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From the Editor

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In this issue a number of papers dealt with community issues, pediatric problems, special education, surgical issues in addition to basic research and oncological problems. A number of papers dealt with pediatric issues Bamatraf F.F et al; did A cross-sectional analytical study to assess the knowledge and attitudes towards childhood immunization among Yemeni parents. Ghasemi, S.F et al tried to determine the clinical symptoms, the results of laboratory tests, and maternal risk factors among neonates hospitalized with a diagnosis of sepsis. The results of this study suggested the need for raising the level of hygiene of the maternity and neonatal wards and the training of mothers and the nursing staff in order to prevent its occurrence.

Helvaci, M.R et al looked at the relationship of Inguinal hernia to metabolic. The authors concluded that inguinal hernia may not have a chronic low-grade inflammatory background on vascular endothelium with a higher prevalence in male gender, younger ages, and right side predominance without any effect of excess weight. Tarbiat. M et al; report a case of hand fingertips ischemia in a 41-year-old female.

Jaff, D., looked comments on a Public Health Initiative to Address Road Traffic Accidents in the Kurdistan Region of Iraq. The authors identifies factors associated with road accidents in Kurdistan specifically but also throughout the wider region, and encourages the development and implementation of preventive initiatives to decrease RTAs in the region. Raheb G et al examined the effectiveness of self-care training program based on empowerment model on quality of life in patients undergoing hemodialysis.

Therefore, using this method in hemodialysis centers could prevent or reduce problems among patients with hemodialysis and improve their quality of life. Ghaffari, M et al; attempt to determine the predictors of nutritional behavior of women referred to health centers to prevent cardiovascular diseases using Health Belief Model.

Bendak, L., highlighted the importance of mobile math games for mildly intellectually disabled students which will reflect positively on their calculations. The results of this study showed statistical differences to the benefit of the experimental group over the control group. Whereas Saki, K et al; investigated the relationship between self-regulated learning, academic self-concept and academic achievement motivation of students in the second grade of high schools of Khorramabad. Naimi, E et al ; conducted a study with the aim of determining the knowledge level, attitude and performance of general practitioners working in hospitals in the city Ahwaz.

Yaseri, H.F, looked at the differences among gastroesophageal reflux patterns, number of reflux episodes and its composition in patients with NERD. The diagnostic value of the DeMeester score, symptom index (SI), and symptom associated probability (SAP) was less than 50%. Ismael, R,J et al ; did a cross-sectional study to determine the rate of inertia among a sample of physician treating diabetic patients and to compare the clinical inertia of physician practicing at different fields of medicine.

A number of papers looked at oncological issues Nezhad H.A et al evaluated the expression of TGF- and its receptor in patients with acute lymphoblastic leukemia. Nezhad H.A et al evaluate p21 and p27 expression in HLA-DR negative AML patients. Salarpour, F et al; looked at the Transcription factors LEF1, PU.1 and IRF8 have decreased expression levels in majority of de novo acute myeloid leukemia patients. Hajigholami, A et al; compared the efficacy of Dexeroyx (Osveral) and Deferoxamine (Desferal) in reducing serum ferritin level in patients with thalassemia major. S et al; did a cross sectional study to look at Plasma ghrelin concentration and pepsinogen I/II ratio as non-invasive markers for upper gastrointestinal malignancy.

Several studies looked at vaccination, Ershadi, F et al; looked at the First Digital Immunization Registry for Health-care Workers in Iran. Keshavarz, S et al; looked at how to build, launch and evaluate a registry system for recording cases of worker exposure to patient blood and body fluids including sharp (needle sticks) injuries and to monitor post-exposure prophylaxis and follow-up procedures

Aliabadie E et al compared the effect of oral administration of dexamethasone and prednisolone on the post-operative pain and swelling of the impacted third molar surgery. Ghobadi, N., reviewed the relation between periodontitis and cardiovascular diseases. Frazadmoghadam, M et al; reviewed the oral health related quality of life in patients treated with implant supported prosthesis. Farrokhnia, T et al; evaluated the effect of educational intervention on musculoskeletal disorders in dentists who work in private dental clinics in Tehran.

Monfared, Y.K; et al looked at the effects of Selenium on Various Sperm Parameters in Varicocele Rats. Results showed that, as an antioxidant, selenium eliminated free radicals in varicocele rats indicating its effectiveness on varicocele-dependent infertilities. Monfared, Y.K; et al looked at the expression of miR135a in serum samples of newborn type 2 diabetic women, diabetic pregnant women and healthy pregnant women was compared with the control group. Rahmani, B et al; evaluated the WT1 gene expression alterations in response to different concentration of omega-3 PUFA alpha linolenic acid (ALA) in pancreatic cancer cell line (MIA PaCa-2) in a time dependent manner. Farmani, O et al; conducted to identify patient's unmet needs and difficulties that they have encountered during the process of diagnosis, treatment and rehabilitation. Harati E et al; investigated the effect of Viola tricolor L. hydro-alcoholic extract on anxiety-like behavior in ovalbumin (OVA) sensitized mice.

Ardashir, A et al; found that group cognitive behavior therapy (GCBT) be more effective to prevent suicidal thoughts and consider as a complementary treatment beside the usual health care for major depression. Samadi, K, et al; in their study to determine whether N2O can aggravate LMA induced gastric distension and pain or not. Katibeh, P et al ; evaluated the prevalence of prolonged QT syndrome in children with first unprovoked seizure.

Masjedi, M et al; in their double blind study found that neither alfentanil nor remifentanil could completely prevent QTc prolongation, following catecholamine surge in anesthetized patients , although remifentanil is more potent in this regard. Davoudimoghaddam, B et al; attempted to determine the effect of hardiness skills training on personal and social adjustment of women household heads in Mashhad, Iran. Khakrangin, M et al; looking at problems and adversities of children that fathers' involvement substance uses

Shabanian, G et al; attempt to determine ETT cuff pressure in comparison with the standard level in intensive care unit (ICU) intubated patients. Shabanian, G et al; conducted a descriptive study to determine the prevalence of infection due to injectable serums administered by the two methods upper and lower blowing. Parvin Delnavaz, P et al; in their study revealed that the quality of nursing documentation in internal surgical pediatric wards had desirable quality and the quality of the documentation was reduced by increasing age and work experience. Masjedi, M et al; evaluated the effect of PLR maneuver on right internal jugular vein (RIJV) diameter in intensive care unit patients under mechanical ventilation. Torki, M.K. et al; investigated the aim of establishment of patient safety standards impact on quality of informed consent. The authors concluded that establishment of patient safety standards as well as observance of its mandatory principles affect the quality of informed consent of patients and increase the quality of informed consent in all aspects.

Azadpour, S et al; investigated the knowledge and attitude of pregnant women about preservation of umbilical cord blood in public and private cord blood banks. ValiPour, A et al; did a a retrospective descriptive-analytical study to determine some epidemiological aspects of this disease in Khorramshahr, one of the cities with high incidence of CL. Ansari, H, investigated the relationship between happiness and self- confidence with the recurrence of addiction among different variables in methadone treated addicts referring to addiction treatment centers in Zahedan.

Ghaderi, A et al did a cross sectional study looking at Determinants of Physical Activity among Iranian Nurses. Alavijeh, M.M et al; did a a cross-sectional study looking at Socio-Cognitive Determinants

of Regular Physical Activity among College Students. It seems the planning and implementation of programs to physical activity promotion among college students is essential by emphasis on outcome expectation, self-efficacy, and social support.

Tahery, N et al; conducted a descriptive, cross-sectional study to determine the frequency of suicide and its related factors in patients referred to emergency department. Behrouzi Rad, E et al; a descriptive correlational to investigate self-care behaviors and the related factors in the older people with diabetes. Shateri, L et al; study was designed to clarify the relationship between emotion regulation and intuitive eating in 60 obese women and 60 normal-weight women. Meybodi, F.A et al investigated the psychometric properties of the ERC for use in Iran. The findings provide the evidence of the validity and reliability of the ERC for use in Iran.

Ebrahim, K et al; assess effectiveness of wrist acupuncture point P6 with pharmacological management to prevent postoperative nausea and vomiting in patient's under laparotomy. Kasiri K et al, did a review to report the findings on the action mechanisms and effects of medicinal plants on the treatment of DD and diaper rash.

Shahsavari, S et al; evaluated the errors in the codes provided for diagnostic and surgical tariffs. According to the results of research is essential the physicians be aware of the importance of documentation and of writing a detailed description of taken procedures and abstaining from providing additional codes. Some proper policies must be adopted to reduce procedure miscoding. Nasrabad, R.R explored the roles and responsibilities of the liaison nurse as a new member of the health care team. Amerai, M et al; aimed to create a mental health minimum dataset through systematic review.

Bahremand, M et al ; done a study with the objective of determining epidemiology, risk factors, and in-hospital outcome of acute coronary syndrome (ACS) patients younger than 40 years admitted to the hospital. Babak, M et al; tried to evaluate the status of obesity, body fat distribution, and blood pressure in people aged from 20 to 65 years old living in Sabzevar.

Clinical inertia in glycemic control among a sample of patients with type 2 diabetes in Erbil City, Iraq

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Abstract

Background: Clinical inertia is a failure of starting or intensifying treatment when indicated. Clinical inertia in glycemic control is an important obstacle in intensification with oral anti-diabetic drugs and insulin therapies.

Objectives: To determine the rate of inertia among a sample of physicians treating diabetic patients and to compare the clinical inertia of the physician practicing at different fields of medicine.

Methods: A cross-sectional study was conducted among a sample of 240 adult patients aged ≥ 18 years with type 2 diabetes who attended two Family Medicine Health centers (Brayatti and Shady Health centers), two Teaching Hospitals (Rizgary and Hawler Teaching Hospitals) and one specialized diabetic center (Layla Qasim diabetic center) in Erbil City. Sixty practicing physicians in different specialties participated in this study during the period from the 1st of April 2017 to the end of 28th of November 2017.

Results: The mean of clinical inertia among doctors treating type 2 diabetic patients was 60.8±24.5, the highest rate of inertia was observed among doctors treating poorly controlled diabetics with haemoglobin A1c ≥ 9%. The rate of inertia was significantly correlated to a higher haemoglobin A1c level, serum cholesterol, triglyceride, and blood pressure (p= 0.038, < 0.001, 0.03, and 0.018 respectively), however it was neither correlated to specialties nor to years of experience of the recruited doctors (p = 0.703, 0.29 respectively).

Conclusion: Clinical inertia among physicians providing health care to type 2 diabetic patients in Erbil city is high, and in all the levels of diabetes control according to haemoglobin A1c levels; however the highest rate of inertia is observed among doctors treating patients with haemoglobin A1c ≥9%. Increasing physicians' awareness to follow the updated guidelines to achieve a greater glycemic control is highly recommended.

Key words: clinical inertia, glycated haemoglobin, Erbil

Introduction

Diabetes affects 387 million people worldwide, about 90% of them are type 2 diabetes mellitus (T2DM) (1). A recent study of eight European countries found only 53.6% of T2DM patients have haemoglobin A1c (Hb A1c <7%) (2). The American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) recommends individualized targets based on various factors, including patient preferences, needs and values, co-morbidities, duration of diabetes, risk of hypoglycemia, costs and, ensuring a patient-centered approach, it also recommends stringent glycated hemoglobin (HbA1c) targets of 6–6.5% in newly diagnosed patients, (3) for instance United Kingdom National Institute for health and Clinical Excellence (NICE) recommends targets of 6.5% in newly-diagnosed patients and <7.5% in patients on two or more therapies (4).

One major reason for not achieving these targets is clinical inertia, defined as failure of physicians to initiate or intensify therapy when indicated (5). Clinical inertia is a main barrier in intensification with both oral anti-diabetic drugs (OADs) or insulin therapies (6). A study of the relationship between inertia and the outcome of diabetes care found that, on average, 15% higher frequency of treatment intensification was associated with a 0.15% lower level of HbA1c (7). The are many reasons for clinical inertia which include physician, patient and system-level barriers (8).

Previous studies in developed countries looked at contributing effect of both physician and patient characteristics on clinical inertia. They distributed greater clinical inertia to patient non-compliance, low information about diabetes, improper consultation, inappropriate data registry, border-high limits blood sugar accepted as normal, no clear treatment targets, lack of teamwork, and having no feedback on performance (9-11).

In the USA, a study revealed a delay of initiation of insulin for almost three years in patients with consistently elevated HbA1c levels despite dual OADs therapy (12) a result which was similar to a study in Japan that stated physicians are strongly resistant to initiating insulin in individuals with T2DM, resulting in high levels of HbA1c (9.6%) at the time of recommending insulin to patients (13). Furthermore, another study demonstrated that "differences in physician and patient perceptions of diabetes therapies could deter patients from accepting insulin therapy" (14). Preceding studies from the USA, Canada, and Europe showed widespread clinical inertia among physicians, with the percentage ranging from 30% to 68% (7).

The aim of the present study to find out the clinical inertia among a sample of physicians involved in care of T2DM in Erbil city, to identify the association of clinical inertia with professional characteristics of physicians and patients characteristics, and to determine the relation between doctors clinical inertia and patients adherence to treatment.

Material and methods

This is a cross-sectional study that was carried out in Layla Qasim diabetic center, Rizgary and Hawler Teaching Hospitals, Brayatii and Shadi Family Medicine Health Centers; between the 1st of April 2017 and the 28th of November 2017, starting from the approval of this research protocol by scientific and ethics committees at Kurdistan Board of Medical Specialties. A convenience method of sampling was used for recruiting 60 physicians who currently provide direct patient health care to diabetic patients at different fields of medicine (family physicians, internists, diabetologists, nephrologists, and others), with 240 patients of T2DM, aged ≥ 18 years. All participants were informed of the study objectives, and recruited after providing verbal informed consent.

A specially designed questionnaire was used to address all relevant physician variables like: age, sex, year of graduation, years of experience, field of specialty, place of work, total number of patients, with number of T2DM patients in care seen weekly and number of consultations per day.

Another questionnaire for T2DM patients was used that included patients variables (age, sex, occupation, residence, marital status, educational level, home ownership, duration of the disease, economic status), data on physical activity, diet, smoking, comorbidities, medication, and lastly their drug adherence were considered and scored according to Morisky Medication Adherence Scale (MMAS-4)15. The body mass index (BMI), Blood Pressure (BP), the recorded investigations in the last 3 months including HbA1c, fasting (FBS) and postprandial (PPS) blood sugar, serum cholesterol and triglyceride (TG) of all recruited patients were obtained. Patients with severe disease (less than 6 months life expectancy) were excluded.

At each consultation setting around 10-15 patients were seen; history, examination and the consultation interview between physician and patients were recorded. The 60 enrolled doctors in the above mentioned places who were providing care for T2DM patients were observed for their way of management of the patients with different HbA1c levels; concerning explanation and advice, promoting patients to continue their own medication or escalating the dose, or adding 2nd or 3rd OADs, and or starting Insulin; if HbA1c was ≤7% and the doctor did not encourage the patient to comply with ordinary therapy this is regarded as clinical inertia. In patients with HbA1c 7.1–7.9%, the doctor should escalate the dose or change the treatment or add a 2nd or 3rd OAD, if it is not to be considered as clinical inertia. In cases where HbA1c was 8.1–8.9%, and previous therapy changed, a 2nd or 3rd drug added, or insulin therapy was initiated this is considered as no clinical inertia and lastly if HbA1c was ≥ 9.0%, only by starting insulin would it not be considered as clinical inertia.

HbA1c levels considered as the reference value for clinical inertia were in agreement with, United Kingdom National

Institute for health and Clinical Excellence (NICE) guideline targets of <6.5% in newly-diagnosed patients and <7.5% in patients on two or more therapies for 3–6 months.

The Socio-economic status (SES) scoring for patients that ranged from 0-12 was calculated from educational level (0 illiterate, 1 reads and writes, 2 primary, 3 intermediate, 4 secondary, and 5 college and above level); house ownership (2 owned, 1 partially owned, and 0 for rented and others); family income (2 if income exceeds needs, 1 if it is enough, and 0 if not enough); and 1 score for each of crowding index (less than 2 persons per room), occupation (if employed), and car ownership. Scoring lower than 5 was considered as low SES, 5-8 as medium SES, and more than 8 is considered as high SES.

Statistical analysis:
Data management and statistical analysis were performed by using Statistical Package for Social Sciences (SPSS, version 22); for comparison between proportions Chi square test was used. Fisher's exact test was used for the expected count, if more than 20% of the cells of the table was less than 5. For comparison the mean of 2 study groups of 2 independent samples Student's t test was used, to compare three means we used (ANOVA) test and to compare each 2 means a post-hoc test (LSD) was used. A p value was regarded as statistically significant if ≤ 0.05.

Results

Two hundred and forty patients were recruited in this study, with mean age (±SD) of 57.3±10.3, median age was 58 years, 63.8% of them were female, most of them (94.6%) from urban areas. Concerning the socio-economic state of the enrolled patients: 53.75% of them were of low SES, 33.75% with medium SES and only 12.5% of patients of high SES.

The mean age ± SD of the sixty doctors who participated in the study were 46.87 ± 8.40, ranging from 33 to 69 years. The mean of duration of service was 23.3 years, and that of years of experience was 12.85 years, 54% of them had more than 10 years specialty experience. The mean number of diabetics examined per day (by a doctor) was 4.75 patients; the details are presented in (Tables 1 & 2).

Table 1: Summary of numerical variables of doctors (n = sixty)

Variables	Mean	±SD	Median	Minimum	Maximum
Age of doctor	46.87	8.41	45.00	33.00	69.00
Duration of service	23.33	8.42	22.00	9.00	45.00
Years of experience	12.85	8.12	11.50	2.00	39.00
Patients examined / week	95.00	56.56	80.00	25.00	250.00
T2 DM patients / week	21.72	18.09	15.00	2.00	80.00
T2 DM patients / day	4.75	4.81	3.00	0.00	30.00
Journals read / month	3.82	3.81	3.00	0.00	20.00
CME scores / year	37.10	45.04	17.00	0.00	207.00

Table 2: Age and gender distribution of doctors

	No.	%
Age in years		
< 40	10	16.7
40-49	28	46.7
50-59	17	28.3
≥ 60	5	8.3
Gender		
Male	52	86.7
Female	8	13.3
Total	60	100.0

The majority of doctors were either board certified (58.3%), or PhD holders (10%). More than half (60%) were specialists in internal medicine, and 25% in family medicine. Regarding the type of facility, many of the doctors, work in more than one facility (Table 3).

Table 3: Distribution of doctors by qualification, specialty, and type of health care facility (n = 60)

	No.	%
Qualification (degrees)*		
Board	35	58.3
Diploma	13	21.7
Master	18	30.0
PhD	6	10.0
Others	4	6.7
Specialty*		
Internal medicine	36	60.0
Family practice	15	25.0
Diabetologist	7	11.7
Neurologist	6	10.0
Nephrologist	3	5.0
Cardiologist	5	8.3
Type of facility		
Private clinic	41	68.3
Multi-specialty group	15	25.0
PHCC	3	5.0
Hospital	33	55.0
Medical college practice	7	11.7

*Some doctors have more than one degree or more than one specialty.

The proportion of doctors at all levels of diabetes control that were assessed by HbA1c was approximately more than 50% and they did not comply with the DM management guidelines. The rate of inertia was 71.7% among doctors treating poorly controlled diabetics (HbA1c ≥ 9%), which was significantly (p = 0.038) higher than the rate (53.3%) among doctors treating controlled diabetes (HbA1c ≤ 7%) (Table 4).

Table 4: Clinical inertia practiced by doctors according to HbA1c levels.

	Clinical inertia		No clinical inertia		p
HbA1c %	No.	%	No.	%	
≤7	32	53.3	28	46.7	Reference
7.1-7.9	34	56.7	26	43.3	0.0713
8-8.9	37	61.7	23	38.3	0.355
≥9	43	71.7	17	28.3	0.038

Although the lowest rate of inertia was observed among family physicians working at family medicine health centers in comparison with other specialties however the difference was not statistically significant (Table 5).

Table 5: Rate of inertia among physicians by specialty of physicians

	Family Physician (n = 15)		Diabetologists (n = 6)		Others (n = 39)		p
HbA1c %	No.	%	No.	%	No.	%	
≤7	6	40.0	5	83.3	21	53.8	0.253*
7.1-7.9	8	53.3	3	50.0	23	59.0	0.856*
8-8.9	8	53.3	4	66.7	25	64.1	0.718*
≥9	12	80.0	2	33.3	29	74.4	0.114*

*By Fisher's exact test (Comparing the three rates of inertia in each category of HbA1c).

The difference in mean inertia scores among different specialties of doctors whether family medicine doctors, diabetologists or other specialties was statistically not significant (p = 0.703) (Table 6).

Table 6. Mean inertia scores by specialty of physicians

Specialty	N	Mean inertia score	SD	p (ANOVA)
Family Physician	15	56.666	31.623	
Diabetologist	6	58.330	13.693	0.703
Others	39	62.821	22.849	
Total	60	60.833	24.515	

In each field of medicine among the studied doctors there was no significant association between inertia and years of experience (p= 0.29); the inertia mean (±SD) for doctors with less than 10 years' experience and those with expertise of more than 10 years was 58.9 (±23.77), and 62.5 (±26.18) respectively.

The mean inertia score among practicing physicians when dealing with uncontrolled diabetics was significantly higher compared to the score of treating controlled diabetics (62.3, 51.5 respectively) (p = 0.020). On the other hand, the mean of inertia among diabetic care providing physicians was significantly higher among corresponding patients with high BP, uncontrolled cholesterol and uncontrolled TG (p=0.018, p< 0.001, p=0.03 respectively). However there was no significant association between mean inertia scores with presence of comorbidities, healthy diet, and physical activity advice (Table 7).

Table 7. Mean inertia scores by patients' characteristics (t test results).

Variables	Categories	N	Mean inertia score	SD	P
Glycemic control	Uncontrolled	207	62.31	23.99	0.020
	Controlled	33	51.51	27.908	
Hypertension	Yes	137	67.5	25.55	0.018
	No	103	54.16	22.82	
Total cholesterol	> 200 mg/dl	165	64.69	22.76	< 0.001
	≤ 200 mg/dl	75	52.33	27.00	
Triglycerides	> 150 mg/dl	199	66.66	26.53	0.03
	≤ 150 mg/dl	41	55	22.16	
Comorbidities	Yes	183	60.93	24.65	0.915
	No	57	60.53	25.42	
Healthy diet	Yes	169	60.50	24.79	0.751
	No	71	61.62	24.94	
Physical activity advice	Yes	43	60.47	28.47	0.915
	No	197	60.91	23.99	

The difference was not significant in the mean inertia scores in different categories of BMI (p = 0.233), and in different groups of drug adherence (p = 0.147). Regarding the number of anti-diabetic drugs taken by the patient, the mean inertia score (73.75) among doctors dealing with patients who take one OAD was significantly higher than the means (55.72 and 61.94) among doctors dealing with patients taking two or three OADs respectively (p = 0.003 and p = 0.045 respectively) (Table 8).

Table 8. Mean inertia scores by patients' characteristics (ANOVA and LSD test results)

Variables	N	Mean scores inertia	SD	p (ANOVA)	LSD (groups)	p (LSD)
BMI						
A)< 25	34	66.18	24.53	0.233	A X B	0.294
B)25-29	87	60.92	24.02		A X C	0.335
C)30-34	86	61.34	25.34		A X D	0.041
D)≥ 35	33	53.79	25.09		B X C	0.912
Total	240	60.83	24.79		B X D	0.160
					C X D	0.137
Adherence						
A)High adherence	100	61.00	24.95	0.147	A X B	0.708
B)Intermediate adherence	133	59.77	24.97		A X C	0.070
C)Low adherence	7	78.57	9.45		B X C	0.051
Total	240	60.83	24.79			
OAD						
A)None	3	66.67	14.43	.024	A X B	0.640
B)1 drug	20	73.75	18.98		A X C	0.447
C)2 drugs	83	55.72	25.40		A X D	0.741
D)3 drugs	134	61.94	24.66		B X C	0.003
Total	240	60.83	24.79		B X D	0.045
					C X D	0.070

Discussion

Attaining strict glycemic control in the early stage of the disease will decline the substantial burden of diabetes related complications. Despite this evidence, globally; only a small percentage of people with T2DM are achieving good glycemic targets (16).

A few studies on clinical inertia in the management of glycemic control among T2DM have been performed in the USA, Europe(7) and Brazil (17) and this is the first study in Iraq and Erbil city designed to find out the clinical inertia among physicians treating T2DM; the mean of inertia among physicians was 60.8% ± 24.5 in the current study, a result which is comparable to a USA study (New England and Florida) finding of 68% inertia in treating patients with HbA1c > 8% over 16 months(18), and another USA (Boston)(19) study and a Croatian study(7) (58%, and 57.7% respectively).

Unexpectedly the rate of inertia among doctors steadily increased with a higher level of HbA1c; the rate of inertia was much higher when they treated those patients with worse glycemic control; about two thirds of them had inertia in HbA1c levels of ≥9%, which was significantly (p =0.038)

higher than the rate (53.3%) among doctors treating more controlled T2DM patients (HbA1c ≤7%).

This difference in the rate of inertia is probably explained by the management intervention of doctors at different HbA1c levels which is nearly the same; where less treatment escalation is needed with better glycemic control (i.e. ≤7), whereas treatment intensification is either by increasing the dose or adding 2nd, 3rd OADs or adding insulin is required.

The doctor's reluctance to initiate insulin to patients with HbA1c ≥9% was the reason for this high mean of inertia. This hesitation in starting insulin therapy may be correlated with insufficient knowledge and professionalism among physicians or inadequate resources.

When there is a high HbA1c it may signify a patient who is more difficult to treat, and may have more comorbidities which could partly clarify clinical inertia. In disparity, we found no relation between the presence of comorbidities and clinical inertia; however in the presence of comorbidities (hypertension, high lipid) controlling of these comorbidities by properly managing them has a significant relation with clinical inertia.

As regards the clinical inertia among patients with HbA1c% (7.1-7.9) and (8-8.9) which necessitates adding 2nd or 3rd OADs, the study revealed around 60% of inertia. This may indicate that such uncontrolled diabetes probably was underestimated by the doctors, and failure to step up the dose of oral diabetes treatment is frequent in diabetes management, with only 22% of patients receiving intensified oral diabetes treatment in hyperglycemic visits (20).

Although the rate of inertia, in the current study among participant physicians was not correlated significantly to their different specialties in spite of having some difference, the lowest rate of inertia was observed among family physicians. One reason could be that majority of family physicians provide more attention and spend more time with their patients.

On the other hand concerning the correlation between rate of inertia and doctor specialties at different HbA1c levels; the highest inertia in HbA1c ≤7% was among diabetologists (83%) compared with only 40% recorded by family doctors. This indicates that they had a significant role in encouraging patients to take the prescribed medication regularly, compared with diabetologists who may pay less attention regarding providing instruction and advice and initiating OADs in this level of HbA1c. Moreover the current study revealed the lowest rate of inertia in HbA1c ≥9% level among diabetologists in comparison with other specialties which means they are more aware about initiating insulin therapy according to the guidelines. Unusually a similar study showed that patients who were treated by diabetologists experience more clinical inertia than those treated by family physicians (7).

Clinical inertia required concurrence of patients with physicians and health system. There are a lot of factors touched by clinical inertia and these are related to patient, physicians and health care resources.

In the current study among 240 enrolled patients with T2DM only 13.7% of them had good glycemic control (HbA1c ≤7). This alarming data could be due to any of three relevant factors; patients themselves (denial of disease, lack of symptoms, medication side effects, too many medication,s cost of medication, poor health literacy, or poor communication with clinician) or the health system (no clinical guidelines, no disease registry, no visit planning, poor communication between clinician and office staff), or related to doctors clinical inertia. We found that the mean rate of inertia among doctors treating such well controlled (HbA1c ≤7) patients was significantly (p= 0.02) lower than that of doctors treating uncontrolled patients and this could be related to more adherence to the guidelines, they have more sufficient focus or emphasis on goal attainment and provide proactive care rather than reactive care for their patients.

The rate of inertia was significantly correlated to a higher HbA1c level, serum cholesterol, triglyceride, and blood pressure (p= 0.038, < 0.001, 0.03, and 0.018 respectively); the above mentioned three variables (HbA1c, serum cholesterol and blood pressure) are truly reflecting the glycemic control of T2DM patient (21), which is why it is clearly correlated with rate of inertia.

The study claimed a significant correlation between the rate of inertia and number of OADs that were in use by enrolled patients; obviously there was more inertia among doctors when they treated those patients taking one type of OAD than those taking 2nd or 3rd OADs (p = 0.003 and p = 0.045 respectively) which means there was reluctance to add further OADs. This may be clarified by more dealing with symptomatic problems of the patient while less pressing issues like intensifying medication therapy may be postponed to future encounters.

Conclusion

This study found that clinical inertia among physicians dealing with T2DM patient was high, and there was inertia in all the levels of diabetes control as assessed by HbA1c. However the highest rate of inertia was among doctors treating badly controlled diabetics (HbA1c ≥9%). Such observations further stress the need for better surveillance, organization and supervision of diabetic care by a better disease registry, arranging a regular planning visit of the patients, and increasing awareness of physicians regarding the guidelines.

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Effectiveness of Self-Care Training Program based on Empowerment Model on Quality of Life among Hemodialysis Patients in the City of Sari, Iran

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Abstract

Background: The purpose of the study was to examine the effectiveness of self-care training program based on empowerment model on quality of life in patients undergoing hemodialysis in the city of Sari, Iran.

Materials and Methods: This experimental research had a pre-test/post-test control group design. The study sample included 60 hemodialysis patients at Hazrat Fatemeh Zahra (SA) Hospital in the city of Sari selected by random sampling method and assigned to two groups: experimental and control. To collect the data and examine the quality of life among patients receiving hemodialysis, a demographic questionnaire and the Kidney Disease Quality of Life Short Form (KDQOL-SF 1.3) were applied. The intervention program of self-care skills training based on empowerment model was administered on the experimental group in 12 sessions; each one lasting 30-45 minutes. Two months after the final session, the form was recompleted and the data were analyzed using SPSS Version 22.

Results: The results showed that self-care training program could improve the aspects of quality of life (general health, physical functioning, emotional role-playing, social functioning, mental health, employment status, sexuality, and family satisfaction) and also a significant difference was observed in the scores of the aspects of quality of life among hemodialysis patients before and after the given intervention.

Conclusions: The self-care skills training program based on empowerment model had an effect on quality of life among patients undergoing hemodialysis. Therefore, using this method in hemodialysis centers could prevent or reduce problems among patients with hemodialysis and improve their quality of life.

Key words: Empowerment, Quality of Life, Hemodialysis Patients

Introduction

Chronic kidney diseases are among the known problems within health systems (1). In this respect, Alvares (2012) shed light on the problems of hemodialysis patients in the domains of functional capacity, physical aspect, as well as social aspect (2). Patients suffering from kidney diseases are also encountered by a sharp decline in quality of life as well as quality of social relationships and social supports (1). Moreover, research studies have shown that part of health that is dependent on quality of life index is lower in hemodialysis patients than that in the general population or even in patients with kidney transplantation (2-6).

Accurate assessment of quality of life in hemodialysis patients and adoption of effective interventions to improve quality of life among these patients are of utmost importance in terms of evaluating and improving the treatment process (2,4,7). According to the definition provided by the World Health Organization (WHO), quality of life refers to individuals' perceptions of their positions in life in terms of culture, value system in which they live in, goals, expectations, as well as standards and priorities (8). Nowadays, improving quality of life in patients receiving hemodialysis is considered as one of the most important therapeutic goals in the domain of working with this target group.

Given multiple drug therapies, special diets, and necessity to acquire the ability to cope with physical and mental disabilities; hemodialysis patients are in need of special and continuous education (9). Thus, it seems that self-care training programs are of importance. Self-care is also recognized as one of the health-promoting behaviors. Such health-promoting behaviors as well emphasize positive patterns of life that can increase health status and quality of life (10), so participation of patients in the processes of treatment and care can be effective in reducing the problems of patients with renal failure and promote their quality of life. Such participations require an increase in patients' awareness of self-care. In this regard, Orem (2005) considered self-care as consciously learned and objective activities performed by an individual to sustain life and promote one's health and those of their families (11,12). The results of various investigations have similarly indicated that poor compliance with self-care behaviors has been associated with a rise in the number of patient re-hospitalizations. Therefore, most chronic renal failure management programs put more emphasis on promoting self-care behaviors as a key to success in improving quality of life and reducing mortality as well as healthcare costs for such patients(13).

Among the self-care training models that can be used by health professionals is a training program based on empowerment model. The empowerment program is an applied tool that can lead to growth and development in individuals' knowledge and skills (11,12). Accordingly, the results of a study by Atashpeykar (2012) suggested that empowerment-based intervention could have a significant impact on improvement of awareness, knowledge, self-esteem, and self-efficacy in patients and in their in-home caregivers in terms of care for patients with chronic diseases (14).

The empowerment components have been also simulated to a triangle whose sides are an individual's behavioral system, an individual's value system, and the social environment in which an individual is living. The behavioral system includes self-care behaviors and the value system for an individual is based on the value given by an individual to oneself which can lead to self-care and controlled living conditions. According to this index, a patient has a sense of responsibility for one's health status and does not evaluate it as affected by external factors such as chance. In the given triangle, the environmental factor involves an individual's social environment and living environment whose essential roles in self-care are a supportive role in personal and social dimensions and an encouraging role in self-care behaviors (15-17).

The purpose of this study was to improve quality of life in hemodialysis patients in aspects such as general health, mental health, physical functioning, social functioning, emotional role-playing, employment status, sexuality, as well as family satisfaction. In order to fulfill this objective, a self-care training program focused on the three-side empowerment triangle including an individual's behavioral system, value system, and social environment, was implemented.

Materials and Methods

This experimental research had a pre-test/post-test control group design. The statistical population of the study included all hemodialysis patients in Hazrat Fatemeh Zahra Hospital in the city of Sari in Iran. The inclusion criteria for the study samples were age range between 20 and 65 years with at least middle school education. The study samples did not suffer from any mental disorders requiring urgent treatments (epilepsy), severe depression, suicidal ideation, types of psychosis, and personality disorders (antisocial). Besides, they were not diagnosed with severe physical disabilities such as liver, heart, and pulmonary failures. Moreover, the sampling was in the form of simple random sampling method in which 60 patients meeting the inclusion criteria were recruited for this study out of the 110 patients selected and then they were randomly divided into two groups of 30 individuals.

The research instrument was the Kidney Disease Quality of Life Short Form (KDQOL-SF 1.3). The given questionnaire is a special tool to assess quality of life in patients with hemodialysis whose reliability and validity had been calculated by Yakaninejad et al. (18,19).

The reliability of the questionnaire for all its dimensions was higher than 0.70. In this regard, all the dimensions of the questionnaire had acceptable internal correlation coefficients. To validate the questionnaire, it was submitted to three faculty members in the field of healthcare and working on quality of life of hemodialysis patients and thus

they confirmed the face validity and the content validity of the questionnaire. The intervention was also administered with a pre-test on experimental and control groups. It should be noted that the intervention was held in 12 sessions and each session lasted about 45 minutes. At the end of the training sessions, a post-test was administered on both groups.

The materials that were taught in the intervention sessions were taken from an information package (1. individuals' empowerment components for self-care; 2. self-care training and information package; and 3. self-care training and information package for self-care). These training and information packages were provided and developed at the Office for Health Education and Promotion in the Ministry of Health and Medical Education of Iran in 2014.

The data were analyzed using SPSS Version.22 using descriptive statistics such as mean, frequency, and standard deviation as well as inferential statistics including Levene's test, Kolmogorov-Smirnov test, and analysis of covariance. The SPSS Software was used for data analysis in which the descriptive statistics included frequency and percentage tables as well as mean and standard deviation and the inferential statistics were comprised of analysis of covariance (ANCOVA).

Results

Considering the descriptive indices of the present study, the demographic characteristics of the samples were as follows.

In terms of gender; 63% of the participants in the study were male and 37% were women. In addition; 11% of the participants were aged between 20 and 35 years, 43% of them were in the age range of 36 to 50 years, and 46% of the given individuals aged between 51 and 65 years. Regarding the level of education, 18.3% of the participants had primary school education, 38.3% of them had middle school education, 36.6% of such participants had high school diploma, and 6.6% of them held a bachelor's degree. Considering the marital status; 56.6% of the samples were married, 13.3% of them were single, 11.6% of these individuals were divorced, and 18.3% of these individuals had deceased spouses.

Table 2 (page 20) illustrates descriptive indices of quality of life components for experimental and control groups in the pre-test and post-test stages with a focus on means and standard deviations.

Using parametric tests in the inferential statistics section, the Kolmogrov-Smirnov test was used to calculate the normal distribution of the data. Since the probability levels in all the variables of the study were larger than the 0.10 error level, the test results of the study indicated the normal distribution of the data.

In order to test the research hypotheses, the mean scores for the pre-test/post-test differences in the experimental and control groups were examined through the ANCOVA.

According to the results of Levene's test indicating equality of variances in all the variables, the ANCOVA was used for the assumptions of the study to test the 3 research hypotheses.

Hypothesis 1: Self-care training program based on empowerment model has an effect on general health in hemodialysis patients.

As seen in Table 3 (page 20) (Eta=0.70, p=0.00, F (1.60) = 0.71), a significant difference was found between both study groups. In other words, there was a significant difference between the general health post-test results in the experimental group and those in the control group. The size of the Eta=0.70 also indicated that 0.70% of the improvement in the general health of the individuals participating in the experimental group was attributed to the effect of self-care training program based on empowerment model on general health.

Hypothesis 2: Self-care training program based on empowerment model has an effect on physical functioning of hemodialysis patients in the city of Sari.

According to ANCOVA (Eta=0.75, p=0.002, F (1.60) = 10.52), a significant difference was observed between both study groups. In other words, there was a significant difference between the physical functioning post-test results in the experimental group and those in the control group. The size of the Eta=0.75 also suggested that 75% of the improvement in the physical functioning of those participating in the experimental group was associated with the impact of self-care training program based on empowerment model on physical functioning of patients receiving hemodialysis in the city of Sari.

Hypothesis 3: Self-care training program based on empowerment model has an effect on emotional role-playing of hemodialysis patients in the city of Sari.

According to ANCOVA (Eta=0.64, p=0.00, F (1.60) = 20.43), there was a significant difference between both study groups. In other words, a significant difference was found between the emotional role-playing post-test results in the experimental group and those in the control group. Moreover, the size of the Eta=0.64 revealed that 64% of the improvement in the emotional role-playing of the participants in the experimental group was attributed to the effect of self-care training program based on empowerment model on emotional role-playing in hemodialysis patients in the city of Sari.

Hypothesis 4: Self-care training program based on empowerment model has an effect on social functioning of hemodialysis patients in the city of Sari.

According to ANCOVA (Eta=0.79, p=0.00, F (1.60) = 21.52), a significant difference was observed between both study groups. In other words, there was a significant difference between the social functioning post-test results in the experimental group and those in the control group.

Table 1: Description of Intervention Sessions

Sessions	Goals	Description
one	familiarity with group members familiarity with patients' problems delineation of training goals for the group	The session began with the introduction of the members, each group member talked about their problems concerning treatment and care, and then the training goals were explained by the social workers to the group.
two	familiarity with self-care and its benefits	The need for self-care among hemodialysis patients was discussed; then the physical, emotional, psychological, social, and spiritual dimensions of self-care were explained; and finally the group members discussed the cases that had been used before the given sessions or how to apply these dimensions.
three	making individuals acquainted with empowerment dimensions with an emphasis on an individual's value system	Understanding self-concept and the value system that a person has about oneself, changing a person's attributes from risky attributes to low-risk ones in order to improve mental health and create a positive attitude towards oneself by which a person can perceive oneself valuable and gain a sense of competence and responsibility about oneself
four	making individuals familiarized with empowerment dimensions with a focus on self-efficacy	Explaining an individual's self-efficacy in terms of self-care dimensions and displaying self-efficacy patterns in self-care, or introducing effective experiences by group members about self-care, expressing negative experiences of members and self-care barriers, and trying to provide solutions or how to resolve such barriers
five	familiarizing individuals with empowerment dimensions with an emphasis on self-regulation	Illustrating self-regulation and its dimensions in self-care, introducing effective self-regulatory patterns
six	making individuals acquainted with empowerment dimensions with a focus on self-management and changing the locus of control from outside to inside	Self-management with an emphasis on cognitive, emotional and behavioral dimensions; individual's perceptions of the disease and what the patient should be aware of, explanation of high-risk behaviors and alternative safe ones, and explanation of the emotional needs of individuals and how to manage emotions
seven	practical work and practice with self-efficacy and self-regulation	Each member of the group was asked to plan on promoting methods for self-efficacy and self-regulation aimed at self-care, identify obstacles and positive points, and provide practical work in group.
eight	practical work and practice with self-management in cognitive, emotional, and behavioral dimensions	Each group member was asked to plan on self-management methods concerning behavioral, cognitive, and emotional self-care; identify positive points and obstacles, and provide practical work in group
nine	identifying effective and facilitating environmental factors and preventive environmental ones in self-care and how to use and apply them	Each member was asked to discuss effective and preventive environmental factors and also how to apply positive factors and eliminate negative ones
ten	introduction of social and therapeutic support networks	Environmental support networks such as associations, community health centers, and healthcare centers were introduced to patients and the family networks affecting treatments were also recognized.
eleven	writing self-care program	Everyone was asked to set a self-care program and then the given program was reviewed and revised by the social worker.
twelve	wrap-up and evaluation	The materials were repeated in brief and summarized and then the results of the sessions were evaluated through interviews.

Table 2: Pre-test/post-test mean scores of control and experimental groups

Variables / groups		Mean	Standard deviation
general health	pre-test (experimental)	66.60	17.25
	post-test (experimental)	64.5	27.61
	pre-test (control)	66.20	16.9
	post-test (control)	65.1	20.28
physical functioning	pre-test (experimental)	16.76	7.75
	post-test (experimental)	32.60	12.38
	pre-test (control)	17.70	7.25
	post-test (control)	18.10	6.32
emotional role-playing	pre-test (experimental)	20.60	5.46
	post-test (experimental)	28.66	6.21
	pre-test (control)	21.43	5.2
	post-test (control)	20.56	7.8
social functioning	pre-test (experimental)	25.30	4.66
	post-test (experimental)	29.36	4.27
	pre-test (control)	23.96	5.02
	post-test (control)	24.40	3.6
mental health	pre-test (experimental)	15.93	7.34
	post-test (experimental)	17.60	5.63
	pre-test (control)	14.13	5.58
	post-test (control)	16	5.003
employment status	pre-test (experimental)	19.60	6.26
	post-test (experimental)	24.93	7.22
	pre-test (control)	18.80	4.85
	post-test (control)	19.33	6.43
sexuality	pre-test (experimental)	19.86	7.78
	post-test (experimental)	23.26	7.70
	pre-test (control)	19.01	6.91
	post-test (control)	19.70	7.80
family satisfaction	pre-test (experimental)	21.50	6.43
	post-test (experimental)	26.03	5.46
	pre-test (control)	21.93	6.01
	post-test (control)	22.96	6.42

Table 3: Summary of ANCOVA for general health in experimental and control groups via removal of interaction effect

Source	Sum of squares	Degree of freedom	Mean squared	F	Significance level of P	Eta
pre-test	64.43	1	64.43	0.10	0.74	0.12
between-groups	1.75	1	1.75	0.71	0.00	0.70

Table 4: Summary of ANCOVA for mental health in experimental and control groups via removal of interaction effect

Source	Sum of squares	Degree of freedom	Mean squared	F	Significance level of P	Eta
pre-test	23.40	1	33.40	1.005	0.32	0.23
between-groups	28.44	1	28.44	73.96	0.00	0.70

Besides, the size of the Eta=0.79 indicated that 79% of the improvement in the social functioning of the individuals participating in the experimental group was attributed to the impact of self-care training program based on empowerment model on social functioning among hemodialysis patients in the city of Sari.

Hypothesis 5: Self-care training program based on empowerment model has an effect on mental health of hemodialysis patients in the city of Sari.

According to Table 4, (Eta=0.70, p=0.00, F (1.60) = 73.96), there was a significant difference between both study groups. In other words, a significant difference was found between the mental health post-test results in the experimental group and those in the control group. As well, the size of the Eta=0.70 showed that 70% of the improvement in the mental health of those participating in the experimental group was associated with the effect of self-care training program based on empowerment model on mental health of hemodialysis patients in the city of Sari.

Hypothesis 6: Self-care training program based on empowerment model has an effect on employment status of hemodialysis patients in the city of Sari.

According to ANCOVA (Eta=0.47, p=0.003, F (1.60) = 9.55), there was a significant difference between both groups. In other words, there was a significant difference between the employment status post-test results in the experimental group and those in the control group. The size of the Eta=0.47 suggested that 47% of the improvement in the mental health of the individuals participating in the experimental group was attributed to the impact of self-care training program based on empowerment model on employment status of hemodialysis patients in the city of Sari.

Hypothesis 7: Self-care training program based on empowerment model has an effect on sexuality of hemodialysis patients in the city of Sari.

According to ANCOVA (Eta=0.41, p=0.00, F (1.60) = 29.86), a significant difference was found between both groups. In other words, there was a significant difference between the sexuality post-test results in the experimental group and those in the control group. The size of the Eta=0.41 indicated that 41% of the improvement in the sexuality of participants in the experimental group was associated with the effect of self-care training program based on empowerment model on sexuality among hemodialysis patients in the city of Sari.

Hypothesis 8: Self-care training program based on empowerment model has an effect on family satisfaction of hemodialysis patients in the city of Sari.

According to ANCOVA (Eta=0.79, p=0.001, F (1.60) =7.74), there was a significant difference between both study groups. In other words, a significant difference was observed between the family satisfaction post-test results in the experimental group and those in the control group. Moreover, the size of the Eta=0.79 indicated that 79% of the improvement in the family satisfaction of those participating in the experimental group was attributed to the impact of self-care training program based on empowerment model on family satisfaction among hemodialysis patients in the city of Sari.

Discussion

The results of this study revealed that social work intervention using empowerment approach aimed at self-care could lead to an increase in the scores of quality of life indices among patients undergoing hemodialysis. In this respect, Cha suggested that hemodialysis patients were better able to cope with their stress associated with their disease and thus the treatment of the disease will be better as the result of learning self-management and self-regulation methods as empowerment indices (20). In another study, Yun demonstrated that improvement of self-management and self-efficacy could significantly influence promotion of quality of life (21). Germin-Petrovic also argued that self-care training for hemodialysis patients and mental-social supports were effective in the improvement of quality of life in patients receiving hemodialysis (22).

Moreover, Naji et al. showed that the use of Orem's self-care model could result in improved quality of life among hemodialysis patients in the city of Zahedan (23). In addition, Goudarzi showed that self-care training could lead to improved self-efficacy in orthopedic immobilized patients (24). As well, Royani concluded that patient empowerment program as an effective program aimed at self-care training could bring about increased self-efficacy and quality of life in patients (25).

In 2005, Esmaieli suggested a significant relationship between self-efficacy and quality of life in patients (26). Shahriari also showed that effective self-care training could influence quality of life in patients receiving hemodialysis (26).

The results of Schron also demonstrated that proper self-care could lead to increased quality of life, prevent recurrence of disease, and reduce number of hospitalizations (27).

Furthermore, Gibson suggested that self-care training could lower concerns such as hospitalization, visits in emergency departments, and impairment of daily functioning. The results of this study also revealed that social work intervention based on empowerment model aimed at self-care could bring about improvements in general health in hemodialysis patients (28). In addition, Buck concluded that self-care training to the elderly could lead to a rise in general health (29).

Besides, the social work intervention model had impacts on reduced depression rates and improved patient ability in terms of emotional role-playing. In a systematic study on 38 investigations of chronic patients, Garina (2014) argued that

that mental and physical stress could significantly affect quality of life in patients (30). Pereira also showed that interventions based on training and psychological-social supports could lead to increased power in an individual to adapt to the environment, reduce patients' problems, and improve mental health status in patients (30).

lyasere et al. in a study on quality of life in patients undergoing hemodialysis showed that the scores of such patients from the depression scale were high. In this study in which social work model based on empowerment approach was employed, an individual's attitude to oneself and their disease was of utmost importance and there were attempts to change patient's attitudes to oneself, the disease, and the surrounding environment in order to improve self-efficacy, self-concept, and quality of life (31). Mau et al. also concluded that quality of life in hemodialysis patients depended on their attitudes towards themselves and their diseases which could be improved through interactions with multiple factors such as social support and care quality (32). Moreover, the results of Habibzadeh et al. suggested that patients' expectations of treatment as well as their attitudes towards ability to manage their health interacted with physical therapy (33).

The model used in the current research study could result in improving mental health among subjects and significantly contribute to improvement in employment status, sexuality, and family satisfaction among patients undergoing hemodialysis. Besides, Brody et al. considered the use of self-care model for the elderly patients as a factor leading to increased mental health (34).

Furthermore, Hassanpour argued that implementation of a training program based on empowerment model would improve mental health (knowledge, attitudes, self-esteem, and self-efficacy) (35). Sahebalzamani et al. also suggested that self-care training could lead to improved physical and mental quality of life in patients (36).

The results of the present study showed that the application of the social work intervention model could result in improved physical and social functioning among patients with hemodialysis. Furthermore, Harris et al. suggested that physical functioning in patients undergoing hemodialysis had dropped (37) and Aliloo (2006) concluded that self-care training program could lead to improved physical functioning in patients and reduce the possibility of complications and recurrences. Raheb et al. in a research study showed that systematic intervention of social work based on group and case work was effective on general health (38).

Conclusion

Self-care training based on empowerment model could assist a patient to overcome the stress and the problems affecting them and the society. The use of this model could enable a patient to have more control over their life and also deal with the negative emotions and stress caused by the disease. This model could also lead to fulfillment of cognitive and behavioral changes in patients along with improvements in behavioral system, self-value, and effective environmental relationships. Moreover, this model led to broadened insight towards life and its events, growth in life management skills, and establishment of communications with the environment and others. The application of the given model also resulted in improvements in social skills, source of inner control, and positive self-concept which could ultimately lead to improved quality of life.

Limitations of the Study
1. The low number of the patients who met the inclusion criteria in this study with the ability to participate in the study sessions
2. The absence of the participants in the study sessions due to their illnesses and physical disabilities

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Knowledge and Attitude Towards Childhood Immunization among Parents in Al-Mukalla, Yemen

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Abstract

Background: According to the World Health Organization, millions of children worldwide are not fully immunized, mostly in developing countries. WHO has estimated that access to services, parental attitudes, knowledge and practices seems to play a significant role in this regard. This study aimed to assess the knowledge and attitudes towards childhood immunization amongYemeni parents in Al-Mukalla city.

Methods: A cross-sectional analytical study was conducted in four governmental kindergartens in Al Mukalla city, Hadhramout Governorate, Yemen, between December 2013 and March 2014. A multi-stage sampling method was used for the selection of participants. Data was collected by using pre-tested self-administered questionnaires.

Results: A total of 400 Yemeni parents participated in the study. Out of them, mothers comprised (73%) of the sample and the remaining (27%) were fathers. In general, the study showed that parents had a positive attitude towards childhood immunization with respect to most of the subjects investigated and (63.3%) had moderate knowledge scores towards them. Health workers were the main source of information for the majority of parents (90.7%). Furthermore statistically significant differences was found in the mean score of parents' knowledge with their age group and the number of their preschool children (P <0.025 and p <0.001, respectively)

Conclusions: Parents demonstrated moderate knowledge scores and a positive attitude towards childhood immunization. There is a need for health education to upgrade parents' knowledge with emphasis on young parents as well as health workers.

Key words: Childhood Immunization, Parents, Knowledge, Attitude, governmental kindergartens, Yemen

Introduction

As highlighted by the World Health Organization (WHO), vaccination is one of the most cost -effective health interventions available, saving millions of people from illness, disability and death each year from vaccine-preventable diseases including diphtheria, hepatitis B, measles, mumps, pertussis, pneumonia, polio, rotavirus diarrhea, rubella and tetanus.(1) WHO reported that "the number of deaths per year in children between the ages of 1 and 59 months was 5.2 million.

About 29% of these deaths in children in this age group are due to vaccine-preventable diseases.(2) In addition WHO estimated that "if all the vaccines now available against childhood diseases were widely adopted as part of the Expanded Program on Immunization (EPI) in some regions of the world. and if countries could raise vaccine coverage to a global average of 90%, an additional two million deaths a year could be prevented among children under five years old".(1)

In Yemen, to maintain high levels of immunization coverage among children, health authorities have taken important steps to support routine immunization and to implement supplementary immunization activities.(3) Yet, despite the concerted efforts of the government, a large proportion of vulnerable infants and children in Yemen remain unimmunized. Although EPI has been implemented in Yemen since 1979 (4) and despite it being available free of charge to the public the full coverage of immunization among Yemeni children in the age group of 12-23 months was only 37.2%.(5)

According to the World Health Organization (WHO), millions of children around the world are not fully immune, mostly in developing countries, because of immunization issues, which are the most common factors that lead to incomplete vaccination of children. (6) In addition, the WHO has estimated that access to services, parental attitudes, knowledge and practices appears to play a greater role among children who have not received any vaccination.(6)

The knowledge, attitudes and practices of parents have also been identified by many studies as factors related to the success or failure of the immunization program.(7,8,9) Previous studies observed that, parents' knowledge and attitudes towards immunization were significantly associated with childhood immunization coverage and can affect the immunization status of children. (9,10) Furthermore, other studies have demonstrated an association between parental sociodemographic characteristics and child's immunization coverage, such as education and age of the parents, number of preschool children, and family income.(11,12,13) Previous studies have shown that healthcare providers also play an important role in the rate of immunizing children.(14,15) It was found that parents' knowledge and attitudes towards vaccinating their children depends on the quality of information provided to them by health care providers about the importance, timing and safety of vaccination.(16,17) They may affect parents' knowledge, practices and their decisions about child vaccination.(18,19)

There are currently no studies available on parents' knowledge and attitudes towards childhood immunization in Yemen, as in Al-Mukalla local area. it is high time for such a study to be carried out to assess the knowledge and attitudes towards childhood immunization and their associated factors among Yemeni parents. It is believed that this study may provide useful information to the Yemeni community and Yemeni authorities such as the Ministry of Health to perform more effective vaccination programs.

Materials and method

This was a cross-sectional study conducted at public kindergartens in Al-Mukalla, the capital of the Hadhramout Governorate, Yemen, between December 2014 to March 2015. The study population consists of all parents whose children were learning in public kindergartens. All public kindergartens (total 4) were selected from the different areas of Al-Mukalla.

A sample size of 384 parents was determined by using recommended statistical methods.(20) It was increased to 400 for an expected non-response. The sample size of parents was distributed proportionally among all four selected kindergartens according to total number of children in each kindergarten and the parents of children were selected randomly. A total of 400 questionnaires were distributed to parents of children attending selected kindergartens. The questionnaire was sent along with a letter explaining the objectives of the study to the parents, as well as an envelope to facilitate the return of the completed questionnaire. Parents were asked to return the completed questionnaires in the envelopes submitted before the deadline by submitting them to the class teacher.

Written consent was obtained for participation in the study from all participants. The researchers collected the completed questionnaires through kindergarten teachers. When a teacher did not receive a questionnaire from a child during 3 to 5 days, the teacher sent a reminder home with the child. Data were collected with self-administered pre-tested questionnaire. The questionnaire was divided into two parts; the first part covered questions on personal and socio-demographic characteristics of parents and the second part covered questions which were pre-designed to assess their knowledge and attitude to childhood immunization.

Responses to the questions of knowledge were recorded as "Yes", "No", and "Don't know". A three point-Likert scale was used to assess parents' attitudes about child immunization, with the following responses: ("Agree", "Not sure", "Disagree",). The pre-testing of the questionnaire of the study was conducted on 15 parents. The sample of parents used in this pre-test was not included in the study. During the pre-test a few difficult words in some questions

were found and these words were changed into simple local words, and the final questionnaire was modified according to the necessary results.

Statistical Analysis: Data was coded, reviewed and entered using Statistical Package for Social Science (SPSS) version 20. Knowledge scores were assessed using a scoring system as following:

Knowledge scale:

The knowledge scale consisted of 15 items. Each correct answer was given 1 score and zero score for a wrong or unknown answer. The total knowledge score ranged from 0 to 15 and was classified as, high knowledge score : > mean + SD, moderate knowledge score: mean −SD to mean + SD and low knowledge score I :< mean −SD. One-way ANOVA was used to assess if there was any significant difference between socio-demographic characteristics and mean scores of knowledge of parents. p-values less than 0.05 indicated statistical significance.

The study protocol was approved by the Medial Research & Ethics Committee of the College of Medicine &Health Sciences at Hadhramout University (HUCOM). A letter was obtained from the Ministry of Education of Al-Mukalla district to the manager of each of the 4 selected public kindergarten to facilitate our data collection. The objective of the study was explained to the subjects, and written consent was obtained from all parents before enrollment in the study as explained above.

Results

Four hundred questionnaires were distributed to parents and 400 participants agreed to participate in the study. Response rate was 100%. Table 1 summarized demographic characteristics of parents. Mothers participants comprised (73%) of the sample and the remaining (27%) were fathers. In terms of age, the parents' age ranged from 25 to 48 years. The mean of their age was 37.01±4.76 years. The majority (64%) of them were in age group 30 – 39 years. University graduates and secondary educated were (34% & 28% respectively). The majority of mothers (73.8 %) have taken decisions concerning the immunization of their children.

Table 1: Demographic characteristics of the parents

Characteristic	No	%
Parental relationship:		
Mothers	292	73
Fathers	108	27
Age group of parents (years):		
< 30	40	10
30-39	256	64
≥40	104	26
Mean age ± SD*	37.01 ± 4.76	
Parents' educational level:		
Illiterate	97	24.3
Primary	55	13.7
Secondary	112	28
Graduate	136	34
Number of preschool children:		
One	68	17
2-3	158	39.5
>3	174	43.5
Decision-maker (on child immunization issues):		
Father	62	15.4
Mother	295	73.8
Both	43	10.8

 * Standard Deviation

With regards to knowledge of childhood immunization, participants answered a total of 15 closed ended, multiple choice questions. Each response was given one mark with a total of 15 marks. The mean knowledge score for the participants was 8.58.± 2.19 (Table 2). Based on the scoring system described in the methodology it was found that the majority of the parents (63.3%) had " moderate " knowledge scores, 23.3% of them had "high knowledge " while 13.5% had "low knowledge (Table 2).

Data revealing the parents' knowledge of immunization are shown in Table 2. It is apparent from the table that all parents (100%) had heard about immunization and the main source of their information were the health workers (90.7%). The majority of parents (93.8%) knew that immunization prevents disease and they know also it's complications and the majority of them considered that vaccination should be completed as per schedule less than 2 years (82.3%) and that a healthy child needs vaccination (92.8%). While only the minority (41.2%) of them know when to start the vaccination schedule.

The results also showed that more than half of the participants (57.7%) correctly answered that the vaccine was for all ages while only 41.3 knew that more than one vaccine at the same time had no adverse effects on the child's immunity. On the other hand, more than half of the parents (51.3%) know that multiple doses of vaccine given at time intervals are important for the child's immunity.

With regards to the name of the diseases against which children are immunized, all parents correctly knew that Oral Polio Vaccine (OPV) protects against polio and measles Vaccine protects against measles disease (100%). While a small percentage of them knew BCG protects against Tuberculosis (17.8%), Hep B protects against Hepatitis B (26.3%) and DPT vaccination protects against three diseases (Diphtheria, Pertussis and Tetanus) (10%). Most of the parents did not accept that harm of the vaccine is more than benefits (92.8%). Common colds, ear infections and diarrhea were considered as contraindications for vaccination by (45%) of the parents Table 2.

Table 2: Parents' knowledge towards childhood immunization

Knowledge items	Response	Frequency	Percentage
Have you heard about childhood immunization	Yes	400	100
	No	0	0
Source of information for immunization program	Radio	20	5
	Television	17	4.3
	Health workers	363	90.7
Immunization prevents disease and its complications	Yes	375	93.8
	No	25	6.2
Healthy children need vaccination	Yes	371	92.8
	No	29	7.2
Immunization start first week of life	Yes	165	41.2
	No	235	58.8
Uniform schedule less than 2 years	Yes	329	82.3
	No	71	17.7
Immunization is for all ages.	Yes	231	57.7
	No	169	42.3
More than one vaccine at the same time has no adverse effects on child's immunity	Yes	165	41.3
	No	235	58.7
Multiple doses of the same vaccine given at time intervals are important for child's immunity	Yes	205	51.3
	No	195	48.7
Name the diseases that the child is immunized against	Polio (OPV)	400	100
	Measles	400	100
	BCG	71	17.8
	Hep B	105	26.3
	DPT	40	10.3
Immunization can be associated with the risk of side effects	Yes	140	35.0
	No	260	65.0
Common colds, ear infections and diarrhea are contraindications for vaccination	Yes	180	45
	No	220	55
Total mean knowledge scores ± SD	8.58.± 2.19		

Regarding parents' attitude Table 3 shows that parents in general had positive attitudes towards childhood immunization. All parents are in favor of vaccination program (100%), and all agree that immunizing children is important (100%). The majority of them agreed that immunization is more beneficial than harmful and agreed that vaccines are safe for the children (92% &71.2% respectively). In addition the majority of parents agreed on the importance of following the immunization schedule and immunization kept the child healthy (94% and 96.5%, respectively).

Table 3: Attitude of parents toward childhood immunization

Questions	Response	Frequency	percentage
In favor of Vaccination program	Agree	400	100
	Disagree	0	0
	Not sure	0	0
Child immunization is important	Agree	400	100
	Disagree	0	0
	Not sure	0	0
Immunization is more beneficial than harmful	Agree	368	92.0
	Disagree	10	2.5
	Not sure	22	5.5
Vaccines for child immunization are safe	Agree	285	71.2
	Disagree	32	8.0
	Not sure	83	20.8
Important to follow vaccination schedule	Agree	376	94
	Disagree	10	2.5
	Not sure	14	3.5
Immunization keeps your child healthy	Agree	386	96.5
	Disagree	4	1.0
	Not sure	10	2.5

Table 4 shows ANOVA statistical results for the knowledge scores by educational level and age group of parents and by the number of their pre-school children. It was found that there was significant difference in the mean knowledge scores of parents with age group (≤30 years and ≥40 years), and between parents with age group (31-39 years and ≥40 years) (p value = 0.025). Mean knowledge scores were significantly lower among those in age group ≤30 years compared to parents in other age groups.

There was also significant difference in the mean knowledge scores between those parents who had one preschool child and those who had 2-3 preschool children and between those parents who had 2-3 children and those who had more than three children (p value= 0.001). Mean knowledge scores were significantly lower among those parents who had one preschool child compared to those who had 2 or 3 and more preschool children. Regarding educational level there was no significant difference of mean knowledge scores between these levels.

Table 4: Mean total childhood Immunization knowledge scores by socio-demographic characteristic among parents (N = 400)

Variable	Categories	No (%)	Knowledge score: Mean ± SD	P-value*
Parents' education	Illiterate	[97 (24.3%)]	8.72 ± 1.09	
	Primary	[55 (13.7%)]	8.46 ± 1.11	0.723
	Secondary	[112 (28%)]	8.82 ± 1.18	
	University	[136 (34%)]	8.85 ± 1.23	
Parents' age group	< 30	[40 (10%)]	7.82 ± 1.27	
	30-39	[256 (64%)]	8.87 ± .956	0.025
	≥ 40	[104 (26%)]	8.63 ± 1.07	
Number of preschool children	One	[68 (17%)]	7.97 ± 1.43	
	2-3	[158 (39.5%)]	8.76 ± 1.13	0.001
	> 3	[174 (43.5%)]	8.84 ± .979	

* One way ANOVA (p < 0.05 is considered statistically significant)

Discussion

It is widely accepted that childhood immunization programs have played a great part in the prevention of many diseases; hence, vaccination coverage is an indirect way to assess child health care.(20) Our study revealed that almost all parents were aware of childhood immunization and the majority of them knew the importance of following the immunization schedule to keep their children healthy. Many studies around the world have shown that successful childhood immunization depends on good knowledge of parents and their positive attitudes.(21,22,23)

The current study revealed that health workers are the main source of vaccination information for the vast majority of participants. Our findings were in agreement with the findings of other studies. where health workers were the main source of participants' information towards childhood immunization.(14,17,18,19) However, our findings were in contrast with other studies which consider media as a strong source for providing of participants' information about vaccination.(24,25,26)

Parental knowledge scores were assessed in this study by collecting the knowledge score for each parent. Data demonstrated that the majority, 63.3% of parents had moderate or adequate knowledge. Unfortunately, previous studies about childhood immunization among Yemeni parents are not available to compare with our findings. However similar results were reported from different countries(27,28,29,30) where the majority of participants had adequate knowledge.

This observation is in contrast with other studies. One of these studies from Libya reported the knowledge of studied mothers about vaccination is not completely adequate.(29) In China, Wang et al observed that 60% of studied mothers were found to have inadequate knowledge towards immunization in childhood.(30) Low levels of knowledge in many countries can be affected by many factors including immunization providers, sources of information and other barriers.

Although the fact that the majority of our participants had awareness about childhood vaccination from the health workers, a good proportion did possess deficiencies in their knowledge about some aspects of it, which could somehow indicate that information given to them was incomplete. However, in the succeeding questions presented to parents, only 41.2% of our participants know when to start the vaccination schedule and slightly more than half of them knew that multiple doses of vaccine given at time intervals are important for child's immunity (51.3%). Most vaccines in the childhood immunization schedule require two or more doses for development of an adequate and persisting antibody response.(31) Our study found that, health workers have a responsibility to inform the majority of parents about immunization. There is a need to educate health workers in this area, and this area also requires further strengthening. Many studies showed that parents' knowledge regarding child immunization varies according to the family physician and other medical staff.(25,32)

Another very important area that the parents lacked knowledge in was that more than half of them (58.6%) do not know that giving more than one vaccine at the same time has no negative impacts on child immunity.(31) In agreement, in another study "a quarter of the parents believed that their child's immune system could become weakened as a result of too many immunizations".(32) To date "there is no scientific evidence that supports parents' fears about combined vaccines causing immune overload".(16)

Our study also revealed that 35% of the parents believe that Immunization can be associated with the risk of side effects. It obvious that parents were not well aware of the potential side effects of immunization. Concerns about immunization safety and regarding the adverse impact of possible side effects on immunization coverage have been reported earlier.(33) It was reported that "the administration of vaccines may be associated with common local reactions like pain, swelling, and redness at the injection site".(31) This area also requires further strengthening and our participants should be educated about these side effects. Another area in which the parents scored low is the question on the name of the diseases against which child is immunized, indicating opportunity for education. Responses revealed that nearly all parents correctly named diseases only polio and measles, while a small percentage of them know the names of diseases prevented by the BCG, hepatitis B and DPT. Furthermore, 55% of our parents believe that common colds, ear infections and diarrhea were contraindications to vaccinate children. Parents need reliable accurate information on true contraindications so that opportunities to immunize an infant or child are not missed. In fact, there are very few true contraindications. "Deferral or delay of immunization based on misconceptions about contraindications puts an infant or child at risk".(31)

With regard to attitudes, our findings generally revealed that participants had a positive attitude towards immunization in childhood. All parents agreed with vaccination programs and agreed that the vaccination was important. As well, the majority of them agreed that they should follow the vaccination schedule to keep their children healthy. Our finding was consistent with other studies from different countries in which the majority of respondents have a positive attitude towards childhood vaccination.(14,25.27) "Understanding parents' knowledge and attitudes towards immunization is important, parent's involvement was shown to be associated with the child's vaccination status".(23)

The findings of the present study showed that there were statistically significant differences between parents in their mean knowledge scores. However the difference between them was found in some variables. With regard to the age of parents, it was found that parents aged 30 years or younger showed significantly lower knowledge scores compared to older parents. This finding is consistent with another study,(28) that reported that older parents have higher knowledge. This may be because older parents are more knowledgeable and experienced. In contrast to our findings, a study in Saudi Arabia conducted by Jamman

(25) observed that "older mothers were less likely to have knowledge towards child vaccination. Perhaps, in older women, this reflects a higher prevalence of traditional nihilistic views, such as destiny being the cause of disease". The same finding has been reported Also by Bernsen et al in UAE.(34)

The study also found statistically significant differences in the average score of parents' knowledge with the number of pre-school children. Mean knowledge scores were significantly lower among those parents who had one preschool child compared to those who had 2 or 3 and more preschool children. This finding is consistent with the study conducted by Al-lela et al (35) where a significant association of parent's KAP with number of children was found.

Conclusions

In conclusion the present study showed that in general parents had moderate knowledge scores and a positive attitude towards childhood immunization. However, a good proportion of them demonstrated insufficient knowledge about some important points such as side effects, timing of the first dose of vaccination and the name of certain diseases that are immunized against in children. Health workers were the main source of their information. There is a need to educate health workers and parents on certain aspects of immunization in childhood, and they should focus particularly on younger parents.

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Inguinal hernia may not have a chronic low-grade inflammatory background on vascular endothelium

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Abstract

Background: Probably metabolic syndrome is a chronic low-grade inflammatory process of vascular endothelium, and there is not enough knowledge about its association with inguinal hernia in the literature.

Methods: Consecutive patients with an inguinal hernia and/or a surgical repair history of inguinal hernia were collected into the first, and age and sex-matched controls were collected into the second, group.

Results: The study included 56 cases with inguinal hernia and 80 cases of controls. Mean age of hernia cases was 45.8 years, and 85.7% of them were male (p<0.001). Interestingly, 46.4% of the inguinal hernias were on the right and 30.3% of them were on the left sides (p<0.05), and 23.2% of them were located, bilaterally. When we compared the groups according to mean weight, height, body mass index (BMI), triglyceride, and low density lipoproteins (LDL) values and prevalences of smoking, white coat hypertension (WCH), hypertension (HT), diabetes mellitus (DM), and coronary artery disease (CAD), there was not any significant difference according to any parameter in between (p>0.05 for all).

Conclusion: Although umbilical hernia may significantly be related with metabolic syndrome with a higher prevalence with advanced age, obesity, and females, we did not find any relationship between inguinal hernia and mean weight, height, BMI, triglyceride, and LDL values and prevalences of smoking, WCH, HT, DM, and CAD. So inguinal hernia may not have a chronic low-grade inflammatory background on vascular endothelium with a higher prevalence in male gender, younger ages, and right side predominance, without any effect of excess weight.

Key words: Inguinal hernia, endothelial inflammation, metabolic syndrome, obesity

Introduction

Due to the prolonged survival of human beings, systemic atherosclerosis may be the major health problem in this century, and its association with sedentary lifestyle, excess weight, smoking, and alcohol is collected under the heading of metabolic syndrome (1, 2). The syndrome is characterized by a chronic low-grade inflammatory process on vascular endothelium in the whole body (3). The inflammatory process is particularly accelerated by some factors including sedentary lifestyle, excess weight, smoking, alcohol, chronic inflammations and infections, and cancers (4, 5). The syndrome can be slowed down with appropriate non-pharmaceutical approaches including lifestyle changes, diet, exercise, cessation of smoking, and withdrawal of alcohol (6). The syndrome contains reversible parameters including overweight, white coat hypertension, impaired fasting glucose, impaired glucose tolerance, hyperlipoproteinemias, alcohol, and smoking for the development of irreversible consequences including obesity, hypertension (HT), type 2 diabetes mellitus (DM), chronic obstructive pulmonary disease, cirrhosis, chronic renal disease, peripheric artery disease, coronary artery disease (CAD), and stroke (7). In another perspective, the metabolic syndrome may be the most significant disease of human beings decreasing quality and duration of human lifespan at the moment. The syndrome has become increasingly common all over the world, for instance 50 million people in the United States are affected (8). The syndrome induced accelerated atherosclerosis in whole body may be the leading cause of end-organ failure, early aging, and premature death for both genders. For example, CAD is the leading cause of death in developed countries. Although sedentary lifestyle, excess weight, smoking, alcohol, chronic inflammations and infections, and cancer induced chronic low-grade inflammation on vascular endothelium may terminate with significant health problems, there is not enough knowledge about effects of the inflammatory process on inguinal hernia in the literature.

Material and Methods

The study was performed in the Internal Medicine Polyclinic of the Mustafa Kemal University between March 2007 and January 2010. Consecutive patients with an inguinal hernia and/or a surgical repair history of inguinal hernia were collected into the first, and age and sex-matched control cases were collected into the second group. We excluded cases above the age of 70 years to avoid debility induced weight loss in elder individuals. Their medical histories including smoking habit, HT, DM, CAD, and already used medications were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride, low density lipoproteins (LDL), and an electrocardiography was performed. Current daily smokers at least for the last six months, and cases with a history of five pack-years were accepted as smokers. Insulin using diabetics and patients with devastating illnesses including malignancies, acute or chronic renal failure, chronic liver disease, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Body mass index (BMI) of each case was calculated by the measurements of the Same Internist instead of verbal expressions. Weight in kilograms is divided by height in meters squared (9). Office blood pressure (OBP) was checked after a 5-minute rest in seated position with the mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked hypertension after a 10-minute education session about proper blood pressure (BP) measurement techniques (10). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5-minutes in the seated position before measurement. A 24-hour ambulatory blood pressure monitoring was not required due to its equal effectiveness with HBP measurements (11). Eventually, HT is defined as a BP of 135/85 mmHg or greater on HBP measurements (10). WCH is defined as OBP of 140/90 mmHg or greater but mean HBP of lower than 135/85 mmHg, and masked HT as OBP of lower than 140/90 mmHg but mean HBP of 135/85 mmHg or greater (10). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already taking antidiabetic medications were defined as diabetics. An oral glucose tolerance test with 75-gram glucose tolerance test was performed in cases with a FPG level between 100 and 125 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level of 200 mg/dL or higher is DM (9). A stress electrocardiography was performed in suspected cases, and a coronary angiography was obtained only for the stress electrocardiography positive cases. Eventually, mean weight, height, BMI, triglyceride, and LDL values and prevalences of smoking, WCH, HT, DM, and CAD were detected in each group, and results were compared in between. Mann-Whitney U Test, Independent-Samples T Test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 56 cases with the inguinal hernia and 80 cases in the control groups. Mean age of the inguinal hernia cases was 45.8 years, and 85.7% (48 cases) of them were male (p<0.001). Interestingly, 46.4% of the inguinal hernias were on the right and 30.3% of them were on the left sides (p<0.05), and 23.2% of them were located, bilaterally. When we compared the two groups according to the mean weight, height, BMI, triglyceride, and LDL values and prevalences of smoking, WCH, HT, DM, and CAD, there was not any statistically significant difference according to any parameter in between (p>0.05 for all) (Table 1 - next page).

Table 1: Characteristic features of the study cases

Variables	Cases with inguinal hernia	p-value	Control cases
Number	56		80
Male ratio	*85.7%*	Ns*	85.0%
Mean age (year)	*45.8 ± 14.6 (18-70)*	Ns	45.9 ± 13.6 (18-68)
Prevalence of smoking	48.2%	Ns	47.5%
Mean weight (kg)	76.5 ± 13.7 (42-108)	Ns	79.4 ± 13.2 (50-116)
Mean height (cm)	169.3 ± 8.5 (137-189)	Ns	170.8 ± 7.6 (153-188)
Mean BMI† (kg/m²)	26.5 ± 4.1 (17.7-38.0)	Ns	27.2 ± 4.4 (17.7-38.7)
Mean triglyceride (mg/dL)	160.6 ± 89.1 (50-381)	Ns	144.0 ± 79.8 (49-385)
Mean LDL‡ (mg/dL)	118.2 ± 26.9 (53-171)	Ns	128.6 ± 34.7 (54-239)
Prevalence of WCH§	32.1%	Ns	35.0%
Prevalence of HT ‖	19.6%	Ns	12.5%
Prevalence of DM¶	10.7%	Ns	20.0%
Prevalence of CAD**	1.7%	Ns	6.2%

*Nonsignificant (p>0.05)   †Body mass index   ‡Low density lipoproteins   §White coat hypertension   ‖Hypertension
¶Diabetes mellitus   **Coronary artery disease

Discussion

Probably obesity is found among one of the irreversible endpoints of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide limited benefit either to heal obesity or to prevent its complications. Overweight and obesity probably lead to a chronic low-grade inflammation on vascular endothelium that is associated with many coagulation and fibrinolytic abnormalities suggesting that excess weight may cause a prothrombotic and proinflammatory state (12). The chronic inflammatory process is characterized by lipid-induced injury, invasion of macrophages, proliferation of smooth muscle cells, endothelial dysfunction, and increased atherogenicity (13, 14). Elevation of C-reactive protein (CRP) levels in serum carries predictive power for the development of atherosclerotic end-points (15, 16), and overweight and obesity are considered as strong factors for controlling of CRP concentration in serum, because adipose tissue produces biologically active leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin. So adipose tissue is involved in the regulation of cytokines, and individuals with overweight and obesity have elevated CRP levels in serum (17, 18). On the other hand, individuals with excess weight will have an increased circulating blood volume as well as an increased cardiac output, thought to be the result of increased oxygen demand of the extra tissue. The prolonged increase in circulating blood volume may lead to myocardial hypertrophy and decreased compliance,

in addition to the common comorbidity of atherosclerosis and HT. In addition to the atherosclerosis and HT, fasting plasma glucose and serum total cholesterol levels were all elevated with the increased BMI values (19). Similarly, prevalences of CAD and ischemic stroke increased with an elevated BMI value in another study (20). On the other hand, the chronic low-grade inflammatory process may also cause genetic changes on the epithelial cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system, effectively (21). Eventually, the risk of death from all causes including cardiovascular diseases and cancers increased throughout the range of moderate to severe weight excess for both genders in all age groups (22).

Hernias develop when an internal part of the body pushes through a weakness in the muscle or surrounding tissue wall. They can even occur anywhere in the abdominal region. The most common kinds of abdominal hernias are inguinal, femoral, incisional, umbilical, and hiatal hernias. In many cases, abdominal hernias cause just a few symptoms. However they may even cause an obstruction in the bowel and interrupt the blood supply of the intestines as medical emergencies. Due to the potential risk of these complications, surgery is usually recommended to repair the hernias. The exception is umbilical hernias since the risks of complications are thought too small to justify surgery for them. Inguinal hernias are the most common types of hernias in both genders in adults (up to 75% of all abdominal hernias), and they are the second in frequency after the umbilical hernias in infants and children. While

the inguinal hernias are much more common in men, they also develop in women with a prevalence of 10% (23). They develop due to a weakness, tear, gap, or opening in the muscular wall of the groin around the inguinal canal region. As a result of this opening in the muscular wall, contents of the abdomen including intestines may protrude by creating a localized bulge or pain. Inguinal hernias may be congenital or acquired. Acquired hernias are the result of repetitive pressure, strain, or injury due to the further weakening of structural integrity and function of the abdominal wall. The process in acquired cases may be acute or chronic, developing slowly over a period of time. Inguinal hernias are also classified as direct or indirect according to their anatomic direction of travel into the inguinal canal. Purely congenital hernias are often called indirect hernias, whereas acquired hernias are referred to as direct hernias. Although femoral hernias occur more often in women, women still get more inguinal hernias than femoral ones. Every year in England, 70.000 surgical operations are required to repair inguinal hernias (24). They can occur at any age, but they are primarily age-related, so older the age, higher the risk of getting an inguinal hernia. Similarly, mean age of the inguinal hernia cases was 45.8 years in the present study, and 85.7% of them were male (p<0.001). As an opposite finding to varicocele (25), the inguinal hernias were significantly more common on the right side (46.4% versus 30.3%, p<0.05), and 23.2% of them were located, bilaterally. Inguinal hernias are further divided into indirect inguinal hernias (2/3 of all), in which the inguinal canal is entered via a congenital weakness at the internal inguinal ring, and the direct inguinal hernias (1/3 of all), where the hernia contents push through a weak spot in the posterior wall of the inguinal canal. The indirect inguinal hernias are congenital hernias and much more common in men due to the way males develop in the womb. In a male fetus, the spermatic cord and both testicles descend from an intraabdominal location into the scrotal sac through the inguinal canal. Sometimes the entrance of the inguinal canal at the inguinal ring does not close as it should just after birth, leaving a weakness in the abdominal wall. Fat or part of the small intestine slides through the weakness into the inguinal canal, causing an indirect hernia. In females, an indirect inguinal hernia is caused by the female organs or the small intestine sliding into the groin through a weakness in the abdominal wall. Premature infants are especially at a higher risk for the indirect inguinal hernias because there is less time for the inguinal canal to close. On the other hand, direct inguinal hernias develop gradually due to continuous stress on the muscles. They are caused by connective tissue degeneration, which causes weakening of the abdominal muscles during adulthood. Although the high prevalence of inguinal hernia in society, its predisposing factors are not clearly known, yet. According to the literature, sudden muscular strains, heavy lifting, straining during constipation, and chronic coughing may cause pressure on the abdominal muscles and worsen the hernia. Similarly, we were not able to find any association between the inguinal hernia and metabolic parameters including mean weight, height, BMI, triglyceride, and LDL values and prevalences of smoking, WCH, HT, DM, and CAD in the present study

(p>0.05 for all). The right side predominance of inguinal hernia cases may also indicate absence of a systemic inflammatory background of the pathology.

Although the inguinal hernia is not related with the parameters of the metabolic syndrome, the umbilical hernia may highly be related with the syndrome. In a previous study, the mean age of the umbilical hernia patients was 62.0 years, and 73.9% of them were female (26). Whereas the mean age of the inguinal hernia cases was 45.8 years, and 85.7% of them were male in the present study that may also indicate the absence of any association of the inguinal hernia with the metabolic syndrome since the syndrome is much more common with obesity, and obesity is much more common in advanced age and in females. Similarly, the umbilical hernia patients were heavier than the controls (85.1 versus 73.1 kg, p= 0.001) and BMI of them was also higher, significantly (33.6 versus 29.1 kg/m2, p= 0.000) (26). Although the prevalence of HT was higher in the umbilical hernia cases (50.0% versus 27.3%, p<0.01), mean triglyceride and LDL values and prevalence of WCH were lower in them (p<0.05 for all) (26). Although the prevalences of DM and CAD were also higher in the umbilical hernia patients, the differences were nonsignificant probably due to the small size of the umbilical hernia group. So there are significant relationships between umbilical hernia and terminal consequences of metabolic syndrome including obesity and HT, probably on the bases of prolonged inflammatory and atherosclerotic effects beside pressure effect of excessive fat tissue on abdominal muscles. The inverse relationships between obesity and hypertriglyceridemia and hyperbetalipoproteinemia may be explained by the hepatic fat accumulation, inflammation, and fibrosis induced relatively lost hepatic functions in obese individuals. Similarly, the inverse relationship between obesity and WCH may be explained by progression of WCH into HT in obese individuals. So obesity may actually be a precirrhotic condition for the human body.

As a conclusion, although the umbilical hernia may significantly be related with the metabolic syndrome with a higher prevalence in advanced age, obesity, and females, we did not find any relationship between inguinal hernia and mean weight, height, BMI, triglyceride, and LDL values and prevalences of smoking, WCH, HT, DM, and CAD. So inguinal hernia may not have a chronic low-grade inflammatory background on vascular endothelium with a higher prevalence in males, younger ages, and right side predominance, without any effect of excess weight.

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Epidemiology, risk factors, and in-hospital outcome of acute coronary syndrome (ACS) patients younger than 40 years in Kermanshah, 2010-11

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Abstract

Background: CAD is the most important public health issue in developing and developed countries. Therefore, this study was done with the objective of determining epidemiology, risk factors, and in-hospital outcome of acute coronary syndrome (ACS) patients younger than 40 years, admitted to the hospital of Kermanshah, Iran in 2010-11.

Methods: In this cross-sectional study, CAD risk factors and in-hospital outcome of ACS patients who were younger than 40 years at the time of admission were extracted from their medical records. A total number of 2,084 medical records were reviewed, of which 125 records met the criteria and were included. The required information were gathered and inserted into the ACS registry developed by the European Society of Cardiology. The data were analyzed by the SPSS software (ver. 20.0) using descriptive indices and the Chi-squared test.

Results: Of 125 patients, there were 98 male and 27 females with age range of 19 to 40 years (mean age of 36.67 ±5.19 years). About 44.8% had unstable angina, 14.4 had Q-wave myocardial infarction (MI) and 27.2% had non Q-wave MI. All patients were alive at the time of the study and only one patient (0.8%) had history of MI.

Conclusion: Unstable angina in individuals younger than 40 years is becoming common and is three times more common in males than in females.

Key words: Risk factors, acute coronary syndrome, in-hospital outcome, Kermanshah

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Introduction

Coronary artery disease (CAD) is the most important public health issue in both developing and developed countries.(1) A major number of patients admitted to the hospitals run by the Iranian Ministry of Health and Medical Education are those with heart diseases, especially acute coronary syndrome (ACS).(2) According to the studies, high social costs and death risk related to cardiovascular diseases are more than any other medical condition. Nowadays, considering the better longevity and change in the lifestyle of the populations, cardiovascular diseases are becoming more common.(3) In the US, up to age 60 years, one male of every three males develops CAD. This rate is 1:10 in females.(1) In Iran, cardiovascular diseases are the most common cause of death and 46% of deaths are attributed to this factor. ACS includes ST-segment elevation myocardial infarction (STEMI), MI without ST elevation (NSTEMI), and unstable angina.(4) ACS encompasses a wide group of heterogeneous diseases ranging from diseases with nonspecific electrocardiogram (ECG) changes and normal cardiac serum biomarkers to STMI and cardiogenic shock. The most important clinical symptoms of ACS are substernal chest pain or epigastric pain which radiates to the neck, shoulders, and left arm. ACS patients may experience some non-specific symptoms for weeks or months before the cardiac event. These include fatigue, dyspnoea, gastrointestinal symptoms, anxiety, and chest discomfort.(5) Traditionally, ACS symptoms are regarded similar in both genders, but studies advocate that there may be relationship between ACS symptoms and gender. Milner et al. (2002) reported that females are more likely than males to experience symptoms other than chest pain like nausea, vomiting, abdominal pain, dyspnoea, and back, jaw or neck pain. Also, some studies report that males are more likely to experience chest pain and diaphoresis than females do.(6) CAD usually occurs in those older than 40 years, however this can occur in younger patients as well.(7) About 10-30% of ACS cases are reported in young patients who are less than 45 years. It is presumed that ACS in young patients presents as the consequence of a thrombotic event and is not related to basic atherosclerotic disease.(8) Generally, accurate assessment of ACS symptoms to initiate intervention is important in three fields. First, the occurrence of symptoms is an important factor which causes the patient to seek medical care. Second, assessment of symptoms is important in correct triage of patients which is usually done by nurses. Third, correct recognition of ACS symptoms is an effective factor in continuing assessment of patients and immediate intervention. The knowledge as to how patients may present with ACS symptoms can both accelerate the diagnosis of ACS and decrease mortality and improve their quality of life.(9) Prompt presentation to hospital is an important factor to achieve better outcome in ACS patients, but only less than 10% of patients present to hospitals in the first 1 hour of symptom onset which is the best time to achieve the desired outcome.(10) Young adults with CAD are an important group to consider with regard to justification of risk factors and secondary prevention as this age group comprises an active group in the population.(7)

There is no explicit report in Iran about the frequency distribution of ACS such as MI, unstable angina, and in-hospital outcomes in patients younger than 40 years. Therefore, this study was done to determine the epidemiology, CAD risk factors, and in-hospital outcome of patients younger than 40 years who presented to Kermanshah hospitals, Iran in 2010-11.

Method

Study population
In this cross-sectional study, the study population consisted of all patients with ACS who presented to the hospitals of Kermanshah, Iran which had cardiology emergency services in 2010-11. A total number of 2,084 records were reviewed, of which 125 records met the desired criteria. The records with incomplete information were not included.

Research Tool
The ACS registry developed by the European Society of Cardiology was used to insert the required data. The variables included the information upon presentation of the patient to the hospital, during hospitalization, and discharge.

Study Design
The medical records of patients who were diagnosed with ACS and who were younger than 40 years were reviewed. The information gathered was age, gender, marital status, educational level, occupation, hypertension, diabetes mellitus, dyslipidemia, body mass index (BMI), and in-hospital outcomes.

Statistical analyses
The data were analyzed by the SPSS software (ver. 20.0) using descriptive indices and the Chi-square test.

Results

Table 1 presents the demographics of the studied population. As shown, there were 98 males (78.4%) and 27 females (21.6%). Most patients were aged 35 to 40 years and age range of 39-40 was the most common age range group (42 patients, 34%). Age ranges of 37-38 years (28 patients, 22.4%) and 35-36 years (19 patients, 15.2%) were respectively the second and third most common age groups. The lowest numbers of patients were reported in age ranges of 19-20 years and 21-22 years (less than 3%). The most common weight range group was 71-80 Kg (57 cases, 45.6%) and then 81-90 Kg (24 cases, 19.2%). The weight group of more than 120 Kg and less than 50 Kg (less than 2%) were the least frequent weight groups.

According to Table 2, most patients did not have history of MI (125 cases, 99.2%) and only one patient had history of MI (one patient, 0.8%). Most patients (110 cases, 88%) did not have diabetes mellitus. Among patients with diabetes, the most frequent patient group was belonging to those who were "medicine takers" (13 cases, 10.4%). About one-fourth of patients (24 cases, 19.2%) had hypertension and most patients (99 cases, 79.2%) were normotensive subjects.

Table 1: Demographic characteristics of the study population

		Frequency	Percent	Cumulative Percent
Sex	Male	98	78.4	78.4
	Female	27	21.6	100
	Total	125	100	----
Age	39-40	42	33.6	33.6
	37-38	28	22.4	56
	35-36	19	15.2	71.2
	33-34	8	6.4	77.6
	31-32	9	7.2	84.8
	29-30	4	3.2	88
	27-28	3	2.4	90.4
	25-26	4	3.2	93.6
	23-24	3	2.4	96
	21-22	2	1.6	97.6
	19-20	3	2.4	100.0
	Total	125	100.0	----
Weight	41-50	2	1.6	1.6
	51-60	4	3.2	4.8
	61-70	22	17.6	22.4
	71-80	57	45.6	68
	81-90	24	19.2	87.2
	91-100	3	2.4	89.6
	101-110	8	6.4	96
	111-120	3	2.4	984
	121-130	2	1.6	100.0
	Total	125	100.0	----

Table 2: Baseline characteristics of the patients

		Frequency	Percent	Cumulative Percent
Stroke	No	124	99.2	99.2
	Yes	1	0.8	100.0
	Total	125	100.0	----
Diabetes	Non-diabetic	110	88	88
	Diabetic (oral medication)	13	10.4	98.4
	Newly diagnosed	1	0.8	99.2
	Unknown	1	0.8	100.0
	Total	125	100.0	----
Hypertension	No	99	79.2	79.2
	Yes	24	19.2	98.4
	Unknown	2	1.6	100.0
	Total	125	100.0	----

About 50.4% of patients (63 cases) were non-smokers (Table 3). But 60 patients (48%) were current smokers and 2 cases (1.6%) were former smokers. Most patients (114 cases, 91.2%) did not have MI and only 11 cases (8.8%) had MI. Regarding the most prominent symptom reported by the patients, the most frequent symptoms was chest pain (114 cases, 94.4%). Regarding systolic blood pressure (BP), most patients had systolic BP measurements between 95 and 155 mmHg (88% of the cases). About 43.2% of the patients (54 cases) had systolic BP range of 116-135 mmHg, 34 cases (27.2%) had range of 96-115 mmHg, and 16% (20 cases) had range of 136-155 mmHg. Regarding psychological variables (depression and anxiety), most patients (106 cases, 84.48%) did not report symptoms of anxiety or depression. About 15.2% of cases (19 patients) had mild anxiety and depression. Regarding the primary diagnosis, 56 cases (44.8%) had unstable angina, 51 cases (40.8%) had NSTEMI, and 18 cases (14.4%) had STEMI or left bundle branch block (LBBB) MI.

Table3: Prevalence of coronary artery disease risk factors

Status		Frequency	Percent	Cumulative Percent
Smoking	Never	63	50.4	50.4
	Current	60	48	98.4
	Former	2	1.6	100.0
	Total	125	100.0	----
HPMI	No	114	91.2	91.2
	Yes	11	8.8	100.0
	Total	125	100.0	----
PPS	Chest pain	118	94.4	94.4
	Dyspnoea	2	1.6	96
	Syncope	1	0.8	96.8
	Other Symptoms	4	3.2	100.0
	Total	125	100.0	----
Systolic	75-95	6	4.8	4.8
	96-115	34	27.2	32
	116-135	54	43.2	75.2
	136-155	20	16	91.2
	156-175	5	4	95.2
	176-195	4	3.2	98.4
	196-215	1	0.8	99.2
	216-235	1	0.8	100.0
	Total	125	100.0	----
Anxiety/ depression	1 - I am not anxious or depressed	106	84.8	84.8
	2 - I am moderately anxious or depressed	19	15.2	100
	Total	125	100.0	----
Working diagnosis	STEMI/LBBB MI	18	14.4	14.4
	NSTEMI	51	40.8	55.2
	Unstable Angina	56	44.8	100.0
	Total	125	100.0	----

HPMI- History of prior myocardial infarction; PPS-Predominant Presenting Symptom

As seen in Table 4, all patients were alive at the time of the study. None of the patients experienced cardiac arrest which required resuscitation during the hospitalization. Most patients (123 cases, 98.4%) did not have coronary bypass surgery (CABG) and only 2 patients (1.6%) received emergency CABG. Most patients (99.2%, 124 cases) did not develop MI during hospitalization. Only one patient (less than 1%) developed hemorrhage during hospitalization. Regarding the final diagnosis made upon discharge, 69 patients (55.2%) had unstable angina, 34 cases (27.2%) had non-Q wave MI, and 18 cases (14.4%) had Q wave MI. Most patients did not develop stroke (124 cases, 99.2%).

Table 4: In-hospital outcome of patients with acute coronary syndrome

Status		Frequency	Percent	Cumulative Percent
Survival status	Alive	125	100.0	100.0
	dead	0.0	0.0	100.0
	Total	125	100.0	----
Resuscitated cardiac arrest	No	125	100.0	100.0
	Yes	0.0	0.0	100.0
	Total	2084	100.0	----
CABG	No	123	98.4	98.4
	Emergency	2	1.6	100.0
	Total	125	100.0	----
MRIH	No	124	99.2	99.2
	Yes	0.0	0.0	99.2
	Unknown	1	0.8	100.0
	Total	125	100.0	----
Bleeding in hospital	No	124	99.1	99.1
	Unknown	1	.9	100.0
	Total	125	99.2	----
Discharge diagnosis	Q wave MI	18	14.4	14.4
	Non Q wave MI	34	27.2	41.6
	Unstable Angina	69	55.2	97.8
	Other	3	2.4	100.0
	Total	125	100.0	----
Stroke in Hospital	Valid No	124	99.2	100.0
	Valid System	1	0.8	----
	Missing Total	125	100.0	----

CABG- Coronary Artery Bypass Graft ; MRIH-Myocardial Reinfarction in Hospital

Discussion

This study was conducted to determine the epidemiology, CAD risk factors, and in-hospital outcome of patients younger than 40 years who presented to Kermanshah hospitals, Iran in 2010-11. Most reported studies in this field have been done in those older than 40 years. The results showed that 78.4% were male and 21.6% were female. Most patients (34%) were aged 39-40 years (34%) and the least frequent age groups were 19-20 and 20-21 years (less than 3%). Regarding weight, the most frequent group was 71-80 Kg (45.6%) and the least frequent group was less than 50 kg (less than 2%). Most patients did not have history of MI, and only one patient (0.8%) stated the history of MI. Also, 88% of patients did not have diabetes which is not compatible with the results reported by Andrikopouloset al. which reported that 27% of patients older than 40 years did not have diabetes (2012). But in the Khalid et al. study (2011), 58.1% of patients older than 40 years were diabetics.(11, 12) About 19.2% of patients had hypertension, but the results of two other studies.(11, 12) reported a higher number of patients

with hypertension (67.9% and 55.3%). In this study, 48% were current smokers and 1.6% were former smokers. In a study by Faizal et al. (2009), 39.13% were current smokers and in the study of Khalid et al. (2011), 32.8% were current smokers(12,13). They reported that the prevalence of smoking is more prevalent in those younger than 40 years than in those older than 40 years. About 44.8% of the patients had unstable angina, 14.4% had Q-wave MI, 27.2% had non-Q wave MI, 40.8% had NSTEMI, and 14.4% had STEMI/LBBB MI. Non-Q wave MI was twice more common than Q wave MI. In a former study by Moludi et al. which was performed among those older than 40 years, non-Q wave MI was twice more common than Q wave MI.(1) We observe a trend in increase in the rate of non-Q wave MI and decrease in the rate of Q wave MI in all ages. All patients survived. Also, none of the patients experienced cardiac arrest. Most patients (98.4%) did not required CABG, and only in 2 patients this procedure was required. Only one patient experienced hemorrhage during hospitalization and most patients (124 cases, 99.1%) did not develop hemorrhage.

Conclusion

Unfortunately the prevalence of CAD is growing in our community which is important from the standpoint of epidemiology. Also, we observe a growing trend of CAD in patients younger than 40 years which seems that hereditary factors, lifestyle, and psychological stress have major roles in this regard. It could be concluded that ACS is growing in patients younger than 40 years which requires more studies to determine its etiology.

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Evaluating Miscoding in the Codes Provided for Diagnostic and Surgical Tariffs

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Abstract

Introduction: Coding errors are inevitable, but an acceptable level of their correctness must be considered.

Aim: The aim of this study was to evaluate the errors in the codes provided for diagnostic and surgical tariffs.

Materials and Methods: This descriptive and cross-sectional study was performed in 2016. Research resources were records in compensation units in the center of medical documents of social security organization. Data were collected using a checklist by compensation unit coders. Validity of checklist was confirmed by six experts. The data were analyzed by SPSS-20 software and provided in descriptive tables.

Results: Findings indicated that 90.7 percent of the accomplished procedures were surgery. 95 percent of them were done in private hospitals of which 61 percent were specialized. 114 tariff codes with relative value of 3338.1 from 260 codes with the relative value of 9696.4 and 62 modification codes with relative value of 910.94 from 301 codes with relative value of 3360.57 were not confirmed. Most types of documentation error were related to not being confirmed, of 106 requested codes according to the documentations by coders.

Conclusion: Therefore, according to the results of research it is essential the physicians be aware of the importance of documentation and of writing a detailed description of taken procedures and abstaining from providing additional codes. Some proper policies must be adopted to reduce procedure miscoding.

Key words: coding, miscoding, tariffs, diagnostic procedure, surgical procedure

Introduction

The proper management of medical centers with the use of the potential of information systems in using available resources can guide the growing hospitals. Failure to accurately record and save data is among the problems that disorder correct decision making and causes waste of resources. Fees of completed procedures for physicians are recorded by codes provided to perform these procedures. Recording the wrong codes causes need for more time devoted to surveying records, injustice to the patient in terms of more reimbursement and multiple deductions for hospitals [1].

The correct and complete data collection using standard coding is crucial for planning, research, analysis, reimbursement and policy-making. The use of coding standards increases data quality and improves the decision-making process [2]. The usefulness of coded medical data relies basically on the same coding on the similar entities independent of the person or coding time [3]. Coding provides the standardization of expressions so that the data can be used by persons other than those who collect the data, so is very important [4].

Coding medical data is important because of the quality of care and the national reports [5]. With regard to the application of coded data in management activities, observing the coding quality and its assessment is necessary more than ever [6]. The use of health information is possible when it is organized and classified correctly, and this can be done through the coding [7]. Coding could be defined as following: assigning a symbol or code for diagnostic terms and procedures based on a common used book of classification [8]. Various studies, recording flawed information in files, lack of familiarity of physicians with the principles of writing diagnosis, lack of familiarity with the classification systems of diseases and inexactness and coders' being inexperienced, are some factors that lead to data miscoding [9].

Coding errors are inevitable. Some of the errors are in the scope of controlling information management process and the others are common in the result of insufficiency of source document or lack of information integration, resulting from current computer programming and software logic [2]. The reality of coding in a hospital system is much more complex than coders think. Poor hand-writing, incomplete or inadequate documentation, lost medical documents and lack of access to electronic documents cause coding to be incomplete or miscoding [10].

Providing intentional wrong codes also causes coding errors. These errors cause, in the first stage, injustice to the patient, because the records are surveyed after discharge, when the patient has paid the cost. In the next step the created errors cause to prolong records and codes investigation time; they cause delayed resource reimbursement by insurance to hospitals and this causes the management of these centers to be confronted with many problems. Most of the documentation difficulties result from a lack of understanding of coding method by physicians and how the documentation is affected because of their coding[1].

In a change in the system it is possible to create the request for getting more by using the code assignation with up-coding. Or multiple codes with up-coding are listed

instead of a correct code. This cheating deceives patients and insurance companies and distorts statistics. A large part of reimbursement of patients admitted to the hospital will be based on the reimbursement systems. Therefore, the appropriate coding of procedures has a financial impact on the Hospital [11]. Investigating strengths and weaknesses and errors in determining tariffs must be taken into consideration. Providing any code should be based on documents, rational reasons and their impact on the health system, insurance and individuals of society [12].

Tariff determination of health services in Iran has been adopted from "Current Procedure Terminology (CPT)" of America; it has been not come about natively nor has it been updated since its implementation. With implementing the health system reformation plan in 2014, the health system tariffs became native and were updated by the Ministry of Health. So with regard to the problems related to the change of system, lack of being familiar with coding rules, the incomplete documentation as well as requesting the error codes to obtain more, this research was conducted surveying a variety of coding errors in diagnostic-surgical procedures related to records of hospitalized patients.

Materials and Methods

The study was applied and performed by descriptive cross-sectional method in 2016. Research resources were records referred to compensation unit in the Medical Documents Center of the social security organization in 2015. The reason why we chose the records of this unit was the lack of modifying documentation and the modification or change of codes for services provided by insurance experts residing in the hospital. The records referred to the compensation unit were selected from the first of April 2014 until the end of March 2015 based on research criteria. The criteria included: being records of hospitalization, codes are not global, being surgical services and not relating to consulting, the record is coded by the center doing services and also the records from the first of April 2014 until the end of March 2015 that were referred to the compensation unit of medical documents of social security organization.

Sampling was census and all the records that met the research criteria (118 files) were investigated. The instrument of collecting data was a checklist. It was designed by researchers based on the type of record data, codes, investigation process and factors affecting confirmation of codes, all kinds of documentation errors leading to miscoding as well as conducted studies; it was divided into seven parts.
1. The first part of the checklist was the patient's demographic information including gender, type of hospitalization, diagnosis and the main procedure.
2. The second part was the information related to the location and service providers. This part included the type of hospital in terms of specialty and affiliation, type of specialty and scientific rank of the surgeon and Anesthesiologist.

3. The third part was related to the type of procedure and classifying it based on the book of surgery diagnostic procedures tariffs approved by the Ministry of health and medical education of the Islamic Republic of Iran in 2014.
4. The fourth part included the surgical tariff codes and the number of modification codes of surgery and anesthesia requested by medical centers.
5. The fifth part was the number of surgery tariff codes and the number of surgical and anesthesia modification codes approved in the medical documents compensation unit.
6. The sixth part was related to the coding errors that were divided into two parts, of surgery and anesthesia. In both parts the first section included the tariff codes and the second section, the modification codes. Coding errors for tariff and modification codes section included: wrong code, i.e. the number of requested codes is correct but the code was wrong. Additional code i.e. the number of codes that were requested by the Medical Center and by the coding expert of compensation unit was not approved and low code i.e. the number of codes that were requested by the Medical Center and were added by the coding expert of the compensation unit. For each of the possible modes in coding error the (tariff or modification) code was collected.
7. The data of documentation errors were collected using the last part of the checklist. Error type not recorded (doing procedure that a code with relative value has been requested for, but its description is not in the record). Illegible (mentioned documents were not legible). Unverified (inserting codes that were not approved with respect to record documents). Inconsistent (mentioned codes were not compatible with documents) and the ambiguous abbreviations (abbreviations that were not standard and there was not any code or value for them) Content validity of checklist was confirmed by six experts (two people for health information management, two people as physicians and two people as coders).

Data collection was done by coders in the compensation unit. During checking of records to verify codes and reimbursement to the patient, the data were recorded in the checklist. The data were entered in SPSS-20 and were analyzed according to the research objectives and questions. Ultimately the results and analysis were provided in the descriptive tables.

The access to data was authorized with the letter of introduction of No.15676 of 14/4/2015 from Kermanshah University of medical sciences for the medical documents center of social security organization and with agreement of its officials. Also the ethical considerations were met to observe privacy principles on the use of data and not mentioning the name of hospital, patients and experts.

The lack of coding procedures of some records was one limitation of the research. In these records an amount has been received from patient for the hospital, surgical and anesthesia services. No code has been mentioned for the surgery and anesthesia procedures; these records were excluded from the study based on the research criteria.

Results

Based on the criteria of selecting study units, 118 records were surveyed. The number of male and female patients was randomly equal and each group contained 59 people. All patients were electively accepted, of whom 9 cases were for Day Care and 109 cases for hospitalization.

Table 1: frequency of type of hospital in terms of affiliation and specialty and the city in which is situated that hospital, surgeon and anesthesia rank and type of procedure

Type of variable	Criteria	percentage	frequency
Type of hospital in terms of affiliation	Treatment-educational	0	0
	Depending on university	0	0
	Social security	0	0
	Military forces	5	6
	Private	95	112
	Petroleum	0	0
	Other	0	0
Type of hospital in terms of specialty	Public	4.2	5
	Specialized	61	72
	Super specialty	17	20
	Specialized clinic	17.8	21
City of hospital	Kermanshah	1.7	2
	Tehran	97.5	115
	Mashhad	0.8	1
Surgeon rank	Specialist	60	71
	Super specialty	40	47
Anesthesia rank	Specialist	94	111
	Super specialty	6	7
Type of procedure	Diagnostic	4.2	5
	Surgery	90.7	107
	Both	5.1	6

95 percent of the patients had referred to private centers and 61 percent of these centers were specialized. For treatment 97.5% of patients had referred to Tehran and 61 percent of them to specialists. 90.7% of procedures done for these patients were surgical.

Table 2: number of patients referring to the surgical specialties

Surgeon's specialty	Number	Surgeon's specialty	Number
Neurosurgery	19	Eye	22
Plastic surgery	5	Heart	2
Digestion	1	Children heart	1
Pain medicine	1	General surgeon	9
Endocrine surgeon	1	Women oncology	1
Vessels surgeon	2	Women	19
Hand repair surgery	3	Urology	5
Physical medicine	2	Children urology	1
Spinal cord surgeon	1	Orthopedic	22
		Children orthopedics	1

The greatest reference was related to the eye and orthopedic specialties (with 22 patients) and in the second stage women and neurosurgery with 19 patients.

Table 3: number of reference, requested and confirmation tariff and modification codes based on tariffs classification

System	Num. of patients		Modification				Tariff		
	patients	relative value	confirmed	relative value	requested	relative value	confirmed	relative value	requested
Integumentary system	11	153.54	18	268.7	25	445.5	13	896.5	31
Musculoskeletal	21	254.86	42	432.29	39	881.9	25	1594	53
Respiratory	1	5.4	2	16.1	4	18	1	30.6	1
Cardio-vascular	5	91	8	138.2	10	445	5	798.8	10
Blood and lymph	0	0	0	0	0	0	0	0	0
Digestion	10	188.8	22	327.2	30	698	10	844.2	13
Urine	4	102	10	109.5	13	236	4	339.5	9
Male genital	2	19.4	2	17.4	2	109	2	132.4	2
Female genital	19	193.43	31	263.4	46	570.2	19	930.2	31
Endocrine glands	0	0	0	0	0	0	0	0	0
Nervous system	24	713.46	58	1219.28	76	1973.2	44	2557.7	67
Eye and supplements	19	506.74	43	414.5	51	774.8	21	1373.5	38
Auditory	2	21	3	54	5	106.7	2	199	5
Total	118	2449.63	239	3360.57	301	6358.3	146	9696.4	260

The majority of the patients related to the nervous system and musculoskeletal system, with 24 and 21 patients, respectively; blood and lymph system and endocrine had no reference. The nervous system with 67 tariff codes and the Relative value of 2557.7 and 76 modification codes with Relative value of 1219.28 had the most requested and modification code. Confirmation codes of nervous system were 44 tariff codes with Relative value of 1973.2 and 58 modification codes with coefficient of 713.46. In the musculoskeletal systems, the modification codes and confirmed Relative value had an increase compared with requested codes. In total 260 tariff codes with the Relative value of 9696.4 and 301 modification codes with Relative value of 3360.57 were requested. 106 tariff codes with Relative value of 6358.3 and 239 modification codes with coefficient of 2449.63 were confirmed.

Modification codes of surgery included multiple surgery (code number 51), assistant surgeon (code number 80) and semi-aggressive technology (code number 85). Based on the classification system, 105 modification codes of surgery were requested; multiple surgery 31 codes, assistant surgeon 48 codes and semi-aggressive technology 26 codes. The most requested modification codes for multiple surgery for integumentary and nervous system were seven codes. The most occurring code for assistant surgeon and semi-aggressive technology in nervous system was 15 and eight respectively. From 105 requested modification codes of surgery 101 codes were confirmed; multiple surgery had 48 codes, assistant surgeon39 codes and semi-aggressive technology 14 codes. For multiple surgeries 17 codes have been added. Assistant surgeon codes and semi-aggressive technology for all systems were the less requested confirmation codes.

Modification codes for anesthesia included position (code number 32), comorbidity (code number 35), emergency patient (code number 36), and age over 70 years (code number 37), difficult anesthesia (code number 38), recovery (code number 39), time (code number 42) and local anesthesia (code number 45). Based on classification system 196 modification codes were requested. The most requested modification code for anesthesia was respectively related to the time of 82 and recovery of 56. Local anesthesia with one code had the most insufficient requested code. From 196 requested modification codes of anesthesia 140 codes were confirmed. For all the systems where there were fewer the confirmation codes from which the recovery with 19 unconfirmed codes had the greatest decrease.

Table 4: coding errors for tariff and modification codes of surgery and anesthesia on the basis of the tariff classification system

Classification system	Anesthesia						Surgery					
	Modification			Tariff			Modification			Tariff		
	Few	Additional	Wrong	Few	Additional	Wrong	Few	Additional	Wrong	Few	Additional	Wrong
Integumentary system	0	2	0	0	5	0	2	4	0	0	6	3
Musculoskeletal	2	6	0	0	1	0	9	6	0	0	15	4
Respiratory	0	1	0	0	1	0	0	0	0	0	0	1
Cardio-vascular	0	0	0	0	1	0	0	3	0	1	4	0
Blood and lymph	0	0	0	0	0	0	0	0	0	0	0	0
Digestive	0	4	0	0	0	0	0	7	1	0	4	4
Urine	0	2	0	0	0	0	1	1	0	0	2	1
Male genital	1	0	0	0	0	0	0	0	0	0	0	0
Female genital	0	12	0	0	1	0	2	7	0	0	11	8
Endocrine	0	0	0	0	0	0	0	0	0	0	0	0
Nervous system	0	10	0	0	4	0	3	16	0	0	14	4
Eye and supplements	1	7	0	1	0	0	12	5	0	0	12	5
Auditory	1	1	0	0	0	0	0	2	0	0	2	0
total	5	45	0	1	13	0	29	51	1	1	70	30

Additional code request was the most occurring error type of tariff and modification codes of surgery respectively with 70 and 51 codes. Musculoskeletal system with 15 codes had greatest requested additional code for tariff of surgery and the nervous system with 16 codes had the greatest additional requested code for surgical modification. Errors related to tariff and modification codes of anesthesia were additional code requests. There was no wrong code request for tariff and modification codes of anesthesia.

Table 5: Frequency of specialist based on the rank and type of coding error

Specialty	Physician's rank	Number	Miscoding		Additional code		Few code	
			Tariff	Modification	Tariff	Modification	Tariff	Modification
Surgeon	specialist	71	23	1	38	33	1	10
	super specialty	47	7	0	32	18	1	19
total		118	30	1	70	51	1	29
Anesthesia	specialist	111	0	0	5	34	1	4
	super specialty	7	0	0	8	11	0	1
total		118	0	0	13	45	1	5

The rank of the 71 surgeons was specialty. Specialists had more coding errors in requesting the wrong tariff code (23), additional tariff (38) and additional modifications (33). The error of requesting few codes with 19 codes was more by the super specialty surgeon. 111 persons were anesthesiologists. 45 additional requested modification codes were the most occurring error type among them. There was no wrong code for coding error request by the specialist and super specialty of anesthesia.

Table 6: Documentation errors based on tariff classification

Book chapter	Ambiguous abbreviation	inconsistent	Not approved	Illegible	Not recorded
Integumentary system	0	3	10	0	0
Musculoskeletal	0	2	19	0	1
Respiratory	0	1	0	0	0
Cardio-vascular	0	0	5	0	0
Blood and lymph	0	0	0	0	0
Digestion	0	1	9	0	1
Urine	0	1	3	0	0
Male genital	0	0	2	0	0
Female genital	0	5	15	0	0
Endocrine glands	0	0	0	0	0
Nervous system	0	3	22	0	0
Eye and supplements	0	1	19	0	0
Auditory	0	0	2	0	0
Total	0	17	106	0	2

Not being confirmed of 106 requested codes of surgeons, according to the documents of coders, were the most occurring documentation error type.

Table 7: Coding errors in modification codes of surgery and Anesthesia

Code	Error	Wrong	Additional	Few	Total
Anesthesia	Total	0	80	5	85
	Local anesthesia (45)	0	0	0	0
	Time (42)	0	37	5	42
	Recovery (39)	0	16	0	16
	Problematic anesthesia (38)	0	1	0	1
	Age higher than 70 (37)	0	7	0	7
	Emergency patient (36)	0	6	0	6
	Comorbidity (35)	0	5	0	5
	Position (32)	0	8	0	8
surgery	Total	1	63	31	95
	Semi-aggressive technology (85)	0	19	2	21
	Assistant surgeon (80)	0	25	0	25
	Multiple surgery (51)	1	19	29	49

Coding errors in surgical modification codes with 95 cases were more than anesthesia with 85 cases. The most occurring error type in modification codes of surgery and anesthesia was additional request with respectively 63 and 80 codes.

Discussion

The procedures taken in indirect care are provided for in the form of tariff codes and the service cost is paid entirely by the patient according to the provided codes. Then for reimbursement the patient refers to the compensation unit in the center of medical documents. In this unit the records are re-surveyed and coded by coders. In the compensation unit the amount of reimbursement specified is based on the codes provided by the coders. There is a difference between the codes provided in the medical centers and the compensation unit. The errors created in codes will cause a change in relative value and the paid cost. The additional paid costs are not refundable to the patient. In this research, the coding errors are associated with errors that have been created due to incomplete, inconsistent and ambiguous documentation or the request of wrong, additional or few codes. Errors were analyzed according to the demographic profile of the patient, illness, procedure, medical specialty and the type of medical centers.

The results of this study showed that 114 tariff codes with relative value of 3338.1 from 260 codes with the relative value of 9696.4 and 62 modification codes with relative value of 910.94 from 301 codes with relative value of 3360.57 were not confirmed. In total the coding errors have caused 4249.04 of the relative value unit to be not confirmed. Given that the basic fee for a unit in 2015 has been equivalent to 380000 Rials, 1614635200 Rials have been requested additionally only from 118 patients. Findings resulting from the research of Cheng indicated that 16 percent of 752 investigated cases had changes in the tariff codes. That is, approximately $US575,300 the additional cost was requested [13].

On the basis of the obtained findings, the greatest error of surgical and modification tariff codes was to request additional code; the tariff codes included 70 additional codes and the modification ones 51 additional codes. Also the request of additional code (relating to the basic code of anesthesia) was the most occurring error type for anesthesia tariff and the requests of additional modification code the most occurring error type in anesthesia. In a study of Karami et al the request of additional modification codes and the request of anesthesia relative value were some causes of imposed multiple deductions [14]. The findings of the research of Mohammadi et al indicated that in the hospitalization section the highest percentage of multiple deductions was dedicated to the costs of anesthesia [1]. In the study of Khorrami as well the greatest multiple deductions were related to surgery sectors [15].

Rank of most of the surgeons who had a coding error was specialty (71 people); this was also true of anesthesia physicians (111 people). Among these experts, the most occurring coding error was related to the request of additional code. In a study of Mohammadi, assigning the wrong code and up-coding were some factors that have led to multiple deductions [1]. In a study of Khorrami physicians' lack of familiarity was the main reason for that [15]. Based on these findings it seems necessary for the physicians to achieve a correct understanding of the levels of required details and limitations to write codes; this shows the necessity of educating in coding (especially among experts). Also in order to prevent the occurrence of these errors it is necessary to monitor the performance of physicians by hospitals and take some strategies aiming to reduce these errors.

Most occurring coding errors (wrong and additional code) on the basis of the tariff classification system were related to the systems that had highest reference (nervous and musculoskeletal system). According to the mentioned findings we can infer that the probabilities of coding errors are higher in cases where the references are higher. The increase in the

confirmation code compared to the request one in some systems was related to the modification code of 51. These codes were requested by the surgeon with the tariff code, but based on the simultaneous surgery law the tariff code was eliminated; they were provided by coder with the modification code of 51. This clarifies the necessity of paying more attention of hospitals to monitor precisely the physicians' performance in the specialties that have greatest reference. In addition, in the areas where the reference is high, educating physicians in the field of coding is more important.

The findings showed that the most important type of documentation was related to the codes not approved by coder (106 items). After that the inconsistent documentation with 17 cases had the greatest documentation error. In this regard, the results of the study of Cheema and Khwaja also showed that the highest documentation error was dedicated to the codes that have not been confirmed by coder; they included 24 cases. After that 2 cases were related to non-recorded codes [16]. In the present study also the unrecorded codes were 2 cases, but before this the error related to inconsistent documentation and had more cases (17 cases). In the research of Naran et al. 266 codes were not approved. Also in this study, the ambiguous abbreviations were one of major reasons for the documentation error [17]. This is while in the present research there was not observed any error related to the ambiguous abbreviations. In a study of Mitra et al as well 6 cases from 47 cases of errors were related to the codes that have not been recorded at all [18]. Given that one of the objectives of the plan for health system reformation is to reduce the patients' payments [19], in accordance with the results of a recent study it appears that the implementation of this plan has been not effective in reducing coding errors of tariff codes, but it could have been successful in reducing coding errors of modification codes.

Conclusion

According to the achieved results it is essential correct policies are adopted in order to decrease the surgical procedures coding errors. To achieve optimal accuracy in coding physicians need to be aware of the importance of documentation and of writing a detailed description of taken procedures. Some of the procedures are complex and sometimes a small change in one procedure can cause a change in the final code. The coding data are the most comprehensive data available for policy-making and decisions in allocation of resources; so coding errors can provide a wrong image of working burden of a department. Based on the findings of the present research and due to a high rate of surgery and anesthesia coding errors, the medical systematic training for physicians to reduce coding errors and additional codes seems necessary. Also it is necessary for hospitals to give importance to educational issues as well as monitor the performance of physicians in order to protect the rights of the patient.

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Rehabilitation services difficulties perceived by Multiple sclerosis patients, their families and professionals in Iran: A qualitative study

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Abstract

Background: Rehabilitation services for people with chronic illness such as multiple sclerosis (MS) have recently come into focus. Adequate and efficient services should be provided based on a deep understanding of patient's difficulties and unmet needs, from different perspectives.

This study was conducted to identify patient's unmet needs and difficulties that they have encountered during the process of diagnosis, treatment and rehabilitation.

Methods: 35 participants (21 patients, 7 professionals and 8 families) were purposively selected for in-depth qualitative research. Interviews were voice recorded and transcribed verbatim. Transcripts were coded thematically using a content analysis approach.

Results: Results are presented in four categories: prerequisites for rehabilitation, treatment administration, awareness level and modification.

The majority of participants highlighted the significance of the patient-doctor interaction and access to competent experts. Also the teamwork as a sub-category of health care service was important from all participants' point of view.

A low level of trust in physicians more likely reduces the continuity of care and adherence to treatment. The unawareness and inadequate information of people, family and patients about the disease can cause stigma, reduced family support, stress and anxiety, respectively.

Transportation and Architectural barriers were the causes of inducing restriction and making the patients house-bound.

Conclusion: Advocating for a rehabilitation service package to consider the social rehabilitation in MS patients is critical. Also the team work approach could facilitate an understanding of the barriers faced by MS persons, thus facilitating patients receiving the right treatment in the right place at the right time.

Key words: content analysis; Multiple Sclerosis; Iran; Rehabilitation,

Introduction

Multiple sclerosis (MS) is a common disabling neurologic disease [1] of young adult people[2] which is more prevalent in the women [3, 4]. More than 2.3 million MS patients in the world are reported[5] and Europeans are more at the risk in comparison to Asians and Africans[6]. About 70,000 patients are diagnosed in Iran [7, 8] and its prevalence has had a significant increase from 26.24 per 100000 in 2006 to 44.53 per 100000 in 2011 [3, 9]. Signs and symptoms of disease (fatigue, depression and anxiety) have impact on patients' daily living and social participation[10, 11].

A comprehensive rehabilitation approach in conjunct with medical treatment should be considered in the treatment process. Providing the right services at the right time induces the optimum treatment outcomes. Prerequisites for providing the right services is based on a deep understanding of patient's barriers, difficulties and unmet needs [12] from different perspectives. The unmet needs from the perspective of patients, healthcare professionals and their caregivers [5, 10, 11, 13, 14] are assessed in different studies and various themes related to service provision are revealed such as "lack of information about services", "lack of continuity and co-ordination of care" [11, 13] "support from family/friends", "healthcare services", "managing everyday life" and maintaining biographical continuity [15]. These differences can be related to a mismatch between perceived unmet needs by professionals, families and the patients. It seems that enrolling the different groups such as MS patients, patient's family and professionals to express their experiences, perceived difficulties and needs are necessary[5]. The present study with the aim of explaining patients' difficulties, barriers and unmet needs from the perspective of professionals, family and themselves simultaneously was therefore conducted.

Methods

Participants

In this qualitative content analysis research, 36 participants (21 patients, 7 healthcare professionals and 8 patients' family) were enrolled voluntarily. They were selected through a purposeful and convenience sampling. Patients with definitive diagnosis of MS aged between 24-65 years from Iranian MS Association (IMSA) and Welfare State Organization (WSO) were selected. The healthcare professionals included social workers (n=3), neurologists (n=1), occupational therapist (n=1) and physiotherapist (n=2) with at least one-year experience of work with MS patients. Patient's family members (a child, a brother, three spouses and three parents) have lived with at least one MS patient and were involved in the treatment process. All of the samples were able to express their experiences and needs. Sampling was terminated when no additional information was acquired and data saturation occurred.

Data Collection

Data was gathered through an in-depth interview with flexible and open ended questions. A prototype interview guide was developed based on the literature [5, 11, 12,

15, 16] and the discussion within the research team. A pilot interview schedule was conducted in three patients and some minor revisions were applied to it. All interviews were conducted in a place that the participants preferred. The interviews usually lasted between 30 and 60 minutes and were tape-recorded and transcribed verbatim.

Trustworthiness

To maximize theoretical sensitivity, constant comparison was done by returning to the data several times during the analysis. All authors participated in the discussions throughout the analysis. All of the transcripts and the preliminary sets of codes and categories were checked by two experts within the research team (Peer review) and some of the participants (Member check).

Ethical Consideration

The study was approved by independent ethics committee of University of Social Welfare and Rehabilitation Sciences, Tehran, Iran (IR.USWR.REC.1395.249) and all participants completed an informed consent form. The purpose of the study and confidentiality of information were explained to the participants.

Data Analysis

The interviews were transcribed and then imported into the qualitative software program MAXQDA (version 10) for analysis. Next open text coding included examining each interview, breaking the transcript down into individual units of meaning, and labeling them to identify categories and concepts that were used. After that, evolving concepts were regrouped to form more abstract categories. Categories were systematically sorted, compared and contrasted, yielding increasingly complex and inclusive themes, until saturated. This analytical process was non-linear in nature, with the analyst going back and forth between the different stages of coding. Finally, the findings were compared with the original tapes, ensuring equality between texts and extracted themes.

Results

The Sample characteristics are presented in Table 1.

Four overall categories were identified based on participations' experiences: "Prerequisites for rehabilitation, Treatment administration, Awareness level and Modification." Subcategories of these four categories are provided in Table 2.

Prerequisites for rehabilitation:

Interpersonal interaction, MS specialists' Competency and sufficiency and Teamwork are grouped into this category. Interpersonal interaction describes physician-patient relationship. The patients and their families explained that physicians had not appropriate interaction with them and did not pay attention. The following example highlights this point:

"As I entered the room, he didn't get up from his seat. He didn't even take my pulse. I was saying to him my symptoms and he was prescribing some medicine without paying any attention to my explanation."(MS P4, man)

Table1: Socio-demographic characteristics of the participation

	MS Patients N (%)	Healthcare professionals N (%)	MS patients' family members N (%)
Gender			
Male	11 (52.4)	4 (57.1)	6 (75)
Female	10 (47.6)	3 (42.9)	2 (25)
Age (year)			
20-30	4(19.04)	1(14.2)	2(25)
31-40	8(38.09)	1 (14.2)	1(12.5)
41-50	7(33.33)	2 (28.5)	-
51-60	-	1 (14.2)	-
61-70	2(9.52)	2 (28.5)	3(37.5)
71-80	-	-	2(25)
EDU (years of education)			
12≤	6 (28.6)	-	3(37.5)
13-16	12 (57.1)	3(42.85)	3(37.5)
17-18	1 (4.8)	2(28.57)	1(12.5)
≥19	2 (9.5)	2(28.57)	1(12.5)
Employment			
Employed	3 (14.3)	6(85.8)	2(25)
Self-employed	6 (28.6)	1(14.2)	2(25)
Retired	5 (23.8)	-	3(37.5)
Not working	7 (33.3)	-	1(12.5)
Time since diagnosis (years)			
0-5	4 (19)	-	-
6-10	3 (14.3)	-	-
11-15	6 (28.6)	-	-
16-20	1 (4.8)	-	-
21-25	5 (4.8)	-	-
≥26	2 (9.5)	-	-

MS is multiple sclerosis

Table 2: Categories and subcategories of the MS patients' difficulties

Category	Subcategory
Prerequisites for rehabilitation	Interpersonal interaction
	MS specialists' competence and sufficiency
	Teamwork
Treatment administration	Treatment adherence
	Trust in therapists
	Controversy on the efficacy of medicines
Awareness level	MS Patients' information about disease and services
	Families' information about disease and services
	People's information about disease
Modification	Transportation barriers
	Environmental barriers

Also, telling the diagnosis directly to the patients usually shocked them and it was so unexpected. The patients preferred that the diagnosis was told initially to their family.

"I didn't expect to hear abruptly that. I had MS. I was really shocked. The doctor didn't bother telling the name of my disease after giving me some preliminary introduction". (MS P21, man)

Participants believed that the MS specialists have the key role in the rehabilitation process. They should have enough knowledge and skills to diagnose the disease, treatment and rehabilitation at early stages. Incorrect diagnosis caused a wrong prescription and secondary side effects. For example:

"I had cramp in my leg and I couldn't raise it then I was referred to a practitioner. He told my father that it is muscular spasm and will be relieved by Piroxicam ointment…,my situation got worse every single day,… once my disease was diagnosed, I was walking with difficulty." (MS P14, man)

Moreover, lack of balance between the number of the patients and the specialists is said clearly by the patients such as 10th patient.

"The doctors try to help the patients but the number of patients and doctors isn't comparable…, Even, we don't have one social worker for a hundred patients. How can just one social worker can deal with all the patients' problems." (MS P10, woman)

The following quotation refers to the lack of teamwork as one of the main problems which participants believed is an essential prerequisite in the treatment process while the most of the patients have not experienced it during the treatment period.

"A doctor just recommends taking some medicine. Now, I realize that psychology and occupational therapy are important. Rehabilitation team doesn't make sense here and the doctor is the therapist." (MS P6, man)

Treatment administration
Medication adherence, trust in physicians and controversy on the efficacy of medicines are comprised in this category, all of them were important in continuity of treatment.

The patients did not follow the medical advice and prescribed treatment. For example:

"The examination fee is really expensive, so we referred to doctors less than before. I used to take my wife to physiotherapy clinics but soon after I gave it up as I couldn't afford it. The truth was that I had to spend all my income on my wife's medicine and I couldn't meet any more expenses. (FM1, husband)

Participants explained that most of the patients spent considerable time choosing the best physician which imposed high stress on them. According to the expert 3 changing the physician makes them tired.

It's so important that patients don't frequent different offices to make their companions tired. They must trust their practitioners and follow their treatment under their observation and this will prevent the occurrence of so many difficulties. (E3, man)

The following quotations show the controversy between the patients and physicians on the efficacy of medicines. Physicians believed that domestic medicine has a high quality while patients do not think so.

Domestic medicine is made with the same quality and under the same standards but the patients imagine that they aren't affective. (E3, man)

Iranian medicines aren't effective. …, when I have an Iranian injection, I get nauseous. I can't bear it. Doctors prescribe all these domestic medicines because people can't afford buying foreign medicine. (MS P1, woman)

Awareness level

This category includes three subcategories: Patients, Families information about disease and services and people's information about disease.

The participants explained that inadequate information about the disease and services are the origin of developed stress and anxiety. For example:

"I didn't know who to refer to. My mother constantly took me to different doctors.

I didn't know what Multiple Sclerosis is. One said "I have Apitherapy. Bee stings are so helpful for you". I was allergic to Apitherapy and as soon as I had it, I was in a coma for three days." (MS P11, man)

Unawareness of the families about the disease reduces their support. The participants explained that the families worried about the patient's conditions. When they have not enough information, they are confused and not able to navigate the challenges of the disease. In this regard MSP 21 said:

"Families don't know anything about the disease. They are worried what changes will happen. Will the patient become wheel-chair dependent in some years? All these factors cause worriedness. If they're informed well, I could be helped by them." (MS P21, man)

Modification

The modification includes two subcategories: transportation and environmental barriers.

Patients described that inadequate transportation facilities have been restricted and made them house-bound. For example:

"If I want to pay a visit to my uncle's house which isn't far, I must get on a vehicle with my wheelchair comfortably. Such a vehicle doesn't exist; therefore, I must call a taxi. Getting in and out of a taxi is so difficult for me, these limitations made me house-bound." (MS P5, man)

Environmental barriers such as unsuitable buildings and non-level pavements have limited the disabled patients from participating in social, occupational and recreational activities. For example:

Many patients used to be potent but they can't steer their wheelchairs. Physical barriers, unsuitable official buildings and their work place, the physical condition of streets pavements have restricted them. (E5, 43 years old, man)

Discussion

The results of 36 interviews showed four categories: Prerequisites for treatment and rehabilitation, Treatment administration, Awareness level and Modification. Some of the difficulties such as physician-patient relationship should be considered before the implementing of the rehabilitation process. This relationship includes respecting each other, spending enough time with patients and sensitive conversation especially in breaking bad news. Similar to the results of Golla et al, spending time with patients as a difficulty, was underlined by most patients[15]. Patients needed empathy from physicians but they did not receive it. Methley et al (2017) similarly have found that the lack of empathy, politeness, respect and active listening skills results in a negative interaction and this negativity challenges the patients' sense of personhood, devaluing them to a number and not taking them seriously.

MS is a complicated disease which leads to extensive unmet needs for the patients but according to our findings, there is a lack of competent MS specialists for appropriate diagnosis, managing and resolving these unmet needs. Moreover, the balance between the patients and the specialist's numbers is also important. The shortage of comprehensive rehabilitation centers and competent specialists were emphasized. Golla et al (2012) believe that the detailed knowledge about the disease nature increases the quality of treatment and the receiving of appropriate care [15].

Neurologists are the professions who diagnose MS but they usually don't refer patients to other professions to assess the other aspects of patients' problems [17]. Patients experience a complex situation thus appropriate care with holistic view is needed which a multidisciplinary team can provide [12, 16, 18]. According to the National MS Society (2015), the treatment goal is to promote comfort, function, independence, health and wellness which can be achieved by a comprehensive, coordinated care system. Unfortunately in our study opposed to the previous research [15] the participants expressed lack of adequate teamwork between the physician and other health care providers such as physical therapist, occupational therapist and social worker.

Poor adherence to treatment, especially during the first months of therapy because of no obvious disease symptoms and experience of relapse or financial distress was another difficulty. Decoo et al, has mentioned that the low quality of life, increased mortality and health care cost are the results of non-adherence. These findings are consistent with our results, where patients reported the increased symptoms, deteriorated health status and increased health cost as a result of non-adherence [19].

MS specialists can explain the importance of accepting and continuing treatment and can play an effective role in resolving the existing barriers if the patients trust them. Furthermore, patient's trust can improve patient-specialist interaction[20, 21]. Our findings showed that unilateral discontinuation of treatment and seeking another physician is the main consequence of lack of trust. Golla et al, have mentioned that lack of trust can hinder constant care[15]. Some other studies emphasized that a low level of trust in physicians is more likely reduce patient satisfaction, continuity of care and adherence to treatment[21].

The efficacy of foreign and domestic medicines is a controversial issue that has not been addressed within the previous studies. From the MS professionals' view the efficacy of domestic medicines is clinically more significant, but this is not confirmed by the patients who experience them. This controversy can raise patients' doubts about the effectiveness of medicines and arbitrarily make decisions to change their medicine.

Our study also highlighted a lack of information about MS disease, its complications and effects on the attitude of people [22]. It also affects patients and families' mental health, stress, anxiety and related decision–making. Understanding the nature of the disease helps the patients and their families to cope much better with it and also in adopting effective interventions [16] and increased empowerment of patients and their family [23].

Methley concluded that the patients who have enough awareness of primary health care services can select the better available care[14].

Another disadvantage of the lack of adequate information about the disease is bad behavior toward the patients such as mocking them, looking compassionately or stigmatizing them as a drunken person. In the long term, unpleasant reactions will cause exclusion of patients and have them stay at home and hide themselves.

The lack of accessibility to environment and appropriate transport facilities, especially for patients with functional limitations, are some of the major barriers. The lack of ramp, elevator and stair-lift, not only restricts their activities but also diminishes their relative's interaction. Existence of accessibility features can decrease the risk of falling and injury, and no participation in social, occupational and recreational activities[24]. Borreani et al, mentioned transportation has a main role in the daily life of patients[10] but handicap transportation and accommodated vehicles are very limited in Iran. So this limitation has effects on the treatment continuity and environment.

Linmitation

Inability of the patients' family to leave the patients alone at home to participate in the interview was a limitation. Generalizability of the results to all Iranian MS patients is another limitation of the study.
Obtaining data directly from patients, their families and specialists was the strong point of this study.

Conclusion

Professionals, patients and their family's perspective are essential to gain a comprehensive view on Patients' unmet needs. It seems that improving public awareness and information about MS disease is an effective way in decreasing patients and their family's stress. It seems that team work approach will facilitate the understanding of the barriers faced by patients.

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Evaluation of body mass index, abdominal fat and prevalence of hypertension among people 20 to 65 of Sabzevar city, Iran 2016

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Abstract

Introduction: The prevalence of obesity has been rapidly increasing in recent years and is considered as the main nutritional-health problem in developing and developed countries. Obesity increases the risk of many diseases, such as diabetes, hypertension, stroke, cardiovascular disease and cancers (1). Inappropriate diet and lack of physical activity are main causes of overweight and obesity which predisposes non-communicable diseases such as HTN (hypertension) (2). Previous studies revealed that both total body fat and central fat distribution are closely related to hypertension (3). The objective of this study is to evaluate the status of obesity, body fat distribution, and blood pressure in people aged from 20 to 65 years old living in Sabzevar.

Method: This is a descriptive-analytic study conducted in Sabzevar, Khorasan Razavi (with a population of 320,000). The target population was people aged from 20 to 65 years old who were randomly selected through cluster sampling. 1,500 citizens (744 men and 708 women) participated in the study. Data was collected throughout the city with collaboration of selected and trained health volunteers. They measured systolic and diastolic blood pressure, waist and hip circumference, height, and weight.

Results: Most samples with systolic blood pressure less than 13.99 had a normal body mass index (564 samples). The results of ANOVA showed that there was a significant difference in BMI between two groups of high and low systolic blood pressure (significant level was 0.35 which is less than 0.05). In addition, the systolic blood pressure was higher in the group with BMI>11.88 (with age over 30) than other groups. Most samples (899 samples) with systolic blood pressure less than 13.99 had normal abdominal fat.

There was a significant difference in WHR index between the two groups of high and low systolic blood pressure (significant level was 0.001 and less than 0.05) and systolic blood pressure was higher in the group with high abdominal fat (11.86).

Discussions and Conclusions: According to the findings of this study, abdominal fat and weight should be reduced to prevent hypertension. Thus, the public educational planning is needed to consider programs for weight loss and reduction in fat intake. People with high blood pressure have more abdominal fat, and most people in Sabzevar are overweight and prone to hypertension.

Key words: hypertension, body mass index, abdominal fat, prevalence

Introduction

The prevalence of obesity is closely associated with increasing hypertension. Both disorders are main risk factors for cardiovascular disease. About 2 billion people in the world are overweight or obese (5). In 2014, more than 1.9 billion people aged 18 and over were overweight, while 600 million were obese. About 13% of adults in the world (11% of men and 5% of women) were obese in 2014. In the same year, 19% of adults aged 18 years and over (38% of men and 40% of women) were overweight. The prevalence of obesity in the world has doubled since 1980. Although obesity and overweight are the health problems of high-income countries, they are also rapidly expanding in middle and lower income countries (especially in urban areas). The rate of overweight and obesity in children living in economically-developing countries (categorized as low and middle income countries based on The World Bank) is 30% higher than those living in developed countries. Obesity and overweight are more associated with death than underweight. The majority of the world's population live in countries where obesity and overweight (and not underweight) kill people (6).

Obesity and overweight are the fifth cause of death in the world. At least 2.8 million adults each year die from complications of obesity and overweight. In addition, 44% of the burden of diabetes, 23% of the burden of ischemic heart disease, and about 7 to 41% of the burden of cancer is due to obesity and overweight (7).

An increase in BMI is the main risk factor for non-communicable diseases such as:
- Cardiovascular disease (especially heart attack), the most common cause of death in 2012.
- Musculoskeletal disorders (especially osteoarthritis, debilitating and degenerative diseases)
- Some cancers (endometrium, chest and colon)
- Hypertension (HTN), known as the main risk for cardiovascular disease in the world, accounting for half of coronary artery disease and about two thirds of cerebrovascular disease (4).

The objective of this study was to evaluate the status of obesity, body fat distribution, and blood pressure in people aged from 20 to 65 years old living in Sabzevar.

Method

This is a descriptive-analytic study conducted in Sabzevar, Khorasan Razavi (with a population of 320,000). The target population was people aged from 20 to 65 years old who were randomly selected through cluster sampling. 1,500 citizens (744 men and 708 women) participated in the study. They were selected with collaboration of active and experienced health volunteers working at health centers in Sabzevar. Volunteers were selected among those who had enough health information in identifying risk factors and preventing chronic diseases. They helped the author in identifying samples and gathering information. A total of 40 health volunteers participated in this study.

First, the number of samples were determined for each center. Then, volunteers visited the target cases in person and asked them if they would like to participate in the research project while noting that their information would be kept confidential. They finally gathered the information of all family members aged between 20 to 65 years old and who qualified through in person interviews.

Prior to starting this, health volunteers participated in training courses for 6 sessions (each session for 2 hours) held in the health department to enhance communication skills, learn how to monitor the completion of the questionnaire, how to measure blood pressure, height, weight, waist and hip circumference. These courses were taught by the researcher through lectures, role play and group discussions. Their ability was ultimately ensured.

The questionnaire was completed by citizens;, the blood pressure (using Beurer blood monitor) and then the body mass index (BMI) and waist to hip ratio (WHR) were measured. (The WHO regards a BMI of less than 18.5 as underweight, 18.5 to 24.9 as normal, 25 to 29.9 as overweight and more than 30 as obese).

Body mass index (BMI) was calculated as the weight (Kg) divided by square of the height (m2), and waist to hip ratio (WHR) as waist circumference (cm) divided by hip circumference (cm). BMI and WHR were evaluated based on the standard defined by WHO: BMI between 25.9 to 29.9 and more than 30 were regarded as overweight and abdominal obesity, respectively. The Content Validity of the Food Habitat Questionnaire was approved by professors and nutritionists. Cronbach's alpha coefficient was used to determine the internal consistency.

To measure blood pressure, people were asked to sit in a comfortable position and after a 5-minute rest, the blood pressure was measured twice by a digital monitor (with a two-minute lag) in the right arm. High blood pressure is defined as a blood pressure higher than 140 mmHg and diastolic blood pressure higher than 90 mmHg, according to the Ministry of Health and Medical Education. Measuring and recording the blood pressure was repeated after 5 minutes by the volunteers (8)

Anthropometric measurements and blood pressure: the weight was measured with a light set of clothes and no shoes using a digital scale (Swca840) and height using a tape meter measuring 0.1 cm. The hip circumference was measured at the widest part of the buttocks and waist circumference between the lower ribs and the ischial ridge at the level of the umbilicus at the end of a normal expiration by a tape meter. Blood pressure was measured after a minimum 5 minutes rest in a sitting position by a digital blood monitor (Beurer). Waist to hip ratio (WHR) and BMI were then calculated.

The most common method for determining obesity is to calculate BMI according to which a BMI of less than 25 is regarded as normal, 25.1 to 29.9 as overweight and over 30 as obese.Data collected from 1,452 samples was first saved in a computer and then analyzed using SPSS software. Data was analyzed based on independent and paired samples t-test, covariance analysis, and logistic regression.

This research was approved by the Ethics Committees of Medical Sciences in University of Hamedan and University of Sabzevar and has received the Code of Ethics. This study was financed by the two mentioned universities. The university ethics code number is IR.UMSHA. REC.1394.217.

Results

The mean age of the participants was 36.83 ± 10.53. The results of other demographic variables are listed in Table 1.

Table 1: Number and percentage of demographic variables

Percentage	Number		Variable
51.2	744	Male	Sex
48.8	708	Female	
17.9	258		Age
43.8	630		
25.9	373		
10.8	155		
1.6	23	Above 60	
3.4	50	Illiterate	Education
18.5	268	Elementary School	
15.6	227	Junior High	
34.0	494	Diploma	
17.1	248	Associate Degree	
11.4	165	Masters	
7.3	106	Single	Marital status
90.4	1311	Married	
1.4	20	Divorced	
1.0	14	Widow	
17.7	257	Employee	Occupation
20.3	295	Self-Employed	
20.5	297	Manual worker	
30.9	448	Housewife	
2.5	36	Retired	
5.3	77	Student	
2.9	42	Jobless	
100	1452		Total

According to the findings of this study, 744 (51.2%) of samples were male and 708 (48.8%) were female. Most of samples (630, 43.4%) were in the age group of 28-38 years old and 13 (0.9%) samples did not report their age. Most samples (1,311, 90.3%) were married. And most of the people under study (448, 30.9%) were housewife.

To investigate the correlation between systolic and diastolic blood pressure with BMI, one-way analysis of variance (ANOVA) was employed and the results are presented in Table 2.

Table 2: Analysis of the correlation between blood pressure and BMI

Test results	Diastolic blood pressure			Test results	Systolic blood pressure			Hypertension BMI index
	Average	≥8.99	<8.99		Average	≥13.99	<13.99	
		Number (percent)	Number (percent)			Number (percent)	Number (percent)	
F=1.196 P=0.310	7.55	15(15%)	86(85%)	F=2.873 P=0.035	11.51	1(1%)	100(99%)	15-18.49 (underweight)
	7.68	115(19%)	500(81%)		11.59	51(8%)	564(92%)	18.5-24.99 (normal)
	7.70	83(18%)	388(82%)		11.76	55(12%)	416(88%)	25-29.99 (overweight)
	7.82	63(24%)	202(76%)		11.88	39(15%)	226(85%)	Over 30 (obese)
	7.71	276(19%)	1176(81%)		11.68	146(10%)	1306(90%)	Total

As shown in Table 2 (blood pressure related to the BMI), a great percentage of population had a systolic blood pressure than 13.99 (90%) and most of them had a normal body mass index (564 people). Also, 81% of the population had a diastolic blood pressure less than 8.99%. Most of the population with blood pressure less than 8.99 (500) and more than 8.99 (115) had a normal body mass index. As seen in Table 2, the ANOVA results revealed that there is a significant difference in BMI between two groups of high and low systolic blood pressure (significance level was 0.35 which is less than 0.05), and systolic blood pressure is highest in the group with BMI over 30 years (11.88). Comparing diastolic blood pressure, the results of ANOVA showed that there is no significant difference in BMI between two groups of high and low diastolic blood pressure and the four groups with different BMI were homogeneous for diastolic blood pressure (P = 0.854).

Table 3: Analysis of the correlation between blood pressure and BMI

Test result	Diastolic blood pressure				Test Results	Systolic blood pressure			
	Average	Over 11	8-11	Under 8		Average	Over 14	12-14	Under 12
		Number (percent)	Number (percent)	Number (percent)			Number (percent)	Number (percent)	Number (percent)
F=4.203 P= 0/006	7.23	0	21(2/29)	51(8/70)	F=2.557 P= 0.054	11.45	1(4/1)	18(0/25)	53(6/73)
	7.63	2(3/0)	216(1/34)	416(8/44)		11.77	39(2/6)	198(2/31)	397(6/62)
	7.75	4(8/0)	180(2/38)	287(9/60)		11.65	22(6/25)	134(5/28)	315(9/66)
	7.67	2(8/0)	86(8/32)	174(4/66)		11.87	24(2/9)	70(7/26)	168(1/64)
	7.66	8(6/0)	503(0/35)	928(5/64)		11.73	86(0/6)	420(2/29)	933(8/64)

As shown in Table 3 (blood pressure related to the BMI), a great percentage of the population had a systolic blood pressure less than 12 (64.8%) and most of them had a normal body mass index (397). Also, 29.2% of the population had a diastolic blood pressure between 12 and 14, and most of them (198) had a normal BMI. As seen in Table 2, the ANOVA results revealed that there is no significant difference in BMI between different groups of systolic blood pressure (significant level was 0.054 which is more than 0.05). A greater percentage of the population had a diastolic blood pressure less than 8 (64.5%) and most of them had a normal body mass index (416). Also, 35% of population had a diastolic blood pressure between 8 and 11, and most of them (216) had a normal BMI. As seen in Table 2, the ANOVA results revealed that there is 1 significant difference in BMI between different groups of systolic blood pressure (significance level was 0.006 which is less than 0.05).

To examine the correlation between systolic and diastolic blood pressure with WHR (waist to hip ratio or abdominal fat), independent 2-sample t-test was used and the results are shown in Table 4.

Table 4: Analysis of the correlation between blood pressure and WHR

Test Results	Diastolic blood pressure			Test Results	Systolic blood pressure		
	Average	≥8.99	<8.99		Average	≥13.99	<13.99
		Number (percent)	Number (percent)			Number (percent)	Number (percent)
T= -3.007 P=0.003	7.65	180(18%)	815(82%)	T= -3.381 P= 0/001	11.60	96(10%)	899(90%)
	7.85	96(21%)	361(79%)		11.86	50(11%)	407(89%)
	7.71	276(19%)	1176(81%)		11.68	146(10%)	1306(90%)

As shown in Table 4 (blood pressure related to abdominal fat), a great percentage of the population had a systolic blood pressure less than 13.99 (90%) and most of them had a normal body mass index (899). Also, 81% of the population had a diastolic blood pressure less than 8.99, and most of those with diastolic blood pressure less than 8.99 (815) and more than 8.99 (180) had a normal BMI. As seen in Table 4, the test (independent 2-sample t-test) results revealed that there is a significant difference in WHR between groups of high and low systolic blood pressure (significance level was 0.001 which is less than 0.05), and systolic blood pressure is highest in the group with BMI over 30 years (11.88). Comparing diastolic blood pressure, the results of t-test showed that there is a significant difference in WHR between two groups of high and low diastolic blood pressure and again, people with high abdominal fat had a higher mean blood pressure (7.85, p=0.003).

For the status of the population in terms of non-behavioral risk factors classified by age, Chi-square test was employed to evaluate abdominal fat (waist to hip ratio) by age in the two sexes. The difference in abundance of abdominal fat by age group was significant in both sexes. In the female group, most of population in the age group over 50 had an inappropriate level of abdominal fat. In addition, most women aged 39-49 years and over 60 years had an inappropriate level of abdominal fat.

Discussion

According to the results obtained in this study, the BMI index was significantly different in both high and low systolic blood pressure groups, which is consistent with the results of Chuang SY, stating that in all ranges of BMI, there is hypertension, but with an increase in the BMI, the possibility of hypertension also increases (9). Almost all studies showed that as weight of the general population decreases, the systolic blood pressure also decreases, even if the weight reduction is low (10). In this study, most of the population with a systolic blood pressure of less than 13.99 had a normal body mass index, and this finding is consistent with the results of the Winkelmayer study. In this study, a unit increase in body mass index (1 kg /m2) led to an 8% increase in risk of hypertension, and it was also stated that more than 75% of patients with high blood pressure had a BMI of more than 25 (11).

The results showed that the systolic blood pressure is higher in the group with high abdominal fat, as revealed by Niazi et al. who reported that abdominal obesity and its rate of increase, independent of the effect of general obesity, would lead to future high blood pressure (12). There is a significant difference in WHR index between the two groups of high and low systolic blood pressure, which is consistent with Fatahi et al. (2011). In this case a study, titled "The relationship between high blood pressure and body mass index, abdominal obesity and dietary habits" was conducted on 270 people aged from 25 to 65 years old. The results showed that there is a significant correlation between high blood pressure and factors such as carbonated-drinks consumption, abdominal obesity, and body mass index. There was a negative correlation between the consumption of wholegrain bread and having breakfast, with high blood pressure (13). In another study on high blood pressure in people with abdominal obesity, it was found that important factors in preventing hypertension are controlling abdominal obesity and waist circumference (11). Epidemiologic studies on obesity and blood pressure also showed that obese men and women are 3 times more prone to hypertension than men and women with a normal body mass index (14). Jonas et al. believed that age and BMI are associated with hypertension (15). Lee et al. (2010) conducted a study to assess the prevalence, awareness, treatment and control of hypertension and its associated risk factors. Awareness, treatment, and control were 60.1%, 91.7%, and 27.2%, respectively. Low BMI was associated with blood pressure control. In high-BMI women with a family history of diabetes, there was a direct relationship with awareness and treatment (16). Thawornchaisit et al. (2013) pointed out that hypertension is a major risk factor for heart attack and brain stroke, and cross-sectional studies revealed the increasing rate. Accordingly, a prospective study was conducted over a 4-year period (2005-2009) with the aim of identifying a number of risk factors for health behavior and lifestyle affecting the prevalence of chronic kidney

disease. Ebrahimi et al. (2010) conducted a study aimed to evaluate the prevalence of hypertension, treatment and control of social demographic factors through the National Monitoring Plan on Risk Factors for Non-communicable Disease In 2006 on a 29,972 sample population in the age group of 15-64 years old. About 45% of the population were overweight or obese, and 3.48% reported diabetes. About half of the population had high physical activity and about 11% were smokers. The prevalence of hypertension in Iranian population aged 15 to 64 was 17.37% and 33.35% of those with hypertension, received treatment (18).

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Comparison of the Effects of Alfentanil and Remifentanil on QT Interval Following Local Epinephrine Infiltration in Septoplasty Under General Anesthesia

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Abstract

Background and Objectives: Corrected QT interval (QTc) prolongation can lead to life threatening arrhythmias. Previous studies denote that many anesthetic drugs and catecholamine release due to endotracheal intubation and surgery could induce QTc prolongation .Short acting opioids such as alfentanil and remifentanil are supposed to reduce the catecholamine release and to prevent QTc prolongation. The objective of this study was to compare the effect of alfentanil and remifentanil on QT interval in patients under general anesthesia following local nasal submucosal epinephrine infiltration during septoplasty.

Materials and Methods: As a double blind study, 84 patients aged 18-50 years old with American Society of Anesthesiologist physical status I and II (ASA PS I&II) scheduled for septoplasty and planned to receive local epinephrine injection under general anesthesia were randomly allocated in to two groups; Alfentanil (A) and Remifentanil (R). Patients in group A, received alfentanil 25-50 g/kg before induction followed by 0.5-2 g/kg/min infusion during maintenance of anesthesia. Group R, received remifentanil 1-2 g/kg before induction followed by 0.2-0.25 g/kg/min infusion through maintenance of anesthesia. Other anesthetics were similar in both groups. Hemodynamic parameters and corrected QT interval were recorded at baseline (T1), 3 minutes after induction (T2), following endotracheal intubation (T3), post epinephrine infiltration (T4),3-5 and also 20 minutes later (T5 &T6).

Results: Our study showed that there was no significant difference in blood pressure changes between group A and R. Heart rate was significantly lower in group R. Development of QTc interval prolongation (QTc>450 milliseconds) occurred in both groups, but shorter QTc interval was prominent in group R at two time-points; post-intubation and 3-5 minutes after epinephrine infiltration .

Conclusion: Neither alfentanil nor remifentanil could completely prevent QTc prolongation, following catecholamine surge in anesthetized patients, although remifentanil is more potent in this regard.

Key words: general anesthesia, alfentanil, remifentanil, QT prolongation

Background and Objectives

Prolongation of QTc interval is associated with life-threatening dysrrhythmia as such as polymorphic ventricular tachycardia (torsade de points), ventricular fibrillation, asystole and sudden cardiac death (1-4) .

It is known that most of volatile and intravenous anesthetics can influence the QTc interval. Many studies have investigated their effects. However it is difficult to determine the exact effect of a single anesthetic agent due to multiplicity of drugs used during anesthesia. For example, in spite of much research , there is controversy about the effect of propofol on QTc interval (2, 5-7).

Short acting potent opioids such as alfentanil and remifentanil which are strong receptor agonists can attenuate the stress induced by intubation and surgery and correlated sympathetic over-activity which is able to induce QTc prolongation (1, 8-13). On the other hand, it is shown that local injection of epinephrine which is a sympathomimetic drug (catecholamine) is able to induce 'torsade de points' in patients with long QT syndrome during surgery (14-16). Although, in a single study ,it was reported to shorten QTc interval (17).

Since there has been no previous study comparing the effect of alfentanil with remifentanil on QTc interval under general anesthesia following local infiltration of epinephrine, we decided to elucidate this issue.

Methods

This clinical trial was approved by research and ethics committee of Shiraz University of Medical Science (No. CT-P-92-6118) and registered in national clinical trial system (registration No.: IRCT2014020816524N1).

Informed consent was taken from participants. This prospective double blind randomized study enlisted 82 patients with American Society of Anesthesiology, physical Status I and II (ASA-PS: I&II), 18 to 50 years old who were scheduled for septoplasty in Shahid Dastghib Hospital (a university affiliated referral hospital of Shiraz, south-west of Iran). All surgery was performed between 08:00 - 12:00 AM to minimize the influence of circadian variation in cardiac autonomic nervous system activity.

Patients were excluded from the study if any of the following criteria were met:

1) Use of any drug affecting QT interval in last 14 days including: tricyclic antidepressants (TCAs), anti-arrhythmic drugs, blockers and calcium channel blockers
2) Idiopathic or acquired QTc prolongation >450 msin preoperative electrocardiogram(ECG)
3) Any electrical conduction abnormality (e.g. bundle branch block, pr-eexcitation syndrome or AV nodal arrhythmia)
4) Any baseline arrhythmia
5) Structural heart disease
6) Electrolyte disturbance

7) Hypo or hyperthyroidism
8) Obesity with BMI >30
9) Diabetic neuropathy
10) Allergy to propofol, egg or soya bean
11) Intra operative administration of blockers or volatile anesthetics to reduce surgical site bleeding

Patients were randomly allocated into two groups, alfentanil (A) and remifentanil (R) based on a computer-generated sequence of numbers.

Standard monitoring including heart rate (HR), non-invasive systolic, diastolic and mean arterial pressure monitoring and pulse oxymetry were established.

Upon arrival to the operating theater, a preoperative 12-lead standard ECG and a baseline recording of study parameters were recorded (T1). All patients received 5-7 cc/kg saline, before midazolam (0.03 mg/kg) and morphine (0.1 mg/kg) as premedication. This was followed by alfentanil 25-50 g/kg or remifentanil 1-2 g/kg in group A or R. Induction was induced by sodium thiopental 4 mg/kg and muscle relaxation by atracurium, 0.6 mg/kg. Three minutes later (T2) and just after endotracheal intubation (T3), data collection was done.

Then, propofol was administered at 100   g/kg/min associated with infusion of alfentanil (0.5-2 g/kg/min) in group A and remifentanil (0.2-0.25 g/kg/min) in group R. A and R solutions were prepared in equal volumes by a nurse and were given to resident of anesthesia who was unaware of the type of opioid. Anesthesia nurse who recorded the parameters was also not aware of the type of opioid infusion.

After prep and drape 20 cc of epinephrine (1/100000 dilution) plus lidocaine (1.5%) was infiltrated at the site of surgery by surgeon.

The 4th,5th and 6th data collection were just after epinephrine infiltration, 3-5 and also 20 minutes later. (T4,T5,T6).QT interval in lead II of ECG were calculated manually and corrected according to Bazett's formula (QTc=) by resident of anesthesia who was not aware of study group.

Data were analyzed by SPSS 19 software and expressed as mean ± standard deviation (SD). Demographic data were also analyzed by the chi-square or ANOVA tests. Inter-group comparison was done by repeated–measures ANOVA and a p-value of <0.05 was considered to be statistically significant. A sample size of 36 patients per group needed with 80% power (α=0.05).

Results

84 patients were assigned to this study, from which 12 were excluded according to exclusion criteria. (Figure 1) Patients in both groups had similar demographic characteristics (that is age and sex). (Table 1)

Figure 1: patients' flow diagram
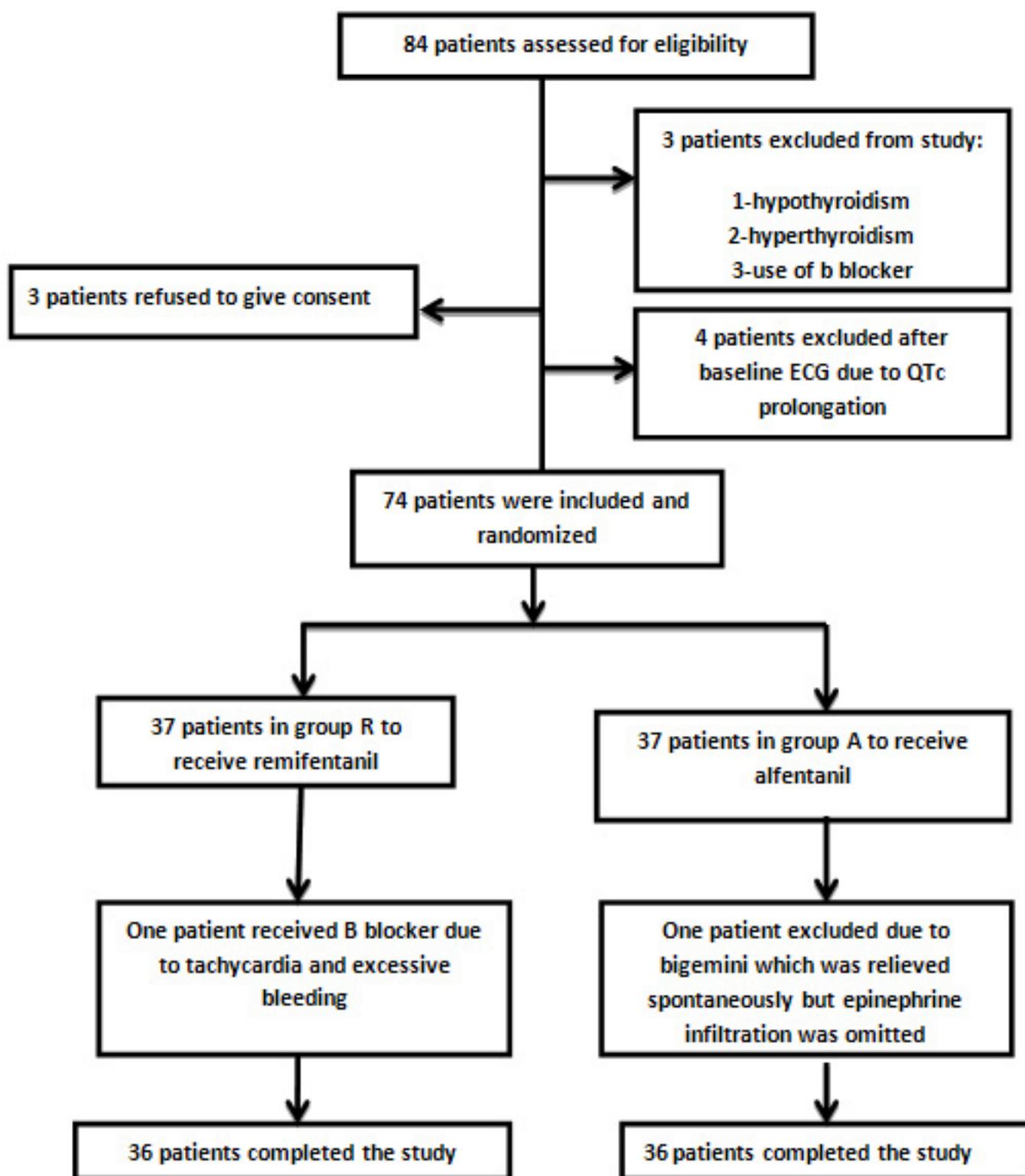
Table 1: Demographic data of the patients in group A (alfentanil) and R (remifentanil)

	Group A	Group R	P Value
Sex (M/F)	18/18	19/17	
Age	27(6.7)	25(7.4)	0.577

Values for age are mean (SD)

There was no statistically significant difference in baseline hemodynamic variables. During the course of study, although trend of changes in systolic, diastolic and mean arterial pressure (MAP) were alike in both groups (p>0.05), heart rates were much lower in group R (p=0.017). (Figure 2)

Figure 2: HR changes during the study
(1:baseline ECG , 2:three minutes after induction of anesthesia, 3:post laryngoscopy and intubation, 4:after epinephrine infiltration , 5&6:three to five and twenty minutes after epinephrine infiltration)
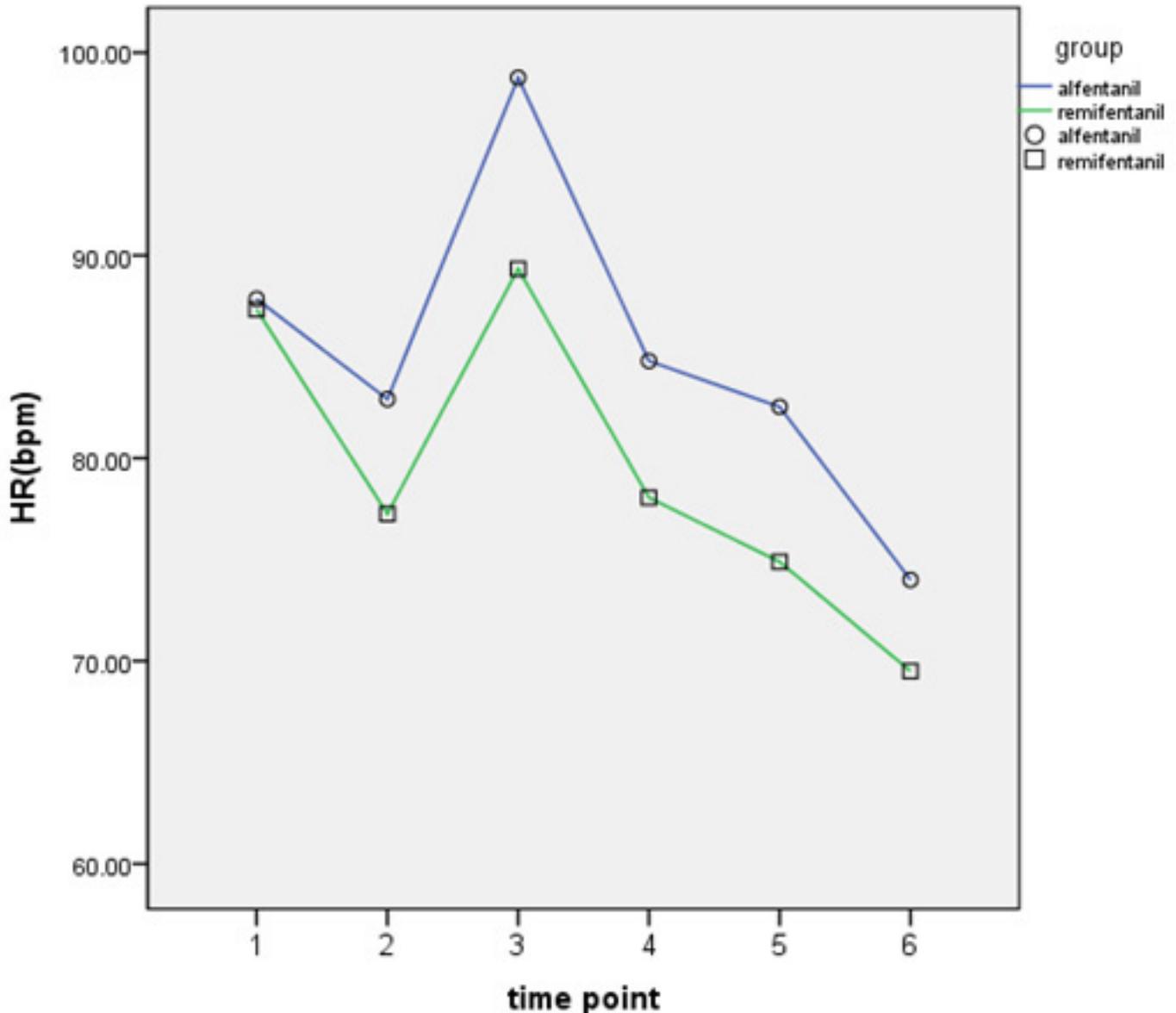
Regarding QTc interval, it was similarly prolonged in both groups (p>0.05). If we consider QTc to be prolonged when it is more than 450 milliseconds, many patients had QTc lengthening from 2nd to 6th time points in both groups.

Meanwhile, more patients with QTc prolongation were in group A at 3rd (immediately after intubation) and 5th (3-5 minutes after epinephrine injection) time points. (P values respectively 0.001 and 0.002) Table 2 and Figure 3.

Table 2: mean QTc interval at six time points (SD).(data in milliseconds)

Time of record	QTc in Alfentanil group	QTc in Remifentanil group	P value
T1	418(24)	411(29)	>0.05
T2	449(37)	443(39)	>0.05
T3	483(50)	440(39)	0.004
T4	444(33)	438(38)	>0.05
T5	461(30)	424(34)	0.004
T6	439(30)	421(35)	>0.05

Table 3: percent of patients with QTc>450 milliseconds (ms) at six time points

	A group>450 ms	R group>450 ms	P value
T1	0%	0%	>0.05
T2	30.6%	47.2%	>0.05
T3	69.4%	27.8%	<0.05
T4	36.1%	36.1%	>0.05
T5	61.1%	25%	<0.05
T6	32.4%	19.4%	>0.05

Figure 3: QTc interval at six different time points in alfentanil and remifentanil groups
(1:baseline ECG, 2:three minutes after induction of anesthesia, 3:post laryngoscopy and intubation, 4:after epinephrine infiltration, 5&6:three to five and twenty minutes after epinephrine infiltration)
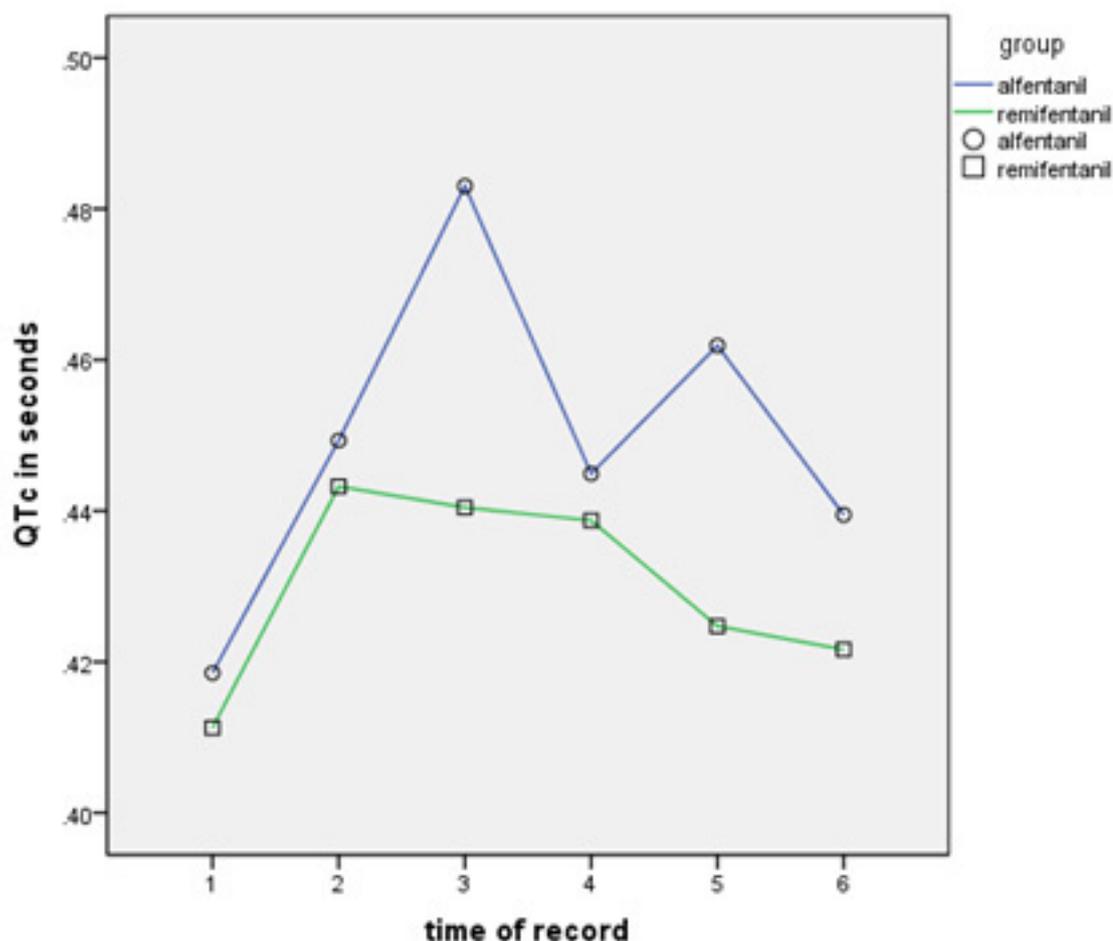
Discussion

The purpose of this study was to compare the effect of A and R on attenuation of prolongation of QTc interval following catecholamine surge (both endogenous and exogenous sources) in patients under general anesthesia.

Previous studies showed that R is capable of depressing sinus node function and so attenuating QTc prolongation during anesthetic induction when used in bolus doses (5) (6) (15). Korpinen et al. and Lindgren et al. showed A could prevent prolongation of QTc interval during induction of anesthesia but there is still some controversy. (8) (9)

Our study showed that, neither A nor R (at prescribed doses) is potent enough to prevent QTc prolongation following endogenous catecholamine release or administration of epinephrine, although no life threatening arrhythmia occurred in each group. It differs considerably from that of Dogan et al. who found that R shortened QTc interval, and those of Kim et al. and Kweon et al. who found that R prevented QTc prolongation. It also differs from findings of Lindgren et al. and Korpinen et al. that A prevented QTc>450 ms after endotracheal intubation (1) (18) (19).

These controversies may arise from different baseline QTc intervals of patients in these studies .Other disturbing factors may include administration of sodium thiopental or propofol infusion during anesthesia; Denoted in both Harvey and Lindgren et al. studies that sodium thiopental can prolong the QTc interval through inhibition of turnover of dopamine and noradrenaline in central nervous system

(8) (20). And in Saarvina et al. and Kim et al. that propofol increases QTc interval (21) (22). The effect of sodium thiopental and propofol could not disturb the result of our study, because both groups (A& R) received the same doses.

Statistically, there was no significant difference between R and A on QTc interval, but some noticeable points need consideration. After laryngoscopy and intubation (T3), QTc interval is shorter in R than in A group (p=0.004). The same happened again 3-5 minutes after local infiltration of epinephrine (T5) (p=0.004). This may be the result of epinephrine surge in blood. In other words, prolongation of QTc interval is more prominent in group A than R at two time points, T3 and T5.

Laryngoscopy and intubation can induce a surge in plasma catecholamine concentration (23). This raise may be associated with QTc prolongation and cardiac arrhythmias. Besides, exogenous catecholamine causes QTc prolongation and U wave amplification even in normal subject (15).

Although various opioids have been used to abolish catecholamine related hemodynamic response to tracheal intubation, ambiguity exists about the efficacy of remifentanil in preventing QTc prolongation and even more about alfentanil (8) (9).

Moreover multiple studies have shown that, the proposed effect of remifentanil on QTc interval is dose dependent (18, 19, 24).

We didn't find any study regarding the effect of injection of epinephrine on QTc interval in subjects receiving remifentanil or alfentanil.

Trend of changes in systolic, diastolic and mean arterial pressure were similar in both A and R groups. Alfentanil was less effective than remifentanil in attenuation of heart rate responses following endotracheal intubation. Previous studies denote controversy about the effect of A or R on suppressing hemodynamic responses following endotracheal intubation (8) (9).

This study has some limitations. First, although the most popular formula to correct QTc interval regarding HR is Bazett's formula, this method is known to overcorrect the QTc interval for fast HRs and under-correct it for slow HRs. Therefore, estimation of the QTc interval with this formula could lead to a false diagnosis of prolonged QTc interval in patients with increased HR (25). This may have disturbed calculation of exact QTc interval in our study.

Secondly, it was performed on a specified subgroup; Healthy young and middle aged patients without any cardiac disorder, and it limits the external validity of our study.

Thirdly, exogenous epinephrine was mixed with lidocaine before local infiltration which may have influenced changes in QTc interval.

Fourthly, the probable effect of other anesthetic drugs, alone or in combination should be considered. We didn't measure the serum concentration of alfentanil, remifentanil and catecholamine.

Conclusion

Neither remifentanil nor alfentanil (at prescribed doses) could completely prevent QTc prolongation following catecholamine surge in patients under general anesthesia. Remifentanil is more potent in this regard.

Acknowledgment

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Comparison of the wrist acupuncture point P6 with pharmacological management to prevent postoperative nausea and vomiting in patient's under laparotomy: a double blind study

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Abstract

Background and Aims: Acupuncture as an available alternative medicine could be effective for some problems such as postoperative nausea and vomiting (PONV).

In high risk patients, the incidence of PONV has been even reported as 70% leading to prolonged hospital stay and need for preventive pharmacologic medication.

We aimed to assess effectiveness of this method, in comparison to common medications, to prevent PONV in these patients.

Methods: This was a randomized double-blinded prospective clinical trial study. 100 scheduled patients who were candidates for elective laparotomy were randomly assigned into two groups: control group (pharmacological) receiving metoclopramide in combination with dexamethasone and acupuncture group receiving P6 acupuncture bilaterally.

Results: The overall prevalence of PONV in the acupuncture group was 4% and in the control group was 2% without significant difference (p = 0.588). In the multivariate regression model and with the presence of baseline variables including gender, type of anesthetic agents, operation time, and recovery time were recorded.

No difference was detected between the prevalence of PONV between acupuncture and pharmacological combination therapy groups (OR = 1.679, 95%CI: 0.122 – 23.076, P = 0.698). Common complications such as tachycardia, local pain, or skin allergy were not detected in any of the study groups.

Conclusion: Single insertion of acupuncture needle could have similar effectiveness on preventing PONV as the pharmacologic combination of metoclopramide and dexamethasone, however due to the side effects of multi medications especially drugs that are used for general anesthesia, the use of acupuncture could be preferred.

Key words: acupuncture, laparotomy, PONV

Introduction

Despite visible progression in prevention and control of postoperative nausea and vomiting (PONV), the overall prevalence of this complication has remained high (1,2).

In high-risk patients, the incidence of PONV has even been reported as 70% (2) leading to prolonged hospital stay and requiring hospitalization in intensive care units as well as a high cost burden. Also, PONV is considered to be a postoperative unfavorable event resulting in high patient dissatisfaction especially in patients under laparotomy.

Regarding pathophysiology of PONV, stimulation and activation of four neural receptors including cholinergic, dopaminergic, histaminic, and serotonergic receptors has been revealed (3,4).

In this line, the main mechanisms of more applicable drugs for preventing PONV are based on affecting these receptors (5-7). Among these, high dose metoclopramide has been successfully used in managing chemotherapy-related nausea. However, because of its potential side effects, the use of a low dose of this drug has been more recommended, but without therapeutic effects in most previous studies (8). Besides, various alternative treatments such as acupuncture have been paid more attention, but with unknown cause of effects on PONV.

According to the importance of presenting a cost-benefit method with minimizing side effects for preventing PONV, the application of alternative methods such as acupuncture is now hopeful(9-14).

According to the advantages of acupuncture regarding its low cost and also low complications, we aimed to assess effectiveness of this method in comparison to common pharmacologic medications to prevent PONV in patients who are undergoing laparotomy.

Methods

In a randomized double-blinded clinical trial prospective study, 100 scheduled patients who were candidates for laparotomy during a one year period in our center were assigned in this study, after fulfilling the eligibility criteria and signing the informed consent.

Inclusion criteria include all patients who were candidates for elective laparotomy , aged between 18 and 70 years old, (ASA) physical status classification of I or II, undergoing general anesthesia, no history of PONV or motion sickness, no use of antiemetic 24 hours before surgery, willing to participate and who signed an informed consent form were eligible for this study

The main exclusion criteria were opium use, drug misuse or alcohol dependency, history of neurological or psychological disorders, the presence of local wound infection or scar at the site of acupuncture needle entry in wrist , age less than 18 years or more than 70 years, or existence of disorders with acute or chronic nausea or vomiting, or prolonged surgery longer than 2 hours,

nausea or vomiting 24 hours before surgery, pregnant or lactating women, recipients of chemotherapy or radiation therapy during the previous 7 days, and refusal to accept acupuncture.

Baseline characteristics including demographics, duration of surgery, length of recovery stay, type of anesthetics, presence of PONV during recovery time and method of preventing PONV, were recorded.

The included patients were randomly assigned according to computer-generated in balanced block randomization and an independent researcher randomly allocated the patients to either of the two study groups following induction of anesthesia.

The patients and investigator who was collecting the data were all blinded to the study groups, the control group (receiving metoclopramide in combination with dexamethasone) and the case group (receiving acupuncture).

In the case group, acupuncture was induced by entering a specific needle at P6 point anterior to wrist nearly 30 minutes before end of surgery.

P6 point was set on anterior to forearm at 2 cm of transverse 'carpal crease' between tendons of flexor carpi radialis and Palmaris lungus muscles.

For the acupuncture group, after skin cleaning with 75% alcohol swab, sterile and disposable stainless steel needles (0.25 × 25 mm, China) are quickly and perpendicularly inserted into the skin at P6 acupoints bilaterally to a depth of 10 mm. In this group, downward pressure and upward lifting combined with twirling the needle was used.

The needles were kept in place for 30 minutes and manipulated manually every 10 minutes to maintain the de qi sensation. When the treatment time was over, all needles were carefully taken out and the puncture sites covered with sterile swabs to avoid bleeding. The control groups received intravenous metoclopramide (10 mg) and dexamethasone (8 mg) after beginning surgery and also the same site of P6 was covered with sterile swabs for blinding.

The study period for each case was 24 hours after the surgery. A nurse researcher who was not involved in the patients management recorded anesthesia time, surgery time, endotracheal intubation time, patient demographics and preoperative data for each patient.

Demographic and preoperative data included: age, gender, race, weight, height, acupuncture experience, Smoking history.

Another blinded observer recorded the postoperative data, which included administration of a rescue antiemetic, patient satisfaction with PONV management, and episodes of vomiting or nausea at postoperative period.

During recovery time, the blinded researcher assessed the patients regarding PONV and side effects of used medications, after fulfilling the eligibility criteria and signing the informed consent.

Nausea is a subjective sensation which should be evaluated by the patient, not by the observer. Thus, the observer requested the patients to evaluate their nausea score using a standard visual analogue scale (VAS) (0, no nausea at all; 10, worst imaginable nausea). Vomiting, which is defined as the ejection of contents of the stomach through the mouth, was reported by the patients and assessed by the blinded observer.

Data were analyzed by the statistical software SPSS version 20 for windows (SPSS Inc, Chicago IL). Quantitative variables were presented as mean standard deviation, and categorical variables were presented by absolute frequencies and percentages. Continuous variables were compared using t test. Whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the group, Mann-Whitney U test was used. Categorical variables were compared using chi-square test. Fisher exact test was used when more than 20% of cells with expected count of less than 5 had been observed. The multivariate logistic regression analysis was used to assess difference in response rate between the two treatment methods with the presence of baseline characteristics. P values of ≤ 0.05 were considered statistically significant.

Results

In this study, 50 patients were treated with acupuncture and 50 with combination pharmacological drug therapy including metoclopramide and dexamethasone. There was no difference in male distribution between the two groups (32% versus 26%, p = 0.509).

Regarding anesthesia protocol, in the acupuncture group, 56% received propofol and 44% received nesdonal, while in the other group, 36% received propofol and 64% were anesthetized using nesdonal (p = 0.45). The mean of operation time in the acupuncture group was 85.50 ± 4.87 minutes and in the control group was 85.00 ± 4.04 minutes with no significant difference (p = 0.578).

Also, mean of recovery time was not different between acupuncture and control groups (19.30 ± 1.75 minutes and 19.1± 1.94 minutes (p = 0.890).

The overall prevalence of PONV in the acupuncture group was 4% and in the control group was 2% without significant difference (p = 0.588).

In the multivariate regression model and with the presence of baseline variables including gender, type of anesthetic agents, operation time, and recovery time, no difference was found between the prevalence of PONV between acupuncture and drug combination therapy groups (OR = 1.679, 95%CI: 0.122 – 23.076, P = 0.698). Common complications such as Tachycardia, local pain, or skin allergy were not detected in any of the study groups.

Discussion

Our study could potentially confirm that acupuncture point P6 stimulation is an effective adjunct similar to the pharmacologic antiemetic drug therapy for the prevention of PONV in patients undergoing laparotomy with just P6 acupuncture points bilaterally for 30 minutes without any electrical stimulation. This is the same result of Jian-qin Lv et al. in 2013 (15) in craniotomy patients.

The results of this study showed no difference in the prevalence of PONV between the two groups which confirms the result of study of Reza Rastegari et al. (16) In fact, the overall prevalence of PONV in the acupuncture and control group was 4% and 2% respectively which was considerably lower than that reported previously (20% to 30%). This be due to a 'placebo effect' induced by the covering on the P6 point.

Also, the effect of acupuncture on preventing PONV was similar to the combination of two common drugs including metoclopramide and dexamethasone that was consistent with other studies.

Chen et al. (17) found that the effect of acupuncture and ondancetrone on laparoscopic-related PONV was similar. In Cheong et al. (18) meta-analysis, acupuncture type P6 point significantly reduced vomiting within 6 hours of surgery and nausea within 24 hour of surgery.

Holmer and colleagues (19) showed that using acupuncture point stimulation before surgery can effectively prevent nausea, but not vomiting occurrence in comparison with oral medications.

In another study, Ouyang et al. (20) indicated that in different study time points, the rate of PONV ranged between 2 to 12 % in the acupuncture group and 2 to 28% in the control group with a significant difference.

Grupe(21) also showed lower postoperative pain as well as lower PONV in acupuncture than in the control group. Finally, Streitberger et al. (22) showed that stimulating with acupuncture could potentially reduce PONV.

In total, considering the side effects of metoclopramide and dexamethasone and according to the similarity of the effects of acupuncture and these two drugs, the use of acupuncture point stimulation can be a suitable alternative for preventing PONV in different types of surgeries.

In conclusion, single insertion of an acupuncture needle could have similar effectiveness on preventing PONV, the same as a pharmacologic combination of metoclopramide and dexamethasone, however due to the side effects of medications, the use of acupuncture point stimulation is preferred.

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The effect of Nitrous Oxide on post-operative gastric pain in Cataract Surgery under general anesthesia with laryngeal mask airway

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Abstract

Background: Gastric distension is one of the troublesome complications of laryngeal mask airway (LMA) use in anesthesia practice. On the other hand, we know that Nitrous Oxide (N2O) can distend the closed gas spaces including in the stomach. We aimed to determine whether N2O can aggravate LMA induced gastric distension and pain.

Method: One hundred and sixty four patients aged between 50-65 years, American Society of Anesthesiologists (ASA) status I and II, and scheduled for cataract surgery under general anesthesia, were randomly allocated in two groups.

After induction of anesthesia, it was maintained with propofol and nitrous-oxide oxygen (60%-40%) in group "A" versus propofol and oxygen 100% in group "B". Quality of mask ventilation before inserting LMA, heart rate and blood pressure were monitored and recorded. Using the Visual Analogue Scale (VAS) pain and also the incidence of nausea and vomiting after the surgery were recorded at 10, 20, 30 and 45 minutes after the operation. Data were analyzed using SPSS software, version 16, and P value less than 0.05 was considered as statistically significant in all instances.

Results: In group "A", 60 patients (72.3%) did not report any pain after operation and 23 patients (27.7%) reported epigastric pain. In group B, 70 patients (86.4%) did not have any pain, and 11 (13.6%) had epigastric pain. Statistical analysis of the results showed that the incidence of epigastric pain in the two groups was significantly different and those who received N2O suffered more postoperative epigastric pain.

Conclusion: According to the results of this study, when we use LMA and we are afraid of postoperative epigastric pain, we can eliminate N2O from our anesthetic drugs.

Key words: General anesthesia, nitrous oxide, laryngeal mask airway

Introduction

Nowadays, using laryngeal mask airway (LMA) for short duration surgery is common, due to a decrease in the complications (1) related to endotracheal intubation. In this regard, many anesthesiologists prefer it to endotracheal intubation. In general anesthesia, laryngeal mask airway (LMA) is the best known supraglottic airway device (SGA) when intubation using laryngoscopy is difficult or when one wants to reduce hemodynamic changes.(2)

In spite of all advantages, gastric distension (3) is one of the troublesome complications of LMA use in anesthesia practice and epigastric pain may be even more troublesome than the surgical site pain for the patient; also, the LMA cuff can cause pressure on the neuropraxia of the lingual nerve, hypoglossal nerve, and recurrent laryngeal nerve.(4)

Nitrous oxide is one of the weakest anesthetic gases with minimum alveolar concentration (MAC) of 104%. It means that even with the maximum permitted prescription (70% concentration), it cannot be used as a sole anesthetic. Therefore, it should be used in combination with other anesthetics (inhaled or intravenous) to induce or maintain anesthesia (Masjedi 5).

The use of nitrous oxide, in the absence of special circumstances indicating its lack of use, is desirable(6). Although nitrous oxide is known as a weak anesthetic, a strong analgesic facilitates reduction of the required dose of other patent anesthetic drugs (7, 8, 9). Nitrous oxide has a low blood solubility (blood/Gas partition coefficient of 0.47) with rapid increase of its relative pressure in blood after prescription (7).

Although few studies have evaluated the effect of this gas on epigastric pain, we know that nitrous oxide which is one of the most common inhaled anesthetics can distend the closed spaces including gastro-intestinal tract (10). We hypothesized that nitrous oxide can aggravate LMA induced gastric distension and accordingly increase epigastric abdominal pain.

Method

Sample size was estimated on the basis of a pilot study on 50 cases. Then, the sample volume was calculated and determined using Med-Calc statistical software with 5% error rate and 80% statistical power (attrition of 20%) as 190 cases. $\alpha=0.05$, $\beta=0.10$, $\mu1=1.1$, $\mu2=2.35$, SD1=2.95, SD2=2.8, Z1-a/2=1.96, Z1-b/2=0.85.

$$n_1 = n_2 = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2 \times (s_1^2 + s_2^2)}{(\mu_2 - \mu_1)^2}$$

This randomized, double-blind clinical trial was performed on 164 patients 55-65 years of age, who were scheduled for Cataract Surgery at Khalili hospital from 2015–2017. After obtaining permission from the ethics committee of Shiraz University of Medical Sciences (2014,246,IRCT20 15010420542) and receiving written informed consent, a table of random numbers was used to divide patients into two groups of 82 through a process of computer-generated block randomization.

Exclusion criteria were emergency operations, full stomach patients, history of abdominal surgery, gastric pain and post-operative nausea and vomiting, patients with uncontrolled medical diseases such as blood pressure above 160/90 mmHg, patients with any contraindication for N2O use, toothless patients, upper respiratory infection, certain co-morbidities (heart failure, congenital heart disease and asthma), use of drugs that have an effect on blood pressure or heart rate, and a long duration of surgery (more than 45 minutes), and finally patients who needed extra doses of muscle relaxation were excluded from this study.

The patients were taken to the operating room and standard monitoring (non-invasive blood pressure, electrocardiogram, pulse oxymetry and Capnography) were applied. Induction of anesthesia was similar in both groups and performed by one anesthesiologist. Premedication, 0.03 mg/kg intravenous midazolam and 2 µ/kg of fentanyl were given to all patients; then, 5 mg/kg Pentothal and 0.6 mg/kg atracurium was administered respectively for induction of anesthesia and muscle relaxation. Mask ventilation before inserting LMA was done by 2 expert anesthesia nurses in 3 minutes and then LMA inserted and fixed in the supraglotic area by the corresponding anesthetist. In the two groups, LMA size 3 was used for patients weighing below 50 kg, size 4 for those weighing 50-70 kg, and size 5 for those over 70 kg. After insertion, the cuff pressure was maintained at 60 cmH2O with a hand pressure gauge (VBM, Germany).

Ventilation continued with tidal volume of 10 ml/kg, respiratory rate of 12/min and the inspiratory:expiratory ratio was 1/2. Anesthesia was maintained with propofol 100 µg/kg/min and O2 (40%) and N2O (60%) in the first group and 100% oxygen in the second group with preservation of normocapnia and normoxia.

Cataract surgery was done and the blood pressure and heart rate were recorded each time. At the end of surgery, all anesthetic drugs were closed and the patient allowed to breath spontaneously and then reversed by 0.03 mg/kg atropine with 0.06 mg/kg neostigmine. All the patients were extubated without exerting any force and so quietly they were transported from the operating room to the Post Anesthesia Care Unit (PACU) immediately after normal awakening of the patient. In recovery the assistant nurse, without any information about group allocations, asked the patients to report epigastric pain according to VAS pain scale and observation.

Furthermore, nausea-vomiting and hemodynamic condition according to blood pressure and heart rate were recorded and registered. (VAS) Visual Analogue Scale is a standard method to measure the severity of pain and the patient's

pain intensity ranging from 0 points (no pain) to 10 points (worst pain). These scores are dependent on the patient's expression; a score of 0 was assigned to no pain, 1-3 light pain, 4-6 moderate pain, and 7-10 worst pain.

Patients were also evaluated as to the received intravenous ranitidine and also in terms of possible side effects such as nausea and vomiting. If there was a pain score more than 0 the patient was given intravenous ranitidine (50mg/2ml) and the data were recorded.

Statistical analysis
All statistical analyses were performed using SPSS, version 16 (SPSS Inc., Chicago, IL, USA). The Kolmogorov Smirnov test was used for normal data distribution; to compare the quantitative variables between the two groups, independent t-test was used, and if the data distribution was abnormal parameters the Mann Whitney U-test was used. The significance level of 0.05 was used in this study

Results and Discussion

There were no significant differences observed in the patient's age, gender, weight, duration of ventilation, duration of anesthesia and quality of ventilation in both groups. (Table 1).

Quality of ventilation			Duration of anesthesia (min)	Duration of Ventilation (min)	Weight (kg)	Sex (M/F)	Age (years)	variable Groups
poor	moderate	good						
3	16	64	32.6 ± 4.4	29 ± 3.5	62.10±5.09	51/32	58± 5.31	Group A
0	9	72	33.5± 4.5	31 ± 3	63.92±4.42	55/26	57±6.01	Group B
P=0.117	P=0.144	P=0.212	P=0.565	P=0.65	P=0.69	P=0.375	P=0.93	Significance

No significant difference was seen in the hemodynamic features of the patients (systolic blood pressure, diastolic blood pressure, and heart rate) between the two groups, both in the period before the operation and in 5, 10, 15, 20, 30 and 35 minutes under the operation.[Table 2 - page 80].

But at the recovery room, systolic blood pressure at 15, 20, 25 and 30 minutes and diastolic blood pressure at 30 minutes, there was a statistically significant difference between the two groups.[Table 3 - page 81]

The severity of pain score at 10-20 minutes and 20-30 minutes after arrival to recovery was significantly different in the two groups.[Table 4]

At the 30-45 minutes (mean±SD)	At the 20-30 minutes (mean±SD)	At the 10-20 minutes (mean±SD)	At the 0-10 minutes (mean±SD)	Pain in RR Groups
1.05 ± 0.30	3.80 ± 0.36	2.38 ± 0.48	2.04 ± 0.35	Group A
0.75± 0.13	0.98 ± 0.33	1.11 ± 0.40	0.86 ± 0.37	Group B
0.10	0.042*	0.048*	0.052	p-value

The patients in both groups did not have post-operative nausea and vomiting.

The results of this study showed that a significant difference was not seen among demographic parameters (age, sex, weight), duration and quality of ventilation, and time of anesthesia.

Gastric insufflation, of course, may happen during mask ventilation before inserting LMA, so we excluded the patients who had poor mask ventilation. Also, quality and time of mask ventilation was not meaningfully different in the two groups; therefore, we cannot relate the increase of pain to poor ventilation or difference between duration of operations.
Ho-Tai L. and colleagues compared gastric distension between LMA and mask ventilation and concluded that in LMA anesthesia less gastric distension happened in comparison with mask ventilation (3).

No significant difference was observed between the two groups in terms of hemodynamic characteristics including heart rate, systolic, and diastolic blood pressure, in 5, 10, 15,20,25,30 and 35 minutes under anesthesia; it means that N2O causes stable cardiovascular status; also, Chizuko's study confirms this matter in Sedation dose of N2O inhalation (11). In the recovery room, we had a statistically significant difference at 20, 25, 30 and 45 minutes in systolic blood pressure and at 30 minutes in diastolic blood pressure.

A significant difference was shown between the two groups in VAS scale pain at the recovery room at 10-20 and 20-30 minutes. The significance level in systolic and diastolic blood pressure parameters in the recovery was closely related to the amount of pain at times asked. For example, at the time of 30 minutes of recovery, we registered the highest severity of pain, increased in systolic and diastolic blood pressure at the same time between the two groups.

In the operating room

Table 2

Variable	Groups	Pre-operative	5 min	10 min	15 min	20 min	25 min	30 min	35 min
Systolic blood pressure	Group A	136.52 ± 19.80	142.52 ± 18.85	140.82 ± 19.40	138.70 ± 18.30	136.42 ± 17.90	133.30 ± 17.60	130.20 ± 17.50	139.65 ± 18.35
	Group B	134.10 ± 19.55	138.52 ± 18.60	135.32 ± 19.35	134.52 ± 18.35	132.52 ± 17.85	129.42 ± 17.70	125.52 ± 16.85	133.50 ± 18.45
	Significant	P=0.31	P=0.29	P=0.27	P=0.30	P=0.29	P=0.28	P=0.25	P=0.22
Diastolic blood pressure	Group A	77.90 ± 18.85	80.75 ± 18.89	79.65 ± 18.40	77.80 ± 18.50	76.75 ± 18.45	76.70 ± 18.63	75.90 ± 17.90	79.81 ± 18.73
	Group B	73.80 ± 18.92	76.81 ± 18.84	75.81 ± 18.55	73.63 ± 18.43	72.81 ± 18.33	72.72 ± 18.22	70.65 ± 17.83	75.81 ± 18.53
	Significant	P=0.31	P=0.30	P=0.29	P=0.28	P=0.29	P=0.28	P=0.28	P=0.31
Heart rate	Group A	89.60 ± 15.43	90.80 ± 16.85	90.89 ± 18.88	88.60 ± 17.75	88.11 ± 17.93	86.81 ± 17.65	84.81 ± 18.53	91.81 ± 18.85
	Group B	85.53 ± 15.33	86.91 ± 16.83	85.80 ± 18.49	84.61 ± 17.83	83.81 ± 17.33	82.50 ± 17.63	79.81 ± 18.49	88.81 ± 18.75
	Significant	P=0.33	P=0.34	P=0.30	P=0.30	P=0.27	P=0.29	P=0.27	P=0.42

In the Recovery Room (RR)

Table 3

variable (Groups)	Pre-operative	5 min	10 min	15 min	20 min	25 min	30 min	35/45 min
Systolic blood pressure	Pre-operative Systolic blood pressure	Systolic blood pressure 5 min	Systolic blood pressure 10 min	Systolic blood pressure 15 min	Systolic blood pressure 20 min	Systolic blood pressure 25 min	Systolic blood pressure 30 min	Systolic blood pressure 45 min
Group A	140.25 ± 16.60	142.95 ± 18.95	145.28 ± 18.44	147.70 ± 18.40	148.42 ± 17.60	155.30 ± 17.65	155.20 ± 17.50	140.95 ± 18.38
Group B	136.15 ± 16.65	133.22 ± 17.70	130.22 ± 18.38	125.72 ± 18.53	122.52 ± 17.58	120.42 ± 17.62	120.52 ± 17.59	118.50 ± 18.40
Significant	P=0.31	P=0.107	P=0.08	P=0.054	P=0.047*	P=0.034*	P=0.033*	P=0.055
Diastolic blood pressure	Pre-operative Diastolic blood pressure	Diastolic blood Pressure 5 min	Diastolic blood Pressure 10 min	Diastolic blood Pressure 15 min	Diastolic blood Pressure 20 min	Diastolic blood Pressure 25 min	Diastolic blood Pressure 30 min	Diastolic blood Pressure 35 min
Group A	80.80 ± 18.45	80.65 ± 18.90	82.65 ± 18.40	85.80 ± 18.50	86.75 ± 18.46	86.70 ± 18.36	87.90 ± 17.50	82.37 ± 18.72
Group B	75.60 ± 18.40	74.81 ± 18.85	73.81 ± 18.55	71.63 ± 18.53	70.81 ± 18.39	68.72 ± 18.32	67.65 ± 17.30	67.40 ± 18.59
Significant	P=0.28	P=0.20	P=0.13	P=0.08	P=0.07	P=0.06	P=0.05*	P=0.07
Heart rate	Pre-operative Heart rate	Heart rate 5 min	Heart rate 10 min	Heart rate 15 min	Heart rate 20 min	Heart rate 25 min	Heart rate 30 min	Heart rate 35 min
Group A	90.60 ± 16.53	92.46 ± 17.85	94.98 ± 18.64	95.55 ± 17.55	95.44 ± 17.93	96.26 ± 17.65	96.47 ± 18.58	89.59 ± 17.85
Group B	86.53 ± 16.43	86.91 ± 17.65	85.80 ± 18.32	84.61 ± 17.53	83.81 ± 17.93	82.50 ± 17.71	79.81 ± 18.29	77.81 ± 17.75
Significant	P=0.33	P=0.21	P=0.13	P=0.12	P=0.095	P=0.08	P=0.06	P=0.10

In the study of Rossi and colleague, it was shown that the stomach distension increased the sympathetic nerve activity and blood pressure in healthy humans, indicating the existence of a functional relationship between gastrointestinal distension and cardiovascular function (12). Hirota stated Nitrous oxide activated the sympathetic nervous system under specific experimental conditions indirectly (13).

At the end of the period of recovery, the patients who had gastric pain received a single dose of ranitidine 50mg/2ml as recommended, and then no significant difference was seen in the hemodynamic features of the patients (systolic blood pressure, diastolic blood pressure, and heart rate) between the two groups (at 45 minutes). None of these patients needed to stay in the hospital due to gastric pain afterwards.

Although not capable of inducing general anesthesia in humans, N2O is a good analgesic agent and commonly used in anesthesia practice in combination with other anesthetic agents (14) and it impacts the patient's comfort after surgery by reducing the incidence of PONV (15). In spite of all that, N2O can distend closed spaces of the body including gastrointestinal tract (10) and, therefore, may aggravate LMA induced gastric distension. We didn't find any study on the effect of N2O on gastric distension during LMA or mask ventilation.

Conclusion

According to the results of this study, whenever we use LMA and we are afraid of post-operative epigastric pain due to poor ventilation or past history of gastric problem, we can eliminate N2O from our anesthetic drugs and replace it with short acting opioids or NSAIDs for augmentation of analgesia.

Limitations

Although most cataract surgery is under topical or local anesthesia in many countries, in our country, it is vice versa. Khalili hospital where this study was conducted, is a referral, university affiliated center for ophthalmologic operations in the southwest of Iran, where more than 80% of ophthalmic operations, mostly cataract, are under general anesthesia due to high enthusiasm for such a procedure from both ophthalmologists and patients.

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A study of evidence-based medicine knowledge and use in general practitioners working in Ahvaz hospitals in 2016

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Abstract

Background and Objective: The need for accurate scientific evaluation of clinical performance was increasingly focused on by medical and sociological societies in the second half of the twentieth century. The present study was conducted with the aim of determining the knowledge level, attitude and performance of general practitioners working in hospitals in the city Ahwaz.

Methods: This study was a cross-sectional study conducted for exploring the knowledge and the use of evidence-based medicine in general practitioners working in hospitals in the city, Ahwaz. The sampling method was random and the sample size was estimated to be 123 individuals. The data were analyzed using the statistical software STATA version 14. Descriptive statistical methods and linear regression model were used for data analysis and the significance level in this study was considered to be 0.05.

Results: The results indicated that 93% of physicians participating in the study were familiar with EBM. In the process of practice, 18 person (14.7%) of the total doctors in prospectuses and clinical professor turned to EBM. 45 person (6/36%) of all doctors, search the Internet for information on clinical experience as the preferred method. 61% of doctors in practice refer to books and printed references and 9.4% used domestic and foreign articles and 56 (4.45%) of all participated in EBP sessions.

Conclusion: In this study, the knowledge, attitude and practice in relation to evidence-based medicine was at a low level. Overall, the findings can be explained that doctors working in hospitals and medical centers in Ahvaz make little use of their scientific resources to increase their scientific information, which is required by the authorities of Ahvaz University of Medical Sciences to promote scientific information for doctors such as launches of science centers in hospitals, workshops and scientific resources and to be familiar with latest references.

Key words: evidence-based medicine, general practitioners, hospital

Introduction

The need for accurate scientific evaluation of clinical performance was increasingly focused on by medical and sociological societies in the second half of the twentieth century(1,2). It is claimed that most of physicians' clinical actions are based not on evidence-based medicine but on tradition, newest experiences gained, the materials they have learned several years before in medical faculties and verbal evidence obtained from colleagues (3). In an applied definition, evidence based medicine (EBM) designates the accurate, explicit and informed use of the best existing evidence in decision-making on patient care individually (4). Therefore, EBM is focused on appropriate use of information (types and levels) for appropriate guidance of objectives and professional medical actions (2). This process is a basis for cautious clinical decision making (2, 5, 6). Therefore EBM requires specific, implicit and cautious use of information obtained from the combination of individual clinical skill and experience with the best evidence obtained from review exploration (2, 5, 6, 7). In a more comprehensive definition, EBM can be defined as an approach in decision making in which the physician, using the best existing scientific evidence and in consultation with the patient regarding option(s), makes a decision on the best balanced option that results in good treatment and positive outcomes. This definition pays attention to patient satisfaction and physician commitment. In this method the physician not only makes diagnostic and prognostic decisions, but also educates the patients regarding the therapeutic options and shares care management decision makings with them (2). This approach supports (1) respecting mutual independence of the patient and the physician, (2) the role of patients in informed decision making, and (3), a consultative technique in which the patients participate in their care (5, 6, 7, 8). Several studies have been conducted in Iran on physicians' view of EBM. In one study, Sadeghi et al (2011) explored clinical residents' knowledge of EBM at the Kerman University of Medical Science. The findings of this study indicated that 83.3 percent of the residents believed that the use of EBM is useful in patient care but only 5.3 percent stated that they had used this approach in their clinical work (10). The study by Gazrai et al (2014) on knowledge, attitude and practice of physicians related to EBM in Hakim and 22 Bahman Hospitals of Neyshabur indicated that 80.4 percent of the physicians viewed EBM as useful in the improvement of care and services provided to the patients and 47.8 percent of them would use this approach most often for making decisions related to patients. Considering the importance of the use of evidence-based medicine, the present study was conducted with the aim of determining the knowledge level, attitude and performance of general practitioners working in hospitals in the city of Ahvaz to determine the strengths and weaknesses of this group of individuals with regard to evidence-based medicine so that favorable planning can be done for meeting the information and developmental needs of this approach.

Method

This study was a cross-sectional study conducted for exploring the knowledge and the use of evidence-based medicine in general practitioners working in hospitals in the city of Ahvaz. The sampling method was random and the sample size was estimated to be 123 individuals. The permits for distribution of the questionnaires among the physicians at hospitals were obtained by obtaining the necessary permits for visiting the hospitals, coordination meetings with the heads and internal managers of the hospitals and giving them explanation regarding the study. The data collection tool was a researcher-made questionnaire. The validity of the questionnaire had been explored by some scholars. For this purpose, the questionnaires were given to 3 faculty members and the final version was prepared after making revisions and corrections. The reliability of the questionnaire, using Cronbach's alpha, was determined to be 0.83. The face validity of this study was verified by 3 experts and researchers in the domain of health services. The questionnaire had two sections; the first section consisted of questions on age, sex, expertise and practice history. The second section of the questionnaire consisted of questions on the role of EBM in daily patient treatments, the percentage of evidence-based activities, search in search engines, familiarity with evidence-based medicine, familiarity with resources such as PubMed and Cochrane and the mastery of some highly employed concepts and principles in epidemiology. The data were analyzed using the statistical software STATA version 14. Descriptive statistical methods and linear regression model were used for data analysis and the significance level in this study was considered to be 0.05.

Findings

In this study, 62.6% of those completing the questionnaires were male and 37.4% were female. 62.6 percent of the respondents had completed their education for becoming a general practitioner in Ahvaz, 22.9 percent had completed their studies in Tehran and 22.9% had completed their studies in other universities in Iran. Their mean practice experience was 8.1(±6.7) years, their mean study time on medicine was 3.2(±2.7) hours per day, the mean time since the end of their education was 8.3(±6.5) years and their mean age was 34(±9.7) years.

The results of this study indicate that 93% of the physicians participating in the study were familiar with EBM. About 70% of the individuals who completed the questionnaire were able to provide a definition and description of EBM. Regarding the impact of EBM on patient outcome, only 70% of the participants expressed their views; 87% of these individuals believed that the use of EBM improves patient outcome and 82% of these residents believed in the usefulness of evidence-based medicine. Regarding the negative impact of EBM on the prestige of medicine as a profession (respect and appearance), 7% agreed on its negative impact, believing that the use of EBM in clinical decision makings results in the reduction of respect and apparent status of medicine and should not be used.

In terms of the way of accessing internet, 95% of the respondents would gain access to internet at home and hospital. In the practice process, 18 physicians (14.7%) would refer to clinical professors and pamphlets and 45 physicians (36.6%) would prefer searching the web in order to gain knowledge of clinical experiences.

Table 1 shows the level of familiarity with some key concepts of EBM in the physicians studied

Table 1: the frequency distribution of the residents regarding familiarity with absolute risk and chance ratio

	I don't know but I am willing to know		I know to some extent		I know and I can explain to others	
	number	percent	number	percent	number	percent
Absolute risk	14	11.47	65	53.28	43	35.25
Relative risk	6	4.91	69	56.57	47	38.52
Systematic review	4	3.3	46	37.7	72	59
Like hood ratio	44	36.07	49	40.16	29	23.77
Confidence interval	52	42.63	54	44.26	16	13.11
Publication bias	43	35.25	47	38.52	32	26.23
Relative risk reduction	56	45.9	38	31.15	28	22.95

61% of the physicians would use printed books and resources, 4.9% would use national and international papers and 56 individuals (45.4%) participated in EBP course. Among the general practitioners, 48% were familiar with PubMed, 22% with Update and 4.9% with Cochrane.

Chart 1 shows the level of knowledge and use of EBM in physicians working in hospitals in the city of Ahvaz by age

Chart 1: the level of knowledge and use of EBM in physicians working in hospitals in the city of Ahvaz by age

Graphs by SEX

Association betwen age and knowledge of physiciation in statistics and epidemiology. Error bar indicate CI.
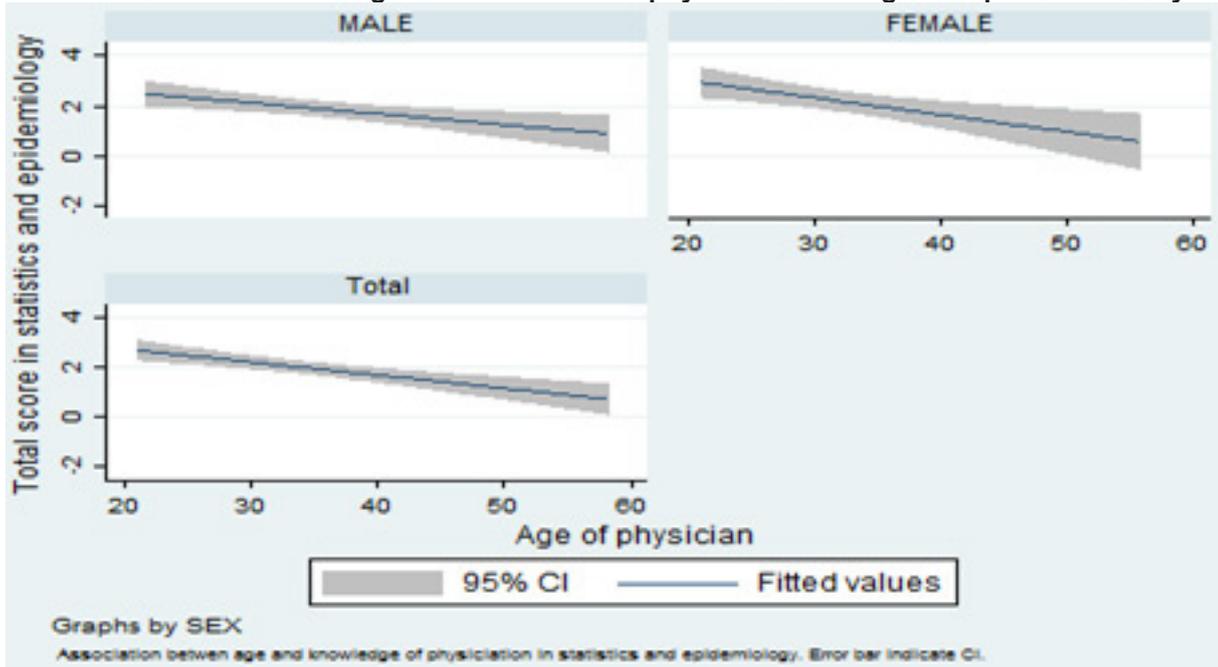
According to the above chart, individuals' knowledge is decreased with the increase of age in a way that highest level of knowledge is found in general practitioners ages 20-30 years and the lowest level of knowledge is found in general practitioners ages 50-60 years. In terms of the respondents' sex and knowledge, the knowledge of female physicians is higher than that of the male physicians. Chart 2 (next page) shows the level of knowledge and the use of EBM in general practitioners of Ahvaz hospitals by sex in 2016.

Chart 3 is related to EBM; the physicians were asked whether they had completed an EBM course and their answers were yes or no.

As age as an independent variable was found to impact the score of the physicians, the elements that have impact (synergistic effect or reducing effect) in this regard are explored. As seen in participation in EBM courses it has not been able to reduce the effect of age and duration from the education end and, unexpectedly, the age and knowledge score of physicians who have participated in these courses are significantly and inversely related.

Chart 2: the level of knowledge and the use of EBM in general practitioners of Ahvaz hospitals by sex in 2016
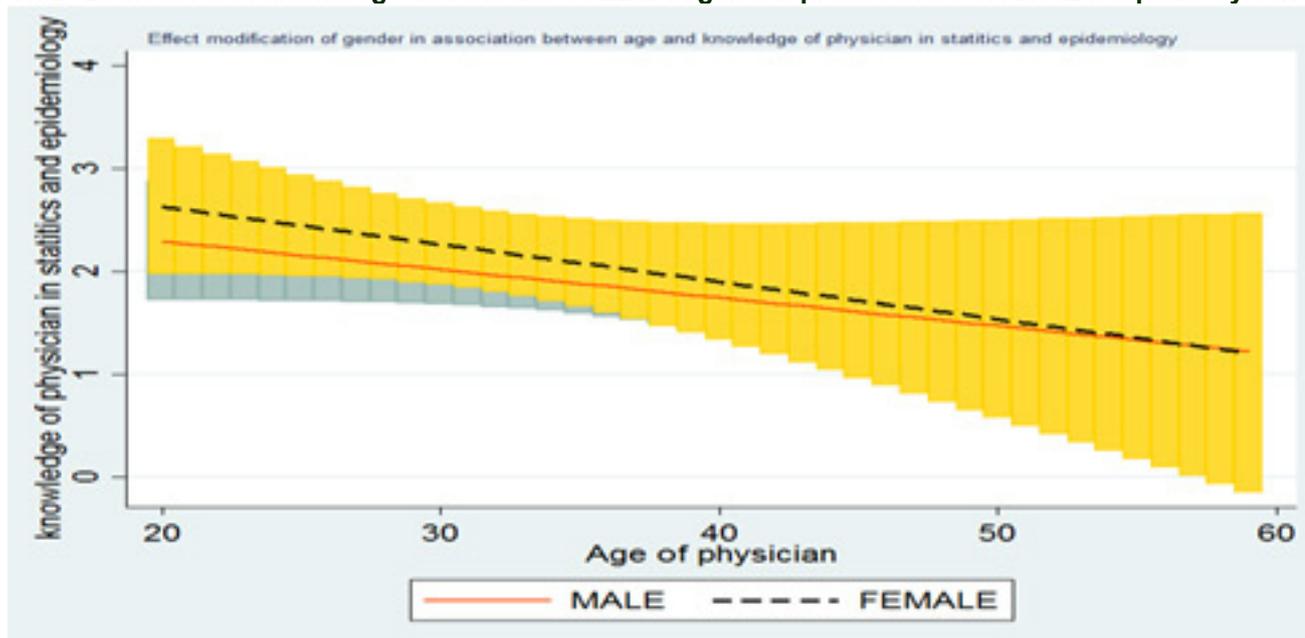
Chart 3: EBM course completion status by the age of the respondents
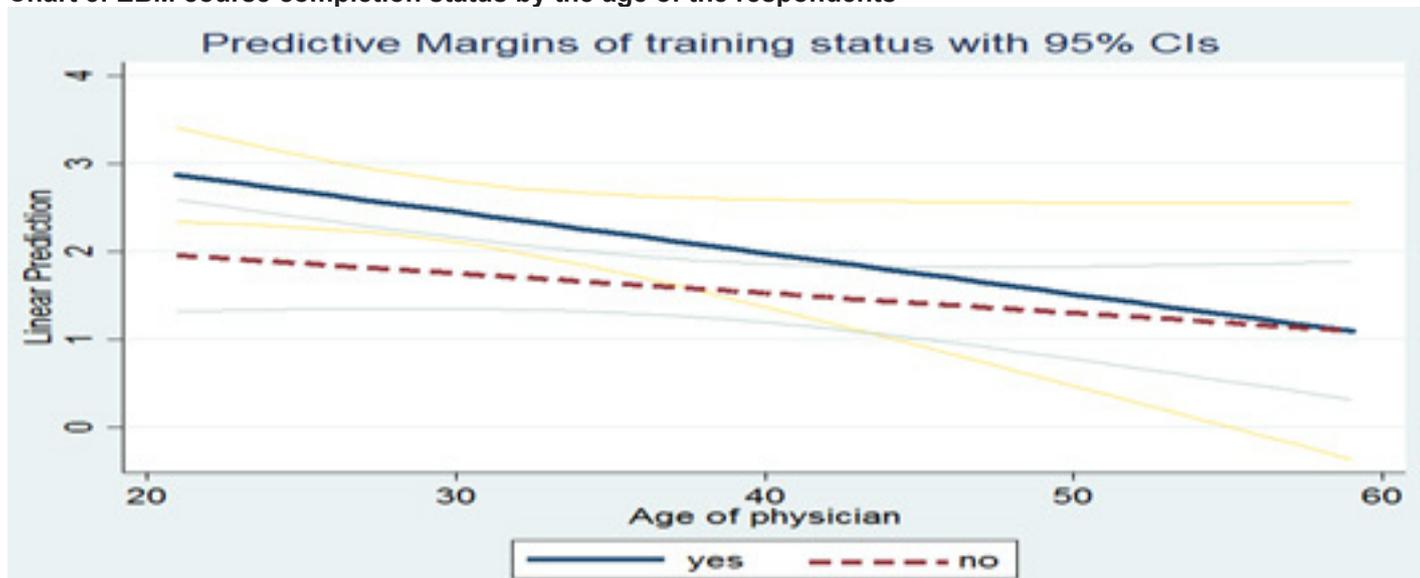
Discussion and Conclusion

A combination of clinical evidence and research evidence is called evidence based medicine. The decision making on patients may be based on old and outdated information, if this method is not used (13). A review of the literature, especially the experiences of foreign universities shows that, in recent years, EBM has become increasingly prevalent and different and diverse efforts are seen in different countries in this regard.

In this study the level of knowledge, attitude and performance in physicians was at a low level in relation to EBM and general practitioners had a low level of familiarity with EBM, assessment and mastery of use of EBM and assessment of mastery of some highly used principles and concepts in epidemiology. The results of this study are consistent with those of the study by Novack et al in which the level of knowledge, attitude and performance of the physicians with regard to EBM was found to be low (14).

In this study, in relation to the level of knowledge and use of EBM in general practitioners by age, the results indicated that the general practitioners in the age range of 20-30 years had the highest level of knowledge and those in the range age of 50-60 years had the lowest level of knowledge. Most general practitioners had had EBM courses and individuals with a lower age had completed more courses, compared with older general practitioners. The findings of this study are not consistent with those of the study by Al-Baghlie et al that showed that 46 percent of the physicians aged over 50 years, in comparison with 72 percent of the physicians below the age of 35, had more mastery of the use of EBM (15). And the findings are not consistent with the findings of the study by Sadeghi et al either as they found that the mastery of the physicians aged over 40 years was higher than the younger physicians (10).

With regard to familiarity with highly used concepts in statistics and epidemiology and the factors impacting them, the results indicated that the highest mean of physician

knowledge was related to the study of the effect of a new drug on blood pressure with 52 percent of correct answers and the lowest mean of their knowledge was related to a type of statistical test for comparing the prevalence of disease in men and women with 11.4 percent of correct answers. The findings of this study indicate that the physicians are more familiar with highly employed concepts in epidemiology than statistical method. In order to improve this, it is necessary to provide necessary education by statistics experts. The results of this study are consistent with the results of the study by Sadeghi et al on the level of knowledge, attitude and use of EBM in clinical residents at Kerman University of Medical Sciences which showed that the familiarity with statistical tests in scientific papers was less than 20 percent. The results are not consistent with the results of the study by Rouhani et al which suggested that the use of statistical methods for treatment of disease by physicians was 54 percent (10).

Regarding the performance of EBM, the physician had poor skills in the use of specialized search methods, familiarity with search engines and understanding of review papers and their performance in this regard was poor. The lack of investment and material and intellectual incentives for physicians as well as the lack of need for learning new skills are the main obstacles in employing EBM. Considering the results of this study, it is recommended that a short-term course on EBM be held each year for improving the statistical knowledge of physicians. In addition, if possible, an educational course should be created in the domain of EBM in universities of medical sciences. And the need for related workshops in all domains of therapy, diagnosis and care is felt. The limitations of this study included the individual characteristics, the different facility levels in different hospitals for accessing the web, crowdedness of hospitals and the lack of objective study of physician with regard to EBM.

Overall, the physicians working in hospitals and health centers in the city of Ahvaz do not use scientific resources for increasing their scientific knowledge much. Thus, it is necessary for the authorities of Ahvaz Jundishapur University of Medical Sciences to create research centers at hospitals, hold workshops for familiarity with scientific resources and the like for increasing the scientific information of physicians. Among the main causes of limited use of scientific resources by physicians can be heavy workload for general practitioners in public hospitals. Appropriate measure should be adopted to make the number of visits proportionate to the abilities of the general practitioners in order to solve this problem. In addition, as general practitioners need to have enough familiarity with websites, references and scientific indices in order to improve their technical knowledge on EBM, it is necessary to hold workshops once in a few years and when general practitioners begin working.

Acknowledgement

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Correlates of Cardiovascular Diseases-related Nutritional Behaviors among Women Using Health Belief Model: a Research from Iran

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Abstract

Background and Aim: Cardiovascular disease is the main cause of mortality and morbidity in the world. Although a large proportion of cardiovascular diseases can be prevented, these diseases have continued to rise due to inadequate preventive measures. The aim of this study was to determine the predictors of nutritional behavior of women referred to health centers in Amol city, to prevent cardiovascular diseases using Health Belief Model in 2016-17.

Methods & Materials: This descriptive-analytical and cross-sectional study was conducted on 180 women of childbearing age, who were randomly selected and investigated. A researcher-made questionnaire was used to collect data and this self-administered questionnaire was designed based on HBM structures (knowledge, perceived susceptibility, perceived severity, perceived benefits, perceived barriers, perceived self-efficacy and behavior). Validity and reliability were determined through face and content validity, and internal consistency and test-retest, respectively. Descriptive-analytical statistical tests (correlation coefficient, regression analysis), ANOVA and T-test were used to analyze the data.

Findings: The results showed that three variables as self-efficacy, level of education and perceived susceptibility among demographic variables and HBM structures were stronger predictors for the behavior, respectively. It should be noted that self-efficacy and perceived sensitivity were direct predictors so that the behavior would be better with the increase of self-efficacy and sensitivity, but it had a reverse relationship with education level; it means that the higher education indicated the lower behavior.

Conclusion: Health Belief Model has very good predictability for preventive nutritional behaviors of cardiovascular diseases. It is recommended to design and implement the educational interventions based on HBM.

Keywords: Nutritional behavior, Women, Cardiovascular disease, HBM

Introduction

Cardiovascular disease is a pandemic that has pressured most of the world's countries; although many cardiovascular diseases can be cured it is still the most important cause of death worldwide(1). According to the report of World Health Organization (WHO), 17.3 million people died in 2008 due to cardiovascular diseases and that accounted for 30% of all deaths in the year. 80% of death has been in low and middle-income countries and is predicted by 2030 reach to more than 23.3 million people per year(2). Cardiovascular disease is the main cause of death and disability in the world. Although a large proportion of cardiovascular diseases are preventable, mainly due to inadequate preventive measures it is still rising(3). Today, most cardiovascular diseases cause frequent hospitalizations with high costs for society and the government(4). Increasing prevalence of cardiovascular diseases (CVD) and human and economic losses due to them has doubled the importance of prevention and control of these diseases(5, 6). According to the World Health Organization (WHO), the majority of cardiovascular diseases can be prevented by identifying risk factors like tobacco use, unhealthy diet and obesity, physical inactivity, high blood pressure, diabetes and fat gain(2, 7).

Many listed factors for cardiovascular disease are strongly influenced by diet(1). High intake of dietary saturated fat, Trans fat, cholesterol and high salt and low intake of fruits, vegetables, and fish have been associated with risk of cardiovascular diseases(3, 8, 9). In addition the importance of habits of eating, cooking and amount of salt intake are considered the factors affecting cardiovascular diseases(10). In the meantime, the role of women is more important than men because many of concepts of diet are achieved by them(4). Today, in the industrial countries by

changes that are created in the lifestyle in terms of reducing the amount of fat intake and controlling tobacco and controlling blood pressure and increasing physical activity and other factors of risk, mortality from cardiovascular disease has been declining over the past 25 years(11). Education plays a major role in this part. The first step in the process of training is needs assessment and value of training programs will depend on their efficiency, and the effectiveness of these programs depends largely on the proper use of theories and models in health education. By selecting a suitable model, the training program will be on the right path(4, 12).

One of the models used at the individual level to change behavior and in fact, one of the most widely used theories and models of health education and health promotion is Health Belief Model (HBM)(13).

According to this model, if people consider themselves susceptible to the condition (perceived susceptibility) and believe that the condition is potentially dangerous for them and has negative consequences for them (perceived severity) and believe that by doing a series of measures they can reduce the risks and effects and doing these actions and measures has interests (perceived benefits) over barriers of the lack of doing the behavior (such as time and money) (perceived barriers), they will do preventive behavior from risk. Individuals to overcome barriers of behavior feel adequacy (self-efficacy)(14). (Figure 1)

Culturally in northern regions of Iran, different nutritional patterns to the Central and South regions as well as the uncontrolled growth of urban population in recent years have followed a change in life style(15). In order to prevent and control cardiovascular diseases associated with nutritional behavior and deal with behaviors and new ways of urban life, no study has been conducted in this

Figure 1: Health belief Model Constructs (9)
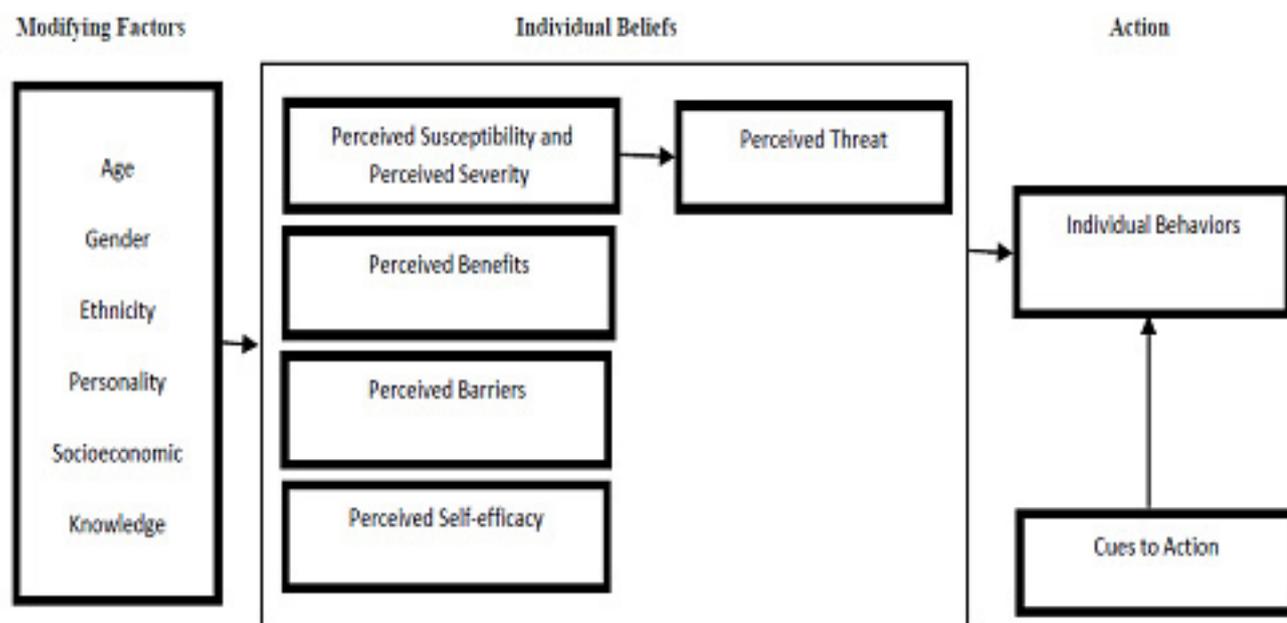
field in Mazandaran province and Amol city. Study conducting research and interventions in this field are inevitable. Given the importance of theories and patterns of behavior change in educational interventions programs should emphasize the most important behavioral determinants so this study is conducted with the aim to determine predictors of nutritional behavior of women referred to health centers in Amol, in order to prevent cardiovascular diseases, using HBM.

Materials and Methods

Study design & sampling
The present study was cross-sectional and was conducted in 2016. The sample size was 180 people and it was calculated utilizing similar precision studies (d) 0.5 and confidence coefficient (z) 1.96 and using the formula (n=z 2× S2/d2). From 18 health centers in Amol, 2 centers were selected randomly. Then the list of women of childbearing age 15-49 years covered who had literacy was prepared from Healthy Reproduction Office, 180 people were randomly selected from 4,300 women of childbearing age.

Instrument
Research-made questionnaire was the tool of data collection on the health belief model. The first part includes background information of women (age, education, occupational status, family history of cardiovascular disease). The second part consists of 24 questions on knowledge, 5 questions of perceived susceptibility, 7 questions of perceived severity, 10 questions of perceived benefits, 11 questions of perceived barriers, 6 questions of perceived self-efficacy, and 4 questions of performance. For questions of awareness, scores 2-1-0 were considered for the options of true, do not know and false respectively and a 5-point Likert scale was used for other structures where the score 5 was considered for the most desirable mode and score 1 considered for the worst mode. The Likert scale of performance measurement was; always, more often, sometimes, rarely, never.

Validity & Reliability
In order to establish the validity of the tool based on HBM, content and face validity was used. Thus, a questionnaire relevant to the aims and hypotheses based on the contents and books and new articles was set. To determine the validity of its content, the comments of 8 professors and experts of health education were used. By doing CVR and CVI of questions of the questionnaire, three questions of perceived barriers were eliminated from the questionnaire. To assess the face validity, the questionnaire was given to 10 women of childbearing age (in terms of demographic characteristics similar to the studied population) to complete, and for any possible defects of the tool (questionnaire) to be resolved in terms of writing, placing of questions and unclear questions for the women and any other apparent difficulties of the questionnaire. To evaluate the reliability of the tool, the test-retest method was used for questions of awareness. This means that among 10 women of childbearing age (in terms of demographic characteristics similar to the studied population), the questionnaire was completed and again

after 10 days, the same questionnaire was given to the same individuals to complete and the correlation coefficient obtained in this way was 0.76, which is acceptable. (It should be noted that these women did not participate in the original plan). To assess the reliability of other questions of HBM structures, internal consistency of Cronbach's alpha was used. To assess the reliability of the questionnaire, other parts of the questionnaire (perceived susceptibility, perceived severity, perceived benefits, perceived barriers, self- efficacy, the performance) was given to 30 women who were later excluded from the main study. Cronbach's alpha related to perceived susceptibility was calculated as 0.74, perceived severity as 0.69, perceived benefits as 0.88, perceived barriers as 0.73, and self-efficacy as 0.46.

Data analysis
Collected Data were analyzed in SPSS 16 software (descriptive and analytical tests such as; Regression, Pearson correlation, ANOVA, T-test).

Ethical considerations
We used unnamed questionnaires in this study. Also, all individuals participated in the research with informed consent and voluntarily.

Findings

The sample was 180 women of childbearing age covered by two health centers in Amol and their average age was 5.88 ± 29.97 years. 53.9% of the women were under 30 years old and 46.1%. over 30 years. Job status of women was 90% housewives, 10% employed. The education level was under high school (31.16%), high school diploma (42.8%), and academic education (26.1%). Family history of heart disease was (28.3%), absence of disease (71.7%).

In the study we entered the model structures of HBM with demographic variables. Among age, education, disease history, awareness, perceived susceptibility, perceived severity, perceived benefits, perceived barriers and self-efficacy with behavior, only three variables were predictors of behavior. These three variables included self-efficacy, perceived susceptibility and education. The strongest predictor among these three variables is the perceived self-efficacy; where perceived self-efficacy was high, the behavior was high and the more the perceived sensitivity was high, the behavior was high, but the more the education was high, the behavior was lower.

In general, three results were achieved in the regression test:
A) The 1st model: self-efficacy has a significant impact on behavior. (Due to the significant level (sig. less than 0.05) and the amount of this effect is 0.28. This means that for a unit change in self-efficacy, behavior changes 0.28.
B) The 2nd model: self-efficacy (0.31) & education level (-0.18) meaning higher education has a less effect on behavior.
C) The 3rd model: According to the values of self-efficacy (0.28) level of education (-0.02) susceptibility (0.18) we understand both of susceptibility and self-efficacy have a good effect on the behavior. But, high education has negative effect on behavior.

Table 1: Demographic characteristics of samples under study

Variable	Sub-Group	(Percent), Number
Age	=<30	(53.9), 97
	>30	(46.1), 83
Education	Under high school	(31.1), 56
	High school and Diploma	(42.8), 77
	University	(26.1), 47
Job Status	Employed	(10), 18
	Housewife	(90), 162
History of heart disease	Yes	(28.3), 51
	No	(71.7), 129

Table 3. The relationship between HBM constructs with behavior using regression analysis

Model	Standard coefficient		Standard coefficient	t	Significant level	R	R²
	B	standard	Beta				
Self-efficacy	0.20	0.05	0.28	4.01	*0.001	2.88	0.83
Self-efficacy	0.22	0.051	0.31	4.37	*0.001	0.34	0.12
Level of education	-0.59	0.23	-0.18	-2.56	*0.001		
Self-efficacy	0.20	0.051	0.28	3.94	*0.001	0.38	0.15
Level of education	-0.67	-0.23	-0.20	-2.94	*0.004		
Perceived susceptibility	0.14	0.058	0.18	2.50	*0.013		

Discussion

The aim of this study was the application of HBM for prediction of cardiovascular disease-related preventive nutritional behaviors among women attending the studied health centers. As the results showed, there was a direct correlation between disease history and perceived sensitivity. People who had disease history had more perceived susceptibility. This finding is logical. Because, people who have history of disease, experience disease and they are familiar with it, thus they perceive themselves as more susceptible to disease, and they believe that they may be re-affected. This finding is consistent with results by Canbulat Uzun(16) on female employees in Turkey. It is not, however, consistent with the study of L. Hasani et al (17) about predictability of health belief model constructs in adopting self-examination of the breast. Perceived susceptibility in people over 30 years is high and in people under 30 years is low. Regarding that the effects of behaviors occur in the long term and lead to chronic or heart diseases, it is required of people in early ages to adopt preventive behaviors. The results show that people who are younger possess do not have desirable behavioral status. Therefore, it is reasonable and necessary to design educational interventions. Among demographic variables, only there was a significant relationship between age and

behavior that was consistent with the research results of Baghiani et al in the field of the role of health beliefs on cardiovascular diseases' preventive behaviors in people at risk (18) and Ammouri et al about risk perception of adults to cardiovascular disease (19), and with the results of Al-Ali Haddad's study in the field of participation of patients with myocardial infarction in sports activities(20). A similar finding was not reported in the studies of Karimi et al in the context of Breast Self-Examination (BSE) (21) and Salehi et al about regular physical activity(22) . There was a significant relationship between education and awareness as well as perceived benefits and perceived barriers and self-efficacy. This finding is quite natural and expected. This is logical that the more educated, the awareness of people in the field of heart disease rises. Meaningful relationship of education with awareness has been seen in the studies of Jalali et al (23) and the Al-Adsan(24) and Avis (25). In the present study, there was no correlation between awareness and behavior observed which is consistent with the results of Imanipour et al research about awareness and performance of teachers on preventing cardiovascular disease (26) and study of Jalali et al about awareness and the performance of people of Babol city on preventing cardiovascular disease(23) . But it isn't consistent with the study of Baghiani et al (18). This is expected and natural, as beliefs such as

Table 2. The relationship between the HBM structures and the demographic variables

	Age			Education				History of Heart Disease		
	≤30	>30	P	Under High School	High School & Diploma	University	P	Yes	No	P
	x̄ ±SD	x̄ ±SD		x̄ ±SD	x̄ ±SD	x̄ ±SD		x̄ ±SD	x̄ ±SD	
Awareness	36.48±5.70	37.84±5.60	0.10	11.34±6.26	37.55±4.87	39.98±4.38	0.001	36.71±6.00	38.14±4.61	0.12
P. susceptibility	18.24±3.06	19.05±2.30	0.07	18.05±3.33	18.51±2.50	19.45±3.39	0.630	17.95±2.89	20.27±2.28	0.001
P. severity	27.08±4.01	28.43±4.16	0.29	27.39±4.36	27.49±4.13	28.43±3.83	0.379	27.5±3.97	28.22±4.56	0.29
P. benefits	44.52±5.19	45.37±4.17	0.22	43.46±5.27	44.84±4.68	46.74±3.52	0.002	44.54±5.00	45.84±3.93	0.09
P. barriers	33.98±8.31	33.70±7.18	0.81	31.68±8.79	33.91±6.93	36.34±7.24	0.010	33.18±7.67	35.55±7.91	0.06
Self-efficacy	25.26±3.45	25.48±3.39	0.66	25.16±3.75	24.88±3.32	25.36±3.41	0.051	25.33±3.32	25.45±3.67	0.82
Behavior	13.99±2.20	14.89±2.64	0.01	14.89±2.70	14.31±2.28	13.98±2.45	0.153	14.37±2.47	14.49±2.42	0.77

perceived benefits are rooted in the awareness of people. As it was seen, awareness of people rises by increasing high educational level, so it is expected benefits rise. Also regarding perceived barriers, the more education rises, people know better the strategies to overcome the barriers. Otherwise, individuals with lower education face more barriers. In general, people who have higher education are probably less influenced by media and less affected by pressures of relatives. Thus, we observed in this study a significant correlation between the level of education and the self-efficacy that is consistent with the study of Taghdisi et al on evaluating pregnant women on infections during pregnancy based on the health belief model (27) while it isn't consistent with the study of Sahar Sabooteh et al on investigating health belief model structures about anxiety in nulliparous pregnant women(28).

In regression findings of the present research, self-efficacy had the most direct effect on nutritional behavior which is consistent with the research results of Mehri et al on factors associated with heart disease preventive behaviors in students of Islamic Azad University(29) and Teimuri et al on mammography treatment in women in Sanandaj (30) as well as studies of Teimuri on factors affecting mammography (31) and the study of Noruzi on factors affecting BSE(32) and on investigating predictors of oral health care in pregnant women. While it isn't consistent with the study of Azam Namdar et al on investigating prediction of health belief model in adopting preventive behaviors of cervical cancer(33) . They reported perceived barriers and awareness as the strongest predictors of behavior. Self-efficacy and perceived susceptibility are two factors predicting behavior in this study. The more self-efficacy, as well as, more perceived susceptibility, adopting preventive behaviors is more. Studies of Karimy et al(34) variables of perceived barriers, self efficacy and perceived sensitivity were identified as the most important constructs of the HBM in predicting nutritional practices, as well as in the study of Karimy et al (35) where a significant correlation was observed in perceived barriers, sensitivity, severity, benefits, barriers and perceived self-efficacy with nutritional practices of pregnant women, and studies of Padula and Sev Livan (36), Yarachesky et al(37) were confirmed in the present study. Based on the findings of this study we can say three variables of perceived self-efficiency, education level, and perceived susceptibility are stronger predictors. So, the necessity of designing and implementing educational interventions related to susceptibility and self-efficacy is seriously required. It could be conducted using role models or using documentation and credible sources to strengthen this belief in people that all men and women in any age are at risk for heart disease. Also, self-efficacy of individuals could be improved using patterns (successful examples) and using peers and successful experiences and also breaking down complex behaviors to simple behaviors.

Conclusion

Health belief model has a very good predictability for cardiovascular diseases-related nutritional behaviors. It is recommended educational interventions based on the HBM be designed and implemented. In this aspect and according to the findings of present research, most emphasis should be on improving perceived susceptibility, and perceived self-efficacy.

Research limitations
This study has some limitations. One is applying self-report questionnaire where people may not have accurately answered the questions. Another is that, only women of childbearing ages were studied here. That is, results may not be generalized to all members of society.

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Newborns and Sepsis: An Overview of the Condition of Neonates Hospitalized with a Diagnosis of Sepsis in Iran in 2014-2015

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Abstract

Background: Sepsis is a serious neonatal infection and is one of the causes of mortality and complications during infanthood. Studies conducted to identify neonatal and maternal risk factors can indicate methods for prevention, better and faster diagnosis, and the selection of the most appropriate antibiotics.

Objective: The Aim of this study was to determine the clinical symptoms, the results of laboratory tests, and maternal risk factors among neonates hospitalized with a diagnosis of sepsis.

Material and Methods: In this descriptive and cross-sectional study, 78 infants who had been diagnosed with sepsis in the Madani Hospital of Khorrmabad in 2014-2015 were included in the study using tconvenience sampling method. Data were collected using a questionnaire, by studying the medical records of the infants, and by interviewing the mothers. Data were analyzed using the SPSS software and descriptive and interferential statistics.

Results: Blood cultures were positive in 16 cases (21.9%). The most prevalent isolated pathogens included Acinetobacter (37.5%) and Staphylococcus epidermidis (37.5%). Urine cultures were positive in 20.3%, the most prevalent pathogens found being various species of E. coli (23%) and Enterobacter (23%). Significant relationships were found between a positive blood culture with mother's urinary tract infections during pregnancy ($p = 0.05$), the presence of maternal risk factors ($p = 0.008$), presentation with respiratory distress ($p = 0.02$), and a WBC higher than 11,000 ($P = 0.036$).

Conclusion: The results of this study suggested the need for raising the level of hygiene of the maternity and neonatal wards and the training of mothers and the nursing staff in order to prevent its occurrence.

Key words: Bacterial sepsis, newborn, risk factors, laboratory tests, Iran

Background

Sepsis is a serious neonatal infection and is one of the causes of mortality and complications during infanthood, which afflicts around 30 million neonates each year and leads to the death of 1 to 2 million [1]. Individuals who live in less developed environments with limited resources are at higher risk, [2]. A study in the UK showed that gram-positive bacteria caused 75 percent of the infections [3]. In another study by Fesharakinia and Miri (2003), 6 out of 67 blood cultures were positive, in which the most prevalent germ was coagulase-negative Staphylococcus [4]. As is apparent, the range of infection-causing organisms is very different in the developed countries as compared with the developing countries [5]. In the developing countries too, regional variation can be observed in the range and varieties of these organisms [6]. This has been attributed to differences in the prescription patterns of antibiotics and differences in lifestyle [7]. Early warning signs and symptoms and clinical manifestations of this disease are few, deceptive, and non-specific [8]. Therefore, the treatment decisions are often based on neonatal, delivery room, prenatal, and maternal risk factors [9]. In their encounters with this uncommon disease, which at the same time has serious complications, most providers of health care services to neonates seek to find ways to identify neonates who are at risk, to quickly identify infected neonates, and start the antibiotic treatment to stop the progression of the disease. Neonates who show symptoms of serious disease at birth receive empiric antibiotic treatment, all over the world, until the presence of sepsis is rejected by negative culture results. Moreover, due to the problem of the presence of infections despite negative cultures, most specialists prefer to empirically treat these neonates with antibiotics for longer periods of time [10]. Due to changes in the pathogenic patterns causing septicemia in neonates over time, the application of various antibiotics, the development of antibiotic resistant species, and variations in the prevalence and causes of septicemia from hospital to hospital and from one community to another, the epidemiological monitoring of sepsis in hospitals, especially in neonatal units, is essential [8]. Currently, neonates suffering from sepsis comprise a large part of the patients admitted to neonatal units and involve great expenditure. Therefore, studies conducted to identify neonatal and maternal risk factors can indicate methods for prevention, better and faster diagnosis, and the selection of the most appropriate antibiotics.

Objectives: The present study aimed to determine individual and familial characteristics of the neonates suffering from sepsis, the bacterial agents causing sepsis in infants, antibiotic resistance among neonates suffering from sepsis, and the relationship between confirmed cases of sepsis with the demographic and familial characteristics, and the clinical and laboratory symptoms and signs that the neonates suffering from sepsis display.

Material and Method

This descriptive cross-sectional study was based on the information obtained from patient records present in the hospital. The statistical population consisted of all the neonates hospitalized in the neonatal units and the NICU of the Shahid Madani Hospital of Khorramabad, Iran, from October 22, 2014 to October 21, 2015. The study sample consisted of 78 neonates who were diagnosed with sepsis by a neonatologist and were hospitalized and treated in the said units during the aforementioned period. The sequential sampling method was used. The data collection instrument was a researcher-designed questionnaire including items related to the demographic and familial information of the neonates and the history of pregnancies and childbirth of the mothers, which was completed via structured interviews with the mothers. The second part of the instrument included the patient information form regarding clinical symptoms, the results of tests, treatments, and the course of the disease. Part of the information recorded in this form was the results of the neonate's blood culture, which is carried out routinely for all neonates diagnosed with sepsis and which determined the type of bacteria causing the sepsis. Moreover, the results of other culture tests such as urine culture, cerebrospinal fluid culture, ocular secretions, and umbilical secretions, which were tested if needed, were recorded in this form. In case blood cultures or other cultures sent to the laboratory were positive (after 24, 48, and 96 hours), antibiotic sensitivity tests were performed on the samples too, and the sensitivity and resistance of the pathogen to commonly used antibiotics was investigated and reported. Based on the results of blood cultures, if gram-negative bacteria were in the blood, resistance to ciprofloxacin, amikacin, gentamycin, and ampicillin would be examined and if gram-positive bacteria were found in the blood, resistance to vancomycin, oxacillin, erythromycin, and ciprofloxacin would be investigated. Additionally, another part of the data recording form included blood index tests, such as CRP, Na, K, BS, CREA, BUN, ESR, Ca, CBC, etc, which were routinely carried out on the neonates and reported. The validity of the questionnaire and the data recording form was investigated and confirmed using the content validity method and by collecting the views of faculty members and neonatologists. After the hospitalization of a neonate and the confirmation of the diagnosis of sepsis by a neonatologist, the objectives of the study were explained to the mother and her consent was obtained. Next, the questionnaire was completed using interviews. The data recording form was gradually completed by studying the patient records during the period of hospitalization of the neonate. The collected data were analyzed using descriptive statistical tests, including frequency, mean, and percentage, and the chi-squared test. If needed, Fisher's exact test, and the independent t-test were also used.

Results

The studied neonates were mostly hospitalized in the neonatal ward (75.6%) and were mostly hospitalized during Autumn (37.1%). The other individual characteristics of the neonates are mentioned in Table 1. The mean and standard deviation of the ages of the mothers of the studied neonates were 27.38 ± 6.28 and their age range was 17-46. The mean and standard deviation of the ages of the fathers were 31.81 ± 5.88 with an age range of 21-48. No significant relationship was found between any of the familial characteristics and the positivity of the blood culture (Table 2).

Table 1: The frequency of the neonates suffering from sepsis based on the individual characteristics of the neonates

Individual characteristics		Number (Percentage)	BC+	Statistic and significance
Hospitalization ward	Neonatal unit	59 (75.6)	15 (93.75)	$X^2 = 3.74$
	NICU	19 (24.4)	1 (6.25)	P = 0.046
Time of hospitalization (in seasons)	Spring	13 (16.7)	3 (18.75)	$X^2 = 1.62$
	Summer	18 (23.1)	4 (25)	P = 0.65
	Autumn	29 (37.1)	4 (25)	
	Winter	18 (23.1)	5 (31.25)	
Sex	Male	44 (56.4)	9 (56.25)	$X^2 = 0.06$
	Female	34 (43.6)	7 (43.75)	P = 0.5
Birth order	1	45 (56.4)	7 (43.75)	$X^2 = 1.28$
	2	23 (29.5)	9 (56.52)	P = 0.19
	3	10 (12.8)		
Embryonic age (in weeks)	Pre-term (less than 38 weeks)	26 (33.3)	3 (18.75)	$X^2 = 2.54$ P = 0.09
	Term (38-40)	45 (57.7)	13 (81.25)	
	41-42	7 (9)		
Birth weight	Less than 2800 g	31 (39.7)	5 (31.25)	$X^2 = 0.44$
	2800 – 4000 g	45 (57.7)	11 (68.75)	P = 0.36
	More than 4000 g	2 (2.6)		
Weight at admission	Less than 2800 g	17 (21.8)	1 (6.25)	$X^2 = 2.56$
	2800 – 4000 g	48 (61.5)	15 (93.75)	P = 0.1
	More than 4000 g	13 (16.7)		
Postnatal age (in days)	3 days or less	15 (20.5)	4 (25)	$X^2 = 0.25$
	More than 3 days	58 (79.5)	12 (75)	P = 0.62
Exposure to second-hand smoke after birth	Yes	26 (33.3)	8 (50)	$X^2 = 2.26$
	No	52 (66.7)	8 (50)	P = 0.12
The use of antibiotics before admission	Yes	9 (11.5)	2 (12.5)	$X^2 = 0.7$
	No	69 (88.5)	15 (87.5)	P = 0.65

51.3% of the mothers had a history of antibiotic use during pregnancy. The other characteristics of the pregnant mothers are mentioned in Table 3. In 60.3 percent of the cases, the type of delivery was cesarean section and 13.9% of the mothers underwent prolonged labor. Fisher's exact test did not show any significant relationships between any of the characteristics of childbirth with the positivity of the blood cultures (Table 4). Table 5 shows the most common clinical symptoms with which the neonates presented. Fisher's exact test showed a significant relationship only between respiratory distress and the positivity of the blood culture (X2 = 5.29, P = 0.02). No significant relationship was found between icterus (X2 = 1.93, P = 0.15) and restlessness (X2 = 0.45, P = 0.36) with the positivity of the blood culture. The range of the time needed for the improvement and resolution of symptoms was 1-12 days and the mean and standard deviation for this resolution were 7.35 ± 2.93.

Table 2: The frequency of the studied neonates based on familial characteristics

Familial characteristics		Number (Percentage)	BC+
Mother's age (in years)	Less than 20	10 (12.8)	2 (12.5)
	21-35	56 (71.8)	11 (58.75)
	More than 35	12 (15.4)	3 (18.75)
Father's age (in years)	21-30	38 (48.7)	9 (66/3)
	31-40	34 (43/6)	6 (37.5)
	≥ 41	6 (7.7)	1 (6.2)
Mother's education	Illiterate	5 (6.4)	0
	Primary school – junior high school	14 (17.9)	4 (25)
	High school – High school diploma	43 (55.1)	10 (62.5)
	University	16 (20.6)	2 (12.5)
Father's education	Illiterate	7 (9)	3 (18.8)
	Primary school – junior high school	11 (14.11)	4 (25)
	High school – High school diploma	36 (46.2)	8 (56.2)
	University	24 (30.7)	0
Mother's job	Housewife	69 (88.4)	15 (93.8)
	Employee	7 (9)	0
	Self-employed	2 (2.6)	1 (6.2)
Father's job	Employee	21 (27)	2 (12.5)
	Self-employed	48 (61.5)	11 (68.8)
	Farmer	3 (3.8)	2 (12.5)
	Unemployed	6 (7.7)	1 (6.2)
Place of residence	Urban areas	56 (71.8)	12 (75)
	Rural areas	22 (28.2)	4 (25)

Table 3: The frequency of the participants based on the characteristics of the pregnancy

Characteristics of the pregnancy		Number (Percentage)	BC+	Statistics and significance level
Problems during pregnancy	Amniotic sac rupture	12 (15.2)	3 (27.3)	$X^2 = 0.22$ P = 0.45
	Urinary tract infections	22 (30.1)	8 (36.4)	$X^2 = 3.84$ P = 0.05
	Hypertension	7 (8.8)	2 (12.5)	$X^2 = 1.03$ P = 0.3
	Vaginal secretions	15 (19)	4 (28.6)	$X^2 = 0.45$ P = 0.36
	Edema	2 (2.5)	-	-
	Spotting	2 (2.5)	-	-
	Diabetes	5 (6.4)	-	-
	No problems	26 (32.9)	1 (4.2)	$X^2 = 6.6$ P = 0.008
The place where pregnancy care was received	Clinics and health centers	36 (46.2)	11 (68.75)	$X^2 = 9.68$ P = 0.08
	Midwife's office	4 (5.1)	2 (12.5)	
	Specialist's office	10 (12.8)	-	
	More than one of the above-mentioned places	28 (35.9)	3 (18.75)	
Having a history of antibiotic use during pregnancy	No	38 (48.7)	5 (31.2)	$X^2 = 2.30$ P = 0.11
	Yes	40 (51.3)	11 (68.8)	

Table 4: The frequency of the subjects based on the characteristics of the delivery

The characteristics of the delivery		Number (Percentage)	BC+	Statistic and significant level
Type of delivery	Natural	31 (39.7)	9 (56.2)	X^2 = 1.28
	Cesarean section	47 (60.3)	7 (43.8)	P = 0.2
Person in charge of delivery	Obstetrician-gynecologist	51 (65.4)	8 (50)	X^2 = 1.50 P = 0.18
	Midwife	27 (34.6)	8 (50)	
Place of delivery	Hospital	77 (98.7)	16 (100)	-
	Home	1 (1.3)	-	-
Problems during childbirth	No problems	59 (74.7)	11 (19.6)	X^2 = 0.73 P = 0.29
	Hypoxia	8 (10.1)	3 (37.5)	X^2 = 1.30 P = 0.24
	Prolonged labor	11 (13.9)	2 (22.2)	X^2 = 0.001 P = 0.64
	Placenta previa	1 (1.3)	-	-

Table 5: The frequency of the participants based on clinical symptoms at presentation

Clinical symptoms	Number (Percentage)	BC+ Number (Percentage)
Poor feeding	13 (17.7)	2 (13.5)
Icterus	12 (16.4)	5 (31.25)
Fever	13 (17.7)	2 (13.5)
Respiratory distress	13 (17.7)	6 (37.5)
Lethargy	12 (15.2)	-
Restlessness	13 (17.7)	4 (25)
Diminished reflexes	1 (1.13)	-
Seizure	3 (3.8)	-
Vomiting	2 (2.5)	2 (13.5)
Distension	2 (2.5)	-
Purulent pustule	2 (2.5)	-
Petechiae and purpura	1 (1.3)	1 (6.25)
Hepatomegaly	3 (3.8)	-
Splenomegaly	1 (1.3)	-
Oral thrush	1 (1.3)	-
Smelly urine	1 (1.3)	-
Ocular secretions	3 (3.8)	1 (6.25)
Umbilical secretions	2 (2.5)	1 (6.25)
Perianal abscess	1 (1.3)	1 (6.25)
Knee joint swelling	1 (1.3)	-
Thigh ulcers and burns	1 (1.3)	1 (6.25)
Ichthyosis	1 (1.3)	1 (6.25)

In the studied neonates, the result of the ESR test was higher than 10 in 55.4% of the cases. The frequency of the participants based on blood test results are presented in Table 6. The time range for the improvement and normalization of laboratory values was 1-13 days and the mean and standard deviation for this time were 7.17 ± 2.94 days. The range for hospital stay was 4-34 days and the mean and standard deviation for hospital stay were 12.19 ± 6.89 days.

Table 6: The frequency of the participants based on blood test results

Test results			BC+	Statistic and Significance
ESR	< 10	29 (44.6)	7 (50)	$X^2 = 0.005$
	≥ 10	36 (55.4)	7 (50)	P = 0.94
WBC	4000 – 11000	53 (67.9)	7 (43.8)	$X^2 = 4.43$
	> 11000	25 (32.1)	9 (56.2)	P = 0.036
Platelet count	< 150000	11 (14.9)	1	$X^2 = 3.06$
	150000-450000	45 (60.8)	9 (56.2)	P = 0.08
	> 450000	18 (24.3)	7 (43.8)	
HB	< 10	22 (29.7)	5 (31.25)	$X^2 = 4.92$
	10-14	28 (37.8)	3 (18.75)	P = 0.17
	14-16	13 (17.6)	5 (31.25)	
	> 16	11 (14.9)	3 (18.75)	
BS	≤ 45	1 (1.3)	-	-
	> 45	77 (88.7)	16 (100)	
Cα	< 8	0(0)	-	-
	8-11	78 (100)	16 (100)	
CRP	Negative	47 (60.3)	14 (87.5)	$X^2 = 6.34$
	1+	12 (15.4)	2 (12.5)	P = 0.02
	2+	15 (19.2)		
	3+	4 (5.1)		

Results of blood and urine cultures in the studied neonates are shown in Table 7. CSF cultures were performed in 3 cases, the results of all being negative. Umbilical discharge cultures were performed in 2 cases. The result of one of them was negative, and the pathogen found in the other culture was Pseudomonas. In one case, wound discharge culture was positive, and the discovered pathogen was Staphylococcus aureus. Ocular discharge cultures were performed in 6 cases. In 2 cases, the results were negative; in one case, the pathogen was gram-positive cocci; and in 3 cases, the discovered pathogen was Staphylococcus epidermidis. In one case, Candida albicans was found in both blood culture and urine culture. Therefore, this neonate was removed from the samples and all calculations and statistical tests were performed on 78 neonates.

Table 7: The frequency of the subjects based on the results of blood and urine cultures

Culture type		Number (Percentage)
Blood	Not performed	5 (6.5)
	Negative	56 (72.7)
	Acinetobacter	6 (37.5)
	Staphylococcus epidermidis	6 (37.5)
	Staphylococcus aureus	2 (13.5)
	Citrobacter	1 (6.25)
	Moraxella catarrhalis	1 (6.25)
Urine	E. coli	3 (23)
	Enterobacter	3 (23)
	Klebsiella	1 (7.7)
	Citrobacter	1 (7.75)
	Pseudomonas	2 (15.4)
	Acinetobacter	1 (7.75)
	Staphylococcus aureus	2 (15.4)

The most frequently administered antibiotics to the studied neonates are listed in Table 8.

Table 9 (page 102) presents the comparisons of the means of some quantitative variables related to the neonates suffering from sepsis based on the results of the blood cultures. From among these variables, only the length of hospital stay showed a significant difference between the two groups.

Table 8: The frequency of the participants based on the administered medicines

Administered medicine	Number (Percentage)
Ampicillin	56 (71.8)
Cefotaxime	63 (79.7)
Vancomycin	50 (63.3)
Amikacin	22 (27.8)
Meropenem	21 (26.6)
Erythromycin	9 (11.4)
Gentamycin	3 (3.8)
Mupirocin	8 (10.3)
Ciprofloxacin ophthalmic solution	8 (10.1)
Cefepime	2 (2.5)
Glucosaciline	2 (2.5)
Acyclovir	2 (2.5)
Ceftazidime	1 (1.3)
Tozacin	4 (5.2)
Metronidazole	1 (1.3)
Fluconazole	1 (1.3)
IVIG	2 (2.5)
Ranitidine	3 (3.8)
Levothyroxine	1 (1.3)
Phenobarbital	6 (7.6)
Hydrocortisone	4 (5.2)

Discussion

The results showed that blood cultures were positive only in one fifth of the hospitalized neonates. Gram-negative bacteria, especially Acinetobacter, Citrobacter, and Moraxella catarrhalis, and gram-positive bacteria, particularly Staphylococcus epidermidis and Staphylococcus aureus, in equal proportions, were the pathogens causing sepsis in the neonates. Infections caused by these pathogens are mostly common opportunistic and hospital-acquired infections, which are transmitted by hospital staff, family members, and contaminated instruments, like venous catheters, etc. Additionally, in the present study, late-onset sepsis was more common. In late-onset sepsis, frequently organisms acquired from the hospital and the community are involved [11]. The results of the study by Movahedian also showed that only 11 percent of neonatal blood cultures were positive [12], However, in another study, the prevalence of neonatal sepsis was 7 percent and the most common bacterial pathogen causing sepsis was group B Streptococcus[13]. Additionally, in a study by Mojtabaei and et al., the most common pathogens causing gram-negative sepsis among neonates and infants were E. coli (46%), and Klebsiella (27%) [13], and the findings of Fallahi et al. showed that among neonates with suspected sepsis, 8 cases (10.5%) had positive blood cultures. In 5 cases (62.5%), coagulase-negative Staphylococcus was responsible for the infection. Escherichia coli, Moraxella, and Pseudomonas aeruginosa were identified in the remaining blood cultures, each bacteria accounting for one positive blood culture (12.5%) [14]. Therefore, our study is largely consistent with the results reported in previous studies regarding the percentage of the positivity of the blood cultures. The high percentage of negative blood cultures in neonates having the symptoms of systemic infection and hospitalized with a diagnosis of sepsis can be due to two factors. First, to improve the processing of microorganisms, taking 3 blood samples with adequate volume is recommended to avoid the dilution of the blood in the culture media [15]. However, due to the condition of the neonates and their blood volume, usually only one sample is taken, and this makes the isolation of the pathogen less likely. Secondly, the use of antibiotics before hospitalization and before the performance of culture tests affects the results of the cultures. However, the results of our study is different from most studies in terms of the types of pathogenic agents. One of the differences is the lower prevalence of Staphylococcus aureus in our study, while in other studies, it was one of the most prevalent. A notable point is the relatively high prevalence of Staphylococcus epidermidis in our study, which is only observed in hospital-acquired infections. Additionally, in the present study, no records were found of group B Streptococcus causing neonatal sepsis. In the developed countries, group B streptococcus is generally the most prevalent pathogen [16], and early-onset sepsis is more common [17]. Lack of reports regarding GBS infections in the neonates investigated by the present study could be due to lower levels of streptococcal infections in our society. Given the fact that most neonates were older than 3 days and late-onset sepsis was more common than early onset sepsis, this finding can be confirmed. Additionally, the lower prevalence rates of early-onset sepsis can be explained by the fact that almost half of the mothers took antibiotics during pregnancy. Studies have also shown that implementing prophylactic antibiotic treatment in the delivery room can considerably reduce the prevalence of

Table 9: The comparison of the mean of some variables related to the neonates suffering from sepsis based on the results of the blood cultures

Characteristics	BC-	BC+	
The age of the neonates (in days)	13.10 ± 48	13.17 ± 10.96	T = -0.42 P = 0.68 df = 71
Birth weight (Kg)	3.46 ± 851.54	3.58 ± 560.47	T= -0.64 P = 0.52 df = 71
Mother's age (in years)	27.53 ± 6.47	26.64 ± 6.04	T = -0.64 P = 0.52 df = 71
Gestational age (in weeks)	37.37 ± 2.24	38.52 ± 2.53	T = 1.12 P = 0.27 df = 71
Birth weight (Kg)	2.93 ± 706.582	3.09 ± 507.54	T = -0.63 P = 0.53 df = 71
ESR (ml/h)	25.56 ± 27.86	21.21 ± 22.92	T = -0.49 P = 0.62 df = 59
WBC (1000/mm³)	10.23 ± 4.18	10.27 ± 3.14	T = -0.73 P = 0.46 df = 71
Neutrophil (1000/mm³)	47.17 ± 18.16	50.15 ± 16.63	T = -0.23 P = 0.82 df = 60
Lymphocyte (1000/mm³)	50.85 ± 17.18	49.75 ± 16.63	T = -0.05 P = 0.96 df = 60
Platelet (1000/mm³)	336 ± 8.535	432 ± 10.996	T = -0.37 P = 0.71 df = 67
BS (mg/dl)	85.24 ± 28.64	73.25 ± 21.11	T = -0.371 P = 0.17 df =64
Ca (mg/dl)	9.61 ± 0.65	9.28 ± 0.69	T = -0.691 P = 0.09 df = 64
Urea	29.66 ± 17.23	26.13 ± 8.28	T = -0.64 P = 0.52 df = 71
The period of time during which clinical symptoms resolved (in days)	6.98 ± 2.78	7.8 ± 3.34	T = 1.10 P = 0.28 df = 65
The period of time during which laboratory markers resolved (in days)	7.07 ± 2.91	6.66 ± 3.77	T = -0.36 P = 0.72 df = 65
Hospital stay (in days)	11.53 ± 6.84	15.65 ± 6.64	T = 2.11 P = 0.04 df = 70

early-onset sepsis caused by GBS [18]. The absence of GBS infection cases could also be attributed to technical and laboratory faults. A study by Maamouri (2013) found that group B Streptococcus grew in none of the ordinary and enhanced culture media and 64 percent of the mothers of the neonates suffering from sepsis had received antibiotics before childbirth [18]. Since in the conventional culture method, the chances of isolating microorganisms decreases, and since the administration of antibiotics before the culture test reduces the opportunity to grow bacteria in the conventional method, the use of newer and faster systems for blood culture like the BACTEC method and the use of more sensitive methods like enhanced blood culture and molecular studies with the PCR test alongside the conventional method have been recommended to achieve faster and more accurate diagnoses, so that treatment starts in time and antibiotics are not administered without adequate evidence [19]. The main causes of neonatal sepsis vary in different geographical regions. The bacterial etiology varies from community to community and from hospital to hospital. The reason for the differences in the reported prevalence rates can be due to differences in the studied environments, differences in the research methods, different criteria used for the diagnosis of sepsis, different culture methods, different sampling methods, and the administration of antibiotics to the mothers and the neonates. Given the fact that sepsis pathogens were mostly opportunistic and hospital-acquired in the present study, being acquired from the hospital or the community, improving the hygiene of maternity and neonatal wards and training mothers and the nursing staff can help prevent the spread of this disease. To prevent late-onset hospital acquired infections, strategies like improvements in hand hygiene, early breastfeeding, meticulous skin care, limited use of invasive procedures, minimizing manipulations when the use of such procedures is required, and the standardization of methods of venipuncture and management of intravenous catheters can be helpful. Additionally, designing the environment so that personal care instrument hygiene is optimized and increasing the number of staff can reduce the chances of transmission of hospital-acquired infections [20]. Moreover, due to the higher prevalence rates of late-onset sepsis in the present study, many microorganisms, such as viruses, fungi, and anaerobic bacteria, which play a role in the development of late-onset sepsis gain importance, because these pathogens can produce clinical symptoms similar to bacterial sepsis [21]. These pathogens were not investigated in the present study, and therefore it is likely that they played a role in the development of sepsis in the studied population.

In the present study, the clinical symptoms of respiratory distress, jaundice, fever, and poor feeding were more common. However, among the clinical symptoms, only respiratory distress showed a significant relationship with the positivity of the blood culture. In the majority of the studies, clinical symptoms of the respiratory tract in the form of respiratory distress were more common [22]. The occurrence of respiratory distress, including tachypnea, nasal flaring, grunting, and intercostal retraction, could

be the only clinical symptom of sepsis with or without pneumonia [23].

In the present study, in the majority of the cases where blood culture was positive, the CRP test was negative. This could be attributed to quick referral after the beginning of the symptoms and the performance of the blood culture in the early stages of the disease, and because the CRP index is a delayed index in inflammatory diseases, its values were reported to be negative in most neonates. In the present study, no significant relationship was found between the values of ESR and the positivity of the blood cultures. Studies have shown that even though ESR, WBC, and CRP are used to diagnose bacterial infections and sepsis, they lack diagnostic accuracy, especially CRP, which is less accurate during the early stages of the disease [24]. In the present study, about one third of the studied neonates had a gestational age of less than 38 weeks, and the majority of them had been born by caesarian section. In the study by Shah Ali et al., the most common underlying factor was preterm birth with a prevalence of 10.2% [25]. In the study by Rafati too, out of the 100 studied neonates, 86 were born by caesarian section and 14 had undergone vaginal birth [26]. The findings of a study by Bailit et al. (2010) showed that as the pregnancy age increases week by week and approaches 39 weeks, when the pregnancy is ended by caesarian section, the prevalence of sepsis is reduced and this should be kept in mind in cases of elective caesarian section [27]. In the present study, from among maternal risk factors, only a history of maternal urinary tract infections during pregnancy showed a significant relationship with the positivity of the blood culture. Neonates, whose mothers did not have any of the risk factors of the pregnancy period, were much less likely to have positive blood cultures. Perinatal and prenatal data can be used to assess risks and as guidelines for action in the delivery room during childbirth and during infancy to make the most appropriate decisions [10].

In the present study, 14.30% of the cases had positive urine cultures, E. coli and other intestinal bacteria being the most common pathogens. However, in no cases, both blood culture and urine culture became positive simultaneously. In the study by Mojtabaei, it was reported that urinary tract infections accompany sepsis in 10.5% of the cases. Additionally, some of the neonates showed symptoms of skin and epithelial infections, such as omphalitis, conjunctivitis, and purulent wounds. In the study by Mojtabaei, too, in 40% of the cases there were symptoms of localized infections, urinary tract infections being the most common [28]. Therefore, given the fact that the clinical symptoms of various neonatal infections appear to be similar, and given that sometimes advanced laboratory equipment is not available, in case sepsis is suspected, it is necessary to investigate the origins of the infection and start treatment measures for the patient. Despite repeated follow-ups, in the majority of the cases, one of the limitations of this study was that, in cases where the blood cultures were positive, antibiotic sensitivity test results (antibiograms) were not included in the patient medical records and the resistance of the

sepsis-causing bacterial pathogens to antibiotics could not be investigated. Moreover, it is obvious that the results of the present study are limited to the studied population and cannot be generalized to the whole city and further studies are needed with larger numbers of participants.

Conclusion

In this study, gram-positive and gram-negative bacteria were responsible for the positivity of the blood cultures in equal proportions. However, in the case of urine culture, enteric gram-negative bacteria, especially the Enterobacteriaceae family were the most commonly found pathogens. Confirmed sepsis was more common among neonates with respiratory distress, white blood cell counts of higher than 11,000, and a maternal history of urinary tract infections. This disease was much less common among neonates who had none of the risk factors of the pregnancy period. These points provide appropriate strategies for fighting the microorganisms causing neonatal sepsis by proper and on-time prescription and administration of antibiotics to prevent antibiotic resistance. Furthermore, it seems that the laboratory tests that are currently used to diagnose sepsis are not fast and accurate enough and require a review.

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The First Digital Immunization Registry for Healthcare Workers in Iran

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Abstract

Background: Health care workers (HCW) are often occupationally exposed to vaccine-preventable diseases. Proper vaccination practices can be highly protective. Yet, healthcare systems ability to ensure vaccination registry accuracy is debatable. Creation of an effective electronic immunization registry system (EIRS) could help overcome this concern. The aim of this study was to develop the first EIRS for use in Namazi Hospital, Shiraz, Iran.

Materials and Methods: A flowchart was designed for each occupationally related vaccine which included decision paths regarding proper immunization. Then, information collection forms were designed based on the flowcharts. After verifying the validity of the paper forms, EIRS data forms were created.

Results: An important result of this study was the development of an EIRS for hospital HCW which is a crucial step in the promotion of a comprehensive vaccination program. An effective and reliable registry could help reduce the chances of occupational disease transmission.

Conclusion: EIRS are more efficient than pencil-and-paper data collection methods and can provide reliable information concerning immunization processes. Other benefits include valid estimations of vaccination coverage rates, development of reminder-and-recall systems that improve vaccine coverage and investigations of factors related to vaccination failure.

Key words: registry, vaccination, hospital, healthcare workers

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Introduction

Proper vaccination is strongly recommended to improve occupational safety and health of healthcare workers (HCW). (1-4) HCW are exposed to a variety of occupational hazards, including infectious disease agents. Vaccination can reduce the risk of some occupational infections, prevent healthcare acquired infections (HAI) and maintain healthcare delivery during outbreaks.

Optimal application of recommended vaccines protects HCW against vaccine-preventable diseases (VPD). Examples include influenza, hepatitis B, rubella, measles, varicella, mumps, diphtheria, tetanus and pertussis. Serious outbreaks of VPD among vulnerable hospitalized patients have been traced to infected HCW. (3-5)

Correct implementation of HCW immunization policies is a crucial step toward reducing healthcare associated infections (HAI) and providing protection for HCW and vulnerable patients. (1)

Several major sets of HCW immunization guidelines have been issued worldwide. (4-8) A study conducted among 30 European countries investigated national HCW occupational vaccine policies. Results indicated each country had specific policies for vaccinating HCW. However, some differences existed concerning the number of recommended vaccines and the target groups involved. (4)

Most countries include influenza and hepatitis B vaccines as part of their HCW vaccination strategy; however, use of vaccines against measles, rubella, varicella mumps, diphtheria, tetanus, anthrax, poliomyelitis, hepatitis A, tuberculosis and Group A meningococcus varied. (4,9-16) HCW immunization not only protects workers and their families, but also vulnerable patients. (1) While countries have different vaccination policies, reports suggest HCW immunity coverage against VPD is often inadequate. (1,6,7,17)

Countries employ different registration methods to determine vaccination status. Performance of healthcare systems concerning the accuracy of their registries has been called into question. (18) Perhaps, an electronic immunization registry system (EIRS) could improve monitoring. (18-21) Investigations indicate traditional methods, such as handwritten charts, vaccination cards and parent reports are not as useful, effective and reliable as EIRS. (18,22,23)   EIRS can be an effective source for healthcare center management and staff to access immunity information and generation of accurate analyses. (18) Planning supported by EIRS can improve immunization coverage, including better recall/reminder schemes. (18,24,25)

EIRS can help study vaccine effectiveness through integration and comparison of data relating to HCW vaccination records, VPD experiences and possible vaccine failures. (21) Also, EIRS can be used to update immunization information.

Canada has established a national EIRS that has become a major component of its immunization promotion program. However, Lorache et al. suggested that despite improvements, comprehensive implementation of the registry project has not occurred. Manual and traditional vaccination data registry techniques have not been widely replaced by EIRS. (25)

Several types of registries currently are used worldwide. For example, Australia and United States have implemented efficient and useful EIRS. Much of this is designed to help achieve Centers for Disease Control and Prevention (CDC) goals concerning HAI prevention. (21,26)

EIRS have the potential to provide accurate data over time and gradually have turned into a powerful information bank for research and policy planning. Unfortunately, EIRS problems have occurred during data collection and identification of demographic and/or socioeconomic factors. (21,27)

In 2009, the Vietnam National Institute of Hygiene and Epidemiology established a National Expanded Program on Immunization which reported an elevated resource burden associated with their manual data registry. (28) This resulted in delayed submission of reports and sometimes inaccurate data. In 2012, Vietnam implemented a pilot EIRS in one southern province and then conducted efficiency studies. Investigated was the rate of timely delivery of pentavalent and BCG vaccines to children before and after implementation. Substantial increases in the rate of vaccination after EIRS use were noted, suggesting a potential for accurate data recording and reminding individuals to be vaccinated. Successful pilot data led the Vietnam Ministry of Health to expand its EIRS system to other areas of the country. (28)

Since 1997, all 50 American states have implemented EIRS; however, efficiency varied. (29) The EIRS in the State of Wisconsin collects a variety of vaccine-related information on children and adults. Important outcomes included faster and better physician access to patient vaccination records, implementation of a reminder system for multi-dose vaccines and increases in vaccination coverage. The Wisconsin EIRS records vaccine type, trade name, manufacturer, serial lot number, vaccination date and any vaccine contraindications and side-effects. CDC considers the Wisconsin EIRS as a model program, recommending it tenets to other states. (29)

Similar reports have pointed out EIRS data can be used in vaccine effectiveness and coverage studies. The system also increased the accuracy and reliability of vaccination data. (30,31)

A 2010 Stockholm conference supported implementation of extended EIRS use throughout Europe to help increase distribution of immunization data. It also requested the vaccine industry to implement a standardized system for bar coding vaccines to better facilitate recording of each vaccine dose. (32) World Health Organization (WHO) lent support to the conference and established a goal that at

least 65% of European children and hopefully other age groups will be covered by an EIRS by 2020. In 1990, Denmark implemented its first immunization registry to record child vaccination data. The aim was to estimate vaccination coverage and conduct vaccine safety and effectiveness studies. In 2008, Denmark's EIRS was upgraded to provide vaccine coverage information and access to vaccination data from all citizens by healthcare personnel. In 2015, these data were used to set up a vaccination reminder system for people with incomplete vaccination histories. Australia, Canada, United Kingdom, Denmark, Italy, Netherlands, Norway and Spain have established effective EIRS programs. (32)

No EIRS currently exists in Iran to collect immunization data. Aims of this study were to develop the first EIRS in Namazi Hospital and to investigate the possibility of extending the program further.

Methods

Phase One
All recorded data came from Namazi Hospital personnel. Exclusion criterion was an unwillingness to be vaccinated. Using a simple sampling method, 50 HCW referred to the hospital's Infection Prevention Clinic were chosen for the first phase of the project.

Software development began with the creation of a paper data collection form. Current HCW occupational vaccination histories were compiled based on WHO, CDC and Iranian national guidelines.

Based on the data collected, specific flowcharts for 10 VPDs were designed. Each flow chart is related to a specific vaccine and was designed by a step-by-step review of current studies, essays, and textbooks and WHO, CDC and Iranian national guidelines, so that the flowchart showed a holistic view of vaccine administration pathways. In fact, they described sequences of events from the arrival of HCW to vaccination decision and follow-up. (2, 4, 33, 34).

Paper data collecting forms then were prepared based on the flowcharts. Forms contained demographic information, workplace position and vaccination information. Forms for each vaccine were prepared and contained information concerning previous immunization , such as disease history, vaccination date(s), allergic responses, side effects and contraindications. Based on responses collected, a determination of vaccine need was made. Forms were given to a group of specialists for verification.

Phase Two
Information was entered electronically using specially designed software. All components of the vaccination process (pathway steps) were evaluated by entering paper form data again and resolving any conflicts. This established software operational precision. After implementation of the electronic registry, all vaccine-related HCW information could be extracted and analyzed statistically.

Results

This study created and evaluated immunization registry software for HCW which can promote vaccination rates and improve infection prevention and control. EIRS is a reliable source of recorded immunization data, capable of replacing paper reporting forms.

As a result, when a HCW was referred to the Center for vaccination evaluation, an initial page containing demographic information is displayed and all related information (e.g., age, sex, education and workplace) is entered (Figure 1). Then, required vaccines appear in 10 separate folders. By entering each folder and following existing options and questions in each folder, users can determine whether a given vaccine is required and records the result in the system (Figures 2-4). Then, a table including all necessary vaccines along with injection dates is printed and given to the HCW to complete his/her vaccination at the specified time. Included is information related to each vaccine (e.g., vaccine name, administration method, place, vaccine serial number, manufacturer country and possible side-effects). Vaccinator information is entered on a separate page.

HCW will have a file with his/her corresponding personal code which contains information on vaccines already administered or need to be given. This information is accessible online. EIRS can provide HCW with a printed vaccination card, documenting immunization status.

Our EIRS has the potential for drawing tables and diagrams (Figures 5 & 6), comparing different information (Tables 1 & 2), estimating the number of vaccines required over time and other statistical analyses. This is a unique capability, rarely found in other similar software.

Figure 1: Example HCW information file

Figure 2: Influenza vaccine file
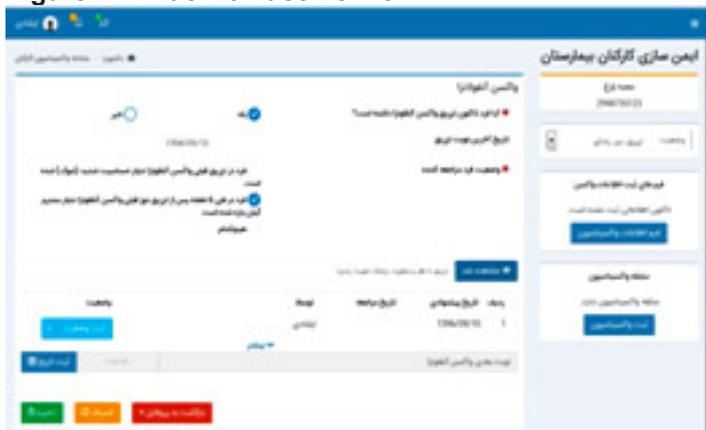
Figure 3. Td vaccine file
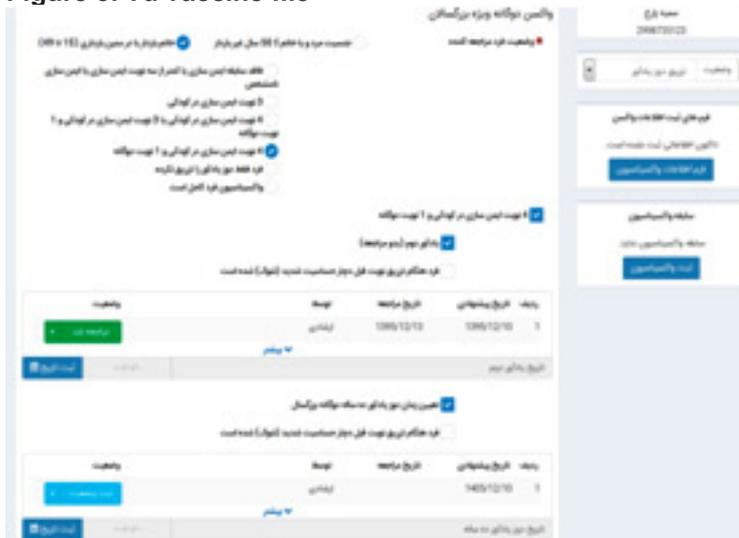
Figure 4: Hepatitis B vaccine files
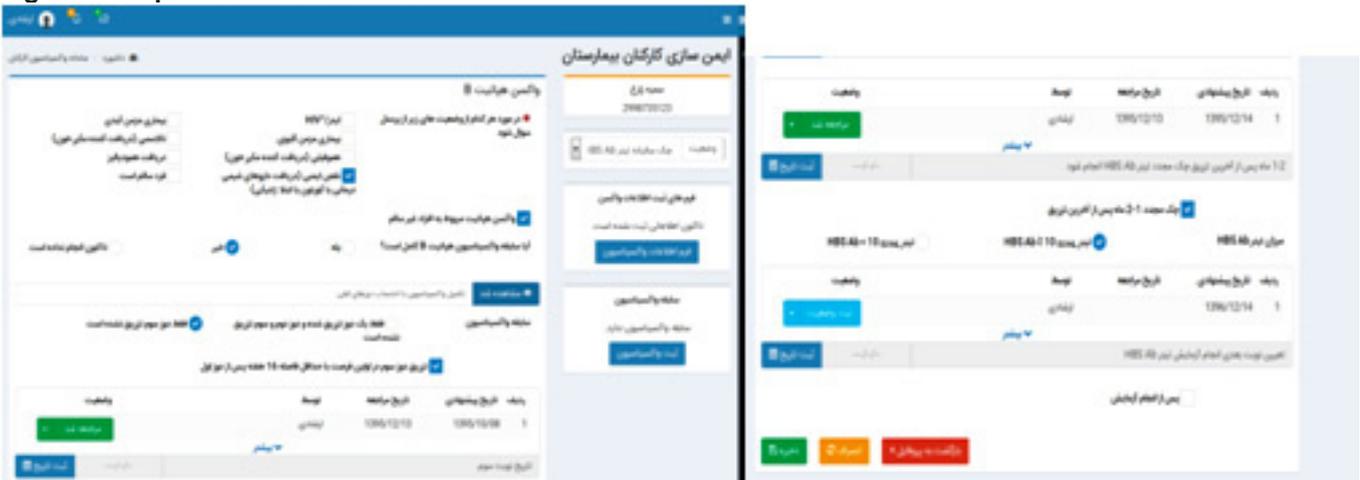
Figure 5. Declination to influenza vaccine based on educational level
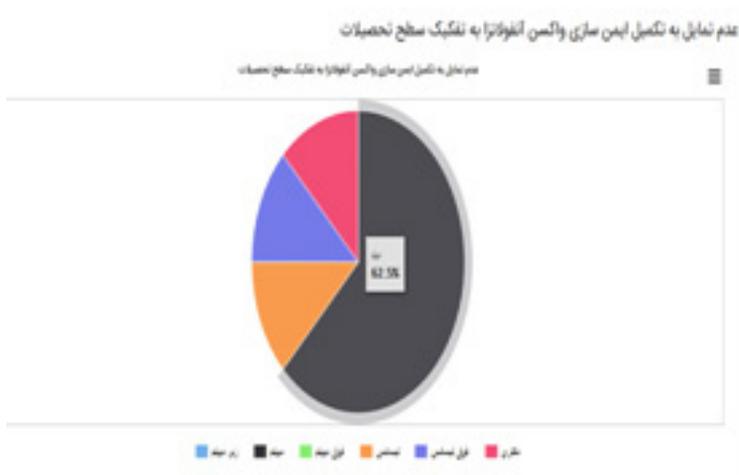
Figure 6. Influenza vaccine coverage

Table 1: General information of influenza vaccination based on sex

Table 2: The vaccination coverage status based on educational level

Discussion

To improve hospital infection prevention and control program, especially HCW occupational safety and health, vaccination is strongly recommended for all susceptible individuals. Universal HCW coverage also protects high-risk hospitalized patients, HCW families and the local community.

EIRS help HCW receive all needed vaccines, properly. Timely immunization and post-vaccination follow-up are essential requirements. (34) Electronic data collection and storage also improves precision, accuracy and reliability of information. Manual data handling is slower and less accurate when compared to digital registries. (35)

For the first time in Iran, comprehensive immunization registry software was developed and implemented with an analytic capacity to evaluate HCW vaccine-related information. It began as a pilot project in Namazi Hospital in Shiraz.

Our EIRS possesses several valuable capabilities. Electronic files for any HCW are easily accessible through individual identifying codes and can help decide which immunizations are needed. Accurate information will help avoid missing an injection, maintain timely vaccine schedules, revaccination when not needed, identify possible side-effects and reduce costs.

An electronic registry will help hospitals estimate the number of vaccine doses needed over a given period and better assure adequate supplies. The registry was developed in such a way that it will increase vaccine coverage and equipped with a reminder messaging system.

Also, reports can be made for individuals, groups, any number of vaccines or even total coverage. Such reports help hospital employee safety and health committees to make informed decisions.

During hospital disease outbreaks, possible vaccine failures can be identified by comparing incidence rates with HCW immunization records using registry software.

Plausible causes of failure could be studied based on information recorded in the system. Registry information also can be used as a reliable source in cohort studies in the future.

Objectives of the prepared software are like those of other registries. A 2014 systematic review indicated that electronic immunization registries can increase vaccination coverage. (36) Specifically, better registries: 1) have "client reminder and recall systems;" 2) can generate and evaluate public health responses to outbreaks of VPD; 3) facilitate vaccine management and accountability; 4) can determine HCW vaccination status, helping make proper decisions and 5) can aid outbreak surveillance, including HCW vaccination rates, missed vaccination opportunities, invalid dose administration and disparities in vaccination coverage.

Immunization registries can provide surveillance information or support specific investigations of changes, trends or gaps in vaccination coverage. In such cases, registries can provide information for decision makers when planning and/or implementing additional interventions. (36)

Goals for the registry system implemented in Vietnam were to increase accuracy and timeliness of immunization records, improving the rate of on-time immunization and reduce the amount of time needed for reporting. (28)

Like the other registries, our software's aim was to promote standards and facilitate sharing of vaccination information. The Canadian registry system is the major tool to evaluate vaccination status, facilitating accurate data collection and assessing and improving immunization rates. (25) The Wisconsin registry system provided physician access to vaccination records and immunization status of their patients, enhancing proper decision making and patient interaction. (29) Such capabilities were designed into our software.

Mahon et al. investigated the role of digital registries in vaccine effectiveness and suggested that registry-based studies on vaccine effectiveness possess advantages compared to traditional observational studies. Registries provide better access to comprehensive immunization data of a population enabling more extensive cohort studies with fewer errors compared to case-control studies. This is especially valid in communities with lower incidence rates of VPD because if an epidemic occurs, it may involve underestimation of vaccine effectiveness. However, vaccine effectiveness studies should not be conducted during an epidemic because this may affect correct estimations of effectiveness. Comprehensive access to accurate immunization data in a registry may avoid errors caused by immunization differences between healthy and ill individuals. (31)

Conclusion

We established the first web-based Iranian immunization registry software for HCW which could be valuable for on-time registration, promoting immunization rates, accurate

data registering and subsequently HAI prevention and control. Also, it is available as a source of recorded immunization data. The analytic capability of our EIRS is unique and the comprehensive capabilities of this software can help health providers adopt better procedures, compare coverage of immunization at the national level and finally managers implement better policies.

Limitations

As a pilot project only 50 HCW were involved. There were difficulties obtaining complete vaccination histories and designing registry software and establishing policies for transfer of information from paper forms to the electronic registry.

Despite experiencing challenges, we designed and developed a digital immunization registry for HCW in Iran for the first time. It been implemented in Namazi Hospital in Shiraz; however, the hope is that it could be used by more Iranian hospitals which would require the support of local and national healthcare officials.

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Post-Exposure Procedures including Prophylaxis: First National Electronic Registry for Iran

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Abstract

Background: An estimated 385,000 percutaneous injuries (e.g., needlesticks, cuts, punctures and other sharp object injuries) occur in United States hospitals each year. Prevention of occupational transmission of bloodborne pathogens requires a diversified approach. This includes reduced exposure to blood and other patient body fluids and prevention of percutaneous injuries through improved engineering controls, work practices and use of personal protective equipment.

Over the last decade, use of electronic data capture systems and devices (EDCSD) has increased, replacing pen-and-paper methods traditionally used during field survey data collection. By combining data collection with data input, EDCSD can lower costs through better data management. Paper-based medical records can be incomplete, lost and difficult to read. Conversely, EDCSD can rapidly retrieve any number of entries; providing up-to-date, accurate information which can be easily shared anywhere in the world.

Method: This study describes the launching of a system that measures exposure to patient blood and body fluids including sharps injuries. The target population was individuals working in Namazi Hospital, Shiraz, Iran. First, a flowchart was created describing movement of data concerning 200 exposed hospital personnel referred to the Infection Control Section of Namazi Hospital from paper forms to an electronic format. The flowchart system was a modification of several mentioned in the published literature. Associated software was designed by hospital computer engineers. The 200 paper forms were used to pilot the new post-exposure registry system.

Results: The aim of this study was to build, launch and evaluate a registry system for recording cases of worker exposure to patient blood and body fluids including sharp (needlesticks) injuries and to monitor post-exposure prophylaxis and follow-up procedures.

Conclusion: Using a coordinated and comprehensive system on a provincial or national level could provide opportunities to compare the performance of the Infection Control Sections in different hospitals concerning causes of occupational exposure and post-exposure procedures, including prophylaxis. Such information could be useful in policy-making processes.

Key words: healthcare workers, sharps injuries, occupational hazards, occupational acquired infections

Methodology

The risk of occupational exposure of healthcare workers (HCW) to bloodborne pathogens, such as hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) through sharps-related injuries, such as needlestick injuries (NSI), especially concerning dental, nursing and midwifery students, is a challenging issue. (1)

HBV, HCV, and HIV account for 37%, 39% and 4% of the infections transmitted through contact with contaminated sharps. (2,3) The risk for transmission after all types of occupational exposure of at-risk HCW is between 30%-60% for HBV, 3-4% for HCV and 0.3% for HIV. (4)

Approximately 64% of healthcare workers are exposed to patient blood or other body fluids during their professional careers. (5). Nurses are the most likely healthcare group to experience a sharps injury. (6,7,8)

Many reasons have been postulated for the occurrence of NSI, including lack of experience, insufficient training, work load, time of day, procedures performed and fatigue. (9) Providing HCW with devices with engineered sharps injury prevention features can reduce exposure. Such devices have built-in safety features or mechanisms that effectively reduce the risk of an exposure incident. Examples include needle-free IV systems, sheathed, blunted or retractable needles syringes with guards or sliding sheaths that shield the attached needle after use, needles that retract into a syringe and blood transfer adapters. (10,11)

The risk of bloodborne pathogens transmission following occupational exposure depends on a variety of factors including source patient characteristics (i.e., viral titer), nature of the injury, quantity of blood/body fluid transferred during the exposure and HCW immune status. The greatest risk of infection transmission occurs through percutaneous routes. However, HBV, HCV and HIV transmission after mucous membrane or non-intact skin exposure has also been reported; however, mucocutaneous exposure is considered to have lower levels of risk than percutaneous exposure. (12)

Every day, more than 1,000 American hospital HCW are injured with a needle or other sharp device. Prevention of occupational transmission of bloodborne pathogens requires a diversified approach to reduce percutaneous injuries and blood exposure, including elimination/substitutions, engineering controls, administrative controls/work practices and use of personal protective equipment (PPE). (12) Following is a diagram that describes a hierarchy of controls, from most to least effective. (13) PPE should be used when more effective controls are not available or possible.
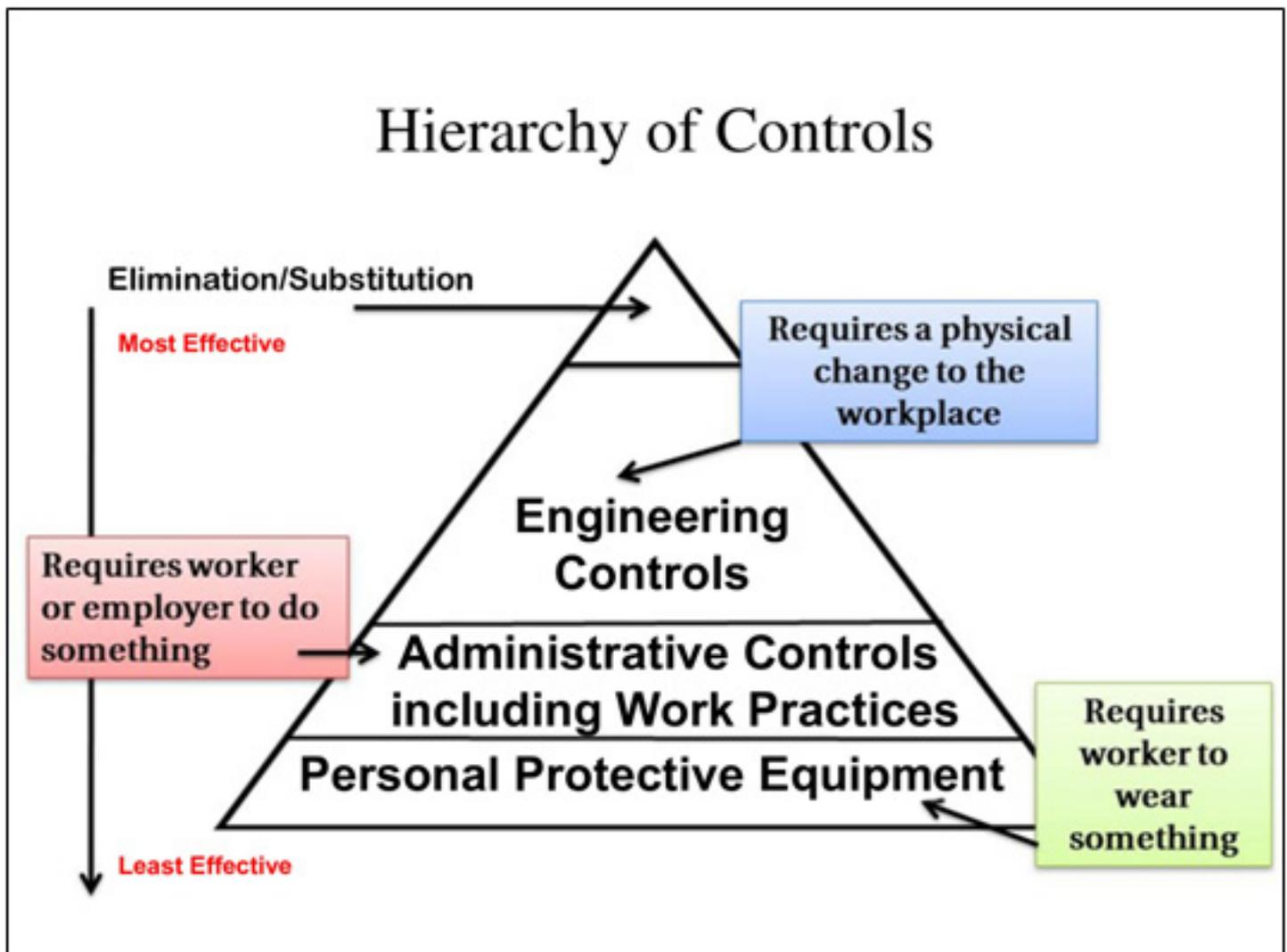
In the past decade, electronic data capture systems have displaced traditional pen-and-paper methods for field survey data collection. (14) By combining data collection with data input, electronic data capture systems and devices (EDCSD) may lower costs and provide better data management. (15,16,17)

Paper-based medical records can be incomplete, fragmented and difficult to find or read. Conversely, EDCSD can rapidly retrieve any number of entries; providing up-to-date, accurate information which can be easily shared anywhere in the world. EDCSD require less space and administrative resources and have the potential for automating structuring and streamlining of clinical workflow.

EDCSD can maintain substantial databases which can readily undergo analysis during a medical audit, research and quality assurance investigations, epidemiological monitoring review, disease surveillance and supporting continuing medical education. (18) The use of EDCSD for cases of exposure to blood and body fluids, including sharps injuries was first developed at the University of Virginia in 1991 and provided standardized methods for recording and tracking percutaneous injuries and blood and body fluid contacts. The Exposure Prevention Information Network (EPINet) consists of a Needlestick and Sharp Object Injury Report and a Blood and Body Fluid Exposure Report and software for entering and analyzing data from the forms. A post-exposure follow-up form is also available. Since its introduction in 1992, more than 1,500 hospitals in the United States use EPINet. It has been adopted for use in other countries (Canada, Italy, Spain, Japan and United Kingdom). (13,19, 20)

Specifically, the EPINet surveillance system gives healthcare facilities the ability to: 1) track occupational sharp object injuries and other blood and body fluids exposure; 2) better prevent occupational injuries and illness; 3) reduce exposure to microorganisms that cause illness and infection and 4) reduce costs and improve quality.

In this study, we used the EPINet model (21,22) to create an Electronic Registry of Data for cases of exposure to blood and body fluids and injuries caused by sharp objects among HCW. The goal was a system with an electronic data collection form having the following capabilities: 1) ease of use at the national level; 2) is in accordance with current CDC guidelines and the new Iranian national protocol; 3) have data collecting properties and decision-making capabilities and 4) be cost effective and easily implemented.

Methods

Phase One
This project involved 200 HCW at Namazai Hospital, who were occupationally exposed to blood and body fluids or were injured by sharp objects and then referred to the hospital's Infection Control Section. Selection was by simple sampling of the exposed HCW pool. Exclusion criterion was an unwillingness to participate in the study.

Flowchart and guidelines development was based on updated guidelines and valid websites such as those of the WHO and CDC as well as the Iranian National Guideline 2017. Flowchart structure begins with emergency actions for exposed personnel and then continues with a referral to a section manager and finally on to the hospital's infection control supervisor.

The supervisor investigates the nature of the exposure, determining infectious source(s) through the presence of HBV, HCV and HIV antibodies and HBV surface antigens. Also, the supervisor investigates the protective controls, including PPE in place when the exposure occurred. The same procedure is followed if risky HCW behavior was noted and the source was unknown.

When a source is known to be HIV-positive, post-exposure procedures, including post-exposure prophylaxis (PEP) are reviewed. Similar activities occurred when the source was HCV or HBV antigen-positive. Finally, a course of action is designed based on currently used flowcharts (Table 1).

Data collection forms were developed based on the tenets of the flowcharts. Form design included variables such as HCW name, age, gender, exposure/injury location, occupation, wound/injury type, location of exposure, type amount of patient body fluids involved, time/day of exposure, treatment provided immediately after exposure, risk assessment for bloodborne disease transmission, description of devices involved, HBV vaccination status and protective controls used, including PPE.

Forms also collected data on HCW post-exposure prophylaxis (PEP) and follow-up experiences. This included the type(s) of prophylaxis offered and received and future referrals and follow-ups (Table 2). After being designed, the paper form was reviewed and approved by a group of infectious disease specialists, with several changes made.

Of the HCW referred to the Namazi Infection Control Clinic, 200 were selected by simple sampling and their information entered onto paper forms. Then, the functionality of the form was reviewed manually and possible errors resolved. Information from the paper forms was entered into the electronic forms and compared.

Phase Two
The next phases of the project involved extraction of HCW information including exposure types and PEP and follow-up procedures which were then comparable.

Various other HCW study factors were also compared which included education level, occupation/position, work experience, location, shift, type of device(s) present, type and amount of body fluids involved, exposed body area(s), injury characteristics and protective procedures and equipment used.

Table 1. Number and title of pathways in flowcharts

Pathway title	Pathway Number
0	Contact with blood and body fluids or damage by sharp devices
1	Screen source patient for HBsAg, anti-HIV, anti-HCV
2	Assessing the risk of exposure to high-risk sources for infection with hepatitis B and hepatitis C and HIV
3	Is the safety of exposed personnel normal and healthy?
4	Is the vaccination of the exposed personnel complete?

Table 2: Number and title of data collection forms

Form Number	Form title
1	demographic questions
2	time and place and type of exposure questions
3	blood and body fluid exposure questions
4	sharps injury and needlestick questions
5	human bites questions
6	when the source of exposure is known questions
7	when the source of exposure is unknown questions
8	a) when source of exposure and HBsAg is known or if source is unknown with high risk for HBsAg b) when source of exposure and HBsAg is known or if source is unknown with low risk for HBsAg
9	when source of exposure and anti-HCV is known or if source is unknown with high risk for HCV
10	when source of exposure and anti-HIV is known or if source is unknown with high risk for HIV
11	when source of exposure is unknown with a low risk for HIV
12	records of all lab data, their answers, prophylaxis, drug usage and drug reactions (summary of HCW medical record)

Results

The aim of this study was to develop and evaluate an EDCSD scheme concerning HCW occupational exposure to blood and body fluids and injuries caused by sharp objects, such as needlesticks and PEP and follow-up activities performed.

Outcomes included creation of a registry system for sharps-related occupational exposures designed to collect, store, recover, analyze and disseminate information of exposed individuals and the appropriateness of PEP and follow-up measures. By creating a registry, the incidence and prevalence of exposures and injuries caused by sharp objects and needlesticks can be examined more carefully and temporal and spatial changes evaluated properly.

Additionally, a registry system could provide evidence of the long-term effectiveness of PEP protocols. The system's web-based software can measure the quality and quantity of care provided, which is not possible using paper forms. It should be noted that this software powers not only registry information, but can also monitor the correctness of the procedures used and the paths that PEP and follow-up took.

Also, it is possible to provide printed records for individuals, if necessary, to relevant specialists, for follow up treatments and to compare feedback forms. The system is also able to generate different tables and charts for registered information, compare different data and other statistical analyses and present results in varying forms (Figures 1-5). These capabilities cannot be performed by similar software. Following are possible examples of analyzed data presentations.

Figure 1. Recording of demographic information

Figure 2. Recording of the related data to time and place of occurrence of exposure

Figure 3. Data recording of cases of exposure to blood and fluids separately based on type of the exposed body fluids, approximate amount of the exposed fluid, type of exposure whether it was dermal or mucosal, type of activity that ended to impairment or exposure and protective conditions of personnel upon incidence of exposure
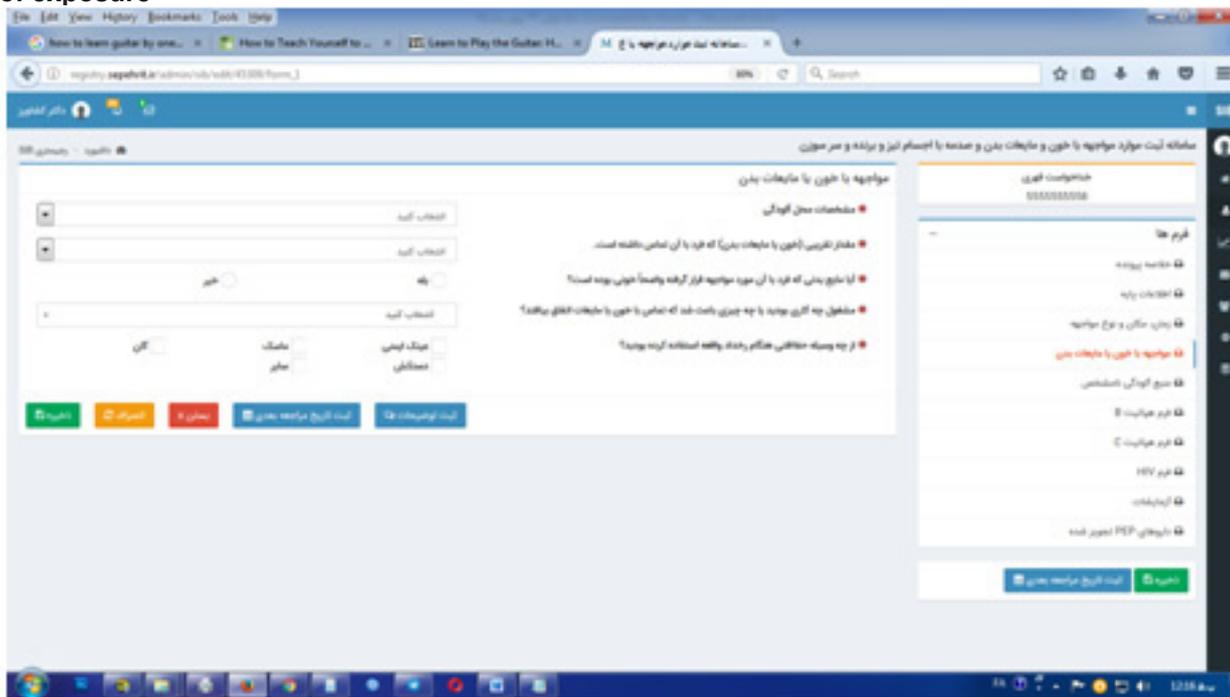
Figure 4. Percentage of exposures to the blood and body fluids based on activity being performed during exposure
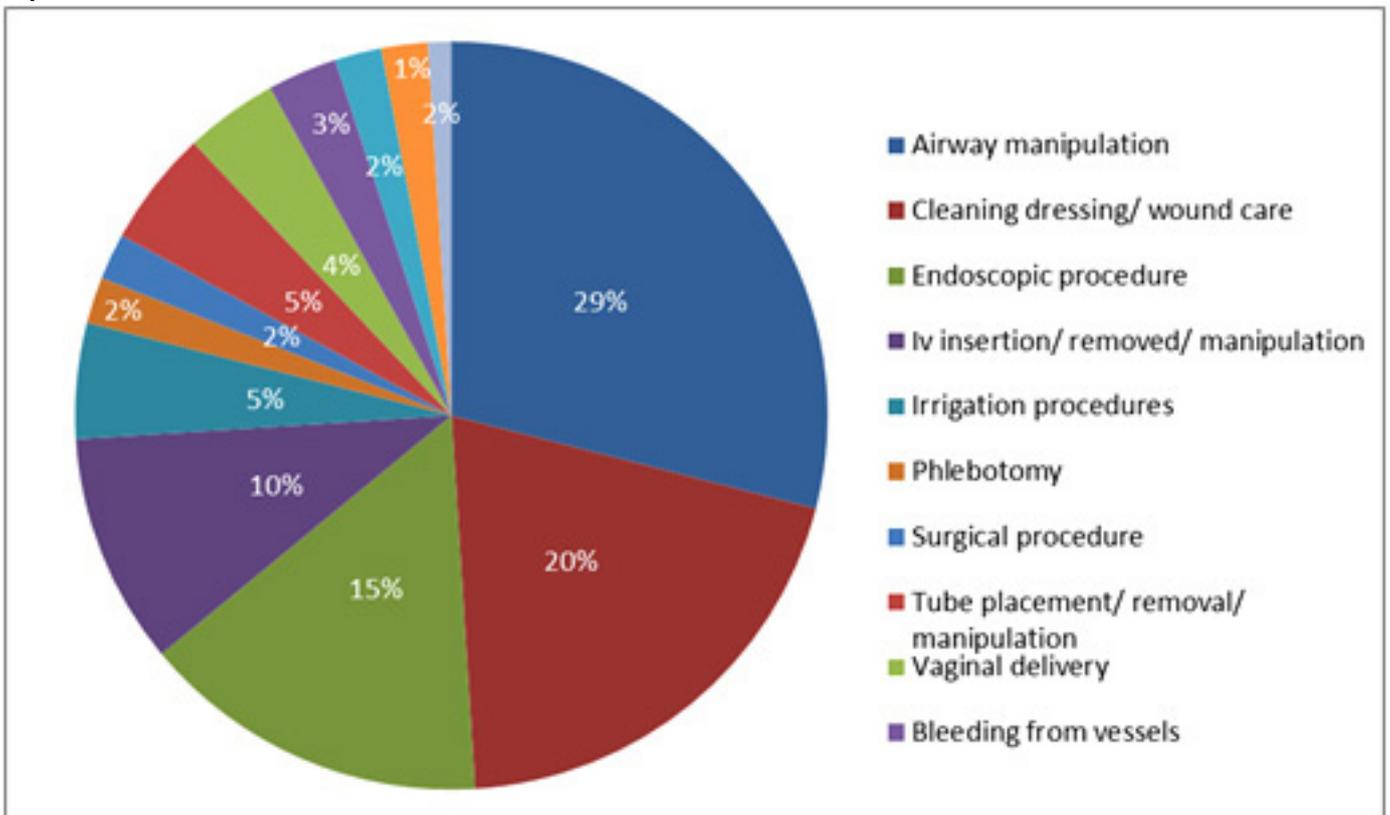
Figure 5. Percentage frequency of human bite cases based on the activity being performed during exposure
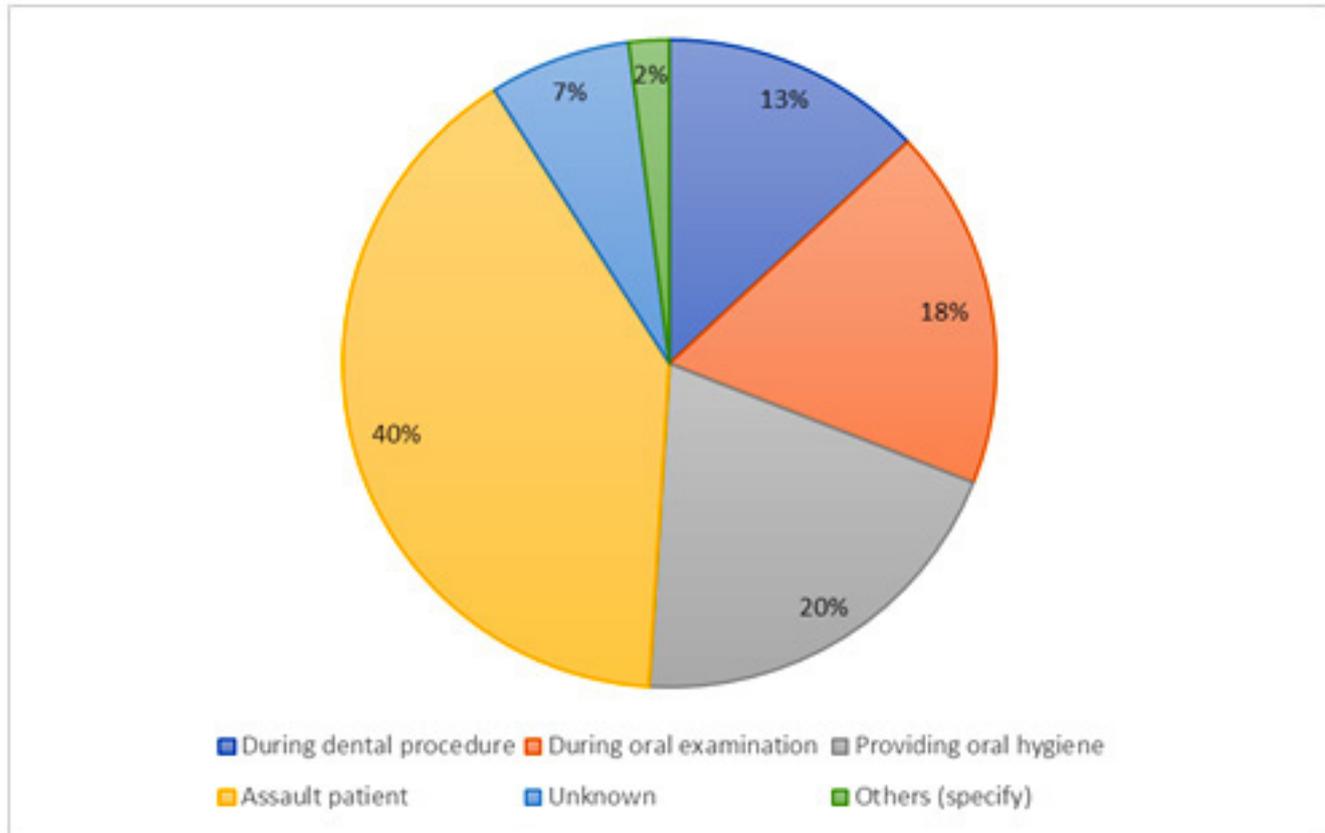
Discussion

Despite the effectiveness of PEP in controlling hospital occupationally acquired infections, no software has been developed to support an electronic registry in Iran concerning HCW exposure to patient blood and other body fluids. This pilot project used PEP software developed at Namazi Hospital in Shiraz.

Currently, EPINet is the most successful software for recording information about sharps injuries and other types of exposure to blood and body fluids and PEP and follow-up practices. Collected information can be used to identify materials and methods that can help reduce the frequency of occupational exposure to bloodborne viruses (21). Specifically, the EPINet system can help: 1) prevent occupational injuries and illness; 2) reduce exposure to microorganisms that cause infections, disease and illness; 3) reduce costs and 4) improve quality. (22)

Paper-based medical records can be incomplete, difficult to read and sometimes, difficult to locate. Electronic registries can provide a single, shareable, up-to-data, accurate and rapidly retrievable source of information, potentially available anywhere any time. Such registries require less physical space and other administrative resources. (23) During the software pilot implementing phase, all these capabilities and benefits of our software were noted, especially concerning accuracy and ease of analysis.

Our software consists of 9 forms with demographic information of exposed HCW recorded on Form 1. Form 2 covers injuries caused by sharp object injuries, while

Form 5 records all forms of exposure. Form responses help develop differing surveillance paths where size and direction can be modified to address the varying types of exposure. While like EPINet, our software also has decision-making capabilities it can readily recognize the proper therapeutic path for an exposed HCW, including PEP and follow-up activities. As with EPINet, our software can generate a variety of illustrations and tables. (19)

Collected data are electronically entered; however, the software will not allow the process to move forward unless all data are entered correctly. This stands in contrast to paper-forms which can contain incorrect and/or missing entries and be erroneously changed. (24)

Electronic reporting systems can be used in any sized healthcare facility. Such technology is relatively easy to install, support and use. Also, it can be adapted to meet local needs and requires a modest resource investment. (25)

An important first step in achieving change is for those involved to realize that change is possible. However, it does require "local ownership." Buying in to the change process involves a local commitment of all involved individuals to solve inevitable problems that arise and to provide local expertise to train and motivate. Appropriate support resources must be provided. Program leadership can be any individual in a facility. However, this person must be highly respected and have the background, motivation and commitment to affect change. (26)

Health Canada commissioned a study of general medical practices in ten countries concerning office automation.

One result was that if a physician is not the champion of change, then a practice administrator can play that role. (26)

A study conducted by African Partnership for Chronic Disease Research compared their electronic data capture system (Electronic Question, EQ) to traditional paper-based data collection methods for a cohort of 200 exposed HCW. EQ increased accuracy and effectiveness, produced similar interview durations and increased data collection costs when compared to paper-based data collection methods. Overall, EQ appears to offer a feasible and cost-effective alternative to paper-based data collection methods in sub Saharan Africa. (27)

Patient charts can be in multiple places (e.g., private physician offices, chart rooms or at nurse stations). An EDCSD saves staff time otherwise used searching for charts and entering change manually. Depending on the size of the practice, this "found time" can be devoted to value-added activities or reducing worker overtime hours. Using EDCSD can improve office productivity and efficiency. (27)

As with other successful registry examples, the accuracy of a data registry is dependent on the quality of its software. Reliable information can be used in future cohort studies.

Conclusion

Our web-based reporting system can be considered a timely registry that properly monitors treatment follow-up. It helps reduce reporting difficulties for personnel working in the Infection Control Section concerning PEP and follow-up activities.

When considering use of a comprehensive reporting system at the provincial or national level, it is possible to review functions and performance of multiple hospital Infection Control Clinics collectively. Results could be useful for policy development and making final decisions to improve PEP.

This web-based system is the first in Fars province. Positive results could be shared with other hospitals and governmental agencies, influencing policymaker, managers and practitioners.

Limitation

It was difficult to develop and implement PEP software. Included are: 1) confidentiality of personnel information; 2) not having valid HCW hepatitis B immunization histories; 3) delays in exposure reporting; 4) transforming data collected by paper forms to an electronic form and 5) coordinating collaboration with expert computer engineers.

Despite difficulties and limitations, PEP software was developed in Iran for hospital use and was implemented at the Namazi Hospital in Shiraz. With support of relevant authorities and health system, we hope that this project could eventually be used in all Shiraz hospitals and even in hospitals in other cities.

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Comparison of the Efficacy of Prednisolone and Dexamethazone on Reduction of Pain and Swelling After Impacted Mandibular Wisdom Teeth surgery

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Abstract

Statement of the Problem: Steroids and Nonsteroidal anti-inflammatory drugs are able to effectively reduce postoperative sequelae of impacted third molar surgery.

Purpose: In this study, we wanted to compare the effect of oral administration of dexamethasone and prednisolone on the post-operative pain and swelling of the impacted third molar surgery.

Materials and Method: 40 patients participated in this study. 5 mg prednisolone was prescribed orally, once 12 hours before and again 12 hours after surgery for twenty patients. The others received 0.5 mg dexamethasone with the same method and postoperative pain and swelling were evaluated in a week.

Results: There were no significant differences between prednisolone and dexamethasone on swelling and pain in the first, third and seventh day after the operation .So we can say that both prednisolone and dexamethasone had equal effect in reducing inflammation and pain in patients.

Conclusion: It was found that the use of a single dose of prednisolone and dexamethasone 12 hours before and 12 hours after surgery can help to reduce pain and swelling of impacted wisdom .

Key words: prednisolone, dexamethazone, impacted tooth, surgery

Introduction

Impaction may be defined as the failure of complete eruption into a normal functional position of one tooth within the normal time due to lack of space in the dental arch, caused by obstruction by another tooth or development in an abnormal position(1). The most often congenitally missing, as well as impacted teeth, are the third molars, which are present in 90% of the population with 33% having at least one impacted third molar (2). They account for 98% of all the impacted teeth (3). The mandibular third molar is the most frequently impacted tooth (4). The incidence varies from 9.5% to 68% in different populations (5-7). According to Elsey and Rock (8) impaction of the third molar occurs in up to 73% of young adults in Europe.

Third molar eruption and continuous positional changes after eruption can be related not only with race but also with nature of the diet, the intensity of the use of the masticatory apparatus and possibly due to genetic background(9).

Surgical extraction of third molars is a traumatic procedure and also is the most common surgical procedure in the Oral and Maxillofacial field (10-14). Wisdom tooth removal is necessary when the jaws are not large enough to accommodate the wisdom teeth or the wisdom teeth are lying in a poor position(12).

The surgical extraction of impacted third molars involves soft and hard tissues and can result in considerable pain, swelling, and trismus. These postoperative sequelae can cause distress to the patient and affect the quality of life of patient after surgery (13, 16-18). Some other complications associated with extraction of impacted mandibular third molars, are alveolitis, infection and paresthesia of the inferior alveolar nerve (19, 20). Hemorrhage during or after surgery and paresthesia of the lingual nerve are relatively rare (21, 22).

Anti-inflammatory drugs with peripheral analgesic action are divided into steroidal (SAID), so called for being analogous to hormones produced by the adrenal glands, and non-steroidal anti-inflammatory drugs (NSAID), which include many drugs that inhibit cyclooxygenase enzyme activity(23).

The introduction of NSAIDs (e.g. diclofenac potassium and ibuprofen) has significantly altered the management of postoperative pain in dentistry and medicine. There are 2 possible mechanisms for the efficacy of NSAIDs when administered prior to surgical trauma. Firstly, the use of the a pharmacokinetic advantage of drug so that with the administration of the NSAIDs prior to pain onset, the absorption of drug would have begun and therapeutic blood level will be present at the onset of pain. Secondly, the presence of a cyclooxygenase-inhibitor at the surgical site may limit the production of prostaglandins and prostacyclins associated with hyperalgesia and edema (24, 25).

Several studies have demonstrated that steroid anti-inflammatory drugs versus non-steroidal anti-inflammatory drugs have a better effect in the control of the swelling and trismus (26-32). Dexamethasone is a type of SAID that inhibits phospolipase-A2 and consequently reduces prostaglandin and leukotriene synthesis and also decreases chemotaxis of polymorphonuclear leukocytes (33). The SAIDs are able to down-regulate many pro-inflammatory cytokines involved in the inflammatory process and immune response (34-37).

The use of the corticosteroids (e.g. dexamethasone, betamethasone) is another preventive strategy for limiting postoperative edema and trismus following third molar extractions(38). Corticosteroids such as dexamethasone have been extensively used in various regimens and routes to lessen inflammatory sequel after third molar surgery (37). In particular, the postsurgical efficacy of dexamethasone administered sub-mucosally remains poorly investigated (37, 39).

Clinical trials in oral surgery have also supported the hypothesis that preemptive NSAIDs and corticosteroids are effective in delaying and preventing of many postoperative sequelae (24). The apparent interactions between the mechanisms of action of the NSAIDs and SAIDs suggests that co-therapy may provide benefits in inflammatory and pain relief without any side effects(38).

When the levels of inflammatory mediators were compared after ingestion of the SAIDs and NSAIDs and placebo, it was observed that both of these anti-inflammatory drugs reduce the levels of prostaglandin E2, and are effective in control of inflammation and postoperative pain(40). For these reasons, researchers have been focusing on alternatives to prevent postoperative pain, by testing different medications and routes of administration (41-43).

In this study, we wanted to compare the effect of oral administration of two types of corticosteroids (dexamethasone and prednisolone) on the postoperative pain and swelling of impacted third molar surgery.

Materials and Method

This prospective randomized clinical study was conducted at the Department of maxillofacial Surgery of dental school of Shiraz University of medical science from 2015 to 2016.

In a year, forty patients with bilateral impacted mandibular wisdom teeth were surgically extracted on both sides by one surgeon. All patients were informed about the study and consent form was completed by all participants. For controlling of postoperative pain and swelling, 5 mg Orally prednisolone was prescribed once 12 hours before and again 12 hours after surgery for twenty patients. The others received 0.5 mg dexamethasone with the same method.

For all patients 2 gr Amoxicillin, 30 minutes before procedure was prescribed. Local anesthesia was obtained using 1.8-3.6 mL Articaine hydrochloride 4% solution with epinephrine 1/100000. A standard incision was used, from the anterior border of the ramus to the disto-facial corner of the second molar following the buccal gingival sulcus along the second and first molar. After periosteal evaluation , surrounding bone of the third molar was removed using a round bur in a low-speed hand-piece and irrigation with copious amount of saline. In the majority of cases, the third molar was split using a tungsten fissure bur and the parts of tooth were then carefully removed with a straight elevator as the routine technique. After the tooth extraction the muco-periosteal flaps were repositioned and partially sutured and an Iodoform drain was inserted for prevention of hematoma formation. We prescribed antimicrobial mouth wash and Ibuprofen for all patients.

Facial swelling was measured by dentist with a measuring tape on the skin surface above the inflation in three dimensions. The pain was evaluated through subjective parameters (visual analogic scale, VAS), so that the pain was declared with numbers between 0 to 10 by the patient. This information was taken on the day before the operation, and the first, third and seventh days after the surgery.

SPSS software version 21 was used for statistical analysis .The cross-table technique was applied for assessment of the variables (pain and swelling) of the two groups: prednisolone and dexamethazone. Pain and swelling recorded by patient and dentist were analyzed by analysis of variance (ANOVA) for repeated measures. The significance threshold was set at 0.05.

Results

As seen in Table 1, there was no significant difference between the two groups (P>0.05) in the first, third and seventh days after the surgery. So we can say that both prednisolone and dexamethasone has equal effect in reducing swelling in patients.

Table 1: The difference between the two groups in terms of inflation (swelling) of patients on the first, third and seventh postoperative days

day	Medicine	N	Mean± Standard deviation	Test statistic (t)	freedom degree	P. Value
1	Prednisolone	20	36.475±1.4279	-0.401	38	0.690
	Dexamethasone	20	36.650±1.3288			
3	Prednisolone	20	37.650±1.3964	-0.853	38	0.399
	Dexamethasone	20	38.000±1.1921			
7	Prednisolone	20	36.650±1.4428	-0.459	38	0.649
	Dexamethasone	20	36.850±1.3089			

As seen in Table 2, the effect of the two medications in control of pain was similar and there was no significant difference between the two groups (P>0.05) in the first, third and seventh days after the surgery.

Table 1: The difference between the two groups in terms of inflation (swelling) of patients on the first, third and seventh postoperative days

Day	Medicine	N	Mean ±Standard deviation	Test statistic (t)	freedom degree	P. Value
1	Prednisolone	20	3.35±1.182	-0.136	38	0.893
	Dexamethasone	20	3.40±1.142			
3	Prednisolone	20	4.35±1.182	-0.136	38	0.893
	Dexamethasone	20	4.40±1.142			
7	Prednisolone	20	3.10±1.373	0.729	38	0.470
	Dexamethasone	20	2.75±1.650			

Three days after operation, the pain and inflation of patients in both groups increased and on the seventh day after surgery, we saw decrease in pain and swelling of patients in both the dexamehazone and prednisolone groups (Figures 1 and 2).

Figure 1: Shows the process of dependent variable (swelling of the patient face) at different levels of the independent variables (the first, third and seventh postoperative day)

**Estimated Marginal Means of group**
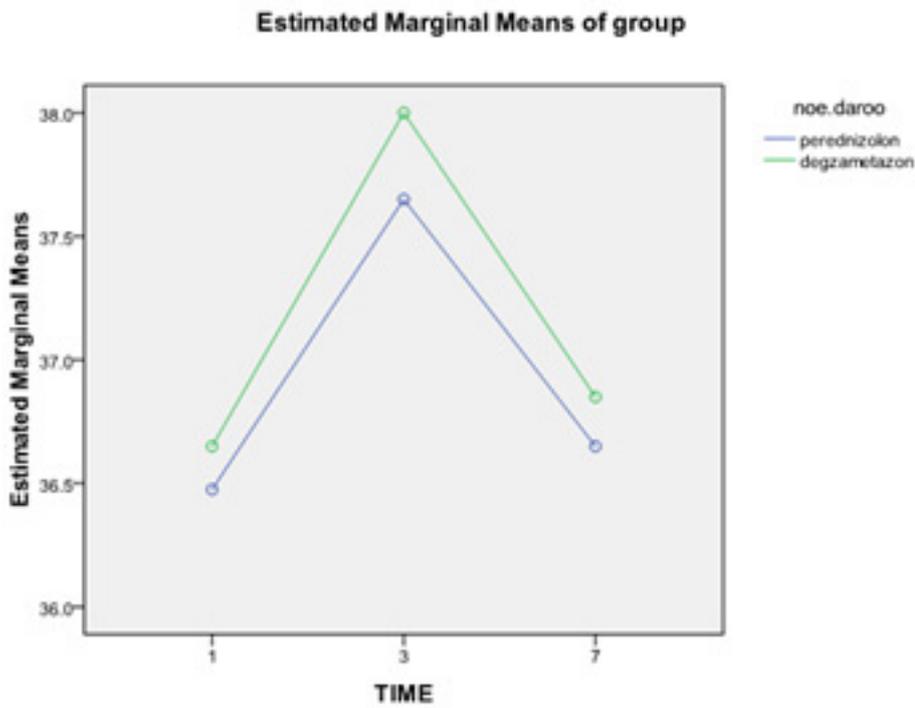
Figure 2: Shows the process of dependent variable (patient's pain) at different levels of the independent variables (the first, third and seventh postoperative day)

Estimated Marginal Means of group
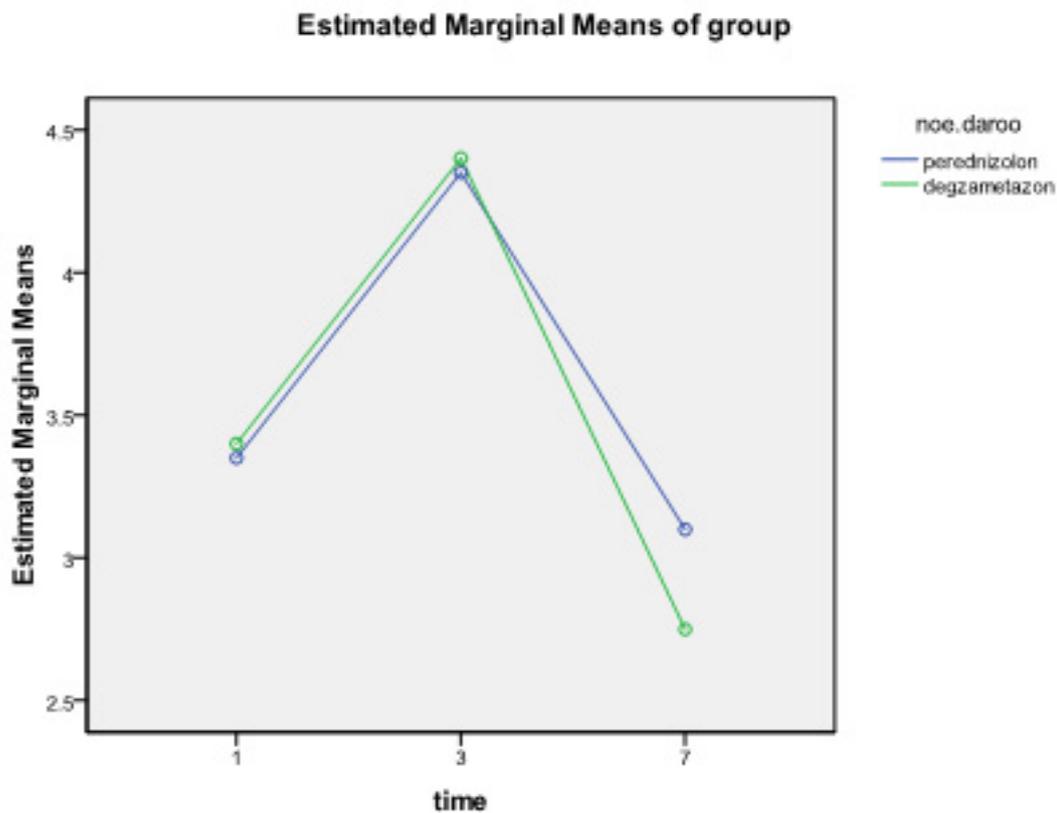
Discussion

In this study we examined the efficacy of prednisolone and dexamethasone on pain and swelling after surgery of impacted wisdom tooth. The results of our study showed that a single-dose (12 hours before and after surgery) of prednisolone and dexamethasone has equal effect on control of pain and swelling. Both drugs reduce swelling and pain within 7 days. This means that on the third day after surgery, we had the highest swelling and pain, while in the seventh day we saw a significant decline in signs and symptoms of these. There was no difference between the two drugs in the first, third and seventh days after surgery.

Various studies have been done in this area. Among them we can cite John Tiigimae-Saar in 2010 who studied The effect of prednisolone on reduction of complaints after impacted wisdom surgery and noted that taking a single-dose of 30 mg of prednisolone after surgery is effective in reducing the pain and swelling caused by surgery on removal of wisdom teeth. Also, they found that one-dose of prednisolone and one of NSAIDs is appropriate for treating lockjaw and swelling after dental surgery (44). In another study in 2006 (35) Mikko Lawrence's review of single doses of 40 mg prednisolone to control complications after surgery of wisdom teeth his result showed that methylprednisolone was effective in reducing the problems.

Schmelzeisen (34) evaluated the effect of oral administration of 6 mg dexamethasone 12 hours before and once 12 hours after surgery of two impacted molar teeth, on postoperative lockjaw and the swelling and pain. The result obtained was that a total of 76% of patients preferred to be treated with dexamethasone. Bamgbose found that the concurrent use of dexamethasone and diclofenac potassium gave significantly more effective for pain relief than a single administration of the diclofenac(38).

Darawade in 2014, with comparison of the effect of methylprednisolone and dexamethasone showed that Dexamethasone is more effective in controlling of swelling, but there was no difference between the two drugs on reduction of pain (45). After this research, our study is one of the few studies that compares the effect of prednisolone and dexamethasone to find the right medication to control complaints after surgery of impacted wisdom tooth. We achieved different results about swelling. Probably, the difference in results may be due to differences in dosage and/or how the drug was administered. In our study, 0.5 mg of dexamethasone, 12 hours before and after surgery, was prescribed, while, Ddarawade used 8 mg dexamethasone one hour before surgery. It seems that he was looking for a quick and short-term effect and perhaps this is the reason why the drug has better results on swelling in his study.

Steroids have many systemic side effects and are not recommended unless in necessary situations. Therefore, when administering these drugs, their benefits and detriments should be measured so that the prescriptive dosage of the medicine is better embedded in the packaging in the market instead of prescribing a number of these pills to reach a higher dose and faster results.

Conclusion

In the absence of contraindications of corticosteroids use a single-dose prednisolone and dexamethasone 12 hours before and 12 hours after surgery can help to reduce pain and swelling and complications of impacted wisdom and NSAID drugs can minimize the problems. However, no differences were found between the performance of these two drugs so it cannot be said for certain which of these drugs are more effective but certainly it can be said that the steroids are very helpful in traumatic and wide surgery, reduce the complications of surgery both for patient and surgeon, and accelerate recovery.

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Evaluation of the prevalence of prolonged QT syndrome in children with first unprovoked seizure

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Abstract

Background: The long QT syndrome (LQTS) is a disorder of myocardial repolarization characterized by a prolonged QT interval on the ECG. This syndrome may be congenital or acquired and it can be associated with seizure-like symptoms. ECG is used routinely to diagnose this syndrome.

Materials and Methods: In this cross-sectional study, we evaluated the ECG of children admitted to the emergency room to estimate the prevalence of LQTS in patients with first unprovoked seizure. Patients with underlying causes like fever and those with previous episode of seizure or electrolyte imbalance at time of admission were excluded. First ECG obtained in the emergency room was reviewed and maximum corrected QT (QTc) was determined.

Results: Out of 100 patients (62 boys, 38 girls), only a 6year old boy showed prolonged QTc (0.53) although 21 patients had borderline QTc (0.42-0.46). Most of the patients (58%) presented with non-generalized tonic-clonic seizures. There was no significant difference in the type of seizure and other electrocardiographic parameters between boys and girls.

Conclusion: Patients with seizure and long QT were considerably lower in number in our study in comparison with other studies. This may be due to our case selection as we excluded the children with a previous history of seizure. Moreover, it seems that ECG solely is not valid or sufficiently reliable to identify LQTS, as this cardiac conductive abnormality is a temporary disorder and may occur only at the time of seizure and disappear when patients are admitted in hospital.

Key words: long QT syndrome, seizure, children, emergency room, ECG, QT interval.

Introduction

Long QT syndrome is a disorder of myocardial repolarization, leading to QT interval prolongation disclosed in electrocardiogram (ECG). This syndrome increases the risk of sudden cardiac arrest and also "Torsade de Pointes", a serious threatening arrhythmia in humans(1,2). Patients are affected congenitally or acquire it due to several reasons, such as electrolyte disturbances or drug interactions(3). The initial symptoms are palpitation, syncope or cardiac arrest in the most disastrous scenario(4,5,6,7), as in the United States congenital long QT syndrome is the main cause of 4000 deaths in children annually (8).

Long QT syndrome is categorized into seven genetic subtypes (LQT1-7) that lead to two distinct phenotypes. One is an autosomal dominant syndrome (Romano ward syndrome) which presents with cardiac manifestations absolutely. The second is an autosomal recessive syndrome (Jervell and Lange-Nielsen syndrome), resulting in neurosensory hearing loss and still more dreadful conditions(7,9). Surprisingly, long QT syndrome may remain obscure, asymptomatic and discovered just after taking incidental ECG or revealed by suspicious sudden death in a family member. In symptomatic patients, it is not uncommon to present with bradycardia (heart rate<60 beats/min) in their first 3 years of life, due to abnormal sodium conduction in the sinoatrial node(10). Also, some external stimulation such as exercise, emotional stress and sudden sleep abruption, swimming, and driving can provoke ventricular arrhythmia in those with long QT syndrome(11).

In spite of the fact that age, gender and genotype can modify the prognosis (Table 1) (13), the clandestine nature of long QT syndrome makes it a potential fatal illness with a remarkable risk of sudden cardiac death, especially for symptomatic cases who have not been treated yet. Overall mortality rate is 20% in the 1st year to 50-60% in the first 10 years, favorably decreasing to 8% in 5 years of age after starting treatment(14,15).

Seizure and long QT syndrome
Occasionally, LQTS manifests with syncope or tonic-clonic seizure-like movements which misleads health-care providers. Thus, identification and management of this complicated group is a major concern, not fully understood yet(13,16,17,18). Pfammatter et al. reported that some cases of LQTS, who presented with falling down, rarely expose obvious QT abnormality in routine ECG after hospital admission and were discovered just by persistent Holter monitoring during exercise(19). Meanwhile, some other reports claim that convulsive disorders may induce QT prolongation in otherwise healthy patients, at least for a transient period of time(20). Hence, one important question is whether ECG is a reliable tool to differentiate LQTS from other common convulsive disorders when patients demonstrate seizure-like movements. Therefore, the purpose of this research was to estimate the number of children with first unprovoked seizure, who exhibited long QT interval in their emergency room ECG. Normal QT interval values are shown in Table 2.

Material and Methods

This cross-sectional study was conducted from 2015 to 2016 on children (1-18 years old) admitted with impression of first unprovoked seizure in the two major and referral pediatric hospitals (Namazi and Dastgheib) Shiraz, Iran. All children with known causes for seizure, such as fever or electrolyte imbalance (hypoglycemia, hypokalemia, hypercalcemia and hypomagnesemia) along with patients with a previous history of convulsive disorders or syndromic or symptomatic epilepsy were excluded from the study.

After admission, ECG was taken in the hospital and in the V5, V6 and II leads, RR and QT intervals were measured to calculate the corrected QT (QTc) interval based on Bazett's formula.

Results

In this study, 100 (62 boys, 38 girls) children with impression of first unprovoked seizure fulfilling inclusion criteria were studied and their QTc were calculated. Seizures in 42 cases were generalized tonic-clonic (GTCS) and in 52 cases they were non-generalized tonic-clonic (NGTCS). The only prolonged QTc was 0.53 detected in a 6 year old boy who presented with NGTCS; however, 21 patients had borderline QTc (0.42-0.46). Differences between boys and girls in ECG parameters or types of seizures were not significant in our study.

Concusion and Dicussion

In Southern Iran, with 100 patients with impression of first unprovoked seizure, one (1%) had long QTc. As expected, there was no significant difference between boys and girls, types of seizure and other ECG parameters among the cases. In research by Davis in 1998, on 126 children who referred to a neurological center, LQTS was diagnosed for 2 patients (1.6%) based on ECG21. In other research by Borzooie et al, also in Iran, out of 273 patients, 32 (11.7%) had long QT syndrome(22). These conflicting results might be due to the selection of cases in different studies. As mentioned before, one of the major exclusion criteria was fever in this study. Febrile convulsion may lead to arrhythmia even in the absence of other factors. In research by Dr Amin et al., fever, alone, has been introduced as a stimulant for ventricular arrhythmia in Brugada syndrome and LQT2(23). Also Burashincov indicated that fever facilitates Torsade de Pointes by prolonging the QT interval(24). Another reason to clarify controversial results was selection of patients with the first episode of seizure and not the chronic, recurrent or complicated ones.

Next to laboratory tests, ECG is almost the only available cardiac evaluation which is implemented routinely on admission in ER. However, many studies questioned ECG's validity and reliability. Kandler et al. pointed out that patients with prolonged QT syndrome usually exhibit ECG abnormality only during the seizure episode(20). Consequently, it is quite possible that ECG shows normal features while most of the patients reach hospital when the seizure is stopped and it is not surprising that some of true

Table.1: Long QT syndrome prognosis QTc: corrected QT interval, LQT: long QT, Sec: Second

High risk (≥50%)	QTc ≥0.50 sec who have LQT1 or LQT2 or (if male) LQT3
Intermediate risk (30 to 49%)	female patients with LQT3 and QTc ≥0.50 sec or patients with QTc <0.50 sec who have LQT3 or (if female) LQT2
Low risk (<30%)	patients with QTc <0.50 sec who have LQT1 or (if male) LQT2

Table.2: Normal value of ECG parameter according to age

AGE	0-7 days	1 wk-1 mo	1 mo-6 mo	6 mo-1 yr	1 yr-5 yr	5-10 yr	10-15 yr	>15 yr
Rate (beats/min)	90-160 (125)	100-175 (140)	110-180 (145)	100-180 (130)	70-160 (110)	65-140 (100)	60-130 (90)	60-100 (80)
QRS axis (degrees)	70-180 (120)	45-160 (100)	10-120 (80)	5-110 (60)	5-110 (60)	5-110 (60)	5-110 (60)	5-110 (60)
PR lead II (msec)	80-150 (100)	80-150 (100)	80-150 (100)	80-150 (100)	80-150 (120)	80-150 (120)	90-180 (140)	100-200 (160)
QRS duration (msec)	40-70 (50)	40-70 (50)	40-70 (50)	40-70 (50)	45-80 (65)	45-80 (65)	50-90 (70)	60-90 (80)
Maximum QTc^f (msec)	450 max	450 max	450 max	450 max	440 max	440 max	440 max	430 max
QRS V₁ Q (mm)	0	0	0	0	0	0	0	0
R (mm)	5-25 (15)	3-22 (10)	3-20 (10)	2-20 (9)	2-18 (8)	1-15 (5)	1-12 (5)	1-6 (2)
S (mm)	0-22 (7)	0-16 (5)	0-15 (5)	1-20 (6)	1-20 (10)	3-21 (12)	3-22 (11)	3-13 (8)
QRS V₃ Q (mm)	0-1 (0.5)	0-3 (0.5)	0-3 (0.5)	0-3 (0.5)	0.5 (1)	0.5 (1)	0-3 (0.5)	0-2 (0.5)
R (mm)	2-20 (10)	3-25 (12)	5-30 (17)	10-30 (20)	10-35 (23)	13-38 (25)	10-35 (20)	7-21 (13)
S (mm)	2-19 (10)	2-16 (8)	1-16 (8)	1-14 (6)	1-13 (5)	1-11 (4)	1-10 (3)	0.5 (2)
QRS V₆ Q (mm)	0-2 (0.5)	0-2 (0.5)	0-2 (0.5)	0-3 (0.5)	0-4 (1)	0-4 (1)	0-3 (1)	0-2 (0.5)
R (mm)	1-12 (5)	1-17 (7)	3-20 (10)	5-22 (12)	6-22 (14)	8-25 (16)	8-24 (15)	5-18 (10)
S (mm)	0-9 (3)	0-9 (3)	0-9 (3)	0-7 (3)	0-6 (2)	0-4 (2)	0-4 (1)	0-2 (1)
T-wave V₁ (mm)	0-4 days = −3 to +4 (0) 4-7 days = −4 to +2 (−1)	−6 to −1 (−3)	−6 to −1 (−3)	−6 to −1 (−3)	−6 to −1 (−3)	−6 to +2 (−2)	−4 to +3 (−1)	−2 to +2 (+1)

Adapted from references 8-10.
*Values reported as 2nd-98th percentile (mean), except for QTC (maximum value only) and >15 yr data, which report ± 1 SD.
^{f}QTc as corrected by Bazett's formula (QTc = QT ÷ square root RR).

LQTS cases would not be identified by ECG in ER. In Davis et al.'s study, 8 out of 126 children previously diagnosed with LQTS had normal ECG at the time of evaluation. Therefore, they concluded that ECG was not sufficiently appropriate to discover LQTS, as cardiac repolarization is a temporary dynamic phenomenon and QT prolongation exists only in 5-10% of gene carriers at rest(21). Furthermore, Kandler et al., who measured QT interval in two separate occasions (2 hours after seizure and 9 days later), reported that out of 7 patients with prolonged QT interval at first, just one revealed long QT interval after 9 days and proposed that seizure itself might actuate the prolongation of QT interval(20).

However, seizure or syncope sometimes do not represent neurologic disorders and follow cardiac electrical conduction disturbances. In Pfammter's study, 8 patients were treated as convulsive cases for about 5 years when finally cardiac arrhythmia was diagnosed as the main cause of their syncope and seizure(19).

Based on all the above-mentioned points, we have to accept that although electrocardiogram is an available simple and inexpensive tool to assess and monitor electrical activity of the heart in emergency situations, ECG alone is not sufficiently valid and reliable for diagnosing new patients with LQTS. Unfortunately, no other modality has been introduced as a golden standard test up to now, but we suggest genetic studies following serial ECGs or Holter monitoring and cardiologist consult as a reasonable plan to diagnose the disease. Thus it might be reasonable that patients with seizure, especially following physical activity and other stresses, or those with family history of syncope, hearing loss or sudden death should be evaluated more precisely using multimodal approach along with an ECG in the emergency room.

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Investigating the relationship between happiness and self-confidence with addiction recurrence in addicted people undergoing methadone treatment referred to addiction treatment centers of Zahedan city with an emphasis on the confounders of demographic variables and variables related to drug taking recurrence

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Abstract

Introduction: One of the major problems in the addicted population is the recurrence of addiction. On the other hand, psychological factors have more effect on the recurrence of addiction than physical factors. Therefore, this research was conducted with the aim of investigating the relationship between happiness and self-confidence with the recurrence of addiction among different variables in methadone treated addicts referring to addiction treatment centers in Zahedan.

Methods: In this study, 250 addicts referring to addiction treatment centers of Zahedan were studied prospectively. The data were collected through an interview using a questionnaireincluding demographic characteristics, addiction related characteristics, and standard self-confidence and happiness questionnaire by the researcher. Data analysis was implemented by Stata.12 software using chi-square test and multiple logistic regression.

Results: Sexual distribution was 206 males (82.4%) and 44 females (17.6%), and age distribution was 37 addicts less than 25 years old (14.8%), and 213 more than 25 years old (21.25%). 162 addicts had recurrence (64.8%) while 88 did not have (35.2%). Variables such as marital status (OR = 4.96, CI=95%: 1.67-14.74) , monthly income (OR=5.28, CI=95%: 2.16-12.90), drug use (OR = 2.25, CI=95%:1.004-5.05), history of previous drug withdrawal (OR=3.40, CI=95%:1.78-6.48), history of alcohol consumption (OR=2.29, CI=95%: 1.09-4.90), and hopes of drug withdrawal from the perspective of addicts (OR=6.65, CI=95%:3.23-13.74), were good predictors of addiction recurrence.

Conclusion: This study showed that self-confidence and happiness are poorly correlated with addiction recurrence, and the main effective variables in the recurrence of addiction are marital status, monthly income, drug use, previous abortion history, history of alcohol consumption before the onset of drug use, and the hope of quitting from the perspective of the addicted person. However, more psychological studies relevant to the recurrence of addiction in other societies and the monitoring of addicts by families with respect to the variables that are influential in this study, are of great importance.

Key words: Addiction, Recurrence, Happiness, Self-confidence

Introduction

Addiction is one of the great problems of human societies which, unfortunately, has plagued all industrial and non-industrial societies, and our society also faces it so much that it threatens the health of society on one hand, and is related to guilt, crimes, and diseases such as AIDS on the other hand(Mirzaei et al., 2010b, Najarzadegan and Tavalaee, 2012). Addiction is a biological, psychological, and a social disease, and several factors are involved in the etiology of substance abuse and addiction which together lead to the onset of drug use and then addiction (JANDAGHI and Alii, 2002). The problem of drug withdrawal is one of the issues that has always been the concern of the authorities and addicts and their families(Laleh, 2003). Unfortunately, the main problem in the treatment of addicts, even with a long period of quitting, is the high rate of recurrence (Yan and Nabeshima, 2009). As according to studies conducted to evaluate the incidence of recurrence of substance abuse in the first and third months in the world, it was shown that, at the end of the third month, 57.3% had recurrent drug abuse (Green Stein, 1996). In Iran, according to Shafie et al's study, 73.1% of drug addicts consumed narcotics over the last 12 months and 72% experienced complete recurrence (Shafiei et al., 2014). Also, Kasani has reported the return rate to drug re-abuse in his study as 30.4% in Ilam (Kassani et al., 2015). Also, according to studies conducted in Zahadan city, it was found that the average age of starting drug use has been 20 years old at Zahedan and there is a significant relationship between marital status, education, and type of substance in the onset of addiction with personal decisions to quitting drug use (Ansari-Moghaddam et al., 2012). In another study, factors such as contaminated living environment, addicted friends, the ineffectiveness of psychotherapy sessions, and the associative factors have contributed to the recurrence of the addiction. The association of these factors with the recurrence of addiction has been similar in the same age group and sex (Nastizayi et al., 2010). According to one study, psychological factors have had a greater impact on the recurrence of addiction than physical factors (Mahdi Karimyar Jahromi 2015), in such a way that happiness and vitality are of great importance in the health, dynamism and mobility of society. Because on one hand, they have role in reducing depression and anxiety and on the other hand, while strengthening self-esteem, feeling safe, reducing the weakness of the body immunity, and improving physical and mental health, speeds up the decision-making process and creates a cooperative spirit and increases the sense of life satisfaction of individuals.

Negative affections are commonly seen among drug addicts during drug use, especially at the time of drug discontinuation, and they are one of the main causes of failure to maintain long-term avoidance from drugs (Tajeri Buick 2011). On the other hand, one of the most important negative emotions is depression associated with thoughts or suicidal behaviors and with a sense of low happiness (Saduk, 2013). Happiness, as one of the variables in positive psychology, is the positive value that a person allocates to himself (Veenhoven, 1997). This structure has two aspects: one is the emotional factor that reflects the exciting experience of happiness, pleasure, euphoria and other positive emotions, and the other one is the cognitive assessment of satisfaction from different realms of life that express happiness and psychological well-being (McKennell and Andrews, 1980). Also, Diner considers happiness as assessment of a person from themselves and their life, and introduces some factors such as life satisfaction, excitement and positive mood, lack of depression and anxiety (Diener and Fujita, 1997). According to the study of Ghobad Pour et al, low levels of happiness are closely associated with psychological disorders and social harm incidence in drug addicts (Saeedeh Ghobadpour, 2016). Also, having the ability to successfully solve the problem of drug withdrawal providess more self-confidence to addicts and makes them more valuable. But, if they lack the necessary skills to solve the problem or use inappropriate and defective methods to solve the issues related to drug withdrawal, they will face difficulty with their environment and their mental health will be threatened (Saeedeh Ghobadpour, 2016). The results of Karim Yar Jahromi et al. study have shown that low self-confidence has had the minimum role in addiction recurrence (Mahdi Karimyar Jahromi 2015). Given that so far, the relationship between happiness and self-confidence with recurrence of addiction has been never studied in Zahedan, and on the other hand, considering happiness and self-confidence as the psychological factors which can be important in substance abuse withdrawal, can addiction recurrence be reduced by creating happiness and self confidence among addicts? So, this study has been implemented with the aim of investigating the relationship between happiness and self-confidence with addiction recurrence along with other independent variables including demographic variables and addiction related characteristics in methadone treated addicts referring to addiction treatment centers of Zahedan.

Materials and Methods

In this cohort study, 250 addicts referring to addiction treatment centers of Zahedan were studied. The sampling method was by preparing the list of the addiction centers of Zahedan city and dividing the city into 6 regions and selecting one center in each region randomly with their cooperation assumption, and in each center, easy or accessible method was used to enter all eligible people in the study. The sampling was continued until completing all samples. Following the selection of patients and passing therapies of addiction treatment and after the physician or a related addiction authority confirmed the withdrawal of the addict during the first days of referral to the center due to clinical tests (morphine and methamphetamine), the patients were followed up for 6 months in order to determine the successful drug withdrawal or addiction recurrence. During these 6 months at different times of the test (morphine and methamphetamine) and telephone call (each week), the subjects were followed up to record the exact time in case of recurrence before 6 months. This was done by retrieving addicts and conducting experiments or companions reporting with the oversight of the centers authorities. To collect data, an questionnaire including demographic characteristics, questions about individual,

social, family and cultural characteristics, standard 10 questions of self-confidence and 29 questions of happiness were completed by a researcher with a personal interview with patients at the beginning of the project. The self-confidence questionnaire was answered by the 4-degree Likert scale, where zero is "completely disagreeing" for the first eight questions, and 4 as "I totally agree", and in the last 2 questions 4 is considered as "I totally disagree", and zero as "I totally agree." For reliability of this questionnaire, Cronbach's alpha was used which was equal to 71%. Also, content validity of this questionnaire was confirmed by the opinion of 10 relevant experts with Content Validity Index (CVI) over 87%. The Oxford Happiness Questionnaire (OHI) was developed by ARGYLO M Argylo MLL in 1989 and is graded into four options from zero to three (Argylo M, 1989). Alipour and Noorbala have reported the reliability of this questionnaire by Cronbach's alpha as 0.93 and 0.92 with two-half way method and 0.79 with retest. Also, in assessing the validity of the questionnaire, 10 experts were polled; all confirmed the ability to measure happiness by this test with CVI over 83% for all questions. Moreover, the reliability of this questionnaire was obtained by Cronbach's alpha in the target population as 76% (Alipoor and Noorbala, 1999). After collecting data and interviewing the person who had discontinued drug use, a specific code was allocated to him and data were entered into the software Stata.12 and were analyzed. Descriptive statistics (relative frequency, tables, and charts) were used to determine the rate of unsuccessful withdrawal, and addiction recurrence. To analyze the data in a single-variable analysis, the relationship between addiction recurrence and independent variables including happiness and self-confidence among controlling other demographic variables and addiction-related characteristics the chi-square test was used with presenting the relevant odds ratio. To control the confounders, data were analyzed using multiple logistic regression.

Results

In this study, 250 addicts referring to the addiction treatment centers of Zahedan who were undergoing methadone treatment were evaluated for their addiction recurrence. The sexual distribution was 206 men (82.4%) and 44 women (17.6%), and age distribution 37 (14.8%) people less than 25 years old, and 213 (85.2%) more than 25 years old. Overall, the results of this study showed that 162 (64.8%) addicts had recurrence and 88 (35.2%) had no recurrence. Table 1 (next page) shows the distribution of the frequency of addict's drug recurrence in terms of demographic variables. According to this table, the variables of housing status (p = 0.034), monthly income (p = 0.004), and marital status (p = 0.61) are correlated with addiction recurrence. As the probability of addiction recurrence was 2.12 times more in residents of a rental house compared to personal housing (OR=2.12, CI=95% : 1.13-3.96) and monthly income less than 500,000 Tomans was 2.93 times more compared to income more than 1,000,000 (OR=2.93, CI=95% : 1.48-5.80). According to the table, although the odds of being addicted in uneducated people was 2.05 times more than the high school diploma

and more education (OR=2.05, CI=95%: 0.64-6.60), it was not statistically significant (P>0.05).

Table 2 shows the frequency distribution of addiction recurrence based on variables related to the history and properties associated with individual addiction. As the table shows, the variables of type of substance used, drug using method, the age of commencement of drug use, the history of previous drug withdrawal, the history of alcohol consumption before the onset of drug use and the hopes of drug withdrawal from the perspective of addicts are associated with recurrence of addiction (p>0.05), in such a way that the chance of recurrence in heroin users was 6.53 times more compared to opium (OR=6.53, CI=95%, 0.82-52/00), 1.99 times more in smoking method compared to eating (OR=1.99, CI=95%: 1.02-3.87), 2.43 times more in having the history of previous drug withdrawal compared with no previous history of drug withdrawal (OR=2.43, CI=95%: 1.42-4.14), 2.71 times more in alcohol consumption before starting substance than non-alcohol use before onset of drug use (OR-2.71, CI=95%: 1.45-5.09), and 4.38 times more in having low hopes for drug withdrawal from the point of view of the addicted person than high hopes for drug withdrawal from the point of view of the addicted person (OR=4.38, CI=95%: 2.37-8.09). Although, the chance of recurrence of addiction in low self-confidence individuals was 1.60 times more compared to high level self-confidence people (OR = 1.60, CI=95%: 0.89-2.89), and was 1.74 time more in those who were not happy compared to happy people (OR = 1.57, CI=95%: 0.92-2.70), but, it was not statistically significant (p >0.05). Also, the highest distribution of the frequency of addiction recurrence in terms of the cause of drug use variables was as 79 (66.4%) for entertainment and pleasures, 116 (60.7) for opium as the most consumed drug so far, 9 (100%) as the history of injection, and 46 (80.7%) as temptations of the drug recurrence in previous withdrawal.

Table 3 shows the coefficients of independent variables related to addiction recurrence in Zahedan addicts in multiple logistic regression model. According to this table, related to addiction recurrence in addicts referring to drug addiction centers in Zahedan, only variables such as marital status, monthly income, drug using way, previous history of quitting, history of alcohol consumption before commencement of drug use, and hopes of quitting from the point of view of addicts have remained in the model (p <0.05). This model shows that in terms of the addiction recurrence, the chance of addiction recurrence in the married couple whose spouse is addicted is 4.96 times more (OR = 4.96, CI=95%: 1.67-14.74) than the married ones whose spouse is not addicted, 5.28 times more when the monthly income is less than 500,000 Tomans than when it is 1,000,000 Tomans (OR=5.28, CI=95%: 2.16-12.90), 2.25 times more when the method was smoking compared to the method of eating (OR = 2.25, CI=95%:1.004-5.05), 3.40 times more in having previous quitting history compared to no history of previous withdrawal (OR=3.40, CI=95%:1.78-6.48), 2.29 times more in having history of alcohol consumption before starting the substance use and no history of alcohol consumption before starting the

Table 1: Frequency distribution of addiction recurrence in terms of demographic variables in addicts referring to addiction treatment centers of Zahedan

Demographic variables	Addiction recurrence	YES n (%)	No n (%)	*p-value	OR(95% CI) Univariate
Sex	Men	137(66.5)	69(33.5)	0.222	1.50(0.77-2.92)
	Women	25(56.8)	19(43.2)		**1
Age	Less than 25 years old	26(70.3)	11(29.7)	0.450	1.33(0.62-2.85)
	More than 25 years old	136(63.8)	77(36.2)		1
Level of Education	Uneducated	16(76.2)	5(22.8)	0.431	2.05(0.64-6.60)
	Elementary School	22(73.3)	12(26.7)		1.76(0.72-4.29)
	Middle School	38(59.4)	25(40.6)		0.94(0.43-2.03)
	High School	47(63.5)	27(36.5)		1.11(0.52-2.38)
	High school diploma and more	28(60.8)	18(39.3)		1
Occupation	Employed	110(65.1)	59(34.9)	0.890	1.04(0.59-1.80)
	Unemployed	52(64.2)	29(35.8)		1
Marital status	Single	38(70.4)	16(29.6)	0.061	***3.02(1.13-8.07)
	Married (his wife is not addicted)	113(66.1)	58(33.9)		***2.48(1.05-5.80)
	Married (his wife is addicted)	11(44)	14(56)		1
Nationality	Sistani	124(65.6)	65(34.4)	0.638	1.15(0.63-2.10)
	Baloch	38(62.3)	23(27.7)		1
Housing status	Residents of rental house	60(73.3)	23(27.7)	0.034	***2.12(1.13-3.96)
	Father's home	48(69.6)	21(30.4)		1.86(0.97-3.56)
	Personal housing	54(55.1)	44(44.9)		1
Monthly income	Monthly income less than 500,000 Tomans	82(70.7)	34(29.3)	0.004	***2.93(1.48-5.80)
	Monthly income 500,000-1,000,000 Tomans	57(68.7)	26(31.3)		***2.66(1.29-5.48)
	Monthly income more than 1,000,000 Tomans	23(45.1)	28(54.9)		1
Number of household members	Less than 5 people	131(67.2)	64(32.8)	0.138	1.58(0.86-2.91)
	More than 5 people	31(56.4)	24(43.6)		1
Divorce history in the family	Yes	19(73.1)	7(26.9)	0.351	1.53(0.62-3.81)
	No	143(63.8)	81(36.2)		1

*p value the result of chi-square test, **basal group, ***significant level of confidence interval (0.05)

substance use and no history of alcohol consumption before starting the drug, (OR=2.29, CI=95%: 1.09-4.90), and 6.65 times more in having low hopes for quitting from the viewpoint of the addicted person to having high hopes for quitting from the viewpoint of the addicted person (OR=6.65, CI=95%:3.23-13.74).

Discussion

Overall, this study showed that 64.8% of addicts recurred over the past 6 months and re-consumed previous addictive substances. According to previous studies in Bangladesh-Dhaka, the rate of substance abuse recurrence was 71.9% in women and 54.5% in men (Maehira et al., 2013). On the other hand, in Iran, the study of Shafi'i et al. reported the rate of addiction recurrence as 73.1% and 30.4% (Shafiei et al., 2014, Kassani et al., 2015). The rate of relapse in this study is almost similar to the reported recurrence rates in some studies and with some others studies is different, which indicates increased incidence of addiction recurrence

in people referring to addiction treatment centers. Due to similar studies, we can mention easy access to addictive drugs, age, number of households, insomnia, temptation, unemployment, family conflicts and lack of adherence to treatment, addiction quitting history, socializing with addicted friends, education, the history of addiction in the family, the employment status, the use of cigarettes, and the type of addictive drug usage as the factors of returning to addiction (Mirzaei et al., 2010a, Rimaz et al., 2013b, Kikhavandi et al., 2015, Tarrahi et al., 2013). Therefore, the difference of the distribution of these variables in different places is due to the different reasons for the relapse of addiction. However, in order to monitor treatment process of addicts to reduce the rate of recurrence more effectively, cooperation of family members and psychologists and experts in addiction treatment centers is necessary, and also reducing the recurrence of addiction should be one of the important priorities of the health system and treatments centers.

Table 2: Frequency distribution of addiction recurrence in terms of variables related to history and properties associated with addiction, happiness and self-esteem in addicts referring to addiction treatment centers in Zahedan city

Variables related to drug recurrence	Addiction recurrence	YES n(%)	No n(%)	*p-value	OR(95% CI) Univariate
Type of substance used	Heroin	10(90.9)	1(9.1)	0.008	6.53(0.82-52.00)
	Hashish	28(82.4)	6(17.6)		***3.04(1.20-7.68)
	Opium	124(60.5)	81(39.5)		**1
Drug using way	Smoking	140(67.6)	66(32.4)	0.040	***1.99(1.02-3.87)
	Eating	22(51.2)	21(48.8)		1
Age of commencement of drug use	Less than 20 years old	75(75)	25(25)	0.006	***2.17(1.24-3.79)
	More than 20 years old	87(58)	63(43)		1
History of drug use in the family	Yes	97(66)	50(34)	0.639	1.13(0.67-1.91)
	No	65(63.1)	38(36.9)		1
History of previous drug withdrawal	Yes	98(74.2)	34(25.8)	0.001	***2.43(1.42-4.14)
	No	64(54.2)	54(45.8)		1
History of drug use	More than once a day	131(65.8)	68(34.2)	0.501	1.24(0.65-2.34)
	Less than once a day	31(60.8)	20(39.2)		1
History of alcohol consumption before the onset of drug use	Yes	61(79.2)	16 (20.8)	0.001	***2.71(1.45-5.09)
	No	101(58.4)	72(41.6)		1
Premarital addiction starting	Single	38(70.4)	16(29.6)	0.287	1.60(0.80-3.21)
	Married (starting before marriage)	56(68.3)	26(31.7)		1.45(0.80-2.64)
	Married (starting married)	68(59.6)	46(40.4)		1
The presence of a addicted person in the family	Yes	121(66.5)	61(33.5)	0.369	1.30(0.73-2.32)
	No	41(60.3)	27(39.7)		1
Self-confidence	Low	127(67.6)	61(32.4)	0.112	1.60(0.89-2.89)
	high	35(56.5)	27(43.5)		1
Happiness	Yes	111(68.5)	51(31.5)	0.095	1.57(0.92-2.70)
	No	51(58)	37(42)		1
hopes of drug withdrawal from the perspective of addicts	Low	83(83)	17(17)	0.001	***4.38(2.37-8.09)
	high	79(52.9)	71(47.3)		1

*p value the result of chi-square test;   **basal group;   ***significant level of confidence interval(0.05)

We can mention the relationship between addiction relapse and housing variables and salary as other results of this study. So that residents who rented houses and monthly income level was less than 500,000 Toman, have the highest risk of exposure to addiction recurrence. In the study of Rimaz et al, there was no significant relationship between addiction relapse and housing status (p = 0.681) and monthly income (Rimaz et al., 2013a). These factors indicate that the socioeconomic status is closely related to addiction and its recurrence. Unemployment and lack of permanent job lead to inadequate income, so that the person is subjected to low socioeconomic status and his/her desire for addiction and its recurrence becomes greater.

Also, there was a significant relationship between the type of addictive substance and the recurrence of it in this study. In another study, a statistically significant difference was found between the type of addictive drug and the incidence of substance abuse (Rimaz et al., 2013a). In other words, in people who consume opium or opium syrup, the possibility of drug abuse was less than those who used other drugs like crack, glass, etc. and took action for quitting addiction. The Farzam study also showed that the percentage of drug abuse in opium users (39.5%) was lower than that in heroin users (62.5%), especially Norfen (42.4%) (Farzam, 2010). Addiction to these substances is considered as final stages and such people are often out of social activity cycle

Table 3: Coefficients of independent variables related to addiction recurrence in Zahedan addicts in multiple logistic regression model

Independent variables		β	S.E	*p-value	OR(95% CI) Univariate	OR(95% CI) Multivariate
Marital status	Single	1.14	0.612	0.61	***3.02(1.13-8.07)	3.14(0.94-10.43)
	Married (his wife is not addicted)	1.60	0.555	0.004	***2.48(1.05-5.80)	***4.96(1.67-14.74)
	Married (his wife is addicted)	-	-		1	**1
Monthly income	Monthly income less than 500,000 Tomans	1.66	0.455	0.001	***2.93(1.48-5.80)	***5.28(2.16-12.90)
	Monthly income 500,000-1,000,000 Tomans	1.56	0.442	0.001	***2.66(1.29-5.48)	***4.77(2.00-11.35)
	Monthly income more than 1,000,000 Tomans	-	-		1	1
Drug using way	Smoking	0.812	0.412	0.049	***1.99(1.02-3.87)	***2.25(1.004-5.05)
	Eating	-	-		1	1
History of previous drug withdrawal	Yes	1.22	0.329	0.001	***2.43(1.42-4.14)	***3.40(1.78-6.48)
	No	-	-		1	1
History of alcohol consumption before the onset of drug use	Yes	0.830	0.378	0/028	***2.71(1.45-5.09)	***2.29(1.09-4.90)
	No	-	-		1	1
hopes of drug withdrawal from the prospective of addicts	Low	1.89	0.370	0.001	***4.38(2.37-8.09)	***6.65(3.22-13.74)
	high	-	-		1	1

*p value the result of multiple logistic regression model, **basal group, ***significant level of confidence interval(0.05)

and, as a result, will have weaker support in the future to avoid drug abuse. In this study, variables such as the age of commencement of drug use, the history of previous abandonment, and the history of alcohol use before drug use were associated with the recurrence of drug addiction. Sayyadi, et al's study also showed that the variables of type of substance, method of use, age of onset of addiction and history of addiction quitting were effective in addiction relapse (Sayyadi Anari et al., 2002). Although the incidence of addiction was higher in people with low self-confidence and those who were not happy, it was not statistically significant, and this may be due to low self-confidence and false happiness in the subjects of this study. But, due to the high chance in people with low self-confidence and those who were not happy, attention to these two psychological factors is important. Also in other studies, there is a link between happiness and self-confidence with addiction recurrence (Saeedeh Ghobadpour, 2016, Mahdi Karimyar Jahromi 2015). So that happiness and low self-confidence lead to psychological disorders and social harm in addicts, and they will not have the skills to solve the problems of

quitting. According to the study of Babamiri et al, stress coping styles are among the factors that are related to addict behavior and happiness (BaBamiri et al., 2013). On the other hand, it is thought that adapting and controlling the painful excitement caused by psychological pressures in people susceptible to addiction, is difficult because of maladaptive coping methods and the inability to correctly and adequately confront addiction leads to showing and exacerbating lack of control over life, lower self-confidence and tendency towards non-adaptive behaviors such as substance abuse. Also, the results of this study showed that the hope to quit from the perspective of the addicted person is related to the recurrence of addiction. So that having low hope for quitting the addiction from the perspective of the addicted person, is more than having high hope for quitting from the same perspective. However, in a case-control study, there was no statistically significant difference between the case and control group in terms of the patient's hope in the treatment process (Rimaz et al., 2013b). There was a significant difference in the Åhary study (Sadegiye Ahari et al., 2004). This finding is in line

with studies that show that the more a person hopes is associated with the completion of treatment and recovery of the patient (Carvajal et al., 1998). It is possible that drug users who have more hope, use more effective remedies for their own treatment instead of common therapeutic courses and are less prone to recurrence. On the one hand, strengthening the problem-oriented coping strategy and hoping with happiness will increase the likelihood of cessation and recovery in addicts.

Conclusion

This study showed that self-confidence and happiness have a weak correlation with addiction recurrence, and the main effective variables that affect the recurrence of addiction are marital status, monthly income, drug using way, history of previous drug withdrawal, history of alcohol consumption before the onset of drug use, and hopes to quit from the perspective of the addicted person. Considering the importance and attention that happiness and self-confidence have found in psychology, further investigation in the addict population and trying to examine the predictions of happiness and self-esteem in these individuals can be significant. Only one factor is not enough for the recurrence of drug abuse, but a set of factors especially individual ones with different proportions can lead to addiction recurrence. However, more psychological studies related to the recurrence of addiction in other societies and monitoring the addicts by families with respect to the effective variables in this study is essential.

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The knowledge and attitude of pregnant women about preservation of umbilical cord blood in public and private cord blood banks in referrers to the therapeutic and health centers affiliated to Abadan School of Medical Sciences

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Abstract

Background: Maintenance and preservation of umbilical cord blood suggests that the benefits of using stem cells in the treatment of many diseases are being considered around the world. The aim of this study was to investigate the knowledge and attitude of pregnant women about preservation of umbilical cord blood in public and private cord blood banks in referrers to the therapeutic and health centers affiliated to Abadan University of Medical Sciences in 2016.

Materials and methods: All pregnant women who referred to the health centers were selected by the census as a sample. In this descriptive cross-sectional study, the instrument was a questionnaire which consisted of three parts: demographic characteristics (7 questions), knowledge (9 questions), and attitude (21 questions) and was filled in by 170 pregnant women. Questions about attitude were based on the proportion of women's knowledge . Scores of knowledge were categorized into three groups: low-level of knowledge (less than 6), moderate (7 to 13) and good (up to 20). The scores of attitude were classified into three groups: negative attitudes (less than 2) indifferent or neutral (2 to 4) and positive attitude (up to 5) were classified. To determine the relationship between knowledge and attitude with age, occupation, education level of descriptive and inferential statistics Spearman correlation coefficient and statistical tests Wallis Kruskal, t. test and one - way ANOVA, were used. Data were analyzed using Statistical Software SPSS, version20. In all cases, p<0.05 was considered as the significant level.

Results: More than half of women had a low-level of knowledge (69.3%) and the majority (57.1%) had a positive attitude, respectively. 78 % of pregnant women chose the storage of umbilical cord blood in public cord blood banks and 13.5% a private cord blood bank. There was no significant relationship between knowledge and attitude with age (p< 0.05) and the relationship between knowledge and attitude with the employment and education was significant (P<0.05). The findings of this study showed that the majority of pregnant women have a positive attitude towards donation of the cord blood, but most of them had low-level of knowledge.

Conclusion: According to our results, the need for training and informing families about donation and the storage of umbilical cord blood for the improvement of the level of knowledge and increase of stem cell donors is essential.

Key words: Attitude, Cord blood, Knowledge, Pregnant women

Introduction

Stem cells are unspecialized cells in the human body that have the ability to become specialized cells with specific functions. These cells with the production of similar stem cells through a process called self-renewal, can provide unlimited proliferation and differentiation into various cells causing the regeneration and repair of damaged tissue in vivo [1]. Actually, these cells by transplanting into those tissue will replace damaged cells and are effective in improving damaged tissues of the body [2]. Since the issue of cord blood preservation has increased, the benefits of using stem cells have been considered in the treatment of many diseases, like cancer so that the patients can receive chemotherapy and radiation therapy. The patients of thalassemia need to replace stem cells because of genetic defects, construction disorder of hematopoietic cells. Stem cells are also used in the treatment of disorders of the immune system and some heart and liver diseases. Nowadays, these cells can be used in the treatment of diseases such as diabetes, cardiovascular and neurogenerative diseases. Although this hypothesis requires further investigation in the future[3], generally we can say that all the treatments based on stem cells are not futuristic. Stem cells are obtained from different sources; one of them is bone marrow stem cells and the other types are obtained from the blood of the umbilical cord and the placenta. Blood of the umbilical cord has younger cells than other sources and do not cause genetic mutation; besides with collection from the cord, there is use of waste tissue unlike adult tissues such as bone marrow, and does not require surgery, and cord blood stem cells are not like embryonic stem cells that are obtained by destroying an embryo. The collection and storage of stem cells provides a good source of cells for transplantation and cellular therapy for persons when it is necessary due to the possibility of rejection, which is caused through transplantation of stem cells, which is nullified for others [4]. Other advantages of umbilical cord blood includes the reduction of the rate of rejection reactions, graft-versus-host, the reduction of immunological rejection of the transplant due to the presence of immature immune cells in cord blood. The possibility of successful transplantation with less similarity of HLA between donor and receiver and the reduction of the possibility of transmission of viral infections of the placenta as a barrier preventing the penetration of the virus to the fetus and the presence of stem cells with high power amplification , etc [5],[6] could be other advantages. Recently, storage of umbilical cord blood stem cells has been done in private and public cord blood banks. 75 % of umbilical cord banks are public and 25 % of them are private, around the world [7]. There are three public cord blood banks in Iran, including Royan Institute of blood transfusion, bone marrow transplant center of Shariati Hospital and a private bank of Umbilical cord stem cells of embryos companies [8]. The public cord blood banks act as donor centers while the private cord blood banks are centers that families can store their child's cord blood stem cells for transplantation when needed. The only difference between them is that the families have to pay money for storage of umbilical cord blood in private cord blood banks. According to the studies, the presence of both banks is essential for our society. In this way, families have the chance to store their baby's umbilical cord blood [8].

The goals of this study were to check the knowledge and attitudes of the pregnant women about the importance of umbilical cord blood storage in public and private cord blood banks in Abadan, and its application therapy. In fact, its importance was furthermore suggested to pregnant women to assure them that their infant's cord blood storage increases the number of Iranian cord blood banks and the recipients over time. Nevertheless, several Asian and European countries have done similar research in this field. Because of the difference in lifestyle, income, culture, religious belief of Iranian people, results of their knowledge and attitude of pregnant women to their babies cord blood storage is not reliable. Therefore, the existence of such contradictions and because a similar proposal in this field has not been done in Iran yet, this research was a new idea for surveying the knowledge and attitude of pregnant women about storage of umbilical cord blood of their newborns and the possibility of establishing of an umbilical cord blood bank in Abadan. Since there is no cord bank in Abadan, the conditions and requirements to establish it are too limited, so this research is different from other studies in this field.

Methods

This cross-sectional descriptive study was performed on pregnant women from 2014 to 2015. In this study, the tool for data collection was a questionnaire compiled by the researcher consisting of three main parts, personal characteristics, and 6 questions about (knowledge), and 20 questions about (attitude), respectively. The information of pregnant women in health centers was recorded for prenatal care; therefore, all of them formed our sampling. People who did not want to participate in this study were excluded from our sample population. The knowledge and attitude of the pregnant women about cord blood storage was checked through the designed questionnaire. The first part of the questionnaire included demographic characteristics such as age, education level, job status, and perceived income level. The second part of the questionnaire consisted of separate questions to assess the knowledge and attitudes of all women who were referred to health centers who were questioned according to the designed questionnaire by Katz et al in 2011,[9],[8]. In connection with the questions related to knowledge, the correct options and YES had a score of 1 and the opposite options and NO had a score of 0. The Score of knowledge was divided into 3 groups: Low level (a score of less than 6), middle (a score of 7-13), and good knowledge level, a score of higher than 20. Also the Score of attitude was classified into 3 groups, negative attitude (a score of less than 2), intermediate or neutral attitude (a score of 2 - 4) and positive attitude (a score of higher than 5). After studying the latest scientific literature, the questionnaire was examined by 3 gynecology and obstetrics specialists and a PhD in Hematology and necessary recommendations and modifications were instituted. Its reliability was evaluated 0.79 by repeated test. The correlation coefficient was calculated and that indicated the reliability of the questionnaire. The internal consistency obtained by Cronbach's alpha for questions of knowledge was 88 % and for questions of attitude was 95.5%. Collected data were analyzed using SPSS version 20, descriptive statistics (in order to provide variable frequency, percent, the mean, standard deviation and other statistics factors)

and tests of t-test, One way ANOVA and Kruskal Wallis.
The significance level of less than 0.05 was considered.

Results

199 people fully completed the questionnaires and the data was studied. Variables included age, level of education, job status, perceived income level, knowledge and attitude. The mean and standard deviation were calculated from obtained scores from the questionnaire. According to the results, the knowledge level of women was divided into three categories of low, intermediate and good. Total frequency of knowledge was 85.4% while the highest percentage of knowledge related to women with weak knowledge was 33.2% (Table 1). Moreover, total frequency of attitudes was obtained at 78.9% with the highest frequency in women with positive attitudes 8%, (Table 2). It was found that about 78.5 % of women's attitude showed agreement to storage of umbilical cord blood in public cord banks while 13.5 percent of them disagreed to store umbilical cord blood in private cord blood banks.

The Kruskal Wallis test was used to examine the relationship between knowledge and attitude with age in four age groups (<18, 18-36, 36-40, >40). The results of the test of non-parametric Kruskal Wallis showed that there was no statistically significant relationship between knowledge ($X2$:1.947, p: 0.583) and attitude ($X2$: 0.314, p: 0.575) and age range in the four age groups.

Table 1: Frequency distribution of knowledge of pregnant women about umbilical cord blood stored in public and private cord blood banks among the patients of health centers in Abadan from 2014 to 2015

Knowledge		Number	Percent	Valid Percent	Cumulative Percent
	Low (a score of less than 6)	138	69.3	81.2	81.2
Valid	Middle (a score of 7-13)	24	12.1	14.1	95.3
	Good (a score of higher than 20)	8	4.0	4.7	100.0
	Total	170	85.4	100.0	
	Missing System	29	14.6		
	Total	199	100.0		

Table 2: Frequency distribution of attitude of pregnant women about umbilical cord blood stored in public and private cord blood banks among the patients of health centers in Abadan from 2014 to 2015

Attitude		Number	Percent	Valid Percent	Cumulative Percent
	Negative (a score of less than 2)	1	.5	3.6	3.6
Valid	Intermediate /Neutral (a score of 2-4)	11	5.5	39.3	42.9
	Positive (a score of higher than 5)	16	8.0	57.1	100.0
	Total	28	14.1	100.0	
	Missing System	171	85.9		
	Total	199	100.0		

One-way ANOVA test was used to check the level of knowledge and attitude with education. The results indicate the meaningful relationship between education with knowledge p(<0.05) while no significant relationship was seen between the attitude and education in the three categories of primary (M± SD ,13.16 ± 6.8), high school (M± SD ,14.4 ± 4.5), university (M± SD ,13.4 ± 0.89) education p(>0.05). The results of post hoc or Tukey test showed that the relationship between the woman's knowledge level and education in primary and high school education was highly significant compared to the group with university education (M± SD ,3.14 ± 1.82), p(<0.05) while significant relationship was not observed between the knowledge of primary (M± SD ,0.44 ± 0.66) and high school education (M± SD ,0.82 ± 1.31) P(>0.05). (Figure 1)

Figure 1: The correlations between women's knowledge about cord blood and their educational level
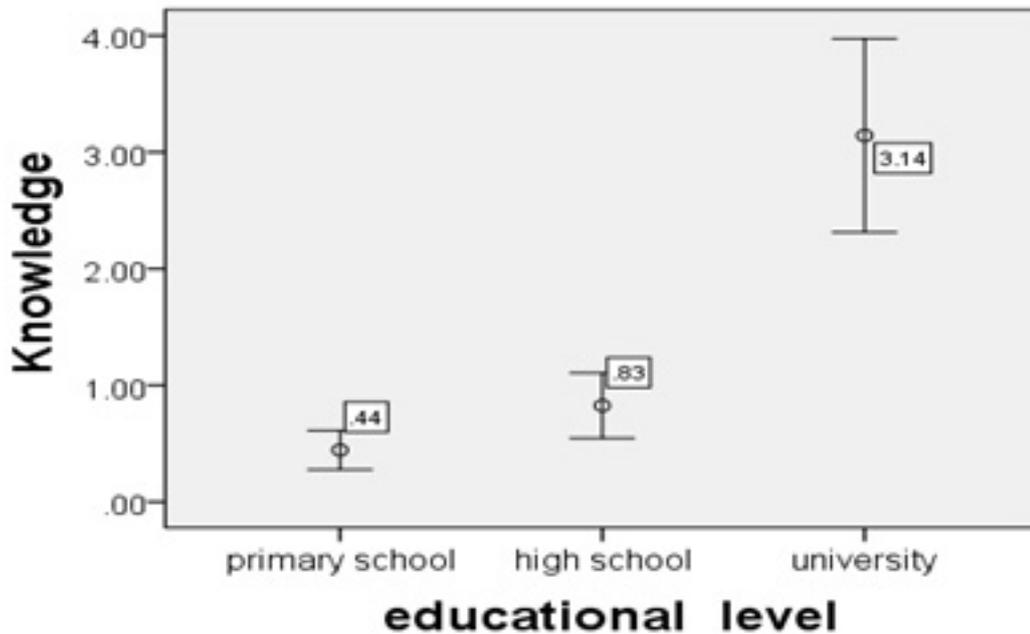
Results showed that there was a significant relationship between the woman's knowledge level and education in primary and high school education compared to the university education p(<0.05). The relationship between woman's knowledge of primary and high school education was not significant difference (p>0.05). The results of the One-way ANOVA showed that there was a meaningful relationship between knowledge and employment (p<0.05). The results of t-test showed that the knowledge of employed women about umbilical cord blood storage(M± SD ,0.71 ± 1.2) had meaningful difference compared to housewives (M± SD ,2.24 ±1.7) (P<0.05), (Figure 2). According to the results of t-test, attitude towards the knowledge did not have any significant relationship with job in both employed (M± SD ,15 ± 2.8) and housewives (M± SD ,13.6 ± 5.1) groups (p>0.05).

Figure 2: The relationship between women's knowledge about cord blood and their job status
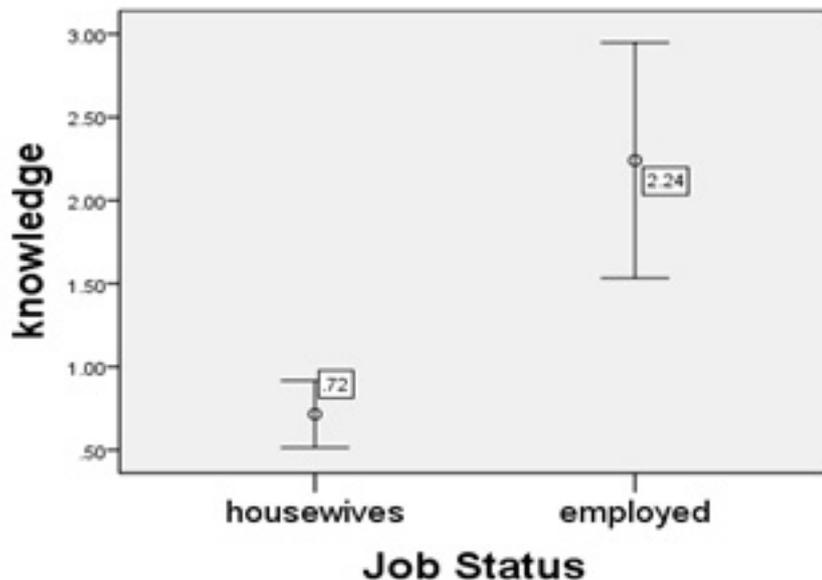
In this figure, it is obvious there is a significant difference of knowledge level of employed women compared to housewives. The results of the t-test analysis was p<0.05.

Results of One-way ANOVA showed that there was a significant relationship between knowledge and perceived monthly income level. In the level of knowledge in three different perceived monthly income levels (low, moderate and high income), there is a significant relationship only between the moderate (M± SD ,0.31 ± 0.51) and high income (M± SD ,1.4 ± 1.7) groups (P<0.05) but in other groups, such as low-income (M± SD ,1 ± 0.75) group the difference was not significant compared with the moderate and high income groups (P>0.05).

Figure 3: The correlations between women's knowledge about cord blood and their perceived monthly income level
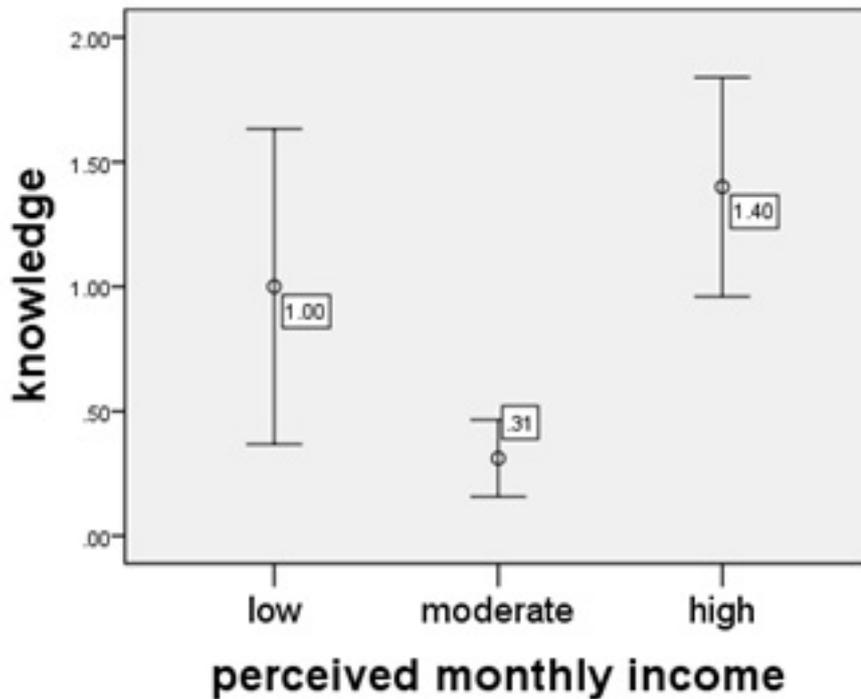
There were significant differences between individuals with moderate income and high income, (p<0.05). There is not a significant difference between people with low-income compared with moderate income and high income (P>0.05).

There was non-normal distribution of attitude survey data of women in the three levels of income related to cord blood storage, so Kruskal-Wallis test was used to compare the results of the attitudes among these three groups. Results certified that there was not a significant relationship between the income level and their attitude (X 2:2.977, p:0.226).

Discussion

Umbilical cord blood is a little blood that remains in the umbilical cord postpartum. Previously, the umbilical cord was discarded as biological waste[4]. But recently, it has been found that umbilical cord blood contains a large amount of stem cells that can be used to treat some types of diseases such as cancer, in the future[3]. Storage of umbilical cord blood and procurement of stem cells from it acts like insurance. In fact, people who make decisions to hold their infants' cord blood in private cord blood banks by paying money, are insuring their children. Although it is possible that the child will not need to use umbilical cord blood and stem cells, the high-risk diseases do not threaten them. Conservation of umbilical cord blood does not need very complicated techniques and its collection does not harm the mother or the baby. There is a very controversial question about storage of umbilical cord blood that has proponents and opponents around the world that relate to the advantage of creating a cord blood bank. Proponents of umbilical cord banks who are mostly from the medical profession and related teams have a duty to save patients in any way. Most opponents of umbilical cord banks, have an economic perspective about storing samples with high costs for several years to possibly use it for the has chance it may be needed for transplantation and its successful is doubtful [10]. The importance of this project was to advise parents to keep the baby's umbilical cord blood until the number of cord blood banks and the recipients increase in Iran. Katz and colleagues (2011) have done a study on the knowledge and attitude of the pregnant women about storage of umbilical cord blood in the European countries. In this study, 79 % of pregnant women had low knowledge of umbilical cord blood storage[9] that was consistent with the results obtained in our study where 32.2 % of pregnant women had low knowledge about umbilical cord blood storage. Most of them declared their conscious satisfaction that the baby's umbilical cord blood is stored in public cord blood banks. A similar study was also conducted by Maryia Scrinci (2011) at the University of Rome in 2012 where 55 % of pregnant women gave conscious satisfaction to store umbilical cord blood[8]. Overall, the women in our study, had low knowledge but positive attitude about their children's cord blood storage. In the other study, Katz and his colleagues (2011) found that attitude of the pregnant women was not a barrier to store umbilical cord blood as well as family income level was not related to umbilical cord blood storage[9]. Similarly, the results of our survey revealed that income levels in the type of attitude of pregnant women to collect cord blood did not have any positive effect. Continuous education for health professionals is the driving force for development and eminency regarding the storage of umbilical cord blood[11]. The results of our studies are in line with the important results of a study in five European countries. Results showed that increasing knowledge about cord blood donors can be done through the increase of educational programs [12].

The results of the questionnaire done by Rucinski (2010), suggested that awareness of married women is higher

regarding donated umbilical cord blood and in educated women and by participating in workshops and conferences they had acquired a positive attitude in relation to donating umbilical cord blood. According to our studies conducted, it was found that there is not a meaningful relationship between the level of education and attitude of married women about cord blood collection which differs from those studies[11].

In this study, the knowledge of employed women showed a significant positive relation with job status than housewives. The management of cord blood donation is based on Clary et al's research (2012), which showed that there was a significant relationship between the type of attitude toward cord blood donation and jobs status which is in agreement with our results[13].

Katz and colleagues (2011) showed that the attitude of pregnant women about the maintenance and storage of umbilical cord blood was not related to family income level. Our study also showed the similar results[9]. There was not a significant relationship between women's attitudes and family income. Studying the relationship between knowledge and the level of education, family income and jobs status about the storage of umbilical cord blood had not yet been done. So we examined such a relationship in our study. Our results showed a significant relationship between the level of education and job status. Highly educated employed women were more knowledgeable than housewives with low education, about their baby's umbilical cord blood storage. This represents the positive effect of university education and their social activities on increasing knowledge and attitude of pregnant women. The results of women's knowledge in families with different income levels showed that families with high income levels have higher awareness than families of low and middle income level. This may be due to the positive role and effect on the welfare of the family, on increasing the public knowledge about the importance of storing cord blood.

According to the findings of this study, less than half of the women had a low level of knowledge about cord blood donation which indicated a lack of suitable education and showed that they did not have training thus it can be concluded from different reasons such as the lack of awareness about donation in clinical field and suitable advertisements. Thus educating programs and creating awareness about this subject, especially in universities, society and public places, is necessary. The study to determine the effect of teaching methods on the knowledge and attitudes related to the donation of umbilical cord blood is recommended. According to the findings, less than half of all women had low knowledge and positive attitude about cord blood donation. Therefore, training programs in this area to improve their knowledge and attitude seems necessary.

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Epidemiologic study of cutaneous leishmaniasis in Khorramshahr, Iran: 2008-2016

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Abstract

Introduction: Cutaneous leishmaniasis (CL) is one of the endemic and neglected diseases known to exist in the world, including in Iran. Therefore the aim of this study was to determine some epidemiological aspects of this disease in Khorramshahr, one of the cities with a high incidence of CL.

Material and Methods: This is a retrospective descriptive-analytical study, which has been performed by examination of Cutaneous Leishmaniasis cases in Khorramshahr during the 9-year period of 2008 to 2016. Further data were gathered using a questionnaire and eventually data analysis was done by SPSS.22.

Results: The number of patients with cutaneous leishmaniasis was 735. According to the population of Khorramshahr, the prevalence of the disease in the studied years was 42 per 100,000 people. 61.6% of the cases were male. Most cases were in children under the age of 10, and in people over the age of 30 years. The highest incidence was reported in December. It was also found that most cases of disease occur in urban areas (68%).

Conclusion: It seems that in the study region, Cutaneous Leishmaniasis is mostly the disease of urban areas; and, since most cases were observed in men, education courses should be planned, focused on men, to prevent the outbreak of the disease in urban areas.

Introduction

Cutaneous Leishmaniasis is an infectious disease mainly in tropical regions with Global expansion and is transmitted from the bite of Phlebotomus mosquitoes to humans. This is one of the six important diseases of the tropical regions induced mainly by two types of Leishmania parasites, i.e., Leishmania Tropica and Leishmania Major (1-3). It is estimated that there are about 12 million patients with Leishmania around the world, which increases every year by 2 million, and 1.5 million of whom have Cutaneous Leishmaniasis (4). Although endemic Cutaneous Leishmaniasis exists in 88 countries around the world, 90% of the cases are residents of the seven countries of Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia and Syria (5, 6). In recent years, Cutaneous Leishmaniasis has been regarded as one of the socially worrying diseases in war-ridden countries like Afghanistan.

Cutaneous Leishmaniasis is still a significant parasitic disease and a health problem in Iran. Prevalence of the disease has been reported to be between 1.8% and 37.9%; and is higher in some provinces, like Isfahan, Fars, Khorasan, Khouzestan and Kerman, than others. Although about 20.000 new cases of the disease are reported in Iran annually, it is believed that the real number is about 4-5 times higher. The report of new infection foci in recent years shows the potential for the spread of disease in Iran (5, 7-9).

Since Khorramshahr is a highly infected town in Khuzestan Province, in terms of Cutaneous Leishmaniasis this study aims at investigation the prevalence, emergence and some epidemiological aspects of the disease in the last 9 years.

Materials and Methods

This is a retrospective descriptive-analytical study, which has been performed by examination of Cutaneous Leishmaniasis cases in Khorramshahr during the 9-year period of 2008 to 2016. Khorramshahr has a population of 170,976, and is located in the south west of Iran.

In this study, the information of patients was gathered by reference to the Health Clinic on Khorramshahr Town by a zoonotic disease expert. All subjects of the study are Cutaneous Leishmaniasis patients, identified by the protocol of the Ministry of Health and were under treatment.

Data required, including age, gender, address, success or failure of treatment, number and position of ulcers, etc., were gathered by a questionnaire and then analyzed by SPSS. 22 software. In statistical analysis, use was made of descriptive statistics to gather primary information like frequency, frequency percentage, mean, maximum and minimum, data number and standard deviation. In inferential statistics, Kolmogorov-Smirnov test was used to gain information on the normality of the variables, and chi-square, Spearman and Eta tests were used for further analyses. In order to accept or reject the hypotheses, P-value=0.05 is used and the results under 0.05 (P<0.05) are considered significant.

Results

A total of 735 Cutaneous Leishmaniasis patients was identified in clinical or preclinical manner from 2008 to 2016 in Khorramshahr. The highest rate was related to 2009 with 327 (44.5%) and 2010 with 35.4% cases. The number of patients in the studied years is depicted in Figure 1.

From among the diagnosed patients, 453 (61.6%) were men and 282 (38.4%) were women, which, with the significance level of 0.000 shows that men are significantly acquiring Cutaneous Leishmaniasis more than women.

Data analysis showed that Cutaneous Leishmaniasis patients are significantly higher in number in urban areas (500 patients, 68%) than rural areas (235). Table 1 shows the demographic characteristics of the patients.

178 patients belonged to the age group of less than 10 years old. However, most of them (243) belonged to the age group of above 30. The age group of Cutaneous Leishmaniasis patients shows significant differences with each other; also, there is a direct relationship between age and patients with P-Value=0.273 (Table 2).

It was revealed by examining the patients that the number of ulcers in the upper limbs was 38.8% (309 ulcers) and the smallest number of ulcers was identified in the neck (16 ulcers or 2%) (Table 1).

Table 3 and Figure 2 show the outbreak of the disease in relation to population, age, and address.

The highest number of diseases was observed in December (157), November (128) and January (115) (Figure 3).

Discussion

Results show that the outbreak is significantly higher in men than women (61.6% vs. 38.4%). This may be due to the presence of men in outdoor areas for longer times than women in the peak activity intervals of the mosquitoes, and wearing less-protective clothes than women, which makes a bite by the Phlebotomus mosquito more probable. In previous studies in Iran and other countries, too, the higher number of bites in men is reported (4, 5, 10, 11); though there are studies in which the number of bitten women is higher (3).

About two thirds (68%) of Cutaneous Leishmaniasis cases live in urban areas. This may be due to unfinished and under-construction buildings which house the mosquitoes for spawning. This is consistent with the results of other studies in Iran (5, 11, 12) and other countries (13). However, a higher number of cases in rural areas are reported in some studies, too (4, 14).

According to the data analysis, the highest number of cases was diagnosed in above-30-year-old subjects. This group consists of the more active people in terms of work, and is predictable. Also, this is consistent with the results

Figure 1: Number of patients with Cutaneous Leishmaniasis in Khorramshahr from 2008 to 2016
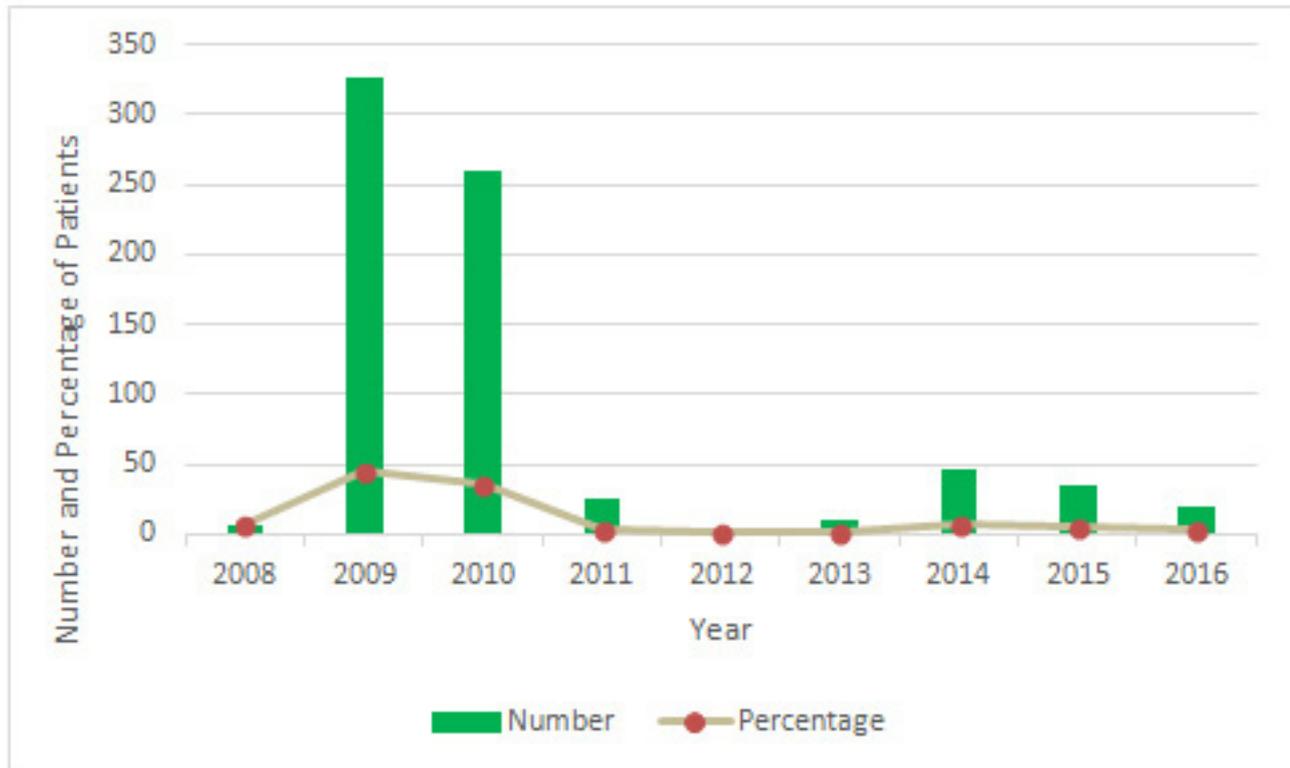
Table 1: Demographical characteristics of the patients with Cutaneous Leishmaniasis in Khorramshahr from 2008 to 2016

		Frequency	Percent
Gender	Male	453	61.6
	Female	282	38.4
Region	Urban	500	68.0
	Rural	235	32.0
Location of the Ulcers	Head and Face	122	15.3
	Neck	16	2.0
	Hand	309	38.8
	Leg	296	37.2
	Trunk	53	6.7

Table 2: Frequency of Patients with Cutaneous Leishmaniasis in Khorramshahr from 2008 to 2016 according to Age

Age Group	Frequency	Percent	
<1	14	1.9	
1-4	77	10.5	
5-9	87	11.8	
10-14	65	8.8	P-Value=0.000
15-19	75	10.2	
20-24	91	12.4	
25-29	83	11.3	
+30	243	33.1	

Table 3: The Prevalence of Patients with Cutaneous Leishmaniasis in Khorramshahr from 2008 to 2016 according to their Gender and Region

	Frequency	Prevalence /100000
Male	453	152.51
Female	282	102.50
Urban	500	39.63
Rural	235	48.07
Total	735.00	41.99

Figure 2: Frequency of Patients with Cutaneous Leishmaniasis in Khorramshahr from 2008 to 2016 according to Age and Gender
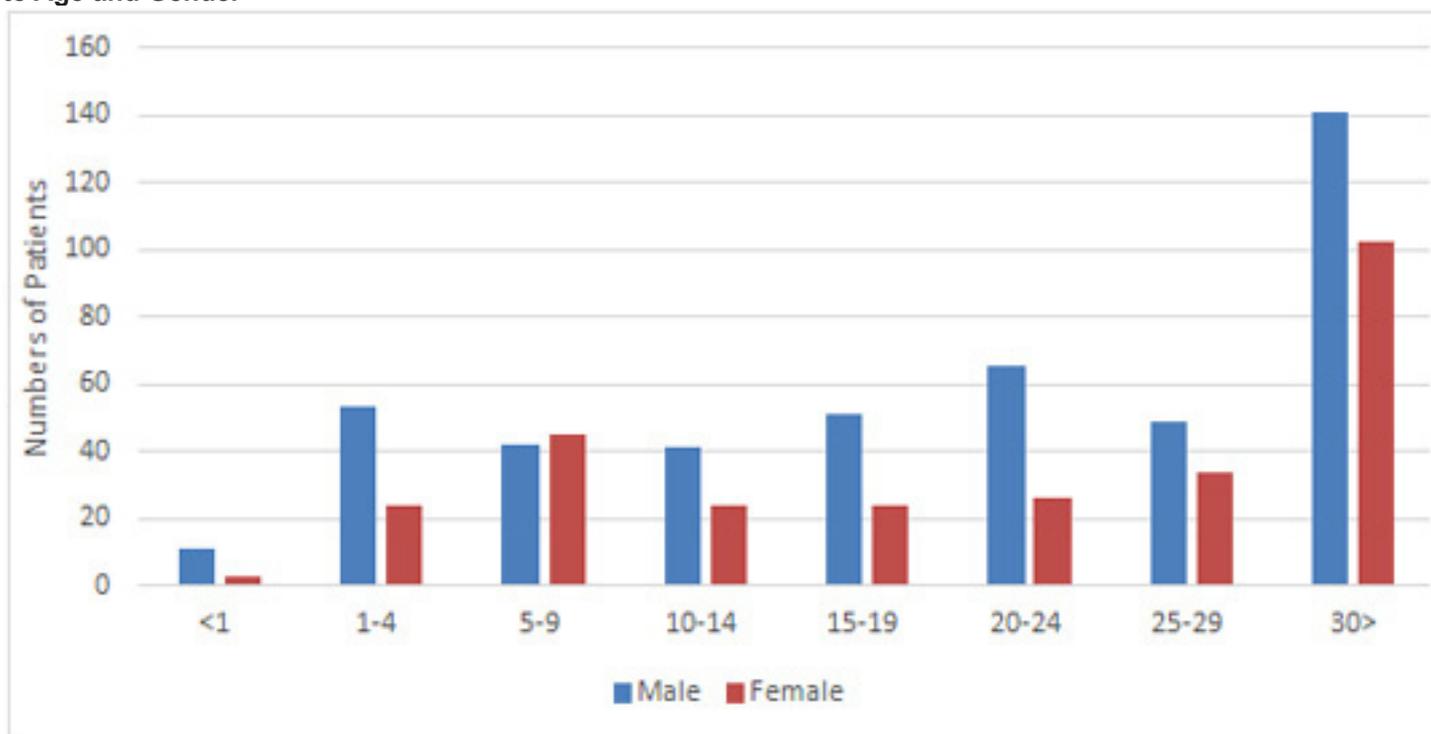
Figure 3: Frequency of Patients with Cutaneous Leishmaniasis in Khorramshahr from 2008 to 2016 according to months of contracting leishmaniasis
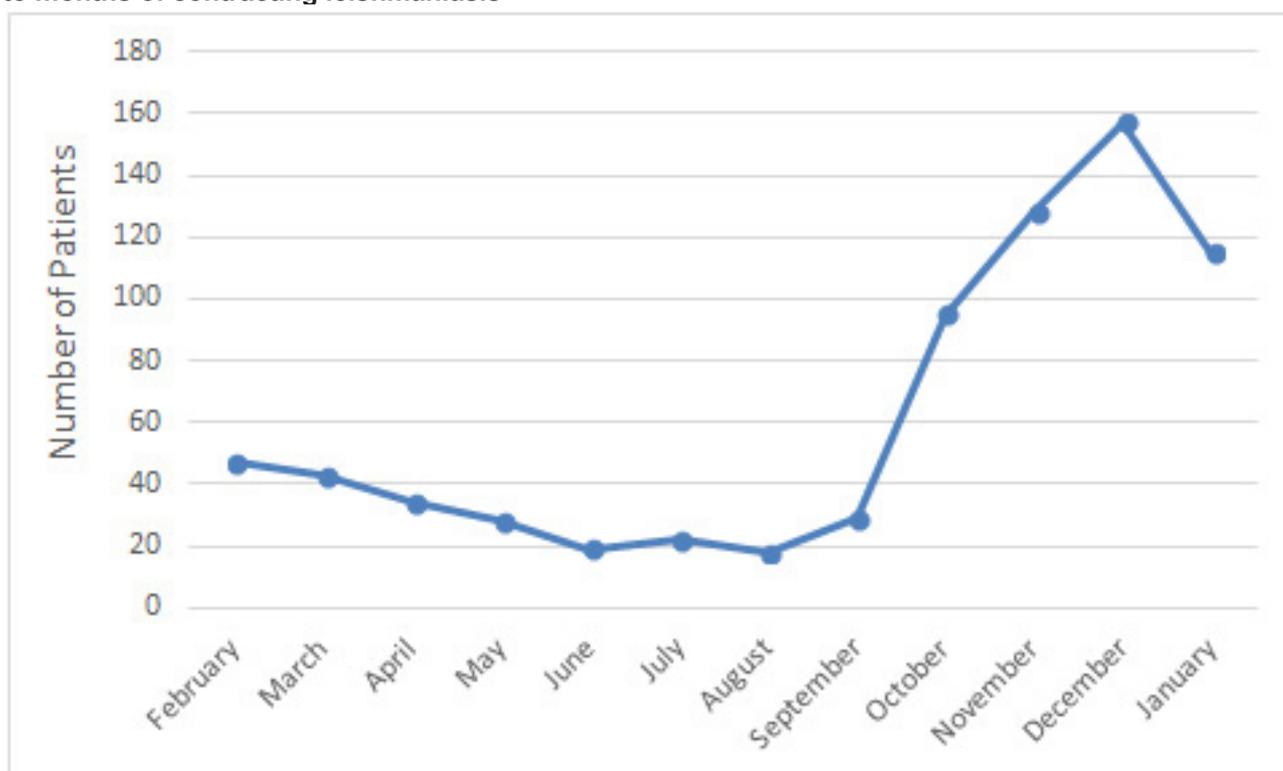
of Galgamuwa in Sri Lanka (4). In the present study, the number of under 10-year-old cases was 178, which is a high number. This is related to both 1) children playing games outdoors in the peak activity time of the mosquito, and 2) the weaker immune system of their bodies. Also, in most studies, children make the highest number of infected subjects (3, 5, 12, 14-16).

In 735 studied cases, the highest number of ulcers was observed in the upper limbs (38.8%), followed by the lower limbs (37.2%). The smallest number of ulcers was observed in the neck (2%). In studies like Galgamuwa in Sri Lanka (4), Pontello in Londrina (10), Vazirian Zadeh in Ramshir (12), the highest number of ulcers was observed on the hands. However, the study by Özkeklikçi in Turkey (16) indicated that the higher number of ulcers was on subjects' faces.

Finally, maximum number of infected cases were observed in December, November, and January, and the minimum number was in August. In previous studies in various places and climates, which determine the peak activity time of the mosquito, various months were indicated for the highest patient number, i.e., September (11), March (12) and February, and lowest patient number, i.e., August, August (12) and March (11).

Generally, it seems that in the study region, Cutaneous Leishmaniasis is mostly the disease of urban areas; and, since most cases were observed in men, education courses should be planned, focused on men, to prevent the outbreak of the disease in urban areas.

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Background Determinants of Physical Activity among Iranian Nurses: A Cross Sectional Study

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Abstract

Introduction: Physical activity as an important health promoting behavior requires understanding and identifying the factors that affect it. Although it is difficult to discover all the factors and components that affect behavior, achieving a number of factors and influential factors in these behaviors facilitates predictive power and helps practitioners to formulate educational programs and interventions. Research has shown that, one of the determinants of physical activity is the underlying and demographic factors. This study aimed to identify the underlying factors affecting physical activity among Iranian nurses.

Methods: This cross-sectional descriptive study was conducted on 418 nurses from Kurdistan and Isfahan Universities of Medical Sciences. In this study, hospitals were considered as class, and nurses were randomly selected using proportional allocation method. Data were collected by a two-part questionnaire including physical activity questionnaire and demographic characteristics questionnaire. Data analysis was performed by statistical tests such as t-test and chi-square test using SPSS 21 software at a significant level of 0.05.

Results: Based on the results, 273 (66.6%) nurses had low physical activity, 104 (25.4%) subjects had moderate physical activity and 33 (8%) subjects had intense physical activity. There was a significant relationship between marital status and physical activity ($x2 = 3.525$, $P = 0.041$), and also membership in sports clubs and physical activity ($x2 = 3.651$, $P = 0.036$) but in other cases, there was no significant relationship. Independent t-test showed a significant relationship between age and physical activity ($P = 0.043$, $t = 2.039$). However, there was no significant relationship between work experience and duration of exercise in the past with physical activity.

Conclusion: Inactive living and physical activity lower than the standard in nurses who are responsible for community health are a danger to health authorities. Given the effectiveness of some of the underlying factors on physical activity, custodians should develop appropriate strategies to moderate these factors. However, some underlying factors may not be adjusted but knowing these factors and their impact, can greatly reduce their negative effects.

Key words: Background Determinants, physical activity, nurses

Introduction

Regular physical activity as a significant health promoting behavior can prevent or delay the occurrence of chronic diseases and early mortality. There is also evidence that regular physical activity leads to mental health promotion, decrease of depression and anxiety symptoms, life satisfaction, and quality of life promotion [1]. It is also effective in reducing the risk of brain diseases [2]. Performing regular exercises (30 minutes in a day, two or three times a week) is a proven way to reduce total cholesterol, increase high density lipoprotein, reduce low density lipoprotein, improve general health [3]; exercise is also effective in improving blood pressure and those exercising if they have a heart attack, they will recover sooner and their blood pressure will be comparatively normal , compared to those wh are not physically active [3 and 4].

Physical activity can also have positive psychological effects, with reduced levels of anxiety and depression and promotes self-confidence. In addition, epidemiological studies have shown that life without physical activity increase earlier mortality rates [5]. Many researchers have emphasized exercise and physical activity as one of the ways to strengthen the immune system and prevent the spread of non-communicable diseases [6]. Physical activity can also promote women's health and prevent major diseases and disabilities in women [7]. Unfortunately, despite the great benefits of physical and mental health, many people do not have enough physical activity [8].

The results of the national survey in Iran, published by the World Health Organization, have shown that the inactivity rate in rural and urban areas with an emphasis on physical activity of leisure time between men and women in the age group of 15-64 years was 76.3% and 58.8%, respectively, and in the same age group was 67.5% [9]. Inactive living is one of the main risk factors for heart disease and it is estimated that in people with low mobility, the risk of these diseases is about two times higher [10].

Physical activity as an important health promoting behavior requires understanding and identifying the factors that affect it. Although it is difficult to discover all the causes and factors affecting behavior, achieving a number of factors and variables that affect these behaviors facilitates predictive power and assists practitioners in their initial prevention and development of educational programs and interventions [9].

Research has shown that one of the determinants of physical activity is the underlying and demographic factors [11] and many studies have been done to identify these factors and how they affect physical activity in different occupational groups [11-12-13-14].

The findings show that the average physical activity of nursing staff is less than average and lack of adequate physical activity and low mental health in nurses are common and this group has a lower level of health than

other health care providers and are exposed to health injuries 4.2% more than doctors [15-16-17-18]. Stressful work conditions and intensive work shifts have put the cortex at risk of developing non-respiratory diseases such as cardiovascular, musculoskeletal, and mental illness [19]. This is despite the fact that the special status of nurses among the members of the health team and their various roles, such as clinical care, counseling and training of patients requires that the nurse has adequate physical fitness and ability [17-20] and nurses cannot meet the needs of the clients unless much attention is paid to promoting their lives and health [16-17].

Therefore, paying more attention to the health status of nurses and determining their risk factors in this group that caters to other people's health is very important [16]. In this research, we have tried to study the underlying factors affecting physical activity among Iranian nurses. The results of this research can be effective in increasing organizational awareness especially among nurses and hospital managers regarding the provision of health promotion programs for nurses and their health improvement. In this study, the status of physical activity among nurses working in Kurdistan University and Isfahan Universities of Medical Sciences has been studied; it is hoped that this research can provide useful results in order to increase physical activity among nurses and thereby increase their health and consequently that of the society.

Methods

This cross-sectional descriptive study was conducted on 418 nurses from Kurdistan University and Isfahan Universities of Medical Sciences. In this study, hospitals were considered as classes then, using random sampling method with appropriate assignment among nurses, participants were randomly selected and a two-part questionnaire including International Physical Activity Questionnaire and demographic information questionnaire was provided to them and the required information was collected. It should be noted that, the subjects of research were instructed on how to make the design and the confidentiality of the information as well as the purpose of this project and all of them volunteered and willingly entered the study. The study population included all nurses working in educational and therapeutic hospitals in Isfahan and Sanandaj. All questionnaires were unnamed and incomplete questionnaires were excluded from the study. The sample size in this study was 348 by the following formula.

$$n = (\frac{Z_{1-\alpha/2}\,\sigma}{d})^2$$

In this formula, for a confidence level of 0.95 from the normal distribution table, $Z_{1-\alpha/2}$ of 1.96 was obtained σ is the standard deviation of the physical activity score and d is the maximum acceptable error in the estimate, which is considered equal to 0.15 σ. Considering the probability of a 20 percent drop in samples, 418 questionnaires were provided to the subjects. Data analysis was performed by statistical tests such as t-test and chi-square test, using

statistical software SPSS 21, at a significance level of 0.05.

Measurements
The information collection tool in this study was a two-part questionnaire and the information was collected by self-report from nurses.

Part One - Demographic Information
This part contains 12 questions that evaluated items such as age, gender, marital status, education, weight, height, waist circumference, membership record in a sports club, membership duration in a sports club, current membership status, work experience, and history of drug or alcohol use.

Part Two - Performance Questions (Physical Activity)
A standard short-form physical activity questionnaire (IPAQ) (21) was used to measure physical activity. This questionnaire contains questions that examine the status of physical activity and categorizes physical activity into three categories: poor, moderate, and intense. This questionnaire has been used to measure physical activity

by the World Health Organization and has been used in various studies in the country and its validity and reliability have been confirmed [22-9-23].

This questionnaire measures physical activity in the last 7 days and according to the final score, the intensity of the activity in the last 7 days is determined. The way it scores is that activities such as aerobics, high-speed cycling, climbing and basketball, which require more than 6 calories per minute, are called intense physical activity; and activities such as volleyball, badminton, room cleaning and walking, which require 3-6 calories per minute, are considered as moderate physical activities. In addition, any activity with a duration of less than 10 minutes will be eliminated. Calculation of energy intensity of total activities in the last 7 days was performed according to the IPAQ instruction and if the total energy calculated during the week is less than 600 met / cal / week, the intensity of the physical activity is poor and, if it is between 600 to 3000 met / cal / week, it is in the moderate class and if it is more than 3000 met / cal / week, it will be classified in the intense category [21].

Results

The findings of 418 completed questionnaires showed that 303 (72.3%) subjects were female participants and 111 (26.5%) were male and four did not answer this question. Of these, 88 were single, 268 were married and 63 did not respond to the marital status question. The average age of people was 33.10 years old and the age range in this study was 21 to 53 years old. In examining the status of educational degree, 90.9% had a bachelor's degree and 9.1% had a master's degree. According to the standard physical activity questionnaire, of 418 nurses participating in the study 273 (66.6%) subjects had poor physical activity, 104 (25.4%) cases had moderate physical activity and 33 (8%) cases had intense physical activity.

Table 1: demographic characteristics related to physical activity - Chi-Square Tests

Variables		physical activity 1= low, 2= moderate + high		Statistics
		1 n (%)	2 n (%)	
Sex	Female	201 (74.4)	98 (72.1)	X^2 = 0.265
	Male	69 (25.6)	38 (27.9)	P=0.344
Marriage	Married	176 (78.2)	85 (69.1)	X^2 = 3.525
	Single	49 (21.8)	38 (30.9)	P=0.041
Education	Bachelor	232 (91.7)	112 (89.6)	X^2 =0.451
	Masters(MA)	21 (8.3)	13 (10.4)	P=0.311
Sport club	Yes	89 (35.0)	59 (45.0)	X^2 = 3.651
	No	165 (65.0)	72 (55.0)	P=0.036
BMI Level	Normal	76 (27.8)	47 (34.3)	X^2 = 3.267
	Overweight	39 (14.3)	20 (14.6)	P=0.352
	Obesity	151 (55.3)	69 (50.4)	

Table 1 shows the results of the relationship between demographic variables and physical activity. In this table, the relationship between sex, marital status, educational status, history of physical activity and BMI status with physical activity status were analyzed using Chi-square test. Considering that among the nurses under study - according to the IPAQ questionnaire - only 33 (8%) subjects had intense physical activity; therefore, in order to determine the most important demographic factors affecting physical activity, intense and moderate physical activity have been combined and physical activity has been analyzed in two levels of people without physical activity (people with poor physical activity) and those with physical activity (those with moderate and intense physical activity).

Findings of this study showed a significant relationship between marital status and physical activity (X2 = 3.525, P = 0.041), and also membership in sports clubs and physical activity (X2 = 3.651, P = 0.036) but in other cases, there was no significant relationship.

According to the results of Table 2, the average age of nurses with physical activity was 31.95 years (SD = 7.91) and the mean age of nurses with no physical activity was 33.61 years (SD = 7.37), the results of independent t-test showed a significant relationship between age and physical activity (P = 0.043, t = 2.039). However, there was no significant relationship between work experience and duration of exercise in the past with physical activity.

Table 2: demographic characteristics related to physical activity - Independent Samples Test

	Physical Activity	N	Mean	Std. Deviation	t	P-value
Work experience	1.00	256	10.0293	7.47795	1.303	P=0.193
	2.00	126	8.9762	7.32471	1.312	
Age	1.00	273	33.6117	7.91240	2.039	P=0.043
	2.00	136	31.9559	7.37249	2.088	
Past exercise duration	1.00	76	3.1579	3.34286	-.950	P=0.344
	2.00	46	3.7826	3.80008	-.920	

Discussion

This study examines the underlying factors affecting physical activity among nurses in Iran. In total, 33.4% of nurses had physical activity (moderate and intense) and the majority of them were physically active in the poor category (66.6%). In this regard, a study conducted by Jalilian et al in 2010 among the staff of Hamedan University of Medical Sciences indicates a high prevalence of physical inactivity among Iranian employees; in his paper, he reported that about 65% of women working in Hamadan University had no physical activity [23], Gharlipour et al. in their study on medical emergency staff in Hamadan province in 2009 reported that, of the 102 participants in the study, 75 subjects (73.5%) had poor physical activity, 25 (24.5%) had moderate activity, and only 2 (less than 2%) had intense activity [24]. Mazloomy et al. also in the investigation of physical activity in employees in Yazd in 2008 showed that 73.6% of employees did not have physical activity [25]. The results of the study by Skaal et al. on employees of a state hospital in South Africa showed that 75.5% of the staff of the hospital had no physical activity [26]. These statistics are consistent with the results of this study and show that nursing society, like other employees, does not have a favorable status in terms of physical activity.

Other findings of the present study showed that there was no significant difference in physical activity among male and female nurses. The incidence of inactivity in women was 67.2% and in males 64.5%, and 32.8% of women and 35.5% of men had moderate and intense physical activity that, in this regard, there is no significant statistical difference between the two genders (X2 = 0.265, P = 0.344). In line with the findings of this study, McNeill et al., in a 2012 study of 850 employees with an average age of 44 years reported that, no significant relationship was found between gender of employees and their physical activity [13]. Contrary to these findings, Miller et al. reported that women have less physical activity than men of all ages [27]. Dishman and colleagues also state that men are twice more engaged than women in participating in sports activities [28]. Heinen

et al reported in their study of 1,370 employees in 2013 that there was a statistically significant difference between gender and physical activity (P = 0.001) [29]. This can be due to the fact that in the nursing profession there is no difference in the hard work and labor pressure due to the job situation with unusual working hours between male and female nurses and this can have adverse and deterrent effects on activities beyond the hours of work such as recreation and sports activities in both women and men's groups.

According to the findings of this research, a significant relationship was found between the current sports club membership (having basic physical activity) and the physical activity score (X2 = 3.651, P = 0.036). Robroek et al. also confirmed the same in a study of 726 employees with an average age of 40 in 2010 [11]. The findings of the study by Gazmararian et al. (2013), which was performed with the participation of 410 employees with an average age of 41.2 years, were in line with the results of the present study [30].

The results of independent t-test showed a significant relationship between age and physical activity (P = 0.043, t = 2.039). In this regard, there is a negative relationship between the level of physical activity and age in various studies [31-32] and the studies mentioned suggest that with increasing age, the amount of attention to physical activity is reduced. Studies by McNeill et al. (2012), Bopp et al. (2013), Heinen et al. (2013) and - VanWormer et al. (2012) were also consistent with the results of this study and had a significant relationship between age and physical activity and this is in line with the results of the present study [14-13-33-29]. As the age increases, the potential and energy of the individual naturally diminishes and on the other hand, the person is more involved in other issues such as family matters, occupations, children's issues, etc. Therefore, it is predicted that there is an inverse relationship between age and physical activity. However, many underlying factors affecting physical activity such as age cannot be adjusted. However, by adopting specific measures, such as reducing work pressures in line with age and placing nurses with

more work experience in lighter areas of work, greatly reduces this adverse effect and allows for addressing side affairs such as physical activity.

Conclusion

Inactive living and physical activity below the standard are known as a risk factor for various diseases and this is among the group that is responsible for the health of the community, and can be a danger to health officials, and this issue should be investigated as to what are the factors affecting physical activity among nurses. Knowledge about physical activity and its effective factors among nurses can help health researchers and planners to develop appropriate strategies for increasing physical activity of nurses and ultimately improving their health and by appropriate educational and executive planning, and timely intervention in modifying the moderating factors,   and encourage nurses to take physical activity at an acceptable level. However, some of the underlying factors affecting physical activity may not be adjusted but recognizing these factors and their impact will help to reduce the negative impacts of these factors by planning and appropriate strategies.

This study also has limitations, such as information gathering through a questionnaire and the collection of information from nurses working in the medical university (which should further inform other people about the benefits of dealing with Physical activity); in this regard, it should be noted that, in questionnaire and self-report studies, it is assumed that the person supplies the correct and true information, however, some respondents may not honestly complete the questionnaires and this is true for the current study. Another limitation of the study was the collection of information from the nursing corps that, it is suggested that in future studies, other staff at different levels of medical and non-medical (health and administrative) will also be examined so that more appropriate analysis can be done on health behaviors and the generalization of its results.

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Socio-Cognitive Determinants of Regular Physical Activity among College Students

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Abstract

Regular physical activity as an important health promotion behavior has many results in prevention or delay of chronic diseases and premature death. The aim of this study was to establish the determinants associated with regular physical activity among college students based on social cognitive theory (SCT). This study was a cross-sectional study carried out among 212 students in Abadan school of medical sciences, in the south west of Iran, during 2016. Data collection was self-report questionnaire in four parts including: demographic information, constructs of SCT, and standard international physical activity questionnaire – short form (IPAQ), social support. Data were analyzed by SPSS-16, and by using bivariate correlations and logistic regression at 95% significant level. About 61.7% (108/175) had low, 33.7 (59/175) moderate, and 4.6% (8/175) vigorous physical activity. Outcome expectation (OR=1.710), self-efficacy (OR=1.523), and friends' support (OR=1.149) was the best predictor for regular physical activity. It seems the planning and implementation of programs for physical activity promotion among college students is essential by emphasising on outcome expectation, self-efficacy, and social support.

Introduction

Regular physical activity is a significant aspect of a healthy lifestyle and has different positive impacts. Generally, individuals who are more active and have a better body fitness will have health related problems less frequently (1). The lack of physical activity is considered as a potential risk for obesity, cardiovascular diseases and death resulting from them. In addition, such problems can account for an immense economic burden of developing countries (2). In many healthcare programs in health related domains, the physical and psychological advantages of regular physical activity for reducing heath is shown with enough evidence (3). The results of numerous scientific studies have verified that even an average level of physical activity reduces the deaths resulting from cardiovascular disease and non-insulin-dependent diabetes mellitus (NIDDM) and has many protective advantages against hypertension, osteoporosis, colon cancer and obesity (4). The minimum physical activity for the protection and improvement of heath in adults is 30 minutes with average intensity and for five days a week (5). Doing regular exercises (30 minutes a day, two or three days a week) is a proven way for reduction of total cholesterol, increase of high-density lipoprotein (LDL), low-density lipoprotein (HDL) and improvement of general health. In addition, epidemiological, clinical and experimental studies indicate that regular physical activity and exercise is critical for maintaining and increasing bone mass and physical strength and helps individuals in preventing osteoporosis-related fractures (6). The inclination towards sedentary lifestyle has increased with the advancement of technology in a way that a lot of time is spent watching television, working with computers, using car and elevator and the like and thus, the time is spent in a sedentary way, and despite the recommendations of health organizations for physical activities with average to high intensity during the week, inactivity is very common (7). On the other hand, many studies indicate that physical activity is reduced from adolescence to adulthood with the increase of age (8). These realities show the necessity of planning for the increase of physical activity in different groups in society and in this regard, different studies have shown that the prerequisite for any planning is the knowledge of the existing status of the problem in the target group of the program (9). In addition, it should be pointed out that human behavior is a reflection of different cognitive determinants and the use of the theories of behavior change, especially social cognitive theory, can guide experts in knowing the cognitive determinants impacting behavior (10). Meanwhile, SCT is one of the most common theories used for the analysis, regulation and change of many human behaviors including physical activity behavior and has a comprehensive view of the aforementioned socio-cognitive determinants (9). In terms of physical activity behavior, structures such as outcome expectation, outcome expectancies, self-efficacy, self-regulation and social support have been paid more attention (11). Comprehensive health education programs need to emphasize on psychological factors that mediate and predict health-related behaviors (12, 13). Considering that many studies were done in Iran without using the comprehensive theory to predict physical activity, and furthermore, students in southern Iran because of hot weather and geographical conditions had lack of regular physical activity, our SCT based study focused on exploring cognitive determinants related to the regular physical activity in a sample of youth college students in Iran.

Material and Methods

This cross-sectional study was conducted among 212 medical college students in Abadan school of medical sciences, the southwest of Iran; during 2016 (total students in this school were 537). Participants were selected in random sampling with probability proportional to size, and data were collected by using questionnaire in self-report. Only the subjects, who were students in Abadan school of medical sciences, were eligible to participate in this study. This study has been approved by the institutional review board at the Abadan school of medical sciences, Abadan, Iran (IR.ABADANUMS.REC.1394.59). Of the population of 212, 175 (82.5%) signed the consent form and voluntarily agreed to participate in the study.

The variables assessed in this study included four sections. Prior to conducting the main project, a pilot study was carried out. Initially the relevant questionnaires were administered to 25 students who were similar to study population in order to estimate the duration of the study conduction and to evaluate the reliability of the questionnaire.

A: Background questions
Included; age (years), sex (male, female), marital status (single or married), live in dormitory (yes or no), and history of participants in sport club (yes, no).

B: SCT constructs
This section included 28 items which were composed under four major constructs including (a) outcome expectation towards physical activity, (b) outcome expectancies towards physical activity, and (c) self-efficacy toward physical activity. SCT constructs was designed based on a standard questionnaire (11, 14). Five items were designed to measure outcome expectation (e.g., if I am active, I will be happy). Five items were designed to measure outcome expectancies (e.g., I will be happy after doing physical activity). Six items were designed to measure self-efficacy (e.g., I think that I can do physical activity every day). In order to facilitate participants' responses to the items, all items were standardized to a 5-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). To estimate reliability alpha Cronbach coefficient was used for each constructs questionnaire: outcome expectation (α=0.83); outcome expectancies (α=0.81); self-efficacy (α=0.84) and social support (α=0.87).

C: Social Support
Social support was evaluated by 12-item standard scale (15). Each item was measured on an ordinal 5-point Likert-type scaling (1=strongly disagree, 5=strongly agree). This included three domains; family, friend and other significant.

D: International Physical Activity Questionnaire-IPAQ
A Persian form of international physical activity questioner -IPAQ (16) was used to measure physical activity.

Data were analyzed by SPSS version 16 using appropriate statistical tests including bivariate correlations and logistic regression at 95% significant level.

Results

The mean age of respondents was 21.01 years [95% CI: 20.79, 21.23], ranging from 18 to 25 years. Almost, 58.9% (103/175) participants were female and 41.1% (72/175) were male. In addition, 3.4% (6/175) participants were married and 96.6% (169/175) were single. Furthermore, based on the results, 61.7% (108/175) had low, 33.7 (59/175) moderate, and 4.6% (8/175) vigorous physical activity.

Table 1 shows mean and standard deviation and bivariate correlations between the SCT constructs, which were statistically significant at either 0.01 level. The findings indicate that for the sample, outcome expectation was significantly correlated to self-efficacy (r=0.177), and outcome expectancies (r=0.662), and not significantly correlated with social support (r=0.122). Outcome Expectancies were significantly correlated to self-efficacy (r=0.143), and not significantly correlated with social support (r=0.058). In addition, self-efficacy was not significantly correlated with social support (r=0.121).

Logistic regression analysis in Backward step-wise model building procedure was conducted and finally on the 4th step the procedure stopped and the best model was selected, among the SCT constructs: outcome expectation (OR=1.710), self-efficacy (OR=1.523), and friends support (OR= 1.149) was the more influential predictor on physical activity (Table 2).

Discussion

The findings of the present study indicated a high prevalence of inactivity in studied students in a way that 61.7 percent of them were in the low category in terms of physical activity and these findings are consistent with the findings of the study conducted by Moeini et al on students in western Iran (17). The findings indicate a low level of regular physical activity in Iranian students, compared with students outside Iran (18, 19). Several studies stated that college students in one of the most important groups should pay special attention to their health problems (20-22). The low statistics of regular physical activity in Iranian students and the lack of enough motivation for participation in such activities indicate the necessity of exploring the socio-cognitive determinants that impact on the creation of such behaviors in students.

Social cognitive determinants have a modifying role and are acceptable intermediates in innovative change in health related behaviors including physical activity. For example, their effectiveness related beliefs regarding the ease or difficulty of overcoming personal or environmental barriers of physical activity modify the relationship between natural occurrence of change in received social support and reduction of physical activity in middle-aged females (23).

Our findings indicated outcome expectation, self-efficacy, and friends support were the more influential predictors on physical activity. In this regard, overall, positive relationships have been verified between support received by individuals, self-efficiency and behaviors related to physical activity in a way that a study has shown a significant positive relationship of perceived self-efficacy, family support and friend support with physical activity related behaviors (24). Also, the social support of friends that has been verified in most studies on physical activity is proved in this study too. In fact, researchers found that

Table 1: Predictor variables of physical activity based on bivariate correlation analysis

	Mean (SD)	Scores Range	X¹	X²	X³
X1. Outcome Expectation	20.86 (3.17)	5-25	1		
X2. Outcome Expectancies	20.02 (3.57)	5-25	0.662**	1	
X3. Self-Efficacy	14.48 (5.01)	6-30	0.177*	0.143	1
X4. Social Support	42.55 (8.77)	12-60	0.122	0.058	-0.121

*P < 0.05;   **P <0.01

Table 2: Logistic regression analysis for SCT variables related to physical activity

Variables	Odds Ratio	95.0% CI Lower	Upper	P value
Step 4				
Outcome Expectation	1.710	1.378	2.106	0.001
Self-Efficacy	1.523	1.330	1.743	0.001
Social Support	1.149	1.001	1.318	0.048

for participation in physical activity young individuals need a motivator and friends are a motivator in this regard (25). This means that the encouragement by friends is a significant variable in doing physical activity by students while such a positive relationship is not observed for family support as students are with their friends in campus and are impacted by their peers more due to their age.

Knowing the amount of physical activity among students and the socio-cognitive determinants impacting them can help in timely intervention and health promotion planning for encouraging students to perform physical activity. The results of the present study indicated that outcome expectation, self-efficacy and friends support are among the socio-cognitive determinants that impact on and predict doing physical activity in students and these findings can be used in designing interventions.

The present study had some limitations such as data collection through questionnaire which can be accompanied by some errors. Also, the present study was conducted only on a small group of medical students in southern Iran and may not be generalizable to the whole Iranian student population.

Conclusion

Overall, 61.7% had low, 33.7 moderate, and 4.6% vigorous physical activity; in addition, outcome expectation, self-efficacy, and friends support were the more influential predictors on regular physical activity among college students.

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Frequency of Suicide and its Related Factors in Patients Referring to Emergency Department of Hospitals of Abadan City in 2014

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Abstract

Introduction: The present study was conducted to determine the frequency of suicide and its related factors in patients referred to Emergency Department of Hospitals of Abadan city in 2014.

Materials and Methods: This is a descriptive, cross-sectional study. The statistical population of the study consisted of all Abadan population and the sample of the study consisted of those who were referred to the Emergency Department of Abadan during the year 2014 which included 282 people who were selected by census sampling method. Data were collected using a checklist and analyzed using relative risk and mental health and SPSS-22. The level of significance was considered (p <0.05).

Results: The results showed that the prevalence of suicide was estimated 2.01 among the women and 4.95 among men in every 100,000 people. The suicide rate in the studied society was 3%, which was not statistically significant in the two genders. In 83.5% of the cases, the method used was medications but it included only 1.7% of the lesions. The highest frequency of suicide attempts was observed in single and employed men and also in married and housewives.

Conclusion: Due to the high rate of suicide attempts in young people, it is recommended that an effective step should be taken through careful planning by the authorities and families and the necessary training in this area. The training of people at risk, including people who have attempted suicide seems necessary.

Key words: suicide, frequency, factors, Abadan

Introduction

One of the major health problems in the whole world is suicide (1). Suicide and suicide attempts are important public health and social behavior issues (2). The phenomenon of suicide can be considered along the continuum of thinking of suicide until action to commit it (3).

The World Health Organization (1993) has defined suicide as a deliberate, voluntarily, and conscious termination of life(4). Some see suicide as a practice in which a person, without interference of other people, may have abnormal behavior such as self-harm or substance abuse (5). Every year, one million people die from suicide in the world (6), and in the past 45 years, the rate of suicide has increased by 60% in the world (7) while suicide is considered as the 13th cause of death in the world (8) and the third cause of death in the age group of 15-45 years (9).

The attempted suicide rate was 10 to 40 times more likely than suicide leading to die in Bahar city, Iran (10). This phenomenon is also considered to be a social loss, in addition to personal and family losses (11), and due to the complexity of interactions and communication in all human societies, the suicide rates are increasing(10), so that the World Health Organization (WHO) reported that suicide rates have been rising over the past half century and have predicted that rates would lead to an increase of 1.5 million people in 2020 (12), and for each suicidal attempt, 10 to 20 suicide attempt cases occur, while more suicide attempts are observed in young people and women (13).

This phenomenon is one of the most complex aspects of human life, and its dimensions and angles are not well understood (14). There are a series of risk factors for this action that include psychiatric disorders, social factors, psychological factors, biological factors and physical illness (10). The age of over 45, females, marital status (single, divorced and widowed), unemployment, conflicting interpersonal relationships, chronic psychological disorders, smoking and alcohol are among the risk factors for committing suicide (15-16).

The results of previously conducted research reveal that issues such as marital conflicts (17) and acute crisis and family problems (15), complications with spouses' families (18), differences with parents (10), forced marriage of women, women's fear of husband, and husband violence (15), unemployment, economic problems are the most common causes of suicide (19).

Recent studies of epidemiology suggest that the prevalence of suicide among adolescents is increasing dramatically, while its prevalence among high school students reaches 3.5 to 11% (20). Suicide is currently the cause for 12% of adolescent deaths, the second most common cause in people between the ages of 25 and 37, and the third most common cause of death in people aged 15 to 24 in the United States (24-21).

Studies also show that nearly half of suicides occur in the three vast countries of India, China, and Japan (25).

But studies during the recent two decades in Iran have shown that suicide and attempting suicide is increasing especially among adolescents and young people of most regions of the country, such as Kerman, Tabriz, Qazvin, Karaj, Shiraz, Kurdoki, Hamedan, Gilan, Masjed Soleiman and Dezful, Ahvaz, Islamabad, and Mazandaran (26), and about ten suicides occur daily and the western provinces of the country account for the largest share (27); however its rate is reducing in most advanced countries, including Britain and Australia. (29-28).

Since Abadan is an industrial city which is very diverse due to the migration of different people and considering the impact of cultural and ethnic factors on the rate of suicide and the difference between Abadan society and other cities in Iran, and the effects of the war and its consequences, such as unemployment and addiction, knowing these factors can provide solutions to prevent suicidal attempts for the Social and health care providers and health authorities. Since there is no statistical data on suicide rate and its causes and methods used by these people in Abadan, we decided to carry out a study to investigate the frequency of suicide and its related factors in Abadan.

Research methodology

The present study is a descriptive and cross-sectional study in order to determine the frequency of suicide and its related factors in patients referred to Emergency departments of Hospitals in Abadan city in 2014. The population consisted of all population of Abadan city and the sample of the study included subjects who referred to the emergency department of Abadan (emergency department of Taleghani Hospital, Shahid Beheshti Hospital) during the year of 2014 with suicidal attempt. Due to the fact that the annual statistics are generally approved by the World Health Organization or forensic medicine, and given that different seasons are effective on suicide rates, it was decided that the timeframe of the four seasons should be considered.

The criterion of the study inclusion is committing suicide (attempting or acting), willingness to participate in the study by a person or companion and literacy, and the exclusion criteria included only those who refused to participate in the project. After obtaining a written license from Abadan Faculty of Medicine and Heads of Hospitals and explaining the objectives of this study to emergency head nurses, the researchers presented the checklist and completed the questionnaires using information from the suicidal person or his companions, orally, through questions and answers. The completion of the questionnaire was considered to be the consent of the subjects to participate in this research project. Unsolicited information on the name was completed. It is worth noting that the information was collected monthly and the sampling lasted twelve months. In order to collect data and carry out the research, a checklist with 20 questions was first set up, in which the questions were closed as response and included the demographic information and the field of suicide (age, gender, marital status, place of residence, occupation, level of education, ethnicity, History of mental illness, addiction, alcohol

abuse, suicide season and suicide), suicide (self-burning, self-mutilation, poison, pills, arms, fall, etc.), the cause of suicide (family differences, differences with the spouse, Emotional failure, academic failure, sexual harassment, etc.) and was confirmed by four faculty members in nursing. It is worth noting that the two hospitals of Oil and the 17th of Shahrivar refused to provide data.

Data analysis was performed using descriptive statistical methods (mean, frequency, percentage, standard deviation) and analytical methods including relative hazard and Mental Hazards-22 and SPSS tests. The data were analyzed using SPSS version 22. The level of significance was considered ($p < 0.05$).

Results

According to the results of this study, a total of 300 people were included in the study. The age range of patients was between 11 and 54 years old with a mean and standard deviation of 25.44 ± 7.50. Among these, there were 199 women (66.3%) and 101 men (33.7%). 253 people were resident in the city (84.6%) and 44 were rural residents (14.7%). The most abundant ethnicities were Arabic with 146 and 48.8%, and the lowest demographic was Kurdish ethnicities with 3 and 1%. 244 subjects (81.6%) had committed suicide for the first time and 55 (18.4%) had a history of suicide. 33 (11%) had mental illness (depression, schizophrenia, and obsession). 29.7% of suicides happened in the Spring, 28.7% in the Summer, 22% in the Autumn and 19.7% in the Winter. 60 people (21.1%) had one child, 33 (11.6%) had 2 children, 8 (2.8%) had 3 children, and 3 (1.1%) had 4 children while 36 (12.6%) had no child.

84.6% were urban and 14.7% were rural. 49.3% of household cases had more than 5 people. 37.3% had 3-5 people. 43.8% had revenue more than 1 million Tomans. The revenue of 30% was between 500,000 and 1 million Tomans and 26.3% of population had less than 500,000 Tomans. 18.4% had previous suicidal experiences.

277 people (92.3%) did not have a history of physical illness. 97.3% had no addiction. 99.7% had no alcohol and no history of suicide. 44.3% of suicide cases happened between 20:00 and 5:00 am and 38.7% happened between 13:00 and 20:00. Information was collected from Shahid Beheshti Hospital and 36.3% was collected from Taleghani Hospital. 97% of suicides were unsuccessful. 66.3% of cases of suicide subjects were female and 33.7% were male.

Table 1: Suicide rates in different age groups of women and men (RR - Relative risk of suicide in men compared to women)

Age	Suicide attempt		Relative Risk	Significance Level
	Male	Female		
10- 24	94.4	97.1	0.972(0.904, 1.046)	0.405
+2	95.7	98.9	0.968(0.908, 1.031)	0.202
Total	95.05	97.99	0.970(0.924, 1.018)	0.158

Suicide attempts in women were more than men with 199 suicide attempts in women against 101 suicide attempts in men, indicating that women nearly doubled the suicide rate of men. As shown in Table 1, men commit suicide in total of 95.05 and in women 99.97, aged between 24 and 10 years, respectively, for men and women 94.4 and 97.1, and at age 25 it is more in 95.7 and 98.9. In two age groups, the rate of suicide in women is higher than the men, although there is no significant difference, and as it is observed that with the change of age, the rate of suicide also increased slightly.

Table 2: Suicide rates in different age groups of women and men (RR - Relative risk of suicide in men versus women)

Age	Suicide attempt		Relative Risk	Significance Level
	Male	Female		
10- 24	5.6	2.9	1.962(0.402, 9.222)	0.694
+25	4.3	1.1	4.043(0.376, 43.456)	0.531
Total	4.95	2.01	2.463(0.676, 8.972)	0.293

Although suicide attempts was higher in women than men, successful suicide rates in men are higher than in women, although this is not statistically significant.

The suicide rate in the population of Abadan males was 5.6 at the age group of 24-10 years and in the population of Abadan women was 2.9. As a result, the relative risk of death from suicide in men compared to women at the age of 10-24 years is 1.926 with a confidence interval (9.222.9, 0.402). The suicide rate in the population of Abadan men over age of 24 was 4.3 and in the population of Abadan women was 1. 1. As a result, the relative risk of death from suicide in men compared to women aged 10-24 years is 4.043 with a confidence interval (0.4456, 0.337). The suicide rate in the population of Abadan men was 4.95 and in the population of Abadan city was 2.01. As a result, the relative risk of death from suicide in men against women is 2.463 with a confidence interval (0.89772, 0.6676). In general, it can be stated that the relative risk of death from suicide is 2.5 times that of women.

Table 3: Frequency and relative rate of suicide in different age groups in two genders

Age	Male			Female		
	Complete Suicide	Suicide Attempt	Rate of lethality	Complete Suicide	Suicide Attempt	Rate of lethality
10- 24	3(60)	51(53.1)	5.55	3(75)	101(51.8)	2.88
+25	2(40)	45(46.9)	4.25	1(25)	94(48.2)	1.05
Total	5(100)	96(100)	4.95	4(100)	195(100)	2.01

Table 3 shows the relative frequency and rate of successive suicides, suicide attempts, and the rate of death in men and women in terms of age. Overall, total suicide in men is 5, of which 3 occurred at the age of 24 to 10 years, and two cases at 25 to 25 years of age. In total, 96 unsuccessful suicides have occurred, 51 of which were at the age of 24 to 10 years and 45 at age of 25. In women, the total number of suicides was 4, of which 3 occurred at the age of 24 to 10 years and one case was 25 years and older. Suicide was unsuccessful in a total of 195 cases, 101 of which were at the age of 24 to 10 years, and 94 cases were over 25 years of age. Death rate decreased with age in men and women.

Table 4: Relative Suicide Frequency and suicide attempt in Career Groups, Marriage and Education of two genders

Age	Male			Female		
	Complete Suicide	Suicide Attempt	Rate of lethality	Complete Suicide	Suicide Attempt	Rate of lethality
Unemployed	1(20)	34(35.4)	2.8	2(50)	139(71.6)	1.4
Employed	4(80)	55(57.3)	6.7	0(0)	30(15.5)	0
Education	0(0)	7(7.3)	0	2(50)	25(12.9)	7.4
			P=0.679			P=0.219
Single	3(60)	67(69.8)	4.3	1(25)	78(40)	1.3
Married	2(40)	29(30.2)	6.5	3(75)	117(60)	1.5
			P=0.645			P=0.545
Illiterate	0(0)	4(4.2)	0	0(0)	16(8.2)	0
High School	1(20)	38(39.5)	2.6	3(75)	65(33.3)	4.4
More than High School	4(80)	54(56.3)	6.9	1(25)	114(58.5)	0.8
			P=0.287			P=0.286

Table 4 shows the prevalence and relative frequency of successive suicides, suicide attempts, and rate of death in men and women in terms of career, marriage and literacy. Overall, complete suicide in males was 5, of which 1 case was an unemployed man, and 4 cases occurred in working men. Suicide was unsuccessful in a total of 96 cases, of which 34 were unemployed men.. In women, the total number of suicides was 4, of which 2 were in housewives and 2 were working women. Unsuccessful suicide happened in a total of 195 cases, of which 139 were in housewives, 35 in employed women and 25 in women in education. There was no significant difference between men and women.

Complete suicide in single men was 3 cases, 2 cases in married men, and attempted suicide 67 cases in single men while in 29 cases in married men. The highest rate was in the married men. Complete suicide included one single woman, 3 married women, and suicide attempts included 78 cases of single women and 117 of married women, while the highest rate was also observed in married women. There is no significant difference in lethality between women and men.

Complete suicide happened in one case with literacy of high school, and in 4 cases of men with literacy higher than high school; however, suicide attempts included 4 cases in illiterate men, 38 cases in men with high school literacy and 54 cases in men with higher than high school literacy. The highest rates of lethality happened in male graduates with degrees and higher education levels. Complete suicide included 3 cases of women with high school literacy, and 1 in women with high school and higher education level, and suicide attempts in illiterate women was 6 cases, in women with high school education was 65 cases and in women with high school and higher was 114 cases, the highest rate. Fatalities in women with a post-secondary education are lacking. There is no significant difference between women and men.

Table 5: Frequency and relative rate of suicide and suicide attempts based on the suicide method in two genders

Method	Male			Female		
	Complete Suicide	Suicide Attempt	Rate of lethality	Complete Suicide	Suicide Attempt	Rate of lethality
Hanging	4(80)	1(1.05)	80	0(0)	0(0)	-
Medicine	0(0)	82(85.4)	0	3(75)	175(90.2)	1.7
Poisoning	0(0)	9(9.4)	0	1(25)	16(8.3)	5.9
Gun	1(20)	0(0)	100	0(0)	1(0.5)	0
Phlebotomize	0(0)	1(1.05)	0	0(0)	0(0)	-
Self- Immolation	0(0)	0(0)	-	0(0)	2(1)	-
Others	0(0)	3(3.1)	0	0(0)	0(0)	-

Table 5 shows the prevalence and frequency of successful suicides, suicide attempts, and lethal rates in men and women. Complete suicide in men was conducted through hanging in 4 cases and guns in 1 case. The highest suicide attempt rate in men was conducted by medicinal drugs in 82 cases. Complete suicide in women was conducted through medicines in 3 cases and poisoning in 1 case, and most cases of suicide attempts, 175 reported use of medicines.

Table 6: Frequency and relative lethal rate of suicide and suicidal attempts based on the suicide causes in two genders

Causes	Male			Female		
	Complete Suicide	Suicide Attempt	Rate of lethality	Complete Suicide	Suicide Attempt	Rate of lethality
Family problems	1(20)	46(47.9)	2.1	1(25)	69(35.5)	1.4
Problems with spouses' family	0(0)	8(8.3)	0	1(25)	35(17.9)	2.8
Emotional failure	0(0)	1(1)	0	0(0)	31(15.9)	0
economic problems	0(0)	1(1)	0(0)	0(0)	3(1.5)	0
Nervous	1(20)	4(4.2)	20	1(25)	12(6.2)	7.7
Addiction	0(0)	18(18.8)	0	0(0)	22(11.3)	0
Others	3(60)	16(16.7)	16	1(25)	21(10.7)	4.5
Educational failure	0(0)	0(0)	-	0(0)	2(1)	0

Table 6 shows the relative rate successful suicides and suicide attempts, and the rate of death in men and women in terms of suicidal ideation. Complete suicide was observed in 1 man due to family history, in 1 case due to the nervousness, and the other 3 cases, and the highest cause of unsuccessful suicide was familial problems. In women, the causes of suicide included familial problems in 1 case, problems with spouse's family in 1 case, nervousness in 1 case, and 'other' in 1 case, and most cases of suicide attempts have occurred due to family problems.

Discussion

In Abadan, as in other parts of the country, suicide is a major public health issue. The present study was conducted on the frequency of suicide and related factors in patients referred to the emergency department of Abadan hospitals. In the present study, the results indicate that suicide attempts in women are more than men, which can be explained by the fact that most suicide attempts occur in the second and third decades of life, which seems to be due to important factors such as puberty, marriage, emotional relationships, responsibility, and finding social status. Therefore, the stresses of a person in this age range are more and more severe and increase the rate of suicide attempts (30). This may be due to less tolerance of women against the problems or more perceived problems and their subordination in some areas due to specific cultural conditions (31).

Due to the many problems that women are exposed to and the social vulnerability of women, which has weakened them more than before, as well as the violence of men against women and sexual assaults that may be directed toward some women, and in some cases women's lack of awareness of their rights or being under control in some

areas due to specific cultural conditions. They may attempt suicide when dealing with problems. In some cases, they use suicide as a means of protesting against problems (32-32).

According to the global statistics, Iranian women commit suicide three times more often than men (32). Suicide among women in the provinces of Ilam, Kermanshah and Lorestan is the highest rate (33). In the study of Golestan province (34), suicide attempts were observed in women more than men which is consistent with our study, but it is inconsistent with the results of a study conducted in Hamadan and (35) showed that female patients were less than men in the hospitals (48% versus 52%).

The study found that suicide rates in men are more than women, which can be explained by the fact that men are more likely to be at risk of suicide compared to women, so that these factors increasingly lead to committing suicide (36). The man's character is such that his job, social relationships, and identity are separate from each other. Similarly, the desire of loneliness is more in men than women even when they are not isolated in society, and they find it difficult to create friendly and social relationships. As it is acknowledged that deaths due to suicide in men is more three times than women (37).

Additionally, the high rate of successful suicide in men depends on the methods used by them; they use harsher methods than women, including shooting and hanging, which can point to (38) the aim of suicide in men is ending their lives, and they don't consider suicide as a means of protesting their status. These findings are similar to the findings of a study in the United States (39). Some internal studies also report the opposite results to this study so that the number of female suicide causing deaths with 32 cases was higher than the number of men with 19 cases (40). This difference can be due to cultural and economic issues in different parts of the country (41).

The finding that, on the contrary unsuccessful suicide has declined with age and this decline is significant in women, can be interpreted that, at adolescence and young age, women seek attention after any failure, and because of lack of familiarity with the correct problem-solving skills and perhaps observational learning, quickly attempt suicide, and this is the dominant mode of life for women during this period, but as the age rises and they find relative stability in their lives, they become acquainted with the correct ways of coping and dealing, and their attitude toward the strain of life changes and it is sometimes due to love for their child and the spouse or parent, they try to raise their threshold of tolerance and solve the problem and help those who are expert in this regard; therefore, the rate of successful suicide decreases.

The finding that the highest rate of suicide and suicide attempts in men and women aged 24 to 10 years can be explained by the fact that this is due to adventure, less tolerance, problems from adolescence to youth, intellectual instability, social, occupational and economic factors, the increasing expectations and sometimes the weakness of

faith. Suicide is also the 11th cause of death in the general population and the third cause of death in the population of 15 to 24 years old (42). In this study, the highest rate of suicide attempt was reported in the age group of 10-80 years old (85%), which is similar to other studies in our country (43), and a study in Greenland reports similar results to this study (44). This finding is consistent with the study of Ardabil with the highest rate of mortality in the group under 25 years of age (45) but inconsistent with studies of Mousavi and Taziki (47-46) in the fact that the mortality rate in the age group over 45 years was several times more than lower ages.

Regarding the level of literacy and the highest rate of lethality in women with high school education, we also saw a similar situation in the way that suicide attempts could be seen as a higher proportion of literacy than in the successful suicide group. In the sense that more literate people are committing suicide, they use this method to solve their problems, while illiterates have had more suicide. Similar results can be seen in several other studies (48-46), (37). Regarding the relationship between suicide and marital status, the situation was different in the two genders. For this reason, we discuss each separately. In women, both in successful suicides (75%), and in suicide attempts, the majority wer married women (60%). Additionally, married women in successful suicide attempts against single women are unfortunately found in most regions of Iran. In most cases, women suffer from more mental stress through marriage, and most of these stresses seem to be related to spouses' misconduct (41).

But in men, while there were not many differences in successful suicides, the number of married and single people showed almost three times the rate of marriage in unsuccessful suicides. In the study of Semnan among suicide committers, married women were reported more than single women with 61%, but it was reported as 34% in married men and 66% in single men, which is almost the same as the results of our study (50).

In a study by Dawas and colleagues in a study, suicide rates in married women and single men were the most frequent (51). Their results are consistent with the present study. Single life is accompanied by failures that may lead to suicide. Given the high rate of suicide in married women, the value of addressing the problems of housewives is doubled (41).

However, it is inconsistent with the studies conducted by Gaidi's (52) and Bakhsha (53) and studies conducted in Italy and Canada (54-55), which shows that suicide rates are more significant in singles. This could be due to the worse economic conditions and the beliefs of families over the years.

The economic situation is related to suicide. Occupation is a good barrier against suicide and, in fact, those who do not have a job and source of income are more suicidal (41). However, the findings of the study revealed the opposite, with 80% of the deceased suffering from suicide in men, and in suicide attempters in employed men with 57.3% and

housewives were 71.6% in most groups (40). Therefore it can be said that the occurrence of suicide is not a single factor, and there are certainly several underlying and revealing factors happening in the life of the individual.

Our findings are inconsistent with the studies of Golder Michael and Yasaki who showed that unemployed people are at risk of suicide and have a positive and specific relationship between unemployment and suicide rates in their studies (56-57).

In the present study, successful suicide rate through hanging, medicine, drug usage, self-immolation and use of weapons was significantly higher than other methods. The results of the Ministry of Health survey in 18 provinces showed that most of the methods used include self-immolation, hanging, drugs, poisoning and weapons (58). In general, there are differences in the suicide methods between different countries. In Sweden, four methods of poisoning, hanging, weapons, and drowning are more common. In the United States, weapons, hanging, poisoning and the use of cold weapons such as knives (59), in Australia high doses of drugs, car carbon monoxide poisoning, weapons, and hanging, in India poisons, hanging, self-immolation, drowning and in China hanging, drowning, poisoning, and jumping from a height make up the most used objects (60).

Meanwhile, the mortality rate of each method is largely influenced by the time elapsed between the use of the method and the time of death, which is more than self-immolation in the use of germination. Therefore, it is possible to save them. (41).

In the present study, a higher percentage of subjects had selected drug consumption and poisoning for suicide attempt (85.4% men and 90.2% women). In other studies, the most common suicide attempt was high-dose (63-61), although in some studies other approaches are at the top (31). Maraveji and colleagues in their study state that the prevalence of suicide with medicine in Iran can be due to availability of drugs, familiarity with various drugs and painlessness of this method. The use of drugs in those whose main purpose of committing suicide is a way of solving their problems, and not death, can be another cause of the high prevalence of this method, which may somehow be used to attract the attention of others to their problems, and this necessitates the increase of emotional communication in this group of people. (31).

Another difference is the relationship between the rate of suicide and sex. In the present study, most men used medicines (84.4%) and then poisons (9.4%), but most women (90.2%) had used medicines followed by poisoning (8.3) to commit suicide, and men used drugs to complete suicide with methods of treating them, using weapons and drugs.

In this study, there was a significant relationship between the outcome of suicide and the seasons of the year. The highest rate of successful suicide was reported in Autumn and Spring, and the highest rate of unsuccessful suicide was reported in Summer and then in Winter. In a study, it has been determined that the difference in seasonal cycles is highly dependent on the method and the results of suicide (64). In these findings, in some internal studies, it has also been proven that there is a significant relationship between season and frequency and the outcome of suicide (65), as well as a seasonal suicide pattern with peak suicide in the Spring and Summer and a clear reduction has been reported in the Winter and Summer (66) which may be due to the climatic and occupational conditions of people in different seasons (67).

However, Sadat did not see any connection in Yasuj between suicide and the season (68). To justify the effect of the seasons on suicide an be referred to two hypotheses. The socio-demographic hypothesis, which clarifies that the social connections of individuals increase with the onset of the warm season. Such connections increase psychological pressure and ultimately commit suicide in them in those who do not tolerate these connections increase while the climate hypothesis states that with the onset of the spring, the temperature of the environment and the length of hours of light per day increases. Such important changes in the environment will increase melatonin and cholesterol, especially changes in the serotonin pathway. Which itself increases the access of brain cells to serum tryptophan and, as a result, to readiness for B One person leads to suicide (69).

Conclusion

Since this study revealed that women are more likely to use less risky methods, and that sedative drugs have been used more than once, and one of the essential requirements and practical steps in reducing suicide attempts, is training and stressing physicians particularly for general practitioners, prescribing drugs to those who do not cause poisoning and death in case of abuse. Other studies also emphasized the role of educating general practitioners for the correct and timely treatment of mental health patients and control of those at risk of suicide.

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Investigation of Self-care Behaviors and the Related Factors in Older People with Diabetes Type 2 Visiting Tehran Selected Hospitals in 2016

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Abstract

Background and objective: Diabetes can affect physical performance, development of disease complications, mental status, and the perception of health. Therefore, one of the main ways of controlling diabetes is to maintain and improve self-care behaviors in these patients. As such, the objective of the present study was to investigate self-care behaviors and the related factors in older people with diabetes.

Method: This is a descriptive correlational study done on 262 older people with diabetes who visited Tehran selected hospitals in 2016. Data collection was done using a demographic information questionnaire and Toobert's and Glasgow's self-care behaviors questionnaire. The descriptive and inferential statistics (Pearson correlation, one-way ANOVA, and independent t-test) in SPSS 20 software were used for data analysis.

Findings: The average age of the older people was 65.78 (±5.69). 152 people (58 percent) of the participants were female and the others were male. The average score of self-care in the study group was 44.74 (±11.90) which is at an average level. The minimum score average of self-care behaviors was related to diet consideration 22.82 (±7.59). There was a significant relationship between self-care behaviors and occupational status, type of treatment, and duration of diabetes.

Conclusion: The self-care behaviors of the research units were at an average level. Regarding the important role of self-care activities in controlling diabetes, some educational programs should be planned in order to empower the patients with regard to self-care. This will benefit the health level of the patients with diabetes and facilitate control of the disease.

Key words: older people, diabetes type 2, self-care behaviors

Introduction

Aging is the gradual passing of time influencing the individual's feelings, performance, and physical and mental ability. Demographers mention that the beginning of aging and becoming elderly is between 60 and 65 years old (1). It is predicted that the world percentage of men and women older than 65-year-old would respectively rise to 9.4 percent and 9.1 percent by 2020. Nearly one million people cross the 60-year threshold each month. These people are from developed countries, such as the United States, where the number of older people has been increasing so rapidly that by the year 2013, 44.7 million people will be aged 65 and older, and by 2023, this number is expected to reach 61.4 million, representing approximately 18% of the total US population. (2). Moreover, The percentage of older persons is expected to more than double from 7.6% to 16.2% by 2050 (3).
Although aging is not disease, a great number of older people suffer from chronic diseases like diabetes. Studies have shown that the prevalence of diabetes type 2 in older people is increasing. Recent statistics show that for each five older persons, there is one with diabetes type 2. (4)

Furthermore, the prevalence of diabetes in the developing countries like Iran has increased by 17 percent and that there is now one person with diabetes per five Iranian people (5). In the future we will have older people (who statistically have a large chance to be or become diabetic). In 2010, the estimations showed that there were nearly 285 million adults with diabetes throughout the world. As such, diabetes in the older people would be the most important factor of disability in Iran and the world during the next 25 years (6).

Diabetes is considered to be the sixth factor of death in the world which decreases life expectancy to one-third (7,8,9). In some of the studies, the prevalence of diabetes and impaired glucose tolerance varied from 10 to 30 percent (10,11,12).

Diabetes is a chronic disease with profound consequences for the individual's whole life. The effects are so extensive that the World Health Organization (2010) has called it a silent epidemic affecting physical performance, mental status, individual, family, and social communication, sexual function, and perception of health. Furthermore, this disease is the main cause of the development of disease complications like amputation, blindness, chronic renal failure, and heart disease. In addition to the said impacts the social and marital relationship, family, and job status are severely negatively influenced and decrease different aspects of the quality of life of the people with diabetes as well as their families (9,13,14). Self-care behaviors are the most important factors in controlling diabetes (15). Monitoring self-care behaviors is of great importance for improving health and preventing chronic diseases among older people (16). According to the studies, the most important reason for death in the patients with diabetes is the lack of self-care (17). With regard to diabetes, self-care includes the following: an appropriate diet, timely use of medicine, self-monitoring of blood glucose (SMBG), doing regular physical exercises, and foot care (18,19). Proper self-care results in an improvement of the patient's general health, which will eventually reduce the treatment costs (20,21). Important factors that play a role in the self-care of patients is individual beliefs and attitudes, values, and the culture of the society the individual lives in (22).

One of the most important differences of diabetes with other chronic diseases is that the patient is supposed to do the main part of disease control by themself (23). Therefore, with regard to the increasing rate of diabetic, older people in Iran the significance of self-care behaviors and the related factors is of prime importance. In 2016, it was decided that this study should be conducted with the aim of investigating self-care behaviors and the related factors in older, diabetic people who visited Tehran selected hospitals.

Method

This is a descriptive correlational study conducted in four selected hospitals in Tehran in 2016. The study concerned older people with diabetes who were visiting Tehran selected hospitals. Availability sampling was used based on the inclusion features.

The inclusion features were: age of >60 years, Persian speaking, willingness to participate in the study, and having been diagnosed with diabetes by an endocrinologist for at least a six-month.

Data collection instruments included demographic information questionnaire and Toobert's and Glasgow's self-care behaviors questionnaire (2000).

The demographic information questionnaire included age, gender, marital status, job status, educational status, duration of the disease, and type of treatment.

Toobert's and Glasgow's self-care behaviors questionnaire is a self-report questionnaire letting the participants report the quality of their self-care activities during the past seven days. This questionnaire was first developed by Toobert and Glasgow in 2000; it includes 11 phrases and evaluates four areas of adherence to the diet, doing regular physical exercises, foot care, and self-monitoring of blood glucose (SMBG)(24). The validity and reliability of this instrument were investigated and confirmed by the previous studies and Cronbach's alpha was estimated as 0.68 (18). Cronbach's alpha was again calculated in the present study and its value was 0.68. Scoring the questions of this scale was in a way that the score of 1 was given to the person who did not do any self-care in the said areas on any days of the past seven days. The person who daily performed self-care in all areas of the seven days received the score of 8. Others received scores from 1 to 8 based on the number of the days they followed self-care behaviors.

To determine the desirable level of self-care, in addition to comparing the mean of the scores, the domain of the scores which was between 11 and 88, was divided into three parts so that patients with self-care scores between 11 and 36 were considered as weak, those with self-care scores between 37 and 62 were considered as average, and those with self-care scores between 63 and 88 were considered as desirable.

The study proceeded as soon as the research subject was approved by the ethics committee of Shahid Beheshti University of Medical Sciences (letter of recommendation and the letter of ethics committee). When coordinating with the authorities of Tehran selected hospitals (Shohada Tajrish, Taleqani, Imam Hossein, and Rasool Akram) was finished, the availability sampling method was applied. From then on, these hospitals were visited and the researcher was present in the diabetes clinics on every day of the week and at their service providing time. Samples were selected after matching the research samples with the inclusion criteria. Informed written consent of all patients was taken in order to conform to the ethical principles and data were collected and analyzed confidentially and anonymously. Then, data collection instruments (questionnaires) were given to the older people visiting the hospitals. The researcher was present in the research environment while the respondents were answering the questions and assisted them if necessary. If the patient could not write the answers to the questions for any reason, the researcher himself completed the questionnaire by asking the patient and writing the exact answer of the patient.

In this study, descriptive (frequency, mean, and standard deviation) and inferential statistics (Pearson correlation test, independent t-test, and one-way ANOVA) were used after investigating the normality of data and confirming the fact that the data followed the normal distribution. Data were analyzed using SPSS 20. The significance level in this study was considered as 0.05.

Findings

262 older people with diabetes who visited Tehran hospitals participated in this study; they were questioned concerning their self-care behaviors and the factors affecting this. The average age of the older people was 65.78 (±5.69). Most of the older people were in the age range of 60 to 64 (50.8%) years old. Among the older people, 152 people (58%) were female and 42% were male. The majority of the patients were married (76.7%) and with regard to their educational level, most of them had a high school degree. The duration of the disease in most of the patients (36.3 percent) was between 1 and 5 years. The job of the majority of the participants (48.5 percent) was housekeeping and 49.6 percent of them used a dietary treatment. The exact numbers are shown in Table 1.

The average score of self-care behaviors was 44.74 (±11.90). According to these results, the self-care of most of the older people with diabetes was estimated at the average level. In this study, self-care behaviors were weak in 15.6% (41 people) of the participants, average in 60.7% (159 people) of the participants, and desirable in 23.3% (62 people). The results of the self-care status and its different areas are shown in Table 2.

According to the results of Table 2, the minimum score of self-care, regarding the range of scores, belongs to physical exercise and activity and the maximum score obtained was in the area of adherence to the diet. Considering all areas, the average score of self-care of the patients was 44.74±11.9; according to the determined desirability level and the domain of scores, indicates a semi-desirable status of self-care in these patients.

The results of Table 3 indicate that there is not a statistically significant difference between men and women in terms of self-care scores. Moreover, there was no difference in the average score of different age groups. In the investigation of the relationship of the other variables with self-care status of the patients based on the results of one-way ANOVA test, it was observed that the educational level and marital status of the patients did not have a significant relation with the quality of self-care behaviors. However, there was a statistically significant relationship between occupational status and the quality of self-care behaviors. The average score of the retired patients was statistically more significant than the others. Furthermore, there was a statistically significant relationship between the type of diabetes type 2 treatment and the quality of self-care behaviors meaning that the average score of the patients simultaneously using glucose and insulin-lowering medication was statistically higher than the other patients.

The self-care status of the patients was different in terms of the duration of diabetes. The average score in the patients who experienced 26 years and more of diabetes was 62.1 ±11.88; according to Pearson correlation test, the correlation value of 0.14 was higher than the other groups.

Table 1¬: Demographic Information of the Older People with Diabetes Type 2 Visiting Tehran Selected Hospitals in 2016

Variable		No.	Percentage
Age (year)	60-64	133	50.8
	65-69	74	28.2
	70-74	36	13.7
	75-79	9	3.4
	80 and above	10	3.8
Gender	female	152	58
	male	110	42
Duration of the disease (year)	1-5	95	36.3
	6-10	67	25.6
	11-15	43	16.4
	16-20	28	10.7
	21-25	19	7.3
	26 and above	10	3.8
Marital status	Single	3	1.1
	Married	201	76.7
	Divorced	3	1.1
	Widow	55	21
Educational level	Illiterate	60	22.9
	Elementary school	60	22.9
	Junior school	31	11.8
	High school	71	27.1
	University	40	15.3
Occupational status	Employed	39	14.9
	Housekeeper	127	48.5
	Unemployed	13	5
	Retired	83	31.7
Type of treatment	A diet	130	49.6
	Diet and insulin	52	19.8
	Insulin	70	26.7
	Diet and physical activity	10	3.8

Table 2: Mean and Standard Deviation of Self-care Behaviors and Their Different Aspects in the Older People with Diabetes type 2 Visiting Tehran Selected Hospitals in 2016

Self-care behavior aspects	Mean ±SD
Diet	22.82±7.59
Physical exercise and activity	5.43±3.6
Blood glucose test	7.07±5.23
Foot care	9.4±3.26
Total	44.74±11.9

Table 3¬: The Relationship between Demographic Information and Self-care Behaviors of the Older People with Diabetes type 2 Visiting Tehran Selected Hospitals in 2016

Variable		Mean and SD of self-care behaviors	P value
Age (year)	60-64	51.87±14.48	0.934
	65-69	52.72±14.59	
	70-74	52.22±14.04	
	75-79	58.55±11.88	
	80 and above	48±22.89	
Gender	female	53±14.13	0.328
	male	51.2±15.49	
Duration of the disease (year)	1-5	51.86±15.59	0.017
	6-10	48.68±13.72	
	11-15	53.44±14.77	
	16-20	53.85±14.58	
	21-25	56.47±12.39	
	26 and above	62.1±11.88	
Marital status	Single	55.66±18.14	0.371
	Married	52.41±15.15	
	Divorced	65.33±7.37	
	Widow	50.72±13.03	
Educational level	Illiterate	50.76±17.72	0.754
	Elementary school	51.03±13.71	
	Junior school	53.19±15.78	
	High school	53.22±12.83	
	University	53.82±13.89	
Occupational status	Employed	45.2±13.99	0.003
	Housekeeper	52.03±14.37	
	Unemployed	50±15.79	
	Retired	56.22±14.3	
Type of treatment	Diet	50±14.55	0.003
	Diet and insulin	58.88±13.53	
	Insulin	51.78±14.04	
	Diet and physical activity	50.1±19.06	

Discussion and Conclusion

The objective of this study was to investigate the condition of self-care behaviors and the factors affecting this in older people with diabetes who visited Tehran selected hospitals. The research findings indicated that the status of the patients' self-care behaviors, generally and in most of its aspects, especially in the area of physical exercise and activity and self-monitoring of blood glucose are not desirable; this finding is in line with the findings of other studies conducted in this regard. Bashar and Rajha 2016 who conducted a study on self-care behaviors in patients with diabetes in Kufa indicated that the status of the patients' self-care is at an average level in terms of desirability (25). In this study, the minimum self-care activity concerned the area of regularly doing physical activities and daily control of blood glucose. This consistency means that the older people with diabetes do not pay enough attention to the daily monitoring of blood glucose and do not exercise or do daily activities sufficiently to control their blood glucose level.

In this study, the score of self-care was higher for women than men, but there was not a significant difference in the average scores of self-care in terms of gender. Although it is expected that men have a weaker self-care status due to business, undesirable adherence to treatment, and usually displaying reckless behaviors such as smoking, this difference was not apparent in the present study. The results of the present study were in line with those of Bigdeli et al. 2015 in terms of gender (26).

Though it is expected that people with higher educational levels have a better insight in to the importance of self-care than others, this difference was not apparent in this study and there was no significant relationship between educational level and self-care behaviors. However, Karter et al. 2000 conducted a study and showed that educational

level is an effective factor in the self-care status of the patients (27). This study concluded that people with an academic educational level are more disciplined in the area of self-care compared to other patients. The reasons for this inconsistency can be due to the difference in the distribution of the educational levels of the population of the present study with the aforementioned study. Furthermore, there was no significant relationship between marital status and self-care behaviors; the reason of which may be the greater number of married patients compared to the other patients. These findings are consistent with those of Wang et al. 2014 (2).

According to the results of the present study, the self-care status showed a statistically significant difference in terms of duration of the disease. This result may indicate that the longer the duration of the disease, the more skillful the patients become with regard to self-care. These results can be observed in the studies done by Fatehi Albikawi and Abuadas 2015, Manjula and Premkumar 2015, and Baghaei et al. 2008 (13,28,29).

Another important factor affecting self-care in this study was the type of treatment. The average score of the patients simultaneously receiving glucose and insulin-lowering diet was significantly higher than the other patients. This high score may be due to the fact that this group of patients have a more regular treatment plan since they fear the mortal complications of the disease and have a higher acceptance of the treatment; this issue makes the patients more disciplined in the self-monitoring of their glucose levels.

As the results indicated, the self-care status of the retired patients was better than the other patients and there was a significant relationship between patients' occupational status and self-care behaviors. However, this relationship was insignificant in the study done by Bashar and Rajha 2016. The reason for this inconsistency may be because of the different occupational status of the two societies. In the present study, the employed individuals were investigated in one group, but in the study of Bashar and Rajha 2016, the employed individuals were investigated in two groups of clerks and self-employed (25). The results of the present study indicate that there was a significant relationship between some of the demographic information and self-care behaviors; the lack of continued adherence to self-care behaviors increases the danger of the short-term and long-term complications of the disease. Therefore, a comprehensive practical training on the quality of engaging in self-care behaviors is of the most important elements of optimally controlling the disease for all the patients. Sufficient awareness of the disease and its complications as well as empowering the patients and their families for controlling the disease lead to success in engaging in these behaviors. Therefore, it is necessary that the health care providers offer some information and instruction on the disease for self-care for different age groups, the two genders, different jobs, and the patients' families.

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The Relationship between Emotion Regulation and Intuitive Eating in Young Women

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Abstract

This study was designed to clarify the relationship between emotion regulation and intuitive eating in 60 obese women (BMI<30) and 60 normal-weight women. There is some significant correlation between the two groups. There is association between unconditional permission to eating subscale and non-acceptance subscale (r= 0.26), strategies subscale and unconditional permission for eating subscale (r= 0.31), Physical emotional eating subscale and strategies subscale (r= 0.30), and also two negative connections between permission for unconditional eating subscale and awareness subscale (r= -0.31), and awareness subscale and Suitable foods election subscale (r= -0.39) in obese women. Other associations are between physical emotional eating subscale and goals subscale(r= 0.29), awareness subscale and Trust in hunger and thirst cues subscale (r= -0.39), and clarity subscale and Trust in hunger and thirst cues subscale (r= -0.35) in normal-weight women. Findings show when obese women have some emotional problems, they cannot accept the situation and do something additional to regulate emotions in the form of unconditional eating.

Key words: Eating, Emotion Regulation, eating disorders, obese

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Introduction

Nowadays we know that over one-third of adults in the United States are obese (Ogeden, Carroll, Kit & Flegal, 2013) and the rate of overweight and obesity have risen (World Health Organization, 1999) and it increases some disease probability such as heart disease, stroke, certain cancers and type 2 diabetes (National institutes of health, 1998). Adaptive behaviors play an important role in maintaining overall psychological health (Seligman & Csikszentmihalyi, 2000). Up to now, research on positive eating behaviors has been sparse and much remains unknown. The focus of the research is on adaptive eating endeavours rather than pathological aspects, predominantly (Tylka, 2006). Adaptive eating behaviors have been investigated both in unrestrained eating (Kahan, Polivy, & Herman, 2003) and in eating disorders (Tylka & Subich, 2004). Primary definition of adaptive eating was the absence of eating disorder symptoms (Garner, 2004), but adaptive eating is wider and not limited to the absence of symptoms (Hawks, Madanat, Hawks, & Harris, 2005; Tylka, 2006; Tylka & Wilcox, 2006).

Extensive research shows that weight loss strategies that promote the restriction of food intake are largely ineffective for long term weight loss and weight maintenance (Mann et al., 2007). Moreover, restrictive eating practices have been associated with a higher body mass index (BMI) (van Strien, Herman, & Verheijden, 2014); weight gain (Mann et al., 2007); an increased risk of disordered eating (Appleton & McGowan, 2006); and psychological problems such as emotional difficulties, body image concerns and reduced cognitive functioning (Appleton & McGowan, 2006; Altuntas et al., 2016).

Intuitive eating which has a powerful connection with internal physiological hunger and satiety signs, is an adapted form of eating (Appleton & McGowan, 2006; Tylka, 2006; Tylka & Wilcox, 2006). The 1980s saw the evolving anti-dieting movement, and the meaning of intuitive eating was based on the claim which restrained dieting is not tolerable and it may have inverse responses such as, negative results as weight cycling, dysfunctional relationships with food, and increasing risk of eating disorders (J. A. Gast & Hawks, 2000). It has continued from those times up to now replacing dieting (J. A. Gast & Hawks, 2000; Tylka, 2006). As argued there is a natural mechanism that good nutrition at a healthy weight is the result of its function (Hawks et al., 2005). It has been suggested that individuals pay attention to their inner body guide and identify their body's physical needs to eat in a good way, and support health, sufficient body weight, and nutrition and it avoids overeating, obsessive food consumption and inadequate dieting (Tribole & Resch, 1996). This type of eating is more reliable than diet plans, environmental cues and emotional states, due to responding to internal physiological needs of hunger and satiety signs (Tylka, 2006).

Intuitive eating has been proposed as an eating style that encourages a positive relationship with food, body, physical activity (Tribole & Resch, 2012). The principles of intuitive eating include: focusing on physical cues for hunger and satiety giving an unconditional permission to eat; making food choices for both health and eating satisfaction; not using food to cope with emotions; respecting the body regardless of weight and shape; and being physically active for the enjoyment and health rather than calorie-burning for weight loss (Tribole & Resch, 2012). This approach discourages a focus on weight control, though the emergence and maintenance of an individual's natural weight and shape is acknowledged as a potential outcome (Tribole & Resch, 2012).

Moreover, it is assumed that disordered eating behaviors are performed as an attempt to regulate or escape from the negative effects (Stice et al., 2001). Studies indicate that many individuals who suffer from excess weight or have an eating disorder show termed emotionally-driven eating which is describe as eating in response to emotions (Goossens, Braet, Van Vlierberghe, & Mels, 2009). It is even suggested that pathological eating behavior may result from maladaptive emotion regulation (Racine & Wildes, 2013). Neurobiological processes concerning self-regulation, including control over one's own eating behavior, are known to be strongly influenced by emotions (Heatherton & Baumeister, 1991). Emotion regulation is defined as the "attempt to influence which emotions we have, when we have them, and how these emotions are experienced or expressed" (Gross & Levenson, 1997). If emotion regulation fails, self-regulation in other areas, like control over eating behavior, can fail as well.

Hence, it seems plausible that explanation models of binge eating behavior in BED and overeating in obesity trace back to self-regulation failure caused by intense emotions. The term emotion can comprise many different meanings ranging from depicting a specific (negative) emotion (e.g. anger or sadness) to simply describing an unspecific emotional state like emotional stress.

From a more behavioral perspective, several emotion regulation theories have been proposed. The theory of emotional eating understands eating as a coping strategy in response to emotional distress (Bennett, Greene, & Schwartz-Barcott, 2013), hence describing a sub-clinical form of disordered eating behavior in response to emotions, especially in terms of obese and normal weight individuals, emotional eating has been investigated (Rommel et al., 2012). There are several theories regarding a more disordered pattern of emotional eating, like overeating (eating a large amount of food) and binge eating (eating a large amount of food and experiencing loss of control). The escape theory (Heatherton & Baumeister, 1991) presumes an alleviation of aversive affects while bingeing, whereas other theories, like the effect regulation theory (Polivy & Herman, 1993), assume an improvement of effect after binge eating.

According to the emotional arousal theory, overeating is evoked by emotional arousals in order to reduce the level of arousal (Pine, 1985). Each of the emotion regulation theories mentioned above includes at least one of the following components:

Figure 1
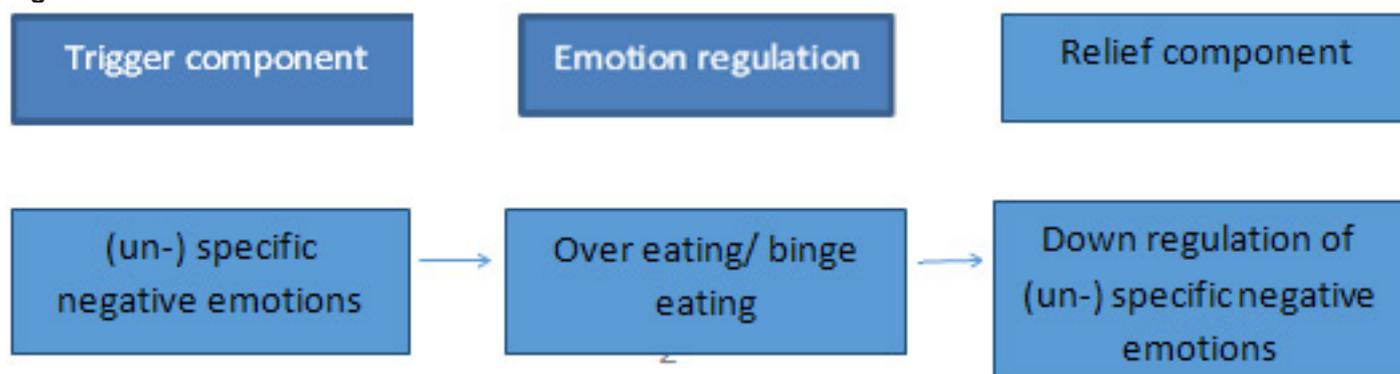
1) specific or unspecific negative emotions as a trigger for binge eating (i.e. trigger component) and **2)** down-regulation of specific or unspecific negative emotions (i.e. relief component) through binge eating in the short-term (while bingeing) or long-term (after a binge episode). To subsume both components, the "emotion regulation model", which includes the whole emotion regulation process (Figure 1), is proposed.

The components of the emotion regulation model as an account of binge eating have also been addressed in previous reviews. (Ganley, 1989) gave an overview of studies investigating the relationship between emotion and eating in obesity; however, he did not differentiate between populations with or without BED. Another more current narrative review investigated capacities in emotion and impulse regulation, considering possible differences between obese people and people with binge eating (BED and BN) (Fischer & Munsch, 2012). Thus, based on previous research, the present study explores the relationship between emotion regulation and intuitive eating in obese and normal-weight young women.

Materials and Method

Data was collected through the cross-sectional method. Participants were selected through accessible sampling. For the first step all participants provided written informed consent. They completed screening questionnaire (included age and educational status), the difficulties in emotion regulation subscale (DERS) and intuitive eating subscale (IES-II).

Participants
The population studied comprised 120 volunteer women aged 18 to 30 who were assigned to two groups according to their BMI score (Normal-weight (BMI<30) and obese (BMI>30)).

Measures
The intuitive eating subscale (IES-T), a subscale developed by Tylka (Tylka, 2006), was used to assess the principles proposed by Tribole and Resch (Tribole & Resch, 2012). The subscale assesses three key features: 1) relying on internal hunger and satiety cues to guide food intake; 2) permitting oneself to eat unconditionally; and 3) eating for physical rather than emotional reasons. Tylka and Kroon Van Diest (Tylka & Kroon Van Diest, 2013) developed a revised version of the subscale and identified a fourth feature: making food choices to

enhance body functioning. An alternative measure is the Intuitive Eating Subscale (IES-H) (Hawks et al., 2005; Tylka & Kroon Van Diest, 2013) which also assesses four features: intrinsic eating (i.e. motivation to eat based on internal cues of hunger); extrinsic eating (i.e. lack of eating based on external cues); anti-dieting (i.e. disagreement with dieting behaviors); and self-care (i.e. focus on health/fitness rather than appearance). A review of the literature conducted by Van Dyke and Drinkwater (Van Dyke & Drinkwater, 2014) has shown that intuitive eating (defined as any eating approach based on hunger and satiety that does not restrict food type, unless for medical reasons) is associated with a lower BMI; weight maintenance but not weight loss; and factors such as body image, self-esteem, affect, optimism, and life satisfaction. The relationship between intuitive eating and health behaviors such as physical activity and dietary intake was less clear (Van Dyke & Drinkwater, 2014).

The difficulties in emotion regulation subscale (DERS) was developed by Gratz (Gratz & Roemer, 2004) to assess the problems in emotion regulation. This subscale has 36 questions and 6 sub subscales that assess difficulties in emotion regulation. These subscales are: 1) Non-acceptance of emotional responses (NON-ACCEPTANCE); 2) Difficulties with engaging in goal directed behavior (GOALS); 3) Impulse control difficulties (IMPULSE); 4) Lack of emotional awareness (AWARENESS); 5) Limited access to emotion regulation strategies (STRATEGIES); and 6) Lack of emotional clarity (CLARITY). The reliability of test-retest was 0.88 and the internal comparison based on Cronbach's alpha was 0.93 and 0.8 for the sub subscales.

Statistical Analysis
Bivariate Pearson correlations were computed to explore the relationship between emotion regulation, intuitive eating and obesity. Table 1 shows means and standard deviation of research variables: the mean of total score of intuitive eating is 3.23 and in permission for unconditional eating subscale the mean is 19.98, and in physical emotional eating subscale the mean is 3.06; the mean of trust in hunger and thirst cues subscale is 3.49, the mean of suitable foods selection is 3.72, the mean of vice scores is 20.31. In the emotion regulation variable, the mean of strategies subscale is 92.78, the mean of non-acceptance subscale is 15.74, the mean of goals subscale is 14.58, the mean of impulse subscale is 12.96, the mean of awareness subscale is 16.44 and the mean of clarity is 12.45.

Table 1: Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Strategies	120	55.00	130.00	92.7833	16.13816
Non acceptance	120	6.00	29.00	15.7417	4.82204
Goals	120	7.00	25.00	14.5833	3.30669
Impulse	120	6.00	25.00	12.9667	3.79281
Awareness	120	8.00	26.00	16.4417	3.99957
Methods	120	10.00	33.00	20.8500	4.88636
Clarity	120	5.00	23.00	12.4500	3.24840
Intuitive eating	120	31.54	72.54	54.0057	8.78597
Permission for unconditional eating	120	11.00	27.00	19.9833	3.20971
Physical emotional eating	120	1.75	5.00	3.0687	.59181
Trust in hunger and thirst cues	120	1.83	6.00	3.4994	.72839
Vices scores	120	9.00	32.00	20.3167	4.92632
Total score	120	1.86	4.21	3.2347	.48295
Suitable foods election	120	1.33	5.00	3.7217	.83303
BMI	120	1.00	2.00	1.5000	.50210
Valid N (list wise)	120				

Results

Pearson correlation coefficient and Fisher Z were used to obtain the results. The results of the bivariate Pearson's correlations between emotion regulation and intuitive eating are shown in Table 2. The results show significant correlation between the two variables. It is worth to note that Fisher Z is not more than 1.96; thus, there is no significant correlation.

Table 2: Comparison of Correlation coefficients between the two groups

		Permission for unconditional eating	Physical emotional eating	Trust in hunger and thirst cues	Suitable foods selection
Non acceptance	obese	0.26*	0.14	0.03	0.08
	Normal weight	0.12	0.22	-0.09	0.22
	z	0.78	0.44	0.32	0.77
Goals	obese	0.23	0.09	-0.002	0.18
	Normal weight	0.07	0.29*	0.05	0.14
	z	0.88	1.11	0.08	0.22
Impulse	obese	0.25	0.21	-0.002	0.16
	Normal weight	0.19	0.20	0.02	0.18
	z	0.34	0.06	0.1	0.11
Strategies	obese	0.31*	0.30*	-0.13	0.09
	Normal weight	0.12	0.02	0.06	0.15
	z	1.07	1.55	0.38	0.33
Awareness	obese	-0.31*	-0.22	-0.12	-0.39**
	Normal weight	-0.16	0.02	-0.39**	-0.16
	z	0.85	1.09	1.55	1.34
Clarity	obese	-0.07	0.10	-0.25	-0.25
	Normal weight	-0.12	0.24	-0.35*	0.11
	z	0.27	0.77	0.59	0.77

There is an association between unconditional permission for eating subscale and non-acceptance subscale in obese women.

Moreover, there is an association between Physical emotional eating subscale and goals in normal-weight women. Also, there is an association between strategies subscale and Unconditional permission for eating subscale in obese women. In addition, there is a relation between Physical emotional eating subscale and strategies in obese women. Moreover, there is a negative correlation between Permission for unconditional eating subscale and awareness in

in obese women. Also, there is a negative association between awareness subscale and Trust in hunger and thirst cues subscale in normal-weight women. In addition, there is a negative significant association between awareness subscale and Suitable food selection subscale in obese women. Another negative association is between clarity subscale and Trust in hunger and thirst cues in normal-weight women.

Discussion

The results indicate an association between unconditional permission for eating subscale and non-acceptance subscale in obese women. This means that when obese women have some emotional problems, they cannot accept the situation and do something additional to regulate emotions in the form of unconditional eating. From a neurobiological viewpoint, hormonal influences and neurotransmitter circuits play a significant role in the explanation of why or how aversive emotional states can trigger binge eating and overeating. Cortisol secretion increases during stress and cortisol also regulates appetite and ingestion (Gluck, 2006). Two studies, one of which is also included in the review, investigated cortisol, hunger, and the desire to binge in BED relative to non-BED women after exposure to stress. Results were contradictory, showing in one study (Gluck, Geliebter, Hung, & Yahav, 2004) a tendency for a higher cortisol level after a painful stressor in BED women as compared to non-BED women, whereas in the other study a blunted cortisol response was obtained (Rosenberg et al., 2013). This finding is in line with previous findings that means when the women are under stress they try to eat more and regulate their emotions and have a sense of control in distressing situation.

Another association is the association between Physical emotional eating subscale and goals in normal-weight women. Intuitive eating is viewed as promoting a healthy relationship with food by discouraging restrictive eating, emotional eating, and eating in response to external cues (Tribole & Resch, 2012). More specifically, intuitive eating is viewed as promoting eating in response to bodily cues for hunger and satiety and permits women to eat unconditionally, thus removing rules for what, when and how much to eat. Regarding goals, it is worth to note that it is associated with goal setting behavior in taught situations. As observed, this association is in normal-weight women which can be accounted for by the differentiation between obese and normal-weight women in emotion regulation and the normal-weight women's ability in responding to internal cues of thirst or satiety. The Eating for Physical Reasons subscale and the reliance on hunger/satiety cues subscale demonstrated small to medium correlations with disordered eating, while the Body-Food Choice Congruence subscale was unrelated with disordered eating (Tylka, 2006; Tylka & Kroon Van Diest, 2013; Tylka & Wilcox, 2006). This finding is in line with the previous findings.

Another finding is about the association between strategies subscale and unconditional permission for eating subscale in obese women. Strategies in DERS subscale have been defined as bounded strategies for emotion regulation.

And as observed, obese women have problems with strategies. Examination of the IES-T subscales, the Unconditional Permission to Eat subscale demonstrated the highest correlation with disordered eating (Tylka, 2006; Tylka & Kroon Van Diest, 2013; Tylka & Wilcox, 2006) thus, suggesting that this feature of intuitive eating is less conceptually distinct from disordered eating (Tylka & Kroon Van Diest, 2013; Tylka & Wilcox, 2006). This finding is in line with previous findings that mean obese women have some problems in permission for eating because of their emotion regulation problems.

The other result of the present research is the association between Physical emotional eating subscale and strategies in obese women. Previous studies showed that intuitive eating correlated with positive emotional functioning in women. This is consistent with not using food to cope with emotions, another principle of intuitive eating (Tribole & Resch, 2012). This contrasts with the studies demonstrating that restrictive and disordered eating practices are associated with depressive symptomatology and poor emotional regulation (Gillen, Markey, & Markey, 2012; İlgün et al., 2016). In intuitive eating, emphasis is placed on being able to distinguish between biological and emotional hunger and regulate emotions with alternative strategies. In the study conducted by Bruce & Ricciardelli(2016), it is also possible that the relationship between intuitive eating and emotional functioning may be bidirectional that is, women may eat more intuitively in the absence of negative emotions but they may also experience more positive emotions as a consequence of intuitive eating. This finding is one of the questions that Lauren J. et al. recommended for further research that can be answered in this research: because of their weak strategies, obese women cannot select better strategies and just use eating for calming themselves.

Moreover, there is a negative correlation between permission for unconditional eating subscale and awareness in obese women. As mentioned in the last paragraph, it can be observed that because of their lack of awareness of their own emotions, they think that sadness and anxiety and any other negative emotions means they should do something, that is eating. Therefore, they use eating to escape their negative emotions. In the Sairanen et al (2015) this hypothesis claimed that mindfulness improves permission for unconditional eating and this approves our result.

Also there is a negative association between awareness subscale and Trust in hunger and thirst cues subscale in normal weight women. The psychosocial correlations of intuitive eating that were found included awareness and responsiveness of women towards bodily states (e.g., sensations, emotions, hunger and satiety) and motivation to engage in physical activity. Greater awareness and responsiveness to bodily states is related to that feature of intuitive eating that focuses on eating based on internal cues for hunger/satiety (Tribole & Resch, 2012; Ur Rehman, 2016). In addition, intuitive eating encourages an attitude towards physical activity that is not focused on calorie-burning for weight control. Instead, the approach

is focused on body's response to exercise and enjoyment of being physically active (Tribole & Resch, 2012). In line with this principle, studies showed that intuitive eating correlated with greater motivation to engage in physical activity when focused on feelings of pleasure (J. Gast, Campbell Nielson, Hunt, & Leiker, 2015), and less motivation when focused on feelings of pressure or guilt (J. Gast et al., 2015) or appearance (Tylka & Homan, 2015; Bilir et al., 2016). Shouse and Nilsson (Shouse & Nilsson, 2011) demonstrated that higher levels of intuitive eating were associated with greater emotional awareness and less self-silencing of emotions. Shouse and Nilsson (Shouse & Nilsson, 2011) demonstrated that higher levels of intuitive eating were associated with greater emotional awareness and less self-silencing of emotions. Schoenefeld and Webb (Schoenefeld & Webb, 2013) found a positive association between intuitive eating and distress tolerance. The finding of the present research is not in line with findings of the previous studies.

In addition, there is a significant association between awareness subscale and Suitable foods selection subscale in obese women. Tylka and Kroon Van Diest (Tylka & Kroon Van Diest, 2013), who found no association between the Body-Food Choice Congruence subscale of the revised IES-T (assessing the extent to which individuals match food choice with body's needs) and disordered eating among university students. The finding of the present research shows that obese women can be aware of their body signals and needs and can choose suitable food based on this need. But with regard to this ability there are other reasons such as emotion regulation that interfere and they eat and choose food based on emotions and circumstances.

Another negative association is between clarity subscale and Trust in hunger and thirst cues in normal-weight women. In addition, Denny et al. (Denny, Loth, Eisenberg, & Neumark-Sztainer, 2013) showed that women who trusted their body to tell them how much to eat reported that they were less likely to engage in unhealthy weight loss practices (i.e. fasting, starvation, food supplementation, skipping meals, smoking) and extreme weight loss practices (i.e., diet pills, laxatives and diuretics). Intuitive eating is viewed as promoting a healthy relationship with food by discouraging restrictive eating, emotional eating, and eating in response to external cues (Tribole & Resch, 2012). More specifically, intuitive eating is viewed as promoting eating in response to bodily cues for hunger and satiety and permits women to eat unconditionally, thus removing rules for what, when and how much to eat. This review also showed that intuitive eating correlated with positive emotional functioning in women. This is consistent with not using food to cope with emotions, another principle of intuitive eating (Tribole & Resch, 2012). This contrasts with research demonstrating that restrictive and disordered eating practices are associated with depressive symptomatology and poor emotional regulation (Gillen et al., 2012; Yılmaz et al., 2016). In intuitive eating, emphasis is placed on being able to distinguish between biological and emotional hunger and regulate emotions with alternative strategies. In our view, it is also possible that the relationship between intuitive eating and emotional functioning may be bidirectional that is, women may eat more intuitively in the absence of negative emotions but they may also experience more positive emotions as a consequence of intuitive eating. The finding of the present research is not in line with findings of previous studies.

Limitations
A limitation of this study is its cross-sectional design. Thus, no conclusion about the cause-effect relationship between intuitive eating and psychosocial correlates is possible. Another limitation is its small population.

Discussion

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Psychometric Properties of the Persian Version of the Emotion Regulation Checklist

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Abstract

Emotion Regulation Checklist (ERC) is a 24 item parent-report questionnaire that evaluates children's emotion regulation. The ERC includes two subscales: Emotion Regulation (ER) and Emotional Lability/negativity. This study aims to investigate the psychometric properties of the ERC for use in Iran. Using convenient sampling, 352 mothers with at least one child aged between 3 to 6 years were selected from 18 preschools in diverse socio-economic areas of Tehran during 2017. Mothers completed measure of the Emotion Regulation Checklist, the Child Behavior Checklist (CBCL), and the Eyberg Child Behavior Inventory (ECBI). Exploratory factor analysis, Cronbach's alpha, test-retest reliability and Pearson correlation coefficient were used to evaluate the psychometric properties of the ERC. The exploratory factor analysis indicated that the most adequate solution is the original two-factor explaining 31.74 % of the variance. The convergent validity was supported by the positive correlations between the Lability/Negativity subscale with mental health problems and disruptive behavior problems. The divergent validity was also supported by the negative correlation between the Emotion Regulation subscale with mental health problems and disruptive behavior problems. These findings provide the evidence of the validity and reliability of the ERC for use in Iran.

Key words: Validity and Reliability, Factor analysis, Emotion.

Introduction

Emotion regulation is a capability to monitor and modify emotional experience in order to achieve personal goals (1). Emotion regulation skills are dependent on emotion expression and emotional knowledge (2). Emotional knowledge and emotion regulation skills develop in preschool years (3). Emotion competence is associated with pro-social behavior, appropriate response to conflicts and physical health (4). Children should be able to manage their emotions to develop adaptive functioning (5). Children with high emotion competence find more adaptive ways to communicate their feelings instead of acting them out (6). The role emotion regulation plays in developmental psychopathology has been documented (1, 7-9). Externalizing behaviors such as attention deficit hyperactivity disorder, oppositional defiant disorders and conduct disorders are associated with difficulties in emotion regulation (10).

Measurement is the main challenge in studying children's emotion regulation (11). There are different methods for assessing emotion regulation in children. Observational methods evaluate how children regulate their emotions provoked by an emotional story. Analyzing mother-child interactions, or children's reaction to emotional photos, drawing and facial expression is a common observing method that has been used in research (12). Some studies have used Interview and tasks including delayed gratification to investigate emotion regulation construct in children (13, 14). Self-report methods are used with school-aged children and adolescents. Researchers studying preschool children mostly use the hetero-evaluation method (parents, teacher or other informants) (15).

The Emotion Regulation Checklist (ERC; Shields &Cicchetti, 1997) is a 24 items questionnaire used for the hetero-evaluation of emotion regulation in preschool and school-aged children. The ERC includes two dimensions

of Emotion Regulation and Emotion Lability/Negativity. Emotion Regulation describes the child's emotional awareness, empathy and constructive emotional expression. Emotion lability/negativity (L/N) describes the child's emotion dysregulation, mood lability, negative affect and inflexibility.

The ERC has been widely used for evaluating emotion regulation in children. Different translated versions of the ERC have been cross-culturally adapted in Italy (16), Turkey (17), China (18) and Brazil (19). As a function of the ERC's extensive use, this study aims to evaluate the validity and reliability of a Persian version of ERC.

Method

Participants
This study was a cross-sectional study using a convenient sampling. The sample comprised 352 mothers with at least one child (girl =168, boy=185) aged between 3 to 6 years (M= 4.5; SD= 1.1). Recruitment occurred through 18 preschools in diverse lower- to upper-class socio-economic regions of Tehran during 2017. Approval was obtained from the research ethics committee of University of Welfare and Rehabilitation Sciences and mothers signed an informed consent form. Mothers who were interested in participating in the research completed measures of the Emotion Regulation Checklist (ERC) (20), the Child Behavior Checklist (CBCL) (21) and The Eyberg Child Behavior Inventory (ECBI) (22).

Instruments
The 24-item Emotion Regulation Checklist (ERC) (20) measures two aspects of children's emotion competence: Emotion Regulation (8 items) and Emotion Lability/ Negativity (15 items). The items are rated on a four point Likert scale (from 1= almost always to 4= never) evaluating the frequency of children's behavior. The Emotion Regulation subscale describes emotional self-awareness, appropriate emotional display and empathy. Emotion Lability/Negativity describes inflexibility, reactivity and mood lability. The ERC has shown a good convergent and divergent validity (20).

The Achenbach Child Behavior Checklist (CBCL) (21) evaluates the mental health of preschool children and includes three domains: externalizing, internalizing, and total problems. The CBCL also has a Syndrome scale including Emotionally Reactive, Anxious/ Depressed, Somatic Complaints, Withdrawn, Sleep Problems, Attention Problems and Aggressive Behavior. Higher scores indicate more mental health problems. The internal consistency of the Persian version has been shown ranging from 0.54 to 0.81 (23). In the present study, Cronbach's alpha was 0.89 for the externalizing subscale, 0.87 for the internalizing subscale and 0.91 for the total problems.

The Eyberg Child Behavior Inventory (ECBI) (22) is a 36-item parent-report scale that was used in the present study to measure disruptive behavior problems in preschool children. The inventory has two subscales: an Intensity score, measuring frequency of disruptive behaviors, and a

Problem score, assessing whether (or not) the behavior is a problem. A higher score indicates more behavior problems. The test-retest reliability and internal consistency 0.74 and 0.93, respectively was reported in the Iranian population (24). In this study, Cronbach alpha's for the Intensity score and the problem score were 0.92 and 0.91, respectively.

Procedure
First, the English version of the ERC was translated into Persian by three independent translators. Secondly, a bilingual psychologist back-translated the Persian version to English. The back-translation version was approved equivalent to the original ERC. Three psychology professors experienced in emotion regulation checked the translation and some words were changed. The resulting version was applied to 15 mothers with a primary education to evaluate problems in the understanding of every item. Items that were not easily understood were changed to be more comprehensible.

Data analysis
The main purpose of the current study was to evaluate the factor structure of the Persian version of the ERC and its psychometric properties including test-retest reliability, internal consistency and convergent and divergent validity. Principal components factor analysis using varimax rotation was performed to evaluate the factor structure of the ERC.

Results

The Kaiser- Meyer-Olkin test of sampling adequacy (KMO =0.83) (25) and the Bartlett's test of sphericity (x^2= 1860 ; df = 276; p < .001) (26) suggested the factorability of correlation matrix. Explorative factor analysis showed that the two-factor solution explained 31.74 % of the variance. The 20.50 % of the variance was explained by the first factor (Lability/Negativity) and the second factor (Emotion Regulation) explained 11.24% of the variance.

According to Cattell's scree plot (See Figure 1) and the clearness of the item loadings, the two-factor solution was the best solution.

In contrast to the solution proposed by the Shields and Cicchetti (20) that item 12 loaded on no factor, this item loaded on the first factor (Lability/Negativity) for the Iranian sample. Items 23 showed positive loading on the first factor (Lability/Negativity) instead of the second factor (Emotion Regulation). As reported by Reis (19) some mothers interpreted "negative" in item 23 as unfavorable behavior and interpreted the item in reverse. Therefore, the item 23 was counted in the first factor (Lability/ Negativity). Consequently, the relationship between two factors rose from – 0.31 to -0.42. Cronbach's alpha was .81 for the Lability/Negativity factor and 0.57 for the Emotion Regulation factor. When item 23 moved to the Lability/Negativity factor, Cronbach's alpha for the Emotion Regulation factor became 0.68. The internal consistency coefficients are in acceptable range for Cronbach's alpha (27).

Table 1. Exploratory Factor Analysis for the Emotion Regulation Checklist

ERC items	EFA two Factors	
	Lability/ Negativity	Emotion Regulation
02: Exhibits wild mood swings (child's emotional state is difficult to expect because s/he moves quickly from a positive to a negative mood)	0.35	-.410
06: Is easily frustrated	0.34	-0.41
08: Is prone to angry outbursts/tantrums easily	0.60	
10: Takes pleasure in the distress of others (for example, laughs when another person gets hurt or punished; seems to enjoy teasing others)	0.34	
12: Is whiney or clingy with adults	0.40	
14: Responds angrily to limit-setting by adults	0.67	
19: Responds negatively to neutral or friendly attempts to interact by peers (for example, may speak in an angry tone or voice or respond fearfully)		-0.53
23: Displays appropriate negative emotions (anger, fear, frustration, distress) in response to hostile, aggressive or intrusive acts by peers	0.37	
24: Displays negative emotions when attempting to engage others in play	0.50	
04: Changes well from one activity to another; doesn't become angry, anxious, distressed or overly excited when moving from one activity to another	0.31	
05: Can recover quickly from upset or distress (for example doesn't pout or remain sullen, anxious or sad after emotionally distressing events)		-0.32
09: Is able to delay gratification (for example, can wait their turn)	0.51	
11: Can manage excitement (for example, doesn't get "carried away" in high energy play situations or over excited in inappropriate situations)	0.45	
13: Is prone to disruptive outbursts of energy and excitement	0.75	
17: Is overly energetic when attempting to engage others in play	0.55	
20: Is impulsive	0.65	
22: Intrusive enthusiasm	0.73	
01: Is a cheerful child		0.70
03: Responds positively to neutral or friendly attempts to interact by adults		0.63
07: Responds positively to neutral or friendly attempts to interact by peers		0.61
15: Can say when s/he is feeling sad, angry, fearful or afraid		0.37
16: Seems sad or listless		0.54
18: Displays flat affect (expression is vacant or inexpressive; child seems emotionally absent)		0.54
21: Is empathic towards others (for example, shows concern when others are upset or distressed)		0.35

Note. ERC = Emotion Regulation Checklist; EFA = Exploratory Factor Analysis. Lability/ Negativity = Factor 1; Emotion Regulation = Factor 2.

To evaluate the test-retest reliability of the ERC, 74 mothers completed the checklist at two-weekly intervals. Test-retest correlations for the Emotion Regulation was 0.84 and for the Lability/ Negativity was 0.68.

The correlation between the ERC, the CBCL and the ECBI scores was evaluated (see Table 2).

Figure 1: The scree plot for the ERC

Scree Plot
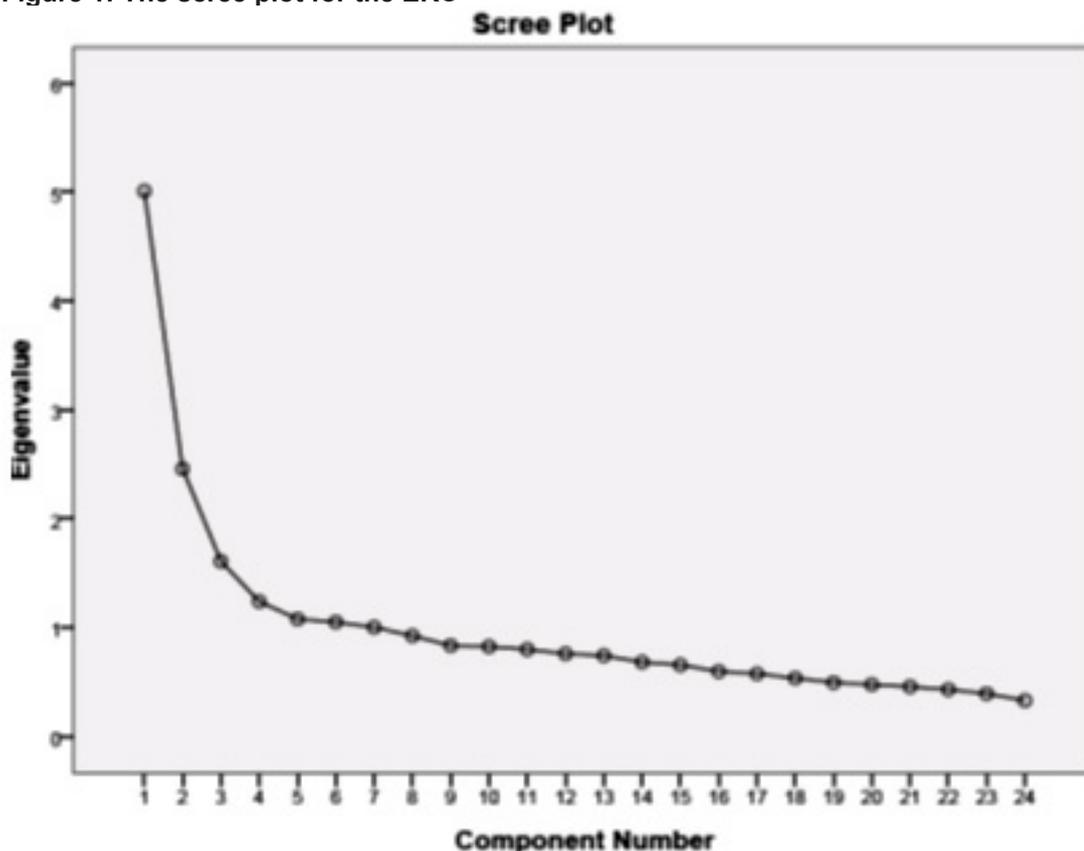
Table 2: Convergent and divergent validity of the Emotion Regulation Checklist

	Emotion Regulation	Lability/ Negativity
Emotionally Reactive	-0.37**	0.44**
Anxious/Depressed	-0.39**	0.37**
Somatic Complaints	-0.15**	0.20**
Withdrawn	-0.39**	0.30**
Sleep Problems	-0.12*	0.24**
Attention Problems	-0.08	0.43**
Aggressive Behaviors	-0.22**	0.53**
Internalizing	-0.25**	0.21**
Externalizing	-0.27**	0.65**
Total problems	-0.35**	0.57**
Intensity score	-0.22*	0.62**
Problem score	-0.33*	0.44**

Note. * P-value ≤ .05; ** p-value ≤ .01.

The Lability/ Negativity subscale had a significant and positive relation with all subscales of the CBCL and the ECBI. The ER subscale has negative relationship with the subscales of the ECBI and all subscales of the CBCL except the Attention Problems. No correlation between children's age and gender with the Emotion Regulation or the Emotional Lability/Negativity were found.

Discussion

The current study was designed to assess the factor structure, the reliability and validity of the Persian version of the ERC. The factor analysis of the Persian version of the ERC supported the theoretical model proposed by the authors of the original version (20). Studies investigating the psychometric properties and the factor structure of the ERC are limited. These findings are consistent with the two-factor model that is proved by previous studies (16, 19, 20, 28, 29).

The Lability/Negativity construct concerns inappropriate emotion displays, emotional intensity, over reactivity and emotions dysregulation. Children with high score on Emotional Lability/Negativity tend to be impulsive and inflexible with low tolerance to frustration and fast shifts from positive to negative emotions (20). The Emotion Regulation construct refers to emotional self-awareness, appropriate emotion expression and empathy. Children with adequate emotion regulation identify and express their emotions properly and manage negative emotions in relation to their goals (20).

As expected, the ERC subscales were associated with several dimensions of children's behaviors. Convergent validity was supported by the positive correlations between the Lability/Negativity subscale with externalizing and internalizing disorders, total mental health problems and disruptive behavior problems. The divergent validity was also supported by the negative correlation between the Emotion Regulation subscale with externalizing and internalizing disorders, total mental health problems and disruptive behavior problems. Emotion dysregulation is associated with developmental psychopathology, and has effects on children's social interactions (30). Children internalizing and externalizing problems tend to have more difficulties in emotion regulation (4).

The present study confirms the two-factor structure of the ERC, offering new evidence supporting the reliability and validity of the ERC and its usage for the assessment of children's emotion regulation in Iran.

Limitations
One of the main limitations of this study concerns sampling. This study investigated the ERC using convenient sampling method in a community sample. The non-randomized sampling limits the generalizability and interpretation of the findings. The findings would be strengthened with large size of clinical and community samples and using randomized sampling. All variables were measured by parent-report questionnaires. Evaluating children's emotion and behavior using observational methods would reduce the expectancy bias.

Conclusion

The present study indicated that the Persian version of the Emotion Regulation Checklist is explained by two-factor structure and has an acceptable validity and reliability. The internal consistency of the Emotion Regulation and the Lability/Negativity subscales was adequate. This study provides evidence for using a widely used instrument for evaluating emotion regulation and dysregulation in Iranian children.

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Determination and comparison miR135a in the serum between women with GDM, non- pregnant type 2 diabetes , healthy pregnant and control group

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Abstract

Objectives: Diabetes is one of the most important endocrine diseases caused by complex reactions between genetic and environmental factors. Recent studies have shown that microRNAs play an important role in the production, inhibition, and secretion of insulin. Identifying the relationship between key miRNAs that control the genes involved in the pathogenesis of diabetes is clinically important because it provides a way to identify preventive methods or treatments. In the present study, the expression of miR135a in serum samples between women with Gestational diabetes mellitus (GDM), non-pregnant type 2 diabetes, and healthy pregnant women were compared with the control group.

Materials and methods: This study was a case-control study and non-random sampling method was used. The present study was conducted among four groups (healthy non-pregnant women (control), non-pregnant Diabetes type 2, GDM, and healthy pregnant). After serum separation, expression of miR-135a was measured using QRT-PCR technique and the results were analyzed by Stata and SPSS21 software.

Results: The results show that the mean expression of miR-135a gene in control group was 0.9 ± 0.06, control of pregnancy was 1 ± 0.1, GDM group was 1.7 ± 0.3 and non-pregnant diabetic type 2 group was 6 ± 6 / 3. The results of analysis of variance showed that the mean difference of miR-135 gene expression was significant higher in the non- pregnant type 2 diabetes than GDM group (F = 2776.3, P <0.001).

Conclusion: The widespread role of miRNAs as post-transplantation gene regulators in gestational diabetes mellitus suggests that miR135a may act as a potential indicator of the prevention, treatment, and management of gestational diabetes .

Key words: miR135a, non- pregnant type 2 diabetes, gestational diabetes mellitus, QRT-PCR

Introduction

Diabetes is one of the most important endocrine diseases that can cause insufficiency or lack of insulin and glucagon production. (1,2) Diabetes is caused by complex reactions between genetic and environmental factors (2, 3). According to the World Health Organization (WHO), diabetes is the seventh cause of death in the world, with the number of diabetic patients estimated to reach 520 million in 2030 (4, 5). Diabetes, includes three types of type 1 , type 2 diabetes and gestational diabetes . Gestational diabetes is diagnosed for the first time during pregnancy. This type of diabetes is usually transient and improves after pregnancy. But these women are at risk of developing type 2 diabetes. (6) Gestational diabetes has many effects on the mother and the fetus, the most common of which are fetus macrosomia, problems during childbirth, cesarean section, polyhydroamenia, preeclampsia and neonatal metabolic disorders (hypoglycemia, hyperglycemia), fetus jaundice and an increased prevalence of pregnancy deaths(7-9). In recent years, various studies have shown that miRNAs are one of the most important genetic factors in the development of diabetes. (10,11)

miRNAs are small intrinsic origin RNAs (19 to 25 nucleotides) that regulate the gene expression by targeting the 3'UTR of the mRNA gene and preventing its transcription (6, 10, 11). miRNA as a regulator of glucose homoeostosis by targeting the genes involved in making insulin, the differentiation of β-pancreatic cells and the agents involved in insulin exocytosis, can play an important role in the development of diabetes can be used as a primary marker for diagnosing gestational diabetes as well as preventing its progress (12). The results of a study on a group of genes expressing the microRNAs involved in pregnancy disorders on chromosomes number 19 and 14 showed that the expression of these microRNAs has a direct relationship with pregnancy disorders, including gestational diabetes (13). Iran is a developing country with limited economic resources and a young population. About 11 million people are women of reproductive age who are at risk of developing the disease (8, 9). As recent studies have shown that the role of miR135a in inhibiting the INSR gene, which targets and suppresses the expression of IRS2 gene, has been shown to reduce glucose uptake in the cell and cause diabetes (14-16). Therefore, the present study aimed to study the effect of miR135a on women with gestational diabetes mellitus(GDM) and non- pregnant type 2 diabetes compared with healthy pregnant women and control group.

Materials and Methods

Characteristics of patients

This study was case-control, It was done on 120 human cases in four groups of 30 (healthy non pregnant (control), healthy pregnant , gestational diabetes mellitus and non-pregnant diabetes type 2). The non-randomized and available sampling method, based on the introduction of the endocrinologist and metabolism specialist, as well as those referring to the Shahid Blindian Diabetes Screening Center, was based on the 2016 health and medical diagnostic laboratories of Qazvin province with a code of ethics REC.1394.191.

Laboratory examination

Peripheral blood samples (2 mL) were collected from women at 16–19 weeks of pregnancy. At 24–28 weeks of pregnancy, a 50-g glucose challenge test (GCT) was conducted. Women with an abnormal 1-hour post-GCT glucose level (≥7.8 mmol/L) were recommended to undergo a 3-hour, 75-g OGTT, during which the blood glucose level would be tested four times after intake of a cola-like drink (at 0, 1, 2, and 3 hours). Women were deemed to have GDM when at least two of the four concentrations measured were above the cutoff values (10.3 mmol/L at 0 hours, 8.6 mmol/L at 1 hour, 6.7 mmol/L at 2 hours, and 5.8 mmol/L at 3 hours.(17)

RNA isolation and Quantitative Real-time PCR

Peripheral blood was obtained by tube containing anti coagulation EDTA and then centrifugation at 2,000 g for 6 minutes. It was then aliquoted and stored at -80C until miRNA detection. Extracted total RNA from 250µl of plasma using TRK- 1001 (LC-Bio, USA) was done according to the protocol 5 µl of plasma RNA containing miRNA and was reverse transcribed to cDNA, reverse transcription solution system that includes 5 µl total RNA, 1 µl M-MLV Buffer, 1 µl M-MLV, 0.5 µl dNTP, and 0.5 µl RRI (Reverse Transcriptase M-MLV (RNase H-), TAKARA, China). Reverse transcription reaction was done in Real Time PCR instrument (MyGene L96G, LongGene, China). Real-time PCR was performed using Platinum SYBR Green qPCR SuperMix-UDG (Invitrogen: 11733-038). RNU6B stable stay in serum and changeless in different people was used as internal control gene according to the Applied Biosystems Application Note ,and it has been widely used in different fields of research. All reactions were run in triplicate.'

To analyze the data, software (Version 14.1: College Station, Texas, USA) STATA, REST 2009 and SPSS 21 were used at the significant level (P <0.05).

Results

This study was performed on 120 human samples including four groups (non-pregnant healthy, non-pregnant type 2 diabetes , healthy pregnant and gestational diabetes mellitus) for measuring the expression of miR135a gene as a diagnostic marker in GDM subjects. At first, the mean and confidence interval of miR-135a gene expression was evaluated by different groups (Table 1). The mean of expression of miR-135a gene in healthy control group 0.9 (confidence interval 95%, 0.8, 0.9) in pregnant control group was 1.0 (confidence interval 95%, 0.9, 1.0) in gestational diabetes group 1.7 (confidence interval 95, 1.6, 1.9) and was reported in the diabetes mellitus group 3.6 (confidence interval 95% 3.4, 3.9).

Table 1: Mean expression of miR-135a gene in healthy control, pregnancy control, gestational diabetes and non pregnant type 2 diabetes

group	mean	confidence interval 95%
Healthy control	0.9	0.9,0.8
Pregnant control	1.0	1.0,0.9
Gestational Diabetes mellitus	1.7	1.9,1.6
non pregnant type 2 diabetes	3.6	3.9,3.4

To determine the difference between the mean expression of miR-135a gene in the studied groups, analysis of variance was used (Table 2). Based on the results of ANOVA, there was a significant difference in the expression of miR-135a gene among the groups ($F_{(0.05, 119)} = 276.3$, P value <0.001). The results of Bonferroni's post hoc test for comparing the two groups showed that expression of miR-135a gene in the healthy control group was significantly lower than the gestational diabetes groups (mean difference of group = 0.8, P value <0.001) and type 2 diabetes (Mean difference of two groups = 2.7, P value <0.001).

Table 2. Evaluation of the difference between mean expression of miR-135a gene in the studied groups using the variance analysis table

Difference Type	SS	Degrees of release	MS	F	P VALUE
The difference between the groups	149.3	3	49.7	276.3	0.001>
Intra-group difference	20.8	116	0.1		
Total	170.2	119	1.47		

Comparison of the mean gene expression in the control group of pregnant women and other groups showed that women in this group compared with GDM groups (mean differences = 0.7, P value <0.001) and non- pregnant type 2 diabetes (mean difference = 2.6, P value <0.001) had lower gene expression and the observed difference was statistically significant. In addition, the difference between gestational diabetes mellitus and non- pregnant type 2 diabetes showed that women with type 2 diabetes significantly had higher gene expression (mean difference = 1.8, p value <0.001) (Table 3).

Table 3: Bonferroni post hoc test result table for comparing two and two differences in the mean expression of miR-135a gene in healthy control, pregnancy control, gestational diabetes and type 2 diabetes

	Healthy control	Pregnant control	Gestational Diabetes
group	Mean difference (P value)	Mean difference (P value)	Mean difference (P value)
Pregnant control	0.09(0.1)		
Gestational Diabetes	0.8(0.001)	0.7(0.001)	
non pregnant Type 2 diabetes	2.7(0.001)	2.6(0.001)	1.8(0.001)

Discussion

Diabetes is now considered one of the most important diseases that has many complications. Despite various treatments, no definitive treatment of this disease has yet been found (18). Gestational diabetes is a major concern for mental health; recent findings suggest that GDM may have long-term implications for mother and child (19).

The pair produces several different microRNAs, some of which are released in the mother's circulation. These genes have been observed in the plasma of GDM-positive women with pregnancy outcomes (21). Based on the results of this study, there was no significant difference between the control and the healthy pregnant control group. However, the mean expression of miR-135a gene in GDM cases was significantly higher than of the healthy pregnant and control group. This illustrates the impact of this Micro RNA in pregnancy-related disorders, such as gestational diabetes, which coincides with the study of Diana M. Morales-Prieto and colleagues to demonstrate the role of microRNAs in the development of gestational diabetes. A study conducted in 2011 with the aim of examining pregnant microRNAs concluded that maternally circulating microRNAs could be a new diagnostic tool for the diagnosis of pregnancy disorders (22); also shown in a study by Nir Pillar and his

colleagues in 2015. It has been concluded that microRNAs play a major role in the pathogenesis of GDM and can be used as a primary bio marker for diagnosis of gestational diabetes, as well as for preventing progression (23). Yanan Zhu and colleagues in a preliminary study concluded that the expression of five positive miRNAs (HSA-MIR-16-5p, HSA-MIR-17-5p, HSA-MIR-19A-3P, HSA-MIR-19B-3P, HSA -MIR-20A-5P) was higher in the GDM group than in the control group and there was a higher amount of these RNAs in these subjects than non-diabetic subjects, which correlated with the expression of miRNA expression. Like the present study, Yanan Zhu's study also identified miRNA in plasma, which predicted GDM in the second quarter. The strengths of the study included the use of a high sequencing platform and the validation of MSRNA results by qRT-PCR. (24)

In the present study, the expression of miR135a in diabetic patients with up-regulate pregnancy was higher than that of healthy pregnant women and control group and according to a study by Chun Zhao and colleagues in 2011 on 16 women with gestational diabetes and 16 non-diabetic (control) subjects. This study examined the expression of microRNAs and their implications in gestational diabetes, and concluded that the expression of miR-132, miR-29a and miR-222 in pregnant women was higher than that of normal and control subjects and prevention of expression. These microRNAs lead to an increase in insulin gene expression (25).

Since the GDM group had a higher gene expression than healthy pregnant group and had less gene expression than non-pregnant type2 diabetes, also considering that studies have shown that women with gestational diabetes are at increased risk for diabetes later in life, (6), and one third of mothers who have gestational diabetes during pregnancy later develop Type 2 diabetes (20). It seems that pregnant women should have diabetes after termination of pregnancy and recovery. Gestational diabetes is monitored for expression of miR135a.

Chen and colleagues compared serum miRNA expression in type 2 diabetic patients with healthy subjects and showed that the serum miRNA expression profile was significantly different between the control and the healthy pregnant group (26). Zampetaki and colleagues performed micronutrient screening and qRT-PCR methods to determine the plasma miRNA expression profile in type 2 diabetes, and concluded that the expression of miR-20b, miR-21, miR-24, miR-15a, miR-126, MiR-191, miR-197, miR-223, miR-320 and miR-486 were more common in type 2 diabetes (10).

Honardoost and her colleagues in their studies have found that miR135a is effective in inhibiting the INSR gene and creating a diabetic state in mouse muscle cells. The goal of this miR is the IRS2 gene, which reduces glucose uptake in the cell. Studies at the molecular level also showed that the suppression of this miRNA reduces hyperglycemia (14, 16, 17, 27).

Conclusion

In general, available data suggest that the serum level of miR135a can be a promising new diagnostic tool for diagnosing gestational diabetes mellitus. However, more research is needed to investigate the mechanism of the effect of mir135a on the incidence of gestational diabetes mellitus.

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The evaluation of the TGF- β1 and TβRII gene expression in patients with acute lymphoblastic leukemia

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Abstract

Background: Tumor suppressors are key molecules involved in the malignant process. TGF- β is one of the most important suppressor genes with a complex role in intracellular processes. Although TGF-β is a traditional tumor suppressor; recent evidence has shown its promoter role in solid tumors. However, it is not determined whether TGF-β has a tumor suppressor or tumor promoter role in hematologic malignancies. In this study we evaluated the expression of TGF-β and its receptor in patients with acute lymphoblastic leukemia, as an important hematologic malignancy.

Material and Method: In this study, the expression of TGF-β and TβRII was analyzed in 52 patients with acute lymphoblastic leukemia in comparison with 13 normal controls; all of them informed volunteers. The mononuclear cell was separated using Ficoll for RNA isolation. After synthesis of c-DNA, the gene expression was measured using cyber green RQ-PCR.

Results: Our results showed that the expression level of TGF-β (3.6 fold) and TβRII (7.7 fold) was significantly decreased in all patient groups in comparison with healthy controls. Reduction in TGF-β was significantly correlated to blast count; TGF-BRII reduction also had correlation with chromosomal translocation, however, we did not observe any correlation with other parameters such as age, gender and leukemic cell immunophenotype.

Conclusion: Altogether our findings suggest defeated TGF-β signaling in patients with acute lymphoblastic leukemia (ALL), and it seems that the targeting of TGF- β signaling component is one of the basic and essential mechanisms in cancer development. More research in this field can help us to design novel methods for ALL diagnosis, classification, monitoring and treatment.

Key words: acute lymphoblastic leukemia, gene, TGF- β , TGF- BRII

Introduction

Acute lymphoblastic leukemia (ALL) is a malignant disorder of hematopoietic stem cells which is characterized by accumulation of immature and inefficient lymphoid precursors (lymphoblasts) in bone marrow and other lymphoid organs (1). Generally the risk classification of ALL patients is based on patient's age, primary WBC count, disease's immunephenotype, chromosomal abnormalities and treatment response rate (2). All of the above prognostic markers are highly dependent on substantial molecular defects of the leukemic cells. Routinely, prognostic categorization of patients based on the molecular features assists physicians greatly in choosing more successful treatment strategies (3).

Tumor suppressors and oncogenes are two types of key molecules involved in the malignant process (4,12). Oncogenes have traditionally attracted more attention in the scientific research. However, recent studies clearly proved the essential role of tumor suppressor defects in cancer development (13,18). In this regard, TGF-β signaling has been reported as a prominent tumor suppressor by several studies (19-21). TGF-β regulates the expression of a wide range of genes involved in critical cellular functions including cell cycle, cell differentiation, cell apoptosis, hematopoietic stem cell dormancy, extracellular matrix formation, genetic integrity and cell migration (22,27).

Naturally, TGF- β induces the expression of cell cycle inhibitors (such as P15, P21 and P53) and inhibits cell cycle inducers (such as c-myc and ID family of proteins) thereby it inhibits tumor formation and induces cell differentiation at the same time(28). Different studies indicated TGF-β signaling abnormalities in tumors. In this way, the aberrant expression of TGF- β has been reported in different kinds of malignancies such as colon cancer, breast cancer and hematological neoplasms (29-32). Other studies demonstrated mutation in other elements of TGF-β signaling pathway including TβRII and SMAD proteins in human malignancies (33,34). In hematologic malignancies it has also been demonstrated that some fusion genes such as AML1-EVI1 and TEL-AML1 inhibits TGF-β signaling pathway elements. All these studies proved tumor suppressor effects of TGF-β signaling (35-37).

Although, these studies indicated tumor suppressor role for TGF-β, recent studies unexpectedly showed tumor promoter function for this signaling pathway in some types of cancers which indicates context dependent function of TGF-β in different kinds of malignancies(32). This complexity is greatly dependent on factors such as the type of malignancy, tumor environment, types of genetic abnormalities, stage of malignancy and the rate of tumor progression (38-40). The tumor promoter function of TGF-β has been mainly explained by alternative signaling. In normal tissues, classic TGF-β signaling occurs through SMAD pathway of proteins. TGF-β signaling by SMAD activates the transcription of several target genes with tumor suppressor activity(41). However, during alternative TGF-β signaling in tumor promoter context, TGF-β signaling doesn't occur through SMADs pathway any more. In this condition, alternative signaling by MAP kinases, PI3K /AKT, GTPase Rho-like leads to malignant cells proliferation and survival (42,43).

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TGF- β has an essential role in the functional regulation of blood cells such as monocytes, macrophages, neutrophils, platelets and even hematopoietic stem cells; moreover, these cells are also the essential sources of TGF- β secretion (44). However, most studies on the role of TGF-β signaling have been performed on solid tumors and the role of TGF- β signaling in hematologic malignancies has been less considered. This study attempts to evaluate the expression of TGF- β and its receptor (TβRII) in acute lymphoblastic leukemia patients to better clarify the possible role of this cytokine in malignant lymphoblasts.

Methods

Patient samples
The present study was performed on the bone marrow (BM) and peripheral blood (PB) samples obtained from newly diagnosed ALL patients and 13 normal control subjects, with informed consent. Consent letter was approved by the local Ethics Committee. The patients were referred to Mofid, Taleghani and Emam Khomeini Hospital, Tehran, Iran with diagnoses based on clinical features and laboratory tests including: morphological assessment, immunophenotyping (according to the FAB classification system) and molecular studies. The median age of individuals in this study was 18 years, with a range of 1–89 years and mean age of 26 years. Samples were taken from 22 female and 30 male subjects.

RNA isolation, cDNA synthesis, quantitative realtime PCR
Total cellular RNA was extracted from MNCs using RNeasy minikit (Qiagen, Germany). The quality and quantity of extracted RNA was measured by NanoDrop (Thermo Scientific, Wilmington, North Carolina, USA) (OD 260/280 nm ratio >1.8). Subsequently, 2 µL (0.5 mg) RNA was used for cDNA synthesize in a final volume of 20 µL using a Thermo Scientific kit (Qiagen, Hudson, NH, USA). c-DNA synthesis was checked by ABL primer as housekeeping gene. An aliquot of 1/10th of the resulting cDNA from control and patient (1 µL) was used as substrate for qRT- PCR amplification. Primers specific to TGF- β1 and TβRII and ABL1 (housekeeping gene) were designed using oligo7 software [Table 1] using data obtained from NCBI databases and designed primers were evaluated for specificity by NCBI primer BLAST. Consequently, the expression of TGF- β1 and TβRII and ABL1 mRNA was analyzed by qRT-PCR (Rotor Gene 6000, Bosch, Qiagen, Germany). qRTPCR reaction components for each gene were composed of 1 µL of template cDNA, 1 µL primer(forward and reverse), 7 µL of RealQ Plus 2x Master Mix GreenLow ROX (Ampliqon, Denmark), and 6 µL water for a total reaction volume of 15 µL. For each qRTPCR reaction, standard curve was considered using five consecutive 1:10 dilutions of cDNA sample (1, 0.1, 0.01, and 0.001). The thermal cycler conditions for each reaction(TGF- β1 and TβRII) consist of initial holding at 95°C for 10 minutes, second phase as denaturation at 95°C for 10 s including 40 cycles, annealing/extension at

65°C for 15 s and final extension at 72°C for 10 minutes. All experiments were performed in duplicate and the relative quantification of mRNA expression for each sample (fold change = FQ) was calculated using the Livak method (2-ΔΔct). (Livak & Schmittgen, 2001; Schmittgen & Livak, 2008).

Statistical Analysis
Data analysis was performed using the SPSS Statistics (V 16.0) and GraphPad Prism (V 6.07) software. The results were represented in form of Mean+SEM. Shapiro Wilk and the Kolmogorov-Smirnov tests were used to evaluate the normal distribution of TGF-β1 and TβRII expression in ALL patients and control group. The t-test was also used to determine whether there was a significant difference in TGF- β1 and TβRII expression between ALL patients and the normal controls. The Pearson's chi-squared test was used to analyze the correlation between TGF- β1 and TβRII expression. The ANOVA test was applied to evaluate the differential expression of TGF- β1 and TβRII according to FAB classification. (p = 0.05 was considered as significance level).

Table 1: The sequence of forward and reverse primers for TGF-β genes, TGF-βRII and ABL1 gene is shown with the length of each primer with unit of nucleotide.

Gene	Premier	Sequence	Length
TGF-β	Forward	AAGGACCTCGGCTGGAAGTG	bp 20
	Reverse	CCCGGGCCATGCTGGTTGTA	bp 20
TGF-βRII	Forward	GGTTTTCAGTTATCTCCAGTCCA	23 bp
	Reverse	GGGGTCCAGGTAGGCAGTG	19 bp
ABL1	Forward	AGTCTCAGGATGCAGGTGCT	20 bp
	Reverse	TAGGCTGGGGCTTTTTGTAA	20 bp

Results

The expression rate of TGF-β and TGF-βRII in case and control groups:
The results showed that the expression of TGF-β (1.19 ± 0.07) and TBRII (1.01± 0.16) in ALL patients was significantly lower compared to normal controls with P value < 0.0015 (mean TGF-β in patients: 0.63 ± 0.08 and mean TGF- βRII in patients: 1.01 ± 0.16). TGF-β expression was 3.6 fold and TBRII expression was 7.7 fold lower than normal controls. There was no significant difference between gene expression levels of TGF-β and TGF-βRII in men and women (P value = 0.69 and 0.62 respectively). The patients were divided into two age classes of younger than 16 and older than 16 years. The expression rate of genes in the two age groups were evaluated, the results showed that there was no significant difference between the two age groups (P value =0.58 and 0.24)

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The expression rate of TGF- β and T BRII in case groups regarding to, translocation and immunophenotype classification:
Regarding existence of chromosomal translocation, patients were divided into two groups (trans positive and trans negative); our results showed no significant changes in TGF-β and Tβ RII expression between these groups(P value= 0.34 and 0.28). On the other hand, TGF-β and Tβ RII expression level was evaluated according to type of translocation including t(12:21), t(9:22), t(1:19) and t(4:11). The results showed that the expression level of TGF-β was not significantly different among patients with t(9:22), t(1:19) and t(4:11) translocations (P value=0.92), while the expression rate of TβRII was significantly higher in patients with t(12:21) (P value=0.04) in comparison with other translocations. Our patients were also categorized into B lineage and T lineage ALL. There was no significant difference between TGF-β and Tβ RII expression in these two groups. Patients were also categorized into 5 groups including T-ALL, Pro B ALL, Early pre B-ALL, Pre B-ALL and B-ALL. The expression level of TGF-β and TβRII was evaluated and the results showed no significant difference in TGF-β and TβRII expression level between different leukemic phenotypes (P value= 0.18 and 0.41)

Figure 1: The expression level of TGF-β and TGF-βRII in case and control groups
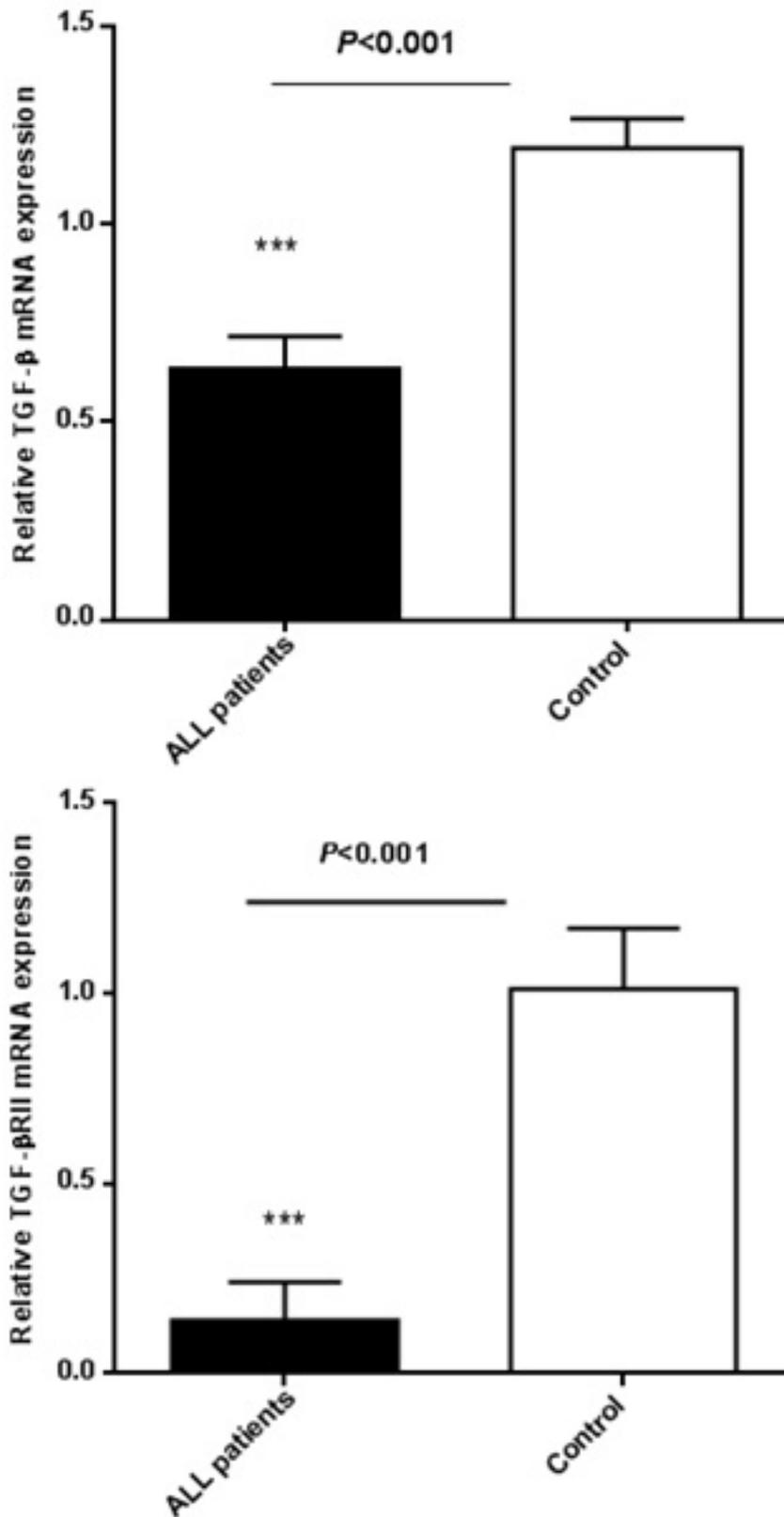
Figure 2: The expression level of TβRII in case groups regarding, translocation and immunophenotype classification
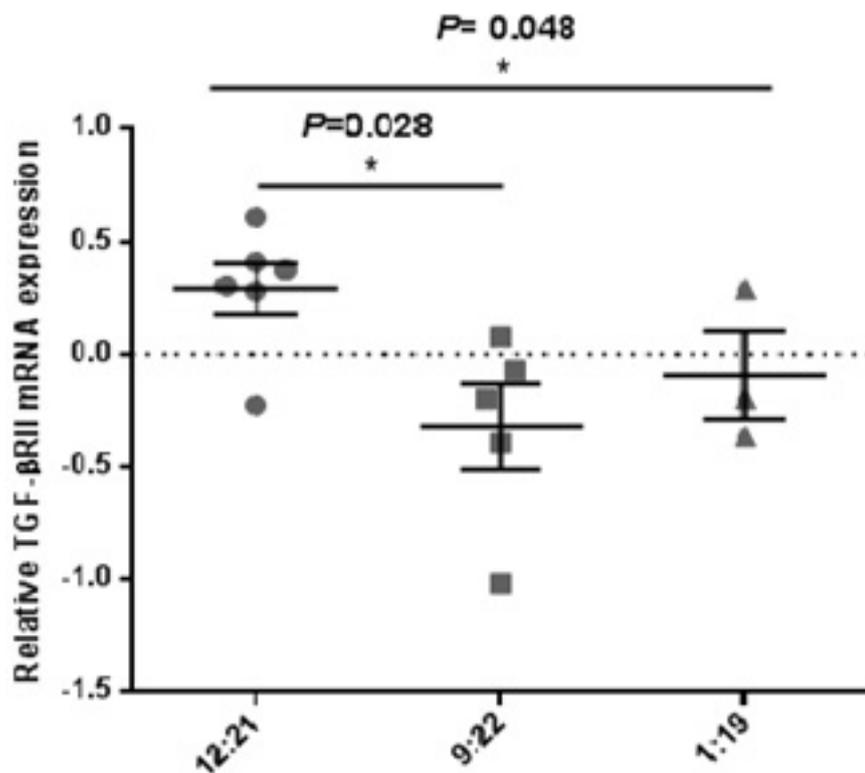
The expression rate of TβRII was significantly higher in patients with t(12:21) (P value=0.04) in comparison with other translocations. Our patients were also categorized into B lineage and T lineage ALL.

The correlation between the expression rate of TGF- β and TβRII:
Our results showed a positive and significant correlation between TGF- β and TβRII expression (p value= 0.015, r=0.33) (Chart 1) in our patients. Also there was a significant correlation between blast count and the expression rate of TGF- β and TβRII (P value=0.043, r=-0.288 and p value 0.74, respectively) (Chart 2), however there was no significant correlation between TGF- β and TβRII expression with age of patients (p value=0.15, r=0.293 and p value=0.089, r=0.293, respectively).

Chart 1: regression between TGF-β with TβRII
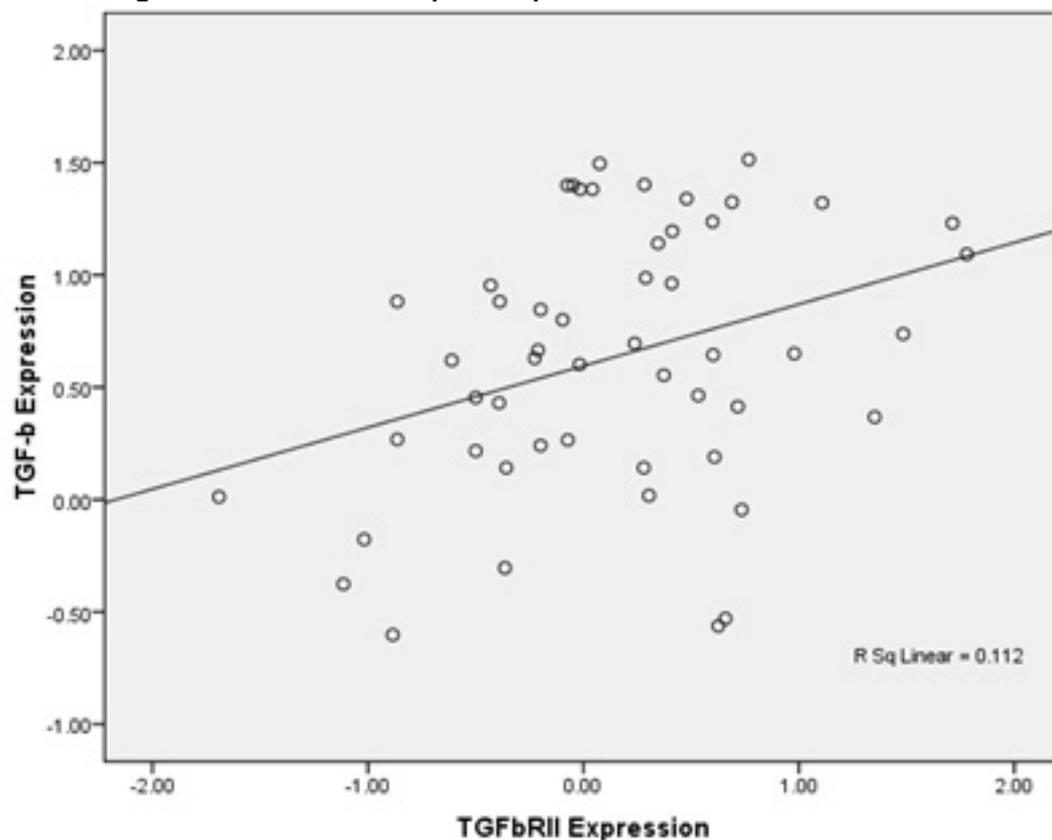
Chart 2: regression between TGF-β with blast count
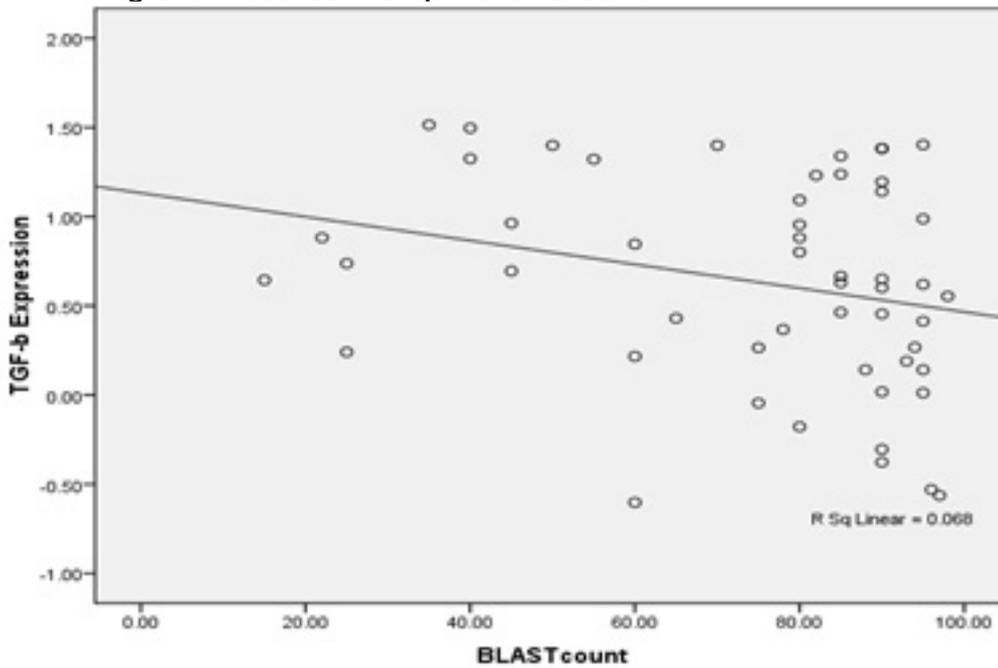
Discussion and Conclusion

Despite all advances in deciphering basic mechanisms involved in ALL leukemogenesis, still ambiguities exist in relation to tumor formation and development (45). While proliferation inducing factors work unrestrainedly in cancer cells, tumor suppressors generally stop their function. Albeit, tumor suppressor defects have an essential role in tumorogenesis, they have attracted less attention (46). There are several potent tumor suppressors, among them TGF-β is one of the most important (47-49). However recent studies have shown that there is also a tumor promoter function for TGF-β signaling in some neoplasms as well (50), thus we decided to evaluate the expression of TGF-β and TβRII as two key molecules involved in TGF-β signaling, in patients with ALL. Our data demonstrated a significant reduction in the expression of TGF-β (3.6 fold) and TβRII (7.7 fold) in our patients compared with normal controls and most cases represented a simultaneous reduction in TGF-β and TβRII expression. Statistical analysis using Pearson test indicated a positive and significant correlation between TGF-β and TβRII expression. On the other hand, we did not observe any correlation in TGF-β or TβRII expression with clinical data such as age, gender and disease immunophenotype. These data suggest that TGF-β signaling may be a defected pathway in ALL patients and malignant cells inactivate TGF-β signaling to escape from anti-tumor effects of this pathway. Such failures in TGF-β signaling can remove negative pressure of TGF-β signaling on the cell cycle and permits neoplastic cells to enter further and faster into the proliferation phase (46, 48). In agreement with our findings, Renald's showed reduced TβRII expression in patients with T cell sezary syndrome (51). Moreover, Swati Biswas et al also demonstrated that TβRII mutations disabled TGF-β signaling and is an important factor in the initiation and progression of colon cancer (52). Nikolaos Soulitzi et al and Dos Reis et al proved that patients with prostatic cancer have reduced TGF-β expression as well (53,54).

The involvement of other TGF-β signaling elements such as SMADs proteins has been observed in other studies, for example, Lin et al have shown that PML-RARα fusion gene inhibits the activation of SMAD2/3 and prevents TGF-β signaling to the nucleus. After ATRA therapy PML-RARα will be degraded and malignant cells respond to TGF-β signaling by their differentiation (55). Jakubowiak et al's study showed that AM1-ETO , another fusion gene in AML, also prevent TGF-β signaling through SMAD3 inhibition (56). A significant reduction in smad3 expression was also reported by Lawwrence et al in T ALL patients (57). All these studies along with our observation strongly suggest tumor suppressor role for TGF-β signaling and TGF-β signaling is inactivated as a possible mechanism for tumor escape from regulatory pressure. Although the natural role of TGF-β pathway indicates tumor suppressor activities, recent studies unexpectedly reported its role in tumor promotion as well; in this regard, Yong Wu, et al study represented over-expression of TβRII in acute myeloid leukemia. In these cases, over-expression of aberrant isoforms of TGF- βRII inhibits normal TGF-β signaling in patients with AML (58). Hui-Jun Zhang et al reported epithelial-mesenchymal transition (EMT) which is a feature of advanced stage of cancer, during TGF-β over-expression in lung carcinoma (59). Mele et al in their study showed the role of this cytokine in colon cancer metastasis also (60). Although in normal condition TGF-β stops cell cycle at G1 stage to inhibit cell proliferation and induces cell differentiation simultaneously. In the mentioned cases, TGF-β over-expression was unable to prevent disease initiation but it unexpectedly acts along with tumor promoter factors. However we did not observe such a finding in ALL patients.

In conclusion; according to our evaluation, TGF-β seems to act as a tumor suppressor in ALL patients because it showed lower expression in ALL patients in comparison with normal controls. It is possible that leukemic cells use TGF-β signaling down regulation for ease in their growth

and survival. Actually, TGF-β acts as a double edged sword in malignancies by contradictory signaling through alternative and classic pathways. The reason for the mentioned contradiction probably lies in natural differences in various tumors context and remarkable genetic and epigenetic heterogeneity between different kinds of malignancies. In this study, although it was not unexpected to see a significant difference in TGF-β expression between adults and children, between male and females and finally between different ALL subtypes, there was not any significant differences. It suggests TGF-β signaling deficiency may act as a general mechanism in tumor formation and promotion in ALL patients. Since simultaneous decreased expression level in both TGF-β and TβRII was seen, it is supposed that tumoral cells benefit from deactivation of multiple target genes in this pathway. Finally, due to the critical role of TGF-β pathway in cell regulatory mechanisms, the evaluation of the significance of TGF-β signaling elements in disease risk stratification, choosing therapeutic options and patient monitoring is highly recommended in future work.

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Transcription factors LEF1, PU.1 and IRF8 have decreased expression levels in majority of de novo acute myeloid leukemia patients

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Abstract

Background & Objectives: The lymphoid enhancer-binding factor 1(LEF1), PU.1 and interferon regulatory factor 8(IRF8) are three important differentiation genes that are commonly defective and associated with the development of leukaemia. Alternations in the expression of these genes can be resulted in malignancy.

Methods: In this study the expression levels of the genes mentioned were analysed using Real Time PCR with SYBR Green and the $\Delta\Delta CT$ method within 96 patients with acute myeloid leukaemia (AML) and 16 healthy subjects as a normal control.

Results: The results presented in this study revealed that PU.1 and LEF-1 gene expression was significantly lower and IRF8 gene expression levels were significantly higher in patients with AML in comparison with the normal control group (P < 0.0001). Furthermore, Analysis determines that the three genes have moderate positive correlation with each other; correlation between PU.1 and IRF-8 is R: 0.378, P <0.0001, expression of PU.1 and LEF-1: R: 0.399, P <0.0001 and the expression of IRF8 and LEF1: R: 0.320, P: 0.001in patients with AML.In our study, the relatively strong positive correlation between these genes was observed which is supported by other studies.

Interpretation & conclusion: It can be indicated in this study that when malignancy for unknown reasons that new connections between transcription factors occur which can affect the malignancy process. Our observations suggest that examining the oncogenic role of these genes and discovering new molecular mechanisms formed in the process of malignancy in each of these differentiation genes can play a role in the design of novel diagnostic methods, monitoring and treatment of patients with acute myeloid leukaemia.

Key words: AML, gene expression, IRF8, LEF1, PU.1.

Introduction

The clonal hematopoietic disorder, acute myeloid leukaemia (AML), is by molecular terms a heterogeneous disease where due to termination of differentiation in the myeloid lineage accumulation of immature progenitors within bone marrow occurs and simultaneously an inability to produce normal blood cells. It is has been widely reported (1,2) that the formation and behaviour of leukemic cells is perpetrated by impaired regulation of the expression of genes involved in cell growth and differentiation(3). Three differentiation genes that are commonly defective and associated with the development of leukaemia are transcription factors PU.1, LEF1 and IRF8 which will be investigated in the present study in the context of gene expression in AML.

Of the key transcription factors under investigation is PU.1, an ETS family transcription factor which is encoded by the SPI1 gene and has multiple roles in the normal haematopoiesis process and is necessary for the lymphomyeloid differentiation of stem cells (4,5). Studies report that in certain subtypes of AML, expression of this gene is decreased due to genetic abnormalities and that this reduced level of expression is pivotal for the induction of AML subtype M3, also known as acute promyelocytic leukemia (APL) as evidence shows that the PML-RARA fusion gene, which characterises this AML subtype, has an inverse correlation with PU.1 (6). A number of studies have demonstrated that PU.1 acts as a tumor suppressor gene in AML, for example by disrupting p53 activity (7).

Another transcription gene that will be considered in this study is the lymphoid enhancer-binding factor 1 (LEF1) which belongs to the LEF1/T-cell factor (TCF) transcription factor family (8). LEF1 has a critical role in myeloid differentiation which has recently been reported in human model studies supported by the observation that in normal conditions mRNA levels of LEF1 reaches its maximum levels in the promyelocytic stage of differentiation and experiences reduction in the final granulocytic stage (9). LEF1 mutations have been identified to be associated with high risk events in AML and lymphomas (10). It has been reported that LEF1 can indirectly promote PU.1 expression by repressing the expression of CEBPA and in turn CEBPA can no longer inhibit PU.1 and monocytosis occurs as observed in the case of congenital neutropenia. A direct relationship between LEF1 and PU.1 has also been identified where in normal conditions LEF1 acts as transcriptional inhibitor of PU.1 thusly alterations in LEF1 expression levels affects PU.1. In addition, LEF-1 is an appealing case of research as it has recently been proposed as a prognostic factor as studies have demonstrated that increased expression of LEF-1 is associated with a favourable prognosis in CN-AML (11-13).

The final gene that will be considered in the present study is interferon regulatory factor 8 (IRF8) which encodes for a protein also known as interferon consensus sequence-

binding protein (ICSBP) (14,15). The fundamental function of IRF8 lies in the regulation of myeloid cell fate moreover in cells of the myeloid lineage IRF8 expression is controlled through means of the myeloid master regulator PU.1. This gene also like PU.1 acts as a tumour suppressor gene in myeloid lineages (16). Recent studies report that IRF-8 is expressed in MDPs, CDPs and in committed granulocyte and monocyte progenitors but absent in GMPs and CMPs which reiterates the crucial function this gene has normal haematopoietic differentiation (14,15). In the case of loss of function IRF8 promotes granulocytic differentiation and represses monocytic differentiation in a disproportionate manner whilst over activation induces the opposite effect. Furthermore, the dysregulation of IRF8 is associated with the development of MDS to AML as seen in murine models and human subjects (17). Moreover, it was observed that in the MDS-AML model there is a positive correlation between IRF8 and PU.1 as lower levels of PU.1 expression were specifically accompanied by lower levels of IRF8 expression in AML patients although no such correlation was observed in normal haematopoietic stem cells (18).

In the present study, we focus on three differentiation related genes, LEF1, PU.1 and IRF8, which have been described as tumour suppressor genes where changes in expression of these genes have been associated to the development of AML. By means of real-time PCR expression levels of the aforementioned genes were measured in AML patients and healthy subjects to analyse relative expression of each gene and further analysed in terms of AML subtype, patient characteristics and to identify potential correlations between the expression levels of these genes.

Methods and materials

Patient samples
Ninety six bone marrow (BM) and peripheral blood (PB) samples with collaborated clinicians were obtained from newly diagnosed patients with de novo AML and 18 samples from healthy subjects (used as a normal control) between the years 2013 to 2015 (Sample size evaluated with

$$n = \frac{\sigma^2 z^2}{d^2}$$

formula).

The patients were referred to Mofid and Emam Khomeini hospital, Tehran, Iran. In addition, Shahid Beheshti University of Medical Science, Tehran, Iran and

Department of Medical Research were laboratory involved in our study. Then receiving informed consent according to institutional guidelines the median age of individuals in this study was 47 years with a range of 2 to 87 years and mean age of 45.39 years. Samples were taken from 44 female and 52 male subjects. The number of patients in each subgroup FAB includes: 10 patients with M0, 20 patients with M1, 14 patients with M2, 30 patients with M3, 14 patients with M4, 7 patients with M5 and one patient with M6. Furthermore, patients were divided into three subgroups based on morphological differentiation status: 34 patients without distinction (M0/M1 /M2), 30 patients with granulocytic differentiation (M3) and 21 patients with monocytic differentiation (M4/M5).

RNA isolation, cDNA synthesis, real-time PCR
Total cellular RNA was extracted from BM and PB using an RNeasy kit (Qiagen, Germany). Following extraction, the amount and quality of RNA was measured by a NanoDrop (Thermo Scientific, USA). All samples showed high purity (OD 260/280 nm ratio >1.8) and integrity. Subsequently, 2µL (0.5mg) RNA was transcribed into cDNA to a final volume of 20µL using a Thermo kit (USA). An aliquot of 1/10th of the resulting cDNA (1µL) was used as substrate for qRT-PCRamplification.

Primers specific to PU.1, IRF8, LEF1 and ABL (house keeping gene) were designed via Oligo 7.56 software (Table 1) which subsequently allowed levels of PU.1, IRF8, LEF1 and ABL mRNA expression in patients and healthy subjects to be detected by qRT-PCR (Rotor Gene 6000, Bosch). The components in the qRT-PCR reaction for each gene consisted of 1µL of template cDNA, 1µL forward and reverse primer, 7µL of RealQ Plus 2x Master Mix Green-Low ROX (Ampliqon, Denmark) and 6µL water for a total reaction volume of 15µL. For each qRT-PCR reaction a standard curve was produced, using five consecutive 1:10 dilutions cDNA sample (1, 0.1, 0.01 and 0.001). The thermal cycling conditions for each reaction included an initial hold at 95°C for 10 minutes followed by 40 cycles of primary denaturation at 95°C for 10 seconds and annealing/extension at 65°C for 15 seconds and a final extension at 72°C for 10 minutes. Additionally, negative controls were included in the assay and the assay was performed in duplicate. The relative quantification of mRNA expression for each sample (fold change=FQ) was calculated using the Livak method (2-$\Delta\Delta$ct)(19).

Table 1. Nucleotide sequences of primers used for ABL, PU.1, IRF8 and LEF1 qRT-PCR reactions

Gene	Forward	Reverse
ABL	AGTCTCAGGATGCAGGTGCT	TAGGCTGGGGGCTTTTTGTAA
PU.1	AGAAGACCTGGTGCCCTATG	GTAATGGTCGCTATGGCTC
IRF8	CAGCCACTTGGAAGACGAG	TTGTATGGCTCGGAAATGTC
LEF1	GAGGAAGGCGATTTAGCTG	AGGTTTGTGCTTGTCTGGC

Statistical analysis

Analysis of the data generated was performed using SPSS 16.0(Universal binary, Chicago) and GraphPad Prism 6.01(California) software. The results were expressed as mean ±standard error of the mean (SEM). A P value of 0.05 or less was considered significant. Shapirovik-Wilk and Kolmogorov-Smirnov tests were used to evaluate normal distribution of data. T-test and ANOVA were applied to determine significant differences between PU.1, LEF1 and IRF8 expression in AML patients and normal control group and to assess differential distribution of gene expression based on patient/disease characteristics. ALSO, the Pearson's chi-squared test was used to measure the linear correlation between CEBPA and RUNX-1 expression.

Results

Variable expression levels of PU.1, IRF8 and LEF1 in AML

By means of real-time PCR, Ct values were obtained for LEF1, PU.1, IRF8 and ABL (housekeeping gene) and subsequently the mean Ct values were measured for all genes for both AML patients and the normal control group (Table 2). For each gene, an expression level in the range of 95% confidence interval was defined as a normal or intermediate expression level for a healthy population. Based on these levels parameters for a range of low expression and high expression for each was also defined (Table 2).

Gene	AML patients Ct values Mean ± S.D	Normal control group Ct values Mean ± S.D	Low expression Range/ number of patients in this range	Intermediate expression (95% confidence) Range/ number of patients in this range	High expression Range/ number of patients in this range
ABL	27.45±0.33	29.10±0.31	-	-	-
PU.1	22.69 ± 0.24	23.16 ± 0.04	0.006-0.76/64n	0.76 − 1.90/20n	1.90-9.88/12n
LEF1	28.89 ± 0.27	26.87 ± 0.25	0.0007-1.04/91	1.04 − 3.36/5n	Until 2.27/0n
IRF8	24.81 ± 0.23	24.19 ± 0.18	0.002-0.79/71	0.79 − 2.23/10n	2.23-96.26/15

Table 2: Average of Ct subjects were obtained for 4 genes ABL, PU.1, LEF1 and IRF8 in patients and healthy according to the above table. An expression level in the range of 95% confidence interval (0.76 – 1.90), (1.04 – 3.36) and (0.79 – 2.23) defined for the average PU.1, LEF1 and IRF8 expression level in the healthy population, was considered 'intermediate', respectively. The majority of patients (64/ 96),(91/96) and (71/96) had an LOW expression level of PU.1, LEF1 and IRF8,respectively.

PU.1 and LEF1 expression is significantly lower in AML patient samples in comparison to healthy subjects.

The resulting Ct values obtained for each gene were normalised against the internal housekeeping gene, ABL, for both AML patients and the normal control group and subsequently compared. An initial comparison by application of the Livak formula (2ΔΔCT) demonstrated that expression levels of the genes PU.1 and LEF1 were lower in AML patients in comparison to the normal control group with a 1.28 and 9.17 fold decrease, respectively (Figure 1, A and B). A statistical analysis by means of a T-test determines that there is a significant difference in expression levels between the two groups for both PU.1 (P < 0.0001) and LEF1 (P < 0.0001) (Figure 1, C and D).
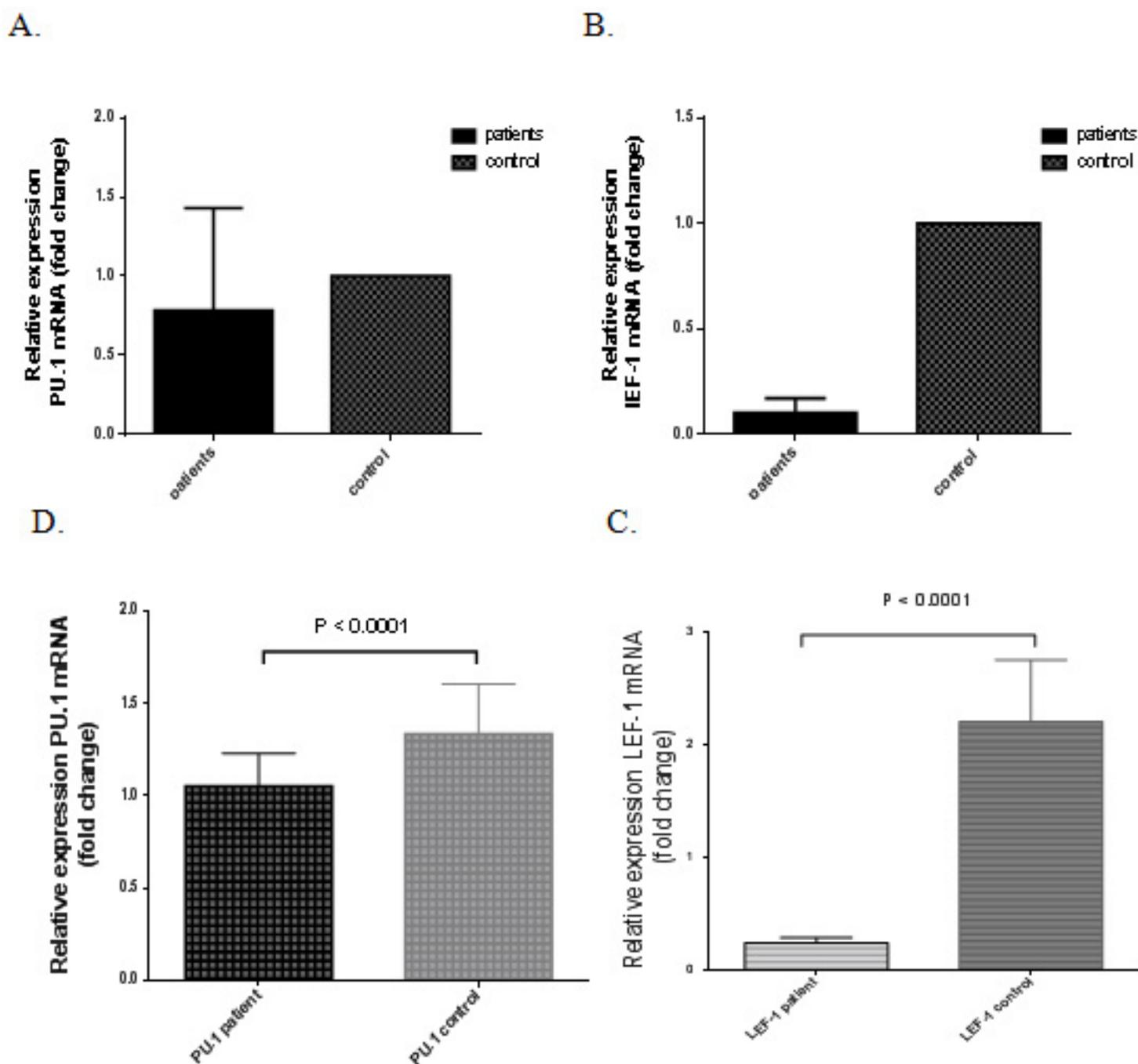
Figure 1: Relative expression of PU.1 and LEF1 in 96 AML patients and 18 healthy patients was measured from Ct values and normalized against a reference gene (ABL). A,B) There is a 1.28 fold decrease in PU.1 expression and a 9.17 fold decrease in LEF-1 expression in AML patients in comparison to the normal control group. C) A mean LEF-1 expression level of 0.24 ± 0.04 (SEM) was measured in AML patients in comparison to a mean LEF-1 expression level of 2.20 ± 0.54 in the normal control group. A significant difference (P< 0.0001) between LEF-1 expression in AML patients and healthy subjects was identified. D) A mean PU.1 expression level of 1.04 ± 0.17 (SEM) was measured in AML patients in comparison to a mean PU.1 expression level of 1.33 ± 0.26 in the normal control group. A significant difference (P< 0.0001) between LEF-1 expression in AML patients and healthy subjects was identified.

IRF8 expression is significantly higher in AML patient samples in comparison to healthy subjects.

As with the PU.1 and LEF1 genes, expression of IRF8 was analysed by normalising the mean Ct values against the housekeeping gene and a comparison of relative expression between AML patients and normal control group was performed by means of the same statistical analyses. In contrast to PU.1 and LEF1, IRF8 gene expression was higher in AML patients than the normal control group with fold increase of 1.87 (Figure 2, A). The increase of IRF8 expression level in AML patients was deemed statistically significant by application of the T-test (P < 0.0001) (Figure 2, B). In our study, this gene significantly increased compared to control group but similar to this study but as in this study when the overexpression is studied in detail in patients we found that only 15% (15 of 96 patients) had increased expression and the rest reduced expression (Figure 3).

A.

B.
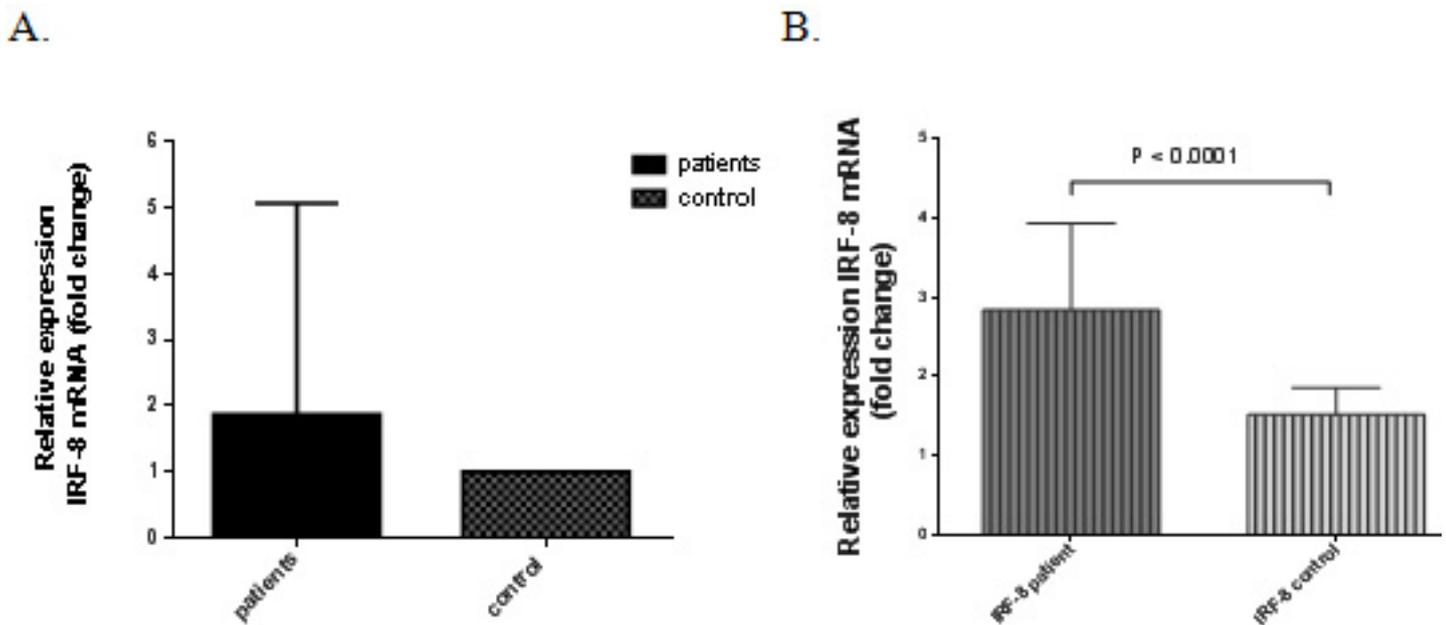
Figure 2: Relative expression of IRF8 in 96 AML patients and 18 healthy patients was measured from Ct values and normalized against a reference gene (ABL). A) There is a 1.87 fold increase in IRF8 expression in AML patients in comparison to the normal control group. B) A mean IRF8 expression level of 2.83 ± 1.09 (SEM) was measured in AML patients in comparison to a mean IRF8 expression level of 1.51 ± 0.34 in the normal control group. A significant difference (P< 0.0001) between IRF8 expression in AML patients and healthy subjects was identified.
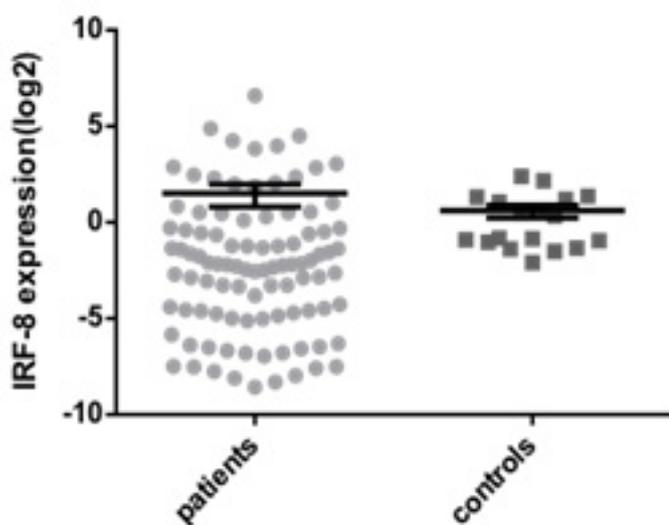
Figure 3: IRF8 gene expression in patients and healthy subjects

PU.1 expression is significantly lower in APL patient samples in comparison to other AML subtypes and healthy subjects.

Expression levels of PU.1 in each FAB subtype (M0-M5) were compared to the normal control group and a statistically significant difference was observed in the APL-M3 subgroup when compared to all other subtypes as a single subgroup (non-M3) (P = 0.027), that there is a 2.27 fold decrease in expression (Figure 4, A). Subsequently, the patients in this study were classified by broader disease subgroups instead of the FAB classification they were initially assigned by. Patients were assigned to a subgroup based on three morphological differentiation statuses; without differentiation (M0/M1/M2 subgroup, 34 patients), granulocytic differentiation (APL-M3 subgroup, 30 patients) and monocytic differentiation (M4/M5 subgroup, 21 patients). When PU.1 expression levels in these subgroups were compared to the normal control group a significant difference was observed between M3 group with normal group (P=0.001), but not the other subgroups.(Figure 4, B) The Tukey test was applied to analyse the relationship of PU.1 expression between AML subgroups and it was observed that PU.1 expression in patients with the APL subtype was significantly lower than the other monocytic differentiation(M4/M5) and undifferentiated subgroups(M0/M1/M2)(P = 0.022 and P = 0.027) (Figure 4, B).
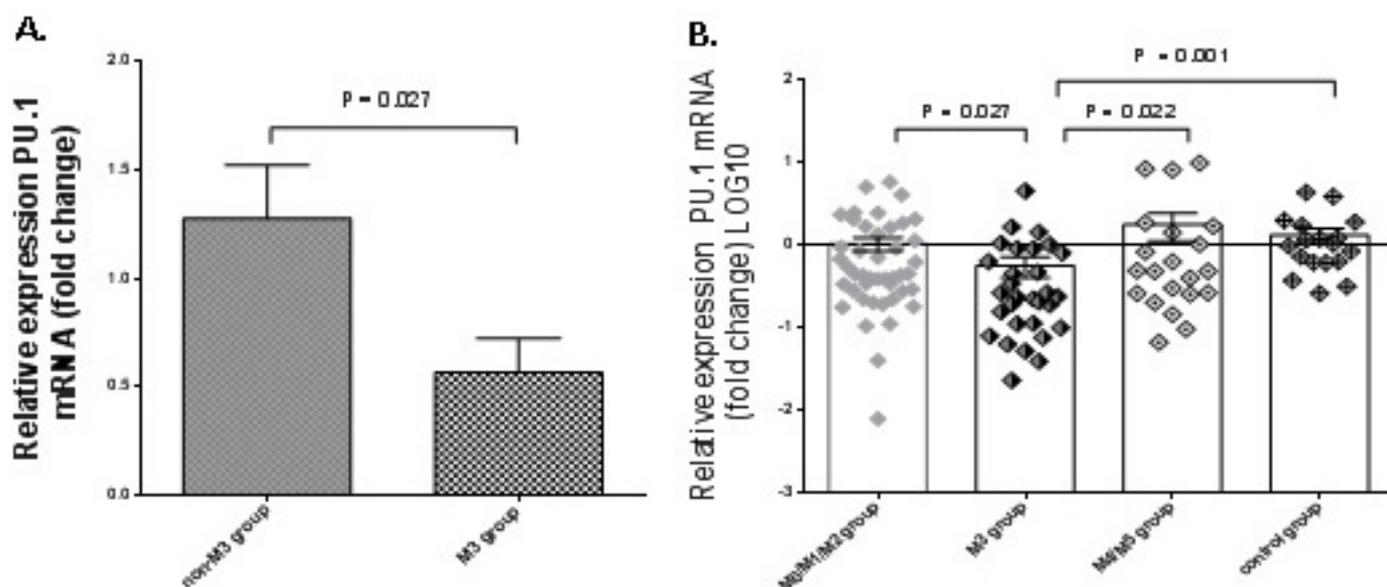
Figure 4: Normalized relative expression of PU.1 in 96 AML patients and 18 healthy patients based on varying disease subtypes. A) PU.1 expression is analysed in patients based on their FAB classification, Patients classified as M3 and non-M3: a 2.27 fold decrease in gene expression levels in the M3 subgroup.B) Patients are classified into three disease subgroups based on differentiation status without differentiation (M0/M1/M2 subgroup), granulocytic differentiation (M3 subgroup) and monocytic differentiation (M4/M5 subgroup). PU.1 expression in comparison to the normal control group was only significantly lower in the M3 subgroup.

PU.1 expression is significantly higher in AML patients with 'some' MPO activity.
Patient samples were assessed for MPO activity by peroxidase staining and subsequently graded and sub-grouped based on the percentage of MPO positive cells: rare (<3%), few (10%), some (50%), most (80%) and strong (100%). PU.1 expression levels were evaluated based on the aforementioned MPO grades and compared. The ANOVA test was applied for normal distribution and as a result a significant correlation (P=0.007) between PU.1 expression and MPO subgroups was observed. The Tukey test was applied to reveal the relationship between PU.1 expression and specific MPO grade and it was observed that PU.1 expression levels in patients with 'some' peroxidase activity was significantly higher than 'rare' (P-value=0.016) and 'strong' (P-value= 0.021) grades (Figure 5).
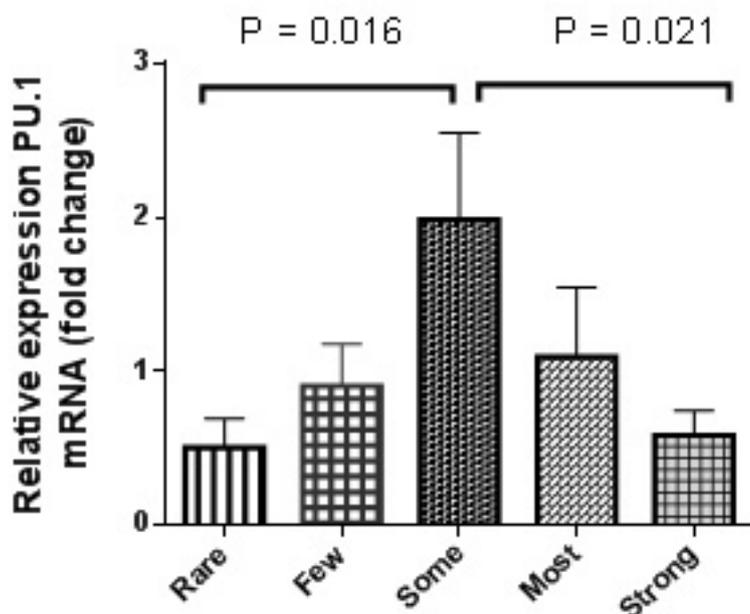
Figure 5: Normalized relative expression of PU.1 in 96 AML patients graded by MPO activity. Patients are graded 'rare' to 'strong' based on the percentage of MPO positive cells. Patients graded with 'some' MPO activity, those with the intermediate number of MPO positive cells, had PU.1 expression levels which were significantly higher in comparison 'rare' and 'strong' group. A significant difference is observed between PU.1 expression levels in the 'some' grade in comparison to the 'rare' grade (lowest number of MPO positive cells) (P=0.016, also a significant difference is observed between PU.1 expression levels in the 'some' grade in comparison to the 'strong' grade (highest number of MPO positive cells) (P=0.021).

Correlation between PU.1, LEF1 and IRF8 in AML patients:

An analysis by means of statistical test was conducted to identify any correlation between the expression of PU.1, LEF1 and IRF8 genes in AML patients. Analysis determines that the three genes have moderate positive correlation with each other; correlation between PU.1 and IRF-8 is R: 0.378, P <0.0001(Figure 6 A), expression of PU.1 and LEF-1: R: 0.399, P <0.0001 (Figure 6 B) and the expression of IRF8 and LEF1: R: 0.320, P: 0.001(Figure 5C) in patients with AML. In comparison, an analysis of the correlation between these genes in healthy subjects determines that there no correlation exists in the normal status; PU.1 and IRF8: R: 0.469, P: 0.049, PU.1 expression and LEF1: R: 0.281, P: 0.259 and between the expression of IRF8 and LEF1: R: 0.418, P: 0.084.
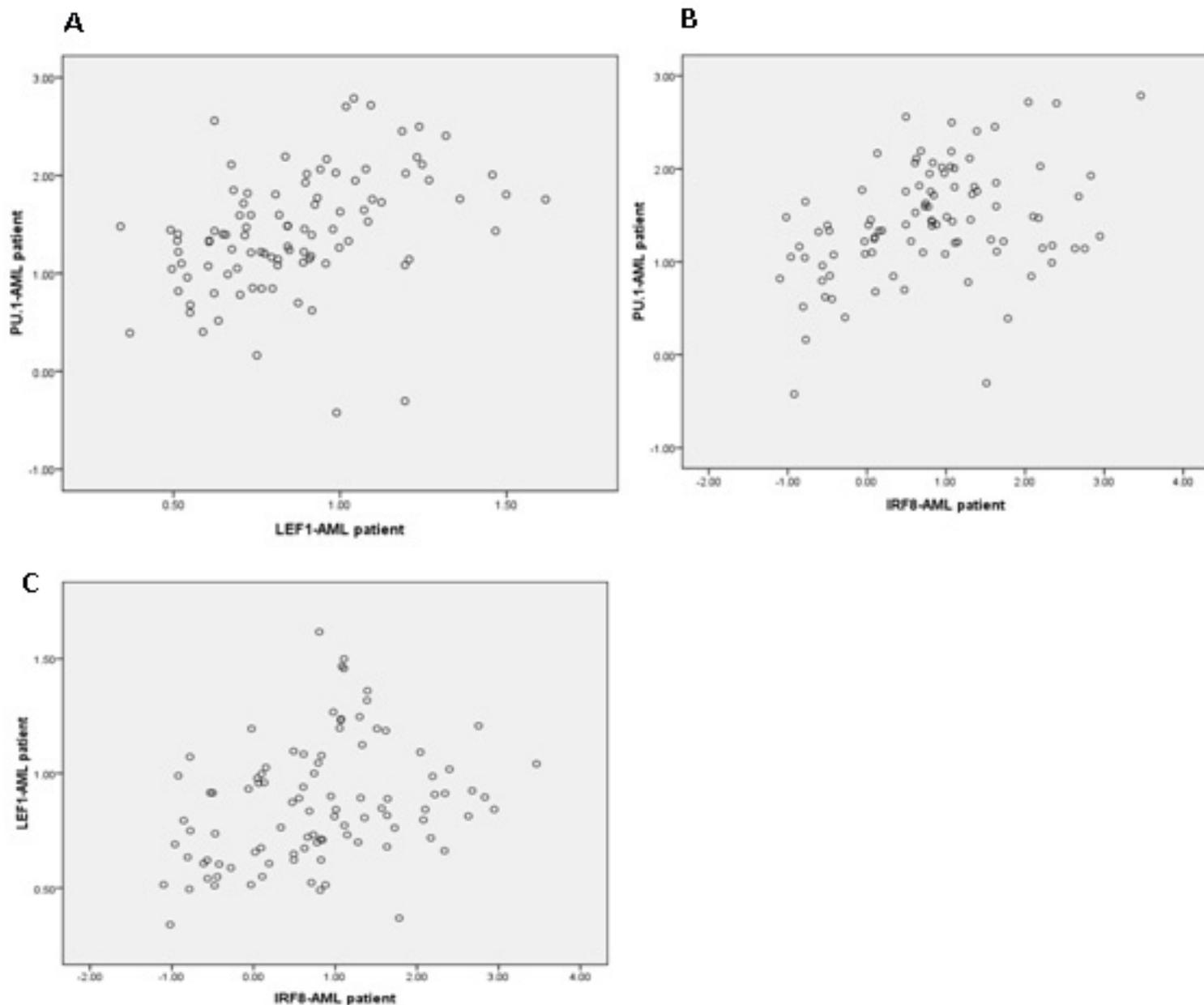
Figure 6: Statistical analysis by means of Pearson's chi-squared test reveals dependence and relation between the expression of PU.1, LEF1 and IRF8. A) Correlation between PU.1 and LEF1 in 96 AML patients was determined to be positive and significant (P < 0.0001, r= 0.378). B) Correlation between PU.1 and IRF8 in 96 AML patients was determined to be positive and significant (P < 0.0001, r=0.399). C) Correlation between IRF8 and LEF1 in 96 AML patients was determined to be positive and significant (P = 0.001, r= 0.320).

Discussion

Several studies together, approve our results associated with decreased expression of PU.1 in AML patients. In studies pointed out that there is a relationship between PU.1 low expression and AML, the absence of this gene leads to stimulation of AML and partial inhibition of this gene is common in AML patients. In other types of leukaemia such as CML also showed reduced expression of the transcription factor (20-22). Thus, this gene in our study has maintained its tumour suppressor role and found decrease and with its decrease in expression also leads to increased tendency towards leukaemia development. In contradictory studies to ours it was shown that IRF8 has significant decrease in expression. In CML it was shown that IRF8 acts as a tumour suppressor as STAT5 is a target gene of the BCR-ABL fusion gene its expression is suppressed (23). Also, reported that decreased expression of this gene in addition to CML and is associated with AML. Since this gene can regulate the survival of progenitors, therefore it can act as a tumour suppressor gene with its decrease cause myelogenous leukaemia formation (14). The absence of this gene leads to granulocytic differentiation and blocking of monocytic differentiation and vice versa. But in a study showed that increased expression of WT-IRF8 transcripts (expressed in hematopoietic stem cell senescent and early leukemic blasts) and SV-IRF8 (identified in malignant cell lines and leukemic blasts in AML patients due to aberrant promotor hypermethylation IRF8 becomes normal) is significantly associated worse with RFS than AML. Since the decreased expression of the gene associated with haematopoiesis dysfunction and promotion of leukaemia it was unexpected that increased expression of the WT transcript is associated with adverse prognosis. Increased expression of this gene likewise to its decrease can have detrimental effects on normal haematopoiesis. Increased expression of this gene blocks the neutrophil differentiation and promotes differentiation towards monocytic, macrophage and DC types. If the overexpression of this gene leads to leukemic cells dendritic cells improperly transport, this change in performance may partly explain the adverse prognosis. In our study, this gene significantly increased compared to control group but similar to this study but as in this study when the overexpression is studied in detail in patients we found that only 15% (15 of 96 patients) had increased expression and the rest reduced expression (Figure 3). LEF1 in our study showed significant decreased expression, in various studies the role of this gene is described as factor in granulocyte differentiation due to decreased expression observed in patients with congenital neutropenia. Moreover, it seems that LIFE-1 gene in leukemic cells acts as a tumour suppressor gene. So its reduction of expression allows leukemic cells to proliferate and increase in growth. (8,10). Studies have shown that overexpression of this gene is associated with a more favourable prognosis in patients with APL. The findings showed that increased expression of this gene in CN-AML is associated with favourable outcome even if the molecular and clinical risk factors are known. Studies have showed that LEF1 is significantly overexpressed compared to controls but the contradictory

results were obtained in our study and in one patient increased expression compared to the normal control was identified. As low expression of LFE1 in AML patients with increased blasts in the bone marrow and is associated with progression of AML. Since this gene is a transcription factor important in the granulocytic differentiation thereby reduction of LEF1 expression may participate in the differentiation block in AML and MDS blasts which an increase in blast percentage and white blood cells in patients with CN-AML is a reflection of reduction of LEF1 expression.

The decreased expression of these genes leads to poor patient prognosis and development of malignancy on the order of PU.1 expression based on subgroups: m3≤m0/m1/m2≤m4/m5. This gene is expressed at the highest levels in monocytes and plays an important role in myeloid differentiation. APL in 98% of cases is accompanied with the PML-RARA fusion gene and the expression of this gene in M3 due to PML-RARA is inhibited as it has been observed that after ATRA increased expression of this gene occurs and differentiation is induced (24). In this study only the M3 subtype was related to the normal control group compared to the other two subtypes. As in other studies our study also showed that PU.1 had significantly decreased expression in APL patients in comparison to the normal control group due to the PML-RARA fusion gene in these patients. This gene in HSCs is expressed lower than CMPs and it this increase in expression which is the factor which promotes differentiation towards monocytes and granulocytes. Expression of this gene was increased from M0 to M5, except in M3. The lowest expression of this gene was found in M0 in blasts with minimal differentiation the lowest expression was seen and average expression in M2 / M1 was shown and expressed higher in M4 / M5. In M2 the fusion gene AML1-ETO is the factor that represses PU.1 inhibition. However the reason M2 was higher compared to M3 is the lack of this fusion gene in 80% of patients. And it was observed that suppression of expression of this gene is essential for the initiation and pathogenesis of APL. Our results on the expression levels of AML subtypes was exactly the same (6). The order of LEF-1 expression in subtypes: M3=M0/M1/M2)>M4/M5 which showed this gene is not involved in cell maturation because with increased differentiation this gene showed reduced expression which contradicts this genes role as a differentiation factor. The more mature the cell this gene is more impaired. This gene in its normal state has a role in the differentiation, proliferation and survival of granulocytic progenitors. In our study in detail expression of this gene in subgroup with granulocytic differentiation was higher than subgroup of monocytic differentiation although this difference was no significant (8). The order of IRF8 expression in subtypes: M0/M1/M2<M3<M4/M5. The more mature the cell, the more this gene was expressed which is why the expression of IRF8 was much higher in the M4/M5 subgroup than the undifferentiated subgroup. It is M3 that confirms the fact that IRF8 has the highest expression in in monocytic differentiation which is the case in normal circumstances. Likewise with consideration to cell maturation it has increased expression which can

be a sign of its proliferation role in AML. In studies it has also been shown that this gene in patients with M5 have overexpression(25, 26).

In our study, the relatively strong positive correlation between these genes was observed which is supported by other studies where it has also been shown that overexpression of PU.1 leads to activation of IRF8 and inhibition of CEBPA, GTA1, GTA2 and KLF4 which are necessary for granulocytic differentiation(6). Since IRF8 acts as a cofactor for PU.1 and based on IRF8 defective mice studies, dysfunction in determining granulocytic and monocytic differentiation and develop towards MDS, slight decreases in PU.1 and defective IRF8 plays a role in the pathogenesis of human leukemia. This means that either IRF8 with lower expression in AML patients with PU.1 lower expression is observed or a positive correlation between the expression of IRF8 and PU.1 exists in LSCs whilst this correlation does not exist in healthy HSCs (17). Furthermore, in other studies it has been reported that LEF1/B-catenin leads to increased regulation of the gene IRF8 (27).

In our study we also showed that between the expression of these three genes in AML patients there is correlation but in the normal control group no correlation was observed. It can be indicated in this study that when malignancy for unknown reasons that new connections between transcription factors occur which can affect the malignancy process. Our observations suggest that examining the oncogenic role of these genes and discovering new molecular mechanisms formed in the process of malignancy in each of these differentiation genes can play a role in the design of novel diagnostic methods, monitoring and treatment of patients with acute myeloid leukaemia(28-32).

Abbreviations:
LEF1, lymphoid enhancer-binding factor 1; IRF8, interferon regulatory factor 8; AML, Acute Myeloid Leukemia; HSCs, Hematopoietic stem cells; bZIP, basic-leucine zipper; WT,wild-type; BM, Bone Marrow; PB, peripheral blood; S.E.M,standard error of the mean; MDS, Myelodisplastic syndrome; CN-AML, cytogenetically normal acute myeloid leukemia.

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Comparing the efficacy of Dexeroyx (Osveral) and Deferoxamine (Desferal) in reducing serum ferritin level in patients with thalassemia major

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Abstract

Background: Considering the necessity of permanent use of iron chelating agents in patients with thalassemia and the difficulty of using injectable drugs such as desferal, has given a special place to research on oral alternatives. The aim of the present study was to introduce oral Dexeroyx as an alternative to injectable desferal and also to determine its efficacy to reduce serum level of ferritin in patients with thalassemia.

Methods: This cross-over clinical trial was performed on 51 thalassemia patients randomly divided into two groups receiving desferal (50mg/kg/day intravenously) or Dexeroyx (20mg/kg/day orally). Serum ferritin levels were determined in both groups before treatment and then they were treated for 6 months and serum ferritin levels were determined on a monthly basis. After this period, with a one-month washout period, the treatment plan was transferred to the two groups.

Results: In the first phase of the study, although a downward trend in the level of ferritin was revealed in both groups within six months of interventions, no difference was found across the two groups. Similar findings were observed in the second phase of intervention so that in both groups receiving desferal or Dexeroyx, the serum level of ferritin gradually decreased within the six months of treatment, but no difference was found between the two groups in the trend of the change in ferritin level. The serum level of ferritin was independent to some baseline factors including gender, age, or history of splenectomy.

Conclusion: Dexeroyx is at least as effective as desferal in reducing serum ferritin levels. If there is no contraindication for using oral medications, Dexeroyx can be prescribed as an appropriate alternative for desferal in thalassemia patients.

Key words: Dexeroyx, Deferoxamine, serum ferritin level, thalassemia major

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Introduction

Thalassemia is a congenital homeopathic illness that appears in two major and minor forms (1). Because of anemia due to hemolysis, these patients are required to suffer repeated blood transfusions that lead to improved oxygen delivery to the tissues, as well as reduce ineffective hemorrhage and eliminate the symptoms of the disease. However, it may result in increasing the body's iron load which can cause early death especially before the age of 30 years (2,3). The ferritin serum level is the most widely used indicator for estimating body iron load (4). In today's world, many drugs are used to treat thalassemic patients, each with its own specific characteristics. These medications aim to reduce the load of excess iron or lower the level of serum ferritin in such patients. The only iron chelator currently available and approved is deferoxamine mesylate (desferal). But it is expensive and slightly absorbed by the digestive tract. Moreover, the method of binding this drug to iron requires its slow and prolonged infusion through the pump. The permanent presence of this drug in the body improves the function of the body and protects the tissues against toxic effects of iron released. Deferoxamine is almost non-toxic, however, cataracts, deafness and local skin reactions such as urticaria have been reported (5). Deferasirox is an iron-chelating agent with a completely different structure as compared to injectable desferal (6). The bioavailability of Dexeroyx in comparison to Desferal is 70%; it is metabolized in the liver and is available in tablets of 125, 250 and 500 mg (7). The starting dose of this drug is 20 mg/kg, taken once a day and half an hour before meals (8). Considering the necessity of permanent use of iron chelating agents in patients with thalassemia and the difficulty of using injectable drugs such as desferal which is used for this purpose, has given a special place to research new drugs that can control iron load in patients with thalassemia. The aim of the present study was to introduce oral Dexeroyx as an alternative to injectable desferal and also to determine its efficacy to reduce serum level of ferritin in patients with thalassemia.

Materials and Methods

This cross-over clinical trial was performed on Thalassemia patients after obtaining written informed consent and approval of the study process by Shahrekord University of Medical Sciences in 2011. All eligible patients were more than two years of age, had serum ferritin level higher than 100ng/dl, suffered more than 10 times blood transfusion with the volume of injected blood greater than 100 cc/kg. All patients had normal serum creatinine level (based on the amount of GFR in terms of weight and age), negative tests for HIV, or hepatitis viruses, normal hepatic enzyme levels (lower than five times normal level), normal CBC and platelet counts, normal cardiac function as left ventricular ejection fraction higher than 55% and left ventricular end diastolic volume less than 40cc/m. Also, none of the participants had visual or hearing problems. No evidence of renal defects (identified as proteinuria or Pr/Cr >0.6) was observed. Pregnant women or those in breastfeeding period were also not included. If the creatinine level was

higher than the normal range or more than 33% higher than the baseline value within the study, the drug dose was halved and creatinine was monitored every week and thus in case of a progressive increase in creatinine, the drug was discontinued for one month; despite decreasing the dose of drug and the dosage of the medicine was reached at the initial level only, in case of normal creatinine. Those patients who faced heart diseases based on annual echocardiography, auditory and ocular problems during the annual examination, the positivity of hepatitis and HIV tests, or increasing liver enzymes more than 5 times of normal range were all excluded from the study. In case with pancytopenia, drugs were discontinued till normalizing the cell counts. In those with the appearance of severe nausea and vomiting, lack of response to antiemetic drugs or presence of skin rash, the dose of drug was reduced or even discontinued and after improvement of rashes, the drug was begun with a low dose and then gradually increased.

The patients were selected from thalassemic patients who referred to a private Thalassemia clinic in Shahrekord city and who were randomly divided into two groups receiving desferal (50mg/kg/day intravenously) or Dexeroyx (20mg/kg/day orally). Then the dosage of drugs was adjusted based on the number of received blood units and serum ferritin levels. Serum ferritin levels were determined in both groups before treatment and then they were treated for 6 months and serum ferritin levels were determined on a monthly basis. After this period, with a one-month washout period, the treatment plan was transferred to the two groups and for the first six months, the first group received Dexeroyx and the second group received desferal and then serum ferritin levels were re-measured monthly. Data were collected by questionnaire including age, gender, type and duration of the disease, as well as serum level of ferritin before and 6 months and one year after intervention.

The required sample size was determined as 30 patients in each group using the formula for estimating sample size for comparing the two means considering the variance of 46 and 25 for serum level of ferritin in the normal population and thalassemic individuals respectively, with the minimum between-group difference of 25%, with 95% confidence level and power of 80%.

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by absolute frequencies and percentages for categorical variables. Normality of data was analyzed using the Kolmogorov-Smirnoff test. Categorical variables were compared using chi-square test or Fisher's exact test when more than 20% of cells with expected count of less than 5 were observed. Quantitative variables were also compared with t test or Mann U test. The trend of the change in study parameters was assessed by the Repeated Measure ANOVA test. For the statistical analysis, the statistical software SPSS version 16.0 for windows (SPSS Inc., Chicago, IL) was used. P values of 0.05 or less were considered statistically significant.

Results

In total 51 patients (26 male and 25 female) were included into the study. The average age of the patients was 14.6 ± 6.9 years ranged 3 to 29 years and most of them (57%) were under 14 years of age. Also, 45.1% underwent splenectomy. Table 1 summarizes the serum level of ferritin within the first 6 months of intervention in both groups. There was no difference in baseline level of serum ferritin between the groups who received desferal or Dexeroyx (1356 ± 770ng/dl versus 1305 ± 515ng/dl, p = 0.79). In the first phase of the study, although a downward trend in the level of ferritin was revealed in both groups within six months of interventions, no difference was found across the two groups (Figure 1). Similar findings were observed in the second phase of intervention so that in both groups receiving desferal or Dexeroyx, the serum level of ferritin gradually decreased within the six months of treatment, but no difference was found between the two groups in the trend of the change in ferritin level (Table 2 and Figure 2). As shown in Table 3, the serum level of ferritin was independent to some baseline factors including gender, age, or history of splenectomy. In the age subgroup of 15 to 19 years, the serum level of ferritin increased after intervention probably due to the lack of appropriate use of medications by patients.

Table 1: Comparing serum ferritin level between the two groups during the first phase of the study

Group	Desferal (SD±Mean)	Dexeroyx (SD±Mean)	P value
Before intervention	1356 ± 770	1305 ± 515	0.79
1 month later	1239 ± 749	1217 ± 448	0.90
2 months later	1286 ± 497	1218 ± 436	0.61
3 months later	1157 ± 412	1226 ± 592	0.47
4 months later	1264 ± 494	1178 ± 310	0.47
5 months later	1195 ± 539	1193 ± 413	0.99
6 months later	1167 ± 487	1134 ± 286	0.79

Figure 1: Trend of the change in serum ferritin level within the first phase of intervention
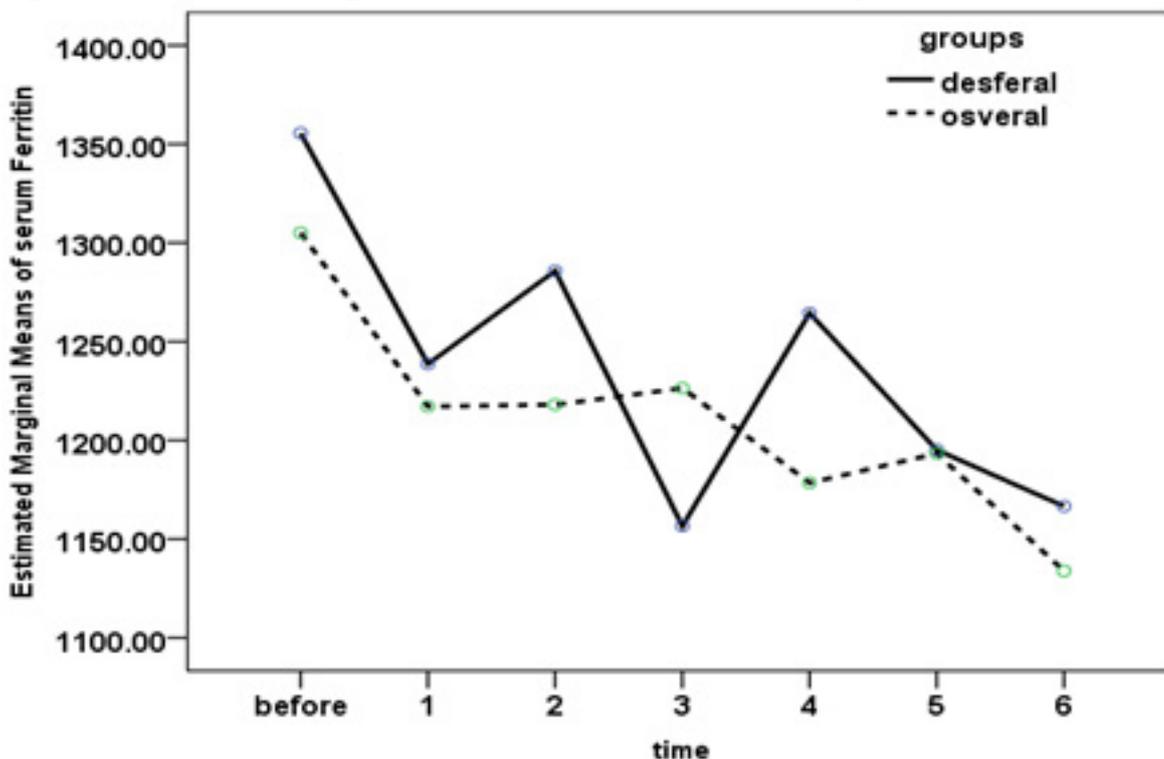
Table 2: Comparing serum ferritin level between the two groups during the second phase of the study

Group	Desferal (SD±Mean)	Dexeroyx (SD±Mean)	P value
1 month later	1125 ± 447	1132 ± 477	0.95
2 months later	1066 ± 423	1139 ± 453	0.55
3 months later	1028 ± 404	1125 ± 437	0.42
4 months later	977 ± 398	1002 ± 408	0.82
5 months later	946 ± 403	994 ± 398	0.67
6 months later	854 ± 389	988 ± 418	0.24

Figure 2: Trend of the change in serum ferritin level within the second phase of intervention
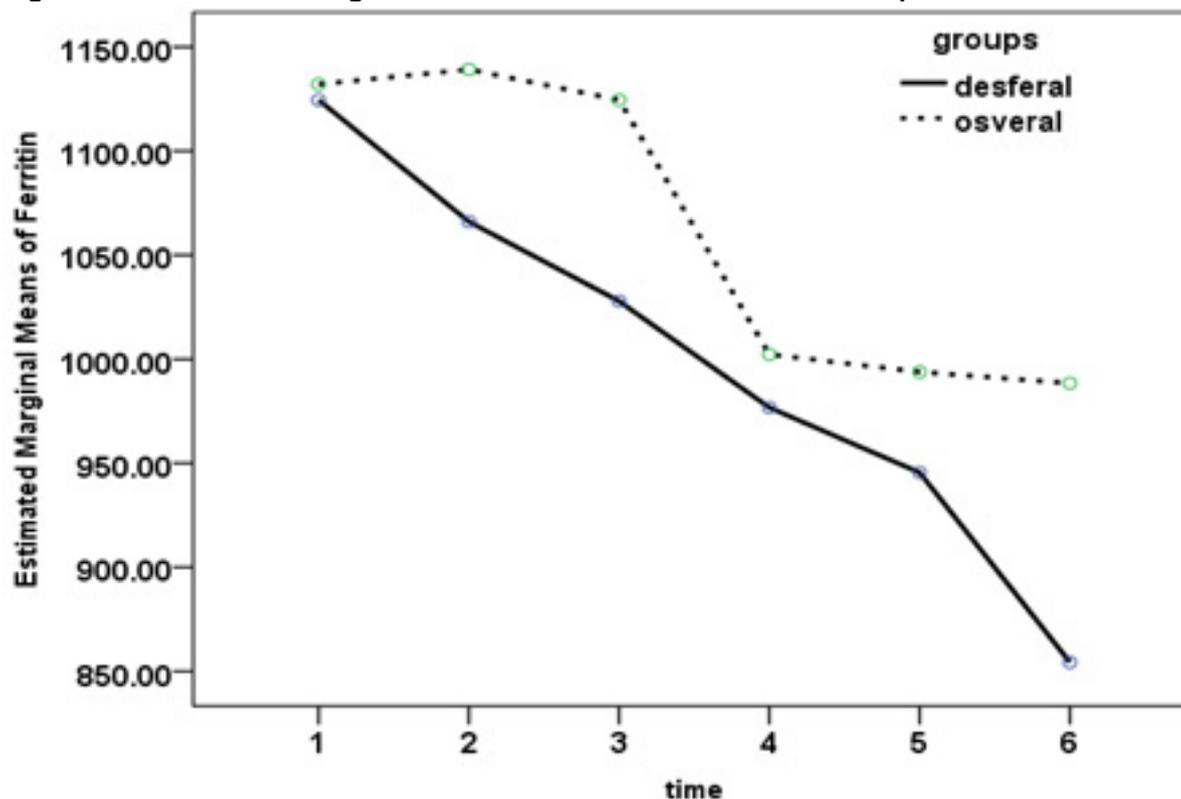
Table 3: mean serum level of ferritin within 12 months of intervention

Group	Before intervention	After intervention	Mean difference	P value
Drug				0.38
Desferal	1356 ± 770	854 ± 386	501 ± 154.3	
Dexeroyx	1305 ± 515	988 ± 418	317 ± 129.5	
Gender				0.21
Male	1226 ± 537	935 ± 313	502 ± 98.5	
Female	1444 ± 765	894 ± 484	907 ± 181.4	
Age subgroups				0.22
< 10 yr	1484 ± 616	745 ± 251	739 ± 153	
10 to 14 yr	1412 ± 963	1011 ± 418	401 ± 290	
15 to 19 yr	1061 ± 373	1064 ± 558	-2.8 ± 209	
20 to 24 yr	1299 ± 452	948 ± 451	351 ± 107	
≥ 25 yr	1179 ± 424	871 ± 337	307 ± 139	
Splenectomy				0.96
Yes	1325 ± 764	902 ± 483	831 ± 173	
No	1339 ± 577	926 ± 331	414 ± 125	

Discussion

According to the findings of this study, age and sex distribution of patients in both groups did not differ significantly. Also, history of splenectomy was not different in patients in both groups. Therefore, the confounding effect of the underlying variables including age, sex and history of splenectomy was neutralized in the two groups and therefore the observed differences between the two groups might be related to the effect of drugs. Also, this study was conducted as a cross-over trial. In fact, each patient was self-examined, and thus the results were believed to be reliable.

According to the results of this study, both desferal and Dexeroyx drugs had similar effects on serum ferritin levels in the studied patients. In this regard, administering desferal and Dexeroyx led to decreasing 501 ± 154.3 units and 317 ± 129.5 units in serum ferritin respectively. But according to the tests, the difference between the two groups was not significant. Several studies have been carried out on the effect of desferal on the reduction of serum ferritin level and the effect of this drug on reducing serum ferritin levels has been well proven in such studies. Nowadays, desferal is approved as a lowering sum ferritin level by the scientific communities and also by the FDA. In a study conducted by Pathare and his colleagues in Amman in 2010 (5), 19 patients with β thalassemia major were treated with Dexeroyx for 18 months indicating high efficacy of Dexeroyx in decreasing iron overload. The results of this study are close to our study results. In a study by Hoffbrand and colleagues (9) in order to investigate the effect of Dexeroyx on the reduction of blood iron levels in patients with thalassemia major in England, it was shown that the use of this oral drug can significantly affect the extraction of iron, which is in line with the results of this study. In a study conducted by Azizi et al (2010), 46 patients with thalassemia were treated with Dexeroyx for at least one year and showed that Dexeroyx is effective in reducing serum ferritin levels with no serious and dangerous side effects (10).

In a study by Molavi et al. (11), the effect of Dexeroyx in reducing serum iron levels was confirmed. In this study, 80 patients with thalassemia major were treated with oral Dexeroyx and patients were followed up for 1 year. In their study, serum ferritin levels decreased from 9494 ± 797 at the beginning of the study to 1578.78 ± 6.6 and the difference was significant before and after the treatment. Eshaghi et al. (12) also evaluated the administration of oral Dexeroyx in thalassemic patients and concluded that the drug could reduce serum ferritin levels. Fathi et al. (2017) showed that Dexeroyx had similar results with desferal in reducing ferritin serum levels, but after 12 months of the intervention, serum ferritin levels in patients who medicated with Dexeroyx decreased more as compared to ferritin levels in patients receiving desferal. Also, the use of Dexeroyx led to lower side effects when compared to the desferal group (13).

Regarding the results of the study and the significant reduction in serum ferritin level in patients with thalassemia, it can be concluded that Dexeroyx oral products are as effective as desferal in reducing serum iron levels. But because of the limited studies, especially the Iranian surveys, there is still no consensus on this finding emphasizing necessity for further studies.

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Plasma ghrelin concentration and pepsinogen I/II ratio as non-invasive markers for upper gastrointestinal malignancy

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Abstract

Malignancy in the upper gastrointestinal tract is an important health problem worldwide. It is often detected late because there aren't typical early symptoms. If the cancer is caught soon enough with identifying useful diagnostic and prognostic markers, patients can have a high survival rate through endoscopy-assisted treatment and surgical therapy.

This cross sectional study was done on 308 referred patients to an endoscopy department of a University hospital affiliated in Iran. Demographic data (age, gender), body weight, stature and any history of systemic disorder were recorded. The blood samples were collected to measure C-reactive protein, fasting blood sugar, Albumin, complete blood count, serum pepsinogen I and II and ghrelin plasma levels after 12 hours of fasting, before upper gastrointestinal endoscopy was performed. Enzyme-linked immunosorbent assay was used to measure serum pepsinogen I and II and ghrelin plasma levels.

The patients were divided into three groups: patients with cancer (14.6%), patients with benign lesions (27.6%), and others with normal endoscopy. Patients with malignancy showed significant lower levels of PGI (median, 73 ng/ml), ratios of PGI/PGII (median, 4.29) and ghrelin (4.94 pg/ml). The average of ghrelin level and PGI/PGII ratio in the women was significantly higher than in the men. The mean of ghrelin level was significantly lower in the stomach lesions than in the esophagus and antrum lesions.

Inverse associations between ghrelin in addition to the PGI/II ratio and some gastrointestinal cancers suggest a potential role for serum ghrelin and in addition to the PGI/II ratio, as two biomarkers of upper gastrointestinal cancers.

Key words: upper gastrointestinal diseases, gastric cancer, ghrelin,
pepsinogen I and pepsinogen II,
non-invasive marker,
endoscopy.
PG: Pepsinogen
Pg/mL: Pico gram/milliliter
Ng/ml: Nano gram/milliliter

Introduction

Malignancy in the upper gastrointestinal tract is an important health problem worldwide (1). Upper gastrointestinal cancer is the fourth-most-common cancer in the world and also the second-highest cause of cancer death. There has been a dramatic decrease in the incidence of this cancer and the death rate during the past numerous years. It is often detected late because there aren't typically early symptoms, so the survival rate drops significantly. The overall prognosis is poor due to high incidence and late diagnosis, nonetheless, the appropriate treatments and early diagnosis improve the prognosis. If the cancer is caught soon enough with identifying useful diagnostic and prognostic markers, patients can have a high survival rate through endoscopy-assisted resection, particularly with submucosal dissection, even without surgical therapy (2).

Barium meal studies, particular double-contrast barium meal, are alternative options to mass screening of gastrointestinal tract in some countries such as Japan, but they are not as sensitive (2). At this time, there are no serum analysis screening tests yet (2). Stomach cancer is the most common cancer with high mortality rate in both sexes in Zanjan of Iran (3), so any study to help resolve this issue is definitely valuable.

Ghrelin is a 28-amino acid peptide hormone that is produced by ghrelinergic cells in the gastrointestinal tract and in other organs and tissues particularly in the stomach. It is the endogenous ligand for the growth hormone secretagogue receptor which present on pituitary cells secreting growth hormone. It is suggesting effects of stimulation of growth hormone in the pituitary and in the regulation of gastrointestinal function (4, 5). Ghrelin exhibits numerous physiological functions, such as stimulation of growth hormone release, anti-inflammatory effects and regulation of energy expenditure. It also exhibits some protective effects (6). The gastric fundus secretes 10 to 20 times more ghrelin than the duodenum; also concentrations of ghrelin in the jejunum and ileum is lesser. In other words, concentrations of ghrelin are generally diminished per gram of tissue with increasing distance from the stomach. Decrease in ghrelin levels following gastrectomy or small-bowel resection inculcate that approximately two thirds of circulating human ghrelin secretes from the stomach and one third from the small intestine (7). Serum ghrelin levels in different gastrointestinal diseases have not yet been determined (8).

Pepsinogen is a substance which is secreted by the chief cells in the fundus of stomach wall before being converted into the proteolytic enzyme pepsin by gastric acid. It includes two major groups: Pepsinogen I and Pepsinogen II. Pepsinogen II is secreted from pyloric glands in the stomach antrum and Brunner's glands in the duodenum (9). Pepsinogen I is released into not only gastric lumen but also into the blood. The serum levels of the two types of pepsinogen represent the morphological and functional conditions of different parts of the gastric and duodenal mucosa, because they are secreted from different sources (9, 10).

Serum pepsinogen has been exerted as biomarkers of gastric inflammation. Serum pepsinogen I and pepsinogen II levels increase in the presence of Helicobacter pylori-related nonatrophic chronic gastritis (9). The serum pepsinogen is measured for information on the presence of intestinal metaplasia in addition to atrophic gastritis. In atrophic gastritis, serum pepsinogen I declines while serum pepsinogen II does not change, therefore the pepsinogen I to pepsinogen II ratio elevates (10). Atrophic gastritis is one of the main precursor lesions of gastric cancer (11). Serum pepsinogen analyses are helpful to screen as a test for cancer. (10).

Early diagnosis of upper gastrointestinal cancer is very important to survival increase in patients. So, this study investigated the serum ghrelin levels and pepsinogen I to pepsinogen II ratio as well as association between these two variables in different places in upper gastrointestinal tract, especially stomach, diseases. Also these two variables were investigated in both benign and malignant gastric ulcers in addition to other upper gastrointestinal tract diseases.

Materials and Methods

This cross sectional study was done on 308 referred patients to the endoscopy department of Vali-Asr University hospital affiliated to the Zanjan University of Medical Sciences, in Iran within one year. The study protocol was approved by the institutional board of human studies at Zanjan University of Medical Sciences (Registration number: A-12-482-6). Furthermore, before the inclusion of cases to this study, the study details were explained to each of the patients and their consent recorded prior to entering the study.

Demographic data (age, gender), body weight, stature and any history of systemic disorder were recorded. The Eastern Cooperative Oncology Group (ECOG) Score was determined to guage ability of all patients to tolerate therapies in serious illness. Data collection device was researcher made check list. Exclusion criteria included: No consent to participate in the study, ECOG Performance Status grade three and more than three, alcoholism and drug abuse, diabetes mellitus, major surgery within recent six months, organ failure and any severe chronic disorder. The blood tests were done to measure C-reactive protein, fasting blood sugar, Albumin and complete blood count. In addition, approximately eight milliliters of blood was collected from each patient after at least 4-hours fasting to measure serum pepsinogen I and II and ghrelin levels. Samples to measure serum ghrelin levels were immediately collected in Ethylenediaminetetraacetic acid and p-hydroxymercuribenzoic acid-containing tubes to prevent acylated ghrelin degradation by protease. Then samples were centrifuged at 3000 rpm for 5 minutes then the serum aliquot were stored immediately at -20°C. Serum pepsinogen I and II samples were kept in the freezer at -70°C. We used Enzyme-linked immunosorbent assay with BioVendor and BioHit Research and Diagnostic kits for ghrelin and pepsinogens tests. Microscopic examination of the gastric biopsies of every abnormal lesion was

conducted after the upper endoscopic process. The patients were divided into three groups: patients with cancer, patients with benign lesions, and patients with normal endoscopy.

Statistical analysis

Data was analyzed by SPSS 20 (SPSS, Chicago, IL, USA). ANOVA, nonparametric tests and Chi-square Test were used. P- Value less than 0.05 was considered to be statistically significant. The results were presented as mean (SE) or number (%) where appropriate.

Results

In the present study; 308 cases (52.6% males and 47.4% females) were investigated by upper gastrointestinal endoscopy. Total of the patients were divided into three groups according to endoscopic Biopsy Specimens: patients with malignant lesions (14.6%) including adenocarcinomas and squamous cell carcinoma, patients with benign lesions (27.6%) including inflammation, erosion, ulcer, hyperplastic polyp, intestinal metaplasia and celiac, and others with normal endoscopy (without lesion). (Table 1) The malignant lesions were especially prominent in men (p-value=0.02). There was no significant difference between body weight index in three groups. (Table 1)

Table 1: Comparison of different characteristics of the study patients including; age, serum concentrations of PGI [ng/ml], PGII [ng/ml], PG I to PG II Ratio and serum concentrations of Ghrelin [pg/ml] among studied groups (n=308).

	Normal group	Benign LESION group	Malignant LESION group	P-VALUE
Age [Median; Mean (SE)]	51.5;53.8 (4.3)	52;56.6(4.9)	70;70.9 (6.1)	<0.0001
SEX				0.002
WOMEN [number(percent)]	95(53%)	37(43.5%)	14(31.1%)	
MEN [number(percent)]	37(46.6%)	48(56.5%)	31(68.9%)	
places of lesions				
Stomach [number(percent)]		23(57.5%)	17(42.5%)	
Esophagus [number (percent)]		15(41.7%)	21(58.3%)	
Antrum [number(percent)]		47(87%)	7(13%)	
total [number(percent)]		85(65.4%)	45(34.6%)	
body weight index	24.99;25.86(2.45)	26.23;27.8(2.5)	24.3;23.1(2.3)	0.051
PGI [ng/ml Median; Mean (SE)]	123.7;145.61(12.3)	117.2;154.44(11.6)	73;117.4(7.2)	0.002
PGII [ng/ml Median; Mean (SE)]	14.2;19.85(1.6)	15.8;23.09(1.7)	20.4;30.66(1.9)	0.069
PGI/PGII ratio	8;9.6(0.8)	6.39;9.03(0.6)	4.29;5.97(0.3)	<0.0001
Ghrelin [Pg/ml Median; Mean (SE)]	16.82;27.19(2)	15.06;19.42(1.3)	4.94;20.41(6.2)	<0.0001
albumin	405;4.54(0.43)	4.4;4.49(0.41)	3.9;4.26(0.39)	0.023
serum C reactive protein	4;21.4(1.2)	5;27.68(1.4)	15;37.3(1.6)	0.014
platelet count*1000	213;200(22)	198;195(23)	254;222(27)	0.021

The mean of age, Serum levels of PGI, PGII, ghrelin and PG I to PG II ratio in the three groups are shown in Table 1. The mean of age of cases in the malignant group was significantly higher than the benign and normal groups (median: 70 years) (p-value <0.0001). Patients with malignancy showed significant lower levels of PGI (median, 73 ng/ml), ratios of PGI/PGII (median: 4.29) and ghrelin (4.94 pg/ml) (Table 1). There was significant difference between Albumins, serum creative protein (CRP) and platelet count in the three groups. (Table 1)

In the cancerous group; the malignant lesions were prominent in 42.5% of the stomach (the fundus, body, and stomach small bend), 58.3% of the esophageal (the lower esophagus and cardia) and 13% of the antral (the antrum, pylorus, and duodenum). The average of ghrelin level and PGI/PGII ratio in the women was significantly higher than in the men (Table 2). There was no significant association between ghrelin levels and age, serum levels of PGI, PGII, and PGI/PGII ratio in total in the three groups. There was no significant association between ghrelin levels and grading of differentiation of adenocarcinoma. The mean of ghrelin level was significantly lower in the stomach lesions than in the esophagus and antrum lesions, but there was no significant difference in mean PG I to PG II among different places of the lesions (Table 2).

Table 2.Comparison of Ghrelin level and PG I to PG II ratio between gender and different places of lesions of the study patients (n=308)

	PGI/PGII RATIO [MEAN (SE)]	GHRELIN [PG/ML, MEAN (SE)]
SEX		
WOMEN	8.78(0.4)	25.15(2.4)
MEN	7.36(0.4)	15.17(1.8)
P-VALUE	0.003	<0.0001
PLACES OF LESIONS		
STOMACH	6.90(0.67)	11.8(1.35)
ESOPHAGUS	6.53(0.53)	17.5(2.52)
ANTRUM	6.85(0.36)	17.17(1.35)
P-VALUE	0.39	0.025

Discussion

Nowadays, several studies have been conducted to find tumor markers for early diagnosis of different cancers (12-13). There was high prevalence of gastrointestinal tract (especially in upper segment) cancers in Asia, especially Japan, Iran and China, so most studies have been conducted in these regions (3, 14, and 15). The purpose of this study was to seek out an appropriate tumor marker for screening of upper gastrointestinal cancer.

According to the results obtained from this study, although the number of men was approximately proportional to the women, malignant lesions incidence in men was higher than in women. In addition, there were significant difference between men and women in ghrelin levels and PG I to PG II ratio, so gender may be a confounding factor in this study. The previous studies did not consider gender as a confounding factor, therefore there is a strength in the current study.

Miki et al. (1991-2005) in Japan pointed to elevation of the PG I to PG II ratio as identifying non-ulcerated differentiated asymptomatic cancer even limited to the mucosa that were well suited for endoscopic treatment (10). Xianghong Zhang et al suggested that the subjects with abnormal serum PG level in China were a high risk population for gastric carcinoma and development of gastric carcinoma (16). Watanabe et al. showed that combining these two serum tests (PGI/II ratio ≤ 3.0) and endoscopic examination for rugal hyperplastic gastritis were identification factors for more active gastritis and higher cancer risk. (17) Murphy et al. presented that low baseline concentrations of serum ghrelin were related with an increase in the risk of gastric non cardia adenocarcinoma and esophagogastric junction adenocarcinoma, as a potential role for gastric hormones in carcinogenesis (18).

In the current study; both the plasma levels of ghrelin and the PGI/II ratio decreased with increasing extent of malignant gastric lesion, but the plasma levels of ghrelin did not correlate with the PGI/II ratio. Suzuki et al. reported that the plasma levels of ghrelin correlated with the serum levels of PGI and also the PG I to PG II ratio in gastric mucosal atrophy as a non-invasive marker for chronic atrophic gastritis (19). They enrolled a small sample size (sixty-nine patients) to confirm their findings in atrophic gastritis. So the results of the two studies were partially different.

In this research, the serum ghrelin levels were associated with location of lesions (stomach, esophageal and antral). This is consistent with findings of Sadjadi et al. that serum ghrelin levels had an inverse relationship with the risk of non-cardia gastric cancer compared to cardia gastric cancer(20), because the main source of ghrelin is the gastric oxyntic epithelium, albeit ghrelin is produced by several different tissues. On the other hand, Huang et al. did not detect influence of the location of gastric cancer (proximal vs. distal) on ghrelin levels (21-26).

In the current study, the ghrelin level and PGI/II ratio were not significantly associated with the grades of tumor differentiation in the malignant lesions. This is contradictory with Isomoto et al's report that ghrelin levels of undifferentiated cases were higher than those of differentiated ones (8).

Conclusion

This study demonstrated that there is significant association between the serum ghrelin levels and PGI/II ratio with the malignant lesions particularly in stomach and esophagus, while there are nosignificant associations between the serums ghrelin levels with PGI/II ratio. Also gender is a

confounding factor, therefore it is recommended to conduct studies for men and women to arrive at more definitive conclusions so that the use of ghrelin and pepsinogen I and II, as tumor markers, to screen for stomach and esophageal cancers can be decided.

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The effects of group cognitive behavior therapy (GCBT) on suicidal thoughts in patients with major depression

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Abstract

Introduction: Depression is one of the common mood disorders. According to the World Health Organization depression disorders will become the second most frequent disorder throughout the world in 2020. So, the present study was designed due to the serious social, economic and familial consequences of depression and to assess the effects of group cognitive behavioral therapy (GCBT) in the major depressive patient.

Methods: Forty patients in Shahid Rajaee hospital were selected, randomly, in the present study as a clinical trial investigation. Major depression was confirmed in them by Beck Depression Inventory and DSM V criteria. The subjects were divided by Control and experimental groups. GCBT sessions were planned for four continuous weeks and there were two 90 minutes sessions every week. Data acquisition consisted of demographic, Beck's suicidal ideation, Beck's depression questionnaires. Beck's suicidal questionnaire (including 19 multiple choice questions) assessed attitude, behavior and planning for suicide in the patients. Data collection by the mentioned tools was established one week and one month after the GCBT. Furthermore, all the patients in the control and experimental groups did not give up their routine antidepressant drug therapy. Finally, the results in both steps of the experiment (pre-& post- GCBT) were analyzed in both groups by unpaired t-test using SPSS software.

Results: This investigation showed that there was a significant reduction between suicidal ideation score in control and experimental groups one week after GCBT, ($p<0.0001$). Moreover, the results demonstrated that one month after GCBT the suicidal ideation score in the experimental group was markedly reduced in comparison with the control, ($p<0.0001$).

Conclusion: Although routine antidepressants can reduce suicidal ideation during hospitalization, cognitive behavioral group therapy accompanied by drug therapy may be more effective to prevent suicidal thoughts and be considered as a complementary treatment beside the usual health care for major depression.

Key words: Major Depressive,
Group cognitive behavioral therapy,
Suicidal Ideation, Beck's suicidal ideation

Introduction

Depression is one of the common types of mood disorders. According to the World Health Organization prediction, depressive disorders will be the second most common disease in the world by 2020. Also, based on existing studies, depressive disorders account for 75% of cases admitted to psychiatric hospitals (Yaeghoobi Nasrabadi et al., 2003, Kenny and Williams, 2007). According to a national survey, the rate of depression risk has been reported to be 21% in Iran (Noorbala et al., 2004). Major depressive disorder is the most common disorder among depressive disorders (Kenny and Williams, 2007). Diagnostic criteria for major depression are defined based on at least 5 cases of clinical manifestations for two weeks or more than two weeks that include at least one of the symptoms of low mood, lack of pleasure, as well as the occurrence of at least four symptoms of overall appetite change, loss of body weight by 5% or more, sleep disturbances, feeling of weakness and lethargy, loss of physical strength or fatigue, feelings of worthlessness, low self-esteem, permanent feelings of guilt, inability to concentrate thoughts of death and suicide (Association, 2013). In general, mood disorders, including major depression and low self-esteem are introduced as the most important predisposing factors for suicidal thoughts (Edalati Shateri et al., 2009). Basically, suicidal thoughts are one of the diagnostic criteria for depression (Kleiman et al., 2014) that is defined as the thoughts associated with death or destruction by planning about the time, place and method of committing suicide as well as its impact on others (Alizadeh et al., 2011). In addition, a range of risk factors of suicidal thoughts or suicide attempts have been proposed, including frustration, negativity, pessimism towards oneself and others (Reinecke et al., 2001), inheritance, family dynamics, communication networks, substance abuse, depression, schizophrenia, personality factors (King et al., 2001, Bearman and Moody, 2004, Gutierrez et al., 2000, Canapary et al., 2002, Zare and Sayadi, 2009, Troister et al., 2008). Assessment of suicide thoughts is not only considered a priority in the prevention process in patients with major depression, but also is a psychiatric emergency in the treatment phase (KaplanHI, 1995). Surveys indicate that about 7% of men and 4% of women with major depression lose their lives due to suicide (Nordentoft and Mortensen, 2011). Also, out of 95% of people with a history of suicide attempts, 80% had depression and 20% of them were diagnosed with major depression (AHMADIAN et al., 2009, Esmaeilnia et al., 2005). Although the exact statistics of suicides associated with affective disorders of major depression has not been reported in Iran, the suicide rate is higher compared to other Middle Eastern countries (MORADI, 2002). Considering that suicide causes a significant challenge for families and society and may result in the loss of active and productive forces of society; also, evaluation and identification of risk factors of suicidal ideation and suicide prevention in patients with major depression, are regarded as priorities in this regard (Vuorilehto et al., 2014). So, in addition to medical and pharmaceutical measures, scholars and researchers focus their attention on non-pharmacological

and support approaches so that they can enhance one's flexibility, resistance, compatibility, stability and self-esteem against suicidal thoughts (Brezo et al., 2006). Considering the various biological, psychological and sociological factors in the etiology of depression and suicidal thoughts, different therapeutic methods have also been suggested such as individual psychotherapy, family interventions, problem-solving treatment training and hospitalization (Shokhmgar and Pakdaman, 2012). In addition to drug therapy, non-pharmacological methods such as cognitive-behavioral method have been of interest for treatment of depression since 1970 (Ghamari et al., 2012). Although this method, whether individual or group, emphasizes on active participation in problem-solving process on the part of the patient, venturesome presence in the environment and improvement of one's ability to interpret events and taking appropriate approach (NAVABIFAR et al., 2008, sotodeh asl et al., 2011), the group method is preferred over the individual method in terms of time, cost and feedback in the treatment group, (Ghamari et al., 2012, Aghaei et al., 2009). Cognitive behavioral approach is a supportive therapy and group psychotherapy for the treatment of mood disorders such as depression, and patients undergo the treatment process during a group process with clear, organized and planned objectives (Noorian et al., 2004). The studies indicate that the effect of this method in the field of depression has been more noteworthy rather than that of suicide thoughts. For example, the effect of this method has been reported in several studies on non-psychiatric patients, including epileptic patients with depression, epileptic patients (Salehzadeh et al., 2010, Macrodimitris et al., 2011), cancer patients (Khodai et al., 2011) and patients with type II diabetes and recovery from depression recurrence (Jacobson and Weinger, 1998) and patients with opioid dependence disorder and major depressive disorder (Rasouli et al., 2009). Therefore, considering the foregoing and the fact that suicide imposes heavy socio-familial and social burden on society, there is a need for low-cost health interventions to reduce suicidal thoughts predicting one's suicidal behavior in the future; so the aim of the present research was to investigate the GCBT impact on suicidal thoughts of patients with major depression The efficiency of this method regarding suicidal ideation in patients with major depression was studied.

Materials and Methods

This study is a clinical intervention, the study population of which included all patients diagnosed with major depression who referred to the Psychiatric Clinic and Hospital of Shahid Rajaie, Yasouj, Iran. Due to limitation of the studied population and lack of computational formula based on probability sampling, available and eligible subjects were used to estimate the sample size. Samples were later divided into two groups, including experimental and control using random allocation. Inclusion criteria included a diagnosis of major depression by a psychiatrist based on the latest version of the Diagnostic and Statistical Manual of Mental Disorders, having a score higher than 29 on the Beck Depression Inventory, the age range of 18-45 years, the ability to be trained, having the physical

and cognitive ability to participate in intervention sessions, obtaining informed consent to participate in the study, obtaining a score higher than 12 for having suicidal thoughts based on Beck Scale for Suicidal ideations (BSSI) and lack of previous participation in similar studies. Exclusion criteria included acute psychiatric condition diagnosed by the psychiatrist, lack of cooperation and willingness to continue the study, incomplete questionnaires or transfer to other treatment centers. Before intervention, the informed consent letter was obtained from the participants after a full explanation about the study's goal. In addition, emphasis was placed on the confidentiality of the collected information, use of the information on the purpose of the study, complete voluntary participation in the study and free withdrawal from the study at any stage. In this research, 40 patients with major depression were studied and no participant withdrew from the study. However, since the above intervention is a GCBT intervention; and thus the experimental group was divided into two groups, 10 participants in each, and both groups were again evaluated one week and one month after intervention in terms of suicidal thoughts. With the start of the study, GCBT sessions began in the experimental group. The intervention protocol was based on the guideline proposed in the literature by a therapist for 8 sessions of 90 minutes twice per week for 4 weeks (Masoudi et al., 2009) (Figure 1). Details of the intervention sessions are listed in Table A (Kith. SD, 2006, Wright.Turkington.Kingdon.Basco, 1st. Ed. Arjamand. 2010). But the control group received no GCBT training but the prescribed medications were administered at the doses ordered by the psychiatrist in both groups. As the intervention protocol was previously mentioned in details, data were collected again and were compared with data before the intervention in both groups after the end of treatment. In this study, in addition to demographic data, data collection tools included Beck's Self-Rating Scale for Suicidal Ideation and the Beck Depression Inventory. Beck's Self-Rating Scale for Suicidal Ideation contains 19 questions with three choices scale (0, 1 & 2), which has been set for measurement of the intensity of attitudes, behaviors and (also) planning for

reliance on suicide. The overall score ranges from 0 to 38 and scores 12-38 indicate high level of suicidal thoughts. Validity and reliability of the Persian version has been evaluated and confirmed (Esfahani et al., 2015). Beck Depression Inventory with 21 multiple-choice questions has been designed to measure feedback and symptoms of depression. The inventory statements are basically prepared on the basis of observation and summarization of attitudes and common symptoms in patients diagnosed with depression. Although the content of this questionnaire is comprehensively dedicated to depression symptomatology, it focuses more on the cognitive content. Beck Depression Inventory is a self-assessment test that is completed within 5 to 10 minutes. It also consists of 21 statements related to various symptoms, 2, 11, 2, 5 and statements of which are dedicated to affective, cognitive, obvious behaviors, physical symptoms among and intra-individual symptomatology, respectively. According to this scale, depression severity ranges from mild to very severe. Also, the total score is obtained by adding the scores of each of the above statements and minimum and maximum scores are equal to 0 and 63, respectively. Lack of, or mild depression, moderate depression and severe depression are respectively classified by scores of 0-13, 20-28 and 29-63. The reliability and validity of the Persian version of this questionnaire have also been approved (Dabson and Mohammadkhani, 2007). The collected data were analyzed using SPSS V.19 and through descriptive statistical tests such centrist indicators, scattering indices, tables, as well as inferential statistics such as t-test and repeated measures considering $\alpha=0.05$.

Summary of GCBT sessions:
First session (A review of depression): welcoming, introducing and making participants acquainted with each other, providing a summary of interventions for each session, emphasis on the need for mutual respect, a sense of security and confidentiality and privacy, a short description of depression, risk factors, cognitive - behavioral model of depression, the importance of activities offered, the necessity of doing assignments, and monitoring activities, mood effects and recognition of emotions.

Figure 1: The protocol of intervention in experimental group in the present study. As seen here, data collection was done in four phases; Pre-GCBT and, 1 week and 1 month after latest session of GCBT.
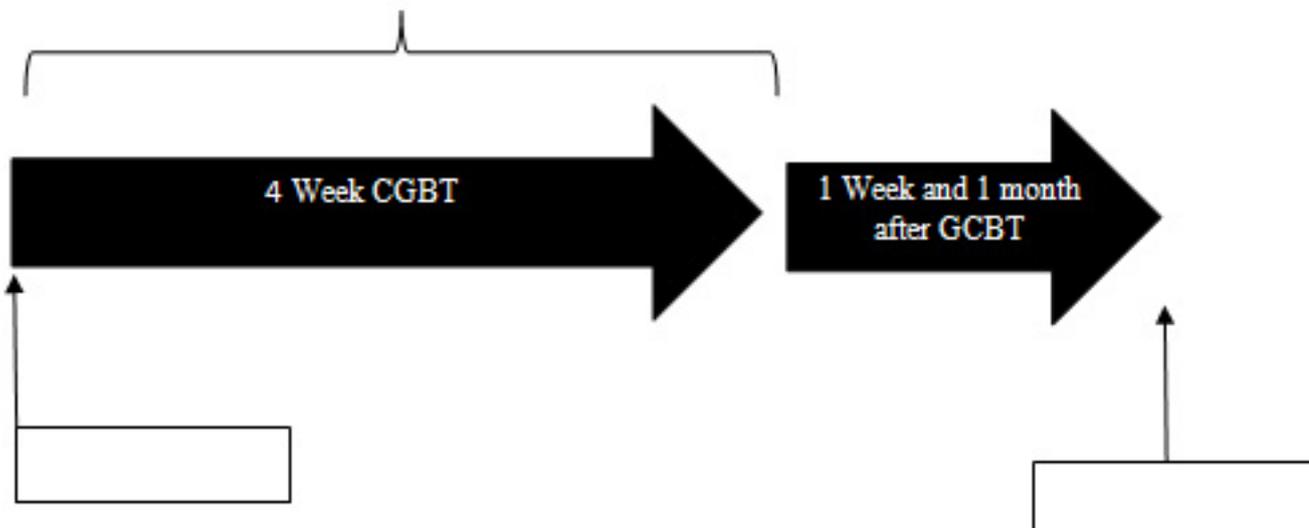
Second session (depression-activity link): reviewing daily activity sheet, completing the mood grading sheet, reemphasizing the importance of doing the assignments, using the experiences of the group members to help increase positive behaviors, providing a list of enjoyable activities to increase positive events or self-caring mood.

Third session (Thought-depression link): reviewing assignments and mood grading sheets, identifying negative thoughts in depression, showing ineffective thought patterns (mental rumination-distraction-distraction), using activity planning strategy to overcome distraction and concern

Fourth session (fighting negative thoughts): reviewing assignments and completing mood grading sheet, mentioning cognitive distortions of depression, fighting useless and negative thoughts through raising three challenging questions

Fifth session (creating hope): reviewing assignments and completing mood grading sheet, providing reasons for an optimistic outcome, organizing the treatment, setting realistic goals, using behavioral methods to foster a more optimistic thinking style.

Sixth session (efficient anti-suicide program): reviewing assignments and completing mood grading sheet, identifying specific reasons of survival, cooperative agreements in the field of precautions, identifying cognitions and adaptive behaviors, fostering strategies to deal with stressful factors increasing suicidal thoughts

Seventh session (meaning of life): reviewing assignments and completing mood grading sheet, setting life goals, providing coping strategies in pressure situations

Eighth session (Conclusion and saying goodbye to the group): - reviewing assignments and completing mood grading sheet, review of what I learned, reviewing the personal operators and depression, stating positive things to each other, saying goodbye to each other.

Findings

After collecting and analyzing data, Chi-square test showed that the control group and experimental groups were homogenous in terms of qualitative variables such as gender, marital status, level of education, employment status, place of residence, history of suicide attempt, history of suicide in the family and the number of hospitalizations. Also, the independent t-test for quantitative variables, including age and duration of diagnosis of depression showed that both groups were homogenous in terms of these variables; so chi-square and t-tests analysis showed no significant difference between the control group and two experimental groups in terms of demographic variables. The average demographic information of samples is shown in (Table 1).

Table 1: The demographic characteristics of variables. All the variables were reported as mean ±SEM.			
The variations		**Control**	**Experiment**
Age		30.35±6.44	28±6.68
Duration of diagnosis		7.3±3.3	8.15±2.87
Gender	Male	12 (52.2%)	11 (47.8)
	Female	8 (47.1%)	9 (52.9)
Marital status	Single	8 (47.1%)	9 (52.9)
	Married	12 (52.2%)	11 (47.8)
Level of education	Diploma	5 (45.5%)	6 (54.5%)
	Associate	4 (40%)	6 (60%)
	bachelor or higher	11 (57.9%)	8 (42.1%)
Job status	Employed	4 (50%)	4 (50%)
	Unemployed	4 (40%)	6 (60%)
	Student of university	12 (54.5%)	10 (45.5%)
Residential location	City	14 (50%)	14 (50%)
	Village	6 (50%)	6 (50%)
Family history of depression	Yes	3 (50%)	3 (50%)
	No	17 (50%)	17 (50%)
History of suicide attempt	Yes	9 (47.4%)	10 (52.6%)
	No	11 (52.4)	10 (47.6%)
Familial history of suicide attempt	Yes	1 (20%)	4 (80%)
	No	19 (54.3)	16 (45.7%)
History of Hospitalization	Once	15 (50%)	15 (50%)
	Twice or more	4 (44.4%)	5 (55.6%)

Before the intervention, there was no significant difference between the average scores of suicidal thoughts intervention in the control and experimental groups (p = 0.023); but immediately after the intervention and one month after the intervention the average score of suicidal thoughts was decreased in the experimental groups compared with the control group subjects who take only their prescribed medications (P = 0.0001 in both cases) (Table 2).

Table 2. The statistical comparison between control and experimental groups by ANOVA. The results demonstrated that there is a significant difference between			
	Control	Experiment	P value
Pre-GCBT	22.85±10.25	28.95±5.30	.023
1 week after of GCBT	6.75±2.82	17.35±6.19	.0001
1 month after GCBT	5.45±3.02	15.35±7.12	.0001
ANOVA (RM)	0001	.0784	

Discussion

As mentioned, the current study aimed to investigate the effect of GCBT on suicidal thoughts of patients with major depressive disorder. Data analysis showed that there was no significant difference between the two groups in terms of effective demographic variables, including age, gender, marital status, level of education , employment status, place of residence, history of suicide attempt, history of suicide or depression in the family and the number of hospitalizations, duration of depression. However, the study suggests that age, gender, marital status, unemployment, low education levels, low economic status, mental disorders, history of self-injury, aggressive behaviors, history of suicide attempt or successful history of suicide in the family and the self-harm thoughts are considered as suicide risk factors (Haerian et al., 2012, Barkhordar and Jahangiri, 2009, Stanley and Brown, 2012, Cheng et al., 2010). But considering the homogeneity of the three groups in terms of all demographic variables, the results can be judged with more confidence. Also, the results showed that there was no statistically significant difference between the mean scores of suicidal thoughts in both experimental groups and control group before the intervention, which is consistent with the results obtained in other studies on the effect of psychological interventions on suicidal thoughts in patients (Cheng et al., 2010). With respect to the mean suicidal thoughts scores in patients with major depression before the intervention, it can be shown that patients in experimental and control groups lack favorable condition in terms of suicidal thoughts scores. In this regard, the results of the study conducted by Sucu et al. (2008), which was conducted on 4,712 young individuals in Italy, the prevalence of suicidal thoughts, planning to commit suicide and lifetime suicide attempts have been reported to be 3%, 0.7% and 0.5%, respectively. The probability of planning, and suicide attempt was respectively 6.24% and 2.18% in those who had a history of suicidal thoughts (Karbalaei et al., 2011). Although the findings of this study showed that the mean scores of suicidal thoughts were decreased significantly in both experimental and the control groups a week and a month after the intervention, the difference between the average scores of suicidal thoughts shows that the decline in the experimental group is more significant than the control group. The results of this study also show that there is no significant change in the declining trend of suicidal thoughts scores within

one month follow-up after the intervention. Regarding the reduction of suicidal thoughts scores in the two groups, it can be said that both drug therapy and drug therapy along with GCBT was effective in reducing suicidal thoughts; but considering the further reduction in the suicidal thoughts scores in the experimental groups, it can be concluded that this reduction is related to the effect of GCBT. Although there are few studies on the superiority of drug therapy over cognitive behavioral therapy, Casacalenda et al. believed that cognitive behavioral therapy is equal to drug therapy (Casacalenda et al., 2002). Furthermore, studies that are consistent with the present study, indicate that psychological therapies, particularly cognitive - behavioral therapy are more effective than pharmacological methods and the results of some of these studies are as follows:

The results of the study conducted by Dimov (2007) who investigated the effectiveness of dialectical behavior therapy, cognitive behavior therapy combined with drug therapy on chronic depressed patients, showed that the recovery of patients who received this type of therapy and in those who were treated using drug therapy alone, was 71% and 47%, respectively (Dimeff and Linehan, 2008). The results of the study conducted by Stanley (2009) who aimed to investigate the effect of cognitive-behavioral therapy on the prevention of suicide in depressed patients aged 13 to 19 years, showed that this approach significantly reduced the suicidal scores among adolescents (Stanley et al., 2009). In a study on the effect of cognitive behavioral therapy (CBT) on suicidal thoughts of schizophrenia patients showed that CBT led to significant reduction in the suicidal thoughts at the end of treatment and sustainability during follow-up (Bateman et al., 2007). Furthermore, the findings of the study conducted by Brown et al. (2005) showed that CBT has reduced suicide attempts by 50% when usual care programs were promoted in patients who committed at least one suicide attempt (Brown et al., 2005). Wales and Hilborn (2012) also conducted a study with the aim of using family-based CBT for the treatment of suicide. The findings show that despite the very complex nature of adolescent suicide, this treatment was critical for saving the life of these individuals (Wells and Heilbron, 2012). Khojasteh, Mehr et al. examined and compared the effectiveness of family-centered CBT and solution to eliminate suicidal thoughts among individuals who committed suicide attempts and were hospitalized in the poisoning ward of Razi Hospital, Ahvaz, Iran. The findings

showed that both methods led to a significant reduction in suicidal thoughts (Abbaspour et al., 2014). According to sources and previous research, we can interpret the effectiveness of GCBT in reducing suicidal thoughts as follows: cognitive behavioral perspective shows the patient that thoughts are always associated with emotions and behaviors. As a result, each time a patient goes in any way to commit suicide, he/she will experience suicidal thoughts or ideas. Therefore, the patient learns the relationship between his/her thoughts and feelings and therefore can better understand and control these thoughts. Cognitive restructuring helps the patients to know their cognitive distortions during treatment and this somehow helps them predict and control the path leading to suicidal attempts (Hassanzadeh and Abedini, 2012, Wenzel and Beck, 2008). Basically, suicidal patients often have mental rumination. They are also extremely irritable, disappointed and pessimistic about the future and tomorrow situations, and feel isolated . These people have low self-confidence and defective thinking about the surrounding phenomena. Assignments help patients recognize the connection between their thoughts and mood states. So, individuals become familiar with a variety of cognitive distortions during therapy sessions and identify their attitude about themselves, others, expectations of others, their abilities, their past and the relationship between these thoughts and destructive daily behaviors using the worksheet. The most common aspects studied in this treatment type include self-blame, shame, inferiority, humiliation, feeling of helplessness, a feeling of emptiness. Also, the group therapy strengthens the communication network by strengthening factors such as group interconnectedness; therefore, the patients experience hope, altruism and tranquility in their interaction (Handley et al., 2013, Ealati and Abonajmi, 2006). Therefore, considering lower scores of suicidal thoughts of the control group who used just the drugs prescribed by the psychiatrist, the results can be explained with reference to previous studies: Based on Henden's view (2009), drugs are taken to prevent suicide attempts according to the rule that a successful drug therapy for an underlying psychiatric disorder (depression) will reduce the risk of suicidal thoughts and attempts (Henden, 2017). In this respect, in a study on the emergence or rise in the suicidal thoughts during treatment with drugs "selective serotonin reuptake inhibitors", Zisuk et al. (2009) conducted, that 57% of patients recovered and 5% were worsened (Biancosino et al., 2010). To justify why the treatment outcomes didn't change at the follow-up phase (one month after the intervention) compared to the post-test phase, it can be said that according to Beck, CBT can be sustained in the long term. Overall, the level of suicidal thoughts was decreased in the experimental and control groups in the present study, but the mean difference was more significant in the experimental group than the control group. Limitations of this study included impossibility of using the placebo group, and lack of annual follow-up. Therefore, to determine the effectiveness of this method, it is recommended to compare it with other methods of suicidal thoughts treatments in future studies as well as to use the placebo group, if possible, and longer-term follow-ups.

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The effect of Hardiness on Personal and Social Adjustment of female-headed Households

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Abstract

Introduction: Women household heads are extremely vulnerable.

Objective: The study was aimed to determine the effect of hardiness skills training on personal and social adjustment of women household heads in Mashhad, Iran. It was assumed that hardiness skill training was effective on the personal and social adjustment of women household heads.

Methods: This study was carried out using a pre-test-posttest control group design. In this study, a sample of 44 women household heads was used, who were supported by the Welfare Organization in Mashhad. The subjects were then randomly divided into two groups composed of 22 individuals. Both the control and experimental groups were asked to complete Bell's Social Adjustment Inventory. Twenty-two subjects in the experimental group underwent a group work training intervention in eight 90-minute sessions (twice a week) in accordance with Kobasa's hardiness training protocol. Bell's Adjustment Inventory (adult form) was used as the instrument in the study. Tables and charts and descriptive statistics including frequency, mean, standard deviation and range of variation were used to describe the data. Moreover, the Kolmogorov–Smirnov test was used to determine whether the data was normally distributed. Due to the normal distribution of the data, t-test, paired t-test and ANCOVA were used.

Results: The hardiness skills training led to the improvement of personal and social adjustment of women household heads. Moreover, the hardiness training intervention effectively improved at-home, health-related, emotional and occupational adjustments among them.

Discussion: The hardiness training as an effective factor in stress management can be effective in improving personal and social adjustment of women household heads.

Key words: Hardiness, personal adjustment, social adjustment, women-headed household

Introduction

The family is the smallest social unit, where both men and women manage and advance its affairs by playing biological, psychological and social roles. However, mostly, heavy responsibilities of this unit are solely given to women due to men's absence. Today, the phenomenon of women household heads is rising worldwide for many reasons. These families often have many problems so that the increase of this group of women is regarded as a social problem (Khosravi, 1999). Different studies show that 60% of women are currently a family's sole breadwinner worldwide and 37.5% of the world's households are run by women (Motee, 2010).

Women household heads have been forced to play multiple conflicting roles since they lost their husbands for whatever reason. A large group of these women face poverty, disability and inefficiency, especially in economic affairs of households, such that their self-esteem and mental health are disturbed, putting them at the risk of depression and other disorders (Langlois & Fortin, 1994). Psychologists believe that women household heads have problems in terms of both financial as well as psychological and emotional aspects and experience more stress and anxiety. According to the results of psychological research, the risk of mental illnesses is higher in women household heads who are divorced than in married women and those who live alone (Simmons, 1994).

The power of confrontation, commitment and coping as well as personal and social adjustment in coping with future stresses is important in women household heads due to the fact that they are exposed to many stresses and problems of biological, psychological and social health (Alipour, Sahraeian, Ali Akbari, & Haji Aghababaei, 2012).

Adjustment is a general concept and refers to all strategies that a person uses to deal with stressful life situations, including real or unreal threats (Sadock, Kaplan, & Sadock, 2003). Adjustment is a psychological process by which a person deals with tendencies and challenges of everyday life or controls them (Chen & Silverthorne, 2008). Adjustment leads to an optimal interaction with others, and results in the process of understanding and predicting others' behaviors, and regulating and controlling social behaviors and interactions with others (Attari, Shahni Yeylagh, Koucheki, & Boshlideh, 2005). Those with low personal and social adjustment may be at the risk of psychological and behavioral abnormalities such as insecurity as well as personal emotional and familial problems (Frydenberg & Lewis, 2012). Azin and Mousavi (Azin & Mousavi, 2011) believe personal adjustment as a factor for emotional stability, which results in good mental health, satisfaction with personal life and coordination between feelings, activities and thoughts. He also sees social adjustment as the result of personal adjustment with the social environment, which can occur by either changing oneself or the social environment (Maddi, 2007). Hardiness is among the personality traits that increase the amount of stress in a person, and seems to be an effective factor in improving personal and social adjustment.

Hardiness is a personality and cognitive characteristic, which results in promoted control, resistance and challenge seeking (Maddi, 1999). Hardy people use problem-oriented strategies in difficult and stressful conditions. This attribute increases the ability of these individuals against tension, depression, disappointment, mental illnesses and behavioral and functional weaknesses (Abdollahi, Carlbring, Vaez, & Ghafarokhi, 2016). Kobasa (1979) recognizes hardiness as an effective factor in reducing stress and increasing mental health, and introduces hardy people with three features of control, commitment and challenge. Hardy people believe that they can control situations and significantly dominate stressful situations. Such people look positively at stressful situations and search for self-made resolutions to problems (Bartone, 2000). Hardy people look optimistically at difficult situations and evaluate these situations positively and easily (Cole, Feild, & Harris, 2004). Hardiness leads to increased adjustive and action-oriented behaviors (Bjørn Helge Johnsen et al., 2017). According to Dreyer (Dreyer, 2004), hardiness can play a protective role since it creates beliefs that affect styles of coping with the stressful event. This belief reduces the stressfulness of an event and helps to improve an individual's adjustment. Seaward (Seaward, 1999) believes hardiness to be learnable and states that the attributes of commitment, control, and challenge can be learned.

Women household heads deal with problems in personal and social adjustment due to being at the risk of numerous stressful factors (Hajjari, Amiri, Yar Mohammadiyan, & Malekpour, 2007). It is important to provide appropriate training and support programs to empower women household heads so that they can challenge future problems, changes and stresses. The main question of this study was whether interventions such as hardiness skills training can improve personal and social adjustment in the vulnerable group of women household heads.

Methods

This study was carried out using a pretest-posttest control group design. In this study, 44 women were randomly selected from the women household heads at the Welfare Organization in Mashhad. The inclusion criteria were being between 30-50 years old, at least two years of self-care and ability to read and write as well as no history of any specific mental illnesses. The subjects were then randomly divided into two groups of 22 individuals. Both the control and experimental groups were asked to complete Bell's Social Adjustment Inventory (Bell, 1962). The intervention group was subjected to a test variable (hardiness training group work), but no selection and intervention was implemented for the other group as the control. At the end, the dependent variable was evaluated by a post-test (Bell's Adjustment Inventory) (Bell, 1962) in both groups.

The intervention group received the group work training intervention in 8 sessions composed of 90 minutes (twice weekly). The hardiness training protocol was an educational package compiled on the basis of hardiness

Table 1: Kobasa and Maddi's hardiness training protocol model (2008)

Session	Topic	Concepts
1	Causing impasse	Familiarity with the concept of stress, familiarity with stress types, different perceptions
2	Different viewpoint	Stress resources, logic of intervention
3	See the event differently	Different perceptions of time, discussion on the hardiness control factor
4	Sink or swim	The Importance of oppositional thinking, effort and challenge with emphasis on the hardiness challenge component
5	Keep calm	Tension relief, mental imagery
6	Dare	Techniques for saying no and expressing emotion
7	Adjustment	Problem solving
8	Restrain	Anger and anxiety control strategies

Table 2: Validity of each of the five subscales of Bell's Adjustment Inventory and its total scores

Subscale	Validity	Subscale	Validity
At-home	0.91	Emotional	0.91
Health-related	0.81	Occupational	0.85
Social	0.88	Total scores	0.94

principles of Kobasa and Maddi (Maddi, 2004, 2007, 2008; Maddi, Harvey, Khoshaba, Fazel, & Resurreccion, 2009). The protocol was trained in 8 sessions of 1.5 hours and in groups twice a week for two months. The important content of the sessions included techniques and skills according to which characteristics of people are considered with a high level of hardiness in cognitive, behavioral and emotional dimensions. In addition, the most important strategies hard-working people choose in facing challenges are considered and implemented for 2 months by the researcher practically and objectively in training women household heads.

Instruments
In this study, Bell's Adjustment Inventory (adult form) was used, which contained 160 items, each with three options including "yes", "no", and "I do not know". This form includes five separate measurement subscales of personal and social adjustment that are: a) at-home adjustment, b) health-related adjustment, c) social adjustment, d) emotional adjustment and f) occupational adjustment.
The validity of each of the five subscales of the inventory and its total scores is reported in Table 2. These coefficients were determined by the odd-even correlation and use of the Spearman-Brown prediction formula.

Results

There was no significant difference between the two groups in examining the demographic variables of age and employment status and income. The mean age was 34.25 in the experimental group and 33.8 in the control group. Moreover, 70% of the women in the experimental group and 65% of them in the intervention group were employed. Further, 40% of the women in the experimental group and 35% of them in the intervention group had an income of

below one million Tomans (Iranian currency). The results of the Kolmogorov-Smirnov test showed that there was no significant difference between the scores observed in the study and the expected scores based on the normal distribution, and the distribution of the components and the overall scale was normal.

Table 3 shows the mean and standard deviation of the pre-test scores of the components including occupational adjustment, at-home adjustment, health-related adjustment, emotional adjustment and social adjustment for both the intervention and control groups. The result of t-test showed no significant difference between the two groups in any of the components at the pre-test stage.

Table 4 shows the mean and standard deviation of the post-test scores of the components including occupational adjustment, at-home adjustment, health-related adjustment, emotional adjustment and social adjustment for both the intervention and control groups. As shown by the results of t-test, there is a significant difference in the mean scores of the post-test of the components including occupational adjustment, at-home adjustment, emotional adjustment and social adjustment between the intervention and control groups. However, the results of t-test showed no significant difference in the mean scores of the post-test of the health-related adjustment component between the intervention and control groups.

Analysis of covariance was used to more accurately investigate the data. The results of the Leven's test showed the equality of the variances of the post-test scores. The results of the covariance analysis are as follows.

The one-way ANCOVA examined the effectiveness of hardiness training on at-home adjustment of the subjects (F=42.886, P<0.1), which indicated the effect of the

Table 3: The mean and standard deviation of the scores of the groups at the pre-test stage

Variable		Mean	SD	t	Significant level	N
Occupational adjustment	Intervention group	21.25	2.04	0.243	0.809	20
	Control group	21.40	1.84			
At-home adjustment	Intervention group	22.50	3.39	0.659	0.514	20
	Control group	21.90	2.24			
Health-related adjustment	Intervention group	16.90	3.39	1.508	0.140	20
	Control group	18.55	2.24			
Emotional adjustment	Intervention group	20.85	1.84	1.449	0.156	20
	Control group	21.85	2.47			
Social adjustment	Intervention group	22.65	2.77	1.652	0.107	20
	Control group	21.10	3.14			

Table 4: The mean and standard deviation of the scores of the groups at the post-test stage

Variable		Mean	SD	t	Significant level	N
Occupational adjustment	Intervention group	19.10	1.58	2.506	0.017	20
	Control group	20.45	1.81			
At-home adjustment	Intervention group	18.20	1.32	6.143	0.000	20
	Control group	20.95	1.50			
Health-related adjustment	Intervention group	16.65	2.79	1.830	0.075	20
	Control group	18.40	3.23			
Emotional adjustment	Intervention group	19.35	1.59	2.249	0.030	
	Control group	20.85	1.51			
Social adjustment	Intervention group	18.90	1.37	2.156	0.038	20
	Control group	20.63	3.31			

hardiness training intervention on the improvement of at-home adjustment among women household heads. As shown by the one-way ANCOVA analysis, given that ETA = 0.537, the hardiness training intervention explained 53% of the improvement of at-home adjustment among women household heads.

Moreover, in the one-way ANCOVA analysis of the effectiveness of hardiness training on health-related adjustment of the subjects (F=1.821, P<0.05), given that ETA = 0.47, the hardiness training intervention explained 47% of the improvement of health-related adjustment among women household heads.

Furthermore, the one-way ANCOVA analysis of the effectiveness of hardiness training on emotional adjustment of the subjects (F=8.271, P<0.01), considering that ETA = 0.183, revealed that the hardiness training intervention explained 18% of the improvement of emotional adjustment among women household heads.

The one-way ANCOVA analysis of the effectiveness of hardiness training on enhancing occupational adjustment skills among the subjects (F=9.742, P<0.01), considering that ETA = 0.208, revealed that the hardiness training intervention explained 20% of the improvement of occupational adjustment among women household heads.

The one-way ANCOVA analysis of the effectiveness of hardiness training on social adjustment among the subjects (F=25.197, P<0.01), given that ETA = 0.405, also indicated the 40% impact of the hardiness training intervention on the improvement of social adjustment among women household heads.

Finally, given that ETA = 0.689, the one-way ANCOVA analysis of the effectiveness of hardiness training on overall adjustment among the subjects (F=82.023, P<0.01) demonstrated the 68% impact of the hardiness training intervention on the improvement of overall adjustment among women household heads.

Discussion

According to the results of this study, training hardiness skills leads to improved overall, health-related and at-home adjustments as well as increased occupational, social and emotional adjustment skills in women household heads. Eschleman (Eschleman, Bowling, & Alarcon, 2010) in a 180-sample meta-analysis study found that hardiness is a critical factor in controlling the sources of acute stress. Johnsen (Bjørn Helge Johnsen et al., 2013) believes hardiness as a major driver of occupational progression. Furthermore, Johnsen (Bjørn H Johnsen, Hystad, Bartone, Laberg, & Eid, 2014) showed that those with low scores in the three components of hardiness (commitment, control, and challenge) had severe problems in various aspects of mental health. Shepperd and Kashani (Shepperd & Kashani, 1991) in their research showed that those who showed less commitment, control and challenge seeking behaviors in stressful situations suffered more severe symptoms of physical and psychological disorders.

Solkova and Tomanek (1994) in their research revealed that hardiness increases individuals' adjustment capability. As a result, these people endure less stress in their daily lives (Moein, Ghiasi, & Masmoudi, 2012). Lee (Lee, 1991) showed that hardiness has a significant positive relationship with psychosocial adjustment. Also, the most important adjustment-related factors are the commitment and challenge components. The results of the study by Filla and Jones (Filla & Jones, 1991) demonstrated a meaningful relationship between hardiness and adjustment among parents. Other variables in this study, which had a significant relationship with hardiness, were social support, preservation of unity among family members and satisfaction with family functioning. Raheb (Raheb, Khaleghi, Moghanibashi-Mansourieh, Farhoudian, & Teymouri, 2016) showed that social work interventions are effective factors in improving the quality of life and personal adjustment of addicts.

Judkins, Arris and Keener (Judkins, Arris, & Keener, 2005) showed that there is a significant negative relationship between hardiness and stress. The control attribute in hardy people increases stress resistance and makes unpredictable stressors less frustrating. In Delahaij, Gaillard and van Dam study (Delahaij, Gaillard, & van Dam, 2010), it was shown that the relationship between hardiness and assessment of stressful situations is moderated by self-efficacy. While in the relationship between hardiness and coping behavior, coping styles are considered as the moderating variable. Subramanian and Vinothkumar (Subramanian & Vinothkumar, 2009) in their study indicated that much role playing, ambiguity in professional role, low professional status and severe working conditions have a direct negative correlation with hardiness and self-esteem. The implications of such a finding suggest that promoting the level of personality hardiness and improving self-esteem can lead to reduced professional stress and enhanced job performance. The findings of the study by Kalantar, Khedri, Nikbakht and Motevalian (Kalantar, Khedri, Nikbakht, & Motevalian, 2013) are indicative of the effect of hardiness training on increasing high school students' hardiness level, and thus improving their psychological health. Yet in another study, Haji Moradi, Poursarrajian and Alizadeh Naeeni (Haji Moradi, Poursarrajian, & Alizadeh Naeeni, 2013) showed a significant negative correlation between control, challenge-seeking and commitment with emotional exhaustion. Hamid (Hamid, 2011) in a study showed that there is a significant positive relationship between hardiness, life satisfaction and hope with the components of hope. Moreover, Moein, Ghiasi and Masmoudi (Moein et al., 2012) showed a positive and significant relationship between the components of hardiness and marital adjustment. Abdollahi (Abdollahi et al., 2016) stated that students containing the hardiness trait experience less anxiety. Johnsen (Bjørn Helge Johnsen et al., 2017) recognizes hardiness as a moderating variable between self-efficacy and performance satisfaction.

Conclusion

These findings indicate that the hardiness personality trait is one of the essential components of a healthy psychological profile. In addition, the existence of such an important attribute is considered as a protective factor against stress in everyday life as well as in unpredictable and high-pressure conditions. Maintaining personal and social adjustment among women household heads is naturally more difficult due to their challenging conditions, as compared to other women. The heavy and sometimes conflicting responsibilities of these women seriously endanger their personal and social adjustment, and thus their mental health. Accordingly, empowering these women and arming them with psychological and social tools will lead them to further adjustment to problems and therefore, towards having greater mental health.

As a general conclusion from the results of this study, the emphasis is on the fact that the psychological and social empowerment of the women surveyed in this study, regardless of all adversities these women deal with, can motivate them to make correct decisions and obtain greater adjustment as well as physical and psychological health.

Limitations

- Insufficient information and resources about women household heads in Iran
- Impossibility to conduct follow-up tests after the research due to the time limit

Acknowledgments

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Explaining problems and adversities of children of fathers' involved in substance abuse: A qualitative content analysis in an Iranian context

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Abstract

The aim of the present study is to identify problems of children of fathers involved in substance abuse, in order to provide some basic guidelines and practical suggestions on reducing the problem and strengthening the children's resilience. The present study employed content analysis, a qualitative research method. The population consisted of children of substance abusing fathers. The study was conducted using a purposive sampling refined by a theoretical sampling of 28 children who participated in the study. Data were collected through in-depth semi-structured interviews and focus group discussions. The trustworthiness of this study was evaluated by the four criteria: creditability, dependability, conformability, and transferability. Seven categories of children's problems were found in the FGD and depth interviews. These categories included: Negative attitude toward oneself, Parental support disorder, Accept the role of the misfortune hero, Violence and maltreatment, The drama of chaos, Family routine/ Disorganization, Exclusion and isolation. The findings of this study indicated that the quality of parental – child relationship and between parents are not satisfied. Domestic Violence is one of the obvious signs of family problems. The offenders often seem to lack emotional involvement with family numbers. The Majority of children in the study had low self-confidence.

Background

Families are hidden victims of drug use. They suffer from Stress and persistent, extreme and intense pain and suffering from depression, deep anxiety and chronic fatigue that stems from anxiety and frustration (Barnard, 2006). Due to the chronic nature of addiction disease, life is very anxious with an abuser. The disease makes them unreliable and aggressive. In fact, these people do not have mood and behavior stability, and their family members do not know how to treat and get along with them. Because of this, in addition to having difficulty communicating and their lifestyle, they often live in anxiety and confusion and suffer from a lot of emotional problems and difficulty expressing feelings (Kimberly et al., 2005; Locke & colleagues 2010; Benishek et al 2011). Over time, the family system undergoes fundamental changes, borders are broken; family members gradually develop alongside the abuser, become sick, and various forms of co-dependency emerge.

Drug abuse and its emotional and behavioral consequences could affect the roles of parents; negative communication and conflicting interactions between parents influence the relationship between them and the performance of children. In family systems in which parents engage in drug use, negative, critical and harassing relationships, along with blame, judgments, complaints, and guilt not only, affect parent relationships but also affect relationships between parents and their children (May & Truman, 2002). Children may experience cognitive impairment and experience feelings of apprehension, hesitation, confusion, anger, and a damaged sense of safety (Haight et al., 2009). These families are often characterized by high levels of dissatisfaction, anxiety, and instability and high prevalence of verbal violence (Fals-Stewart et al., 1996). Children who are exposed to conflict with parents have anxiety and lot of fear (Jets et al., 2003). These negative impacts on children could prevent their confidence in the family and increases the probability of bullying, aggression, violence, delinquent behaviors, victimization, and addition of stress to the family system (Morti et al., 2006). Studies show that among the families involved with drug use, both parental weakness and parental conflicts may have similar outcomes for the child (Kelly et al., 2010). Thus, simultaneous attention should be considered to the relationship between parents and parent-child interactions in the interventions of the family system involving parents involved in drugs.

Denial and silence is one of the basic principles in many families that involve substance use, which makes children unable to easily talk about their experiences and feelings (Haight et al., 2009). Several studies have also shown the relationship between drug use and violence against children and spouses (Hartley, 2002; Donovan & colleagues, 2006; Greer & Taylor, 2006; Freistler et al., 2017). Based on the attachment theory, the result of the experience of domestic violence for children can be the loss of sense of trust, high violence, anger and fear (Lieberman & Van Horne, 2005). Children may choose anger and aggression as an adaptation path to cope with the stresses in their relationships (Haight et al., 2009). In other words, children in the families' using drugs suffer from multiple harm, because in addition to simultaneously tolerating the observation of parental abuses and the suffering of child abuse, the expression of anger and aggression as an adaptive mechanism, they also have to endure the negative feedback of social environments.

Research shows that, children with drug addicted parents often face emotional, behavioral, physical, cognitive, educational and social problems (Anda et al., 2006; Peleg-Oren & Teichman, 2006). Also children and generally girls may experience intrinsic behaviors, such as social abandonment, low self-esteem and loneliness and these behaviors and feelings could predispose them to depression, suicide and addiction during adolescence. (Straussner & Fewell, 2011).

Given the vulnerability of children and the need for parental support, parenting and parental care to achieve optimal growth and livelihoods and survival, the dangers of drug abusing by parents are more for them. Despite the devastating and prolonged effects of the use of drugs by the parents on children, few studies have been conducted in Iran on the field of evaluating physical, psychological and social performance of children in families involved in the use of drug and no serious consideration has been given to the problems of the children. What is primarily important in protecting children with drug addicted parents is the recognition of the effects of drug use on psychosocial development of children and their problems. This recognition is important in the framework of support services, drug abuse prevention, mental health services and other forms of intervention. This research seeks to grasp the needs, issues and problems of children of substance user fathers (COSUFs) in order to provide supportive solutions to reduce these problems.

Method of study

The present study employed content analysis, a qualitative research method. The population consisted of children of fathers' of substance abuse. Coordination with four centers in 2015 (in Tehran the capital city of Iran) was taken and all interviews, after winning the trust of participants, were conducted by the researchers. The study was conducted using a purposive sampling refined by a theoretical sampling of 28 children who participated in the study. Data were collected through in-depth semi-structured interviews and focus group discussions. Interviews began with simple and general questions followed by questions that were more detailed. The average interview time was about 60 minutes. Immediately after each interview, the data were transcribed verbatim and simultaneously analyzed. In coding, transcripts of interviews were investigated line by line and word by word, and coded by key phrases in the text or inferred by the researchers; codes of similar nature and meaning were placed in a category. Categories and codes for each interview were compared with the next interview to identify the properties and relationships between them, and then similar categories were conceptually and characteristically merged, located around a joint axis

which then formed a wider category which was related to other categories.

The trustworthiness of this study was evaluated by the four criteria: credibility , dependability, conformability, and transferability. Credibility was assured via the triangulation strategy – in addition to semi-structured interviews, field notes and the researchers' prolonged engagement in the subject matter. Dependency was provided by peer reviews and group member checks. Conformability of the data was accomplished by the researcher, who conducted thorough reviews to gather ideas from other researchers and maintained the study documents. Transferability of data was provided by offering a comprehensive description of the subject, participants, data gathering, and data analysis. This description offers other researchers the opportunity to extend the study. In this study, which received ethical permission from the University of Welfare and Rehabilitation Sciences, the researchers observed ethical considerations such as obtaining informed consent, maintaining anonymity, confidentiality, and the right to withdraw from the study at any time.

Results

The analysis of the information obtained from the collaborators on the problems and issues of children with drug user fathers led to the following categories and concepts:

1. Negative attitude toward oneself
In this research, the negative attitudes toward self are one of the main issues and categories concerning children's difficulties. This category consists of the following three themes, overlooking the strengths of the children in the shade of addiction stain, the child's doubts about being worthy to get kindness, and Children's Concerns for other's Confirmation.

1-1- Overlooking the strengths of the children in the shade of addiction stain
The addiction problem affects a family in such a way that it is less important to address some issues for both children and healthy parents. One of these cases is the appreciation of the strengths and efforts to discover it. It seems that the pressure from perceived differences and focusing on it and spending energy to hide the differences has led to the child's presence in the school environment and the success of education and good behaviors are also not much to be considered. On the other hand, the heavy shadow of addiction makes some of the strengths of the family seem insignificant to others.
"I think that when it comes to the family, they cannot see their own success. There is a great disgrace to this issue that successes become small and trivial."

1-2. Doubt the child is worthy to receive kindness
The need for children to love and good-natured behaviors has not been well addressed from parents and especially the fathers. Some interactions formed in the family induce a sense of misuse and the formation of this conception that the child is loved for matters outside his being. On the

other hand, the children analyzes the love received from others considering the conditions of the family. Therefore, the child's perception of family differences, especially in families with a poor financial status, which has more differences externally, love has the meaning of pity (again, a matter beyond the child's existence).
"He would take us out on holidays on the pretext of having fun, we would end up in deserts around Tehran, and he would go after drugs. No matter what we said, he would not listen to us, we were very afraid."

1-3 Concerns for other's Confirmation.
Children in the family are less likely to be approved and esteemed by their parents, and their successes are less visible. On the other hand, differences in the family make it doubtful whether family patterns are appropriate and good, so that children wait for others to comment to be evaluated for the desired behavior.
"Confirmation to be seen is too great among kids. I was studying to be seen. My interaction with others was good to say he is a polite kid, he is an intelligent child, and to get me up there, Let my teacher support me."

2. Parental support disorder
Parental support disorder consists of four sub-themes: over support, Family's desire not to attend needs and feelings, unstable security and stability in the family, and the lack of attention to the relationship between the siblings.

2-1. Over support
An imbalance in the protection of children is one of the common problems of a family whose father is a drug abuser. Over protection is one of them and is done by mothers.
"I never let the kids lift a finger, since they were going through adverse life; I tried to pamper them as much as I could."

2-2. Family's desire not to attend needs and feelings
Essentially, the expression of needs and emotions require to be replied, and families usually are not prepared to respond to the needs of children and family members. Family members refuse to express their feelings and needs in order to support family stability and not impose a negative emotion on the system.
"It's as if there were always mechanisms in the house that these feelings should be suppressed and poured into the inside until they talked about it. In our family it did not come up that if it caused something to hurt us, we can talk about it. And to some extent the mother tried to cover these issues."

2-3.Unstable security and stability in the family
One of the challenges posed by all children was the existing threats to the family's psychological stability and security, the probability of parental separation, the concern of children to worsen family situations in the absence of father, domestic violence and parental conflicts, and etc... All are annoying experiences for children, which mothers also confirmed their prevalence in the family. The concern of the children for the deterioration of the situation in the case of leaving the family by the father was reported only by sons and in the case of girls; this concern was a form of compassion for the father.

"The father who uses crystal is aggressive, insulting, beating, threatening, has abnormal behavior, the child seeing all these, giving the child a humiliation, fear and panic. He wants to take refuge, but there is no place. And the child loses his trust."

2-4. Lack of attention to the relationship between siblings

The lack of encouragement by parents to improve the relationship between sisters and brothers are other problems reported by children in this study, which a number of children referred to.

"My relationship was not good with my brother; we always struggled with each other. My mother did not try to improve our relationship. She would say that it's better that you keep being sulky."

3- Accept the role of the misfortune hero

The topic of accepting the role of the hero of misfortune refers to the reproduction of the roles played in the family by the child and the other members of the family. A child living in silence, isolation, denial, high self-sacrifice and violence has a negative attitude toward him/herself. He/she is also inconsiderate to his/her health status and cares for the wellbeing of family members. Children reported that she/he committed to bad mood.

This category is characterized by three themes; sacrifice responsibility for the release of others from suffering and resistance to earn comfort.

3-1.Sacrifice

The children consider addiction as an unresolved, big and unique problem therefore the individual's and the family's positive points are unimportant too. The unwillingness to recount their family problems with others and he/she has a few opportunities to discover the problems of other families and children, as a result they induce that are stuck in a disappointment situation.

"I felt very lonely. I thought I was tainted. Because my father was addicted I was separated from others. I cannot feel good in life, because I have an addict in my life, I must always experience anger. Feel negative. It was one of the emotions that separated me from others."

3-2.Responsibility for the release of others from suffering

This theme refers to the fraternal efforts and concerns to protect others, including family members or friends, and reduce their hardship, so that children prefer to meet the needs and concerns of others rather than address their needs and provide comfort for themselves.

"What's common among kids is that you want to find the role of a savior, if one asks for us, we will do it perfectly and it will be confirmed; as far as we can play the role of a hero, help everyone, if we are given a responsibility we can do it in the best way"

3-3. Resistance to earn comfort

The children reported a kind of resistance to physical and mental well being, an inner desire to maintain the conditions and negative emotions that prevented them from enjoying the opportunities of being happy, and relieving the painful circumstances.

"I think, because I have a problem, I should not be happy and I do not have the right to be happy until this problem is resolved. I do not know correctly, maybe we are accustomed to tension and worry, although sometimes I have the opportunity to something, it's as if I lose my balance, as if I'm afraid and feel guilty."

4. Violence and maltreatment

Violence and misconduct are other hardships of children in addiction situation, characterized by mental maltreatment, neglect, and physical abuse and exploitation of children.

4-1.Mental maltreatment

Creating fear and panic in children, observing domestic violence, insulting and humiliating, frightening children, mastering and controlling mentally, and proxy attacks are instances of mental abuse that has been extracted from interviews.

"The child wouldn't forget when he is out of the house at midnight (mother says). He couldn't forget it that he'she is forced to sleep in other people's houses because of the risk he/she will be killed by their father. Well, that's a lot of pain."

4-2. Neglect

According to the children's statements, mental neglect has been the greatest pain of children in life. Despite experiencing other types of maltreatment (except sexual abuse), all children had complained of suffering from not being seen. Mental neglect, inadequate supervision, educational neglect, and physical neglect were examples of neglect, extracted from interviews.

"It's as if we're waste. Nobody (parent) see us, nobody cares for our needs."

4-3. Physical abuse

Most children indicated physical abuse by family members. Contrary to other types of maltreatment that fathers were the first guilty, but mothers also participated in physical abuse of kids.

"Our mother would beat us up time and again. We got used to it like our meals".

4-4. Exploitation of children

A number of children referred to forms of exploitation by the father, such as abuse of them to cover the purchase of drugs and forcing them to work for the cost of drugs.

"My dad would take me with himself to buy a drug so that police don't suspect t him."

5. The drama of chaos

The category of chaos drama is related to the confusion and conflict of children, unpredictable events, and the prediction of the annoying events with the root of drug abuse. This category consists of the following three themes: unpredictable behaviors and events, lack of respect for family privacy, and emotional conflict or ambivalence.

5-1.Unpredictable Behaviors and Events

Living in addiction conditions would place children in a confusing and vague environment in which proceedings are not necessarily predictive of outcomes. By the impact of drugs, family happiness is quickly replaced by unhappiness, often which is not controlled by family. Use

of drugs is the cause of many family conflicts and children are confused by the lack of awareness about using drugs or knowing its effects on the father's behavior. Life events have taught the children that the family environment has the aspect of controversy and the children are presentiment to bad events.

"Sometimes even though they were fine, Fear would come to us. What thought was in their head? What the hell does he want of me? Why is he laughing so much with that person? Maybe he wants to get some money that he is so kind to her?"

5-2. Lack of respect for family privacy

It seems that in families for reasons such as dispute and conflict, violence and leaving home by a parent, interference of others in family problems, financial dependence and commuting of abuser friends, resulted in that family privacy has not been well preserved and children's safety has been endangered.

"Once I came home from school with my brother, father brought someone to our home to use drugs. As he saw us said that he is an engineer and we are working on a project! We did not dare to say anything. At this moment, my mother came home and kicked the engineer out of the house!"

5-3. Emotional conflict or ambivalence

Because of the father's appearance, dressing and behaviors, sometimes the children are ambivalent, angered and guilty in the presence of the father in the familial and social interactions.

"I really wanted to go anywhere with Daddy but it did not happen. I understood that time ... my father was really a disaster I did not even want to see him. I was afraid of other people's judgments. They would understood that he was addicted. I tried not to think about these but it was in me."

6- Family routine / Disorganization

The stresses on life and escorting the flow of life into emotions, the struggle to control and prevent the formation of negative emotions and the lack of adequate support, have led families to passively deal with the disruptive processes of consumer life, financial difficulties and life tribulation and be content with living in an unplanned process and being engaged in daily struggle. Family Daytime / Disorganization themes are; faulty cycle of life, neglect of planning, interpersonal barriers and passivity to external conditions.

6-1. Faulty Life Cycle

The faulty cycle of life refers to the reproductive processes of family life that limits the opportunities for change and growth.

"Somehow, I can tell you that we were used to the same routine way that we followed the process of life. In the morning, when we get up, what a bad day, the conflict, fights and this same mental groove always repeated, my father started to use drug and my mother to nagging And call everybody and the conflict with our father and we were watching all these."

6-2. Neglecting to plan

Family focusing to encounter everyday difficulties and financial bottlenecks has disrupted long-term planning, and children do not have the skills to pursue long-term targeting and planning to take on new responsibilities and roles.

"When we were a kid, we were mostly disturbed by the financial issues and the same disorder. Disorder means that we never had a specific plan, we could never have a plan for ourselves, and we could not plan to buy something or go somewhere in the future".

6-3. Interpersonal barriers

Mental employment with lost opportunities, depression, feeling guilty, perfectionism, and low self-esteem are the inner barriers of children to change living conditions and get out of the routine.

"I treat myself very arbitrarily, I cannot accept my mistakes and misunderstandings, I cannot accept that I am a human being, and I can make a mistake and compensate in another opportunity."

6-4. Passiveness to external conditions

Interview analysis shows that although children blame themselves for their own problems and have special focus on themselves in identifying problems, they are waiting for a change outside of themselves in order to change their living conditions, so that external factors have impacted them to a great extent and as a factor of changes have less authenticity.

"This disorder affects us. I cannot behave arranged. I cannot plan for our lives. Let's say I'll get up, I do our work, and I'm going to party. Our schedule has no specific time. Our program is more chaotic."

7. Exclusion and isolation

Deprivation results from the relation between two main mechanisms: Exclusion and isolation. Abnormality of life conditions and Mental employment of children toward the judgments of others including peers, the fear of the secrets of the family to be revealed and the lack of family's competitive advantage to share family experiences among peers (such as family travels, family recreations, parental reward, etc.) caused children and, in some cases, families, to restrict their communication as a mechanism for self-protection. Exclusion and isolation are the main themes extracted in this study; Isolation is more tolerable than humiliation, interaction with others is a threat to reveal the differences, the unwillingness of others to communicate with the family, and disregard of the norms and rules of the situation display power are the themes.

7-1. Isolation more tolerable than humiliation

It seems that curbing relationships for children and families is a shield that protects them from contempt, judgment, and banishing, while due to the low credibility of the family, the children are not as well considered in the Family relationships.

"It was frightening for me that very soon they ask me how my family was, when I was communicating with others."

7-2. Interacting with others is a threat to reveal the differences

One of the interaction results for children is that they further recognize aching differences between their family and others.

"These children, mother said, are definitely isolated. Children cannot have a comprehensive analysis, but when they see how normal families behave with their kids, how they participate in their games, how they will be rewarded, how they are encouraged, and the child will compare and find out. Therefore, in itself, there is a fundamental difference that affects him\her and leads to a deterioration."

7-3. Unwillingness of others to communicate with the family

Other reasons for limiting family relationships are the reluctance of others to communicate with the family.

"The one that happened (mother said) to me was from my brother that he said they may have AIDS. Do not have much contact with them. It's a pain, a scar. My husband quickly took us to a Hepatitis Vaccine."

7-4. Disregard of the norms and rules of the situation to display power

This theme reflects the fatigue of children from obtaining the consent and approval of others. By spending the childhood and finding sources of power and support (such as jobs, new friends, etc.), children would experience the freedom from constraints and established criteria by others (individuals outside of themselves). This experience of power is so dangerous because it is leading to job loss or school drop-out.

"I did not study at high school. I played stock and laughed. I joked. I dropped out of the class. I was playing volleyball. I did not care what others would judge about me. I wanted to live comfortably. I did not want to live for others."

Discussion

In this study, negative attitudes toward themselves were the main themes extracted and were the main complaints of children. Many studies have also shown that children of parents of alcohol and drug users are at risk of problems, including negative attitudes toward themselves and low self-esteem (Lutharet al., 1998; McNichol & Tash, 2001; Haight et al., 2008; Bee & McDaniel, 2013). Family flaws and most importantly, having an unusual father has caused doubt in the children regarding their worth. Shame caused by the inner family problem may also lead to sentimental forms such as being bad, lack of energy, hesitate to br self-affirming, and a feeling that he\she does not deserve the other's love and pain (Straussner & Full, 2011)

Violence and maltreatment are one of the other hardships of children in the condition of addiction, characterized by mental maltreatment, neglect, physical abuse and exploitation of children. The results of this finding are consistent with the studies by Hartley, 2002; Donohue et al., 2006; Graber & Taylor, 2006; Jeffreys et al., 2008; Bee &McDaniel, 2013; and part of the study by Freisthleret al (2017) which showed that there is a relationship between drug use and violence against children and the wives. But it does not coincide with the section of their study, in which the use of drugs by parent is not related to the neglect of children.

Disputes and conflicts between parents were also a common problem in families involved in drug use. The results of Falless Stewart et al. (2005), as well as the results of the National Surveillance on Domestic Violence and National Family Surveillance (O'Leary & Schamcher, 2003), showed that the likelihood of violence against a spouse during drug use is three times as high.

One of the key assumptions of attachment theory is that the experiences of the child with their caregiver during childhood play a central role in their mental health and development. When children experience violence in their families, their sense of trust may be distorted and lead to anger, excessive alertness, and fear of them. In addition, children may use aggression and anger as a way to cope with stress in other close relationships. The children of addicted families may experience parental failure in their role as supporter. Parents may behave in a dangerous or scary way for the child, or allow others to harm the child. Such experiences often scare children very much. These experiences may leave scary images and memories in the minds of the child that are difficult to understand, as well as feelings of apprehension, uncertainty, confusion, and anxiety may also be created (Haightet al., 2009).

Parental support disorder is another major issue in this research. According to the findings of previous studies, the lack of stable security (Tyson, 1998; Semidei et al., 2001), the experience of unsustainable care and disturbance in the life-order (Jeffreys et al 2008), the probability of parental separation and divorce (Bee &McDaniel,2013), and the separation of the child from the family and being deposited into welfare systems (Jeffreys et al., 2008; Haightet al., 2009), the family's desire not for unmet needs (Black, 2001; Haightet al. 2009) has also been reported in research. As well as having a secure sibling subsystem helps the children to deal with the drug abuse of parents (Walk and Lee, 1998); the analysis of interviews in this study points to its importance as a supportive factor. There were no research cases regarding the over protection of children in family with substance use parent. It should be explained that in this research over protection was provided by the healthy parent. The lack of parental protection was also reported in previous studies (Haight et al, 2009). Silence is a feature that has been mentioned in previous research (Black, 2001; Haight et al, 2009; Bee &McDaniel,2013); essentially, the need for. and expression of. emotions need responsiveness, and families are often not equipped to respond. Therefore, in order to support the family and not to impose a negative emotion on the system, mechanisms are created in the family that people ignore or refrain from talking about the needs, questions and feelings that upset the healthy members of the family .

One of the main issues encountered in this study is the drama of chaos. This category is based on three themes: Unpredictable behaviors and events, Lack of respect for family privacy, emotional conflict or ambivalence. The drama of chaos was further reported in Bee research and McDaniel(2013) in African-American Adult Children of

Alcoholics who referred to confusion, disorder, instability and ambiguity in the family as a direct result of having alcoholic parents.

Children are more affected when stress factors disrupt family processes (Patterson, 1983). An important part of this effect is the emotional dimension of high-pressure situations in the family with father's substance use. In addition to damage to the children from dangerous factors such as isolation and exclusion, family routine, drama of chaos, maltreatment and other adversities, there is another damaging capacity in the family, which is less clear, but it affects children too. In this research, most contributing children referred to an essential suffering and it was mental pain due to the observation and knowledge of the suffering of parents, in which they experienced different sentimental feelings similar to parents and especially the healthy parent in difficult situations. And they also took roles beyond their power. This finding is consistent with the results of Benishk et al., 2011; Locke et al., 2010; Kimberly et al., 2005).

The stresses on life and dedicating the flow of life into emotions, attempt to control and prevent the formation of negative emotions, financial problems, lack of adequate support, led families to passively deal with the disruptive processes of abuser life, financial difficulties, and hardship living in life and living in an unconventional way and being entertained with daily routines. Routine and disorganized way of family life is the main theme. This finding matches with the results of other researchers (Benisheket al. 2011; Luk et al., 2010; Kimberly et al., 2005) that the prevailing mistrust and anxiety-free living along with a substance consumer, as well as lack of program Life. Because the addiction disease is a chronic and progressive nature, over time, the family system is undergoing fundamental changes, and borders are broken up or disturbed; members of the family gradually become addicted to the addict and various forms of co-dependence are created.

Children spend a lot of energy on making things normal, hiding defects and avoiding inappropriate judgments, but this effort is not always successful because others are aware of family defects, and they also do not tend to relate with the family; by growing up and gaining power and resources of more children, others who have been the stress factor in many situations and worsen their psychological energy, will lose their degree, and children, indifferent to their rules and judgments, show their power and this time these are the children that others get away from, a demonstration of power that it's result is that is is not necessary in order to progress and gain social status. Another of the main issues in the current research is the withdrawal and isolation. Unconventional way of children's living condition and mental conflict to the judgments of others, including peers, the fear of exposing the secrets of the family, and the lack of family's competitive advantage to share family experiences among peers, causes children and families to restrict communication as a mechanism for self-protection. Although the problems caused by addiction caused others to leave the family, evidence suggests that gaining social support for members of the family involved

in addiction is very difficult. Most contributors believed that others' awareness of drug abuse of a person would lead to their embarrassment. While it may lead to a worsening of their behavior; or others engage in their own activities and do not do anything about them. This finding is consistent with the results of Straussner & Fewell(2011) and Orford et al's (2013) research.

Since awareness of addiction is associated with the stimulation of strong emotions in people and how answering to them is difficult and controversial, others may be unprotected, criticized or hostile, some members of the family are accused of being tolerant, and some are criticized for lack of tolerance (Orford et al., 2013), which leads to a desire for isolation. The present study showed that deprivation of relationship is related to the two mechanisms of withdrawal and exclusion. Isolation More tolerable than humiliation, interacting with others is a threat to reveal the differences, Unwillingness of others to communicate with the family and Disregard of the norms and rules of the situation to display power is its themes. This finding is in line with the results of research by Ashenberg Straussner & Fewell (2011), which are based on the tendency to withdrawand isolation and the inability to confide in others and to take their assiatance , are the consequences of parental addiction on children. Disregard of norms and rules is the negative response of children to pressures from community judgment, and refer to a time when the conformance with society imposes a lot of pressure on them, they show their power by disregarding some of the social norms.

Another major issue in the research is the acceptance of the role of a misfortune hero. This category is characterized by three themes of Sacrifice, Responsibility for the release of others from suffering and Resistance to earn comfort. The acceptance of the role of the "hero of misfortune" refers to the reproduction of roles played in the family by the child and the healthy members of family. A child living in silence, isolation, denial, sacrifice and violence, in adulthood, is also careless to his or her well-being and cares for the well-being of others, and in spite of having the facilities doesn't do anything for his well-being, as Black says (2001) in The role of responsible children in alcoholic families that these children do not know how to act in adulthood, be carefree and enjoy. They have essentially serious problems for future prospects.

Although, as in Whig Wegscheider-Cruse's work (1989), there was evidence of survival roles such as hero, scapegoat, lost child and mascot, but as Black (2001) refers to the children of alcoholics, children take on several roles to adapt to The conditions; he points out that children play three roles, as an adjuster, placater and a responsible child, and that few children tend to play the sole role of the acting out child who through the disorder and misbehaviors gets attention. This research also shows that children play different roles in different situations, but these roles include a forgotten Placater, responsible child and a lost child. In only one case, the child was careless to the family and has played the role of acting out with incompatibility at home and creating school problems.

Conclusion

The final outcome from the research findings suggests that children with a father who abuses drugs have many problems, including a negative view of themself, Parental support disorder, Accept the role of the misfortune hero, Violence and maltreatment, The drama of chaos, Family routine / Disorganization and Exclusion and isolation.

Although numerous studies have shown that parent drug abuse is dangerous for children but Deren (1986), Gifford and Humphreys (2007) believe that drug addiction has a strong correlation with other factors, and only drug abuse is not a problem identified for children; on the social level, drug addiction has a strong connection with poverty and deprivation. At the psychological level, it's likely that people who use drugs are abusive, have low self-confidence and are depressed. Even at the genetic level, it's possible that some of the tendencies that lead to addiction are themselves causes for children's adversity. So, perhaps these variables are the factors that are the cause of problems, either separate or in interaction with substance use. Drug use disorders are therefore not a single issue, and it will not be possible to determine its specific role alone.

To mitigate the effects of life with the misuser father on children, protecting factors such as promoting the resiliency of children and family members, and increasing informal support (relatives, neighbors, friends) and formal (supportive organizations) in order to adapt to Difficulty in life must be considered. To reduce the transaction of drugs and child abuse, community based prevention and neighborhoods should be prioritized.

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The evaluation of p21 and p27 expression in HLA-DR negative AML patients

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Abstract

AML is a heterogeneous type of leukemia with a high variation in the biological features of the leukemic cells and disease outcomes. The biological features of the leukemic cells have a very close correlation with the disease outcomes. In this way, leukemic cells with higher levels of proliferation and lower levels of maturation undoubtedly would lead to poorer outcomes. Based on immunophenotyping, HLA-DR negative AMLs constitute an important category in AML classification. The majority of patients with this immunophenotype belong to APL subtype with PML-RARA fusion gene and the others are non-APL subtype without PML-RARA fusion gene. As disease outcome and cell biological features have a very close correlation, it is important to evaluate essential molecules involved in the biological processes of the leukemic cells which are helpful in the determination of disease outcome. Therefore in this study we evaluated the expression of p21 and p27 as two key molecules involved in the regulation of cell cycle, proliferation, maturation and apoptosis to determine whether there is any significant difference between these two subgroups of HLA-DR negative AMLs. We studied p21 and p27 mRNA levels by real-time RT-PCR in 41 primary HLA-DR negative AML samples, compared with normal bone marrow and peripheral blood cells. p21 expression was significantly higher in APL cases than non-APLs but there was no significant difference in p27 expression between APL and non-APL patients. According to our results, it seems that p21 can be considered as a critical gene involved in the determination of the levels of cell differentiation between these two subtypes.

Key words: Acute Myeloid Leukemia;
HLA-DR negative; p21; p27

Introduction

Acute myeloid leukemia (AML) is a cancer of hematopoietic system which results from a clonal proliferation of hematopoietic precursors that have lost their maturation capacity to various degrees (1, 2). Patients with AML constitute a highly heterogeneous class of neoplasms because of their variation in the biological features of the malignant cells and disease outcome. Disease outcome is strongly dependent on the biological features of the malignant cells. In this way, leukemic cells with higher levels of proliferation and lower levels of maturation undoubtedly would lead to poorer disease outcomes (3,4). The importance of disease outcome prediction in designing best treatment strategies led to various AML classifications including FAB, WHO 2001 and 2008 and finally the 2016 revision. These classification systems have been introduced mainly based on the leukemic cell features including morphology, immunophenotype and genetic abnormalities (5). Standing on these criteria, human leukocyte antigen-DR (HLA-DR) negative AMLs represent an important category with prognostic significance in most cases. Most patients with HLA-DR negative AML belong to acute promyelocytic leukemia (APL) cases which lack HLA-DR antigen on their surface. However infrequent cases of non-APL AMLs do not express HLA-DR as well. The APL cases have PML-RARA fusion gen as their underlying genetic defect and they represent good prognosis; however, other non-APL cases do not have a common known genetic defect and prognostic significance until now. Thus the biological characteristics of these non-APL HLA-DR negative cases and their outcomes have remained elusive. It has been shown that both subgroups are biologically distinct in some aspects (6). These two categories are also morphologically distinct, as APL cases show higher levels of maturation and differentiation than non-APL cases. Some key molecules involved in the cell cycle regulation, including the CIP/KIP family and the INK4 family, play a pivotal role in the determination of the extent of cell proliferation and differentiation. Their functional inhibition can induce cell proliferation and inhibits differentiation while their activation do vice versa (4). In other words, in leukemic transformation, they are at the center of cell transformation (7). The CIP/KIP family includes p21, p27 and p57 genes. They do their role by binding to and inactivating cyclin-CDK complexes; hence, they halt cell cycle in the G1 phase (8, 9). They directly regulate cell proliferation, maturation and apoptosis. In this way, they have opposite effects on the extent of proliferation and maturation (10,16). Since they induce a delicate and opposite balance between proliferation and differentiation, whenever cells are let go faster through the cell cycle, they proliferate but do not differentiate and thus have leukemic transformation without maturation. Defects in p21 and p27 have been demonstrated in a wide range of human malignancies and usually these defects have value in determination of patient prognosis (17-19). The purpose of this study was to evaluate the expression of p21 and p27, as two key molecules in cell cycle regulation, in HLA-DR negative AML patients. In this study the expression of p21 and p27 genes as two biological targets which are critically involved in the determination of the extent of cell proliferation and maturation was considered to determine whether there is any significant difference in the pattern of these key molecules in HLA-DR negative APL and non-APL cases. Any difference can help us to further sub-classify AML patients based on their leukemic cells biological features which have shown to greatly affect disease outcomes.

Material and Methods

Patients and normal controls:
Bone marrow and peripheral blood samples were obtained after obtaining informed consent from 41 patients who were subsequently diagnosed with HLA-DR negative AML between July 2013- and June 2015 (20 male and 21 female subjects, age median 48 years, range 18-80 years) and from 14 healthy donors that included bone marrow samples from five patients with early stage Hodgkin and non-Hodgkin Lymphoma and peripheral blood samples from eight normal donors. (6 males and 8 females, age median 44 years, range 3-81 years). The diagnosis was established by morphologic examination, cytochemistry staining, flow cytometric analysis and molecular testing. All of the patients were new cases and the mean proportion of leukemia cells (blasts, promyelocytes) was 60±2.0 (mean±S.E.M) in BM and PB samples, which were enriched by Ficoll density gradient centrifugation of sample.

Immunofluorescence staining and flow cytometry:
Flow cytometric analysis was performed through mixing between 30-50 Micro L of BM or PB sample mix with 5 Micro L of monoclonal anti bodies including HLA-DR, CD3, CD13, CD33, CD14, CD64, CD11b and CD45 Labeled with PE/FITC (all of them DAKO Ab, DAKO company, Denmark) and they were incubated for 20 minutes at 2-4ºC. The sample was prepared with RBC lysis buffer (DAKO-, Denmark) and analyzed by flow cytometery instrument (Beckman-coulter XL, USA). Threshold for confirmation of marker positive was more than or equal to 20% of the cells.

RNA isolation, c-DNA synthesis, real-time PCR
For the isolation of mononuclear cells from peripheral blood and bone marrow of both patient and control samples; Ficoll density centrifugation was used according to the manufacturer's instructions. Then for total RNA extraction QIAmp RNA blood extraction kit was used and total RNA was extracted using the manufacturer's instructions. We determined the quantity and purity of total RNA by Nano drop (Thermo fisher USA). All samples had an OD 260/280 nm ratio of 1.8-2.0, indicating their high purity. The integrity of RNA was confirmed by agarose gel electrophoresis.
One µg of RNA was transcribed into first-strand c-DNA using random hexamer primer and First Strand c-DNA Synthesis Kit (Thermo-scientific, USA.) in a 20 µl reaction, under standard conditions.

The expression level of p21, p27 and ABL as reference gene was determined with SYBR Green I real-time PCR. An aliquot of 1/10th of the resulting c-DNA was used for

quantitative PCR amplification. Real-time PCR amplification was performed with Rotor-gene 6000. The master mix was prepared in 15µl mix containing 1.5µl cDNA samples, 7.5µL of 2.5× SYBR Green mix (Ampliqon, Holland), 1.2 µl 10 pmol forward and reverse primer and 4.8 µl water. The thermal cycling conditions included 10 minutes at 95 ˚C followed by 40 cycles of denaturation for 15 s at 95˚C, annealing at 62˚C for 15 s and final extension at 72 ˚C for 20 s. To check the PCR mix for any kind of contamination, we took a negative control (2 ml water instead of c-DNA). Additionally, the specific amplification of the PCR products was analyzed by melting curve analysis and agarose gel electrophoresis.

The Standard curve was produced by four continuous 1:10 dilutions of a positive sample, for each PCR. Using the following calculation: the relative rate of mRNA in the samples was counted as the percentage of ABL gene.

Statistical analysis:
Skewness, kurtosis and Kolmogorov-Smirnov tests were applied for normality. The distribution of relative expression of p21 and p27 in control normal samples and HLA DR-negative AML samples was normal. Differential p21 and p27 expression between the two groups was evaluated using t-test. Differential distribution of p21 and p27 expression in HLA DR- negative AML according to FAB classification was assessed using the Kruskal-Wallis test. Data are presented as mean ± standard error of the mean (SEM). Spearman's rank correlation analysis was used to analyze the p21and p27 mRNA levels in different samples and evaluate correlation with age and blast count using the SPSS 11 statistical and GhraphPad Prism5 software. Differences were considered statistically significant at $p < 0.05$.

Results

Patient's characteristics
HLA-DR negative AML cases were divided into two subgroups, APL and non-APL based on immunophenotyping, cytochemistry, morphology and molecular testing for PML/RARα fusion gene. Thirty APL and eleven non-APL cases were diagnosed in this study. According to FAB classification, non-APL cases were M1 and M2.

p21 and p27 expression:
The expression of the p21 and p27 was evaluated in HLA-DR negative patients (n=41) in comparison with healthy control samples (n=14). In this regard, p21 expression was significantly lower in HLA-DR negative patients (mean p21in patients: 1.00±0.13) compared with normal controls (mean p21 in controls: 1.44± 0.14) (p<0.05, Figure 1).

But p27 expression levels did not show significant difference between patients (mean p27 in patients: 0.82±0.12) and control groups (mean p27 in controls: 0.63±0.10) (p> 0.05, Figure 2).

After that, we evaluated the expression levels of p21 and p27 between HLA-DR negative APL versus HLA-DR negative non-APL patients. P21 expression levels were significantly higher in APL cases compared with non APL cases (mean p21 in APL: 1.17±0.15 vs non-APL: 0.55±0.20, p<0.05, Figure: 3A). But it was not significant for p27 expression (mean p27 in APL: 0.82±0.15 vs non-APL: 0.82±0.20, p>0.05, Figure 3B).

p21 and p27 expression according to FAB classification: The expression levels of p21 and P27 were not significantly related to sex and age in patients and control group. We did not see any difference between groups with different blast percentage. As we evaluated a variety of FAB subtypes including M1, M2 (known as non-APL) and M3 (known as APL) in HLA-DR negative AML subtypes, fluctuation in p21 and p27 expression levels was observed subjectively; but it was not statistically significant (p>0.05, Figure 4A and 4B - page 256).

In particular, although the p21 and p27 did not demonstrate significant difference between different subtypes of FAB (M1, M2, and M3) in our patients, we can see variable expression in p27 and trend to increase in p21 expression from M1 to M3, respectively.

Discussion

The classification of AML attempts to identify biologic entities of leukemic cells in the hope that future work will clarify molecular basis of the disease; this might help us to employ targeted therapies. Now evidence strongly suggests that AMLs consist of a group of relatively well-defined hematopoietic neoplasms affecting hematopoietic precursors and they should not be considered as a uniform kind of disease any more. Therefore these neoplasms should be divided into separated entities based on their unique biological characteristics. To date literature has classified AML patients as HLA-DR positive and negative subtypes based on their leukemic cells immunophenotype. Although the majority of HLA-DR negative cases have PML-RARA fusion gene (APL cases) as their underlying genetic defect, others do not have such a certain genetic lesion (non APL cases). Because of this, they are completely separated entities. As a general rule, APL cases enjoy a better prognosis due to their higher levels of cell maturation while non-APL cases mostly exhibit lower levels of cell maturation, so they have poorer prognosis and outcome. As we know, cell differentiation occurs in parallel with proliferation arrest which is mediated by up regulation of cell cycle regulators particularly cyclin-dependent kinase inhibitors. In the present study, the investigation of any significant difference in p21 and p27 expression (as two keys cyclin-dependent kinase inhibitor) was undertaken in a number of experimental steps in HLA-DR negative AMLs in comparison with normal controls. Firstly, we aimed to characterize the nature of p21 and p27 in HLA-DR negative AMLs and secondly we decided to determine the relationship between HLA-DR negative/ APL and HLA-DR negative/non APL cases with p21 and p27 expression. Any significant difference in p21 and p27 expression can possibly somewhat justify different extent of cell maturation/differentiation in our evaluated patient subtypes. It helps us to more differentiate these

Figure 1: comparison between patients and control, p21 expression
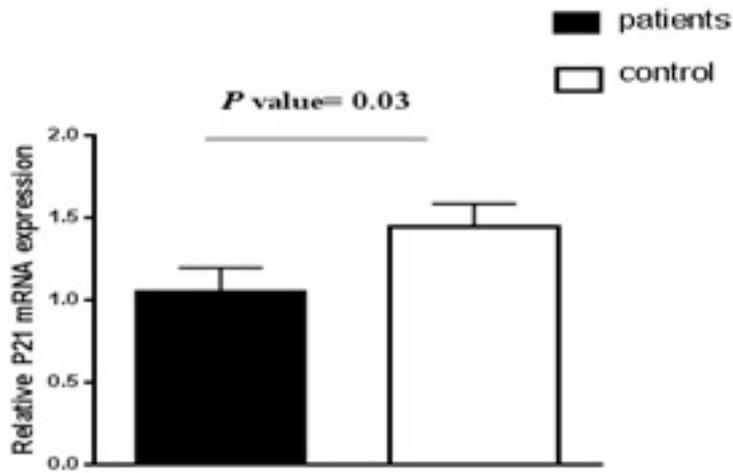

**Figure 2: comparison between patients and control, p27 expression**
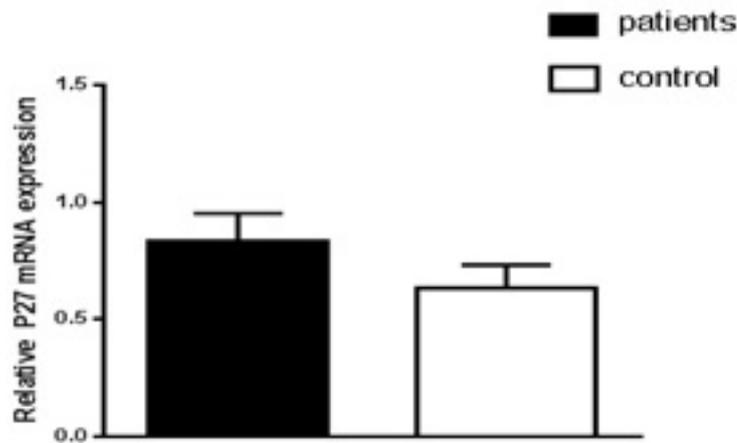
Figure 3: comparison between HLA-DR negative APL and HLA-DR negative non-APL, p21 (A) and p27 (B) expression
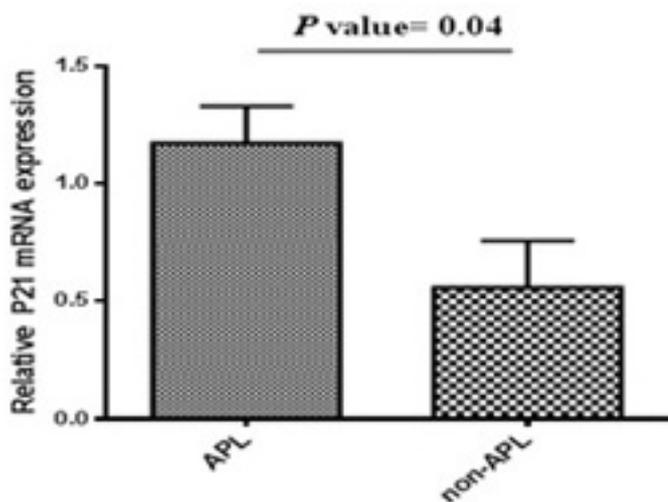

Figure 3A
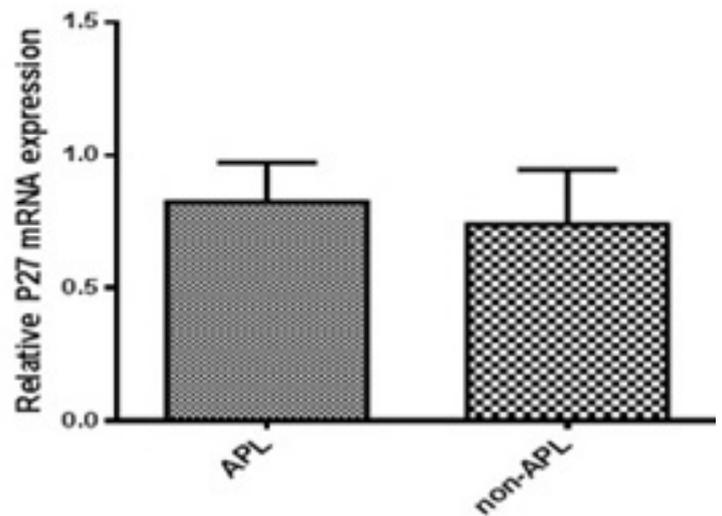
Figure 3B

Figure 4: gene expression in according to FAB classification, p21 expression (A), p27 expression (B)
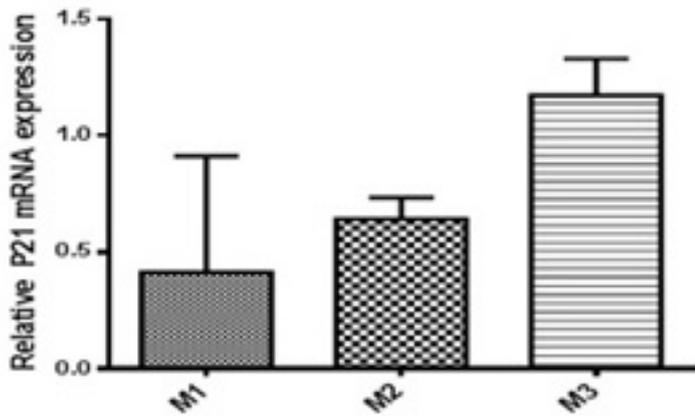

Figure 4A

Figure 4B

subtypes based on their molecular features. P21 and p27 expression levels were measured in HLA-DR negative AML patients and compared with a normal control group. It was found that p21 but not p27 is markedly decreased in HLA-DR negative AML patients compared with normal controls (mean p21: 1.00 ± 0.13 vs 1.44 ± 0.14, $p<0.05$) and it increased in HLA-DR negative/APL cases compared with HLA-DR negative non-APL cases (mean APL: 1.17 ± 0.15 vs non-APL: 0.55 ± 0.20, $p<0.05$). It strongly suggests that p21, but not p27, has a role in leukemic cells differentiation in AML. In contrast, p27 expression did not show any significant difference between HLA-DR negative AML patients (mean p27: 0.82 ± 0.12) and normal controls (mean p27: 0.63 ± 0.10, $p>0.05$). Also it was not expressed significantly different between HLA-DR negative/APL cases and HLA-DR negative/non APL cases (mean APL: 0.82 ± 0.15 vs non-APL: 0.82 ± 0.20, $p>0.05$. In this study we also detected a trend in p21 expression from a lower level of expression in M1 to a higher level of expression in M2 and M3 respectively, although it was not statistically significant. This pattern of increase in gene expression was compatible with the increase in the maturation levels through the FAB classification from M1 to M3 and indicates the possible role of p21 in myeloid differentiation.

In agreement with these findings, Taniguchi and colleagues in 1999 demonstrated that p21 mRNA expression increases in all myeloid colonies (granulocytes, macrophages, megakaryocytes, and erythroblasts) during differentiation of normal hematopoietic stem cells (HSCs), but they could not show increase in p27 mRNA expression except for erythroid bursts (20). In addition, Yaroslavskiy and colleagues in 1999 also studied normal CD34+ HSCs which were motivated to differentiate through the myeloid lineage. They found that the p27 but not p21 was expressed in freshly harvested resting CD34+ cells. During differentiation, p21 levels peak synchronized with cellular proliferation and then drop in expression when cells undergo terminal differentiation but p27 expression was steady (21). Moreover, Weng-Lang Yang and colleagues in 1999 in their study concluded that APL cells treated with retinoic acid (RA) show p21 transcription up regulation. They suggested that APL cells differentiation induction using RA may be due to P21 activation (22). Steinman and colleagues in 1998 have shown that P21 was elevated in myeloid maturation of CD34+ precursor
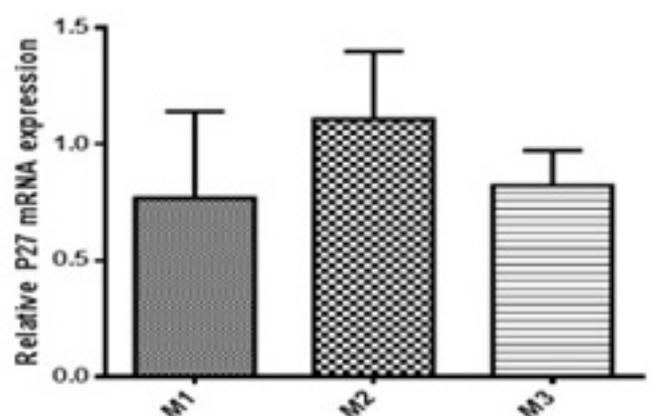
cells and this increase was associated with decreased binding to a highly conserved 44-bp fragment within the p21 promoter (23). However other studies somewhat contradict the aforementioned observations as they observed both P21 and P27 are mainly involved in cellular differentiation. In one study conducted by Muto and colleagues in 1999, they reported that the induction of RA-resistant UF-1 cells by 1,25(OH)2D3 toward granulocytes differentiation was associated with the G1 arrest of the cell cycle and an increase in the expression of the both cdk inhibitors p21 and p27 (24). Another study by Jean Q. Tian and colleagues in 1999, observed that p21 and p27 are strongly overexpressed during intestinal epithelial cells differentiation but with different kinetics: p21 induction was rapid and transient while the p27 induction was delayed and sustained (25). Overall our results and these recent studies clearly indicate that p21 may be strongly involved in the myeloid differentiation of hematopoietic precursor cells. It also can be concluded that the levels of P21 expression may be an important molecular difference between HLA-DR negative/APL cases and DR negative/ non APL cases. It might be concluded that P21 induction in HLA-DR negative AMLs leukemic cells can induce cell differentiation and malignancy resolution. Although we expected that like p21, p27 expression be lower in leukemic cells in comparison with normal controls, the level of p27 in HLA-DR negative AML cases did not show significant difference in comparison with normal controls. These findings demonstrate that more studies may be needed to be done to clarify the reason for this controversy about P27 and why p27 expression does not show any significant changes in HLA-DR negative AMLs. Although some studies demonstrated that P27 expression has a differentiation role, they were not in myeloid cell differentiation or they have not been performed on AML patients. These findings suggest that p21 and p27 may have distinct functions in controlling cell differentiation and maturation in myeloid cells and these two highly related proteins perform unique biological activities during myeloid differentiation and cannot simply substitute for each other to facilitate hematopoietic differentiation. Altogether, according to obtained results in this study it seems that p21 is a more critical factor in differentiation and maturation of DR-negative AMLs in comparison with p27 and it can be one of the discriminating factors between

these two closely related groups of DR-negative AMLs. However, there is controversy about the behavior of p21 in malignancies. Some observations have demonstrated that p21 have opposing functions in some kind of malignancies in a tissue-type dependent manner or localization menner (whether it has nuclear or cytoplasmic localization). For example, p21 can be both pro- and anti-apoptotic, and can both promote and inhibit differentiation and transcription (26). As we did not observe increase in p21 or p27 expression, we could not suppose oncogenic or tumor promoting role for p21 or p27 in our study.

Conclusion

The aim of this study was to evaluate the p21 and p27 expression in HLA-DR negative AMLs (APL and non-APL) to determine whether there is any difference in the pattern of expression of these two critical factors in myeloid differentiation. The main conclusion to be drawn from this study was that p21 expression in this category of AML was higher in APL cases with more maturation levels versus non-APL cases with lower levels of maturation. But there was no significant difference in p27 expression. It was supposed that p21 might be determinant factor that differentiates HLA-DR negative APL cases from non APL cases in comparison with p27. Considering the significant role of cell cycle regulatory proteins in differentiation and maturation of hematopoietic cells and according to the acquired results in this study, we suggest that further experimental investigations should be done to determine whether other critical cell cycle regulatory proteins such as p14, p16, p53 and c-myc have difference in their expression pattern between these two categories (27-29).

Conclusion

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Reflux Patterns Characteristics of Iranian Patients with Nonerosive Reflux Disease (NERD) Based on 24-Hour Multichannel Intraluminal Impedance-pH (MII-PH) Monitoring Tests

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Abstract

Introduction: Nonerosive gastroesophageal reflux disease (NERD) is the most common gastroesophageal reflux disease (GERD) and is associated with acid, weakly acid, nonacid, liquid, and mixed reflux. The present study aimed at evaluating the differences among gastroesophageal reflux patterns, number of reflux episodes and its composition in patients with NERD using combined multichannel intraluminal impedance-pH (MII-pH) monitoring tool in the Iranian population.

Materials and Methods: This study was conducted on 670 participants aged 11 to 65 years, with nonerosive gastroesophageal reflux disease (NERD). They were selected using a questionnaire and esophagogastroduodenoscopy findings. Esophageal multichannel intraluminal impedance-pH (MII-pH) monitoring test was performed for all the patients. The number of reflux episodes and their composition, DeMeester score, symptom index (SI), and symptom associated probability (SAP) were recorded.

Results: Of 670 patients who had NERD, 49.5% (332/670), 65.1% (436/670), and 4.0% (27/670) had acid, weakly acid, and nonacid reflux, respectively. Moreover, 11.8% (79/670), 89.2% (598/670), and 77.5% (519/670) had liquid, mixed, and gas reflux, respectively. DeMeester scores were above the normal range in 39.4% (264/670) of the patients. The symptom index (SI) and symptom-association probability (SAP) score, regardless of PH, were 34.6% (232/670) and 58.4% (391/670) above the normal range, respectively.

Conclusion: The present study revealed that weakly acid reflux was more prevalent in patients with nonerosive reflux disease (NERD) than in those with acid or nonacid reflux. Also, gas (and mixed) reflux was more frequent than liquid reflux. No significant difference was found between upright and supine position of acid, weakly acid, and nonacid reflux in patients with NERD (P>0.05). The diagnostic value of the DeMeester score, symptom index (SI), and symptom associated probability (SAP) was less than 50%.

Key words: GERD, Heartburn, NERD, MII-pH, EE

Introduction

Gastroesophageal reflux disease (GERD) is currently defined as a condition that develops when the reflux of gastric contents into the esophagus leads to troublesome symptoms or complications. The prevalence of GERD based on symptoms has been reported to be 20% and is increasing in both Western and Asian populations [1]. Recent studies documented that most patients with GERD have typical symptoms such as heartburn or regurgitation in the absence of endoscopic esophagitis, which is called nonerosive esophagitis (NERD) [2]. Impedance is a new tool that can measure the electrical impedance (bolus transit) among the closely arranged electrodes assembled on an intraluminal probe. Reflux is defined as either pure liquid or a mixture of liquid and gas detected by impedance. One can determine whether a reflux episode is acid, weakly acid, or nonacid when it is combined with pH monitoring. However, the bile or pepsin in refluxate cannot be determined by this method. Acid reflux episodes are defined as a pH fall <4. An overall score, known as DeMeester score, is calculated using a special formula; this value should not exceed 14.7 in healthy individuals [2].The relationship between symptoms and reflux episodes is usually expressed in NERD patients using the symptom index (SI) or symptom association probability (SAP). Conchillo et al found that acid and liquid reflux had a lower incidence in patients with NERD than in those with erosive esophagitis (EE). However, the incidence of nonacid reflux was equal in patients with NERD and EE [3]. It has been found that 30% to 40% of weakly acidic reflux events correlate with GERD symptoms [1]. The present study aimed at prospectively evaluating the differences in the total number of reflux episodes and its composition in patients with nonerosive esophagitis (NERD) based on the new technique of combined multichannel intraluminal impedance-pH(MII-PH) monitoring in the Iranian population.

Methodology

1. Patients

This study was conducted on 950 patients (11-84 years) with gastroesophageal reflux disease (GERD) during August 2012 and July 2017. GERD was defined as having any degree of reflux esophagitis on endoscopy, heartburn, regurgitation, or noncardiac chest pain (NCCP) on a weekly basis during the last 3 months. The participants were selected from those who referred to our endoscopy ward. All the patients provided informed consent and accepted to complete a standard questionnaire on heartburn, regurgitation, and NCCP. Esophagogastroduodenoscopy (EGD) was done for all the patients in the same center by expert endoscopists. Reflux esophagitis was diagnosed and graded using Los Angeles classification. Of the total participants, 70.5% (670/950) aged 11 to 65 years had GERD symptoms without esophagitis (nonerosive reflux disease (NERD). Esophageal manometry and esophageal multichannel intraluminal impedance-pH (MII-pH) monitoring were performed for all patients. The exclusion criteria were as follow: previous foregut surgery,

cardiovascular diseases, history of malignant diseases, pregnancy, breastfeeding, psychiatric illness, history of alcohol or drug abuse, large hiatal hernia, and esophageal varices. GERD symptoms (heartburn, regurgitation, and NCCP), and negative esophagitis in EGD were included. Achalasia findings in barium swallow, esophageal manometry, or EGD were excluded. All patients accepted to undergo esophageal manometry before MII-pH.

2. Esophageal Multichannel Intraluminal Impedance-pH (MII-PH) Monitoring:

Esophageal multichannel intraluminal impedance-pH (MII-pH) monitoring was performed on an outpatient basis using an ambulatory MII-pH system (manufactured by Mui Scientific, Ontario, CA). The MII-PH catheter (Unisensor AG, Bahnstr, Switzerland), with 6 impedance electrodes and 1 pH sensor (K6011-EI-0632), was inserted transnasally. Impedance measuring sites were located in the distal esophagus at 3, 5, 7, and 9 cm and 2 impedance measuring sites in the proximal esophagus at 15 and 17 cm above the LES. One antimony pH sensor was located 5 cm above the LES, allowing the simultaneous pH analysis in the distal esophagus. MII-PH data were recorded for at least 23 hours and properly downloaded. The location of the lower esophageal sphincter (LES) was determined by high resolution manometry (HRM) using 23-channel silicone-customized water-perfused catheter (manufactured by Mui Scientific, Ontario,CA). The proton pump inhibitors (PPIs) were evaluated and the patients were asked to discontinue PPIs for at least 2 weeks, and H2-antagonist, prokinitic agents and antacid for at least 3 days prior to MII-PH study. The patients were advised to continue daily regular activities and have a minimum of 3 standard meals during the study period. In addition, the patients were asked to avoid eating fruit juice and acidic beverages including apple, orange, or lemon juice during the examination and to push the symptom indicator button on the MII-pH each time they experienced heartburn or regurgitation and chest pain. The following parameters were obtained from MII-PH recordings. The esophageal acid exposure of time (EAET) provided a quantitative measure of the time when esophageal pH remained below 4 in the distal esophagus, expressed as a percentage. A total EAET of >4.0% was used to define elevated acid exposure, then, upright and recumbent were separately calculated. This test had a sensitivity of 91% and specificity of 85% for discriminating acid reflux [4, 5].

3. Data Analysis

Impedance and pH tracings were analyzed by the researcher. Analysis of the impedance signals included the total number of reflux episodes as regards to composition (liquid, gas, and mixed reflux episodes) and pH (acid, weakly acid, and nonacid). Liquid reflux was defined as a sequential decrease in impedance to a minimum of 50% of the baseline value, beginning at the most distal recording site. Gas reflux was defined as a rapid (3 kOhm/s) increase in impedance, occurring simultaneously in at least 2 esophageal measuring segments in the absence of swallowing. Mixed liquid-gas reflux was defined as gas reflux that occurred during or immediately preceding liquid reflux. For each reflux, episodes detected by impedance

at 5 cm above the LES were calculated as the time(s) between the 50% drop in impedance until the 50% recovery of the impedance baseline. Acid reflux is defined as a reflux event associated with a drop in esophageal pH <4, weakly acid is associated with a pH drop between 4 and 7, and nonacid is a reflux event associated with a pH drop <7.

The meal periods were excluded from the analysis. DeMeester score was calculated based on 6 variables (percentage of the total time that pH was <4; percentage of upright and supine time that the pH was <4; number of reflux events; number of reflux events longer than 5 minutes; and longest reflux event). Acid reflux episodes are defined as a pH fall <4. An overall score, known as DeMeester score, is calculated using a special formula; this value should not exceed 14.7 in healthy individuals [2]. The symptom index (SI) and symptom association probability (SAP) were calculated according to the formula described previously. SI was defined as the number of symptoms associated with reflux divided by the total number of symptoms; at least 1 symptom is required for SI to be positive. SAP was calculated by dividing 24- hour pH data to 2-minute segments; the probability of symptom distribution and reflux episodes in a 2 minute-window was then calculated to determine if it could have occurred by chance (Fisher test); SAP = 1-p.SI and SAP were considered to be positive at ≥ 50% and ≥ 95%, respectively. The normal values of the MMS MII-PH system were reported by Zerbib et al. [6].

Statistical Analysis
Data were entered into SPSS Version 19 after encoding for each participant. Age was reported as mean ± standard deviation. Comparison of statistical significance was made between the symptom categories using either the Mantel-Haenszel chi-square test with Yates correction, or the Fisher's exact probability test. A p value less than 0.05 was considered statistically significant.

Results

This study was conducted on 670 patients, who met our inclusion criteria and had GERD symptoms (heartburn and/or regurgitation and noncardiac chest pain) without esophagitis. The mean age of the patients was 40.4±9.6 years (range: 11-63 years), and of them, 62.4% (418/670) were female. The mean age of the female and male patients was 39.5±9.3 years (age range: 11-63 years) and 41.2±8.4 years (age range: 12-63), respectively. Based on the total number of reflux episodes, of the patients, 49.5% (332/670), 65.1% (436/670), and 4.0% (27/670) had acid, weakly acid, and nonacid reflux, respectively. Also, 11.8% (79/670), 89.2% (598/670), and 77.5% (519/670) of the patients had liquid, mixed, and gas reflux, respectively. DeMeester scores were above the normal range in 39.4% of the participants (264/670). The symptom index (SI) and symptom association probability (SAP) score, regardless of PH contents (acid, weakly acid, or nonacid) were above the normal range in 34.6% (232/670) and 58.4% (391/670), respectively (Table 1). The acid, weakly acid, liquid, mixed, and gas reflux were more frequent in males than in females, but gas reflux was more frequent in the upright position than in the supine position and weakly acid and mixed

reflux were more frequent in the supine position than in the upright position. There were not any significant differences between upright and supine position in acid, weakly acid, nonacid, liquid, and mixed reflux in patients with NERD (P>0.05). Nonacid and liquid refluxes were not prevalent, but gas reflux occurred more frequently in patients in this study. SI was 23.6% (158/670), 2.4% (16/670), and 0% (0) above the normal value in acid, weakly acid, and nonacid reflux, respectively. SAP was 48.8% (327/670), 32.7% (226/670), and 7.2% (48/670) above the normal value in acid, weakly acid, and nonacid reflux, respectively (Table 2).

Discussion

To the best of our knowledge, this was the first Iranian study to date to examine the prevalence of esophageal multichannel intraluminal impedance-pH (MII-PH) monitoring findings in patients with nonerosive reflux disease (NERD) associated with diverse types of reflux patterns. The results of this study revealed that weakly acid was more prevalent than acid in patients with NERD. DeMeester score number was positive in less than 50% of the total patients.

The symptom association probability (SAP) score was 48.8% positive in acid reflux and more frequent than weakly acid and nonacid reflux. The acid, weakly acid, liquid, mixed, and gas reflux were more prevalent in males than in females, however, nonacid reflux was more prevalent in females. Although acid, nonacid, and gas reflux were more frequent in the upright position than in the supine position and weakly acid and mixed reflux were more frequent in the supine position, no significant differences were found between upright and supine positions in acid, weakly acid, nonacid, liquid, and mixed reflux in patients with NERD (P>0.05). Nonacid and liquid refluxes were not prevalent in this study, but gas reflux was more prevalent. It seems that SI and SAP are more closely correlated with symptoms in acid reflux than in nonacid reflux.

Although Gastroesophageal Reflux Disease (GERD) Questionnaire and Proton pump inhibitor s(PPIs) test could diagnose patients with GERD, the definitive diagnosis of GERD still depends on endoscopy or MII-pH monitoring. Savarino et al. have proposed subtypes of NERD patients based on cooperation between MII-pH findings and symptom association probability (SAP) results as pH-positive and negative NERD (including hypersensitivity esophagus and functional heartburn)(7). On the other hand, if the parameters of reflux such as total number of reflux episodes based on acid, nonacid, or mixed reflux were above the normal limits and SI or SAP parameter were positive, then, the patient would be considered to have a reflux related disease. However, if the parameters of reflux such as total number of reflux episodes were within the normal limits but SI or SAP indexes were negative, then, the patient would be considered to have a non-reflux related disease. NERD is the most common presentation of GERD and comprises up to 69% of all Iranian patients with GERD [8], which suggests that the chemical stimuli (acid, weakly acidic, bile and proteolytic

Table 1: Demographic Information and reflux characteristics of 670 Patients With non-erosive reflux disease (NERD) and correlation between onset of reflux episodes to the symptoms index

Findings	NERD, n (%)
Numbers	670(100)
Age(years)	
Mean ±SD	40.4±9.6
Range	12-63
Sex	
Female, n (%)	418(62.4)
Male, n (%)	252(37.6)
Reflux episodes (Total)	
Acid, n (%)	332(49.5)
Weakly acid, n (%)	436(65.1)
Non acid, n (%)	27(4)
Reflux composition (Total)	
Liquid, n (%)	79(11.8)
Mixed, n (%)	598(89.2)
Gas, n (%)	519(77.5)
De Meester Score, n (%)	264(39.4)
SI Total, n (%)	232(34.6)
SAP Total, n (%)	391(58.4)

Table 2: Demographic Information and prevalence of reflux episodes of 670 Patients With non-erosive reflux disease(NERD), reflux episodes based on body position and correlation between onset of reflux episodes to the symptoms index

Findings	Patients with NERD ,n=670					
	Acid reflux +	Weakly Acid reflux+	Non Acid reflux+	Liquid reflux+	Mixed reflux+	Gas reflux+
Patients, n (%)	332(79.5)	436(65.1)	27(4.0)	79(11.8)	598(89.2)	519(77.5)
Gender						
Female, n (%)	110(33.1)	204(46.8)	21(77.8)	35(44.3)	253(42.3)	234(45.1)
Male, n (%)	222(66.9)	232(53.2)	6(22.2)	44(55.7)	345(57.5)	285(54.9)
Body position:						
Upright, n (%)'	177(26.4)	208(31.0)	16(2.4)	21(3.1)	286(42.7)	519(77.5)
Supine, n (%)	155(23.1)	228(34.0)	11(1.6)	58(8.6)	312(46.6)	265(39.5)
Symptom Index:						
SI, n (%) **	158(23.6)	16(2.4)	0(0)	-	-	-
SAP, n (%) ***	327(48.8)	226(32.7)	48(7.2)	-	-	-

enzymes), mechanical stimuli (distension or contraction), peripheral, and central hypersensitivity are the main causes of NERD (or GERD). The esophageal sensitivity, large volume, and proximal extent of refluxate are other putative mechanisms of patients with NERD. The pathogenesis of NERD for each patient is based on the results of MII-pH monitoring. The multiple intraluminal impedance pH (MII-PH) monitoring has been introduced as a new and reproducible technique to diagnose and assess the outcome of anti-acid secretory drugs. This tool could detect reflux episodes independent of the pH of the refluxate, so it identifies who has nonacid reflux. Combined pH and intraluminal impedance monitoring could identify all types of reflux events with respect to acidity (acid, weakly acidic, weakly alkaline) and its composition (liquid, gas, and mixed), and it is more accurate than pH alone in detecting both acid and weakly acidic reflux. The direct positive relationship between the esophageal acid exposure time (EAET) and the degree of mucosal damage have been shown by several studies [4]. Bredenoord et al. recommended that MII-PH monitoring esophageal manometry be done based on PPI because it can show the correlation between native oesophageal acid exposure and degree of mucosal damage [4]. In this study, total acid reflux episode was (49.5%) lower than the previous report. Conchillo et al. found that acid and liquid reflux in the supine position of the patients with NERD were lower than erosive esophagitis (EE), but patients with EE and NERD have similar nonacid reflux patterns [3]. Namasivayam et al. found that 30% to 40% of weakly acidic reflux episodes

episodes correlate with symptoms [1]. Weakly acidic reflux is uncommon in patients with GERD, who are tested for acid suppressive medication (14.8%); it mainly occurs in patients treated with PPI and in the postprandial period. However, in this study, weakly acid was more frequent than acid and nonacid reflux; they were tested based on PPI. It is suggested that preceded acid reflux before weakly acid reflux is the pathogenesis of esophageal symptom in NERD patients [1]. NERD patients with pH-negative are more sensitive to weakly acidic reflux than patients with erosive esophageal reflux disease (ERD) [9]. Moreover, experiments have revealed that exposure of nonacid materials and bilirubin to esophagus can provoke esophageal injuries and heartburn, but it is a mechanism in patients with NERD, which is not fully elucidated [6]. Although nonacid reflux was not prevalent in this study, several studies have supported the role of nonacid reflux as a cause of symptoms in NERD patients, especially those not responding to proton pump inhibitors (PPIs) [6]. Gas (and mixed) reflux was more frequent than liquid reflux in this study, suggesting that the presence of gas in the refluxate of patients with NERD significantly enhances the probability of reflux perception. These patients are also more sensitive to less acidic reflux than patients with oesophagitis. Temporal relationship between symptoms and reflux episodes is a method used in evaluating the results of combined pH-impedance monitoring in NERD patients. This method is only recommended for NERD patients with hypersensitivity esophagus and functional heartburn, those whose EAET results was negative in MII-pH test [10]. In this study, the frequency of the patients with positive SAP (48.8%) was more than patients with positive SI (23.6%) in acid reflux pattern. The present study had some limitations. First and foremost was that nonacid reflux had overlap symptoms with bile reflux that could not be identified with MII- pH technique. Second, not all our patients had accepted MII-pH-monitoring, so it could have had a different prevalence. Third, some patients on long-term PPI therapy who referred to the Motility Disorders Laboratory of Firoozgar Hospital before, met our exclusion criteria.

Conclusions: The present study revealed that weakly acid reflux was more prevalent in patients with nonerosive reflux disease (NERD) than those with acid or nonacid reflux. Also, gas (and mixed) reflux was more frequent than liquid reflux. There were no significant differences between upright and supine position of acid, weakly acid, and nonacid reflux patients with NERD (P>0.05). The diagnostic value of the DeMeester score, symptom index (SI), and symptom associated probability (SAP) was less than 50%. Further studies should be conducted to determine the effectiveness of other stimulates as bilirubin and pepsin on esophageal symptoms and histological injuries.

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The effect of Viola tricolor L. flower hydro-alcoholic extract on anxiety-like behavior in a mouse model of chronic asthma

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Abstract

Background: Since anxiety may aggravate asthma outcomes and current anti-anxiety drugs may cause respiratory depression, the development of new anxiolytic therapies for asthmatic patients is critically needed. Viola tricolor L. has been used empirically for asthma remedy, but its anxiolytic effect has not been evaluated yet. Here, we investigated the effect of Viola tricolor L. hydro-alcoholic extract on anxiety-like behavior in ovalbumin (OVA) sensitized mice.

Methods: BALB/c mice were randomly divided into six groups: normal control, OVA (asthma) control, OVA + Viola tricolor (50, 100 and 200 mg/kg) and OVA + dexamethasone (3 mg/kg). Allergic asthma was induced in mice by sensitization and challenge with ovalbumin. Asthmatic mice were treated orally in the last 7 days of the OVA challenge. One hour after the last administration of therapeutic regimen, the anxiolytic activity was evaluated by elevated plus maze. Next day, the body weight of the animals and OVA-specific immunoglobulin (Ig) E levels in serum were measured.

Results: Viola tricolor at all three doses as well as dexamethasone significantly suppressed OVA-induced IgE production, although IgE level in dexamethasone-treated group remained significantly higher than the normal control group. Viola tricolor treatment particularly at 200 mg/kg increased open arm activity and improved body weight in asthmatic mice. However, treatment with dexamethasone in asthmatic animals did not induce significant changes in open arm activity and body weight.

Conclusions: Unlike corticosteroid therapy which did not improve anxiety, Viola tricolor can be a good remedy for treating asthma associated anxiety.

Key words: Anxiety, Asthma, Immunoglobulin E, Viola tricolor L

Introduction

In the recent years, asthma has emerged as a major public health problem and affects about 300 million people worldwide (1). Allergic asthma is a chronic inflammatory respiratory disease driven by Th2 lymphocytes activation which leads to increased synthesis and release of IgE from B-cell following allergen exposure. IgE is a critical mediator of early and late phase of allergic reaction and plays an important role in the pathophysiology of allergic asthma (2-4). Although the cellular mechanisms underlying allergic asthma are well understood, little is known about its effects on brain function and behavior. Moreover, recent evidence has reported that allergic responses could modulate brain functioning in the areas that are involved in behavior, and these allergic responses are implicated in the development of psychiatric diseases, such as asthma associated anxiety (5, 6). Clinical studies have reported a high prevalence of anxiety in asthma patients (7, 8). The comorbidity of anxiety disorders is responsible for poor prognosis of asthma and impaired quality of life. Therefore, managing anxiety is a critical aspect of asthma treatment (9).

Some classes of currently used anxiolytic drugs (e.g. benzodiazepines) may increase the possibility of asthma exacerbation and induce adverse effects such as addiction and respiratory depression. Therefore, anxiety-reducing medications may not be ideal for managing comorbid anxiety in patients with asthma (10, 11). Although, steroid therapies are effective in controlling asthma, they have anxiogenic effects and may induce insomnia, and neuropsychiatric disorders (12, 13). Therefore, a drug bearing anti-inflammatory and anxiolytic potentials may impart significant benefit for managing comorbid anxiety in asthma patients.

There is increasing scientific evidence demonstrating that traditional medicine has the potential for treating asthma and comorbid conditions, such as asthma associated anxiety (14). Viola tricolor, belonging to the Violaceae family, is a traditional medicinal plant widely distributed throughout Europe, Asia, America and Australia (15). It contains flavonoids particularly rutin, and other compounds, like anthocyanins, coumarins, tannins, saponins, phenolic acids and cyclotides (15, 16). Viola tricolor has a long history in folk medicine for treating bronchitis and asthma. It has remarkable pharmacological properties like anti-inflammatory, antioxidant, antitussive, expectorant effects (17, 18). In addition, this herb has immunosuppressive activity and can block proliferation of activated lymphocytes (18). Keeping in view the traditional use of Viola tricolor against asthma, the current study was designed to evaluate the anxiolytic effect of Viola tricolor L. hydro alcoholic extract on asthma associated anxiety-like behavior in ovalbumin (OVA) sensitized mice.

Materials and Methods

Plant extraction
The Viola tricolor L. was purchased from the garden in Tehran. Flowers of the plant were dried at room temperature. 100 grams of dried flowers were ground, added to 800 ml of 96% ethyl alcohol (Kimia alcohol Zanjan Co., Iran) and water (1:1) and kept for 3 days. The suspension was filtered through filter paper and concentrated using rotary evaporator vacuum system (Heidolph, Germany) until the solvent was evaporated. The resultant product was kept in 2-8 °C and freshly dissolved in normal saline before used.

Animals
Sixty adult male BALB/c mice (6–8 weeks old) (18±2 g) were purchased from Pasteur Institute of Iran. The animals were acclimatized to the laboratory conditions one week prior to the study. They were maintained at 23±1 °C in a 12 hour light-dark cycle with free access to rodent food and water. This study was carried out in strict accordance with the guidelines for the care and use of laboratory animals of the Tehran University of Medical Sciences. Study procedures were approved by the Animal Ethics Committee of Tehran University of Medical Sciences (Number: IR.TUMS.REC.1395.2465).

Establishment of a murine model of chronic asthma and treatment regimen
Sensitization and challenge were performed as described by Mohammadian M (2016), with some modifications (19). Mice were randomly divided into six groups as follows (n=10): normal group, OVA (asthma) group, OVA + Viola tricolor treated groups (with 50 mg/kg, 100 mg/kg, and 200 mg/kg), and OVA + dexamethasone (DEXA) group.

For asthma modeling, the mice were sensitized with intraperitoneal injection of 20 µg chicken OVA (grade V; Sigma, USA) and 2 mg aluminum hydroxide (Sigma, USA) on days 0 and 14. Then mice were challenged with a 1 % OVA solution in normal saline, using an ultrasonic nebulizer (Omron CX3, Japan) for 30 minutes daily. The challenge was carried out from day 21 of protocol for 8 weeks, 3 times in a week (19). The normal group received intraperitoneal injections of 2 mg aluminum hydroxide gel and were challenged with normal saline alone. Mice were orally treated with Viola tricolor at different doses (50 mg/kg, 100 mg/kg, and 200 mg/kg) from day 68 to 74 (the last 7 days of OVA challenge). Dexamethasone (3 mg/kg) (Iran hormone Co., Iran), used as the reference drug for the positive control (20), was orally administered from day 68 to 74. Normal group and OVA group received only saline. Animals were sacrificed 24 hours after the last challenge (thus on day 75) to investigate the therapeutic effects of Viola tricolor. A schematic diagram of the treatment schedule is shown in Figure 1.
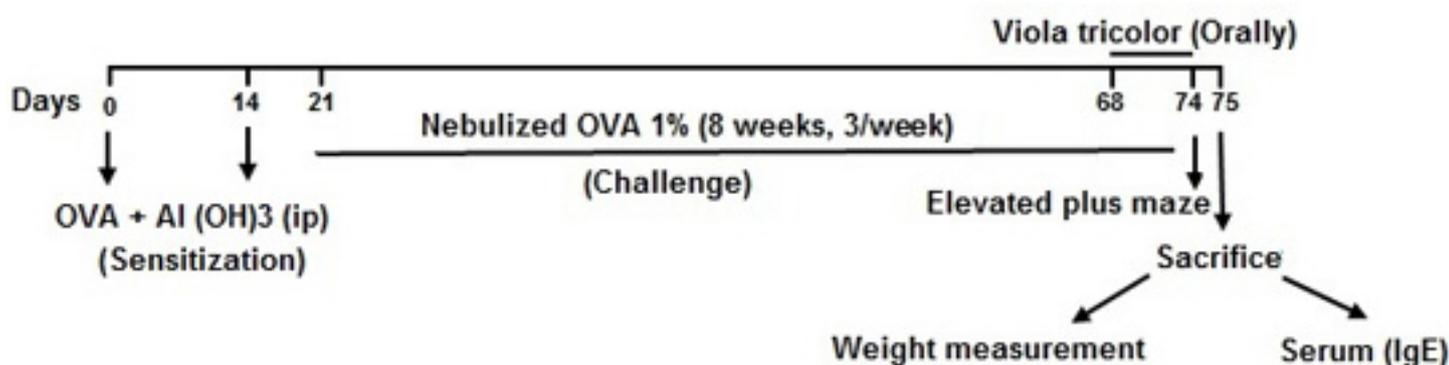
Figure 1: Time schedule of the chronic asthma mouse model and treatment with Viola tricolor.

Elevated plus maze test

The elevated plus maze test was performed to measure anxiolytic properties of pharmacological agents as described previously by Lister (21). The EPM apparatus consisted of two open arms (35 cm × 5 cm) and two closed arms (35 cm × 5 cm × 15 cm) that extended from a central platform (5 cm × 5 cm) which was elevated to a height of 50 cm above the floor.

One hour after last administration of extract, on the day of the last challenge (day 74), the mouse was placed in the center of the maze facing toward an open arm. The number of entries and the time spent in closed and open arms were recorded over 5 minutes. The criterion of an entry was the presence of all four paws inside an arm. The maze was cleaned with 96% ethanol and dried after each trial to prevent a bias based on olfactory cues.

The percentage of open arm entries (100 × open/total entries) and open arm time (100 × open/open + closed arm time) was calculated for each animal. An increase in open arm activity (duration and/or entries) indicates anti-anxiety behavior. The total number of entries (numbers of entries into open and closed arms) was determined as an index of locomotor activity.

Measurement of body weight

At the end of the experiment, the body weight of the animals was measured before euthanasia, using the digital electronic balance (Vibra, SJ 620 model, Japan), 620 g capacity and sensitivity of 0.01 g.

Measurement of OVA-specific IgE level in serum

Blood was obtained from the heart; sera were collected by centrifugation (3000 rpm, 10min) and stored at −70 °C. Then, the serum level of OVA-specific IgE was measured by a sandwich enzyme-linked immunosorbent assay (ELISA) kit using commercially available reagents, according to the manufacturer's instructions (BioLegend, Cat. No. 439807, USA).

Statistical analyses

Data are represented as mean ± standard error of mean (SEM). Statistical analysis was performed using GraphPad Prism Software (the version of 5.0). Differences between experimental groups were first analyzed by ANOVA. When a statistical significance was detected, post hoc Tukey test was used to determine statistical significance between multiple testing groups. P-values less than 0.05 were considered significant.

Results

Viola tricolor increased open arm activity in the elevated plus-maze

As it can be seen in Figure 2, animals from the OVA group in the elevated plus maze test showed a slight reduction in the percentage of both time spent in the open arms (OAT %) and the number of entries to open arms (OAE %) when compared with animals in the normal group, but the differences did not reach statistical significance. Animals treated with Viola tricolor (50, 100, or 200 mg/kg) showed an increase in both percentage of time spent in the open arms and the percentage of open arm entries when compared with the OVA group and this increase was significant only in the 200 mg/kg Viola tricolor-treated group. Administration of the extracts at all three doses had no effect on locomotor activity (Figure 2C). However, dexamethasone at 3 mg/kg had no significant effects on any of the parameters that were measured on the EPM (Figure 2).

Viola tricolor extract reduced the level of OVA specific-IgE in the serum

Figure 3 shows that the serum level of OVA-specific IgE significantly increased in the asthmatic group compared with normal control group (P <0.001). However, treatment with Viola tricolor at all three doses as well as dexamethasone significantly suppressed OVA-induced IgE synthesis (P<0.001 and P<0.01) but the level of OVA-specific IgE in the DEXA group did not reach the normal value and was significantly greater than the normal control group.

Viola tricolor extract improved body weight of the asthmatic animals

The body weight of the animals at the end of the experiment is presented in Table 1. The weight of animals in OVA-group was significantly lower than the animals in the normal control group (p<0.05). However, the weight of the mice treated with Viola tricolor at all three doses was significantly higher than the OVA-group (P<0.005).
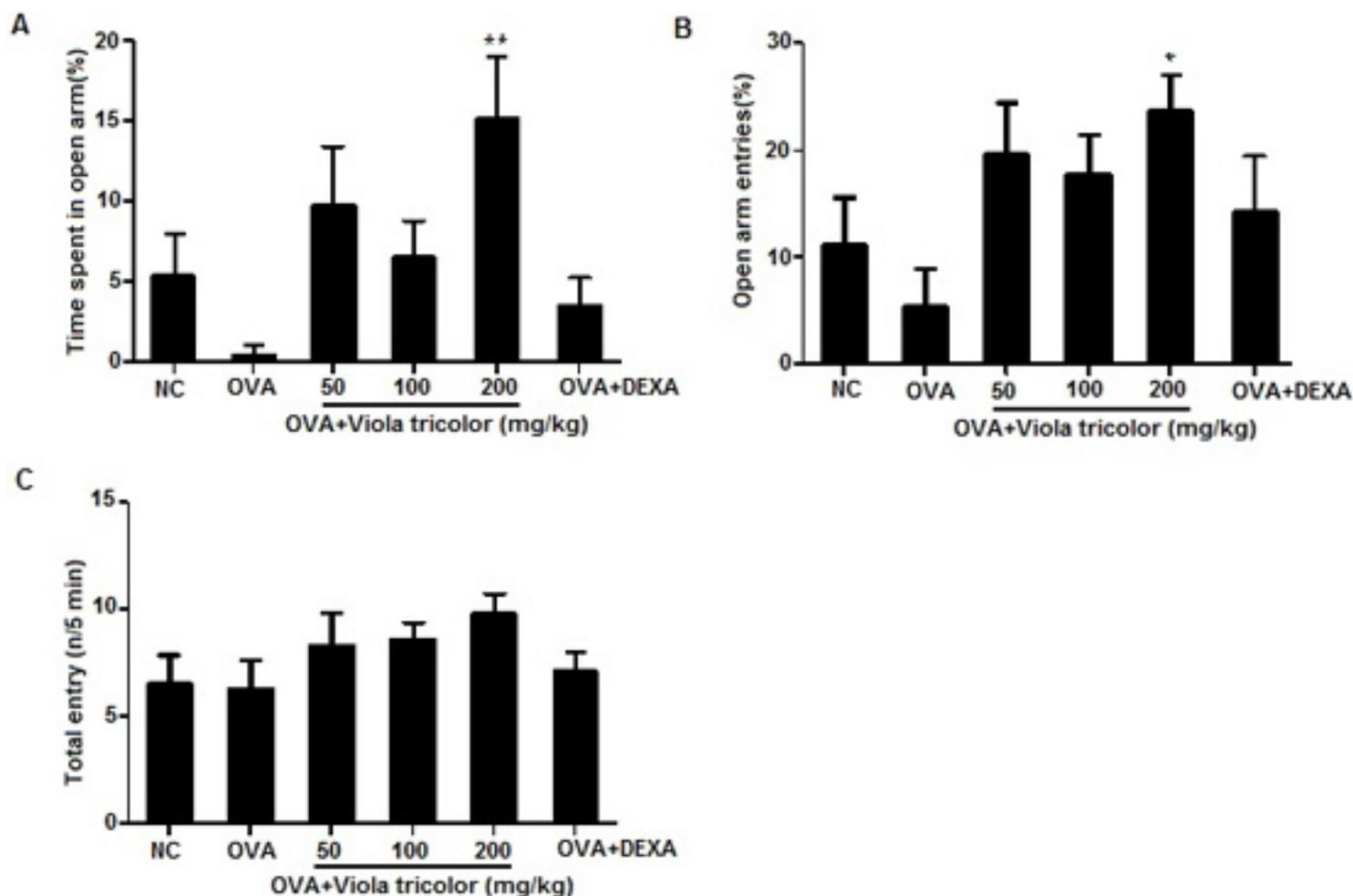
Figure 2: The effect of Viola tricolor extract on (A) the percentage of time spent in the open arms; (B) the percentage of open arm entries; (C) the numbers of total entries of the elevated plus-maze during a 5 minute test. In NC, Normal control animals, OVA (asthma) animals and asthmatic animals treated with Viola tricolor (50, 100 and 200 mg/kg) or dexamethasone (DEXA) (3mg/kg). Data are expressed as means ± SEM (n=9/group). *P<0.05, **P<0.01 vs. OVA group.

Treatment with dexamethasone in asthmatic animals did not induce significant changes in body weight. Furthermore, dexamethasone-treated mice had lower body weight compared to normal control and extract-treated groups.

Table 1: Effect of Viola tricolor extract on weight of asthmatic animals

Groups	Weight (gr)	P-value
Normal control	23.37 ± 0.77	
OVA (Asthma)	20.70 ± 0.83	P = 0.05 #
OVA + Viola tricolor 50 mg/kg	24.63 ± 0.45	P = 0.003 *
OVA + Viola tricolor 100 mg/kg	25.03 ± 0.99	P = 0.000 *
OVA + Viola tricolor 200 mg/kg	25.04 ± 0.29	P = 0.001 *
OVA + Dexamethasone (3mg/kg)	19.77 ± 0.96	P = 0.015 #

Data are expressed as means ± SEM (n=9/group); # Significant difference from normal control group; * Significant difference from OVA group. OVA = Ovalbumin
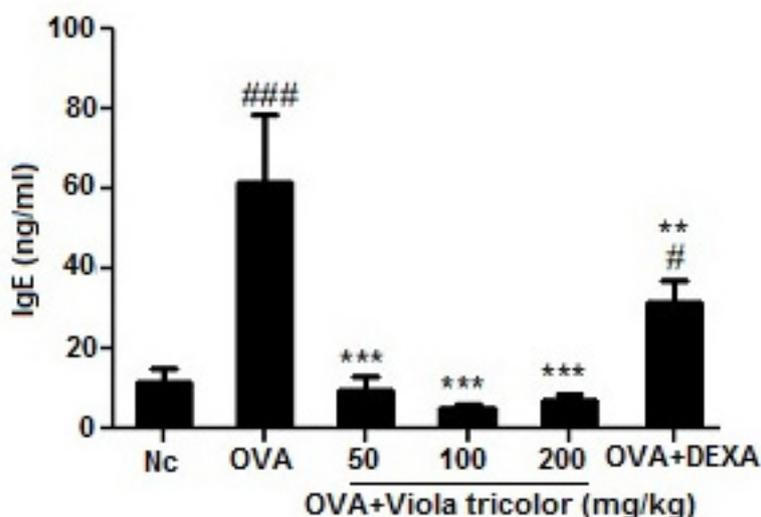
Figure 3: Effect of Viola tricolor extract on the level of OVA specific-IgE in the serum. In NC, normal control animals, OVA (asthma) animals and asthmatic animals treated with Viola tricolor (50, 100 and 200 mg/kg) or dexamethasone (DEXA) (3mg/kg). Data are expressed as means ± SEM (n=9/group). #$P<0.05$, ###$P<0.001$ vs. normal control, **$P<0.01$, ***$P<0.001$ vs. OVA group.

Discussion

The prescription of anxiolytic drugs in asthmatic patients is frequent and these medications tend to have adverse effects on the respiratory system (11). Therefore, there remains a crucial need for the development of new anxiolytic therapies for patients with asthma. Viola tricolor is a medicinal herb that has been used for centuries in the traditional treatment of asthma (18). To the best of our knowledge, this is the first study that investigated the effects of Viola tricolor on asthma-associated anxiety in the chronic asthma mouse model.

Elevated serum allergen-specific IgE is the hallmark of allergic asthma and is correlated with the disease severity (3, 22, 23). In our study, the OVA-sensitized animals showed higher levels of serum OVA-specific IgE versus normal control animals (Figure 3), confirming that the sensitization was effective. Although dexamethasone significantly inhibited OVA-induced IgE synthesis, IgE levels did not return to the normal levels and remained significantly higher than the normal control group (Figure 3). Consistent with our findings, some evidence suggests that dexamethasone may have little or even no effect on serum IgE levels (24, 25). Interestingly, treatment with Viola tricolor at all three doses reduced IgE titer to the normal level, suggesting that the extract effectively reduced sensitization process in mice (Figure 3).

Numerous studies demonstrated that psychiatric disorders, mainly anxiety and depression are more prevalent in asthmatic patients than the general population (7, 8, 26). Similar to the human studies (8, 26), results of this study demonstrate that asthmatic animals rated higher in anxiety tests as compared to the normal group (Figure 2). Basso et al. found serum IgE levels to be positively correlated with anxiety (5). Therefore, increased anxiety in asthmatic animals (Figure 2) may be at least partially attributed to asthma-induced rise in IgE levels (Figure 3).

There are a lot of natural herbs that can reduce stress and anxiety without causing many side effects as currently used anti-anxiety medications do (27, 28). Our study demonstrates that treatment with Viola tricolor, especially at the dose of 200 mg/kg, reduced behavioral markers of anxiety in OVA-challenged mice (Figure 2). This effect of extract may be partially related to the suppressive effect of Viola tricolor on IgE production. Jyonouchi showed that controlling allergy symptoms with the use of a humanized anti-IgE antibody unequivocally improves neuropsychiatric symptoms (27). Viola tricolor and dexamethasone both resulted in reduced IgE levels. However, anxiety levels were markedly reduced with Viola tricolor treatment. These findings suggest the presence of another prominent mechanism beside IgE that would have led to the anxiolytic effect of Viola tricolor. We speculated that the anxiety-reducing effect of Viola tricolor may be associated with the stimulation of GABA receptor by rutin, the main component of Viola tricolor. A previous study suggested that rutin induces anxiolytic-like effects through modulation of GABAA receptors in the basolateral amygdala (29, 30).

In this study, dexamethasone as a conventional anti-asthma drug had no effect on anxiety (Figure 2) and body weight (Table 1). On the other hand, Viola tricolor, a traditional remedy for asthma reduced anxiety (Figure 2) and improved body weight of the asthmatic animals (Table 1). These results suggest that Viola tricolor induced improvement in body weight may be attributed to its anxiolytic effects and not to its anti-asthmatic effects. In accordance with our findings, a recent study indicates that rutin treatment has anti-anxiety effects and ameliorates various impairments related to physical fatigue including body weight (31).

Furthermore, previous studies indicate that psychotropic drugs increase appetite and result in weight gain over a long-term period of consumption (32, 33). A study shows that GABAergic neurons within the hypothalamus positively regulate feeding behavior and body weight (34). Since rutin, the major component of Viola tricolor, has GABA agonistic property (29, 30), Viola tricolor's effect on body weight may have been exerted through stimulation of GABA receptors.

Conclusion

The results of the present study showed that the hydro alcoholic extract of Viola tricolor reduces anxiety-like behavior in OVA-sensitized mice. These results suggest unlike corticosteroid therapy which cannot improve anxiety, Viola tricolor appears to be beneficial for managing asthma-associated anxiety. However, future studies are warranted to evaluate the role of GABA receptors in mediating anxiolytic effects of Viola tricolor.

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Effects of Selenium on Various Sperm Parameters in Varicocele Rats

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Abstract

Aim: Varicocele is an abnormal enlargement of the pampiniform venous plexus and blood blockage in the spermatic cord. Among major effects on male fertility is oxidative stress and metabolites reflex to testicles, which in turn have a significant part in producing free radicals (reactive oxygen species =ROS). As a micronutrient, selenium has an antioxidant characteristic to normal spermatogenesis and combats oxidative stress. The present study aimed at examining selenium effects, as an antioxidant element) on sperm parameters (sperm count, motility, morphology) in varicocele rats.

Methods: This study was a case-control. It was done in 2017 in the Qazvin University of Medical Sciences on 24 male Rats that were divided randomly to four 6-subject groups of control, sham, varicocele, and treated varicocele. A daily 0.2-mg selenium diet was injected intraperitoneally to the treated varicocele group. After four weeks, sperm indices were examined among all the groups and the data was analyzed by one-way ANOVA.

Results: All the indices in this study (sperm count, motility and morphology) had a significant decline in the varicocele group compared to the control group (p<0.05). Results also indicated an effect of selenium as an antioxidant on the number of sperm as well as their motility. This led to improvement of these parameters having no effects on sperm morphology among varicocele rats.

Conclusion: Results showed that, as an antioxidant, selenium eliminated free radicals in varicocele rats indicating its effectiveness on varicocele-dependent infertility.

Key words: varicocele, spermatozoa, sperm count, sperm motility, sperm morphology, Rat

Introduction

Infertility is a prevailing problem among couples who have over a one-year struggle to have a child. About 50% of infertility relates to male factors [1]. Male infertility may have various causes among which are genetic mutations, changes in chromosome counts or morphology, infectious diseases, varicocele, chemotherapy, radiotherapy, ejaculation disorders. Varicocele is paid much attention as a cause of infertility [2-5]. Varicocele is an abnormal enlargement, as well as blood blockage, in the plexus of vein (pampiniform) within the spermatic cord that drains the blood through testicles. Its occurrence rate among fertile men is 15-20%; 30-50% among primary infertile men; and 50-80% among infertile men. The mechanism involving varicocele leading to male infertility has not been identified yet. However, theories have identified factors like reflection of poisonous metabolites from kidneys or adrenals, rise in testicle temperature, testicular hypoxia resulting from venous stasis and malfunction of hypothalamus or hypophysis in varicocele. Recent studies report that the main influencing factors on infertility include oxidative stress and reflection of metabolites to testicles. In this regard, ROS plays a major part [6]. Oxidative stress is a result of imbalance in production of ROS and antioxidants defence resulting in damage to DNA integrity in sperm nucleus, leading to many changes in parameters, especially sperm motility, within 90% of cases and decline in sperm count parameter up to 20 million in 60% of cases. ROS production is a physiologic process, which can cause sex cells' death, dysfunction of Sertoli–Leydig cells and spermatogenesis disorder. High levels of ROS in semen was reported in 80% of varicocele patients [7-8]. Selenium acts as a micronutrient and is required in mammals' diets like all other vital elements such as zinc, taking a crucial part in normal sperm spermatogenesis to protect sperm against oxidative substances. Protective effects of selenium are shown through building structures called selenoproteins that are part of antioxidant enzymes like superoxide dismutase, glutathione peroxidase, and catalase that are important for cellular health protection against oxidants and oxidative stressors like ROS. Recent studies show that defects in selenium production can lead to smaller testicles and, in the long run, to sperm impairment through spermatogenesis and sperm maturity processes [9-11]. Because expression of selenium (as an oxidant) is of great importance for normal spermatogenesis in sperm, and to defend against oxidative stress, the present study was initiated with the aim of investigating selenium effects on various sperm parameters in varicocele rats.

Materials and Method

This was a case-control study done in Qazvin University of Medical Sciences in 2017 according to the moral code of IR.QUMS.REC.1394.213. The sample of the study consisted of 22 mature male rats or mice with 250-350 gram weight. The rats were kept in 12 hours of light and 12 hours of darkness and 20°C temperature, then divided randomly to four 6-rat groups. These groups included the control group (with no surgery), the Sham group (varicocele was induced on them without any renal vein blockage), varicocele group, treated varicocele group (underwent surgery to induce varicocele with a daily selenium diet of 0.2mg during 8 weeks based on Koksal et al method) [12]. Eight weeks after the surgery, rats from varicocele, sham and control groups were killed by chloroform. In order to examine the sperm indices (count, motility, morphology), testicular fascia was torn by sterile scissors. After observing the left epididymis (the coiled tube) its tail was cut to be kept in Hams_F10 medium. Epididymis was divided into various parts and placed in the incubator for 15 minutes in order for the sperm to be released from the testicles into the petri dish.

To count the sperm, a Neobar light was employed. There were two sections for counting. Each section was a large 3×3mm box fragmented to 9 smaller curved 1×1mm boxes. The Neobar lam was covered with a special lamel which produced a 0.1mm when put on the lam. The semen was diluted with 1:2 proportion and all the squares (1 to 9) were counted. Only the sperm with head and tail (a complete sperm) were counted [13]. The border of each of the 9 boxes had three lines. If sperm head was located inside the box or on its internal margin, the sperm was counted, but if it was on the two exterior lines, it was not counted. To identify the percent of motile sperm, a droplet of the sample was placed on the lam. This parameter was examined by a 40-magnification microscope based on WHO criterion [13]. To determine the morphology of sperm, Papanicolaou staining was used. In this type of staining, the acrosome part of a sperm turned light blue and it was dark blue in the rear part of the acrosome. The neck was a little reddish, the tail blue and the cytoplasmic parts around the neck were pink. After that, using a microscope with 400×magnification, at least 200 sperm were examined [13]. In order to evaluate the viability of sperm, eosin-nigrosine staining procedure was employed, which is based on solubility level of eosin-nigrosine to cell membrane of the damaged cells as well as on insolubility of the colour in healthy cells [13]. A dead sperm is of red or pink colour; the living ones are light pink to white. If the neck is pink but the remainder of head doesn't absorb colour, this sperm is alive too showing that the membrane is permeable in neck. After staining, 100 sperm were evaluated from each sample, by CX31 microscope with 100×magnification. SPSS 16 and two-way ANOVA were employed to analyze the data.

Result

All sperm parameters (motility, normal morphology, the number of viable sperm) had a significant decrease in the varicocele group compared to the control group and selenium diet improved these parameters (see Table 1).

The percentage of sperm with good motility was significantly higher in the control, sham and treated groups than the varicocele group (p<0.05). The percentage of sperm with good motility was significantly different in the treated group from that of the varicocele group (p<0.05) (Diagram 1).

Table 1: Mean of sperm parameters among the different groups

Group / Sperm Parameters	Control	Sham	Varicocele	Treated
Mobility (%)	33.2±4.5	29.8±3.2	24.2±5.2	**27.1±2.5
Count	145±3.2	144±4.2	75±3.1	**129±4.1
Normal Morphology	44±1.2	41.3±3.2	37±1.8	40.1±3.1
Dead Sperm (%)	16.1±4.2	15.8±3.2	29.8±1.8	**20.1±2.2

** significant difference between the varicocele and the treated groups

Diagram 1. Comparing the mobility of sperm among the mentioned groups
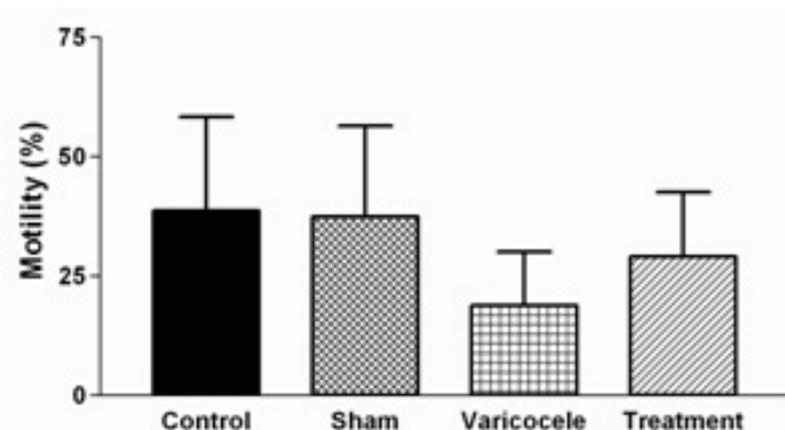
The number of sperm was significantly higher in sham, control and treated groups than the varicocele group ($p<0.05$). On the other hand, sperm count of the treated group had a significant increase compared to the varicocele group ($p<0.05$) indicating the positive effect of selenium on the sperm count in varicocele rats (Diagram 2).

Diagram 2. Comparison of sperm counts among the groups
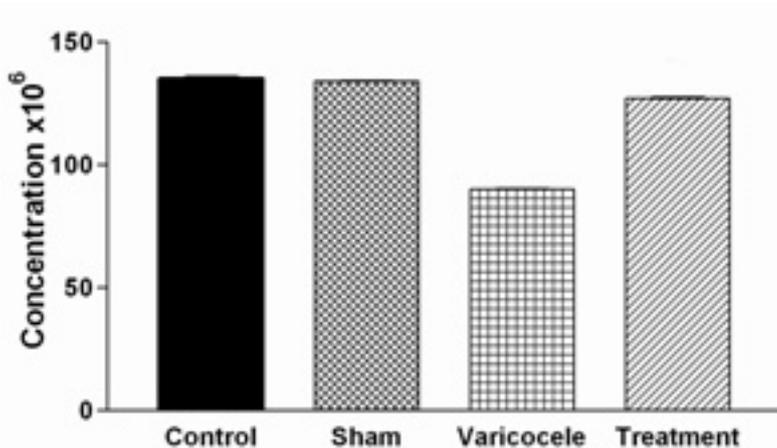
The percent of sperm with normal morphology in sham, control, and treated groups was significantly higher than the varicocele group ($p<0.05$); however, in the treated group, no significant difference was found between the treated group and the varicocele regarding normal morphology ($p>0.05$) showing that selenium had no effects on sperm morphology (Diagram 3 - next page).

Percent of dead sperm in sham, control, and treated groups was significantly lower than the varicocele group ($p<0.05$) but this parameter declined significantly in the treated group compared to the varicocele group ($p<0.0$(, showing a positive effect of selenium on the mentioned parameter in varicocele rats' sperm (Diagram 4 - next page).

Diagram 3. Normal morphology of sperm among different groups of the study
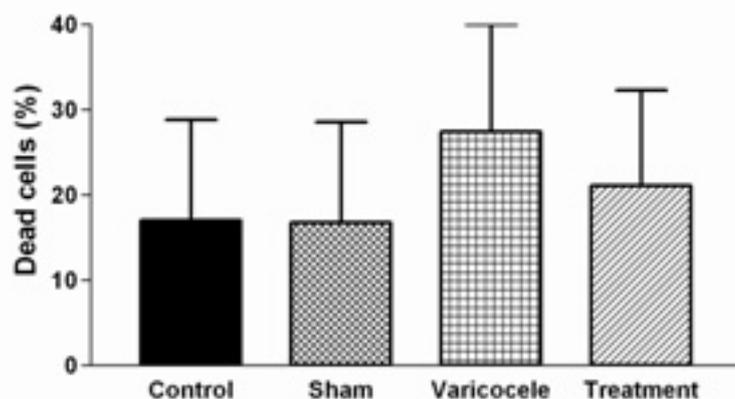
Discussion

It was reported in this study that selenium could improve the parameters of sperm count and the percent of dead cells in varicocele rats. A study by Camejo et al on infertile men reported that a decline in selenium in semen significantly decreased sperm count, motility as well as good morphology [14]. Another study (Molina et al) reported that lower levels of selenium would lead to higher levels of oxidative stress in testicles. They also showed that a diet of 0.1 – 0.3 selenium per one kilo of antioxidant is required for a good production of sperm in animals. This study was consistent with the present study regarding the effect of antioxidants on male infertility resulting from varicocele [15]. It was reported in a study (2016) that selenium, along with carnitine, improved sperm parameters like motility, count, viability and normal morphology [16]. Sobhani et al (2015) examined the effects of antioxidants on sperm parameters and found a significant difference in sperm morphology between the control group and the case group, which was inconsistent with the present work [17]. Amidi et al reported that saffron had a significant positive effect on sperm morphology. Unlike Amidi et al, in the present study, selenium improved sperm morphology but no significant difference was found [18]. This study found significant higher sperm counts in the treated group than in the varicocele group. Testai et al (2016) investigated the relationship between oxidative stress and damage to mitochondrial membrane which reported that, because internal mitochondrial membrane contain cytochrome c, mitochondrial collapse by oxidative stress would result in cytochrome release from mitochondrial membrane, which in turn leads to cell death. This death might lead to exacerbate negative effects of the stressors' activities like collapse of DNA [19]. Based on this study, significant decline in sperm counts in varicocele group compared to other groups is justified. Mostafaeroglue et al conducted a study on men suffering from varicocele. They showed that selenium expression improved sperm parameters including sperm counts, which was consistent with the present study, although inconsistent regarding the positive effect of selenium on normal morphology and mobility of sperm [20]. Seminal leucocytes and abnormal sperm are the main sources of free radicals in infertile people. Protective factors like antioxidants, act as a treatment in infertile men. Investigating creation of oxidative stress by ROS production, Alaa Hamada et al concluded that, as an antioxidant, selenium could control oxidative tension in sperm of infertile people [21].

Conclusion

Generally speaking, selenium is an antioxidant that can have a positive effect on sperm counts and viability in varicocele rats. Further study is needed to better demonstrate effects of antioxidants like selenium because oxidative stress involves different parts of the body.

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The effects of omega-3 PUFA (ALA) on WT1 gene expression in pancreatic cancer cell line (MIA PaCa-2)

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Abstract

Background: Cancer starts by cells acquiring a number of characteristic alterations especially abnormal cell growth. These properties reflect faults in signalling pathways in cancer cells. Wilms' tumor 1(WT1) acts as a tumor suppressor by negative regulation of WNT/beta-catenin signaling pathway. The role of WT1 in many cancers has been studied.

Aims: To evaluate the WT1 gene expression alterations in response to different concentrations of omega-3 PUFA alpha linolenic acid (ALA) in pancreatic cancer cell line (MIA PaCa-2) in a time dependent manner.

Methods: MiaPaca-2 cell line was cultured in monolayers. After that began the cells treatment with omega-3 fatty acid (ALA) using different concentrations of 25, 50, 100, 250, 500 and 1000 µM for 24, 48 and 72 hours. The RNA was extracted from both control (untreated) and treated cells. Viability was checked by MTT assay and WT1 expression was evaluated by RT-PCR.

Results: Real-time RT-PCR analysis showed that the level of WT1 mRNA, was decreased after 24, 48, 72 hours treatment with omega-3 fatty acid (ALA) for 100, 250, 500 and 1000 µM concentrations but not 25 and 50 µM. Data obtained from MTT revealed antiproliferative effects of omega-3 fatty acid (ALA) for 100-1000 µM concentrations but not 25 and 50 µM.

Conclusion: Our findings indicated that the cell viability and level of WT1 mRNA was decreased during Omega 3 ALA Treatment. So, it a potential role of Omega 3 in prevention or as a supplementary for pancreatic cancer treatment has been suggested.

Key words: omega-3 PUFA (ALA), pancreatic cancer, MIA PaCa-2, WT1

Introduction

Cancer is one of the world's biggest challenges. It is the cause of every four deaths in the United States. [1] Pancreatic cancer is a fatal disorder with the 5-year survival of lower than 5%, and the fourth leading cause of cancer-related deaths in the world. Pancreatic cancer is aggressive with few symptoms until the cancer is advanced. Symptoms may include abdominal pain, weight loss, diarrhea, and jaundice. Treatments include surgery, chemotherapy, and radiation. [2] Because of high fatality rates, pancreatic cancer incidence rates are almost equal to mortality rates. [3]

Risk factors for pancreatic cancer are summarized as follows: age, sex, race, smoking, obesity and low physical activity, family history, certain jobs and some genetic diseases like ovarian cancer and breast cancer, gastric disorders (H. pylori infection). [4]

Wnt proteins are extracellular signaling molecules. Canonical Wnt signaling has a great impact on embryonic development, tissue homeostasis, cell division and cancer. Thus deregulation of Wnt signaling causes uncontrolled proliferation and unstable chromosomes duplication. [5]
The Wilms' tumor gene (WT1) provides information for making a zinc finger domain that is crucial for the organogenesis and development of the kidney. Furthermore this gene encodes a transcription factor and a RNA-binding protein and was revealed to be connected with kidney disorder in children and gonadal dysgenesis. The expression of WT1 gene is tissue specific and has been indicated to occur in kidney stem cells, gonads, adult spleen, heart, lung, thymus and mesothelium perdurable. [5, 6]

Omega-3 (n-3) fatty acids are long-chain polyunsaturated fatty acids (LCPUFA) with a first double carbon bond at the third carbon atom counting from the methyl end of the chain. Several studies have recently reported the cancer preventing effects of polyunsaturated fatty acids (PUFAs) in vitro. Indeed n-3PUFAs including α-linolenic acid (ALAor18:3n-3), eicosapentaenoic acid (EPA or 20:5n-3), docosapentaenoic acid (n-3 DPA or 20:5n-3), and docosahexaenoic acid (DHAor22:6n-3) are the most important for human nutrition. [7] Moreover the hypothesis that PUFAs can reduce tumorigenesis has been supported by many scientists using animal models worldwide. In any case epidemiologic studies have suggested the cancer preventing effects for n-3 PUFA and demonstrated the tumor inducing role of n-6 PUFA contrarily. [8, 9]Some studies showed that pretreatment of colon cancer cells (COLO 320 DM) with 25 µM Ecosapantanoic acid (EPA), increases sensitivity of total cell population to chemotherapy in both 24, 48, 72 and 96 hours after treatment. [10] Treatment of MDA-MB-231 breast cancer cell line with 100 µM LA (60 µM EPA+ 40 µM DHA), decreased cell growth about 40%. [11] Apoptotic activity of omega-3 PUFAs (ALA) alone [12] or in combination with other anticancer therapies [13, 14] are illustrated. Although potential of omega-3 PUFAs for target protein alterations in chemotherapy resistant SW620 colon cancer cells are demonstrated, the mechanisms by which these PUFAs assert their effects are not fully understood. [15, 16]

Materials and methods

MiaPaca-2‹ cell line was purchased from Pasteur Institute of Iran and cultured in monolayers using RPMI 1640 Biosera supplemented with 10% fetal bovine serum and 1% antibiotic (100 U/ml of penicillin, 10 mg/ml of streptomycin) at 37°C under a humidified atmosphere of 5% CO2. The cells were seeded in 6 well cell culture plates, each well containing 8x105 cells for all concentration and control. After treatment of the cells with omega-3 fatty acid (ALA) using concentration of 99% ethanol we prepared dilutions 25, 50, 100, 250, 500 and 1000 µM. At intervals of 24, 48 and 72 hours, cells were harvested and isolated from medium. RNA was extracted using total RNA purification kit (GeneAll RibospinTM), according to the manufacturers. For quantitative analysis of RNA extraction, we used Nanodrop techniques. For cDNA synthesis we used RT reagent kit Revert A-L, Extraction Kit from AmpliSens®. Real-time RT-PCR was performed using Rotor-Gene Q instrument (QIAGENE co.) and analyzed by Rest 2009 software.

Primers used for WT1 expression were 5′-GCGGCGCAGTTCCCCAACCA-3′ and 5′-ATGGTTTCTCACCAGTGTGCTT-3′ for forward and reverse respectively. [17]

Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was used as a RNA integrity control and amplified using primers 5′-CAATGACCCCTTCATTGACC-3′ and 5′-TGGAAGATGGTGATGGGATT-3′ for forward and reverse respectively. [18] The cycles were as follows: 95°C for 5 minutes, followed by 35 cycles of denaturing at 95°C for 30 seconds, annealing at 56°C for 40 seconds and extension at 72°C for 40 seconds. This was followed by the final extension at 72°C for 10 minutes.

For MTT, cells were cultured in 96-well tissue culture plate (2x103 cell/200µl). 24 hours after the first culture, we replaced ambient with 0.1% ethanol as control and concentrations of 25, 50, 100, 250, 500 and 1000 µM omega-3 fatty acid (ALA). Each concentration was performed as a quadruplet. After 24, 48, 72 hours of treatment, cells were washed with PBS and MTT solution (Sigma) was added at a concentration of 0.05 mg/ml diluted in PBS. Cells were incubated at 37°C for 4 hours to allow the formation of purple formazan crystals due to mitochondrial dehydrogenase activity. Then 100 µl of filtered DMSO was added to each well followed by 25 µl glycine buffer. The color intensity was then measured by spectrophotometric at 570 nm using a micro plate reader (ELISA reader, BioTek ELX800, USA). Data were analyzed by one-way analysis of variance ANOVA followed by Dunnett's multiple comparison test using graphpad prism 7 software where $P < 0.05$ was considered to be statistically significant.

Results

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As shown in Figure 1, real-time RT-PCR analysis revealed that the level of WT1 mRNA, was decreased after 24, 48, 72 hours treatment with omega-3 fatty acid (ALA) in a time dependent and concentration manner for all concentrations but 25 and 50 µM of omega-3 fatty acid (ALA). (Data for 48 hours are shown here).
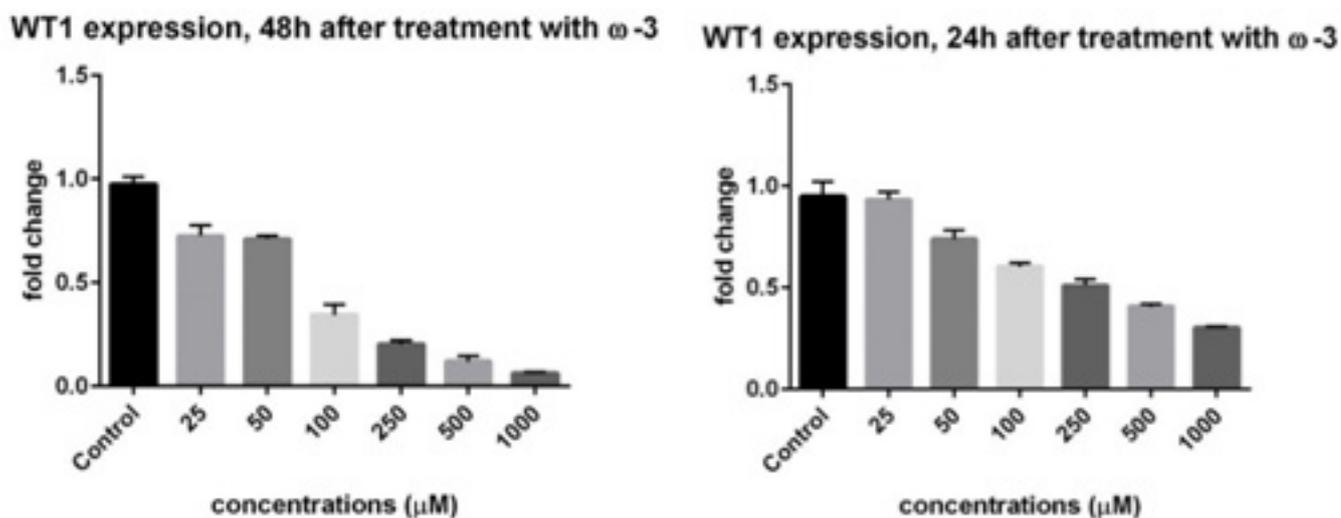
Figure 1: Omega-3 fatty acid (ALA) induced downregulation of WT1 expression in a time and concentration manner. Detecting the transcription of WIF mRNA using real-time RT-PCR. MiaPaca-2 cells were treated with 25, 50, 100, 250, 500 and 1000 µM ALA for 24, 48, 72 hours. The levels of WT1 mRNA were analyzed by REST 2009 software ($P < 0.05$) (only data for 24 and 48 hours are shown here).

To confirm the anti-proliferative activity of omega-3 fatty acid (ALA) in pancreatic cancer cells, we performed a cell viability assay (MTT) in both concentration and time dependent manner as described in Material and methods section. As shown in Figure 2 (only data for 48 and 72 hours are shown here) the anchorage-dependent cell viability of MiaPaca-2 cells after exposure to omega-3 fatty acid (ALA) was decreased significantly. These data demonstrate that omega-3 fatty acid (ALA) have antiproliferative activity in pancreatic cancer cell lines.
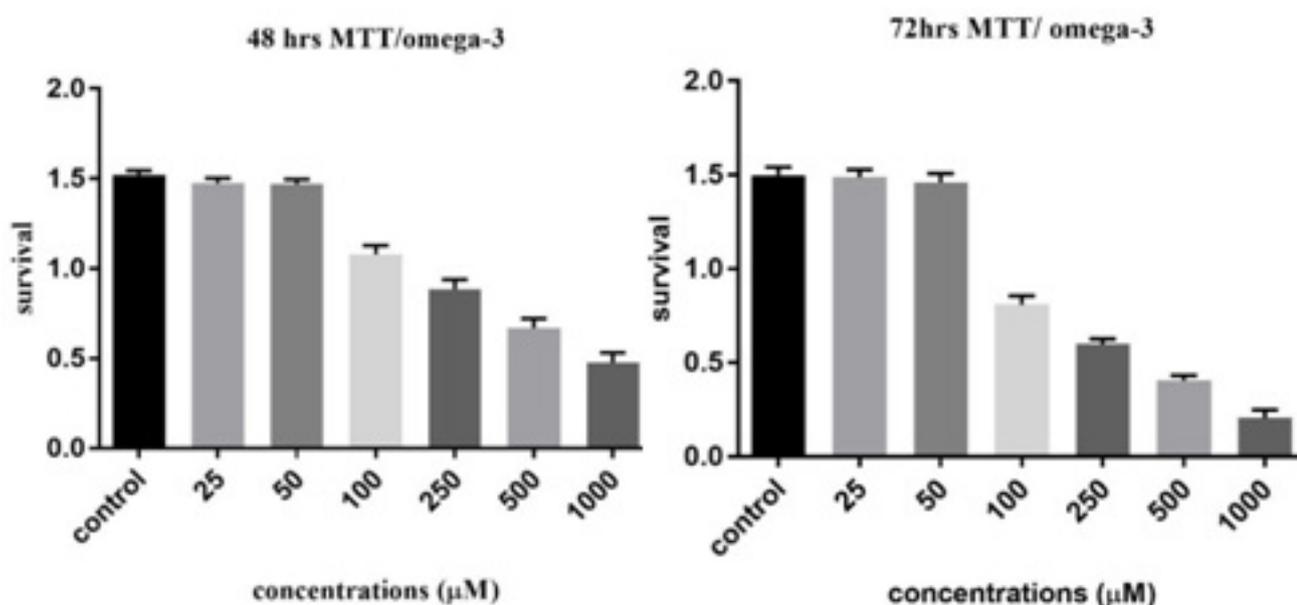
Figure 2: Anchorage-dependent cell viability of pancreatic cancer cell line (MiaPaca-2(, after treatment with different concentrations of omega-3 fatty acid (ALA) as described in material and methods. Antiproliferative effects were seen at 100 to 1000 µM of ALA with a time- and concentration-dependent manner ($P < 0.05$).

Discussion

In line with our study anticancer potential of omega-3 rich foods that have been reported in previous studies. [19, 20] As illustrated in Figure 1 and 2 the antiproliferative and downregulation of WT1 expression effects of ALA at 100 to 1000 µM treatment concentrations were seen in pancreatic cancer cell line (MiaPaca-2), respectively (P<0.05). The first WT1, has been identified as the tumor suppressor gene in Wilms' tumor, a kidney cancer with an incidence of 1 in 10,000 children. Its target genes are involved in cell growth, metabolism, extracellular matrix components and growth factors. [21, 22] During embryogenesis in mammals, WT1 has firmly been indicated in the kidneys, gonads, spleen and mesothelioma. After birth, its expression in renal glomerular epithelial cells it continues in this area probably to maintain skin performance [23] WT1 expression in lung cancer, colon cancer and glioblastoma cell lines has been detected. [24] Recently, oncogenic properties of WT1 in both various hematological malignancies and solid tumors have been documented. [25] So, this study emphasizes the oncogene suppression role of omega-3 PUFA (ALA) particularly in pancreatic cancer cell line (MiaPaca-2). Many studies have established global and/or local toxicity of anticancer drugs on normal cells. [26] Some chronic diseases such as cancer and inflammatory disease can be affected by omega-3 PUFAs . [27] Also EPA, in human colon cancer cell lines, HT-29 and Caco-2, decreases proliferation. . [28] In fact either PUFAs or its purified EPA and DHA form have proven anti-neoplastic functions which enable them to play an important role in cancer prevention or therapy. [29-31] EPA and DHA at concentrations of 40 and 60 µg/mL respectively increased apoptosis of SW1990 cells in a concentration-dependent manner. [32] Many biological functions including cancer cells invasion, metastasis, apoptosis and proliferation are shown to be affected by omega-3 PUFAs . [33, 34] In summary, in confirmation of the above studies pancreatic cancer cells proliferation was inhibited in 100, 250, 500 and 1000 µM ALA in all three times studied. Besides, WT1 was downregulated by omega-3 PUFA (ALA) at the same concentrations in a time- and concentration- dependent manner. Overall, these findings are consistent with others, proposing a potential role for omega-3 PUFA (ALA) as an anticancer dietary/drug supplement that affects on WT1 gene as a therapeutic target in pancreatic cancer. Further studies are suggested for investigating the mechanisms by which omega-3 PUFAs (ALA) assert their anticancer effects. Investigations for clearing omega-3 PUFA (ALA) functions as a supplementary combined with anticancer drugs in pancreatic drug resistant cells remains to be shown.

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A Public Health Initiative to Address Road Traffic Accidents in the Kurdistan Region of Iraq

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Abstract

The human and financial toll from road traffic accidents in the Kurdistan region of Iraq is high. In a small population of 5.2 million, there are currently three fatalities and 28 injuries daily. According to local authorities, many factors contribute to this problem. Speeding, failure to wear seat belts, and aggressive road behavior are among the principal causes. The local public health system is working to reduce deaths and injuries from road traffic accidents, a problem common not just to the Kurdistan region but throughout the Eastern Mediterranean region. This article identifies factors associated with road accidents in Kurdistan specifically but also throughout the wider region, and encourages the development and implementation of preventive initiatives to decrease RTAs in the region.

Key words: Road safety campaigns, World Health Organization, behavior change.

Introduction

The Decade of Action for Road Safety (2011-2020), (1) a resolution of the United Nations General Assembly, was formulated with the goal of first stabilizing and then reducing road traffic casualties globally. In the Kurdistan Region of Iraq at present the human and financial toll of road traffic accidents (RTAs) is high and, in some locations, trending upward. For example, in 2012, there were on average two deaths and 17 injuries for every RTA in the region (2). Currently the daily average is three deaths and 28 injuries per RTA (3). In other words, more than 1,000 preventable deaths and 10,000 injuries are occurring annually. In 2012 there were 567 deaths and 3,141 injuries while in 2016, 614 lives were lost and 7,724 were injured from the 4,268 road traffic accidents [Table 1] (4,5). Thus, between 2012 and 2016 there was an 8% increase in deaths from traffic accidents and a 145% increase in injuries. This suggests that health personnel may be preventing deaths from traffic accidents while overall accidents and injuries are increasing.

Table 1 (next page) suggests that deaths in Erbil and Sulaimaniya are decreasing while deaths in Dohuk are increasing. In addition, injuries have been reduced substantially in Erbil but have increased dramatically in both Sulaimaniya and Dohuk.

Table 1: Deaths and injuries from RTAs in the three provinces of the Kurdistan Region of Iraq: 2012 and 2016 (4, 5).

Province	Deaths		Injured	
	2012	2016	2012	2016
Erbil	216	215	1441	1191
Sulaimaniya	242	206	1155	2808
Dohuk	109	194	545	3725 *
Total	567	615	3141	7724

[*The increase in deaths and injuries in Dohuk might be attributed to the large number of displaced people from Syria and Mosul being re-located in the province and also to the increase in traffic from Turkey due to the increase in cross-border trade and transportation.]

In a study on road traffic fatalities in Iraq from 2010 to 2013, which included Erbil and Sulaimaniya in the Kurdish region, both governorates had the highest fatalities when compared with other locations in Iraq (6). Fatalities were high among children, adolescents and young adults. In Erbil, the capital of the Kurdish region, RTAs were the second major cause of death (7). These estimates are very high especially when under-reporting is common throughout in the region (8).

Many factors contribute to the current situation. After the war in Iraq in 2003, the Kurdish region witnessed rapid economic growth reflected in an increased number of cars travelling on the major roads, from 200 to 500 per day in 2003 to 5,000 to 8,000 per day in 2013 (9). This rapid motorization combined with reckless behaviors, largely by young drivers, has made the highways "death roads," as described by the local population. As Sabey and Taylor report, drivers are responsible for 65-77% of all road crashes (10). According to local traffic police, aggressive road behavior by young drivers, who are less than 33 years old and predominantly male, is one of the principal causes of fatalities and injuries (2). A study by medical students in Erbil identified several risky driving behaviors exhibited by younger drivers; these include speeding, failure to use seat belts and texting/calling while driving (11).These findings suggest that the behavior of drivers is the principal cause of accidents and that an effective road safety education program is urgently needed.

While excessively aggressive driving, sometimes termed 'road rage,' has been identified as a factor in road deaths and injuries in Kurdistan, the problem is considered common throughout the Middle East and North African (MENA) region (12). Countries like Oman, Saudi Arabia, Iran and other countries are aware of this condition. The literature on road deaths and injuries suggests that deaths have a profound psychological impact on the families of the deceased and on a large proportion of survivors (13). Many suffer from post-traumatic stress disorder, major depressive disorders, anxiety disorders, as well as grief, panic and bereavement.

Given the decreasing number of deaths from RTAs, it may be that the public health system in the region is working effectively to reduce fatalities from road accidents but having only modest success in preventing RTAs from occurring and in rehabilitating the survivors of the accidents. It is suggested, therefore, that the development and implementation of effective preventive initiatives and comprehensive rehabilitation services are critical.

At present there are few public health initiatives, like road safety campaigns, in place to inform the public and to mitigate the injuries and trauma caused by RTAs in the Kurdistan Region of Iraq and throughout the region. Road safety campaigns are defined as "purposeful attempts to inform, persuade, and motivate a population (or sub-group of a population) to change its attitudes and/or behaviors to improve road safety, using organized communications involving specific media channels within a given time period" (14).

Adopting behavior change strategies is of considerable interest to road safety professionals because it (is) or (may be) one of the most cost-effective interventions to address RTAs (14). A main purpose of these campaigns is to convince people to abstain from hazardous behaviors and to adopt safe practices. According to current research, behavior can be influenced by delivering well-designed and well-implemented road safety campaigns based on a solid theoretical foundation (15). A well designed campaign takes into account an analysis of local data on road accidents and their outcomes, a more detailed analysis/understanding of why people are engaging in excessively aggressive driving behavior, and developing and implementing a campaign of messaging to change behavior (15). According to Neil Fleming's VAK (visual, auditory, kinesthetic) model, individuals learn new information and change behaviors depending on how the information is delivered and promoted (16). Successful campaigns include various resources and materials that reach and influence the behaviors of that segment of the population most likely to engage in aggressive driving (15). Evidence suggests that effective evidence-based behavior change campaigns should contain four phases: research/design, production, dissemination and evaluation (17).

There are many resources that can be adapted and used to design and implement these campaigns in the Kurdistan Region of Iraq and throughout the region. The online library of road safety mass media campaigns was produced to

Table 2: strategies to achieve immediate, intermediate and long-term results in road safety in the Kurdistan Region of Iraq and other counties in the region are listed below:

Strategies expected to produce results in 18 months
• Start road safety campaigns through an illustrative and animated website in local language
• Create cost effective, accessible and easy to comprehend multimedia materials in local language
• Reinforce road safety messages especially during the time of religious and cultural feasts and events
• Create and put in public places resources like stickers, and posters on road safety in local language
Strategies expected to produce results in 36 months
• Train local authorities and NGO staff in proper public health and road safety education
• Reach out to local remote communities through local community (NGOs) to deliver road safety messages and education
• Develop and implement school education curriculum in all schools and academic institutions
• Create a core action/working groups of community members, volunteers, public health professionals to address the barriers to decreasing RTAs
Strategies expected to produce results in 60 months
• Improve surveillance, data collection and reporting methods
• Establish a program in high-school education focusing on the preparation of young adults for safe driving
• Start partnerships and coalitions with public- and private-sector organizations able to share knowledge and resources to address this problem more efficiently
• Engage concerned policy and decision makers to foster political commitment and enhance leadership
• Measure and evaluate all interventions to determine whether activities are implemented as planned and identify program strengths, weaknesses, and areas for improvement.

inspire, and save time and money for governments and concerned actors willing to develop their own mass media campaigns. This library has materials from the best campaigns from around the world. These campaigns reflect high-quality productions with clear and targeted messages to promote good road safety practices as identified by WHO and others.

In addition, there is an urgent need to implement road safety education on a wide scale in the Kurdistan Region of Iraq and throughout the wider region. Road safety education is "the totality of measures, which aim at positively influencing traffic behavior patterns" (18). This education program has three pillars - promotion of knowledge and understanding of traffic rules and situations, improvement of skills through training and experience, and strengthening and/ or changing attitudes towards risk awareness, personal safety and the safety of other road users.

High death tolls and injuries can be cut sharply if these campaigns are implemented effectively. But behavior change initiatives alone will achieve only modest results and cannot be sustained unless coupled with other measures such as improving roads, law enforcement and driving training (19,20).

There is an urgent need to promote preventive measures and complementary strategies. Some steps have been taken by the Kurdish authorities, like mandatory training

and tests before issuing driver licenses, periodic car inspections, and enforcing speed limit in the urban areas. However, these measures are not enough, and many challenges remain (5). Local authorities and NGOs should identify and adopt approaches and interventions that have proven effective in preventing and reducing road traffic causalities especially among youth. The Global Road Safety Program in Turkey and the Zusha sticker intervention in Kenya, which contributed to improvements in road safety, are examples of such interventions (21,22).

Table 2 (previous page) summarizes strategies to enhance road safety education in the Kurdistan Region of Iraq and other countries in the region. Road safety campaigns utilizing social media to improve road user's behavior and decrease causalities should be considered one of the main initiatives. It is well known that social media - Facebook, YouTube, Twitter and the use of mobile phones - is growing in popularity across the region and is especially popular among youth. Research conducted by the Broadcasting Board of Governors (BBG) and Gallup on media consumption in Iraq reported that 72% of homes in the Kurdistan region of Iraq use the internet and mobile phones to access news and that these media are especially frequented by young adults (23). The success of social media campaigns like the "Embrace Life" YouTube campaign in the United Kingdom, which attracted world-wide acclaim for its content and delivery, is the case in point of the effective use of social media to improve road safety (24). The effectiveness and efficiency of these campaigns could be assessed in Kurdistan before extending these approaches throughout the region. The ultimate success of these campaigns should be measured in terms of reductions in fatalities and RTA rates, and increases in "good", safe behavior/s (25). In addition, the differences in the functional effectiveness of the various social media types should be assessed at the same time to determine which might be most effective in changing behavior and reducing traffic accidents.

Investment in public awareness especially among the youth will increase awareness about the importance of road safety in the region. Failure to seize opportunities to stop this carnage will cost more lives.

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Endotracheal tube cuff pressure in comparison with the standard pressure in intensive care unit intubated patients

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Abstract

Background and aim: The balance of endotracheal tube (ETT) cuff pressure is necessary to prevent complications and to perform a proper therapeutic treatment on the patient. The aim of this study was to determine ETT cuff pressure in comparison with the standard level in intensive care unit (ICU) intubated patients.

Methods: In this descriptive-analytical study conducted in Kashani Hospital in Shahrekord, southwestern Iran in 2014-2015, the 200 ICU patients intubated for any reason participated. All measurements of ETT cuff pressure were conducted by researchers using a manometer, and were expressed as mmHg. In this study, a checklist was used to record the data and then the data were analyzed by the SPSS version 16 using descriptive statistics, ANOVA, t-test, and chi-square test.

Results: Mean cuff pressure was 30.97 ± 16.53 mmHg. The cutoff point of cuff pressure with 95% confidence interval was obtained 28.66-33.28 mmHg. Since this range overlaps the standard range (30-25 mmHg) for cuff pressure, it can be said, with 95% confidence, that the cuff pressure in the target population is in concordance with the standard range. Gender, height, the mean number of intubation days, level of consciousness and decrease of oxygen saturation, lung pharyngeal reflex, and work experience of the cuff filler were not significantly associated with cuff pressure (P > 0.05), but there was a significant association between weight and cuff pressure (P = 0.01).

Conclusion: Although in this study, the cuff pressure in a number of patients was outside the standard range, the cuff pressure was generally in concordance with the standard range.

Key words: Endotracheal tube; Cuff pressure; Intubation

Introduction

Airway management is the first step in treating all patients who are in critical, life-threatening conditions and who have a depressed level of consciousness or a respiratory problem.

To achieve this purpose, various measures are taken, including the insertion of an endotracheal tube (ETT) in the patient's trachea, by a skilled person, thereby providing a safe airway tract for the patient, apart from the gastrointestinal tract, and serving as a respiratory and ventilatory support and exerting positive airway pressure (1, 2).

Despite the great benefits of this therapeutic measure for patients who need it, as with other therapeutic measures, if the complications are not addressed, there may be dangerous and sometimes irreversible complications, one of the most important of which is mucosal injury due to excessive dilation of the ETT, causing certain complications such as erosion, inflammation, softening of the articular cartilage, tracheal dilation, bleeding and infection, and tracheal stenosis. On the other hand, insufficient dilation of ETT cuff leads to pulmonary aspiration and upper airway secretions (3-5).

In order to deal with these complications, the use of the ETTs with low-pressure and high-volume cuffs and adjustment of the pressure inside the cuff to 20-30 cm of H2O is an appropriate and efficient support to prevent aspiration (6, 7).

Due to the known complications of inappropriate ETT cuff pressure, maintenance of cuff pressure during hospital stay at appropriate intervals is important for intensive care unit (ICU) patients.

Therefore, considering the importance of appropriate ETT cuff pressure, to prevent the occurrence of the injuries due to very high or very low cuff pressure, we decided to study the effect of ETT cuff pressure in comparison with the standard range in ICU intubated patients.

Materials and methods

In this descriptive-analytical study conducted in Kashani Hospital in Shahrekord, southwestern Iran in 2014-2015, the participants were the 200 ICU patients intubated for any reason, aged over 8 years, and admitted to the hospital during the study.

History of trachea disease, according to their medical records, the age of under 8 years, and lack of volunteering to participate in the study were considered the exclusion criteria. The participants were selected using convenience random sampling and the sample size was determined to be 200 using a sample size calculation formula.

In this study, a manometer, specifically designed for measuring cuff pressure, was connected to the outer cuff of the ETT and fixed. Pressure was expressed as mmHg, and in all shifts, cuff pressure was recorded. In this study, the measurements of ETT cuff pressure measurements were conducted randomly and subtly by a medical student using a manometer for the 200 patients. The results were expressed as mmHg and then compared with the standard range [25-30 mmHg] (8).

In this study, a checklist was used including information such as age and sex of the patient, height and weight of the patient, systolic and diastolic blood pressure, cause of intubation, the mean number of intubation days, pulse rate, level of consciousness, lung pharyngeal reflex, the work experience of the cuff filler in the ICU, and the level of cuff pressure (9, 10). In this study, the cuff pressure above 30 mmHg was considered to indicate over-inflation and the pressure between 30 and 25 mmHg was considered normal pressure (8).

Data were analyzed by the SPSS version 16 using descriptive statistics, ANOVA, t-test, and chi-square test.

Results

Mean cuff pressure was 30.97 ± 16.53 (range: 9-91) mmHg. 44% of the patients had lower-than-standard range cuff pressure, 16% had standard cuff pressure, and 40% had higher-than-standard range cuff pressure.

The cutoff point of cuff pressure with 95% confidence interval was obtained at 28.66-33.28 mmHg. Since this range overlaps the standard range (30-25 mmHg) for cuff pressure, it can be said, with 95% confidence, that the cuff pressure in the target population is in concordance with the standard range.

Age, height, and the mean number of intubation days, were not significantly associated with cuff pressure (P > 0.05), but there was a significant association between weight and cuff pressure (P = 0.01) (Table 1).

Table 1: Correlation Coefficients and P Values for Relationship between Cuff Pressure and Variables

Variable	Age	Weight	Height	The average of the days of intubation
The correlation coefficient	0.08	0.18	0.11	-0.01
p-value	0.09	0.01	0.09	0.15

The results showed that gender, level of consciousness and decrease of oxygen saturation, lung pharyngeal reflex, and work experience of the cuff filler were not significantly associated with cuff pressure (P > 0.05) (Table 2).

Table 2: Distribution of mean cuff pressure in terms of gender, decrease of oxygen saturation and level of consciousness, work experience of the cuff filler, and lung pharyngeal reflex

Variable		Cuff pressure (MmHg)	p-value
		Mean±SD	
Sex	Male	29.32±17.22	0.12
	Female	28.56±15	
Reduced oxygen levels and consciousness	Reduced oxygen levels in patients	30.96±93.15	0.99
	Reduced consciousness levels in patients	30.98±17.41	
Work experience	1-5 years	27.08±14.23	0.43
	5-10 years	32±17.92	
	>10 years	31±14.89	
Laryngopharyngeal reflux	Intact	32.55±17.99	0.35
	Non-Intact	30.21±15.79	

Discussion

The general objective of this study was to determine ETT cuff pressure in comparison with the standard level in the ICU intubated patients in Ayatollah Kashani Hospital in Shahrekord.

The analysis of the results showed that 95% of the recorded results of cuff pressure in these patients were within the standard range. Therefore, it is necessary to measure and record other vital variables in patients admitted to ICU to measure ETT cuff pressure at appropriate intervals.

A study by Sole et al. to investigate the factors influencing cuff pressure, showed that cuff pressure was within the recommended range in 60% of the patients, but the rest of the patients had a cuff pressure higher or lower than normal range. That study emphasized frequent cuff pressure monitoring to reduce false positives (11).

The study of Vyas et al., showed that in 32 ICU patients, the measured ETT cuff pressure was higher than the recommended range in 62% of these patients (12).

In the study of Sharifi et al., in Hamedan Hospital, 65% of the ETT cuff pressure measurements for the patients were higher than the recommended range (13). It is obvious that several factors affect the ETT cuff pressure. For example, with an increase in the duration of the intubation, the ETT cuff pressure is gradually reduced.

The result of our study showed that there was not any significant association between cuff pressure and height (P = 0.09), age (P = 0.9), duration of intubation (P = 0.15), and gender (P = .12), but the cuff pressure was significantly associated with the weight of the patients (P = 0.01) so that cuff pressure was observed to increase with increasing weight of the patient. Ezri et al. also emphasized, in their study, that according to their results, the incidence of intubation increased in male patients with overweight (BMB/BMG > 35 kg/m2) (14).

In the study of Sengupta et al., the relationship between the ETT cuff pressure and demographics was investigated in 93 patients.

The results of that study showed that there was no significant relationship between age and height of the patient and even the place of admission (private or public hospital) and the size of the ETT, and the ETT cuff pressure.

In addition, in that study, 27% of the cuff pressure measurements were within the standard range, and 27% of the measurements exceeded the standard range (15).
In our study, the work experience of the cuff filler and cuff pressure were not significantly associated (P = 0.43).
In a similar study by Hoffman et al., they determined the correct level of cuff pressure adjusted by the experienced physicians in emergency departments, and concluded that the physicians were not able to estimate the ETT cuff pressure and recommended that more precise instruments be used to evaluate this pressure (16).

In our study, it was found that there was no significant relationship between cuff pressure and the level of consciousness, heart rate, systolic pressure, and diastolic pressure in the patients (P < 0.05). In addition, changes in the ETT cuff pressure were investigated by the patient's activity and position on the bed.

The results showed that in patients with more in-depth anesthesia and lower GCS score, the cuff pressure was lower than the patients with less in-depth anesthesia and higher GCS score.

As these patients are more active, this study recommends more frequent monitoring of the cuff pressure in patients with a higher level of consciousness, because the changes in cuff pressure are more pronounced in these patients. The height of the head from the bed and the neck position also affects the cuff pressure (11).

Conclusion

Although in this study, the cuff pressure in a number of patients was outside the standard range, the cuff pressure was generally in concordance with the standard range.

Therefore, precise monitoring of the ETT cuff pressure at proper intervals is necessary, which, necessitates, an efficient and defined management in the ICU. It is suggested that future studies assess the incidence rate of pulmonary complications and pulmonary function.

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Comparison of infection of injectable serum solutions administered by upper and lower air bleeding in patients hospitalized in surgical wards

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Abstract

Background and Aim: Because hospital infections are one of the major causes of increasing the length of hospital stay, increasing the cost of treatment and mortality and morbidity in patients hospitalized in different wards of the hospital, especially the surgical wards, this study was conducted to determine the prevalence of infection due to injectable serums administered by the two methods upper and lower air bleeding.

Materials and Methods: This descriptive-analytical study was conducted in 2014 at Kashani Hospital in Shahrekord, southwest of Iran. The microbial samples of 250 serums attached to patients hospitalized in different wards of the hospital were collected and were cultured in vitro. Data for serum characteristics, serum bleeding method, and patient's characteristics were collected by a checklist and analyzed by the SPSS version 22.

Results: There was a significant association between the average time interval between serum attachment and sample collection in positive and negative culture samples, and the frequency distribution of microbial culture results with respect to time interval (P < 0.001).

The result of microbial culture was negative in 247 cases (98.8%) and positive in 3 cases (1.2%). The bacteria grown in the culture medium were Acinetobacter in 1 case (0.4%), fungus in 1 case (0.4%), and Staphylococcus epidermidis in 1 case (0.4%). There was no significant difference in the culture result in terms of bleeding method (P=0.59).

Conclusion: Bleeding of injectable serum due to air pollution in hospital wards has contributed to the infection of these serums, and although the serum bleeding method did not differ in the number of cases of infection development, the number of infection development was higher for the serums administered by lower bleeding.

Key words: Infection; Injection; Serum; Hospitalization; Patients.

Introduction

Injections are one of the most common methods in prescribing drugs and pharmaceutical derivatives. Obviously, in the case of non-compliance with the therapeutic standards, it creates many dangers such as infection in health care service users (1).

Infection of the skin and soft tissues are some of these infections (2, 3), ranging from Staphylococcal infection to dangerous infections such as HIV and hepatitis B and C (4-8). Injection infections, in addition to causing illness in hospitals highly frequently, impose high hospital and medical costs (9), which require health care personnel and nurses to adopt preventive strategies (10).

Bacteria and other airborne objects in the hospital may enter the serum solution during infusion and infect the contents of the serum. In addition to the factors contributing to the contamination of the serum, such as personnel's hands, contamination of the infusion site, contamination of the secondary equipment such as infusion set and vein set and the primary contamination of the fluid, the contents of the serum can be contaminated during bleeding and the airborne bacteria may enter the solution through a pore that has been created to let the air enter (11).

Hence, considering this issue important, not only leads to saving so many lives, but also affects the health of the community (12). Therefore, it is very necessary to find preventive methods to deal with this problem (13).

Currently, in hospitals of Iran, for the bleeding of injectable serums, a pore is created by the needle in the upper part, or the air is drawn through the lower part, i.e., lower bleeding, which in both ways allows the serum fluid to be contaminated.

However, so far, no study has been done on this issue. Therefore, considering the importance of preventing hospital infections and the possible transmission of infection through serum bleeding, it seems necessary to investigate this issue. The aim of this study was to determine the frequency distribution of microbial contamination of injectable serums in the two methods of bleeding, i.e., upper and lower bleeding.

Materials and Methods

This is a descriptive-analytical study conducted in 2014 at Kashani Hospital in Shahrekord, southwest of Iran. The study population of this study consisted of inpatients in surgical and internal wards and under serum therapy from whom our patients were selected by convenience sampling.

Inclusion criteria were treatment with serum injected into the patient in various internal and surgical departments, agreement of the departmental authorities to sample the serum injected, and not adding antibiotics to the serum content.

The accidental contamination of serum during injection, such as the fall of serum from the hands of the administrator staff, and exit of serum from the patient's hand before it was completed, were exclusion criteria. Based on the sample size calculation formula, the number of the samples for each group was estimated at 125.

After labeling the serum with adhesive labels, the serum characteristics including the type, volume, production date, expiration date, and the type of auxiliary equipment, such as the type of set, the type of vein set or branula and their expiration dates, as well as the time of serum injection and the patient's characteristics, including age, gender, and the type of illness were recorded in a special checklist.

Serum characteristics, bleeding method, and other information were collected by one of the research team members and recorded in a checklist that had been designed, for this purpose, by a group of infectious specialists, surgeons, and statisticians. The results of microbial culture of the samples were also recorded in the checklist after they were received from the laboratory.

Bleeding method was also determined randomly; in the upper bleeding, the sets without bleeding pore (simple sets) were used, and a needle no. 22, after attaching the serum to the upper level of solution, was introduced into the container; and in the lower method, the sets with lower air inlet pores were used. After the completion of the serum, when 10 cc of the serum was left, 10 cc of serum solution was collected with a 10 cc syringe under sterile conditions and then was sent to the laboratory for microbial culture.
In the laboratory, the samples were cultured in eosin methylene blue agar and blood agar and a smear was prepared for simultaneous hot staining. After 72 hours, the growth of the bacteria in the samples was examined and the type of bacteria grown in the culture medium was determined and the results were recorded in the checklist for each serum.

Data were analyzed by the SPSS version 22. Statistical tests used for data analysis were t-test, Fisher's exact test, Chi-square test, and one-way ANOVA.

Results

Of the samples collected, 198 cases (79.2%) were 1/3–2/3, 25 cases (10%) Ringer's lactate, 15 cases (6%) normal saline, 4 cases (1.6%) Dextrose, and 8 cases (3.2%) other injectable serums (1 case of albumin, 1 case of homoxyl, 2 cases of vellon, and 4 with half-saline). In the upper bleeding group, 114 samples, and in the lower bleeding group, 84 samples of the injectable serum were 1/3–2/3 (82.6% vs. 75%).

Also, in the groups upper bleeding and lower bleeding, there were 15 and 10 serum solutions of Ringer's lactate type (10.9% vs. 8.9%). On the other hand, in the groups of upper bleeding and lower bleeding, there were 3 and 12 normal saline solutions (2.2% vs. 10.7%), 3 and 1 glucose solutions (2. 2% vs. 0.9%), and 3 and 5 injectable serums of other types (2.2% vs. 4.5%), respectively. According to the Fisher's exact test, the serum type was not significantly different between the two groups (P = 0.06).

The volume of injectable serum was 250 cc for 180 cases (72%), 1000 cc for 62 cases (24.8%), and 500 cc for 8 cases (3.2%). Serum expiration date was 1 year for 4 cases (1.6%), 2 years for 116 cases (46.4%), 3 years for 57 cases (22.8%), 4 years for 49 cases (19.6%), and 5 years for 5 cases (9.6%). The average interval between serum attachment to the patient and sample collection was 1.92 ± 1.19 hours.

Also, the time interval between serum attachment and sample taking for 116 cases (46.4%) was less than 2 hours, for 114 cases (45.6%) between 2 hours and 3 hours, and for 20 cases (8%) over 3 hours. 172 cases (68.8%) of the samples were collected in the morning shift, 42 (16.8%) in the evening shifts, and 36 samples (14.4%) in night shifts.
Of the 250 serum samples, 55 (22%) were collected from the surgical ward, 77 (30.8%) from the internal ward, 16 (6.4%) from the intensive care units, 28 (11.2%) from the pediatrics and gynecology wards, and 74 samples (29.6%) from the emergency department.

Among the 250 studied serums, upper bleeding was performed for 138 cases (55.2%) and lower bleeding for 112 cases (44.8%). The result of microbial culture was negative for 247 cases (98.8%) and positive for 3 cases (1.2%). The bacteria grown in the culture medium were Acinetobacter in 1 case (0.4%), fungus in 1 case (0.4%), and Staphylococcus epidermidis in 1 case (0.4%). There was no significant difference in the culture result in terms of bleeding method (P=0.59) (Table 1).

Interestingly, the Acinetobacter-containing samples were from the serums administered by upper bleeding and the fungus and S. epidermidis-containing samples were from the the serums administered by lower bleeding.

Table 1: Distribution frequency of culture results for the two methods of bleeding

Bleeding method	Negative		Positive		Total		P value
	Number	Percent	Number	Percent	Number	Percent	
Upper	137	55.5	1	33.3	138	55.2	
Lower	110	44.5	2	66.7	112	44.8	0.59
Total	247	100	3	100	250	100	

On the other hand, there was no significant difference in serum type between the two groups (P = 0.20) (Table 2). It should be noted that the Acinetobacter and fungus samples were observed in 1/3–2/3, and S. epidermidis in another type of serum (albumin).

Table 2: Distribution frequency of culture results for different types of serum solutions

Culture result in different types of serum solutions	Negative		Positive		Total		p-value
	Number	Percent	Number	Percent	Number	Percent	
Dextrose saline	196	79.4	2	66.7	198	79.2	
Ringer's lactate	25	10.1	0	0	25	10	
Normal saline	15	6.1	0	0	15	6	0.20
Dextrose	4	1.6	0	0	4	1.6	
Others	7	2.8	1	33.3	8	3.2	
Total	247	100	3	100	250	100	

There was no significant difference in the result of the culture according to the expiration date (P = 0.22) (Table 3). In addition, the expiration date for the Acinetobacter-, fungus- and S. epidermidis-containing samples was 3 years, 3 years, and 4 years, respectively.

Table 3: Distribution frequency of culture results for the expiration date of serums

Culture result based on serum expiration	Negative		Positive		Total		P value
	Number	Percent	Number	Percent	Number	Percent	
1 year	4	1.6	0	0	4	1.6	
2 years	116	47	0	0	116	46.4	
3 years	55	22.3	2	66.7	57	22.8	0.22
4 years	48	19.4	1	33.3	49	19.6	
5 years	24	9.7	0	0	24	9.6	
Total	247	100	3	100	250	100	

There was no significant difference in serum microbial culture among different hospital wards (P = 0.44) (Table 4). It should be noted that the Acinetobacter-containing sample was collected from gynecology surgery ward, the fungus-containing sample was collected from neurosurgery ward, and S. epidermidis-containing samples were collected from the urology ward.

Table 4: Distribution frequency of culture results in different hospital wards

Culture result in different wards	Negative		Positive		Total		P value
	Number	Percent	Number	Percent	Number	Percent	
Surgery	54	21.9	1	33.3	55	22	
Internal	77	31.2	0	0	77	30.8	
Intensive care unit	16	6.5	0	0	16	6.4	
Pediatrics and gynecology	27	10.9	1	33.3	28	11.2	0.44
Emergency	73	29.6	1	33.3	74	29.6	
Total	247	100	3	100	250	100	

The average time interval between serum attachment and sample collection for the positive culture samples was 5.83 ± 0.29 and for the negative culture samples was 1.87 ± 1.01 hours. According to the t-test, the difference between the two groups was significant (P < 0.001) (Table 5). Fisher's exact test also showed that there was a significant difference in the frequency distribution of microbial culture results in terms of the time interval between serum attachment and sample collection (P < 0.001).

Table 5: Distribution frequency of culture results for the time interval between serum injection and sample collection

Culture result based on interval between serum attachment and sample collection	Negative		Positive		Total		P value
	Number	Percent	Number	Percent	Number	Percent	
< 2 hours	116	47	0	0	116	46.4	
2-3 hours	114	46.2	0	0	114	45.6	0.00
> 3 hours	17	6.9	3	100	20	8	
Total	247	100	3	100	250	100	

According to the results, there was no significant association between the shift of sample collection and the microbial culture result (P = 0.13) (Table 6).

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Table 6: Distribution frequency of culture results for the shifts of sample collection

Culture result based on shift of sample collection	Negative		Positive		Total		P value
	Number	Percent	Number	Percent	Number	Percent	
Morning	171	69.2	1	33.3	172	68.8	0.13
Evening	40	16.2	2	66.7	42	16.8	
Night	36	14.6	0	0	36	14.4	
Total	247	100	3	100	250	100	

There was no statistically significant difference in age, length of hospital stay, gender, and having catheter between the positive culture and negative culture groups (P > 0.05) (Table 7).

Table 7: Frequency distribution of microbial culture results with respect to demographic characteristics

Culture result Variable		Positive Mean±SD	Negative Mean±SD	P value
Age		70.7±15	57.3±23.6	0.33
Length of hospitalization		4.33±2.08	8.77±12.8	0.55
Variable		N (%)	N (%)	p-value
Sex	Male	1 (33.3)	159 (64.4)	0.30
	Female	2 (66.7)	88 (35.6)	
Catheter	Yes	3 (100)	191 (77.3)	0.59
	No	0 (0)	56 (22.7)	

Discussion

The general aim of this study was to determine the frequency distribution of microbial infection of injectable serum solutions in the serums administered via upper and lower bleeding. In this study, of the 250 serum samples collected from injectable serum solutions administered to hospitalized patients, 3 samples (1.2%) had culture positive. The study by Gupta et al. also showed that unsafe injection increased the incidence of hepatitis B in the community (6).

For serum type, the bacterial infection for 2 cases (66.7%) was found in 1/3–2/3 solutions and 1 case (33.3%) was observed in another type of solution (albumin).

The point to consider is that serums containing biological compounds such as albumin and blood, due to providing a good environment for bacterial growth, are more exposed to contamination, and in contrast saline serum solutions, such as normal saline, due to being an unsuitable environment for microbial growth, have less potential for contamination. Thus is especially important for storage of injectable serums (14).

In terms of expiration date, out of three positive cultures, the expiration date of 2 samples (66.7%) was 3 years and the expiration date of 1 sample (33.3%) was four years; and although there was no significant difference between the two methods of bleeding due to the small number of cases of positive culture, several studies have shown that injectable solutions, after expiration date, in addition to being predisposed to potential chemical changes in the solution, are also predisposed to microbial growth, which can be due to the provision of suitable conditions for microbial growth in the deformed solution, damaged package, or preservatives (15).

In terms of hospitalization, of the three positive culture samples, one was collected from the surgical ward, one from the gynecology ward, and one from the emergency ward. So far, numerous studies have been performed on environmental contamination in different wards of the hospital, most of which have shown that infectious disease and surgical wards have higher environmental contamination than other wards, and, in contrast, transplantation and surgical have the lowest environmental pollution (16).

Another noteworthy point is the storage conditions of injectable solutions in drug depots and hospital wards, which may lead to contamination and the growth of microbial agents due to possible damage and unfavorable storage conditions. Even, in certain cases, skin contamination can cause infection despite performing decontamination. A study conducted by Wang et al. in 2015 showed that Staphylococcus aureus could cause infection in a standardized decontamination device because of resistance to disinfectants (17).

Injectable serum solutions are completely sterile liquids and no microbial contamination, whether pathogenic or non-pathogenic, should be detected in them, and the contamination of the samples studied is likely to be due to secondary contamination during injection due to non-

compliance with sterile conditions when installing fittings to the solution.

On the other hand, the contamination of the air in different wards of the hospital with bacteria is also likely, and therefore it is argued that the passage of air bubbles from the solution that is being infused in the serum solutions that are administered by lower bleeding causes solution contamination. In our study, 3 cases of contamination were observed, of which 2 cases were found in the serum solutions administered by lower bleeding.

However, because of the very low prevalence of microbial contamination in injectable solutions, the observation of 3 cases of contamination can be an accidental finding and not related to the method of bleeding, although other studied variables in the samples of positive culture and negative culture also showed that the interval between serum attachment to the patient and sample collection had a significant effect on the contamination of the solution.
Therefore, the microbial contamination of injectable solutions is most likely to be due to the entry of the air with bacterial contamination during bleeding or non-compliance with sterile conditions when connecting the injection set to the serum solution bottle.

Conclusion

The bleeding of injectable serum solutions has contributed to the contamination of injectable serums due to indoor air contamination in the hospitals, and although the bleeding method did not cause any significant difference in the number of infection development, the number of infected cases was higher for the serum solutions that were administered by lower bleeding.

Therefore, it is recommended that for the injectable serum solutions, upper bleeding be used as much as it is possible so that the likelihood of contamination of injectable serum solutions is minimized. It is also recommended that long-term serum administration of the serum solutions to patients be avoided, especially if the patient is transferred to different wards.

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Evaluating the quality of nursing documentation in pediatric wards of Motahari Hospital of Urmia in 2017

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Abstract

Introduction

Nursing documentation is a set of written information, transmitted in the form of a document with regard to patient's health and care status (1). It is a legal and professional action for people involved in health care affairs, including nurses (2). One of the important elements of medical documentation is patient records (3). It involves a process, indicating the activities performed by nurses for patients (4). Thus, it should have desirable quality.

Observing the standard principles in recording the nursing reports results in an exchange of information among the members of the care team, ensuring care is provided for clients (2), understanding the defects in the measures taken (5), the continuity of care provided for patients, enhancing the quality of care provided for client, increasing nurses' professional credibility, and increasing the credibility of the therapeutic-care institute and ensured nursing work. In contrast, undesirable recording would result in some problems, for example, the nurses may be sentenced in the legal authorities and slowdown in the treatment process. Legally, the function or performance is accepted and defended in the medical team where it is recorded (3).

Hence, given their importance, nursing documentation should have desirable and comprehensive conditions, in a way that it results in acceding to documentation goals, such as communication, educational, research, monitoring and evaluation goals of the health system and obtaining necessary information on patients based on proper principles (6). Additionally, desirable documentation should have accurate information on nursing examinations, patient problems, caring plans, daily progress course, educational plans and discharge plan. The nursing reporting principles include two dimensions of structure and content, in which the content includes recording the general status, drugs prescribed, instructions and acute changes, preventable cases, paraclinical findings, vital signs, and the recording of the discharge programs. In the structural dimension, the author characteristics, the time and date of the report are considered (7).

Despite the importance of recording nursing reports, various studies have indicated that nursing reports do not have desirable quality and standard. Findings of a study conducted in England revealed that 83% of medical records are incomplete in terms of documentation of the vital signs and the course of disease completed by physicians and head nurses (5). Findings of research conducted on 457 hospital records in the Educational Hamedan University of Medical Sciences in 2010 revealed that none of the medical records was fully completed (8). The research conducted by Paans et al in 2010 (9) showed that only 28% of the reports had a full nursing process.

The research conducted by Jasemi et al in 2012 on documentation (10) also provided the same results. They indicated undesirable quality of documentation at the content dimension and lack of paying attention to the

eleven principles by nurses during recording of reports (11). As observing the proper principles in recording the nursing documentations plays a major role in protecting the patient's life and the safety of nurses, and as no research has been conducted so far on the quality of nursing documentation in pediatric wards in Iran and other countries, and given the fact that the pediatric wards are considered among the most critical wards of the hospital and nursing reports require high accuracy in providing the care, investigating this issue in the pediatric wards has high importance. Thus, the current research was conducted to evaluate the quality of nursing documentation in the pediatric wards of the Shahid Motahari Hospital of Urmia in 2017.

Methodology

The current research is a descriptive study (with ethical code of IR.TBZMED.REC.1395.1326, approved by Tabriz University of Medical Sciences), in which the quality of nurses' documentation in the internal surgical pediatric wards of Shahdi Motahari Hospital of Urmia was investigated. The research population included all nursing staff of the hospital. Inclusion criteria of research included having at least three months of work experience, having a bachelor degree and higher and direct clinical work with the patient. Lack of willingness to participate in the research was the exclusion criterion of the research. The sample size was calculated to be 159 nurses using the previous studies. Considering the probability of sample drop out, all 175 qualified nurses were selected as sample of study using the census method (12). In order to evaluate the quality of each nurse's documentation, a number of medical records in the ward were selected randomly after obtaining informed consent from them. Among the reports of working shifts and previous days, three reports (one report of each shift) were evaluated for each nurse, and if three reports of one nurse were not found in one medical record, other records were used.

The data collection tool was a demographic questionnaire (including questions on individual and job information of the nurses) and a checklist for reviewing the documentation. Demographic characteristics were completed through interviewing with nurses and information recorded in the reporting book of the ward. A 59-item checklist was used for examining the documentation of the patients' record. It was developed by reviewing the research literature and standards developed by the Ministry of Health. It included 4 options, in which the option "yes" received the score 2, option "relatively" received the score 1, and the option "no" received the score 3, and if one of the items in the checklist was not true in a medical record, that item was not considered in calculating the total score. The mean score of each checklist was obtained by dividing the total scores of the used items on the number of items. To match all items uniformly, the mean score of each item was converted to a percentage. In order to facilitate the process of judgment on quality of the documentation, the obtained scores were classified and reported in three levels of poor (less than 33%), moderate (33-66%) and desirable (66-100%). The validity of this checklist was evaluated by obtaining the view of 10 nursing professors and required corrections were

applied. The level of agreement of observers was used to determine the reliability of the checklist. Accordingly, 10 primary medical records were examined and scored by two people and the level of agreement between the observers was evaluated by using Cohen's kappa coefficient and it was obtained to be 0.70%, which is an acceptable value.

After entering the data into SPSS 21 software, they were analyzed using descriptive statistics and reported in the form of mean, SD, number, and percentage.

Findings

In the present research, 525 reports of 175 nurses were evaluated. The mean age of employed nurses was 28.48 ± 5.57 years and their mean work experience was 5.09 ± 4.86 years, and they cared for 9.55 ± 3.06 patients on average. Investigations revealed that nurses had physical overtime of 76.98 ± 19.31 hours per month on average, in addition to their obligatory shifts. Other demographic characteristics of nurses are presented in Table 1.

Table 1: Demographic characteristics of nurses working in pediatric wards

Variable		N (%)
Gender	male	2(1.1)
	female	173 (98.9)
Marital status	Single	73 (41.7)
	Married	102(58.3)
Educational level	Bachelor	173(98.3)
	Master	3(1.7)
educational courses on documentation	Completed	139(85.8)
	Not completed	23(14.2)
Age (year)	mean± SD	28.54± 5.49
	Min-max	22-46
Overtime (per month)	mean± SD	76.98±19.31
	Min-max	20-120
Work experience (year)	mean± SD	5.09±4.86
	Min-max	1-20
Number of patients of nurses	mean± SD	9.55±3.06
	Min-max	4-20

The statistical investigations revealed that the documentations of morning shift had desirable and moderate quality, and the quality of the documentations in different shifts was in the range of 83.4 to 95.4%, and all of them were placed in the range of desirable quality. While the general score of documentation quality in the evening shift was low, no significant difference in the quality of the reports of different shifts was seen (Table 2).

Table 2: Quality of reports of nurses working in pediatric wards in different shifts

		Quality					
		Desirable		Moderate		Poor	
Variable		n	%	n	%	n	%
Working shift	morning	167	65.4	8	4.6	0	0
	evening	146	83.4	28	16.0	1	0.6
	night	166	94.9	5.1	9	0	0
	total	165	94.3	10	5.7	0	0

With regard to the relationship between the quality of nursing documentation and some individual and social characteristics of nurses, findings revealed significant and inverse relationship between the age and work experience and quality of the documentations, so that quality of nursing reports is reduced by increasing the age and work experience of nurses (Table 3).

Table 3: The relationship between some of the individual and social characteristics and research subjects' documentation

Individual and social characteristics	age		Work experience		Completing the educational course		Educational level		Marital status		Number of patients	
	P	R	P	R	P	R	P	R	P	R	P	R
Total score of quality of documentations	0.000	- 0.28	0.000	-0.27	0.30	0.08	0.84	0.01	0.15	0.10	0.89	0.01

Discussion

Research findings in general revealed that the documentation examined in the pediatric ward of Motahari Hospital of Urmia had a desirable and moderate quality. In line with present research findings, in the research conucted by Rangraz et al to examine the quality of 540 records of nursing documentation, it was found that only 11% of these medical records did not include the necessary information (13). In addition, in the research conducted by Aryaee, findings revealed that all nursing documentation had necessary information on the nursing care (14). One of the reasons for desirability of nursing documentation in the present research might be holding educational courses on in-service reporting.

Based on the nurses' demographic characteristics, 139 nurses completed the educational courses on in-service reporting. Findings of the research conducted by Abbas Zadeh et al indicate that continuous educational programs have significant impact on knowledge, attitude, and performance of nurses in the reporting area (3). Moreover, findings of the research carried out by Asghari et al suggest the positive impact of continuous educational programs on knowledge and performance of nurses (15). In the research carried out by Karimi et al to identify the factors affecting the quality of documentation of medical records, it was found that the quality of documentation increased as a result of high knowledge and attitude. Thus, holding educational courses on documentation would have great impact on improving the quality of nursing documentation (2), which is in line with the result of the current research.

Findings of our research were not in line with those of some studies conducted in this regard. Examining 140 medical records of nursing reports, Ghasabi et al concluded that the nursing reports did not have desirable quality at content dimension (11). In the research carried out by Nohi et al, findings revealed that nursing reports did not have desirable status (16). Moreover, in the research carried out by Mahjub et al, findings revealed that the completion of the examined papers was not at the desirable level and it was very poor in some cases (17). Some reasons for this inconsistency might be using different sample sizes, general structure of the checklists used to examine the quality of documentations, the wards examined, and different research methods. Investigating the relationship between the quality of nursing documentation and some of the demographic

variables in the current research revealed a significant and inverse relationship between the age and work experience and quality of the documentation, so that the quality of nursing documentation was reduced by increasing the age and work experience of the nurses (Table 3). This finding is consistent with findings of the research carried out by Hallajpour in 1997, in which the researcher examined 50 medical records in Tehran. In the mentioned research, the researcher concluded that factors of age, experience, and type of employment affect the quality of recording the documentation, so that quality of nursing documentation is reduced by increasing the age and work experience (17). In a study conducted on 170 nurses working in internal surgical wards of Tabriz hospitals in 2010, Madineh Jasemi et al examined the quality of nursing documentation and factors affecting it. They concluded that there is a significant relationship between demographic variables such as ward type, employment, the hospital where nurses are working, and work experience (10); that finding was consistent with the findings of this research. The inverse relationship between the quality of documentation and work experience and the age of nurses could be attributed to the impact of increased work experience, reduced motivation of nurses, high workload, excessive fatigue during work shift, in which older people experience this fatigue more, passage of time from educational course. In research conducted in 2002, findings revealed that by increasing the work experience of nurses, the educational needs of them also increase (18).

Given the importance of nursing documentation in recent years, authorities have paid increasing attention to quality of documentation. Thus, it is recommended that workshops be held in hospitals in order to enhance quality of the documentation. In this regard, the pediatric ward in Motahari Hospital of Urmia has used these programs. Findings of the current research suggest that these workshops have been effective and they could enhance the quality of nursing documentation. This research suffers from some limitations: first, the wards examined in this research included internal surgical pediatric wards, while intensive care and emergency units were not examined in the present research. Second, only 3 sets of documentation were examined for each nurse, so the number of the examined cases for samples might be low. Thus, it is recommended that other studies with better research methods, larger sample size, and other wards and hospitals be examined. Given the significant relationship between the quality of the documentation and some

of the individual and social characteristics, it is recommended that some studies be conducted on the impact of these factors on the quality of documentation.

Conclusion

According to findings of the present research, the nursing documentation had a desirable quality and examining the relationship between demographic variables and the quality of documentation showed that the quality of nursing documentation is reduced by increasing age and work experience.

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The effect of passive leg raising maneuver on right internal jugular vein dimension in ICU patients under mechanical ventilation

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Abstract

Introduction: To improve accessibility, central vein catheterization in the upper body region is classically done in Trendelenburg position but it may impose potential disadvantages to respiratory system and disturb physiologic status of many other organs. Passive leg raising (PLR), a simple maneuver, widely used to improve cardiac preload and to predict patients' volume responsiveness could be an alternative.

Objectives: In this study, we evaluated the effect of PLR maneuver on right internal jugular vein (RIJV) dimension in intensive care unit patients under mechanical ventilation.

Methods: As a prospective study, twenty patients under synchronized intermittent mandatory ventilation (SIMV) without valvular heart problem or heart failure and acute respiratory distress syndrome were studied. RIJV dimension was measured with bedside ultrasonography of neck, first in supine position and then for second and third measurement, after 30° PLR for 1 and 5 minutes. Measurements were at the end of inspiratory cycle with positive end expiratory pressure of 5. We chose 30° PLR to keep bedridden patients away from possible damage that may be induced with higher upward slope.

Results: RIJV diameter increased with 30° PLR maneuver, and reached its utmost at 5 minutes in comparison to 1 minute point (p < 0.0001). Mean RIJV diameter was 10.2 mm in supine, increasing to 11.2 mm and 11.5 mm, 1 and 5 minutes after 30° PLR maneuver respectively. Increments in diameter were slightly lower than that associated with Trendelenburg position reported in other studies. No complication was noted.

Conclusions: PLR maneuver can be safely considered as an alternative to Trendelenburg position to increase internal jugular vein dimension in mechanically ventilated patients.

Key words: internal jugular vein, passive leg raising, mechanical ventilation, ultrasonography

Introduction

Passive leg raising (PLR), a maneuver of bringing both legs up from supine position, is a surviving method used by emergency paramedics in times of circulatory collapse. Recently this procedure has been under interest for assessing hemodynamic status and diagnosis of intravascular volume depletion as it is observed that it could increase cardiac preload(1) easily and non-invasively. Raising legs induces transferring of blood reserved in lower extremities to the central compartment and finally to the heart. In a study on radioactive tagged erythrocytes, following PLR, blood content of calves depleted about 150 cc and this volume of venous return enhances circulation by augmenting right ventricle preload(2).

Multiple studies show different aspects of hemodynamic change following PLR such as increase in pulmonary artery occlusion pressure(3,4), end diastolic dimension of left ventricle (3,5), enhancing E wave of mitral valve flow(3,6,7), prolongation of left ventricle ejection(8), also improving sublingual microcirculation and perfusion(9). All of these changes confirm that the volume of blood redistributing after PLR is sufficient to possibly expand left heart preload. Surprisingly, preload expansion disappears after returning legs to supine position thus this maneuver is assumed as a reversible intervention(4,8,10,11). Furthermore, some studies indicate that PLR is capable of boosting cardiac output such as intravascular administration of 300 cc colloid even in patients under mechanical ventilation (MV) (4). Moreover this enrichment is not affected by arrhythmia or ventilator setting. In a survey of 71 patients suffering from hemodynamic shock, PLR increases aortic flow time, a marker of increased left ventricle preload. Also it is proved that PLR can be used as a measure to anticipate responsive and non-responsive patients in time of fluid therapy(8).

Central vein catheterization (CVC) is a standard way of measuring central vein pressure and a route of vasoactive drugs` and chemotherapy agents` administration as well as intravascular volume resuscitation or evacuation of embolized air bubble in affected patients. This is a safe method for multiple sampling in admitted patients when peripheral lines are not accessible. More than that, through central veins we can install temporary hemodialysis, catheterize pulmonary artery or implant pacemaker`s wires(12). From the introduction of this method in 1960, right internal jugular vein is the most preferred location by the anesthesiologist to access upper body central veins(13,14). A maneuver conventionally tried for successful catheterization is to lower head below body level, known as Trendelenburg (TDB) or head down position, which makes cervical veins congest, and helps to reach central veins more easily (15,16,17).

Unfortunately, TDB position has serious consequences on cardiovascular, respiratory and cerebral systems. In a review study on more than 290 articles in 2010, authors concluded that this position not only causes disadvantage on cardiac output but also some undesirable effects

observed even after returning patient back to supine position(18). Also seen is increased intra-cranial and ocular pressure(19,20), edema of face, eyes, tongue and larynx with feasible risk of upper airway obstruction, when individuals are placed in head down position for a long period of time. Besides that, patients are in danger of regurgitation or aspiration due to upper displacement of stomach(20,21). Moreover functional residual capacity of lung diminishes, leads to aggravation of breathing work in individuals with spontaneous respiration as intra abdominal organs are pressing on the diaphragm as well as in patients under MV in some settings (e.g. peak airway pressure) should be changed to maintain adequate ventilation(22,23).

Due to near similar consequences of both PLR and TDB on increase of jugular vein dimension, we evaluated the possibility of using PLR as an alternative maneuver. The effect of PLR to expand right internal jugular vein already has been determined in healthy volunteers in relation to controls, in a study performed by Kim et al. Their measurements showed about 25% increases in vein diameter (P < 0.0001) but it was lower than TDB change (25% vs. 48%), they noted (24). Another study in 2013 on anesthetized pediatric cases with cardiac shunts, candidates for repairing of congenital heart diseases, demonstrated that both maneuvers were successful in engorgement of jugular vein(25). Considering the necessity of access to central veins in critical care units, where patients are usually ventilated by mechanical ventilators and in situations when TDB or head down position is harmful to particular patients, PLR advantages should be confirmed again. If we want to apply this method, the first step will be demonstrating PLR effects in increasing jugular vein diameter.

Materials and methods

Our study is a prospective clinical trial performed on 20 patients aged between 20 to 70 years, admitted in intensive care unit (ICU) under MV with synchronized intermittent mandatory ventilation (SIMV) mode. Unstable respiratory and cardiovascular patients or those in danger of complications due to change in position or whose treatment processes were threatened by our intervention (e.g. patients with lower extremity fracture or deep vein thrombosis) were excluded. To avoid confusion in interpreting results, cases with any type of valvular or congenital heart disease, heart failure, pericarditis or pericardial effusion were also refused. Likewise, patients sufferering from abdominal compartment syndrome, with history of trauma and surgery in neck and patients receiving intravascular inotropes or vasoactive drugs were not involved.

Our purpose was to examine possible effects of PLR in right internal jugular vein (RIJV) dimension and for exact evaluation we tested it in three separate phases. At the first phase (supine pre-test), cases were examined with portable bedside Doppler sonography, RIJV dimension and cross sectional area were measured. In the second

(PLR phase) both legs were raised straight up to 30 degrees, stabilized as safe and then measuring repeated, 1 and 5 minutes after staying in PLR position. In the last phase (supine post-test) we returned legs to supine and after 5 minutes remaining in flat position, RIJV diameter and cross sectional area were measured again with the aid of Doppler sonography. Thus we evaluated each patient at four time points and recorded 8 measurements for each case to be compared later. The intervention sequences are shown in Figures.1 and 2.

Ultrasonography device SonoSite®M-Turbo was used and the same vascular probe (HFL 38 E) applied for all cases. Method of sonographic evaluation (depth, place and direction of probe) followed standard studies(15.26.27). Patient`s head was stabilized in neutral posture, without flexion or extension, then slowly turned about 20 degrees to left side. In this position and at the level of cricoid cartilage, the maximum anterior-posterior RIJV diameter and cross-sectional area were measured with minimal pressure to avoid vascular compression. We saved each ultrasonic frame of displayed view to be studied later, for further evaluation, by another examiner. This blinded radiologist supervisor repeated measurements on recorded images and was not informed about patients` positions or intervention phases while frames were captured. We observed periodical fluctuations in vein diameter due to ventilation cycle, however we recorded maximal diameter on assisted ventilation. During the intervention we carefully monitored patients to interrupt examination in times of medical instability, although we did not encounter any complication during study phases.

Results

We studied twenty cases, 11 men and 9 women; mean of age was 50.5 as the youngest was 25 and the oldest was 75 years old. All of them were ventilated by SIMV mode, set tidal volumes were 6 to 8 cc/kg and positive end expiratory pressure (PEEP) was 5 cmH2O. Patients were not completely paralyzed but were completely comfortable and had spontaneous breathing, sometimes. Data were analyzed with SPSS®ver.21 and paired t-test. Difference of RIJV diameter and cross-sectional area in supine position versus one and five minutes after PLR showed to be significant ($p < 0.0001$). Mean RIJV diameter in supine position (1st phase) was 10.2 mm, that was increased to 11.2 (9%) and 11.5(12%) mm, one and five minutes after PLR (2nd phase) respectively and decreased again to 10.6 mm 5 minutes after returning to supine position (3rd phase) (Figure 2). Mean of RIJV cross-sectional area in supine position (1st phase) was 1.25 cm2, that was increased to 1.40(12%) and 1.49(19%) cm2, one and five minutes after PLR (2nd phase) respectively and decreased again to 1.26 cm25 minutes after returning to supine position (3rd phase) (Table 1) (Figures 3 and 4).

Figure 1. Sequence of study phases on patients (black arrow: time of measuring)
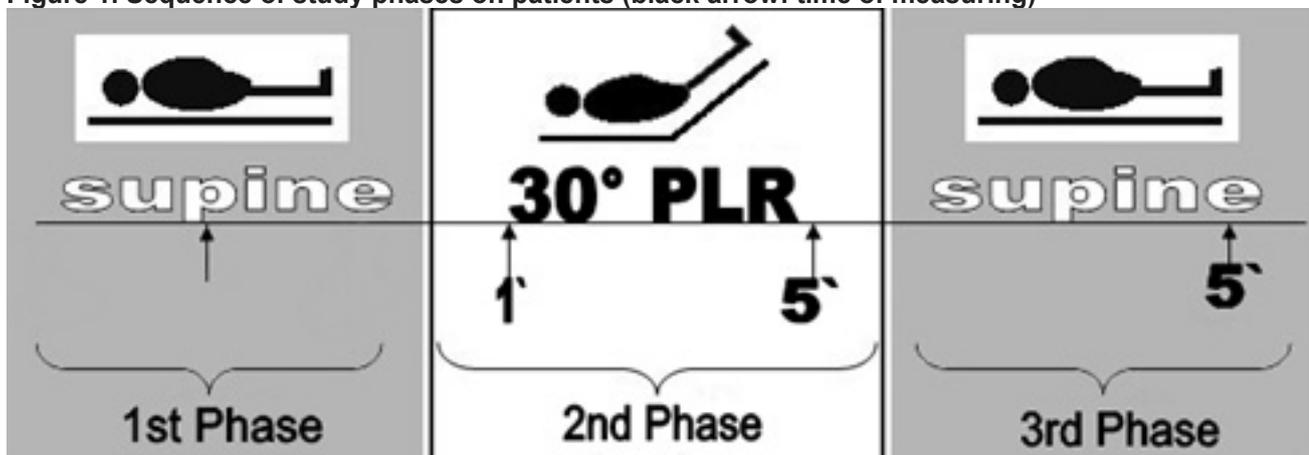
Table 1: Results

Means	SUPINE Pre-test	30°PLR		SUPINE Post-test
		1min	5min	
RIJV Diameter (mm)	10/2	11/2	11/5	10/6
RIJV Cross-Sectional Area (cm²)	1/25	1/40	1/49	1/26

Figure 2: An example of measuring and saved frames of displayed ultrasonography views in different study phases (v: right internal jugular vein)
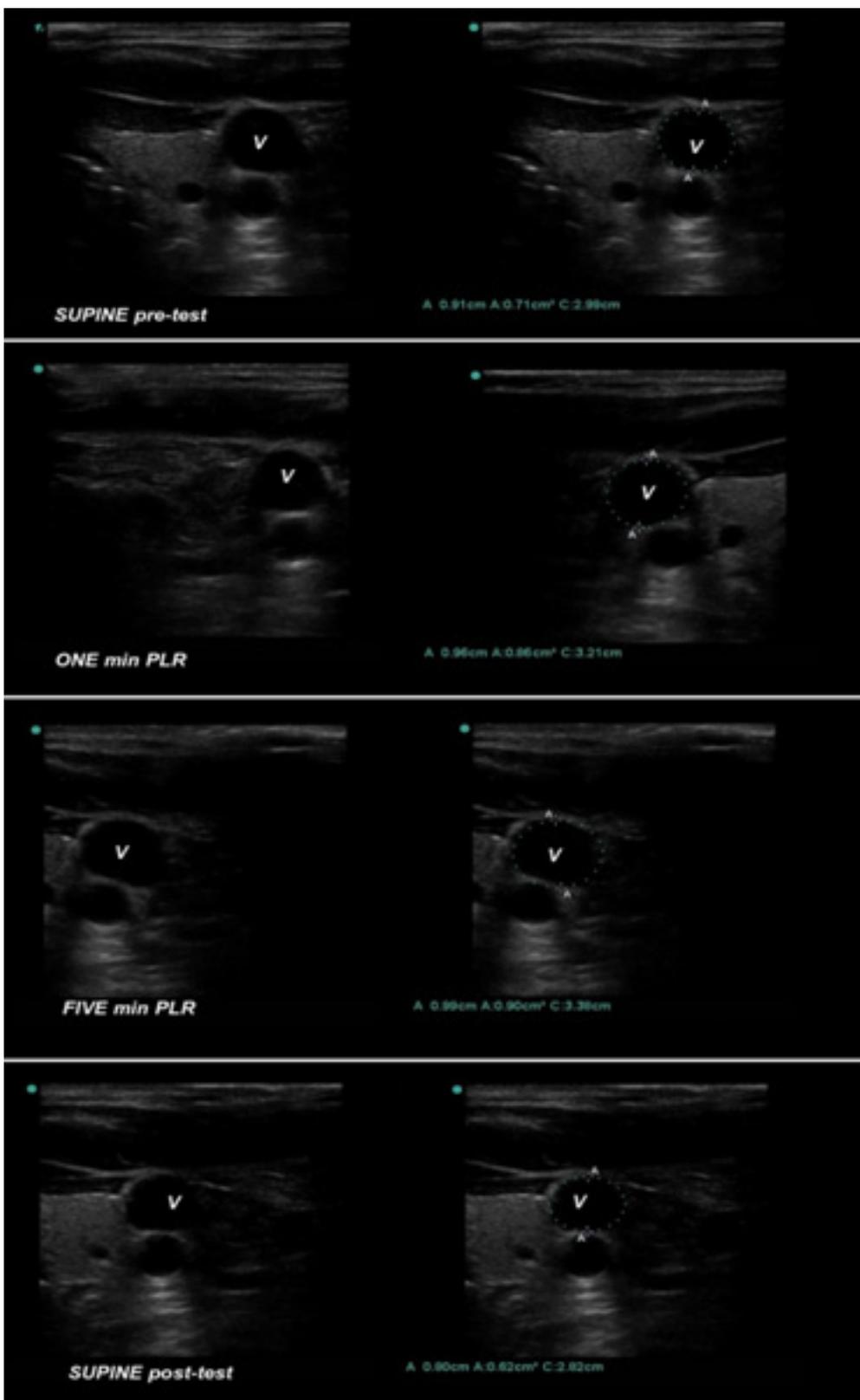
Figure 3: Changing in RIJV diameter during study phases
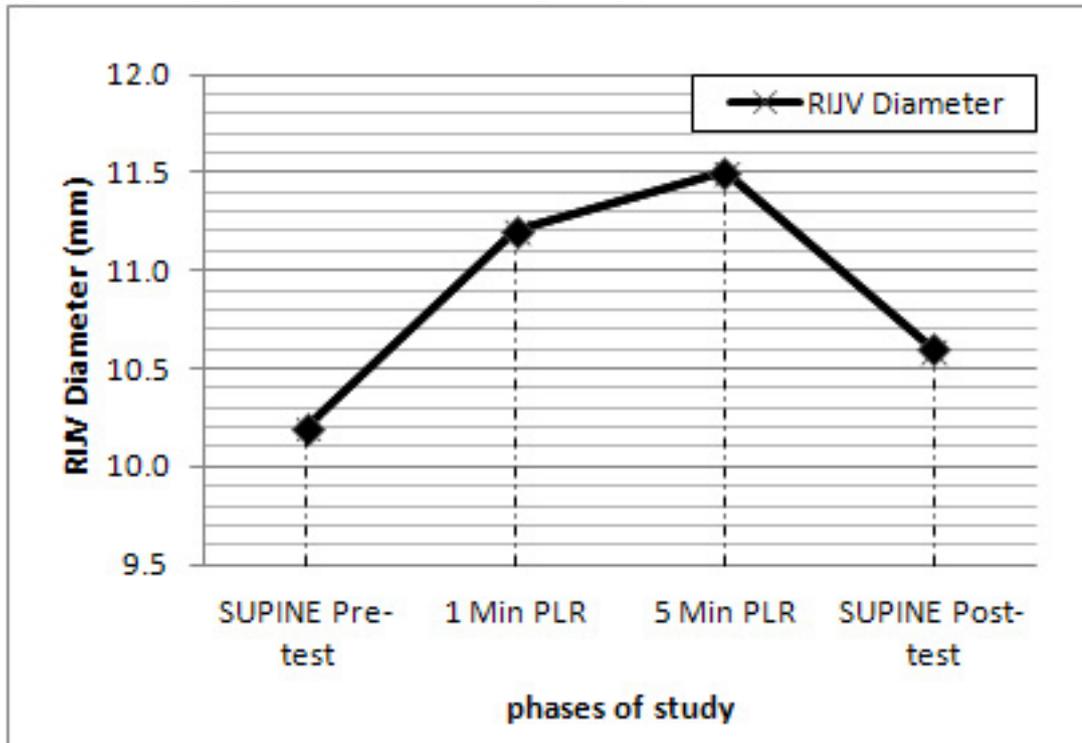
Figure 4: Changing in RIJV cross-sectional area during study phases
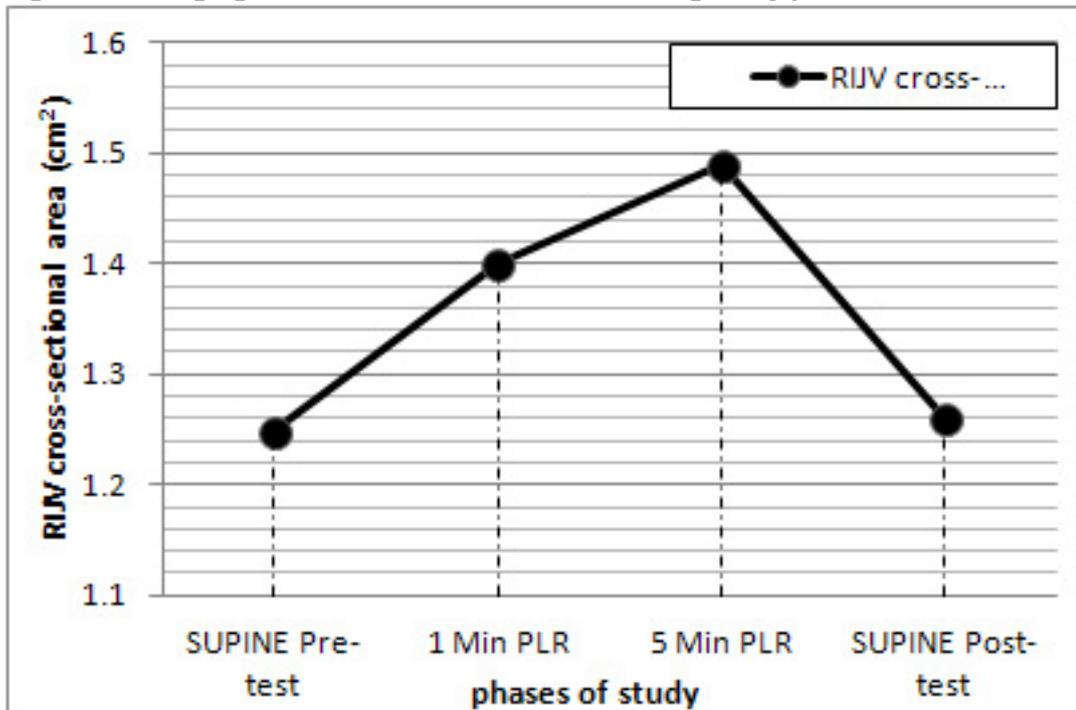
Discussion

Change in RIJV diameter and cross-sectional area after 30° PLR in comparison to supine position was significant. Venous engorgement was more obvious after five minutes sustained leg elevation. Additionally, increase in cross-sectional area of vein denoted that enhancement occured in multiple, not only one direction. Extent of increased cross-sectional area after 5 minutes seems to be enough (19%) that may be considered to facilitate RIJV catheterization. To prove that rise in diameter and surface area of RIJV were caused by PLR and were rapidly reversible, we repeated measurements, five minutes after returning the legs to neutral position. A little difference between 1st versus 3rd phase measurements indicate that venous size alteration is transient and reversible and PLR does not induce permanent effects as revealed in other studies(4,8,10,11).

Increase in diameter and cross-sectional area of RIJV has been already investigated in previous studies on healthy volunteers but we wanted to demonstrate its effects in ICU patients under MV. Application of positive pressure ventilation leads to multiple hemodynamic changes in patients which to a great extent, depend on their basic

condition and ongoing status. In spite of the fact that there are too many factors to be considered, it is almost impossible to find similar ICU patients with exact similar conditions. Moreover, if a specified group of the same patients had been chosen, the result of study would be limited to that small group only. Although our patients had different intravascular volume, cardio-respiratory and hemodynamic status at the time of intervention and showed different amounts of alteration, changing style in RIJV size was identical among cases.

According to study of Kim et al(24), RIJV cross-sectional area was 1.12 cm2 reaching to 1.40 cm2 after one minute 50° leg raising (p < 0.0001). These findings are similar to our results but smaller changes in our cases might be due to lesser degree of leg raising (30°vs. 50°). In respect to ICU patients` vulnerable situation and to prevent plausible injury induced by coarse or excessive displacement, we were limited to PLR to 30°. Nonetheless, to clarify the exact size suited for RIJV catheterization with the least risk to patients requires further studies.

Many surveys concluded that increment in RIJV dimension after TDB position, is more than PLR maneuver(17,24,25,28,29). This is probably due to excessive blood which redistributes from lower, central and upper parts of body toward head and neck, in comparison to PLR maneuver that only draws in lower extremity blood. The goal of our study is just to show the effects and extent of PLR maneuver on RIJV dimensions; the first essential step to utilize this maneuver in catheterization.

Although positive results were achieved by this study, it had some limitations. One of the most challenging subjects is bias related to examiner, the fact that exists in all studies where a specific person or tool used to measure a variable. For all cases in our study, examiner was a specified and constant physician who was inevitably aware of patient position. We tried to minimize this bias by saving displayed frames and measured them again by another blinded examiner, who did not know anything about patients` positions or phases of intervention. Our study encompassed a limited group of ICU patients. We excluded patients suffering from hemodynamic or respiratory instability, therefore limiting external validity of our results. However, it could be suggested to health-care providers to apply PLR for internal jugular catheterization, when other conventional positions may have undesirable consequences. Further studies focusing on PLR facilitation of catheterization should be undertaken.

Conclusion

Passive leg raising maneuver can be safely considered as an alternative to Trendelenburg position to increase internal jugular vein dimension in mechanically ventilated patients. Future studies are needed to clarify possible pros and cons of PLR when utilized for central venous catheterization.

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Investigating the Effect of Educational Intervention on Musculoskeletal Disorders in Dentists

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Abstract

Background and Objective: Work-related musculoskeletal disorders (MSDs) are highly common and considered as the main factor leading to lost work time, increased costs, and hazards of manual labour work. Dentists are predisposed to work-related MSDs due to their job and methods of service delivery. Surveys have indicated that ergonomic design of job equipment and environment, proper posture, regular rest breaks and stretching exercises between patients can positively effect on the musculoskeletal system of dentists, reducing work-related musculoskeletal disorders. The aim of the present study was to evaluate the effect of educational intervention on musculoskeletal disorders in dentists who work in private dental clinics in Tehran, Iran during 2016.

Materials and Methods: This study was carried out on 84 dentists working in private dental clinics in Tehran using before-after method. The data were gathered using demographic characteristics questionnaire and standardized Cornell Musculoskeletal Discomfort Questionnaire (CMDQ). Educational intervention was implemented distributing educational pamphlets among all participants. Data were re-measured 2 months after educational intervention using CMDQ. Data and changes in them were tested before and after educational intervention using SPSS 22 Software, Wilcoxon Signed Rank Test, McNemar test, and Linear Regression test.

Findings: 51 male and 33 female dentists participated in this research. 86.9% of dentists reported some problems in at least one part of the body during the last week. There were larger numbers of dentists with musculoskeletal pain in neck, low back, right shoulder, and upper back. There was a significant reduction in musculoskeletal pain in neck, right shoulder, left shoulder, upper back, and right wrist (P<0.05) after implementing educational intervention in terms of good body posture and stretching exercises, while there was not any considerable change in other considered limbs. Findings obtained from the study indicated a significant statistical relationship between short break in appointments and musculoskeletal disorders (P<0.05); in this case, the expanded break time between appointments resulted in less musculoskeletal disorders.

Conclusion: Work-related musculoskeletal disorders are more prevalent among dentists and can be reduced by educational interventions teaching proper posture, regular rest breaks and stretching exercises between working hours. Therefore, it is essential to perform further educational interventions to promote occupational health among dentists.

Key words: Musculoskeletal Disorders, Ergonomics, Posture, Dentists

Introduction

Musculoskeletal disorders caused by work are a major health, social, and economic problem in all communities; this problem is created because of various ergonomic reasons such as imposed force (lifting or pulling objects), repeating gestures, static and fixed posture, vibration and environmental factors such as heat [1-2]. Musculoskeletal disorders are common and costly occupational harm since one-third of work-related harm comes from such disorders annually [3-4]. Work-related musculoskeletal disorders are considered as the most significant reason for lost work time, increased costs, and hazards of manual labor [5]. Researchers have revealed since 1950 that dentists are at risk of musculoskeletal disorders because of harmful factors related to routine dentistry so pain and musculoskeletal disorder can be seen among dental care staff. Repetitive activities in abnormal postures deviating from the normal skeletal position, long-term static spasm in muscles of neck, back and limbs, strong gestures in hand, non-ergonomic and unsuitable equipment, improper design of work office, and disarrangement of work instruments can be mentioned as some reasons leading to musculoskeletal disorders in this occupational group [6-8]. Some of these disorders occur because of non-observance of ergonomic principles, non-standard conditions of work environment and the occupational process of individuals. It can be expressed obviously that not only ergonomic issues in work environments lead to musculoskeletal damage but also cause dropped efficiency and productivity, increased errors, fatigue, lack of comfort and environmental stresses [9]. Dentistry is a job full of repetitive movements, long-run and continuous activity in static and fixed positions, inappropriate position of body, such as long bending posture, careful work, and low break time leading to musculoskeletal disorders such as pain and dysfunction in various parts of the body. Prevalence of musculoskeletal disorders among dentists has been reported by research carried out in different areas of the world [10]. Nokhostin et al. (2016) conducted a study entitled "Musculoskeletal problem: Its prevalence among Iranian dentists" on 600 dentists and showed that 67.5% of participants had musculoskeletal disorders. These problems were reported mostly in neck (51.87%) and less in shoulder (7.40%). There was a direct relationship between age (p=0.0001), high body mass index (BMI) (p=0.021), number of patients per day (p=0.002), low physical activity (p=0.0001) and musculoskeletal problems [11]. Ancuța et al. (2016) carried out a study about ergonomics and prevention of work-related musculoskeletal harm in dentists; they conducted a prospective study on 30 dentists (20 female dentists) at age range of 30-60 during 12 months to examine occupational disorders in hand using CMDQ. There was a wide range of hand-related job occupational disorder among dentists due to various occupational factors such as occupational posture, work experience, and quality of tools and instruments. According to the results obtained after 12 months, those dentists who had performed 30-minute kinetic exercises 5 days a week had no musculoskeletal pain in their hands compared to the group who had no physiotherapy; hence, it is concluded that such exercises had a positive effect on their quality of life and ability [12].

Dehghan et al. (2013) carried out a study to investigate the effect of a multifaceted ergonomic intervention program on reducing musculoskeletal disorders in dentists. This interventional study was conducted on 102 male dentists working in dental clinics in Tehran. Prevalence of musculoskeletal disorders in both groups (case and control) was measured before intervention, 3 months and 6 months after intervention using Nordic Musculoskeletal Questionnaire (NMQ). Results showed reduced musculoskeletal disorders in neck, shoulder, forearm, wrist, waist, hip, knee and lower leg (P<0.05) after educational intervention. On the other hand, prevalence of musculoskeletal disorders was increased in neck, shoulder, forearm, wrist, waist, hip, and knees of individuals in control group. According to the results obtained from this study, multi-dimensional ergonomic intervention consisting of improving work circumstances, exposing ergonomic risk factors, regular exercises, and group discussion could positively reduce prevalence of musculoskeletal disorders among dentists [13]. Morshedi et al. (2014) conducted a study under the title of "Assessment of effectiveness of an educational intervention using the theory of planned behavior to modify posture of operating room personnel in Qazvin educational hospitals". They selected 130 staff from the operating room from 4 educational hospitals in Qazvin using random sampling method and assigned them to experimental (65 members) and control (65 members) groups. Demographic information questionnaire, 31-item questionnaire of Planned Behavior Theory, Ergonomic Awareness Questionnaire, and Nordic Musculoskeletal Disorders Frequency Measurement Questionnaire, Pain Intensity Tool with REBA method for posture status measurement were used as data collection tools. Data were measured at three time sections before, immediately and 3 months after educational intervention. Results obtained from this study in the experimental group showed a significant increase (P<0.05) in attitude, abstract norms, perceived behavioral control, and behavioral intention after intervention. Moreover, mean score of REBA was reduced among operating room staff within the third appraisal (P<0.05) indicating reduced level of risk in terms of body posture. In addition, pain intensity and frequency of musculoskeletal disorders in wrist, neck, shoulder, arms and lower back of the experimental group were significantly reduced after intervention (P<0.05) [14]. Saremi et al. (2006) carried out a study under the title of "The effects of ergonomic intervention on musculoskeletal disorders among dentists". Nordic Musculoskeletal Questionnaire and ergonomic appraisal method of REBA (Rapid Entire Body Assessment) were filled out before and after intervention. According to the results obtained from this study, more than 90% of dentists had problems in at least one of their limbs within the last year. Most of the complaints were in neck and shoulder so that these pains put 83% and 62% of individuals at risk, respectively. Results obtained from REBA method indicated 94% of dentists at risk of such disorders; 60% needed certain ergonomic actions, and 34% needed essential ergonomic actions. To modify existing conditions, human-based ergonomic principles were taught. There was a significant reduction (P<0.05) in scores and risk rate obtained from REBA method after intervention; in addition, there

was a significant reduction (P<0.05) in musculoskeletal disorders in neck, shoulder and upper back while there was not any considerable change in other limbs (P>0.05) [15]. Sharma et al. (2010) carried out a study under the title of "Awareness among Indian dentists regarding the role of physical activity in prevention of work related musculoskeletal disorders". The applied instrument was a questionnaire consisting of some questions related to physical volume of work, public health and musculoskeletal problems. 80 male and 22 female dentists at age range of 36.2 participated in this study. Most of reported work-related musculoskeletal disorders in the past 6 months were related to lower back, neck, and shoulder so that more than 97 dentists were looking for medical advice in order to reduce these disorders and 74 dentists set appointments with physiotherapists to follow ergonomic advice and exercises. There was a direct relationship between number of physical activities and improved symptoms. According to the results obtained from this study, not only work-related musculoskeletal disorders in dentists reduce their power but also are important concerns among them [16]. Rahnamaye Tamrooiy et al. (2015) carried out a study under the title of "A survey on Prevalence of Musculoskeletal Disorders in Dentists of Tehran and their posture assessment by RULA method". Data were collected referring to dental clinics, taking pictures, and recording films. Postures were evaluated in two ways, manual and automatic (use of software) after data collection using Cornell's questionnaire. The highest prevalence of musculoskeletal disorders was reported in neck (78.3%) and shoulder (76.4%) and the lowest prevalence was related to elbow (47.6%). According to statistical analysis, there was a significant relation between gender, height, weight, number of patients per day, obesity, marital status, and prevalence of musculoskeletal disorders (P>0.05) while there was not any significant relation between work hours per week, work experience, training experience in field of ergonomics and prevalence of musculoskeletal disorders (P<0.05). Findings showed the suitable interventions such as re-design of work place and instruments, creation of basic information about proper posture, and introducing the role of body posture and biomechanics in prevalence of musculoskeletal disorders to dentists and passing ergonomics by dentistry students are essential actions regarding reduction in musculoskeletal disorders and increase in dentists' productivity [17]. Dentists are at risk of more occupational musculoskeletal disorders due to their job and services. Researches have indicated that optimal and correct posture can positively effect on the musculoskeletal system leading to improved performance and reduced occupational events and harm [9]. To prevent musculoskeletal harm, it is essential to be aware of role of biomechanical factors such as awkward or fixed posture, imposed force and repetitive actions in order to find controlling strategies [18-19]. Besides sufficient teaching and design of work experience and instruments, ergonomically, regular aerobic exercises and stretching between work hours are recommended to prevent musculoskeletal disorders [20].

Methodology

This study was conducted using before-after method and convenient sampling method among dentists working in Tehran. In this regard, a list of private healthcare centers with dental clinics was prepared and the 84 dentists who were working in these centers were asked to fill out questionnaires after obtaining their consent. The brand of dental unit and chair of dentist was recorded at the next step. Questionnaires consisted of the following parts: demographic characteristics questionnaire and standardized Cornell Musculoskeletal Discomfort Questionnaire (CMDQ). Primitive status of musculoskeletal disorders was determined and recorded using CMDQ. An educational program was performed through brief face-to-face teaching and distributing pamphlets. Data were re-measured 2 months after educational intervention. Disorders were tested again after performing educational interventions using Wilcoxon Signed Rank Test, McNemar, and Linear Regression test.

Findings

51 male and 33 female dentists participated in this research; they were at age of 43.99±8.86 with BMI of 35 that was at normal range of (18.5-24.9). 4 members were overweight (25-29.9kg overweight) and 9 members were obese (30kg and above). Selected members had average work experience of 17.14±8.43 years. Of them, 59 members were general dentists and 25 members were specialized and a large number of them were periodontists (6 members). Average number of patients per day was equal to 10.24±6.63 and work hours reported to 37.43±15.99 weekly. 32 dentists had no short break between treatments as follows: 24 dentists once per day, 10 dentists twice per day and 16 dentists more than two breaks per day. 41 dentists had regular exercise weekly and 40 dentists had no regular exercise activities weekly.

According to the results obtained from CMDQ, dentists had musculoskeletal problems in their neck (64.3%), lower back (51.2%), right shoulder (41.7%), and upper back (39.3%); so that negative effect of these problems in neck (45.2%), lower back (40.5%), upper back (31%), and right shoulder (28.6%) interfered with their ability to work. Right wrist (33.3%) and left shoulder (31%) were at next importance in terms of creating musculoskeletal disorders. In case of pain intensity (score of 0-90), dentists reported more intensive pain in neck (score of 10.97±20.44), right shoulder (8.85±19.76), upper back (6.92±17.59), and lower back (6.90±14.33) (Table 1).

86.9% of participants had problems in at least one of the mentioned limbs before intervention and only 13.09% of them expressed no pain in their limbs. 19% of participants reported no pain in mentioned limbs after intervention. There was a significant reduction (P<0.05) in intensity of musculoskeletal pains in neck, right shoulder, left shoulder, upper back, and right wrist after educational intervention using Wilcoxon Signed Rank Test while there was not any considerable change in other limbs. There was not any significant difference in frequency of dentists with

Table 1: Distribution of dentists based on intensity of musculoskeletal disorders before and after intervention considering the involved body area

Intensity of musculoskeletal disorders (score 0-90)	before intervention		after intervention		P value
	Mean	Standard deviation	Mean	Standard deviation	
neck	10.97	20.44	7.91	17.01	0.004
right shoulder	8.85	19.76	5.24	13.51	0.003
left shoulder	5.80	17.21	2.95	9.33	0.008
upper back	6.92	17.59	4.53	14.35	0.003
right upper arm	1.98	7.51	1.17	5.36	0.200
left upper arm	1.78	10.34	0.79	3.30	0.609
lower back	6.90	14.33	6.54	15.83	0.692
right forearm	3.03	12.16	1.42	7.20	0.123
left forearm	2.96	14.51	1.29	7.04	0.305
right wrist	5.12	13.35	3.81	12.96	0.028
left wrist	3.79	14.73	2.55	11.98	0.099
hip	0.92	4.21	1.11	5.44	0.906
right thigh	1.21	5.35	0.51	2.31	0.191
left thigh	1.65	10.36	0.26	1.20	0.440
right knee	3.27	14.07	2.35	8.66	0.300
left knee	3.22	12.94	3.73	14.75	0.776
right lower leg	1.95	7.15	1.17	5.19	0.090
left lower leg	1.78	5.79	1.04	4.97	0.108

musculoskeletal disorders in different parts of the body before and after intervention using McNemar test.

Presence of musculoskeletal disorders (as a separate variable) and its significance was compared with other variables using Linear Regression test and there was a significant relationship between short breaks between patients and presence of musculoskeletal disorders (P<0.05); in this regard, more short breaks between patients led to lower musculoskeletal disorders. Moreover, there was a significant relationship between pain in neck, gender, and age (P<0.05) so that the pain in neck was higher in men and increased age led to more pain in neck. In addition, there was a significant relationship (P<0.05) between intensity of pain in lower back and dominant hand so that left-handed individuals had more pain in lower back. There was not any statistical significant relationship between musculoskeletal disorders and other variables including BMI, smoking, marital status, specialty, regular weekly exercise activities, use of mirror, history of particular disease, history of accident or trauma, history of surgery of the spine and upper and lower extremities, type of dental unit and chair, work experience, number of patients per day, and working hours per week.

Discussion

This study was conducted to examine effect of educational intervention on musculoskeletal disorders in dentists working in private healthcare centers of Tehran. For this purpose, we went to a private healthcare center with dentistry clinic in Tehran and selected some participants using convenient sampling method; we spoke with dentists about importance of prevention of musculoskeletal disorders then proposed educational intervention through face-to-face teaching and distribution of educational pamphlets. Ultimately, results of training effect were evaluated 2 months after intervention. According to findings of this study, 86.9% of dentists had problems in at least one of their limbs before the educational intervention. A study conducted by Ísper Garbin et al. (2017) on 204 dentists [21], a study carried out by Nokhostin and Zafarmand (2016) on 600 Iranian dentists [11], a study of Munshi et al. (2016) on 420 Indian dentists [22], and a study conducted by Abi Aad (2016) on 218 Lebanese dentists [23] showed prevalence of musculoskeletal disorders equal to 81.4%, 67.5%, 90.7%, and 92.7%, respectively. According to the mentioned studie that confirmed the results of each other, there is a considerable prevalence of musculoskeletal disorders among dentists indicating lack of awareness of correct ergonomic principles and lack of stretching exercises between patients. Findings obtained from extant study showed larger number of dentists with musculoskeletal disorders in neck (64.3%), lower back (51.2%), right shoulder (41.7%), and upper back (39.3%) compared to other parts of the body. Musculoskeletal disorders in the right wrist (33.3%) and left shoulder (31%) had lower importance rate. Similar results were obtained in other research. Ísper Garbin et al. (2017) carried out a study on 204 dentists and reported more musculoskeletal disorders in neck, shoulders, and lower back [21]. Munshi et al. (2016) carried out a study on 420 dentists and reported neck (73.8%), lower back (70%), wrist and hand (64%), and shoulders (62.4%) as the most involved parts of body [22]. Abi Aad (2016) conducted a study on 218 dentists and reported lower back (61.8%), neck (51.5%), and shoulders (39.5%) as the most involved parts of the body [23]. Moreover, Nokhostin and Zafarmand (2016) conducted a study on 600 Iranian dentists and reported neck (51.87%), wrist and hand (29.62%), back (11.11%),

Figure 1: Distribution of dentists based on intensity of musculoskeletal disorders before and after intervention considering the involved body area
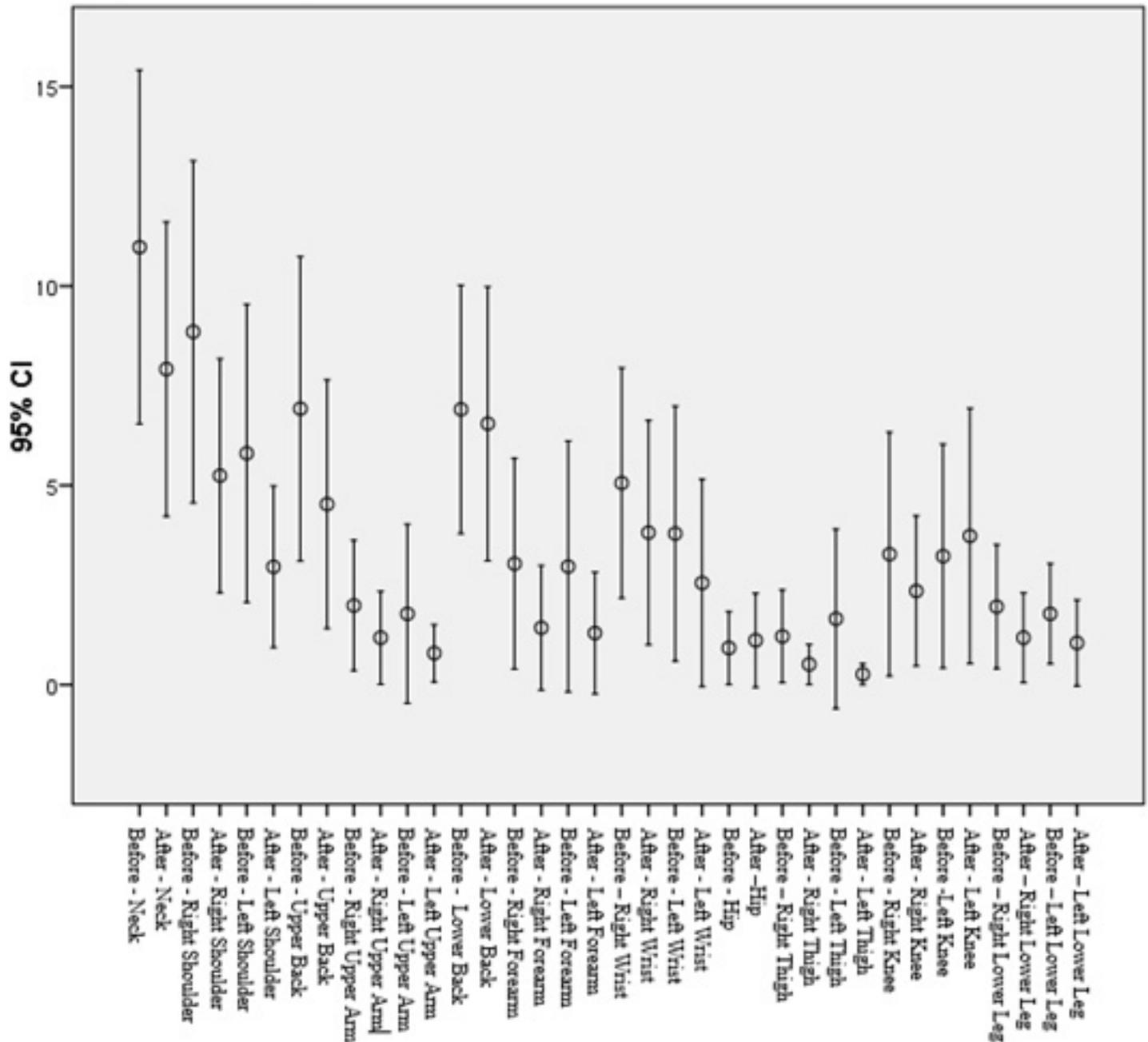
and shoulder (7.40%) as the most involved parts of body [11]. The study carried out by Rahnamaye Tamrooiy et al. (2015) examined 98 dentists in Tehran and reported the highest prevalence of musculoskeletal disorders in neck (78.3%), shoulder (76.4%), wrist (68.5%), and lower back (55.4%) [17]. Sharma and Golcha (2010) conducted a study on 102 dentists and reported the highest prevalence of work-related musculoskeletal disorders in lower back, neck and shoulder within recent 6 months [16].

Saremi et al. (2006) conducted a study on 47 dentists and reported the highest complaint of pain in neck (83%) and shoulder (62%) [15]. Two other studies were carried out in a dentistry school of Islamic Azad University and obtained similar results in this field; Momenabadi (2013) reported the highest prevalence of musculoskeletal problems in neck (50.7%), waist (38.7%), and back

(37.4%) among specialized students in dentistry [24]. Jahangir (2005) reported the highest rate of pain in neck (42.2%) among faculty members of dentistry school of Azad University and Shahid Beheshti University [25]. According to the mentioned studies that confirm each other, musculoskeletal disorders most frequently involve neck, shoulder and back of dentists due to more loads on these muscles because of dentist's type of work and working conditions, awkward body postures and lack of attention to ergonomic principles. Results obtained from the present paper showed a significant relationship (P<0.05) between short break and musculoskeletal disorders so that increased short breaks between patients led to decreased musculoskeletal disorders. In addition, there was a significant relationship between gender, age and pain in neck (P<0.05) so that men feel more pain in their neck because of more working hours they spent in the

clinic. On the other hand, increase in age led to more pain in neck. Also, there was a significant relationship (P<0.05) between intensity of pain in lower back and dominant hand so that left-handed dentists had more pain in their lower back because of awkward postures. There was not any statistical significant relationship between musculoskeletal disorders and other variables and this may be related to the small number of samples. Kierklo et al. (2011) conducted a study and reported a significant relationship between musculoskeletal disorders, standing position, lack of short break, and lack of attention to ergonomic principles [9]. According to the study conducted by Abi Aad (2016), chronic pain in different parts of the body was reversely related to physical activity of the person [23]; the reason for such a relationship may be because of regular exercises and physical readiness that lead to flexibility of tendons and more ability of muscles to support the spine [26].

Sharma and Golcha (2010) conducted a study on 102 dentists and reported a significant direct relationship between number of physical activities and improved musculoskeletal symptoms [16]. A study of Nokhostin and Zafarmand (2016) on 600 Iranian dentists indicated a direct relationship between old age, high MBI, number of patients per day, low physical activities, and increased musculoskeletal disorders [11]. There was not any statistical significant relationship between musculoskeletal disorders and variables including age, BMI, number of patients, and physical activity in the present study and this may have been due to small number of sample members. The mentioned research shows that musculoskeletal disorders can be controlled in the case of following ergonomic principles, having short breaks between appointments, having a suitable lifestyle, doing regular exercises and controlling weight. According to the findings obtained from present paper, there was a significant reduction in musculoskeletal disorders in neck, right shoulder, left shoulder, upper back, and right wrist (P<0.05); however there was not any significant difference in various parts of body before and after intervention in terms of dentists with musculoskeletal disorders; this case indicates that intervention could significantly reduce intensity of disorders in some parts of the body but was not able to remove them completely since data were re-measured 2 months after intervention and it was a short-term follow up to reveal effects of intervention. Nevertheless, 86.9% (73 members) reported pain in some limbs before receiving educational intervention and this rate dropped to 81% (68 members) after intervention. In general, reduced musculoskeletal disorders in neck, right shoulder, left shoulder, upper back, and right wrist indicated effectiveness of intervention among dentists. Saremi et al. (2006) conducted a study on 47 dentists and reported a significant reduction in musculoskeletal disorders in neck, shoulder, and upper back 4 months after educational intervention (P<0.05) [15]. Dehghan et al. (2016) carried out a study to examine effect of educational intervention on reducing musculoskeletal disorders in dentists. Results obtained from this study in case group (n=52) indicated reduced musculoskeletal disorders in neck, shoulder, forearm, wrist, waist, tight, knees and lower leg 3 and 6 months after intervention (P<0.05) [13]. Ancuța et al. (2013) conducted a study on

30 dentists to examine occupational disorders in the hand and prevention from work-related musculoskeletal harm using exercise and stretching programs. It was revealed in this study that dentists in group A who did 30-minute kinetic exercises 5 days per week reported no musculoskeletal pains in hand after 12 months of intervention compared to group B who did not receive physiotherapy. This study showed effectiveness of stretching exercises in reducing musculoskeletal pain [12]. According to the mentioned studies that confirm each other and that confirm the results of our study, there was considerable effectiveness in reducing musculoskeletal disorders after intervention indicating effects of ergonomic design of work place and instruments, proper posture, regular rest breaks, regular aerobic exercises, and stretching activities between working hours on reducing musculoskeletal disorders. The positive point of our study was implementation of educational intervention to promote musculoskeletal health in dentists leading to effectiveness of training in promotion of occupational health of dentists. Although there have been various studies about musculoskeletal disorders in dentists, few interventional studies have been conducted to reduce these disorders.

Conclusion

Work-related musculoskeletal disorders are common among dentists; in this case, teaching suitable body posture, regular rest breaks, and doing stretching exercises between working hours can reduce and prevent musculoskeletal harm in dentists so that more rest breaks lead to lower musculoskeletal disorders.

Problems and limitations
There was poor collaboration of some centers and dentists, too much time spent visiting dental clinics to answer the questionnaires.

Recommendations

We recommend performing similar interventional research in educational centers and clinics, poster design and installation in the dentists' offices and dental schools, holding retraining courses and workshops for dentists and dental students, Inclusion of ergonomic training course in the educational curriculum of dental students and Sending questionnaires and training tips via email to save time.

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The Quality of Informed Consent After the Establishment of Patient Safety Standards: The Consent of the Physician, The Presence of a Third Party, The Description of the Type of Procedure, The Description of the Benefits of the Procedure

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Abstract

Objectives: The present study was to investigate the aim of establishment of patient safety standards' impact on quality of informed consent in Baharlo Hospital in Tehran.

Research Method: This is descriptive-survey research that was done by cross-sectional method. The statistical population of the study consisted of all patients who underwent surgical procedures since the establishment of patient safety standards from 2011 to 2016. 200 people were selected using target and convenient sampling method. The data were collected using a checklist and were analyzed using inferential statistics of paired t-test.

Findings: The findings of the study showed that the establishment of patient safety standards has a positive and significant effect on the quality of informed consent (p = 0.001) and also on 4 variables: 1) the consent of physician or the person performing the procedure (p=0.001), 2) presence of a third party (nurse or companion) at the time of obtaining consent (p = 0.001), 3) description of the type of procedure by the physician to the patient (p = 0.001), 4) description of the benefits of the procedure to the patient (p = 0.001) in Baharlo Hospital.

Conclusion: Establishment of patient safety standards as well as observance of their mandatory principles affects the quality of informed consent of patients and increases the quality of informed consent in all aspects.

Key words: Patient Safety Standards, Quality of Informed Consent

Introduction

In the current world, the quality of health care and the improvement in hospital performance has been a global issue and one of the main goals of the health system of all countries. Among the most important reasons for addressing the issue of quality in health care, there are problems with the safety of providing these services (Emami Razavi et al., 2011).

Patient safety standards are a set of requirements that are critical to patient safety planning in the hospital setting. These standards provide operational forms that empower hospitals to evaluate patient care in terms of patient safety, empowerment of staff in patient safety, and empowerment of service users in promoting health in healthcare services (Emami Razavi et al., 2011).

Patient safety is a global concern in all health care settings. Inadequate care and services, besides imposing suffering on patients, cause heavy economic costs. Although significant advances have been made in the last decade in terms of patient safety, there are still many shortcomings; and the degree of damage inflicted on patients is unacceptably high (Parsapur et al., 2009).

The World Health Organization has recognized the importance of patient safety and prioritized it as a public health concern. The Eastern Mediterranean World Health Organization has launched a safety hospital program. This program is considered necessary to implement a set of patient safety standards for the hospital and staff to provide the best performance in this regard (Emami Razavi et al., 2011).

Patient safety standards are comprised of five main groups and subdivided into 24 subgroups. This section includes guidelines for assessors, including documentation to be reviewed for each standard, relevant interviews, guided visits and group visits, and rating guidelines. (Farkhondeh, 2010).

The five groups that meet the following standards are:
A. Leadership
B. Attracting patient and community engagement
C. Clinical-safety and evidence-based services
D. Safe environment
E. Continuous training

Every living human has life, health and death rights. One of the most fundamental rights of patients is the right of consent to treatment. Logically every person with a healthy mind has the right to decide on what action is conducted on his or her body (Farzandipour, 2012).

According to law any medical action should be permitted by the patient through informed consent, and the most important principle in obtaining consent is consciousness (Bateni, 2013; quarterly journal of Jamaran Heart Hospital) and the patient has the right to have the right information as without this, informed consent is not obtained. Therefore, the failure to provide adequate and accurate information to a patient is a breach of the contract, according to which the patient can lodge an action for any damages (Darmal, 2009)

As a general rule, patient treatment is unlawful without their consent, except in cases such as real-life emergency situations (Voura, 2010).

Conscious consent is not just signing the consent form, but also informed consent. There must be 6 conditions met: "Provide information, understanding, decision competence, consent signature or oral satisfaction, and factors relating to the interaction between the doctor and the patient". (Sheikh Taheri, 2008).

The legal origin of informed consent lies within the context of the law, which is based on the principle that each individual "has the right to know what action is conducted on his body" (Sklundorf, the New York Hospital Association of 1914, quoted by Hiller 2008) and they must be medically satisfied. The legal aspect of more informed consent is used in negligence cases, so that the patient has permitted doctor to take steps to improve his condition when he / she consents to the intervention of the physician, but the physician may not describe the risks and possible consequences (Abbasi Nejad, 2011).

Despite research on patient consent, the research on the impact of establishing patient safety standards on the quality of informed consent has not been investigated. Therefore, the aim of this study is to answer this question. The research is carried out in Baharlo Hospital, the first ranked hospital in terms of establishment of patient safety standards. Therefore, the findings of this study can be used as a model for other health centers in this area.

There are few studies in Iran in this regard. In some studies, this topic has been partially discussed from the point of view of the patient rights charter. A study in Yazd has reported mediating the patient's right to inform the nurses. (Nasiriyani, 2007)

Studies in Iran show that Iranian physicians generally provide general information about the illness to the patient. Doctors also seem to be more prudent in reporting side effects and other treatment options. In this study, 50% of the respondents believed that the information given was not understandable. (Vahdhani Nia, 2007; Amini, 2008; Taghadosi nezhad, 2008)

Studies in Iran have shown that generally enough information about diagnosis or treatment is not provided to patients, and patients do not understand the information provided (Tariqat, 2007; Davar Panah, 2002; Dengirz, 2007; Wahdadi, 2004).

The study of CD Coy (2009) also referred to the same subject. Though studying Jawf (2001) reported in America, 86% of patients considered the information understandable.

A study in Sydney showed that 74.6% of cancer patients knew that their disease was untreatable (Gatthalari, 2002). Hawolder's (2004) study also found that most patients were aware of the complications of surgery and even the possibility of death.

Butachyara et al concluded that informed consent in admissions was associated with the risk of an increase in compensation (P ≤ 0.000). In other words, by increasing the risk of surgery, the team needs to be more responsible for providing appropriate information to patients and reducing future reimbursement. (Quotes, 2012).

Yang's study 2010, also revealed that cancer patients studied were aware of the untreatable nature of their illness and its complications. A study in Switzerland also found that patients considered the amount of information provided (both written and oral) to be good and adequate (Qulam, 2006) The study of CD Coy (2009) also referred to the same subject. A study by Jaff (2001) in the United States reported 86% of patients considered the information understandable.

Research method

The overall aim of this study was to investigate the effect of establishment of patient safety standards on the quality of informed consent in Baharlo Hospital in Tehran. This study is a descriptive-survey study that was conducted in Baharlo Hospital. This research was a semi-experimental study that was carried out before and after establishment of patient safety. This research was done on a field scale and the information gathering tool was a checklist for the standard of quality of information for informed consent. Through direct observation, interviews were conducted with the patient and, if necessary, with the nurses.

The tool used in this study was a checklist. The checklist is available to expert users (professors, responsible for improving the quality of the hospital, a patient safety expert, doctors of the Forensic Medicine Group and a senior evaluator of the ministry at Baharlo Hospital). For each statement, the check list has three weak options (zero score), average (score of 0.5) and good (score 1) and the score obtained from the check list is between zero (at least) and 12 (maximum)

The statistical population of this study included all patients who underwent surgical procedures since the beginning of the establishment of patient safety standards in all parts of the Baharlo hospital in Tehran (from 2010-2016).

Sample size: The sample number was estimated by Cochrane formula 200. The sampling method was targeted and available at the time of the study in Baharlo Hospital of the patients undergoing surgery.

To analyze the data of the present study, we use the inferential statistics of the paired t-test.

Table 1: Comparison at a Glance Informed consent centers in the hospital at the beginning and after the establishment of patient safety standards

Hypothesis	Items	Before establishment	After establishment	Mean difference	Degree of freedom	t	p value
Hypothesis 1	Obtain informed consent by the doctor or the person administering the procedure	1.02	2.98	1.96	199	22.279	0.001
Hypothesis 2	The presence of a third party (nurse or companion patient) at the time of consent from the patient	1.11	2.97	1.86	199	29.283	0.001
Hypothesis 3	The quality of the description of the type and manner of conducting the procedure by the physician to the patient	0.73	2.52	1.89	199	26.34	0.001
Hypothesis 4	Quality description of the benefits of the procedure by the physician to the patient	1.01	2.15	1.14	199	11.20	0.001
Main hypothesis	Total score of all dimensions	3.87	17.12	10.47	199	22.297	0.001

Findings

The findings of this study showed that the establishment of patient safety standards has a positive and significant effect on the quality of informed consent. (P = 0.001) Although patients in the hospital should be informed about their legal rights, the legal and ethical awareness of informed consent is often limited. Sufficient information before surgery is fundamental and the basis for patient's informed consent. Information should include the description of surgical usefulness, risk and complexity during the surgical procedure and various treatment regimens. Many studies have shown that providing information has a very beneficial effect. Patients who receive information in writing during treatment can better understand their information and recall after surgery (Rajesh, 2013). The results of this study indicate that the establishment of patient safety standards has improved all the information that was considered in the study, as well as the length of the treatment and information provided by the doctor or the person performing the procedure.

In studies in Iran, it has been shown that sufficient information about the diagnosis is not available to patients (Sheikh Taheri, 2010), while in the present study safety standards have affected this item. The doctor writes the type of diagnosis in the informed consent form, after a written explanation. In other countries, studies show that patients receive better information about their illness in this format which is consistent with the current study (Gatlari, 2002; Gulam, 2006; Jacick, 2009; McIntosh, 2010).

The findings of this study showed that the establishment of patient safety standards on the quality of third-party presence (nurse or companion) has a positive and significant effect on consent. (P = 0.001) According to Rajesh (2013) research, in the UK, the physician is obliged to obtain consent, and individuals over the age of 18 years are qualified to give consent. Patient consent is not just a signed form. Consent should be obtained regarding complications for as high a prevalence of 1%, which was congruent with the present study in which consent is obtained by physician except in rare cases, where it is obtained by nurses.

The study, by Golam (2006), found that patients considered the amount of information (both written and oral) to be good and adequate. A study by Gathlory in Sydney showed that 74.6% of cancer patients know that their disease is untreatable. Hawolder's (2004) study also found that most patients were aware of the complications and even the possibility of death.

Conclusion

The findings of the study showed the benefit of establishment of patient safety standards on the quality of informed consent (p = 0.001), as well as on 4 variables, namely, (1) obtaining consent by the practitioner or the person performing the procedure (p = 0.001) 2) The presence of a third party (nurse or companion) at the time of obtaining consent (p = 0.001); 3) Description of the type of procedure by the physician to the patient (p = 0.001); 4) Description of the benefits of the procedure, by the physician (p = 0.001) and it has a positive and significant effect in Baharlo Hospital. Establishing patient safety standards as well as observing its mandatory principles will affect the quality of informed consent of patients and will increase the quality of informed consent in all aspects.

Recommendations

Based on the results of the research and the achievement of the effect of establishing patient safety standards on the quality of informed consent, it is suggested that, with more comprehensive coordinated studies, a national medical consensus form could be designed and developed to be used in all treatment units which could help to unify the procedure. And the information forms of informed consent by the physician should be simple and understandable, with less use of medical terms. The complications and side effects of surgery should be explained by the doctor and the patient should be the ultimate decision maker.

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Using Math App Monster Numbers for improving Calculation of Mild Intellectual Disability Students

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Abstract

The purpose of this study is to highlight the importance of mobile math games for mildly intellectually disabled students which will reflect positively on their calculations. The quantitative approach was adopted where the total number of the intellectually disabled students in the study was 10 from two private schools. The study was limited to grades 1, 2 and 3, whose ages ranged from 6.8 to 9.10. The students were divided into two groups, where the control group had 5 mildly intellectually disabled students and the experimental group also had 5 mildly intellectually disabled students. The measuring instrument or tool that was used in this study is the Woodcock-Johnson III, Test of Achievement limited to the calculation section. The pretest was done during the first trimester of the school year. Then the educational math games for kids "Monster Numbers": addition, subtraction, numbers intervention was applied for two trimesters. After that, the posttest was done and the results were submitted for analysis, where the means and standard deviations, the independent samples T- test, and the paired samples T- test were calculated. The results of this study showed statistical differences to the benefit of the experimental group over the control group.

Key words: intellectual disability, mathematics, Woodcock-Johnson III,
test of achievement-calculation

Using Math App Monster Numbers for improving Calculation of Mild Intellectual Disability Students

The Diagnostic and Statistical Manual of Mental Disorders DSM-5, places intellectual disability under the Neurodevelopmental Disorders section; which was previously called Mental Retardation. Intellectual Disability refers to a disorder that starts during the developmental period (American Psychiatric Association, 2013). It consists of certain intellectual deficits and challenges handling aspects of daily life like school, work, home, social life, health, and other things as well. Intellectual disability (ID) is an explanatory phrase for sub standard intelligence that occurs below the age of eighteen, which is the developmental period. According to DSM-5, there are three criteria that must be fulfilled in order for the diagnosis of ID:

(A) Deficits in intellectual functions, such as reasoning, problem solving, planning, abstract thinking, judgment, academic learning, and learning from experience, confirmed by both clinical assessment and individualized, standardized intelligence testing.
(B) Deficits in adaptive functioning that result in failure to meet developmental and socio-cultural standards for personal independence and social responsibility. Without ongoing support, the adaptive deficits limit functioning in one or more activities of daily life, such as communication, social participation, and independent living, across multiple environments, such as home, school, work, and community.
(C) Onset of intellectual and adaptive deficits during the developmental period. (American Psychiatric Association, 2013).

While DSM-4 emphasized IQ scores, this is not so with DSM-5. Instead, no particular score is indicated to establish diagnosis, and the assessment is done based on the individual's complete clinical presentation (American Psychiatric Association, 2013). The basis regarding this development was that this definition leaned more towards a conceptual rationale, and was not applicable to actual real-life cases. With the previous definition, an individual who met the cut off score could have adaptive issues in key areas of adaptive functioning which makes the

individual's actual functioning similar to that of people who have a much lower IQ score.

The various levels of severity (mild, moderate, severe, profound) are defined on the basis of adaptive functioning, and not IQ scores, because it is adaptive functioning that determines the level of support required. The severity level for mild ID is divided into three domains:

Conceptual Domain
For Preschoolers: There may be no obvious conceptual differences. For School-Age children and Adults: Difficulties in learning academic skills such as reading, writing, arithmetic, time or money. Support may be needed to meet age related expectations. For Adults: Abstract thinking, executive function (planning, strategizing, priority setting, cognitive flexibility) as well as functional use of academic skills (reading, money management) are impaired. There is a somewhat concrete approach to problems and solutions compared with age-mates.

Social Domain
Compared with typically developing age-mates, the individual is immature in social interactions. Examples: Difficulty in accurately perceiving peers' social cues. Communication, conversation and language are more concrete or immature than expected for age. Difficulties regulating emotion and behavior in age appropriate fashion. Differences are noticed by peers in social situations. Limited understanding of risk in social situations. Social judgment is immature for age. The person is at risk of being manipulated by others (gullibility)

Practical Domain
ID children may function age-appropriately in personal care, and sometimes need some support with complex daily living tasks compared to peers. In adulthood, supports typically involve grocery shopping, transportation, home and child-care organization, nutritious food preparation and banking and money management. Recreational skills resemble those of age-mates, however judgment related to wellbeing and organization around recreation requires support. In adulthood, competitive employment is often seen in jobs that do not emphasize conceptual skills. Individuals generally need support to make health care decisions and to learn to perform a skilled vocation competently. Support is typically needed to raise a family. (American Psychiatric Association, 2013).

The educational math games for kids (monster numbers) methodology aims to mix fun with learning. It is an android application that can be downloaded for free containing addition, subtraction, numbers, times tables, division, counting numbers, multiplication and sequence for kids. Designed by EducaGames, specialists in educational Videogames, fashioned by psychologists and professionals with extensive experience in the educational field, monster numbers is an excellent educational game for learning mathematics for kids and adults of all ages. It is described as a fun edutainment application. Run, jump, count, add, subtract, multiply (times tables) and divide to win. It's an actual game, with a highly adaptable edutainment design.

It is age oriented; for ages: 4-5 (Preschool), kindergarten students will find age appropriate games to match their maturing level in mathematics: counting coins, logical sequence, number recognition, association quantity and numbers, sums of sets of coins (easy addition). While ages: 6-7 (first grade and second grade of elementary school) practice math activities: logical sequences, additions without regrouping, subtractions with coins and subsequently subtraction without regrouping.

The best part is that children will engage in learning math without realizing, due to the great adventure they are experiencing with Tob the squirrel. Our squirrel is lost in the world of monster numbers and the children will have to come to the rescue. To do this, they must overcome countless obstacles and try to recover Tob's spacecraft pieces. They can jump, run, slide, fly, shoot, all while doing fun math facts (addition, subtraction, multiplication….) that can always be adapted to the students' level.

Recent development of tablet computers offers new potential for math learning. Compared to desktop and laptop computers, tablets are light and portable. For example, the iPad weighs 1.44 pounds (0.653Kg) and the ipad mini weighs only 0.68 pound (0.308Kg). Most tablets have a long battery life that can last an entire school day without recharge. In addition, touch screens are easier to use than a mouse and a keyboard, and offer a better sensory experience to children by direct touch and physical movement (Paek, Saravanos, & Black, 2013). Moreover, the average weight of a mobile is 0.1 Kg. Now there are over one million apps in online stores. Moreover, an abundant amount of math apps are available in both the App Store and Google play (Zhang, M., Trussell, R. P., Gallegos, B. et al. 2015).

Literature review

A study on engaging students with intellectual disabilities through games based learning and related technologies (Brown, D., et al., 2013) has shown that Digital Game Based Learning (DGBL) can have a positive effect on some of the core development needs of people with intellectual disabilities and associated sensory impairments. Of current interest is the expansion of DGBL activities on mobile platforms. The RECALL Project describes the development and evaluation of a novel route learning system for people with disabilities using location based services (on the Android OS). Research has shown that route guidance systems suppress cognitive map development, and for a target audience described as having 'poor spatial skills', systems that develop route learning rather than guidance are required. Two studies are reported here. The first demonstrates that there were less navigational errors made, and less help required in the more independent usage of the system, than in the earlier training stages. The second focuses more on qualitative evaluation of soft skills and personal development via the use of the system, and of the gamified version of the software. It looks specifically at how a playful approach can aid the understanding of map based representations.

Another exploratory study on using math apps for improving student learning: an exploratory study in an inclusive fourth grade classroom (Zhang, M., Trussell, R. P., Gallegos, B. et al. 2015), was conducted in an inclusive fourth grade classroom, in which about half of the students were either at risk or had disabilities. The students used three math apps that employed different scaffolding strategies to support learning of decimals and multiplication. Pre- and Post- tests showed that use of the math apps improved students learning in mathematics and reduced the achievement gap between struggling students and typical students.

Another study on support to pupils with learning difficulties in mathematics (Zakelj, A., 2014) presents a model of assistance to pupils with learning difficulties in mathematics - Implementation of modifications for pupils with learning difficulties in mathematics (hereinafter – the model LDMAT) and LDMAT model's contribution to the teachers' competence to implement the support measures to pupils with learning difficulties in terms of the empirical study. The conceptual platform of the model LDMAT is based on the following principles: giving sense to mathematical knowledge, instruction as mutual activity of pupils and teachers, and the principle of participation. The results of the study have shown that LDMAT model's contribution to the qualification of teachers to assist pupils with learning difficulties is very positive and represents a significant contribution to the improvement of teaching practices in overcoming learning difficulties in mathematics. Among teachers, the LDMAT model was evaluated as the highest in the field of selection, planning and use of appropriate didactic tools; they also highlighted the key factors for raising pupils' learning achievements: an individualized approach, promotion of the use of multi-sensory learning, timely support, cooperation with parents, encouragement for continuous work, discussion between teachers, pupils and parents, early involvement of pupils and parents in the preparation of the assistance plan, encouraging pupils to self-learning, etc.

Statement of Research Question
Does the tablet or iPad math app "Monster Numbers"; the educational math game for kids: addition, sutraction, numbers improve the calculation of mild intellectual disabled students?

Design and method

The quantitative method was used in this research. The total number of mildly intellectually disabled students in this study was 10 from two private schools. The study was limited to grade 1, 2 and 3, whose ages ranged from 6.8 to 9.10. The students were divided into two groups where the control group had 5 students, and the experimental group had 5 students. The pretest, the Woodcock-Johnson III, Test of Achievement limited to the calculation section was done during the first trimester of the school year. Then the intervention was applied, that is the educational math games for kids: addition, numbers for two trimesters one session per week for 20 minutes each session. The level of the play was set for each student based on their result at the pretest, as the game depends on the chronological age which is not effective in our study and we set it according to the calculated age level of the Woodcock-Johnson III, Test of Achievement calculation section. Then the posttest was done and the results were submitted for analysis, where the means and standard deviations, the independent samples T- test, and the paired samples T- test were calculated.

Limitations
The intervention of educational math game for kids: addition, numbers for mildly intellectually disabled students was limited at school hours, so that it would have given a better perspective if students were able to play it at home with their parents or guardians.

Results

Two independent sample t-tests were used in this research and two paired tests, the independent sample t-tests were used to compare if the experimental and control groups were the same at the beginning of the study, the second independent samples t-test was applied after the posttest to compare whether there was a difference between the control group and the experimental group. The results of the independent samples t-test proved that our hypothesis was supported but not significantly. Two paired tests were used to check whether there is a difference before and after applying the Math app Monster training for both the control and experimental group.

Descriptive Statistics
The mean and the standard deviations of the experimental and control group are presented in the table below:

Table 1: Mean and Standard Deviation

	PRETEST		POSTTEST	
	Mean	SD	Mean	SD
CONTROL	3	2.550	5	2.550
EXPERIMENTAL	4	2.739	8	3.082

It is clear that there is a difference in the means between the control and experimental group. The means in the posttest for the Experimental group is higher than that of the control group.

Independents Samples T-test

An independent sample t-test was conducted between the control and experimental group before applying the test and after applying the test. The results are presented in Table 2.

Table 2: Independent t-test

	T	DF	SIGNIFICANCE
CONTROL-EXPERIMENTAL PRETEST	-0.598	8	0.567
CONTROL-EXPERIMENTAL POSTTEST	-1.677	8	0.133

Table 2 reveals a high significance in the posttest between the control and experimental group. According to the test, the posttest values are t(8)=-1.677, p-value = 0.133 which is more than 0.05. The significance should be less than 0.05 in order to consider that the posttest between the two groups is significantly different; however it's not the case here. On the other hand, the pretest values are t(8)= -0.598, p-value=0.567 which is greater than 0.05, so the pretest is the same for both groups. This shows that both groups are homogeneous before the test. It appears that there is some effect of the training on the experimental group since the significance of the posttest is less than that of the pretest.

The effect size was calculated using the following formula: d= (x1-x2)/mean SD= 3/2.816=1.065. This value is considered large, and thus an independent t-test showed that the difference between the two conditions was significant. Another way to show the effect of the test is by viewing the error bar chart which showed the 95% confidence interval of both groups.

Figure 1: Error Bar Chart for Pretest
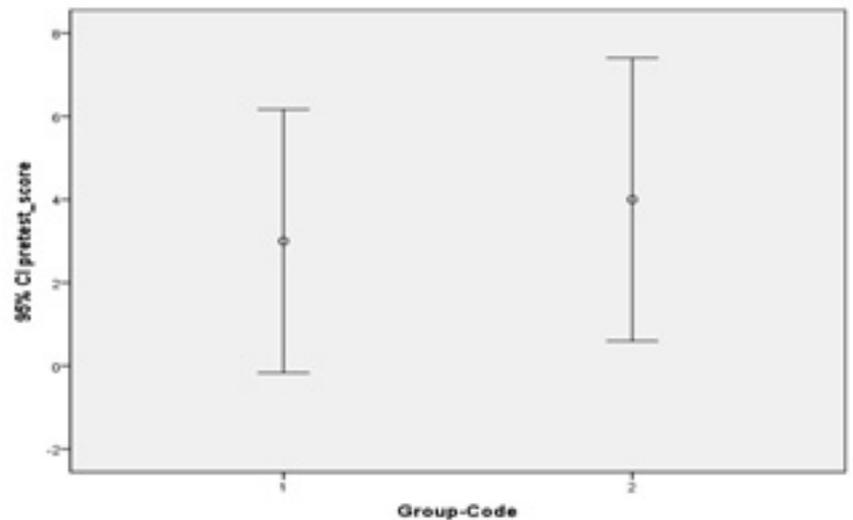
Figure 2: Error Bar Chart for Posttest
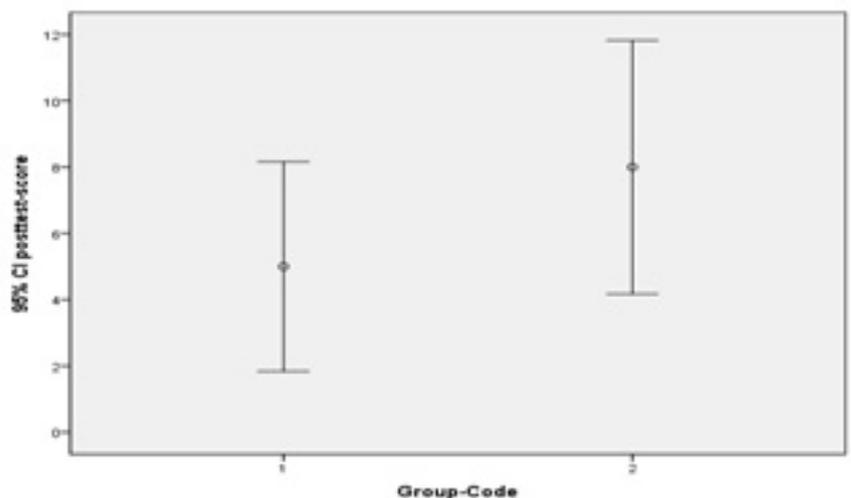
For the Error Bar Chart for the Calculation it is clearly shown how using the Math app Monster Numbers affected the results. The group code 2 which is the experimental group has a higher posttest range than group code 1 which is the control group.

Paired Samples T-test
The paired t-test is used to study if using the Math app Monster Numbers was effective or not. If the significance was less than 0.05 then this means that the group differs, and if the significance was more than 0.05 it means the group acted the same before and after the training. The paired t-test was applied on both experimental and control group before and after applying the Math app training and the results are shown below in Table 3.

Table 3: Paired t-test

	T	DF	SIGNIFICANCE
PRETEST-POSTTEST SCORE	-8.216	9	0.000

Table 3 shows that the results are: t(9)= -8.216, p-value =0.000. (The value is never zero but according to SPSS it is shown like this because usually SPSS rounds the values to 3 decimal places, so p must be less than 0.0005). So the significance is less than 0.05 which means that the group is significantly different and this proves the variation in the mean that SPSS calculated and it is shown in the table below.

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pretest score	3.50	10	2.550	.806
	Posttest score	6.50	10	3.100	.980

This confirms that using the Math app Monster Numbers training has an effect on the groups, The mean of the posttest score is higher than the mean of the pretest score. Pair 1 represents pairs of pretest and posttest from the control and experimental groups.

The effect size was measured to be 0.6875 which isn't considered to be large effect size.

Conclusion

The tablet or iPad math app "Monster Numbers"; educational math games for kids: addition, numbers intervention did help the intellectual disabled students in developing their calculation skills. Based on the Woodcock-Johnson III, Test of Achievement limited to the calculation section, the experimental group showed significant improvement in calculation. It is therefore recommended that mobile applications are to be used in the teaching learning process.

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The relationship between self-regulated learning, academic self-concept and the academic achievement motivation of students in the second grade of high school

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Abstract

Background: The purpose of this study was to investigate the relationship between self-regulated learning, academic self-concept and academic achievement motivation of students in the second grade of high schools of Khorramabad.

Materials and Methods: This was a descriptive-correlational study in which all the second-grade high school students in Khorramabad city in Iran who numbered 382 (201 boys, 182 girls) were selected as case study subjects. Data collection tools were Pintrich & De Groot Self-regulated learning strategy questionnaire and Karal Rodgers academic self-concept questionnaire. Pearson correlation and multivariate regression analysis were used for data analysis.

Results: The Pearson correlation coefficient test showed that there was a positive and significant relationship between self-concept and intrinsic motivation as well as between self-concept and extrinsic motivation of academic achievement (p <0.05). But, the relationship between self-concept and lack of motivation for academic achievement was inversely significant. The relationships between self-regulated learning and intrinsic motivation and the relationship between self-regulated learning and extrinsic motivation of academic achievement among secondary school students were also positively significant (p <0.05). There was a negative and inverse significant relationship between self-regulated learning and lack of academic motivation. The results of regression analysis also showed that self-concept and self-regulated learning variables were suitable predictors for academic achievement motivation.

Conclusion: According to the results of the research, in the educational system, the academic self-concept and self-regulated learning can be improved by counseling and clinical psychology programs in schools in order to develop academic achievement of students.

Key words: Academic achievement motivation, Academic self-concept, Self-regulated learning strategies

Introduction

Motivation is an important issue in the learning of trainees and students. Indeed, some professionals consider motivation to be the primary responsibility of instructors and teachers [1]. Despite the excitement of learners, it is unlikely that they would show enough effort to gain skills. Unfortunately, even the best training and educational program would not work if there was no "motivation" in trainees and students. There are still people who already have signs of motivation. Individuals from the very beginning to the last moments of life have self-arousal. Motivation is one of the characteristics of every living creature [2]. But in some cases, it is seen that learners do not like to perform based on the desires of teachers or instructors, they are motivated in any case. Therefore, the instructor and teacher play the role of controlling the learners' motivation and pushing the motives to learn a task or special work, rather than to play the role of creating motivation. It means that their attention is attracted in some ways and their energy is directed to engage in serious activities [3].

Sometimes, motivation is instinctive and sometimes logical decision making; often motivation is self-centered and in personal service [4]. Motives are a powerful force in the learning process. Motivation is not only a guiding force but is also confusing [5]. If you are motivated by something, the other things that you have to do, will cause bewilderment. This is the way you prefer to do something, and you have to choose another method [6].

Regarding the role of motivation in academic achievements, it can be said that motivation makes the learners strong. This force makes them active and involved in the work and responsibility. Motivation is a factor for insistence on work and continuity of activity [7]. Motivation is goal-centered and leads learners to complete their work and estimate the comprehension of an objective goal. Motivation is selective. It determines what action to take. Motivation determines the priority. It is a model for learner behavior, and organizes the activities, adds to workforce and efficiency, and leads to mapping or designing. The effects of four factors of persistence, orientation, prioritization and planned behavior are necessary for learning [8]. They create a rich source that can benefit the instructors, teachers and learners. No-one will remember anything without motivation, although the genetics and environment or intelligence and enriched teaching environment and improving teaching methods, have effects, to a large extent, on improving the educational situation. The heart of education is motivation. Motivation is a general tendency to achieve academically and motivation is a special way to comprehend a specific lesson. Today, with deeper attention to the new horizons of psychology, the interests and wishes of students are better known to teachers [9].

Students are the focus of training activities and find the necessary motivation and curiosity for learning. The third millennium education is different from the education of the past. The dramatic changes in behavioral sciences and the discovery of new horizons, meta-cognitive, self-concept

theories and confidence reinforcement are among the most important priorities of education. Students are not able to achieve great and supreme goals without being assured about moderate goals and strengthening their sense of accomplishment. Objectives must be moderately complex and should be guided in relation to everyday life issues and with regard to childhood interests in the primary school (with stories, the story of the display of childhood poetry (child literature)) and in middle school with regard to the psychology of puberty and the cognitive development of their interests and they should be educated as curious people and researchers.

Motivation is mixed in the world of children at initial stages of development. Children have a learning motive from birth, and for the same reason they continually interact with the environment. The more they grow, the stronger this motive. They want to act independently and learn as much as possible until it is time to read and write. At this stage, the child continues to strive and occasionally stops trying, or enjoys learning, and thinks that those who succeed are different from him. Therefore, they become distanced from the learning of science and knowledge. This distance is increased due to psychological and spiritual characteristics and culture of family or environmental factors, and sometimes it is irreparable, and thus they do not like and think about it [10]. Regarding what has been stated, the current research considers to answer if there is a significant relationship between self-concept, self-regulated learning and the academic achievement motivation in students in the second grade of high schools of Khorramabad.

Having the power of learning and remembering the materials included in the curriculum will lead to success and motivation for academic achievement [11]. Academic achievement motivation will require quantitative and qualitative changes in students' knowledge and skills through formal education that is measured by their annual average. Learning and teaching have a social context and occur in the classroom. Academic achievement motivation in terms of cognitive skills is not the sole educational goal. Self-esteem and social skills are both necessary as a condition for cognitive skills [12].

Absolutely, studies have shown that academic self-concept affects academic achievement motivation. Magno (2010) showed that students were at risk of dropping out of school, with negative attitudes toward education, and have poorer self-concept, and tendency to more external control. They described their parents as low-expectation and superficial subjects [13].

The strategies of learning motivation were above moderate among the students, but self-regulated learning strategies had no significant difference with the average level. Considering the structure of educational settings, the method of compiling educational content as well as the teaching patterns used by the professors, low self-regulated learning strategies of students seem to be logical.

The results of Delavar et al. (2015) in studying the relationship between self-regulated learning strategies, types of goal orientation and academic achievement of students confirmed that the self-regulated learning strategies and the dominant goal orientation predicted positively as well as the functional goal orientation negatively predicted students' academic achievement and the contribution of self-regulated learning strategies in this field is more than other variables [14].

.Deci & Ryan (2015) found a significant relationship between self-concept of the ability and academic achievement motivation (correlation of about 0.60) [15]. Zimmerman and Schunck (2015) in examining the relationship between self-regulated learning and academic achievement motivation found that there was a significant relationship between students' self-regulated learning and their academic achievement motivation and those with higher academic achievement have higher self-regulated learning [16]. Research results of Zimmerman and Schunck showed that self-regulated learning with very high percentage predicted students' academic achievements.

In a longitudinal study of four groups, Pajares & Kranzler (2014) measured the academic achievement of students at the ages of 9, 12, and 15 and their total self-concept was measured at the age of 12. The control variables, social class and ability, were measured at the age of 7 years. They did not find any evidence that academic achievement and self-concept had a causal relationship to one another, and stated the third variable (for example, social class and ability) as the cause of academic achievement and self-concept [17].

Mostafaei (2015) in a study compared the effect of smart and ordinary schools on critical thinking skills and academic achievement motivation of high school students in Tehran. The study was conducted as a causal comparison and the statistical population of the study was students in the third year of Tehran high school and pre-university in the field of mathematics [18]. The results of the research showed that the mean of critical thinking skills of students in smart schools was higher than that of ordinary school students. There was no significant difference among students of ordinary and smart schools in terms of academic achievement motivation. By analyzing the data of a large sample of high school students and measuring their academic achievement and total self-concept within two years, Malmberg (2014) found no evidence that the performance of a variable was more prominent than other variables. They suggested two possible explanations: self-concept and academic achievement might be the effect of a third variable, or both variables have the same impact in a cyclic form [19]. Therefore, even if academic achievement, self-concept of total ability and self-esteem interact with each other, the dominant causal direction is from achievement in the self-concept of the ability to achievement motivation [20]. Another study showed that the mean score of behavior and attitude increased after the intervention. But, no significant association was obtained between the mean scores of behavior and attitude prior to and after the intervention in the traditional group [21].

Self-regulated learning is one of the variables that are related to academic achievement motivation. Self-regulated learning is now considered as an important building block in education and has been addressed by policy makers, teachers, educators and parents. Self-regulation is the ability of a person to develop knowledge, skills and behaviors that can be transmitted from one field to another and from learning situations to work and leisure activities. This new construct has sparked discussions on school reform around the world. The self-regulated learning term has been rooted in the 1980's. Since then, self-regulation has been emphasized in learning, responsibility and commitment to learning in students [22]. Research conducted in this field focused on the interaction between cognitive, metacognitive and motivational strategies in a rational structure [23]. Also, the term self-regulated learning is valuable because in such behavior, "self" mediates between individuals and their learning objectives on the one hand and their goals on the other hand. For example, one's perception of their ability and one's perception of the difficulty of homework affects the quality of his or her learning [3].

The concept of self-regulated learning is a multifaceted construct, which involves complex interactions between the use of cognitive, meta-cognitive and motivational strategies. Self-regulated learning is a type of learning that results from the effects of self-produced thoughts, emotions, strategies and behaviors of students that are directed towards achieving goals. On the other hand, self-concept is a collection of perceptions or an overall evaluation of one's personality [11]. This assessment comes from mental evaluation that each person obtains from their own behavioral characteristics. Rogers defined self-concept as an interpretation a person has of his or her own self, or, in other words, what the individual feels of their own existence [6].

The importance of students' academic achievement has been addressed in many studies on facilitating predictors to achieve this goal. One of these predictors is the self-concept of a person. Self-concept can be understood as the perception of an individual that is formed as a result of the experiences of the individual with the environment and their relationship with others [11]. Self-concept is a dynamic system related to the beliefs, values, desires, talents and abilities of the individual. These factors determine the direction of individual life. Academic self-concept is also the process of formation of evaluation of self-concept influenced by the students' educational experiences and the interpretation of the educational environment and expresses the individual's knowledge and perceptions of weaknesses in a certain academic discipline and belief in their ability to successfully accomplish academic tasks at designed levels. Also it is one of the best predictors and mediators for effective and non-effective motivational variables and is one of the most important and influential factors in the learning process. Academic self-concept is strongly dependent on relative social information and is a reflection of others' evaluation with a normative nature. In other words, the academic self-concept of each person is a result of their comparison with others [24].

What further emphasizes the necessity of the present research with regard to the above issues is the study of the relationship between self-concept, self-regulated learning and the level of students' academic achievement, which is carefully considered in the present paper. The basic necessities of the research are as follows:

The first requirement was that education policy makers have a special and more specific view on self-regulated learning in the development and improvement of low-attained and unpromising students. The second requirement was that, for better student performance in school, the subject of self-concept was paid attention to based on the results of this study in a more planned form (a meeting with the parents, instructors and educational workshops). The third requirement was that, given the fact that the vast majority of students with lack of academic motivation are at risk of developing disorders, the academic achievement motivation should be taken into consideration by teachers in form of conference and group discussions in the classroom. The fourth requirement was that families and teachers should pay attention to the students' self-concept, and that students who are weak in this regard can provide their own self-esteem by contributing to classroom activities. The fifth requirement was that the research flaws were resolved in relation to the examination of these three variables (self-concept, self-regulated learning and academic achievement motivation). Researchers have also devoted part of their research to the study of these variables, as conducting educational research in education can create a growing environment for the development of a country. Therefore, according to the discussed issues, the purpose of the present study was to determine the relationship between self-regulated learning, academic self-concept and academic achievement motivation in the second-grade high school students in Khorramabad, Iran.

Research methodology

Research method:
Since the purpose of the research was to describe the conditions or phenomena under study and the implementation of the research can help to learn more about the existing conditions and help the decision-making process, the present research method was descriptive and correlational.

Statistical population of the research
The statistical population of the research included all the second-grade high school students in Khorramabad, Iran (8254), who were studying in the academic years 2015-2016.

Sampling method and sample size:
Based on Krejcie & Morgan tables, 382 individuals were selected to determine the sample size. The questionnaires were distributed among them to collect the data. 95 people were in the field of mathematics-physics, 95 people were in the field of experimental sciences, 94 in the field of humanities, 115 in technical sciences and 75 in the field of skill and knowledge. Out of 382 in the sample; 118 were

14-15 years old; 217 were at the age of 16-17, and 47 were between 18 and 19.

Measuring tools
Self-regulation strategy inventory
This questionnaire was arranged in 47 items by Pintrich et al. (2009) in two sections: Motivational beliefs and self-regulated learning strategies (Cognitive and Metacognitive Strategies) [25]. The subscale of self-regulated learning strategies includes 22 phrases and measures three aspects of academic self-regulation, namely cognitive strategies, metacognitive strategies and resource management. Cognitive strategies have 13 phrases. The Likert scale was used (I totally agree, agree, no idea, disagree, and totally disagree).

Pintrich and De Groot (1991) reported cognitive strategies as 0.88, meta-cognitive strategies as 0.83, and motivational beliefs as 0.76 by Cronbach Alpha [25].

Pintrich self-regulation learning strategies questionnaire (1990) was scored as follows (I totally agree: 5, I agree :4, I have no idea: 3, I disagree: 2 and totally disagree:1). Also, the cognitive strategies include 11 phrases as follows: repeating and reviewing contain phrases 77,14,24; expansion includes note taking with phrase 17; summarizing contains phrases 73,11; Organizing contains the phrases 74.72.14.24.24; and comprehension includes phrases 11,12. Metacognitive strategies and resource management include 4 phrases as follows: Planning includes phrases 74, 14; monitoring and control include the phrases 71, 71, 13, 24; the ordering includes attempts and. the perseverance with phrases 14 ,13; and the ordering activity contains phrase 73. The motivational beliefs section includes 23 phrases with four components of self-efficacy, goal orientation, internal evaluation, and exam anxiety as follows: self-efficacy includes phrases 22, 21, 14, 17, 12, 13, 4, 4, 2; goal orientation includes phrases 27,14,11,7,1. Internal evaluation includes 23, 14, 4, 3; exam anxiety includes 23, 21, 14, 13; 11, 4, 1. By adding each of the questions, the score of each sub-scale is obtained.

Vallerand Achievement Motivation scale. AMS (1992):
The scale of academic motivation is the translation of the English sample of the academic motivation scale. This scale is built on the theory of "self-determination" and has 28 questions with seven options that measure three dimensions of intrinsic motivation, extrinsic motivation and lack of motivation. The intrinsic motivation refers to a person who voluntarily and inwardly carries out a specific task, and, besides the external rewards, doing homework is worthwhile and satisfactory for a person. But extrinsic motivation refers to the motive which forces people to do their homework for external rewards and reinforcements as well as when people are excited externally and act to accomplish something more than their own pleasure. To assess psychometrically the questionnaire, all face validity and content validity stages were performed (qualitative and quantitative). Reliability of the questionnaire was verified by Cronbach's alpha (a = 0.88) and splitting (r = 0.73). In the study of Veysani et al. (2012), Cronbach's alpha for

subscales of intrinsic motivation, extrinsic motivation and lack of motivation were 0.84, 0.86, and 0.67 respectively [26]. Also, the academic motivation questionnaire was approved by faculty members of school of Education Sciences of Shiraz University in terms of face validity and content validity. The reliability of the tool was calculated by Cronbach's alpha method. At the time of the test, it was 0.73 for two weeks. Cronbach's alpha coefficient for the whole questionnaire was also reported at 88%.

Akbari (2007) evaluated the validity of the achievement motivation test among high school students in Gilan province [27]. Cronbach's alpha for the whole questionnaire was 0.84.

Content validity was confirmed by several psychologists, psychometrists and advisers in education. The criterion validity was 0.42 obtained through correlation coefficient of a person's score made by an average of two years ago and the correlation coefficient of the individual score in the scale made by the average opinions of high school teachers and assistants was 0.56, which is evidence of the criterion validity. The correlation between the score of each question and the total test and the correlation of the triple components suggest the construct validity. The response to each item is based on a seven-point Likert scale (not at all, very low, small, medium, high, very high, perfectly) and they were scores from 1 to 7, respectively. Then, the amount of academic motivation is ranked according to obtained score, so that the scores between 27 and 70 are poor academic motivation, scores from 70 to 112 show motivation at a moderate level and the scores above 112 are considered very good at academic motivation.

Academic self-concept questionnaire

This questionnaire was prepared in 1938-1957 to measure the level of self-concept of individuals. This test consists of two forms, in both of which the same set of 25 pairs of opposite personality traits are presented. The subject is asked to answer the first form based on how he sees himself and in the second form how he wishes to be. In this test, high self-concept means no matching between the actual and ideal selves. The self-concept question has six distinct dimensions, namely self-concept, physical, social, rational, moral, educational, and temperament.

Molaei (1998) reported the criterion validity by 0.59 and the reliability of the tool as (0.78) by the alpha method [28]. Zarei (2006) reported the criterion validity as 0.71 and the reliability of the tool was 0.82 by alpha method. Respondents have four choices and should choose one based on their self-concept ranging from completely disagree to completely agree [29]. The choices or responses are in a way that the scoring system remains the same for all questions, namely 1- 2- 3- 4-5 whether the question is positive or negative. If the respondent ticks the first choice (P), the score will be 4, the score 3 is for the second choice and 2 for the third choice is and the score 1 is for the fourth choice. The total scores of 60 questions show the total score of the individual's self-concept, in this questionnaire the high score reflects a higher self-concept and low score shows lower self-concept.

Data analysis and processing

In order to analyze the data in this research, the following statistical methods and SPSS version 22 were used: In the descriptive analysis section the mean, standard deviation and percentage of scores and variables along with plotting a column chart were used. In Inferential Analysis: Kolmogorov Smirnov Test to examine normal distribution, Pearson correlation coefficient and multivariate regression with SPSS 22 were used. Also, for all hypotheses, the significance level was considered to be P <0.05.

Research Findings

The Pearson correlation coefficient test showed that there was a positive and significant relationship between self-concept and intrinsic motivation as well as between self-concept and extrinsic motivation of academic achievement (p <0.05). But, the relationship between self-concept and lack of motivation for academic achievement was inversely significant. The relationships between self-regulated learning and intrinsic motivation and the relationship between self-regulated learning and extrinsic motivation of academic achievement among secondary school students were also positively significant (p <0.05). There was a negative and inverse significant relationship between self-regulated learning and lack of academic motivation. The results of regression analysis also showed that self-concept and self-regulated learning variables were suitable predictors for academic achievement motivation. The results of this study are shown in Tables 1 to 22.

Inferential analysis
Testing statistical data for normalization

For data inferential analysis, the data were first tested by the Kolmogorov-Smirnov test to determine which statistics are used for analysis. The results of this test are shown in Table 1.

Table 1: Test of Questionnaires for normalization (Kolmogorov-Smirnov test)

Indicators		Mean	Standard deviation	Z	Probability value	Type of distribution
Variables	Self-concept	40.397	5.94	7.85	0.01	Normal
	Self-regulated learning	125.591	32.89	7.37	0.01	Normal
	Intrinsic motivation	56.82	9.26	10.39	0.01	Normal
	Extrinsic motivation	57.16	9.47	8.41	0.01	Normal
	Lack of motivation	16.92	4.73	9.15	0.01	Normal
	Academic achievement motivation	130.911	18.92	11.41	0.01	Normal

According to Table 1, the distribution of the response of the samples to each of the variables is significant with 0.05, it is concluded that the distribution of these variables is normal, therefore, parametric tests were used in the analysis of information.

Test of research hypotheses:
In the test of research hypotheses with SPSS 22, Pearson correlation coefficient and multivariate regression analysis were used to investigate the relationship between variables and determine the effect of independent variable on dependent ones. In this section, firstly, the results, correlation coefficient and regression are discussed.
The main hypothesis: There is a significant relationship between self-concept, self-regulated learning and the academic achievement motivation in the second-grade high school students in Khorramabad.

Table 2: Correlation coefficient of self-concept, self-regulated learning and academic achievement motivation in the second-grade high school students

Variable		Academic achievement motivation
Self-concept	Correlation	0.44
	Significance	0.00
Self-regulated learning	Correlation	0.40
	Significance	0.00

Based on the results of Table 2, the correlation coefficient for self-concept is (r = 0.44) with significance level of (sig = 0.00) and for self-regulated learning, it is "r = 0.40" with significance level of (sig = 0.00). There was a positive and significant relationship with p <0.05 (more than 95% confidence). Therefore, the hypothesis contrary to the hypothesis of the investigator was confirmed and the null hypothesis was rejected. That is, the higher the self-concept and self-regulated learning of students, the higher the academic achievement motivation.

Table 3: Regression (coefficient of determination) of self-concept and self-regulated learning with extrinsic motivation of academic achievement in the second-grade high school students

	Correlation	Squared correlation coefficient	Standard error estimate
Self-concept	0.44	0.19	6.38
Self-regulated learning	0.40	0.16	6.39

The results of Table 3 indicate that according to the correlation coefficient of 0.44, the self-concept predicts 0.19 of academic achievement motivations and according to the correlation coefficient of 0.40, self-regulated learning predicts 0.16 of academic achievement motivation of students

Table 4: ANOVA analysis of self-concept and self-regulated learning with academic achievement motivation of the second-grade high school students

	Squared sum	Freedom degree	Mean squares	F	Significance level
Regression	2561.87	2	2561.87		
Residual	10465.41	379			
Total	13027.29	381	40.72	62.91	0.00

Table 4 shows that according to the total sum of regression squares of 13027.29 with mean squares of 2561.87, F = 62.91, p = 0.00, the predictive value of self-regulated learning and self-concept for the academic achievement motivation is significant.

The first hypothesis: There is a relationship between self-concept and the intrinsic motivation of academic achievement in the second-grade high school students in Khorramabad.

Table 5: Correlation coefficient of self-concept with intrinsic motivation of academic achievement in the second-grade high school students

Intrinsic motivation		
Self-concept	Pearson correlation coefficient	0.91
	Significance	0.00
	Number	382

Based on the results of Table 5, Pearson correlation coefficient of (r = 0.91) with significance of (sig = 0.02) indicates that there is a positive and significant relationship between self-concept and intrinsic motivation of academic achievement in the second-grade high school students with p <0.05 (with confidence greater than 95%). Therefore, the hypothesis contrary to the hypothesis of the investigator is confirmed and the null hypothesis is rejected. That is, the higher the self-concept of students in the second grade of high school, the greater the intrinsic motivation of academic achievement.

Table 6: Regression (coefficient of determination) of self-concept with intrinsic motivation of academic achievement in secondary school students

Correlation	Squared correlation coefficient	Standard error estimate
0.91	0.83	0.79

The results of Table 6 show that with respect to the correlation coefficient of 0.53, the self-concept predicts 0.28 of the intrinsic motivation of academic achievement of the second-grade high school students.

Table 7: ANOVA analysis of self-concept and intrinsic motivation for academic achievement of the second-grade high school students

	Sum of squares	Freedom degree	Mean squares	F	Significance level
Regression	887.354	1	887.354		
Residual	181.03	380			
Total	1068.38	381	0.64	1387.16	0.00

Table 7 shows that according to the total sum of regression squares of 326.989 with mean squares of 91.76, P = 0.003, F = 0.77, predictive value of self-concept is significant for intrinsic motivation of academic achievement.

The second hypothesis: self-concept is associated with the extrinsic motivation of academic achievement in the second-grade high school students in Khorramabad city.

Table 8: Correlation coefficient of self-concept with extrinsic motivation of academic achievement in the second-grade high school students

Extrinsic motivation		
Self-concept	Pearson correlation coefficient	0.10
	Significance	0.048
	Number	382

Based on the results of Table 8, the Pearson correlation coefficient of (r = 0.10) with significance of (sig = 0.48) indicates that there is a positive and significant relationship between self-concept and extrinsic motivation of academic achievement in the second-grade high school students with p <0.05 (with confidence greater than 95 percent). Therefore, the hypothesis contrary to the hypothesis of the investigator is confirmed and the null hypothesis is rejected. That is, the higher the self-concept of students in the second-grade of high school, the greater the extrinsic motivation of academic achievement.

Table 9: Regression (coefficient of determination) of self-concept with extrinsic motivation of academic achievement in the second-grade high school students

Correlation	Squared correlation coefficient	Standard error estimate
0.10	0.010	9.43

The results of Table 9 show that with respect to the correlation coefficient of 10.0, the self-concept predicts 0.010 of extrinsic motivation for academic achievement of the second-grade high school students.

Table 10: ANOVA analysis of self-concept and extrinsic motivation for academic achievement of the second-grade high school students

	Sum of squares	Freedom degree	Mean squares	F	Significance level
Regression	348.80	1	348.80		
Residual	33829.80	380			
Total	34178.61	381	89.02	3.91	0.048

Table 10 shows that according to total sum of regression squares of 34178.61 with a mean square of 348.80, F = 3.91, p = 0.048, the predictive value of self-concept is significant for the extrinsic motivation of academic achievement.
The third hypothesis: There is a relationship between self-concept and lack of academic achievement motivation in the second-grade high school students in Khorramabad.

Table 11: Correlation coefficient of self-concept with lack of academic achievement motivation in the second-grade high school students

Lack of motivation		
Self-concept	Pearson correlation coefficient	- 0.148
	Significance	0.004
	Number	382

Based on Table 11, Pearson correlation of (r = -0.1488) with sig of (004/0004) indicates that there is a negative, reverse and significant relationship between self-concept and the lack of academic achievement motivation in the second-grade high school students with $p < 0.05$ (with confidence greater than 95%). Therefore, the hypothesis contrary to the hypothesis of the investigator is confirmed and the null hypothesis is rejected. That is, the higher the self-concept of the second-grade high school students, the lower the lack of motivation for academic achievement.

Table 12: Regression (coefficient of determination) of self-concept with lack of academic achievement motivation in the second-grade high school students

Correlation	Squared correlation coefficient	Standard error estimate
0.27	0.077	96.70

The results of Table 12 show that with respect to the correlation coefficient of 0.27, the self-concept predicts 0.077 of lack of academic achievement motivation of the second-grade high school students.

Table 13: ANOVA analysis of self-concept and lack of academic achievement motivation of the second-grade high school students

	Sum of squares	Freedom degree	Mean squares	F	Significance level
Regression	961.04	1	961.04		
Residual	11494.78	380			
Total	12455.83	381	44.90	21.40	0.00b

Table 13 shows that according to total sum of regression squares of 961.04 with mean squares of 961.04, F = 21.40, p = 0.00, the predictive value of self-concept is significant for the lack of academic achievement motivation.

The fourth hypothesis: There is a relationship between self-regulated learning and intrinsic motivation of academic achievement in the second-grade high school students in Khorramabad

Table 14. Correlation coefficient of self-regulated learning and intrinsic motivation of academic achievement in the second-grade high school students

Intrinsic motivation		
Self-regulated learning	Pearson correlation coefficient	0.15
	Significance	0.002
	Number	382

Based on the results of Table 14, Pearson correlation coefficient of (r = 0.15) with significance of (sig = 0.002) indicates that there is a positive and significant relationship between self-regulated learning and intrinsic motivation of academic achievement in the second-grade high school students with p <0.05 (with confidence greater than 95 percent). Therefore, the hypothesis contrary to the hypothesis of the investigator is confirmed and the null hypothesis is rejected. That is, the higher the self-regulated learning of students in the second-grade of high school, the greater the intrinsic motivation of academic achievement.

Table 15: Regression (coefficient of determination) of self-regulated learning and intrinsic motivation of academic achievement in the second-grade high school students

Correlation	Squared correlation coefficient	Standard error estimate
0.29	0.086	8.52

The results of Table 15 show that with respect to the correlation coefficient of 0.29, the self-regulated learning predicts 0.086 of intrinsic motivation for academic achievement of the second-grade high school students.

Table 16: ANOVA analysis of self-regulated learning and intrinsic motivation for academic achievement of the second-grade high school students

	Sum of squares	Freedom degree	Mean squares	F	Significance level
Regression	1746.67	1	1746.67		
Residual	18584.22	380			
Total	20330.90	381	72.59	24.06	0.00

Table 16 shows that according to total sum of regression squares of 20330.90 with mean squares of 1746.67, F = 24.06, p = 0.00, the predictive value of self-regulated learning is significant for intrinsic motivation of academic achievement. The fifth hypothesis: There is a relationship between self-regulated learning and extrinsic motivation of academic achievement in the second-grade high school students in Khorramabad.

Table 17. Correlation coefficient of self-regulated learning and extrinsic motivation of academic achievement in the second-grade high school students

Extrinsic motivation		
Self-regulated learning	Pearson correlation coefficient	-0.25
	Significance	0.00
	Number	382

Based on the results of Table 17, Pearson correlation coefficient of (r = -0.25) with significance (sig = 0.00) indicates that there is a negative, reverse and significant relationship between self-regulated learning and extrinsic motivation of academic achievement in the second-grade high school students with p <0.05 (with confidence greater than 95 percent). Therefore, the hypothesis contrary to the hypothesis of the investigator is confirmed and the null hypothesis is rejected. That is, the higher the self-regulated learning of students in the second-grade of high school, the lower the extrinsic motivation of academic achievement.

Table 18: Regression (coefficient of determination) of self-regulated learning and extrinsic motivation of academic achievement in the second-grade high school students

Correlation	Squared correlation coefficient	Standard error estimate
0.24	0.065	20.51

The results of Table 18 show that with respect to the correlation coefficient of 0.24, the self-regulated learning predicts 0.065 of extrinsic motivation for academic achievement of the second-grade high school students.

Table 19: ANOVA analysis of self-regulated learning and extrinsic motivation for academic achievement of the second-grade high school students

	Sum of squares	Freedom degree	Mean squares	F	Significance level
Regression	114314.35	1	7384.88		
Residual	106929.47	380			
Total	11.4314.35	381	420.98	17.54	0.00

Table 19 shows that according to total sum of regression squares of 114314.35 with mean squares of 7384.88 and F = 17.54, p = 0.00, the predictive value of self-regulated learning is significant for extrinsic motivation of academic achievement.

The sixth hypothesis: There is a relationship between self-regulated learning and lack of academic achievement motivation in the second-grade high school students in Khorramabad

Table 20: Correlation coefficient of self-regulated learning and lack of academic achievement motivation in the second-grade high school students

Lack of motivation		
Self-regulated learning	Pearson correlation coefficient	-0.178
	Significance	0.004
	Number	382

Based on the results of Table 20, Pearson correlation coefficient (r = -0.178) with significance (sig = 0.004) indicates that there is a negative, reverse and significant relationship between self-regulated learning and lack of academic achievement motivation in the second-grade high school students with p <0.05 (with confidence greater than 95 percent). Therefore, the hypothesis contrary to the hypothesis of the investigator is confirmed and the null hypothesis is rejected. That is, the higher the self-regulated learning of students in the second-grade of high school, the lower the extrinsic motivation of academic achievement.

Table 21: Regression (coefficient of determination) of self-regulated learning and lack of academic achievement motivation in the second-grade high school students

Correlation	Squared correlation coefficient	Standard error estimate
0.178	0.032	6.99

The results of table 21 show that with respect to the correlation coefficient of 0.178, the self-regulated learning predicts 0.032 of lack of motivation for academic achievement of the second-grade high school students.

Table 22: ANOVA analysis of self-regulated learning and lack of motivation for academic achievement of the second-grade high school students

	Sum of squares	Freedom degree	Mean squares	F	Significance level
Regression	410.03	1	410.03		
Residual	12510.97	380			
Total	12921.00	381	48.87	8.39	0.004

Table 22 shows that according to total sum of regression squares of 12921.00 with mean squares of 410.03 and F = 8.39, p = 0.004, the predictive value of self-regulated learning is significant for lack of academic achievement motivation.

Discussion

Regarding the main hypothesis of the research, there was a positive and significant relationship between self-concept, self-regulated learning and academic achievement motivation. Also, the results of regression analysis showed that self-concept and self-regulation variables predict respectively 0.19 and 0.16 of academic achievement motivation of the second-grade high school students. The results of the analysis of the fourth hypothesis of the research were consistent with the result of Zimmerman & Ponz, 2017[16], Pintrich (2016) [25], Jing (2017) [30]. Regarding the first hypothesis, there was a positive and significant relationship between self-concept and the intrinsic motivation of academic achievement among the second-grade high school students. Also, the results of regression analysis showed that self-concept predicted 0.28 of the intrinsic motivation of academic achievement of the second-grade high school students. The results of the

first hypothesis of the research are consistent with results of Pintrich (2016) [25]. Regarding the second hypothesis, there was a positive and significant relationship between self-concept and the extrinsic motivation of academic achievement among the second-grade high school students. Also, the results of regression analysis showed that self-concept predicted 0.010 of the extrinsic motivation of academic achievement of the second-grade high school students. The results of the second hypothesis of the research are consistent with research results of Pintrich (2016) [25] and Hansford & Hattie (2017)[1]. Regarding the third hypothesis of the research, there is a negative and significant relationship between self-concept and lack of academic achievement motivation. Also, the results of regression analysis showed that self-concept predicted 0.077 of lack of academic achievement motivation of the second-grade high school students. Regarding the fourth hypothesis, there was a positive and significant relationship between self-regulated learning and the intrinsic motivation

Regarding the main hypothesis of the research, there was a positive and significant relationship between self-concept, self-regulated learning and academic achievement motivation. Also, the results of regression analysis showed that self-concept and self-regulation variables predict respectively 0.19 and 0.16 of academic achievement motivation of the second-grade high school students. The results of the analysis of the fourth hypothesis of the research were consistent with the result of Zimmerman & Ponz, 2017[16], Pintrich (2016) [25], Jing (2017) [30]. Regarding the first hypothesis, there was a positive and significant relationship between self-concept and the intrinsic motivation of academic achievement among the second-grade high school students. Also, the results of regression analysis showed that self-concept predicted 0.28 of the intrinsic motivation of academic achievement of the second-grade high school students. The results of the first hypothesis of the research are consistent with results of Pintrich (2016) [25]. Regarding the second hypothesis, there was a positive and significant relationship between self-concept and the extrinsic motivation of academic achievement among the second-grade high school students. Also, the results of regression analysis showed that self-concept predicted 0.010 of the extrinsic motivation of academic achievement of the second-grade high school students. The results of the second hypothesis of the research are consistent with research results of Pintrich (2016) [25] and Hansford & Hattie (2017)[1]. Regarding the third hypothesis of the research, there is a negative and significant relationship between self-concept and lack of academic achievement motivation. Also, the results of regression analysis showed that self-concept predicted 0.077 of lack of academic achievement motivation of the second-grade high school students. Regarding the fourth hypothesis, there was a positive and significant relationship between self-regulated learning and the intrinsic motivation of academic achievement among the second-grade high school students. Also, the results of regression analysis showed that self-regulated learning predicted 0.086 of the intrinsic motivation of academic achievement of the second-grade high school students.

Regarding the fifth hypothesis, there was a negative, reverse and significant relationship between self-regulated learning and the extrinsic motivation of academic achievement among the second-grade high school students. Also, the results of regression analysis showed that self-regulated learning predicted 0.065 of the extrinsic motivation of academic achievement of the second-grade high school students. The results of the fifth hypothesis of the research are consistent with result of Hansford & Hattie (2017) [1]. Regarding the sixth hypothesis, there was a negative, reverse and significant relationship between self-regulated learning and lack of academic achievement motivation among the second-grade high school students. Also, the results of regression analysis showed that self-regulated learning predicted 0.032 of lack of academic achievement motivation of the second-grade high school students.

Conclusion

According to the results of the research, in educational system, the academic self-concept and self-regulated learning can be improved by counseling and clinical psychology programs in schools in order to develop academic achievement of students.

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Effects and mechanisms of medicinal plants on diaper dermatitis: A systematic review

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Abstract

Diaper dermatitis (DD) is one of the most common skin disorders in infants and, if not treated properly, causes several complications such as infection, pain, and itching. The present review was conducted to report the findings on the action mechanisms and effects of medicinal plants on the treatment of DD and diaper rash.

The key words "diaper dermatitis" or "diaper rash" or "nappy rash" in combination with "medicinal plant", "herb*", and "phyto*" were used to conduct this review. Relevant articles were retrieved from databases including Institute for Scientific Information (ISI), PubMed, Scopus, Islamic World Science Citation Database (ISC) and Google Scholar.

Medicinal plants and plant-based compounds reduce and treat DD mainly due to their anti-inflammatory, antimicrobial (mainly antibacterial and antifungal), and antioxidant properties. Helping to accelerate the recovery and regeneration of the skin and to reduce moisture in the diaper environment is another mechanism of medicinal plants, for treating DD. Plants such as Calendula officinalis, Matricaria chamomilla L., A. barbadensis Mill., Prunusdulcis, Hamamelis, and Lawsonia inermis L. can be useful to treat this condition.

Medicinal plants and their compounds comprise an effective treatment for DD and can be used as a supplementary or adjuvant therapy because of low cost, easy use, availability, and lack of systemic effects.

Introduction

Diaper dermatitis (DD) is one of the most common disorders in infants (1), which is caused either directly by diapers or by the environment caused by the diaper (2). DD is associated with several factors; for example, contact dermatitis (3), allergic contact dermatitis, and fungal, viral, and bacterial infections that can cause suck disorder and, following such infections, certain complications such as skin rashes appear. (4).

Itching, infection, and pain are the symptoms of DD (1, 5). If this disorder is caused by allergic reactions and leads to an increase in IgE, it requires a more complex treatment process (6). There are several therapies for treating this disorder depending on pH balance, microbial load, and moisture (6-8).

Today, chemical and plant treatments are of particular importance for the treatment of various disorders and diseases (4, 9, 10). Meanwhile, the use of medicinal plants is increasing due to their comparatively fewer side effects and lower cost. Medicinal plants can represent effective treatments for various disorders (19-19), including dermatological diseases (20). Hence, in this study, we examined the medicinal plants and plant-based compounds affecting the treatment of DD and diaper rash.

Materials and Methods

The key words diaper dermatitis or diaper rash or nappy rash in combination with medicinal plant, herb, and phyto as well as the Endnote software were used to retrieve the relevant articles from the databases Institute For Scientific Information, PubMed, Scopus, Islamic World Science Citation Database, and Google Scholar. Then, the plants and the plant-based products that had been reported to be effective on diaper dermatitis and diaper rash were selected according to the comments of two colleagues. The articles included in this review were published between 2005 and 2017. The articles whose full texts were not accessible, studies with non-positive effects, published in non-English and non-Persian language, and not related to the purpose of this study were excluded after the authors' agreement was achieved. Figure 1 illustrates the process of selecting the articles for final analysis.

Figure 1. Flowchart of the process of selecting articles
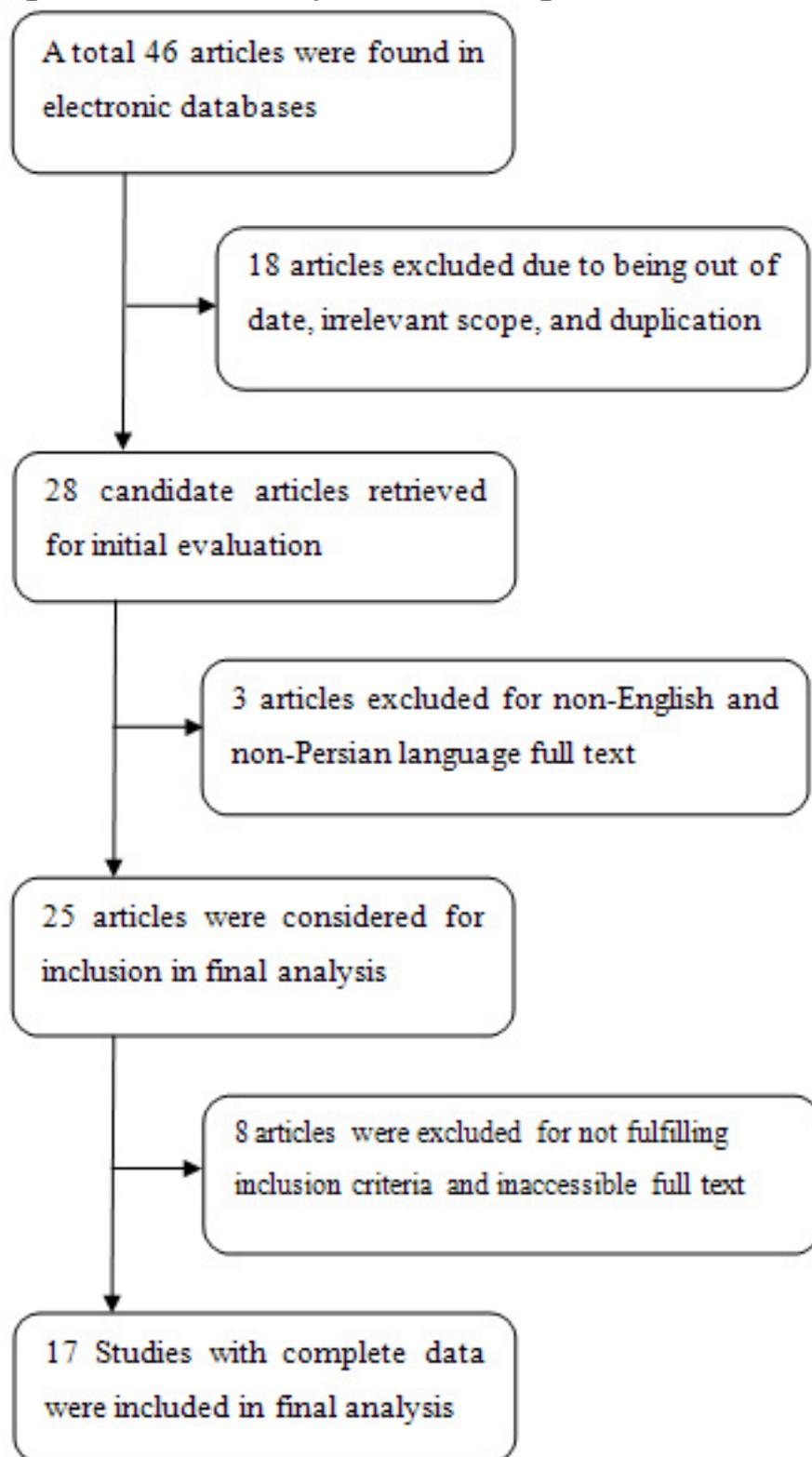
Results

Plants are rich sources of effective compounds that can be used to treat skin diseases and cutaneous lesions by certain routes of administration such as topical, oral, and acupunctural use (20, 21). Medicinal plants and plant-based compounds, through various mechanisms, can be effective in reduce complications of, or treatment of DD (Table 1).

Table 1: Effective medicinal plants for diaper dermatitis

Plant names	Method of application	Main effects and action mechanisms	References
Calendula officinalis	Cream/Ointment	Antibacterial, anti-inflammatory, water-absorbing and skin-protecting properties and as a result accelerating improvement of lesions	(22-27)
Matricaria chamomilla L. (Chamomile)	Ointment	Antibacterial and anti-inflammatory effects and reducing rash sites	(24, 27)
A. barbadensis Mill. (Aloe vera)	Methanol extract	Antibacterial and anti-allergic effect	(28)
Lawsonia inermis L. (Henna)	Dried leaves	Reducing the severity of diaper dermatitis	(29)
Prunus dulcis (Almond)	Oil-based ointment	Decreasing frequency or completely treating diaper dermatitis, improving dryness and exerting protective effect against future episodes of diaper dermatitis	(7)
Hamamelis (Witch-hazel)	Ointment	Reducing total scores of signs and symptoms of skin injuries, diaper dermatitis, or localized inflammation of skin	(30)

In addition, there are other medicinal and nature-based compounds that reduce the symptoms of DD in many ways. As an example, a natural combination of honey, olive oil, and beeswax can reduce the complications of DD by reducing prostaglandin synthesis, inhibiting fungal or bacterial growth, increasing nitric oxide concentrations in the lesions, and exerting antioxidant and anti-inflammatory effects (31).

A topical application of a plant combination was investigated in an innovative manner. This combination consisted of zinc oxide (serving as a barrier material), cod liver oil (for conditioning; source of vitamins A and D), lavender and chamomile (for fragrance), natural vitamin E (for skin conditioning), lanolin (for skin conditioning), fragrance, petrolatum or petroleum jelly (serving as a barrier material), talc, and purified water. It was found that this combination can be used to treat diaper rash by exerting antimicrobial effects and due to a compound, namely, anthocyanin (32, 33).

In the study of Chatterjee et al., a herbal cream was studied for its therapeutic effects on diaper-like skin rashes. That study showed that its antibacterial properties were due to a compound called zinc calx, *Aloe vera, Vitexnegundo*, and *Rubia cordifolia*, its anti-inflammatory properties were attributed to *A. vera, V. negundo*, and *R. cordifolia*, which in turn have wound-healing activity due to the presence of *A. vera*, and its antioxidant properties were due to *V. negundo, Prunus amygdalus*, and *R. cordifolia* (34).

Another compound consisting of honey, beeswax and olive oil was studied by El Sakka et al. In that study, it was found that this natural combination could be used as an alternative or a complementary treatment for the treatment of DD (35).

Obviously, it should be kept in mind that some herbs (even those that have been reported to be effective in the treatment of dermatitis) have not only no healing properties for the skin, but their use or contact with skin can cause dermatitis as an allergen.

Therefore, necessary precautions should be taken into account even in local and dermal application of medicinal plants (36, 37).

In some studies, the response to herbal treatments was less encouraging than that to chemical treatments, and was found to have no effect on the treatment of DD (38). The design, sample size, and randomisation can lead to different results in clinical trials.

But, in general, it seems that medicinal plants protect against H2O2-induced oxidative stress due to their antioxidant properties (such as phenolic compounds) on keratinocytes (39, 40).

Also, medicinal herbs can reduce the microbial activity of damaged skin environment by affecting certain bacteria such as *Streptococcus pyogenes*, *Staphylococcus aureus*, and methicillin-resistant *S. aureus* (MRSA), exerting anti-bacterial effect, and making growth medium inappropriate for bacterial growth and pathogenic fungi (41-44).

For example, the ethanolic extract of Calendula officinalis can have antimicrobial activity against *Escherichiacoli, Vibrio cholera*, and *Candida albicans*.

Its methanol extract can also have antifungal activity against *C. albicans,* and its chloroform and acetone can have antimicrobial activity against *E. coli* (45).

Medicinal plants and their derivatives have generally been shown to reduce Scoring Atopic Dermatitis (SCORAD) index, erythematic intensity, pruritis, itching, and trans-epidermal water loss (TEWL), as well as to improve skin sebum contents, hydration level, and expression of various inflammatory mediators (21). Considering the increasing importance of taking medicinal herbs in the treatment of various diseases in Iran (46-58), topical use of medicinal herbs can be used in children for safety reasons.

Conclusion

The use of medicinal plants and their compounds is an effective therapeutic strategy for DD. They can be used as supplementary or adjuvant therapy because of their low cost, easy use, availability, and lack of systemic effects. But using them in some infants and children may have allergic reactions that should be addressed and avoided.

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Investigation of periodontal infections and its relation with cardiovascular diseases

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Abstract

The relationship between periodontitis and cardiovascular diseases has been of interest in recent years. Cardiovascular diseases in the developed countries account for 50% of the mortality rate and are the principal causes of death. Periodontitis, one of the most common diseases of humans, is an infectious condition that can result in inflammatory destruction of the peridontal ligament and alveolar bone. Periodontitis and atherosclerosis have complex etiologies such as genetics and gender, and they potentially share many risk factors, the most significant of which may be smoking. A number of studies have shown a significant relationship between periodontitis and cardiovascular diseases, but the need for further studies of new definitions of the relationship between them, especially in women, seems to be required.
Key words: Periodontal infectious diseases, Cardiovascular diseases, Periodontal
diseases as a risk factor.

Introduction

Cardiovascular disease is one of the most common medical problems and the main cause of death in the world. (1, 2) The relationship between periodontitis and cardiovascular diseases has recently been considered. Periodontitis is an infectious disease that results in gum inflammation, periodontal tissues, and progressive alveolar bone loss and is considered as an important focus of infection in the body. (3) Increased levels of acute inflammatory phase have been seen in patients with periodontitis as well as in cardiovascular patients. 2, 5, 4) Several studies have been done on the relationship between periodontal and cardiovascular disease. In some studies, periodontitis has been introduced as a risk factor for cardiovascular disease, while the results of some studies do not support this issue (Janket et al., 1997). In a meta-analysis, seven studies were conducted on nine cohort studies in this regard. Based on the results of these studies, the risk of such events and those with periodontitis increased by 19%. (8) In a study by Arbes et al., A direct correlation between coronary artery disease and severity of periodontitis has been emphasized. (9) Beck et al. In a broad prospective study. A total of 921 men without coronary artery disease were studied for 18 years and during the aforementioned period, they monitored the periodontal condition and the probability of developing coronary artery disease. The results showed that the probability of this disease was 2.8 times higher. (6)

Coronary artery disease is one of the most common causes of premature death in industrialized countries. (10) Various studies confirm the effect of oral cavity diseases, especially periodontal diseases on systemic diseases, such as cardiovascular diseases (29,25,26,24,23,22,30,14). Many of these studies are long-term and retrospective. Destefano, in a 14-year study reported that there is a statistically significant relationship between periodontal disease and cardiovascular disease. The present study is an overview of the mechanisms of communication between cardiovascular diseases and periodontal diseases. To better understand these mechanisms, information is provided on the pathology of cardiovascular diseases, periodontal diseases and their related risk factors.

Cardiovascular diseases
According to World Health Organization statistics, in 1995 around the world, 20% of deaths were due to cardiovascular disease, which is increasing by 50% in developed countries. (25)

Hardness of the arteries (Atherosclerosis)
The basis of pathology of cardiovascular diseases is the severity of arterial disease (26).

This condition has been known for more than a century, and clinically involves moderate-sized vessels. One of the most commonly involved vessels is coronary arteries. Early damage to the arteries can be found in children, called a fatty streak, and an advanced type of injury, called the fibrous plaque, in the adult. There are various views about the problems with arteries, but the Response-To-Injury Hypothesis approach is more likely to be confirmed (28).

Periodontal infectious diseases (periodontitis)
Infectious disease, is caused by a small group of gram-negative bacteria, anaerobic bacteria. The presence of bacteria to cause the disease is an essential factor, but host readiness is also one of the essential factors in the development of the disease. In the course of periodontal disease, connective tissue and bone destruction occurs, and inflammatory cytokines, such as (Interleukin-I) IL1 and (TNF), producing MMPS (Matrix metalloproteinases) and (Prostaglandin E2) PGE-2. The mentioned materials are mediators of intercellular matrix destruction in the gum, PDL and bone. Heritable and environmental factors vary in different stages of the disease and in different types of diseases. These conditions affect the onset of the disease, tissue degradation, the rate of progression of the disease, and response to treatment. In addition, the severity and rate of progression of the disease depends on the quantity and quality of the microbial biofilm, the pH of the environment, the amount of the oxygen and the nutrients contained in the periodontal envelope. This view can show individual differences in the susceptibility to disease. (14) Among the different species of bacteria in the oral cavity, three types of Gram-negative bacteria are found in most cases of periodontal disease, namely Porphyromonas gingivalis (P.G), Actinobacillus, Bacteroides forsythus (BF), the latter species. Actinomycetemcomitans (Aa). Most are seen in progressive periodontal disease. Of course, spirochetes are also involved in the disease process (14). Microorganisms live in a special environmental gathering called bacterial biofilm, in which the features of this biofilm are as follows: An environmental gathering, which causes the group to survive. The bacteria have a fuel cell contribution. The environment has a large number of microorganisms with varying pH, oxygen concentrations, and electrical power. Biofilm creates an environment that causes micro-organisms to resist hostile defense mechanisms. The microorganisms in the biofilm are resistant to antibiotics and anti-microbial agents (antibiotics). In patients who are prone to develop periodontitis, microbial biophilia progresses to gingivitis, causing damage to the graft (coronary part of the sticky epithelium junctional epithelium), thereby increasing the availability of bacterial products such as Lipopolysaccharides (LPS)

lipoplasty saccharide to connective tissues and veins. lipopolysaccharide bacteria, by stimulating epithelial cells, secrete IL8, IL-I. These cytokines cause accumulation and activity of neutrophils, and other inflammatory cells, such as B cell, T-cell macrophages, and also play a role in the immunopathogenesis of periodontal diseases. Types of cytokines, including 1,2,3,5,6,9,10, result in the secretion of TNF and IL. Due to these cytokines, lymphocyte B cells differentiate into plasma cells and secrete immunoglobulins. The highest immunoglobulin is secreted from the IgG2 species. Macrophages, due to medium stimulation of lipopolysaccharide, secrete substances such as TNF and high levels of MMPs, PGE2, TNF, and IL-1. Due to these materials, periodontal tissues are destroyed. (14)

Mechanisms of communication between periodontal diseases and cardiovascular diseases
Dental health plays an important role in factors associated with increased cardiovascular disease. In addition to risk factors such as high cholesterol, obesity, diabetes, smoking, which are considered as classical factors, chronic infection is also a risk factor for cardiovascular disease (28). The most common chronic infections, dental caries and periodontal diseases can be mentioned. Periodontal diseases are among the risk factors for cardiovascular disease. (Cardio vascular accidents) A variety of studies show the relationship between periodontal disease and cardiovascular disease (11,27,24,25,22,14,12).

Mechanisms Effective in Infection Influence on the Hardness of the Arteries
The direct effect of infection
There are three reasons for the direct effect of periodontal bacteria on the formation of hardness of the arteries.
1. P gingivalis I=in plaques on cardiovascular and carotid arteries.
2. In the study of Deshpade and colleagues in 1993, the ability to invade of P.Gingivalis and its proliferation in endothelial cells has been identified.
3. Research by Meyer, Herzberg in 1998, P.Gingivalis

P.Gingivalis can cause platelet accumulation and an antigen such as the PAA (Platelet Aggregation Association protein) and its expression on the microorganisms. Coagulation power (thrombogenic) of this bacterium is exacerbated by high blood lipids (hyperlipidemia). Lipid elevation is one of the risk factors for stroke (MI). With this classic risk factor, is the presence of specific bacteria from species that have the ability to clot (thrombogem). They cause inflammation injuries, and active platelets play a regulating role in the release of chemokines from monocytic cells. Here, it should be noted that platelets and leukocytes are activated during bacteremia, and active platelets can regulate the release of chemokines from monocytes in inflammatory injuries. Platelets are part of the process of hemostasis, which is essential for the formation of the hardness of the arteries, and is thought to be a target cell for a number of microorganisms (29,26,20). Despite all of the above, the direct role of microorganisms in the etiology and pathogenesis of arterial stiffness is still not fully understood (27, 28). The study of Kuramitsu in 2001 showed that in the outer membrane vesicles P.Gingivalis

causes the formation of fat cells, which is an important feature of cardiovascular disease. In addition, it acts as a mediator in the oxidation of LDL and ruptures the arterial hardness plate. (32)

Indirect effect due to host intermediates

Another mechanism that supports the effects of periodontal diseases on cardiovascular disease is the creation of cytokines. The role and effect of gingival microbial plaque due to the relatively large surface area of periodontal packs (especially in the course of periodontal diseases, which is an ulcerative epithelium), high levels of endotoxin, the gram-negative bacteria are in contact with the connective tissue and enters it. Tissue defenses act to destroy bacteria and we are less likely to get bacteria in the bloodstream. But this leads to an increase in cellular debridement and lipoplasty of saccharides in the bloodstream. The effect of increasing the material on the fibrinogen is observed. Increasing fibrinogen will act as a coagulation disorder preparatory factor and will lead to coagulation changes. Studies have shown that the incidence and prevalence of cardiovascular disease are related to hemostatic and rheological changes. Rheological variables include plasma viscosity and hematocrit. The effect of plasma viscosity, is partly by fibrinogen and partly by the lipoproteins. The viscosity of the whole blood is associated with plasma viscosity and hematocrit, and the count of white blood cells. The hemostatic variables include the Von Willebrand factor, which is released by endothelium damage. One of the mechanisms of communication between cigarettes is the increase in lipid and infection, such as oral infections based on hemostatic and rheological changes. For example, in people who use cigarettes, rheological changes are high in non-smokers. In a case control study in Glasgow in 1998, the concentration of plasma fibrinogen and white blood cell count in patients with chronic gingivalis and periodontitis were significantly higher than those in other individuals. (11) A large number of studies suggest that increased white blood cell counts are an agent for ischemic heart disease. The increase in circulating leukocytes results in the closure of micro vascular arteries, especially if this increase is acute. In inflammatory periodontitis, there is the potential for making cytokines and inflammatory mediators and lipid compounds. These substances affect endothelial cells of the blood vessels in other areas. (25) Endotoxin and lipopolysaccharide gram-negative bacteria, which are microorganisms of the peri-gland in periodontal diseases, also cause damage to endothelial cells. The damage to endothelial cells causes the release of various factors, such as Von Willebrand, which can justify an increase in the size of this factor in the process of periodontal disease.

Effect of lipopolysaccharides

Infection causes the metabolism of lipids to change. IL-1 and TNF inhibit lipoprotein lipase activity, and bacterial products such as lipopolysaccharide and Muramyl dipeptide, can directly affect endothelium. Perhaps for this reason, lipid elevation is a clear indication of chronic infections. (25) In the study of peripheral blood monocyte in patients with Early-onset periodontitis and Refractory periodontitis revealed that these cells secrete 3 to 10 times the normal levels of PGE2, IL-1, and TNF. (28)

Increasing the secretion and production of cytokines from gingival tissues to the general flow of blood and in distant areas. (25) Lipopolysaccharides are released from the microorganisms of the periodontal envelope, and into tissues. Periodontium is entered into the patient. lipopolysaccharide are not free in plasma, they are bound to plasma proteins. In the event of bacterial invasion and the formation of bacteremia, free lipopolysaccharides are found in plasma. Bacteremia is caused by treatment such as scar=ring and during acute and chronic abscesses, and the availability of warm bacteria causes a negative blood flow. Following is the activation of leukocytes, platelets, and endothelial cells. Circulating microorganisms liberate lipopolysaccharides, which affect fat metabolism. When lipopolysaccharide is bound to a lipopolysaccharide-binding protein, a high affinity protein, it finds the ability to transplant CD14 receptors, by binding the compound to the receptors on endothelial cells, monocytes and macrophages, and these cells are activated. By activating these cells, the appearance of adhesion molecules and release of cytokines and chemokines, and with increasing molecules, adhesion at the level of endothelial cells, leukocyte migration to (sub intima), which is explained by the effect of this event in the process of causing arterial stiffness. (28,27,26,23,15)

Hyperactive mononuclear phagocytes

We observe high activity macrophages in smokers and periodontal patients. Monocytes are highly active macrophages in high levels of inflammatory cytokines, lipopolysaccharides, and the activity of Matrix metalloproteinases (MMPs) and prostaglandin and protease. Such macrophages are involved in causing arterial stiffness in susceptible areas of the arteries, such as the placement of arches. In patients with periodontal disease, polymorphonuclears are about twice the FCR (receptor (FC) more than control group. These PMNs, in the bloodstream, contribute to the formation of the hardness of the arteries. The mechanism of this change is not known. In patients with topical periodontal disease, peripheral blood monocytes secreted high levels of PGE2 in response to lipopolysaccharide, but this reaction is not related to CD14. Laboratory studies have shown that the presence of chronic infection in periodontium causes this reaction, and this is not a characteristic of monocytes in people with progressive localized periodontal disease (15,16).

Inheritance

A recent survey of epidemiology suggests the role of hereditary factors and suggests various genes in this regard. For example, several forms of the Interleukin-1 gene are associated with periodontal disease and cardiovascular disease. The proof of this relationship requires further examination. (31)

Conclusion

Frequent studies confirm the association between oral infections and cardiovascular diseases. Longitudinal, cross-sectional and case-control studies confirm the association between periodontal diseases and other oral conditions

with cardiovascular diseases and infective endocarditis (17,21,27). In a 1998 study, Matyla et al. examined the relationship between coronary artery disease and dental infections. In this study, on 100 patients in terms of body mass index, age, lipid profile, economic status, and blood pressure, using Pantomography, they found that, Coronary atheromatosis (p = 0.003) is associated with dental infections In 1993, Mattila et al. conducted a study on 100 patients with angiography who had a degree of coronary artery bypass graft or history of stroke. They measured the patient's age, serum lipids, body mass index, economic status and blood pressure, and found that coronary arthromotosis with p = 0.001 was associated with dental infections. One of the first long-term studies was carried out by Handfano and colleagues in 1993. (27) They surveyed 9,760 people. Examination of caries and loss of teeth at the onset of cardiovascular disease were investigated over14 years. The findings showed that in subjects who at the beginning of the study had periodontal disease, the risk of cardiovascular disease was 25% higher. In this study, smoking and oral hygiene were not matched. Beck and colleagues surveyed 1,147 men in 1996 (23). Initially, bone Height was determined by radiography. In patients with a high bone fracture assay, the risk of cardiovascular disease was higher after 18 years. Joshipura. (16) A six-year study was conducted on 44,119 men. In men who reported periodontal disease and less than 10 teeth at the beginning, the risk of developing cardiovascular disease was higher than that of men who had 25 or more teeth. The periodontal disease report was studied by an individual, which is a deficiency in this study. Genco (25) and colleagues in a 10-year report from the use of the ECG in 13 patients identified age, diabetes, sex, cholesterol, weight, and blood pressure in matching patients with periodontal diseases who were below 60 years old, were 86.2 times more likely to have cardiovascular disease. In the study group, smokers were very low. In this way, cigarettes have been eliminated as a risk factor. In summary, the mechanisms of communication between cardiovascular diseases and periodontal diseases include the following: the role of lipopolysaccharides in periodontal pathogenic bacteria in the process of causing arterial hardness by transplantation to CD14 and the activation of macrophages and endothelial cells and following the release of inflammatory cytokines. These cytokines cause hemostatic and rheological changes. The effects of the changes mentioned in the pathology of heart disease have been reported. Macrophages, in areas that are lipopolysaccharides or inflammatory cytokines, have macrophages with excessive activity. The role of macrophages in causing severe arterial injury has been shown. The direct role of microorganisms in the periodontal pathogens, despite the evidence referred to, has not been completely established. Recently, studies have focused on the key role of the host's response to the microorganisms and the incidence of cardiovascular disease (30). Finally, despite the mechanisms that have been mentioned and the various studies, the abbreviations of which have been given, it has been concluded that periodontal diseases can be a risk factor for developing cardiovascular disease. Of course, it should be noted that more studies are done in men and information about the association of these two diseases in women is not enough and requires further examination (10,26,27)

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Oral Health Related Quality of Life in Patients Undertaking Implant Treatments: A Review of Literature

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Abstract

Tooth loss is one of the factors which affects on oral health related quality of life because of impaired aesthetic, speaking, and mastication. Replacement of lost teeth by prosthesis options is ndicated for regaining aeshetic, speech, function, and psychological improvement. Fixed partial dentures, removable complete and partial dentures are usual treatment options to regain the function of patients. But, today implant treatments are preferred by patients due to functional and psychological factors. Replacement of teeth by implants has become popular among both patients and clinicians. This paper has reviewed the oral health related quality of life in patients treated with implant supported prostheses.

Key words: Dental implant, Tooth loss, Dental prosthesis, Quality of life

Introduction

For a more valuable assessment of health status and treatment results, factors related to quality of life must be considered [1]. Tooth decay and periodontal problems are two prevalent oral diseases which do not manifest symptoms in early stages. Therefore, clinical signs of tooth decay and periodontal disease such as number of missed teeth, loose teeth and periodontal pockets are not strongly related to poor oral health related quality of life factors [2]. Tooth decay and periodontal problems, are progressing disease and if left untreated lead to tooth loss. Depending on type and location, missing teeth can influence oral health in terms of mastication, speech and aesthetics [1]. Clinician's consensus is that more preserved teeth result in better mastication [3]. Replacement of missed teeth with prosthesis is among the most complicated dental procedures for regaining function, aesthetics, speech and psychological improvement. Although full crown, bridge and removable dentures are usual treatment options, today, patients' attitudes seem to be changing and many prefer implants due to functional and psychological factors.

Implant treatments have gained popularity among both patients and clinicians [3]. Patient and clinicians opinions are both important regarding the assessment of treatment outcomes. In patients' point of view, psychosocial effects, cost-effectiveness, cost-benefit and quality of life factors are all considered important. Many studies show higher patient satisfaction of implant-based prosthesis when compared to conventional prosthesis [4-6]. This paper has reviewed the quality of life in patients treated with implant based prostheses.

Tooth loss

Regarding oral health related quality of life, tooth loss is a significant influencing factor [7]. Tooth loss mostly appears as a result of tooth decay or periodontal disease. More than 50% of tooth loss is related to tooth decay and periodontal disease accounts for 30-35% of tooth loss [8].

Today advances in oral health, has lead to lower cases of edentulous patients in North America and European countries [9]. Compared to men, women consider aesthetics as a more important factor in oral utility. Nevertheless, considering shortened dental arches, this is not statistically significant. Although aesthetics is more important in women, oral function was known to be equally important in men and women [10]. Fixed tooth-based or implant-based prostheses, removable partial dentures and removable over dentures, are usual recommended treatment options for replacing missing teeth. In the past, tooth loss was little concern to patients and the majority of them easily adapted to usual tooth replacement methods [11]. Due to functional and psychological reasons, today this attitude has changed and many people prefer implant-based treatments [12]. Up to year 2030, the population of USA above 65 will double thus increasing the need for replacing lost teeth [13, 14].

Implant

Implant is an alloplastic, biocompatible material for replacing teeth. It increases retention and stability of dentures. Also it will avoid the cut of adjacent teeth in cases of partial dentures [12,15]. Prevention of bone loss and increased aesthetics especially in anterior parts of the oral cavity are other advantages of implant based treatment options [16 , 17]. Many studies have assessed the utility of various replacement methods for lost teeth. Although results show higher utility of implant-based replacement methods, cost of such treatments has remained a huge impediment to their demand [4,18,19]. Dental implantology is a popular treatment option which has shown high success [20]. Available studies about dental implants have mostly investigated implant clinical success, titanium surface and surgical and prosthetic procedures. Recently dentistry and especially implant dentistry has focused on patient centered treatments in which patients' needs and success of treatments are assessed [21]. More than four decades has passed since the first published paper about titanium dental implants [22] but a low percentage of them have emphasized on patient-centered implant treatment results [23]. Most studies have revealed that implant treatment in cases of partial and full edentulous patients increases quality of life and in the long term, is considered a more cost-effective treatment compared to other tooth replacing options [6,24,25,26]. Evaluation of patient's utility values for the methods of teeth replacement showed that implant supported prosthesis was the best method for replacement of lost teeth [27].

Quality of life

Four basic parameters are described to evaluate dental treatment results. Biological and physiological parameters are health of oral structures, mastication, nutrition, and aesthetics. Longevity and survival rate parameters include tooth, restorations and implant; psychological parameters incude satisfaction, self-esteem, body image and quality of life and economic parameters include direct and indirect costs. Most research has focused on the first two parameters whereas little focus has been placed upon psychological outcomes of treatment [28]. Oral health related quality of life (OHRQOL) is an important patient centered endpoint which needs to be considered when evaluating professional interventions and treatment results. In the general population, number of teeth has the most significant effect on patients' OHRQOL [29]. WHO defines health as complete social, psychological and physical well-being and not only the absence of disease [30]. Quality of life is the perception of one's situation in life based on individual cultural values.

Quality of life and its relationship to goals, expectancies, standards and anxiety is considered a valuable parameter in patient's oral health evaluation [31]. Subjective evaluation of OHRQOL, reflects patients comfort while eating, sleeping and participating in social activities, self-esteem and satisfaction with oral health [32]. OHRQOL will evaluate both positive and negative domains of health perceptions [33,34].

Single tooth implant

Due to following reasons, single tooth implants are suitable treatment options:
1) They avoid the cut of adjacent teeth.
2) They are ideal treatments for spaced dentitions.
3) They have high prognosis and require little maintenance.
4) Preserves the height and width of alveolar ridge [12].

Fixture survival, limited bone loss and minor prosthetic problems are contributing factors to implants' clinical success [35]. In a systematic review carried out in 2007, Jung et al, revealed that single crown supporting implants show a survival rate of 96.8%. Also single crowns which were supported by implants gained a survival rate of 94.5% after 5 years. Likewise the survival rate of metal-ceramic crowns (95.4%), was significantly higher than full ceramic crowns (91.2%) [36]. In another research, single crown supporting implants' survival rate was 97.2% after 5 years and 95.2% after 10 years [37]. These two Meta-analysis studies show a high survival rate for single crown supporting implants. Another Meta-analysis, reported a 5 year survival of 93.8% for conventional tooth supported FDPs and 94.5% for implant supported single crowns. After 10 years this was reported to be 89.2% and 89.4% respectively [38]. In a case control study carried out by Raes et al, quality of life of people in need of implant-based single tooth replacement was assessed in a group with healed bone and a group with fresh socket. At base line there was no significant difference in quality of life factors. After a year, in the healed bone group, all seven domains of OHIP-14 improved significantly whereas in the fresh socket group, only three of seven domains of OHIP-14 improved. According to OHIP-14 score, people in need of single tooth replacement had limited oral health related problems, although OHIP score was not significantly different between the two groups [39]. Regarding quality

of life in people treated with endodontic procedures and implant procedures, both treatment methods achieved high clinical success with similar OHIP-14 scores. Overall participants were satisfied with the treatment. Their clear message was "preserving natural teeth as long as possible". Therefore in addition to prognosis and clinical results, patient preference and long term and short term effect of treatment on quality of life should also be considered when evaluating treatment outcomes [40].

Single implants versus fixed partial dentures (FPDs)
Fixed partial denture is used to replace single or multiple teeth. In this method, significant cutting of adjacent teeth is needed to gain optimal functional and aesthetic results. This can cause endodontic, periodontic or tooth structure problems [41]. In a systematic review, Creugers et al, analyzed 26 studies in which FPDs were followed for more than 15 years. The overall 10 year and 15 year survival rate was 90% and 74% respectfully. This means that after 10 years less than 15 percent of FPDs needed removal or exchange whereas after 15 years one third of FPDs were in need of exchange [42]. Considering removed or failed FPDs (a broader definition of failure), Walter reported a 87% survival rate after 10 years and 69% after 15 years [43]. In 2015, Pjetursson et al, noted survival rate of all types of all-ceramic FDPs to be less than metal-ceramic FDPs [44]. Using implants for teeth replacement is a predictable method. Walton reported the 15 year survival rate of posterior FPDs and implant supported single crowns to be 92.7% and 95.9% respectively. This difference was not statistically significant. In contrast the survival rate of anterior implant-supported single crowns (93.3%) was significantly higher than anterior FPDs (82.8%). Both treatment options were similar in complications, whereas FPDs economic burden was considered to be higher [45]. Park et al compared the quality of life in 35 people treated with single tooth implants and 36 people treated with FDPs. In both treatment options, OHRQOL increased but no significant difference existed between the two groups [46].

Implant supported over dentures
For more than a century, soft tissue supported maxillary and mandibular dentures have been an acceptable treatment method. Over time and especially in the mandible, bone loss leads to loose dentures, thus functional, social and psychological failure [47]. Bouma et al, reported improved OHRQOL 12 months after over denture treatment. In spite of better OHRQOL, general quality of life did not improve [48]. Implant supported over denture increased patient satisfaction in terms of aesthetics, denture stability, comfort, speech, food choice and social activities [49]. In a systematic review carried out by Thomason et al, strong evidence supported the fact that implant supported over dentures increase quality of life more than conventional dentures. Although patients show high satisfaction after maxillary implant supported over dentures, compared to conventional dentures, no significant superiority existed [49]. Wilfried Kleis et al concluded that type of attachment did not influence OHRQOL in cases of mandibular over denture supported by two implants [50]. Regarding mandibular over dentures, it cannot be concluded that

level of bone loss, patient satisfaction and after treatment complications is related to the number of supporting implants [51]. Evidence shows that an over denture supported by two implants, should be the first and least treatment option offered to edentulous patients. Although this treatment option is not the gold standard for mandibular edentulous patients, regarding time, cost and patient satisfaction, it is considered to be adequate for most patients [52].

Implant supported removable partial dentures
Removable partial denture is a prevalent method offered to partially edentulous patients. Lower cost, easy hygiene and replacement of several teeth all in one denture are advantages of this treatment option. On the other hand lower retention and stability (especially in cases of free end, occlusal disharmony and soft tissue pain are among disadvantages of such treatment. Any way prosthesis clinical success does not necessarily show patient satisfaction [53]. Patient age, previous experience of a denture, number and location of replaced teeth are factors contributing to the clinical success of removable partial dentures [54].

In a study by Ali et al, anterior teeth replacement with removable partial denture increased OHRQOL [54]. In another assessment of OHRQOL, partially edentulous patients without dentures, reported higher OHRQOL compared to partially edentate patients who used a removable partial denture [55].

In cases of anatomical or economical limitations, Implants are used to support partial dentures instead of using fixed prosthesis [53]. In a 3-16 year retrospective study, class 1 Kennedy edentulous patients who used implant supported partial dentures reported an implant survival rate of 91.7%. Also level of implant surrounding bone loss was 0.9mm. In this study the mean overall OHIP score was 16.7 and patient satisfaction was reported high [56].

Gates study reported a 41 unit decrease in OHIP score after replacing removable partial denture with implant supported partial denture [20]. According to Campus et al, the strategic replacement of implants in posterior alveolar ridge, significantly increases patients' quality of life, retention and stability of denture in patients with implant supported partial removable dentures [53].

Implant supported fixed prosthesis
For people who prefer this treatment option or those who previously had a removable partial denture, implant supported fixed prosthesis are recommended (57). The 10 year survival rate of implant and the prosthesis is reported to be 96% for mandibular implant fixed complete dental prosthesis. Also survival rate of implants with coarse surfaces were similar to implants with smooth surfaces. Number of implants and anterior–posterior position of implants did not influence survival rate [58].

In a systematic review, Kern et al, reported implant survival rate to be 97.9% for maxilla and 98.9% for mandible. Implant loss was significantly higher in maxilla and lower in implant supported fixed dentures compared to implant supported

fixed prostheses, implant supported removable prostheses and conventional dentures. Although quality of life increased in all three groups after treatment, OHRQOL was significantly higher in patients with implant supported fixed prostheses and implant supported removable prostheses, compared to patients who used conventional dentures. Specifically, compared to conventional dentures, functional limitation, physical pain and psychological problems significantly improved in implant supported fixed prosthesis patients and functional limitation improved in implant supported removable denture patients [4]. Brennan et al, noted lower quality of life and satisfaction in patients with implant supported over denture in comparison to implant supported fixed prosthesis [60].

Conclusion

Patients with conventional dentures, were lower in quality of life compared to patients treated with implant supported fixed prosthesis, implant supported removable partial dentures and implant supported over dentures hence showing the importance of implant use for teeth replacement according to clinician and patient perceptions.

Acknowledgement

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Roles and Responsibilities of the Home Care Liaison Nurse: A Review of the literature

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Abstract

Introduction: The purpose of this study was to explore the roles and responsibilities of the liaison nurse as a new member of the health care team.

Methods:. Six scientific databases were reviewed for articles published between 2007 and 2017 in English language among peer-review journals. A total of 80 articles were obtained. After applying the inclusion and exclusion criteria, 5 articles were retained. These articles propose some tasks, roles and responsibilities for the liaison nurse to provide continuous care. But to address these issues, structural and educational changes are necessary to improve nurse performance.

Results: The results showed that liaison nurse roles are defined differently from the common roles of nurses.

Conclusion: The caring gap has always been a concern for the health system. The role of liaison nurses has been defined to maintain continuous patient care.

Key words: liaison nurse, continuity of care, home care, caring gap, nurse performance

Introduction

Today, the number of clinical nurses' roles has expanded in various areas of health and treatment (1). These roles vary from primary care provider to specialist nurses in different domains. However, the main roles of the nurse include providing patients with services, facilitating the admission and discharge of patients, making clinical decisions, supporting, directing, coordinating, organizing care plans, and providing mental and psychological support to patients. Here is the question: what can be done to increase the effectiveness of nurses and consequently increase the quality of care provided especially after discharge? Evidence suggests that a large group of specialized nurses called liaison nurses play specific roles in the hospital and community. A liaison nurse is supposed to be a patient advocate at the time of the patient's admission to the hospital and thereafter in the field of continuing care(2). They provide special care for sedation, diabetes, asthma, stoma wound, infection control, AIDS and intensive care units.The provision of these care services will result in a nurse's association with the community and the continued provision of care, especially in chronic diseases (3). The clinical function of these nurses is at two basic and advanced levels(4). At these levels, nurses collaborate and communicate with the patient and his or her family as well as different groups to meet the patients' mental and psychological needs, diagnose diseases, plan, implement, and assess nursing care. The most important actions of these nurses focus on promoting mental health, preventive measures, training for patients with self-care, implementing and monitoring prescribed therapies, health education, performing specific actions in critical cases, and specific patient counseling and management. Research has shown that the presence of a liaison nurse improves the quality of care, increases the knowledge of nurses, and creates better communication between the hospital and the community(5). The liaison nurse is not solely responsible for providing conventional nursing services, but is also responsible for providing information, as well as pastoral care to the patient at the time of diagnosis

and subsequent therapies. In fact, the liaison nurse is to provide a reliable communication channel between the treatment team, patients and their families (6). Liaison nurses are also responsible for the psychological and emotional support of patients and their families.

Liaison nurses can play an effective role in providing the necessary care at home, as well as providing recommendations for changing lifestyle and behavioral risk factors for the patient and family in addressing the concerns of the disease.

Liaison nurses are also able to facilitate early discharge from the hospital by providing care at home and acting as the main pillar between hospital and home and even replacing certain specific needs that are more relevant to nursing(7). Actually, the Liaison nurse position was established in the clinical setting to support integrated care of the patients by coordinating and encouraging inter-professional and inter-organizational collaboration to address the patient's needs (8). The purpose of this literature review was to explore the details of the roles and responsibilities of the liaison nurses.

Methods

In the present study, the literature was reviewed using the five-step protocol of conducting a systematic review process described by Khan et al, 2003. These steps included, (1) framing questions for a review, (2) identifying relevant work, (3) assessing the quality of studies, (4) summarizing the evidence and, (5) interpreting the findings (9).

Inclusion and exclusion criteria
Only original articles published on the subject of liaison nurses including quantitative, qualitative, and systematic reviews were included in this review. The search was carried out using specific key words such as liaison nurse, care gap and after care in combination with terms such as role, task and responsibility. Likewise studies which included liaison nurse positions in hospitals and official liaison nurse responsibilities were included in this review literature.

Search and selection
Searching in six scientific databases such as ISI, Scopus, PubMed, EBSCO, CINAHL and Cochrane database was conducted. A total of 80 related original articles between July 2007 and May 2017 were retrieved. Based on the study objectives and relevance of the research title, 20 articles were selected by the researcher for further review. Selected articles were reconciled across the two reviewers for assessing the quality of studies until a consensus was reached. Finally 5 full text articles were approved for study inclusion. A narrative summary of the selected articles follows below.

The results of a 2016 US interventional study on the role of liaison nurses in hospitals suggest that liaison nurse interventions (counseling, informing, supporting the patient and family) have a major impact on the patient's recovery and the speed with which the patient returns to social activities. Clinical studies on the impact of the liaison nurse

as a coordinator to provide care for patients who are at the end of their illness emphasize the cost-effectiveness of services provided to patients with a life expectancy of less than a year, by the nurse (10).

In the context of the role of the liaison nurse in the hospital, an interventional (case-control) study was conducted at the Clinical Research Center of the Griffith University in 2007. The purpose of this study was to investigate the effect of liaison nurses on patient and family anxiety experiences before transferring from the intensive care unit to the normal ward. This interventional study, with a pre and post test design along with the control group, was conducted for four months. In the intervention group, the liaison nurse prepared the patient and family to transfer to the normal ward, but in the control group, the patient was transferred to the ward in the usual way. The results of the study showed statistically significant anxiety reduction among patients and their families in the intervention group (11).

In 2010, another study was conducted in Australia. The purpose of this study was to identify the effect of ICU liaison nurse on reducing the complications and possible injuries after the discharge of the patient from the ICU. The research method was case-control. In this study, the control group did not receive any care after discharge from the ICU, but in the case group, patients were visited by the ICU liaison nurse at least three times in three days. Patients were evaluated for three possible post-discharge incidents, including unexpected death, need for surgical procedures, and improved care. The data collection tool was a researcher-made questionnaire. In this study, 388 patients (201 controls and 187 cases) participated. After controlling other incidents, patients who received liaison nurse interventions achieved 1.82 times higher levels of care (p = .028) and needed surgery 2.11 times less (p = .006). These results indicate that the interventions performed by the liaison nurse are effective in preventing post-discharge incidents and improving their health (12). A similar case control study was conducted in 2007 at the pediatric ICU Melbourne Hospital, Australia. In this study, it was assumed that a liaison nurse would reduce the readmission of children in an intensive care unit within 48 hours after discharge from this department. After a year (July 2004 to June 2005), 1.388 children were discharged from ICU. During this period, 67 patients were never re-admitted; overall, the rate of children's re-admission decreased from 5.4 to 4.8%. After a year, staff and patients were asked about the impact of the liaison nurse. A majority of staff members (98.5%) in ICU believed that the liaison nurse's measures are positive and useful, and 99% of the parents of the children considered the idea of liaison nurse as a positive role (3).

Objectives of the interventional study that was conducted by Carson and his colleagues in 2014 was to develop job descriptions and standards of care for the liaison nurse in preoperative settings. In this study, liaison nurse was a health care team collaborator, patient and families councellor, coordinator and manager for 12 months. Research results showed improvement in patient

satisfaction and increased patient responsibility in their own health care during the twelve month without quality of care sacrificing. Staff nurses, patients and their families found that the liaison nurse role was essential in the heath care team (Carson, 2014).

Studies Characteristics

To determine the level of evidence of the selected articles, using the Melnyk Pyramid (2011) for hierarchy of evidence.

> **Levels of Evidence**
>
> **Level 1** - Systematic review & meta-analysis of randomized controlled trials; clinical guidelines based on systematic reviews or meta-analyses
> **Level 2** - One or more randomized controlled trials
> **Level 3** - Controlled trial (no randomization)
> **Level 4** - Case-control or cohort study
> **Level 5** - Systematic review of descriptive & qualitative studies
> **Level 6** - Single descriptive or qualitative study
> **Level 7** - Expert opinion

Source: Melnyk, B.M. & Fineout-Overholt, E. (2011). Evidence-based practice in nursing and healthcare: A guide to best practice. Philadelphia: Lippincott, Williams & Wilkins.(13)

The table includes seven levels of evidence, Level IV ideally describes a well-designed case-control or cohort study. In the present study, Methodology in all five studies were interventional (case-control) that reflected level 4 of the evidence in this rating system.

Thematic Analysis

The five articles shared commonalities about the roles and responsibilities of the liaison nurse. Themes across the articles were identified. In total, the five articles covering four principle roles for the liaison nurse included caring, educational, counselling and managerial roles. Also selected studies showed several tasks and responsibilities for the liaison nurse in the area of each of the liaison nurse's roles.

Results

In this review article, exploring the role and responsibilities of the home care liaison nurse, five case control studies were reviewed and the results of the selected articles are summarized in Table 1.

Table 1: Roles of the Liaison Nurse

Brief Bibliography	Research Objectives	Results (liaison nurse roles)
Hanson et al (2016)	Achieve the impact of the liaison nurse	Liaison nurse has a positive role in counseling, informing, coordinating, supporting the patients and their families.
Carson et al (2014)	Develop a job description, guidelines and a standard of care for the nurse liaison in the perioperative setting	The liaison nurse is a manager, coordinator, supporter, teacher, collaborator in the health care team.
Endacott (2010)	Identify the role of ICU liaison nurse in reducing the complications and possible injuries after the discharge of the patient from the ICU	Liaison nurse is effective in preventing post-discharge incidents and improving patients' health through caring, counselling, training, coordinating, supporting and managing the patient
Caffin (2007)	Identify the role of liaison nurse in preventing rehospitalization of the pediatric patient in ICU units after discharge.	Improving communication between parents and health care staff and community services after discharge, improving the quality of training provided in the department, improving patient outcomes and reducing re-hospitalization
Chaboyer et al (2007)	Effects of the liaison nurse in intensive care unit	Support the patient and relieve patient stress and anxiety

Based on the above table and the results of the selected articles, generally, the liaison nurse has four principal roles that the researcher classified as caring, educational-counseling and managerial fields. Also there are some documents that support this classification. For example Jowett in 2000 classified the roles of the liaison nurse in three levels, educational, training and counseling(14). This classification and the definitions are summarized in Table 2.

Table 2: Roles of the Liaison Nurse

Liaison Nurse roles to provide home care	Essentials	Definitions
Educational-Counseling Role	Ability and knowledge to provide necessary training for patients and their families	Patient and family education is a set of experiences a nurse gives the patient and their family with a positive impact on their knowledge, performance, and attitude of self-care.
Caring Role	Assessing the patient's condition at home to meet patient's care needs	Determining the patient's educational needs is the first step in educational planning at the time of discharge and then at home
	Ensuring the receipt of home care services	Ensuring that patients at home receive the best health care services upon request such as physiotherapy and nutrition therapy
	Availability part-time or full-time	Effective performance of liaison nurses will be achieved when patients have the best access to them at different times and in different ways. Liaison nurses must be present in person or available by phone and telegram full-time to patients.
	Professional competency	A liaison nurse must have the proper qualifications to provide home care and have completed the relevant course and be committed to his/her profession.
Managerial Role	Communicate with social health services	In order to provide patients with better services, liaison nurses must recognize and communicate with the community-related social services so that patients can be referred to these centers if necessary.
	Organizational affiliation	The main place of liaison nurses is in the hospital. They are hired by the hospital and trained to provide home-based services and have the necessary authority in this area.
	Meeting organization and patients' needs	For more efficacy, the liaison nurse needs to be flexible in her/his role so that s/he can respond to changing needs of organization and patients.

based services in the healthcare system of all countries and also on the basis of the long-term program of this organization, liaison nurses play a role in the following forms:

- As a skilled general practitioner who is the primary point of contact of the patient with the hospital and, if necessary, the referral of the patient to the relevant specialist, patient support during the hospital admission and the design of the discharge plan
- As a health professional who cares about health more than illness and carries the role of patient and family guidance in disease prevention and health promotion as well as care provision.
- As a skilled caregiver focusing on the principle of patient care at home.

Obviously, changes in roles and responsibilities of nurses require a change in their educational programs during education or the development of short-term educational programs in the form of continuing education programs in the field of nursing at home, as well as changes in the structure of hospitals and the establishment of a post for liaison nurse(5, 15).

According to the liaison nurse' roles and based on the research results, there are some tasks and responsibilities in the area of each of the liaison nurse roles. The liaison nurse's tasks for providing home care are described in Table 3 (4, 11, 16).

Table 3: Tasks of the Liaison Nurse

Liaison Nurse Roles	Liaison Nurse Tasks
Educational –Counseling Role	-Solving patients' problems by consulting with patient care-providers to provide standard care at home, collecting relevant information, consulting with other colleagues and assessing the needs of the patient at home. - Providing self-care education to patients, especially patients with common chronic diseases (diabetes, cancer, cardiovascular diseases, trauma and chronic obstructive pulmonary disease) - Using Tele Nursing Care 'remote contact with patients and their families using ICT' to provide family education and family preparation - An effective company in the home care program by identifying the short and long term problems that need to be addressed, recommending different actions and providing information and interpreting its relevance to the patient's existing conditions. -Updating information and knowledge through participation in relevant training courses, studying papers and scientific documents, maintaining a professional information network with other members of the treatment team, participating in professional organizations
Caring Role	-Transferring patient services from hospital to home through establishing and maintaining contact with the reference hospital, hospital staff and consulting with nurses as well as other services. - Improving the results of home-based care by studying, evaluating and re-designing the care program and measuring the results - Adhering to professional standards in the home care program, maintaining local and national policies in the home care program. - Filing a case for patients covered in order to follow up health issues - Assessing patient's progress in health - Surveying the ability of the family to care for patients - Drug administration based on specific protocol and defined instructions - Working with the health team to provide a patient care plan
Managerial Role	- Providing an effective and interactive collaboration between the family and the providers of health care and educational services. - Establishing a patient care plan in collaboration with the treatment team - Effective and mutual cooperation with social organizations such as the welfare organization, support units, refugee and drug addiction centers, the relief committee, and emergency centers - Providing information in response to a hospital request, communication with a doctor and care team, categorizing and distributing messages and documents, answering questions and requests - Informing the relevant physician about the patient's condition by monitoring and reporting the services provided at home, monitoring patient progress, reporting on emergency patient visits at home, anticipating other home-based care needs -Establishing home care policies at home similar to hospital through consultation with hospital staff, facilitating group discussion on the patient's condition, and social survey on this care method.

The liaison nurse has some responsibilities in the area of his / her tasks. The main responsibility of the liaison nurse is to increase the continuity of care through meetings and establishing a relationship between the hospital, the physician and the patient's family(3, 4, 17). Other responsibilities of the liaison nurse include:

1. Promoting patient care quality, expanding nurse presence in the hospital and easy access to counseling at any time.
2. Developing, training, implementing, and patient counselling. Also, palliative care, and pain management.
3. A nurse as a liaison in the admission and clearance of patients from the hospital

4. Ensuring that care plans are implemented during the hospitalization of the patient.
5. Collaboration with physicians, nurses, social workers and other personnel (forming a liaison team) to ensure that palliative care is provided to patients in accordance with the instructions.
6. Evaluation of any counseling in order to provide the best and most suitable program for each patient based on personal criteria.
7. Providing proper information to the patient and their family about the philosophy, goals and services of the hospital
8. Giving appropriate guidance and complete patient evaluation in accordance with existing protocols

9. Proper patient referral for discharging

10. Collaboration with the hospital staff, patient and family, and doctors to ensure that the discharge process is facilitated.

11. Consultation with other patients involved in the process to facilitate decision-making and strengthen communication and team collaboration.

12. Recording and monitoring and maintaining clinical information systems including: duration of hospitalization, referral cases, number of patients covered at home, evaluations, therapeutic outcomes and patient satisfaction rate and other related activities.

13. Cooperating and participating in studies on palliative and end-of-life care or other fields, as the case may be.

14. Collaborating with hospital managers in order to examine the daily statistics of patients and to find appropriate cases to provide counseling and follow up of patients, and provide home care and make necessary coordination.

15. Considering the timely encouragement by the hospital authorities for members of the liaison team to assist in identifying patients with the aim of correcting and relieving symptoms and supportive care for patients who need home care.

Conclusion and Discussion

Certainly, nurses, along with other medical professions, must work to reduce costs by designing, modifying and promoting care systems and processes. Therefore, in order to provide quality care at an affordable cost, best practice should guide all service delivery (5, 18). In this regard, one of the interventions that has recently been considered for specialist nurses, which encourages nurse involvement with the community as well as continuity of high quality care, is liaison nursing.

Creating a position for liaison nurses with several roles and responsibilities in the hospital that can fill the gap between the hospital and home could potentially improve the efficiency and continuity of the provided care, bridge the care gap and establish a relationship between the hospital and the patient's home, increase satisfaction of patients, increase patient safety due to the presence of nurses at the bedside of the patients at home, increase nurses' satisfaction by improving their experience and skills in providing hospital care, increase their commitment to advanced processes, professional development, increase patients' access to care and treatment, and also decrease hospitalization costs and shorten the length of stay in the hospital(12).

But the liaison nurses should have been trained and certified to gain required skills and competencies to play their effective roles and responsibilities in health care and community settings. Liaison nurses must have an RN or LPN degree. Since it is necessary for the liaison nurse to meet the needs of patients in different areas, having training and experience in specialized areas is very important and helpful and may be evaluated by some medical centers for the use of liaison nurses. In some countries such as the United States, liaison nurses need

to pass a one-year course on home care and receive an end-of-course certificate (3, 19). Liaison nurses who are interested in their work can enter the undergraduate degree program at the hospital or faculty and complete the theoretical and practical / clinical course and acquire the necessary skills. After completing the training course, the liaison nurses will be required to take part in the home work permission exam that is held in each country internally and obtain the necessary permission to provide care at home. At the moment, a 4-year liaison nursing course is held in a limited number of countries. According to the Association of American Nursing Colleges, four years of liaison nursing education for providing nursing care at home is a great potential for advancing nursing knowledge and thus increasing the accountability of nurses to the growing need of the community (20).

Among the general skills required for the liaison nurse, the following appear to be critical:

Drug therapy, creating a safe and effective environment for the patient and family, maintaining and improving the patient's health, having nursing skills, communicating effectively, listening to the patient, confidentiality of patient information, self-confidence and self-control, and skill in doing team work (10, 21)

According to the World Health Organization, the ultimate goal for liaison nurses is that they can play a key role in promoting the health of the people and society with the participation of families, communities and other professionals in the health sector(22).

In this regard, and according to the World Health Organization, the competencies expected of the liaison nurse responsible for providing home care include five main areas:
• Care provider
• Decision maker
• Communication establisher
• Community leadership
• Care management

Despite the importance of the role of liaison nurse in health care setting, and based on evidence, currently, in most of countries there is no position for liaison nurse in the organizational hospital structure, but with the development of the role of the liaison nurse as the link between the hospital and the home, and subsequently the change in the duties and roles of the medical staff, changes are required in clinical posts and a place for liaison nurses should be considered in the organizational structure of the hospital in order to stabilize the role and continuity of care at home. In each unit, it is also necessary to identify the number of liaison nurses, the scope of activities, and their contact numbers for ease of communication, and provide for the patients in need (23, 24).

In addition to the importance of establishing a position for the liaison nurse in the hospital structure, evidence shows that continuity of care requires major changes in nursing education. Although many educational programs have been developed at the macro level for nurses, there is a

need to make changes to these programs based on the needs of each educational institution, in order to assess the educational needs of home care and other social care. Results of the studies required three types of changes in nursing education in order to prepare nurses to play the role of liaison nurse in the future, including:

1. Introduction of home-based care in theory and practice in a basic nursing education program

2. A home care study should be added to educational courses and developed over time

3. It is necessary to include the concept of continuity of care and its various aspects as a central and dominant concept in all basic nursing education programs.

A change in the continuity of education program is also suggested. Experience has shown that nurses who complete a course of social care or home-based education are knowledgeable and skilled and have different social behaviors (16, 25). In addition, in order to change the educational curriculum, nurturing skilled nurses in social care is necessary to develop this kind of care. In the changes to the curriculum, it is necessary for the liaison nurses to have a separate educational program to prepare them for their roles in the future.

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