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Special Issue: Focus on Iran

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FOCUS ON IRAN



This is the first issue of a special series of the journal where we have focus on researchers and writers from Iran. In addition there are a number of papers from medical students. Iran is a country situated in southwest Asia in the part of the globe generally known as the Middle East. It has functioned for at least 5000 years as a civilization and as fecund ground for the emergence of the world's first state in the modern sense of the word. This issue reveals the wealth of research and academic activities in Iran.

The topics vary from basic research to clinical trials, to community studies to review. Chafjiri, M, investigated the effect of vocational rehabilitation of the governmental sector in the year 2000 relative to that of the private sector in 2014 for employment of persons with disabilities. The authors concluded that based on those results, it is concluded that the performance and efficiency of the private sector was lower than that of the governmental sector in 2000. Hence, it is necessary to evaluate, grade and improve the performance of the private sector.

Halime Raeisi Sarbizhan, Nahid Hatam and Mehrdad Askarian developed a national immunization electronic registry system to improve immunization levels. This system of immunization

coverage facilitates shared experiences, information and specialized consultation. The aim of the study is to establish an immunization registry system in the Health- Therapeutic center in Shiraz city and for the country as a whole.

Sarmadi, F investigated the effects of factors related to food consumption in health workers of Najaf Abad-based healthcare centers, in 2012. The results of the present study revealed that the bread and celery group had the highest mean of consumption in employees (4.4 ± 9.1). The author concluded that the underlying factors be recognized before education in advance to improve nutrition and prevent diseases caused by malnutrition.

Norouzi L et al looked at the Effect of Internet Usage on Relations between Members of the Iranian Family in Tehran City. The authors stressed that Iran has a society which is highly driven by religious cultural values. The findings suggested that the Internet use has affected familial relationship including wife-husband and siblings. The authors concluded that the internet use had also effects on Iranian families' traditional culture and beliefs.

Taghipour, A et al carried a qualitative study comparing Dyspepsia Symptoms from the Viewpoints of Traditional vs Modern Medicine. The symptoms of dyspepsia were collected from literatures of modern and Persian traditional medicine. The authors concluded that diseases causing dyspepsia are very similar from the viewpoint of Persian traditional and modern medicines.

Kalhor R.P et al did a survey on Inter urban Taxi Drivers' driving Behaviors across Kermanshah, Iran, in 2015. Data were collected from the cluster random sampling was employed, and the final volume of sample population 226 subjects were selected. The findings of this study showed psychometric properties of dangerous driving behavior in deliberate volition and slaps in Kermanshah taxi drivers. The authors suggest starting teaching driving workshop and safety driving education for taxi drivers.

Kazemi. M et al looked at Serum level of ionized calcium in patients with migraine during a migraine attack and times without migraine. The study was performed

on 50 patients who were referred to the Jahrom, Honari Clinic. The authors concluded that serum levels of Ca^{2+} during migraine attacks decreased significantly compared with normal mode, which seems Ca^{2+} have an impact on these attacks. However, more research in this area appears to be needed.

Babadi1, F et al did a clinical trial on 30 patients referred to the Department of Oral Disease of Faculty of Dentistry with the diagnosis of minor oral aphthous. The participants were divided randomly into two groups of 15 persons. Each group was given one of the two drugs: salvizan gel or teriident ointment. The results indicate the both medicines, have a significant effect on reducing the pain and the oral aphthous ulcer size; so, salvizan gel and teriident ointment are markedly effective respectively in the control of pain and in reducing the ulcer size.

Mehri-Ghahfarrokhi. A et al reviewed the possible use of Restoration of Let-7: as a possible approach for increased sensitivity to paclitaxel in ovarian cancer. Paclitaxel is the first-line treatment of ovarian cancer and the second-line treatment of advanced ovarian cancer. Although let-7 is a potential therapeutic target for therapy resistant ovarian cancer, further studies should be conducted to investigate clinical use of let-7 to treat or suppress ovarian cancer.

Hafizi. M et al compared standard triple therapy regimen with sequential therapy regimen containing levofloxacin used for the eradication of H. pylori in patients with gastrointestinal infection caused by H. pylori using single blind design. Given the low rates of H. pylori eradication in both sequential and triple therapy regimens observed in the present study, it seems that it is necessary to conduct further researches on the bacterial resistance to the prescribed antibiotics.

Shahdadi. H et al examined the relationship between information technology and employees productivity with mediating role of knowledge management. A descriptive, quantitative, correlational design was used. The statistic population of research consist all employees of Imam Reza Hospital in Sirjan. According to the results, there is a significant relationship between knowledge management and productivity.

Tarhani, F et al investigated the clinical and laboratory predictive resistance factors for intravenous immunoglobulin in patients with Kawasaki. Patients were divided into two groups: a) responders to IVIG treatment, consisting of 47 patients (90/4 %); and b) resistant to treatment, consisting of 5 patients (9.6%). The authors found that high ESR and CRP and lower serum sodium levels can be considered as predictors of resistance to intravenous immunoglobulin therapy in patients with Kawasaki.

Saied, A et al led a population study that examined for the presence of the Palmaris longus tendon and for variations of the fifth superficial flexor. By the end of the study, 1180 individuals were enrolled and their data were recorded. Of the total 2360 hands studied, 1688 had a Palmaris longus tendon (71.4%) and 1284 had a functional fifth superficial flexor (54.4%). It seems that Palmaris longus and the fifth superficial flexor function are not evolutionarily determined, at least in the studied population.

Nikseresht . A et al carried a descriptive study to measure the precompetitive anxiety and two its subcomponents (somatic and cognitive) and its relationship with age, weight, height and body mass index. The mean score of precompetitive, somatic and cognitive anxiety was 17.93 ± 3.25 , 14.71 ± 2.95 , 3.21 ± 0.97 , respectively. The authors concluded that the swimming competition equally effect on somatic and cognitive components of anxiety.

Golkhani, S et al looked at the effects of Matricaria Chamomilla extract during neonatal period of rats on pituitary-gonadal hormone axis and changes in testicular tissue of male progenies. Results showed that the extract increased FSH not significantly whereas increased LH, testosterone and also male sexual cells including spermatogonia, spermatocytes, spermatids, sertoli cells, and leydig cells significantly ($P < 0.05$).

Zahabi1. M & Sadeghi N looked at the Moral challenges in the provision of care for Infant and Family: a qualitative study. The first mentioned challenge connected with issues such as nursing workforce shortage or lack of facilities and equipment as a factor in defects of neonatal care that implicitly affect nurses' per-

formance and were beyond the control of nurse. The second mentioned challenge was due to the lack of attention to family-centered care.

Nikkerdar, N. et al studied Radiological and clinical evaluation of maxillofacial cysts and tumors in patients referred to Hospitals in Kermanshah during 2008-2012. Overall occurrence of maxillofacial lesions was 24.5% (85/347) including 41 cysts, 14 benign tumors, 10 malignant tumors, and 20 bone diseases in jaws. The most common cyst, benign tumor, malignant tumor, and jawbone disease was radicular cyst (41.5%), ameloblastoma (57.1%), squamous cell carcinoma (75%), and central giant cell granuloma (65%), respectively. The authors concluded that their findings are generally consistent with those reported in the literature. However, there area few dissimilarities that may be due to racial and/or environmental differences.

Nasrin, A et al assessed the efficacy and safety of ascorbic acid in the treatment of keratoconus by increasing the number of "anchors" that bond collagen fibers together in human in vitro cornea using electron microscopy. In this semi experimental study keratoconus cornea is divided into six equal parts after keratoplasty. Results showed that ascorbic acid strengthen the cornea and decrease the distance between collagen fibrils (consequently increase cross-linking). Therefore, the efficacy of ascorbic acid is observed by more recovery through increasing its doses and passing time.

Zamani, N et al, investigated the prenatal exposure of hydro-alcoholic extract of ginger on the function of Pituitary – Gonad axis in male mature offspring rats. In this experimental study, 40 Pregnant female rats were divided into four groups. The authors concluded that consumption of HEG in perinatal period results in increase in function of Pituitary – Gonad axis in born male adult rats.

Salehiforouz, B et al attempted to answer the questions about whether exposure to benzene is associated with changes in the level of human blood parameters under normal conditions.

The results of blood tests showed that the mean concentration of red blood cells (MCHC) in the control group was

higher and Erythrocyte sedimentation rate (ESR) in exposed benzene workers was higher than control group. The authors concluded that the average exposure of workers at different workshops with benzene vapors is not great, than the exposure limit values of these compounds. In the results of this study, other factors such as alcohol consumption, smoking, non-vegetarian diet and exposure to benzene are effective.

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Serum level of ionized calcium in patients with migraine during a migraine attack and times without migraine

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Abstract

Introduction: Migraine is known as a debilitating headache. The aim of this study was to compare the level of serum ionized calcium in patients with headache attack and in normal subjects. To assess and compare the serum ionized calcium, which is the active form of this ion level during the migraine attack and in the normal subject (with no headache).

Material and Methods: The study was performed on 50 patients who were referred to the Jahrom, Honari Clinic. Migrainous patients were selected according to the Criteria of International Headache Society (IHS). Serum ionized calcium level was measured by Ion Selective Electrode (ISE) method.

Results: Seventy- six percent of all patients who participated in this study were women, the rest of them were men. Mean age for women was 34.8 years old and for men 37. Mean serum level of ionized Ca²⁺ was 3.5 mmol/L and 4.5 mmol/L in women during the headache attacks and normal subjects respectively and Mean serum level of ionized Ca²⁺ was 3.7 mmol/L and 4.3 mmol/L in men during the

headache attacks and normal condition (with no headaches) respectively. There was a significant difference in serum Ca²⁺ level during migraine attacks which decreased significantly compared with normal mode in women and men (P<0.05).

Conclusion: According to the results obtained in this study, serum levels of Ca²⁺during migraine attacks decreased significantly compared with normal subjects, which indicates Ca²⁺ has an impact on these attacks. However, more research in this area appears to be needed.

Key words: Serum ionized calcium, migraine, headache attack

Introduction

Migraine is a common headache that may be accompanied by symptoms such as nausea, vomiting and increased sensitivity to light and sound, which is called migraine with aura (MA) (1). The main symptom of a migraine is usually an intense headache on one side of the head (2, 3). This debilitating progressive and chronic neurovascular disorder affects approximately 6% of males and 18% of females worldwide (4). Migraine is more frequent in midlife with 3- fold more prevalence in women. The prevalence of migraine in European adults is 14.7% and in Asian countries is 3% in men and 10% in women (5, 6).

In Iran, migraine is of the most common types of headache. Evidence shows that migraine prevalence is 95% in south of Iran, which is considered high (3). Regarding the high incidence and prevalence of migraine and its disabling nature, it seems crucial to detect the exact mechanism. This can guide us through better plans for disease management. Extensive research has been done on the role of minerals and many studies have been made on the role of magnesium and calcium in the pathophysiology of migraine (6).

Previous studies described that neuromuscular disorders may be due to changes in amount of active form of calcium (7) and also calcium-phosphate metabolism disturbance was seen in relapsing-remitting multiple sclerosis (RRMS) patients, which increases during disease progression (8).

In addition, some probable mechanisms have described the relationship between calcium level and migraine headache attacks (9). For example, studies have shown that serum magnesium levels in migraine patients compared to healthy controls is slightly lower and the level of serum calcium is higher (3). Overall most research has been done on the effect of magnesium on migraine attacks and less research has been done in the case of calcium. Calcium is known to have anti-spasmodic action, which helps alleviate headaches and migraines (10).

However, studies have shown that when calcium is administered along with Vitamin D, it reduces the frequency of migraines in a considerable number of patients (11). Magnesium and calcium interact with each other. If blood has overly high calcium levels, the body may excrete the extra calcium (1). This can trigger a loss of magnesium, which is expelled along with the calcium, leaving a magnesium deficiency and conflicting results have been reported in association with calcium levels in patients with migraine (1, 5).

Due to the high prevalence of migraine, complications, medical and psychological comorbidities and effective symptoms on patient quality of life, limitations on the use of appropriate treatment and the need to prevent attacks of the disease (12), doing research on this disease is essential to evaluate the hypothesis that serum ionized calcium is a causal risk factor for migraine headache.

The aim of this study was to assess and compare the level of serum ionized calcium, which is the active form of this ion, during the migraine attack and in normal subjects (those with no headache).

Materials and Methods

This cross sectional and analytical study has been done on 50 patients with headache referred to Honari Neurology Clinic of Jahrom, Iran, who had inclusion criteria for migraine (13).

Patients completed a questionnaire containing information such as age, sex, history of trauma, smoking, family history of migraine or a history of mental disorder.

In this study 5 mL of blood sample was taken from each patient during the migraine attack and when they were in a normal condition (no headaches at the time of blood sampling). The blood samples were centrifuged at 3000 rpm for 10 minutes. After separation of the serum, 300 microliters serum were collected from patients to determine serum level of Ca²⁺ by Ion Selective Electrode (ISE) method using ISE analyzer (14).

An ion-selective electrode is a transducer (or sensor) that converts the activity of a specific ion dissolved in a solution into an electrical potential. The voltage is theoretically dependent on the logarithm of the ionic activity, according to the Nernst equation. Ion-selective electrodes are used in analytical chemistry and biochemical/biophysical research, where measurements of ionic concentration in an aqueous solution are required (15, 16).

Prior ethical approval was obtained, and in using these human tissues, safety and ethical guidelines were conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent before entry, and the research study was approved by the Human Ethics Committee of the Jahrom University of Medical Sciences with ethics research committee number: JUMS. ERC.1392-1125.

Results were reported as mean \pm Standard deviation (SD). The groups were compared using t tests (and non-parametric tests) comparisons using Graph pad prism (version 6) software. P values < 0.05 were considered as significant difference between groups.

Results

The patients were aged 21-60 years who were 76% women and the rest = men, with a mean age of 34.8 years for women and 37 years for men.

Mean serum level of Ca²⁺ was 3.5 mmol/L and 4.5 mmol/L in women during the headache attacks and normal respectively and Mean serum level of ionized Ca²⁺ was 3.7 mmol/L and 4.3 mmol/L in men during the headache attacks and normal condition (with no headaches) respectively. There was a significant difference on serum Ca²⁺ level during migraine attacks decreased significantly compared with normal mode in women and men (P values <0.05).

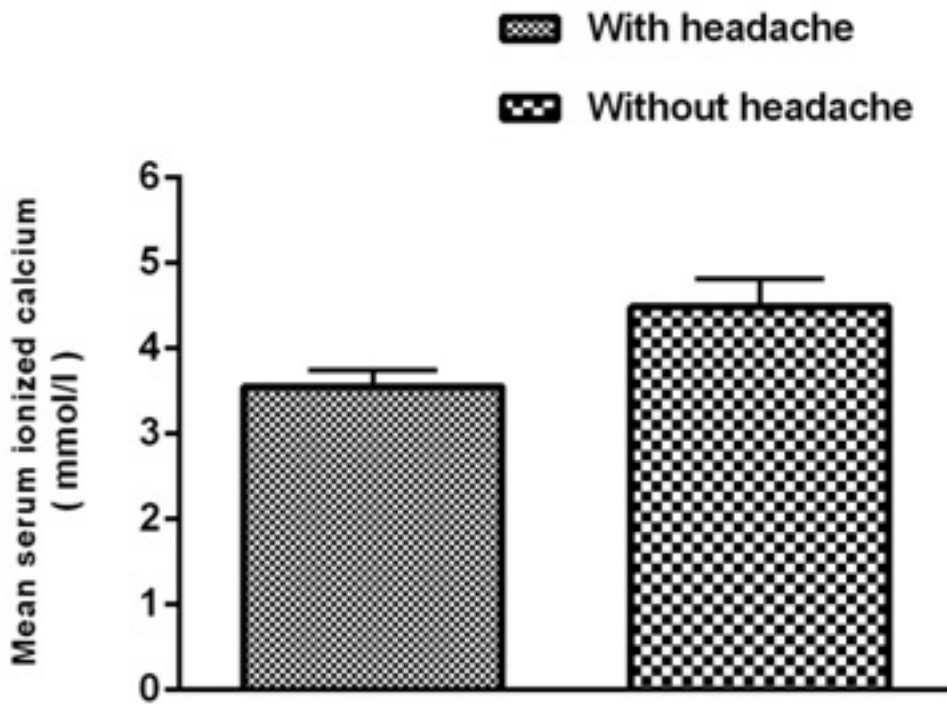


Figure 1: Decreasing ionized calcium level during migraine headache

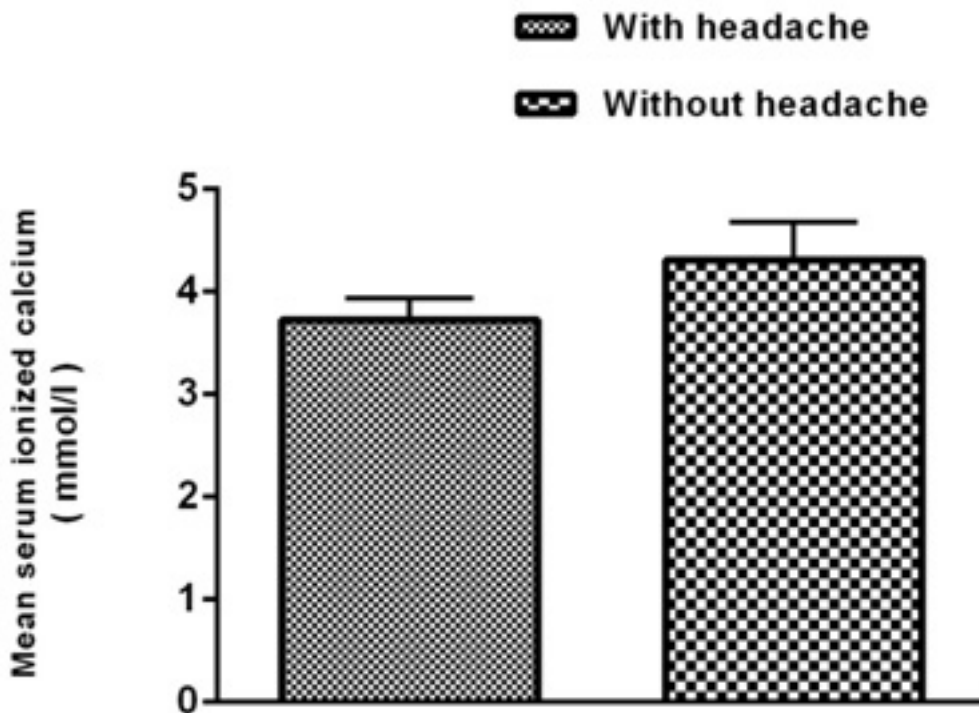


Figure 2: Mean serum ionized calcium level reduced significantly during migraine headache in women

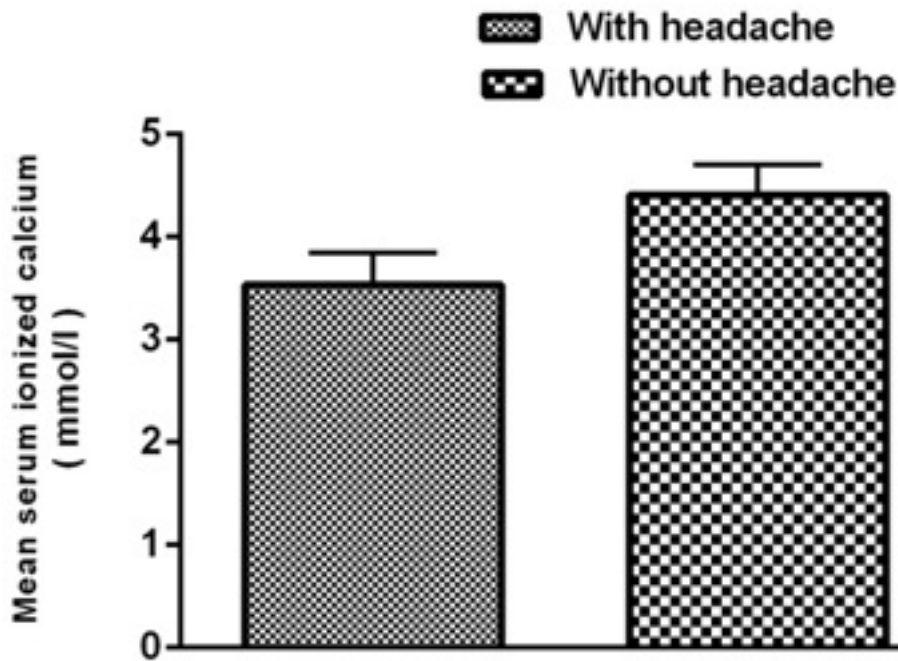


Figure 3: Mean serum ionized calcium level decreased significantly during migraine headaches in men

Discussion

Migraine seems to have a complex pathogenesis (2). Several theories have been suggested to explain the mechanism of migraine. A phosphorylation oxidative defect, malfunction of intra neuronal voltage gated calcium channels, intracellular magnesium (Mg) deficiency or a combination of these may make the cells susceptible to spontaneous depolarization (17).

Many patients with familial hemiplegic migraine have a missense mutation in the P/Q calcium channel, so that this form of migraine, at least, is associated with a demonstrable calcium channelopathy. In menstrual migraine, ionized Mg level is decreased and the ratio of Ca/Mg level is increased. Therefore, serum Mg level may have a role in pathogenesis of menstrual migraine (18).

The results of the present study showed serum ionized calcium level decreased substantially in migraine headaches compared to normal subjects. Also examining the ionized calcium level in men and women separately showed that the ion level in both genders reduced significantly in migraine headaches than normal subjects.

Findings may also add to the growing evidence for involvement of magnesium in migraine pathophysiology (1). Other studies show that Ca²⁺ and other ion channels are important in the mechanism of cortical spreading depression, which is believed to initiate migraine attacks (2). Thus, impaired function of cerebral Ca²⁺ channels may facilitate the initiation of attacks (10). Recent studies have also concluded that abnormalities in the channels within the cells that transport calcium, magnesium, sodium and potassium contribute to the onset of migraines (3). The calcium channels are known to regulate the release

of serotonin. with impaired functioning of the channels, serotonin may not effectively be released or may be released in low quantities (2). As a consequence of this dip, a range of migraine symptoms begin to occur (19).

Previous study suggests that the abnormality of glucose level, insulin resistance, and β -cell function have significant correlation with alteration of serum calcium homeostasis (20). As these factors were not adjusted in our study, this is a limitation for the present study.

Conclusion

Based on the results obtained in the present study, there was a significantly decreased serum ionized calcium level in patients during migraine attack in males and females compared to in normal subjects (those with no headaches).

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Comparative study of vocational rehabilitation among governmental and private sectors on employment of disabled persons

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Abstract

Objectives: The aim of the present study was to investigate the effect of vocational rehabilitation of the governmental sector (Welfare Organization of Rasht, Iran) in the year 2000 relative to that of the private sector in 2014 for employment of persons with disabilities.

Methods: In this study, a total of 154 disabled persons who were trained and skilled under the vocational training program of the private sector in 2014 were compared with 140 disabled persons who were trained and skilled under the vocational training program of the governmental sector in 2000. In this study, we used an interview method with managers of training centers and corrected the obtained data based on available data from the Welfare Organization of Rasht Rasht, Iran as well as Nazari (2000).

Results: Results indicated that 24 trained/skilled individuals among 140 disabled persons who were trained/skilled under the vocational training program of the governmental sector were employed (17.14%). Conversely, 7 trained/skilled individuals among 154 disabled persons who were trained/skilled under the vocational training program of the governmental sector were employed (4.54%).

Conclusion: Based on those results, it is concluded that the performance and efficiency of the private sector in 2014 was lower than that of the governmental sector in 2000. Hence, it is necessary to evaluate, grade and improve the performance of the private sector.

Key words: rehabilitation, employment, disabled person, skill, training

Introduction

Importance of employment in disabled persons is more significant than for normal persons in society, both socially and economically, because disabled persons feel more threatened than normal persons when unemployed. Conversely, job/employment restrictions based on their disabilities decreases job selection opportunities for these disabled persons and they therefore become costly and consumers (Zarneshan, 2008).

Having a job is one of many important aspects of culture and identity for each person. Most people organize their life based on job/employment. Unemployed persons are set aside for important activities and social roles (Obermann, 1980).

Employment as one factor affecting human life is supported by international and national rules. It is recognized as a right and is one of the human rights. Disabled persons, due to their physical situation, need appropriate public support and social cooperation to obtain employment (Zarneshan, 2008).

Technical and Vocational Training Organization (TVTO) could train many Iranian youth. Education is one way to improve human resources and capital. Education should act as a lead to employment. In fact, education should include the principal skills required for job capacities and achievement. Technical and vocational training of disabled persons should be organized based on their individual properties. Training should emphasize practical skills and programs and should be adjusted based on degree of disability and the specificity of the situation (Amiri, 2010).

Based on the International Labour Organization (ILO) definition, vocational rehabilitation is an on-going process including coordinated services. Vocational rehabilitation of disabled persons includes vocational guidance, vocational education, job seeking, and employment so as to provide appropriate jobs for disabled persons. Vocational rehabilitation starts with the identification of a disabled person until he/she is leading a normal social life and career (Asad-Alavi and Roshd-Caboli, 1994).

Employment of each person leads to his/her economical independence. Employment leads to improvement of social dignity and identity and hence employed persons have increased self confidence. Unfortunately, many disabled persons cannot access appropriate jobs despite the fact that they are educated as well as skilled (Habooti, 2014).

Until recently, many people believed that disabled persons could work and be employed. For example, before the vocational rehabilitation program of 1973 in the USA, disabled persons could not participate in employment tests (Blanck, 2001).

Negative attitude of people, especially private employers, toward disabled persons leads to less attention given to their capabilities. People, even highly educated people, do not recognize the potential and acquired capacities of disabled persons. These people think disabled people cannot work and need continuous help (Fleih and Vazooji, 2003). The United Nations (2009) reported that 1.3-3.4% world people are disabled. Italy has the most disabled people among European countries. India and China have the most disabled people among Asian countries. Based on Italian rules, disabled people have services similar to those as remnants of war (Italy had the most disabled people due to the 2nd world war), and 9% of job opportunities in industries and social services belonged to disabled individuals. Meanwhile, if a job opportunity for a disabled person was occupied by a normal person, the same wage was paid to the disabled person (Koucharian, 2014). In as much as all valid data are not available about the recruitment of disabled persons, available data shows there is lower recruitment of disabled individuals compared to normal persons (International Disability Rights Monitor, 2004).

There are at a minimum 650 million disabled individuals worldwide. Approximately 15-20% of people have disability. In developing countries, 80-90% of disabled people do not have a job (Zarocostas, 2005). In developed countries, 50-70% of disabled individuals do not have a job, which at a minimum is twice the rate of normal people. There are 370 million disabled individuals in Asia; of those 238 million seek employment. In Asian countries, 80% of disabled people do not have a job, which is at a minimum twice the rate of normal people (Perry, 2002). In European countries, 43-54% disabled people do not have employment, which is 2-3 times the rate for normal people (International Disability Rights Monitor, 2004). In Latin American countries, 80-90% disabled people do not have a job, and also disabled careers are associated with low income (World Bank, 2004). A total of 0.03% of gross non-net income in the USA is used to support disability institutes. In addition, 0.02% of the total state budget is used for social services to create employment for disabled individuals. Examples from different countries: handicraft produced by disabled persons in India, monitoring of traffic performed by disabled persons in China, traffic light control by disabled persons in France. In addition, 3 disabled individuals work in the navigation and control

tower of the Charles de Gaulle airport in Paris. There were approximately 1 million disabled individuals in 2006 in Iran, and that number increases annually by about 25,000-30,000 persons due to congenital diseases, road accidents, occupational accidents, biological and medical failure, and natural disasters. Hence, there were about 1,120,000 disabled individuals in 2012 in Iran. Nevertheless, there are no valid statistics concerning the number of employed disabled persons in Iran (Koucharian, 2014).

In spite of the ratification of the Disability Rights Protection Act in 2004, there are no real and valid data about their occupation. Hosseinpour (2008) reported that only 600 disabled individuals worked in the public sector. Based on the Disability Rights Protection Act, 60% of operators should select workers among disabled persons, nonetheless they are not employed.

Different countries can create employment for disabled persons in the private sector by means of various actions and politics. For example, governments can use incentive quota, occupation of disabled persons for special jobs, loan or grants for occupation of disabled persons, exclusive contracts, giving priority of production, tax rebates, technical support for companies which employ disabled persons, etc. Countries should support initiatives for providing facilities required by disabled persons.

There are some resources for occupation of disabled persons in Iran. For example, self-employment loans based on the annual budget law, loan and facility available in the Mehr-Imam-Reza Fund, facilities available for quick small business and entrepreneurship, grants available based on law article 17, allocation of as much as 3% of total employment for disabled persons, occupation of disabled persons by the private sector, construction of cooperatives for employment of disabled persons, payment of premium employer's share by the government, issuing work permits for charities to employ disabled persons, providing loans available through national banks for the employment of disabled persons, etc. (Amiri, 2010).

Previous studies reported that disabled persons usually work in low level jobs and income. There is discrimination for occupation between disabled and normal individuals. Although the government should allocate as much as 3% of total employment for disabled persons, the reality shows that this rule is not well implemented. Therefore, disabled persons' lives are difficult (Habooti, 2014).

In the present study, we will compare vocational rehabilitation among governmental (2000) and private sectors (2014) on the employment of disabled persons. Other studies focused only on one type of disability or one time period. In the study herein, however, we studied and compared two methods (governmental and private sectors) for vocational rehabilitation. As no report exists for investigating the performance and efficiency of the private sector, this research was conducted to monitor their performance concerning the employment of disabled persons.

Materials and Methods

This research was conducted based on a descriptive-analytical approach. Samples were selected among all vocational rehabilitation centers at Rasht city, Iran. Samples were all disabled persons who trained and were skilled in these centers at Rasht city, Iran.

Firstly, all available statistics (address and telephone number) of vocational training centers (private and governmental sectors) of Rasht city, Iran were collected in 2014 from the Welfare Organization of Rasht, Iran. Then, all available statistics (address and telephone number) of vocational training centers (private and governmental sectors) and also from all occupied disabled persons in the year 2000 were collected from Welfare Organization of Rasht, Iran.

We collected data via managers of all vocational training centers by verbal or telephone interviews. The number of skilled and occupied disabled persons collected were based on the type of disability and sex. Then, collected data were validated, based on data available in the Welfare Organization of Rasht, Iran, and incorrect data removed.

Results and Discussion

Results are summarized in Tables 1 and 2. Based on obtained results, there were four vocational training centers in Rasht city, Iran in 2000:

1-Rofeideh supportive workhouse for mentally retarded and deaf persons. This center included 50 disabled persons (27 males and 23 females).

2- Fayazbakhsh center for blind and mobility impairment persons. This center included 8 disabled persons (5 males and 3 females).

3- Koosesh center for mentally retarded persons. This center included 50 male disabled persons.

4- Tavana center for mentally retarded persons. This center included 32 female disabled persons.

Therefore, there were 140 trained/skilled disabled persons in the four above centers. A total of 24 disabled persons were able to find a job among the 140 above disabled persons (17.14%) in 2000.

Table 1. Summary of data obtained for 2000

Institute	Disability type	Sex		Type of education	Number	Number of employed persons	Sex of employed person	
		Male	Female				Male	Female
Rofeideh	Mentally retarded and deaf person	+	+	Carpentry, tailoring, broom making, mat weaving, nylon making, artificial flowers	50	17	14	3
Koosesh	Mentally retarded person	+	-	Sweep making, mat weaving, nylon making, doll making	50	-	-	+
Tavana	Mentally retarded person	-	+	Knitting yarns, artificial flowers, crocheting, embroidered Gobelins	32	5	-	5
Fayazbakhsh	Deaf person	+	+	Telephone operator, Sweep making, mat weaving	8	2	1	1
Total		+	+	-	140	24	15	9

Table 2. Summary of data obtained for 2014

Institute	Disability type	Sex		Type of education	Number	Number of employed persons	Sex of employed person	
		Male	Female				Male	Female
Center for mentally retarded person above 14 years	Mentally retarded and semi-deaf person	+	+	-	52	3	3	0
Center for mentally retarded person above 14 years	Mentally retarded and semi-deaf person	-	+	-	40	0	0	0
Blind society	Blind person	+	+	Computer, life skills, hymns	10	1	0	1
Dasthaye-Shokoofa	Blind person	+	+	Telephone operator, theatre, computer	52	3	3	0
Total		+	+	-	154	7	6	1

There were some vocational training centers in Rasht city, Iran in 2014:

- 1- A private supportive workhouse for mentally retarded males above 14 years of age.
- 2- A private supportive workhouse for mentally retarded females above 14 years of age.
- 3- and 4- Two private supportive workhouses for mixed mentally retarded persons under 14 years.
- 5- A private supportive workhouse for mixed mobility impairment persons above 14 years of age.
- 6- A private supportive workhouse (blind society) for blind persons. This center included 10 disabled persons.
- 7- A private supportive workhouse (Dasthaye-Shokoofa) for blind persons. This center included 52 disabled persons.

There were 154 trained/skilled disabled persons in the five above centers in 2014. A total of 7 disabled persons could find employment among the 154 above disabled persons (4.54%) in 2014.

Comparison of results obtained from governmental (2000) and private (2014) sectors showed that the private sector was not successful in creating employment for disabled persons, and there was a decline in job creation relative to the governmental sector. Hence, there are some questions:

- 1- Was the privatization of government agencies executed properly?
- 2- Does the private sector with respect to the objectives of the Welfare Organization of Rasht perform their tasks properly?
- 3- If the budget paid as subsidies to the private centers for the disabled was transferred to governmental sector to pay for their training and vocational rehabilitation, would the outcome not be better?
- 4- It is recommended that the Welfare Organization be careful and have an appropriate target concerning the assignment of governmental centers to the private sector.
- 5- Private centers should be monitored periodically.

6- The level of education of disabled persons should be evaluated periodically in the private sector.

7- The employment rate of disabled persons should be selected as one of the important items to be considered in grading these centers.

8- Type of education should be organized based on community and labor market needs.

9- Follow-up and evaluation of employers' satisfaction should be scheduled periodically.

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A Survey of Interurban Taxi Drivers' driving Behaviors across Kermanshah, Iran, in 2015

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Abstract

Introduction: Car accidents in developing countries are one of the major causes of mortality and injuries. Human errors are the most important causes of traffic accidents. The skill of safe driving a taxi was an important part of job behaviors for drivers of public transport. The aim of this study was to determine the factors affecting driving errors in Taxi Drivers' driving Behaviors across Kermanshah 2015.

Methods: The descriptive cross-sectional study was performed in 2015. Data were collected from the cluster random sampling that was employed, and in the final volume of sample population 226 subjects were selected. The samples consisted of all interurban taxi drivers with a driving license and at least one year of driving experience. Data were collected using two questionnaires, a researcher-made questionnaire and the Manchester Driving Behavior Questionnaire. The validity of the first questionnaire was confirmed by the experts' opinions while the second questionnaire was validated in previous studies. The qualitative and quantitative analysis of data was conducted using the SPSS Statistics Software Version 20.0.

Findings: The reliability of the Manchester driving behavior questionnaire measured 0.92. Exploratory Factor Analysis showed differences between slips, lapses, deliberate violation and unintentional violation clearly. Internal consistency were unintentional violation 0.42, deliberate violation 0.85, lapses 0.77 and slips 0.88. The most dangerous driving behavior related to slips and deliberate violation.

Conclusion: The findings of this study show psychometric properties of dangerous driving behavior in deliberate violation and slips in Kermanshah taxi drivers. It is suggested that driving teaching workshops and safety driving education are initiated for Kermanshah's taxi drivers.

Key words: Manchester Questionnaire, Driving behavior, taxi driver.

Introduction

Car accidents and their consequences, especially in developing countries, are seen as one of the major causes of mortality and injuries. In addition to economic losses, car accidents pose serious loss of life in Iran (1). It is estimated that roughly two million people lose their lives as a result of car accidents in the world annually (2). The estimated number of driving casualties is over 15 million people per year (3), and Iran is no exception, but what distinguishes Iran from other countries is the growing trend of car accidents compared to other countries. In most countries, the growth trends of the accident index have been either negative or sluggish from 1990 to 1993. For instance, this trend has measured 18% in France, 16% in England, 7% in Denmark, 2% in Pakistan, and 1.2% in India, while the very same index measured 55% in Iran between 1994 and 1996 (4). In other words, the mortality rate resulting from car accidents was 29 deaths per 10,000, while the very same index indicated 1-2.5 people for developed countries and 3-15 persons for developing ones (4).

In Iran, 64 people are killed in car accidents every day, and 1967 injured people are hospitalized, of which 640 people are disabled in car accidents. Every day, the incomes of 450 families are severely decreased, and with the assumption of the existence of four people in each family, about 1,300 people are severely affected by the financial pressures of death or disability in the family. Every year, 23,300 are killed and 718,000 are injured in car accidents, of which 200,000 victims are disabled. In other words, a total of 753,000 Iranians (equivalent to one percent of the whole population of Iran) are killed or injured. The estimated costs of accidents outside cities alone have been 10 times higher than the budget allocated to the construction and maintenance of roads. If the effects of human factors are controlled, accidents and driving violations will probably be reduced (5).

Driving violations have always been one of the leading causes of traffic problems and accidents in all societies, and their rates and types are different depending on the cultural, socioeconomic and geographical contexts of societies. Notwithstanding the environmental, controlling and executive factors as well as the disproportion of road structures to the number of vehicles and traffic units and other factors contributing to driving violations, the human factors, as the leading cause, constitute the highest percentage of violations. One of the major duties of health researchers is to conduct research into the related issues with the aim of having a more accurate classification and understanding of human factors that play prominent roles in road accidents. It is noteworthy that all human factors involved in driving accidents are not covered by rectifying human errors by any means. In fact, it's important to distinguish between errors and violations (6).

Errors are interpreted as one's inability or failure to make sound judgments or to perform a series of designed actions to achieve the intended results (7). Violations are those behaviors that endanger the driving safety, for

example, excessive speed or driving without observing the safe following distance from other vehicles ahead (8). According to consensus, errors are categorized into two distinct types. The first type is about errors that are caused by problems in attention, memory and information processing, which include two major categories: lapse and slip. The first type refers to errors that are caused by the wrongly adopted approaches to achieve a goal without awareness of one's wrong choice. Violations fall into two major categories: unintentional violations (e.g., driving too slowly on narrow two-lane highways) and deliberate violations (e.g., overtaking other cars on solid white lines in crowded two-way roads) (9).

Various studies have referred to the role of human factors as the main cause of traffic irregularities, particularly in driving offenses and accidents. Disregard for traffic regulations and evasion of law as the causes of problems, dilemmas and traffic accidents in many societies depend on the cultural, social, economic and geographical conditions of societies. The statistics in Iran are indicative of the high and unusual rates of driving violations which cause irreparable economic losses and social damage, not to mention, human factors have been reported as the main cause of driving violations (10). All interurban taxi drivers are to have the required knowledge and various skills to provide safe travel service in the urban transport fleet. Further, they must all have a driving licence class B2 and adopt the correct driving behaviors while moving along the traffic and avoid accidents using their driving skills.

In a study conducted on 293 drivers with driving licence class B2 in Isfahan, Iran, Oreyzi and Haghayegh (2009) assessed the reliability and validity of Manchester driving behavior questionnaire and determined the types of traffic anomalies. First of all, lapses, slips, unintentional violations and deliberate violations were differentiated from each other to examine the validity of the instrument through the exploratory factor analysis. The results of the final analysis showed that all four factors had high internal consistency: unintentional violations (0.65), deliberate violations (0.86), lapses (0.81), and slips (0.77). The results of this study demonstrated that the Manchester driving behavior questionnaire could be used as a valid and reliable instrument for assessing the driving behaviors (11).

In a descriptive and analytical study conducted on 1,286 interurban drivers in the United Arab Emirates by Beneret al. (2011), the driving behaviors were investigated in terms of unintentional violations, deliberate violations, lapses, and slips. The results indicated that the unintentional violations, lapses, deliberate violations and slips accounted for 48%, 10.6%, 7.2% and 6.3% of injuries caused by accidents, respectively (12). The results showed that there was a difference between the errors and violations performed by the subjects under study. Furthermore, the rates of slips, violations and lapses were higher compared to those in Australia and European countries (13).

In a study performed on driving examinees in Shiraz, Iran, 537 subjects were selected using convenience sampling through visiting places such as the center for replacement

and issuance of license plates and a central specialized clinic based in Shiraz. For data collection, a demographic questionnaire, the Manchester driving behavior questionnaire, and NEO Personality Inventory were utilized. In addition, correlation and variance analysis were used for data analysis. The results of this study demonstrated that there was a significant positive relationship between the scores of neuroticism and the levels of error types and unlawful actions ($p < 0.05$). Additionally, it was shown that the scores of agreeableness and extraversion significantly and inversely correlated with the levels of error types and unlawful actions ($p < 0.05$). It was demonstrated that only the factors of age and years of driving experience significantly and negatively correlated with dangerous violations ($p < 0.05$). Interestingly, there was a significant positive relationship between the years of formal education and each of the rates of error types and dangerous violations ($p < 0.05$). Also, the results indicated that there was a significant relationship between the personality traits and driving behaviors (14). The results of Ozkan et al. study (2006) on 242 drivers selected from Finland, England, Greece, Iran, Norway and Turkey showed that lapses were the most common factor in connection with driving accidents, and a relationship was found between the patterns of driving behaviors and accidents. So, it was concluded that driving accidents could be estimated based on the patterns of driving behaviors (15).

Given the significance of this skill, the necessity of correct driving behaviors to minimize loss of life and property caused by accidents, lack of previous research in this respect across Kermanshah, and the fact that a major portion of urban transport is performed by interurban taxi drivers, the present study aimed to investigate the interurban taxi drivers' driving behaviors across Kermanshah, Iran, in 2015.

Methodology

The descriptive cross-sectional study was performed in 2015. The statistical population consisted of all interurban taxi drivers with a driving license and at least one year of driving experience. As for sampling, the cluster random sampling was employed, and the final volume of sample population was estimated to be 200 taxi drivers based on the fact that there were 260 interurban travel agencies across Kermanshah which fell into 20 clusters, and 10 people were selected from each cluster. The final volume of the sample population was estimated to be 184 taxi drivers using the study performed by Oreizy and Haghayegh (2009), but 220 subjects were selected due to the possibility of sample attrition. After the distribution and collection of questionnaires, the final volume of the sample population reached 226 subjects. To encourage the taxi drivers to complete the questionnaires, one car air freshener was given to each of the participants (11).

For data collection, a researcher-made demographic questionnaire and the Manchester driving behavior questionnaire, were utilized. In addition, the face and content validities of the demographic questionnaire were approved by a panel of 10 faculty members at Kermanshah

University of Medical Sciences. The Manchester driving behavior questionnaire was developed by Reason et al. (1990) in the Department of Psychology at the University of Manchester. Furthermore, the reliability and validity of this instrument has been confirmed in different countries of the world, including Iran (11). This questionnaire was designed based on the basic theory that errors and violations have different psychological causes and correction procedures, and they should be differentiated. Moreover, given the prohibition of alcoholic beverages in most countries the questions relating to the permitted consumption of alcoholic drinks were modified. Also, this questionnaire consisted of 50 items with five-point Likert scale (0=never, 1=rarely, 2=sometimes, 3=often, 4=usually, 5=Always). The questions were different in two aspects: the kind of behaviors and the extent of danger that the behavior causes for other drivers. The abnormal behaviors fall into four categories: lapses, slips, unintentional violations, and deliberate violations. Also, in terms of the extent of danger that each of these categories cause for drivers, there are three categorizations: 1) low-risk, 2) average-risk, and 3) high-risk (see Table 1).

The qualitative and quantitative analysis of data were conducted using the SPSS Statistics Software Version 20.0. Furthermore, the statistical tests of mean and variance were employed for the descriptive analysis of the demographic characteristics and driving cultures of the samples under study. To investigate the factor structure of the Manchester driving behavior questionnaire, the principal components analysis, one of the procedures of exploratory factor analysis, with varimax rotation method were utilized and items were operating under factor loading to separate from each other factor and will be calculated error. After performing the factor analysis; the internal consistency was analyzed based on the extracted factors. To commence the study, the required permits were obtained from the Vice Chancellery for the Department of Research and Technology at Kermanshah University of Medical Sciences.

Findings

Of the total of 226 subjects of the present study, 64.2% of drivers were married, and 35.8% were single. The average age of subjects was 34.86 (± 11.33), the average work experience measured 9.94 (± 8.27), and the average driving history was 5.24 (± 3.86). In terms of education, 5.8% of the respondents were illiterate, 32.3% had middle school education, 17.3% were high school graduates, 29.6% had A.A. degrees, 12.4% had B.A./B.Sc. degrees, and 2.7% held M.A./M.Sc. degrees. Besides, 23.9%, 47.3%, 11.5% and 17.3% had class 1, class 2, class B1 and class B2 driver's licenses, respectively. In Table 2, the drivers' behavioral characteristics are shown in terms of traffic violation records and normal behaviors.

To investigate the factor structure of the Manchester driving behavior questionnaire, the principal components analysis, one of the procedures of exploratory factor analysis, with varimax rotation method were utilized. The results showed that the KMQ index measured 0.867. In addition,

Table 1: The Structure of the Items of the Questionnaire Based on the Classification of Abnormal Behaviors and Their Risks (High, Average, and Low)

Risks	Low-risk	Average-risk	High-risk	Total
Abnormal Behaviors				
Slips	10	2	9	21
Deliberate Violations	1	2	14	17
Lapses	3	3	3	9
Unintentional Violations	1	1	1	3
Total	15	8	27	50

Table 2: The Frequency Distribution of the Drivers' Behavioral Characteristics in Terms of the Traffic Violation Records and Normal Behaviors

Row	Traffic Violation Records and Normal Behaviors	Frequency	Percentage
1	History of traffic tickets	181	80.1
2	Suspended driver's license due to high-risk driving	13	5.8
3	History of arrest due to high-risk driving	9	4
4	History of accidents leading to injury	22	9.7
5	History of accidents leading to death	7	3.1
6	Fastening seat belt upon riding or driving a car	180	79.6
7	Talking on cellphones while driving	99	43.8
8	Eating and drinking while driving	102	45.1
9	Observing the speed limit	173	76.5
10	The difference between ordinary driving and driving an ambulance	138	61.1

Table 3: The Cronbach's Alpha Coefficients Based on the Standardized Items in Manchester Driving Behavior Questionnaire

	Slips	Deliberate Violations	Lapses	Unintentional Violations
Number of items	21	17	9	3
Cronbach's Alpha Coefficient	0.880	0.859	0.779	0.426

the four factors of slips, lapses, deliberate violations and unintentional violations were differentiated from each other. The results indicated that these four factors determined 42.169% of the variance of behaviors. The reliability of the Manchester driving behavior questionnaire measured 0.92. After performing the factor analysis, the internal consistency was analyzed based on the extracted factors. In Table 3, the internal consistencies of the four factors are shown.

In the first factor (slips), 21 items were examined, and the 9th and 15th questions had the highest (0.873) and lowest (0.869) factor loadings, respectively. In addition, the internal consistency was 0.880 (see Table 4 - next page).

In the second factor (deliberate violations), 17 items were examined, and the 44th and 29th questions had the highest (0.845) and lowest (0.623) factor loadings, respectively. In

addition, the internal consistency measured 0.859 (see Table 5 - page 19).

In the third factor (lapses), nine items were examined, and the 33rd and 49th questions had the highest (0.772) and lowest (0.756) factor loadings, respectively. In addition, the internal consistency measured 0.779 (see Table 6 - page 20).

In the fourth factor (unintentional violations), three items were examined, and the 28th and 22nd questions had the highest (0.214) and lowest (0.239) factor loadings, respectively. In addition, the internal consistency measured 0.426 (see Table 7 - page 20).

Table 4: The Statistical Indexes of the First Factor (Slips)

Row	Items	Mean	STDEV	Type of Behavior	Possibility of risk	Reliability after removing the question
1	Attempt to drive away from traffic lights in third gear	0.7	1.08	Slip	Low	0.869
3	Lock yourself out of your car with the keys still inside.	1.15	1.38	Slip	Low	0.871
6	Prior to starting the car, you have tried to drive	0.63	1.69	Slip	Low	0.874
8	Forget where you left your car in a multi-level car park.	0.83	1.20	Slip	Low	0.873
9	Distracted or preoccupied, realize belatedly that the vehicle ahead has slowed, and have to slam on the brakes to avoid a collision	1.46	1.34	Slip	High	0.873
10	Intend to switch on the windscreen wipers, but switch on the lights instead, or vice versa	1.01	1.12	Slip	Low	0.871
13	"Wake up" to realise that you have no clear recollection of the road along which you have just travelled	1.15	1.21	Slip	Low	0.869
14	Miss your exit on a motorway and have to make a detour	1.47	1.07	Slip	Low	0.871
15	Forget which gear you are currently in and have to check with your hand	1.11	1.05	Slip	Low	0.869
7	Intending to drive to destination A, you "wake up" to find yourself en route to B, where the latter is your more usual journey	1.07	1/08	Slip	Low	0.868
20	Try to overtake without first checking your mirror, and then get hooted at by the car behind, which has already begun its overtaking manoeuvre.	1.04	1.01	Slip	High	0.871
23	Lost in thought, you forget that your lights are on full beam until "flashed" by other motorists	0.75	1.01	Slip	Average	0.869
24	On turning left, nearly hit a cyclist who has come up on your inside	0.51	0.99	Slip	High	0.868
25	Attempt to overtake a vehicle that you hadn't noticed was signaling its intention to turn right	0.64	1.07	Slip	Average	0.868
30	Misjudge the speed of an oncoming vehicle when overtaking	0.88	1.02	Slip	High	0.867
32	Fail to notice someone stepping out from behind a bus or parked vehicle until it is nearly too late	0.7	1.04	Slip	High	0.875
38	Fail to read the signs correctly, and exit from a roundabout on the wrong road	1	1.02	Slip	Low	0.869
41	Fail to check your mirror before pulling out, changing lanes, turning, etc	0.93	1.16	Slip	High	0.869
42	Fail to check your mirror before pulling out, changing lanes, turning, etc.	1.07	1.07	Slip	High	0.872
45	Drive with only "half an eye" on the road while looking at a map, changing a radio channel, etc.	1.59	1.29	Slip	High	0.880
46	Fail to notice pedestrians crossing when turning into a side street from a main road.	1.21	0.88	Slip	High	0.873

Table 5: The Statistical Indexes of the Second Factor (Deliberate Violations)

Row	Items	Mean	STDEV	Type of Behavior	Possibility of risk	Reliability after removing the question
4	Become impatient with a slow driver in the outer lane and overtake in places where it is not allowed (outside urban areas, for example).	2.21	1.31	Deliberate Violation	High	0.852
7	Drive especially close or "flash" the car in front as a signal for that driver to go faster or get out of your way	1.34	1.25	Deliberate Violation	High	0.851
16	Stuck behind a slow-moving vehicle on a two-lane highway, you are driven by frustration to try to overtake in risky circumstances	0.75	1	Deliberate Violation	High	0.839
18	Take a chance and go through lights that have turned red	0.82	0.97	Deliberate Violation	High	0.842
19	Angered by another driver's behaviour, you give chase with the intention of giving him/her a piece of your mind.	0.59	0.93	Deliberate Violation	High	0.837
21	Deliberately disregard the speed limits late at night or very early in the morning.	1.01	1.17	Deliberate Violation	High	0.842
26	You have noticed that you are in no condition to drive due to certain medical restrictions such as blood sugar, high blood pressure, etc.	0.56	1.06	Deliberate Violation	High	0.841
27	Have an aversion to a particular class of road user, and indicate your hostility by whatever means you can	0.55	0.05	Deliberate Violation	Average	0.843
29	Park where it is not allowed and risk a fine.	0.65	0.97	Deliberate Violation	Low	0.845
35	Overtake a slow-moving vehicle in the inside lane or on the hard shoulder of a motorway.	0.95	1.12	Deliberate Violation	High	0.845
36	Cut the corner at a right-hand turn and have to swerve violently to avoid an oncoming vehicle.	0.93	1.14	Deliberate Violation	High	0.836
39	Fail to give way when a bus is signalling its intention to pull out.	0.46	0.98	Deliberate Violation	Average	0.856
40	Overtake from left to avoid traffic congestion	0.79	1.09	Deliberate Violation	High	0.842
43	Deliberately drive the wrong way down a deserted one-way street.	0.62	1.05	Deliberate Violation	High	0.838
44	Disregard red lights when driving late at night along empty roads.	0.75	1.36	Deliberate Violation	High	0.845
47	"Race" oncoming vehicles for a one-car gap on a narrow or obstructed road.	0.6	1.07	Deliberate Violation	High	0.839
48	"Race" oncoming vehicles for a one-car gap on a narrow or obstructed road	0.55	1.09	Deliberate Violation	High	0.837

Table 6: The Statistical Indexes of the Third Factor (Lapses)

Row	Items	Mean	STDEV	Type of Behavior	Possibility of risk	Reliability after removing the question
5	Drive along country roads at night as fast with dipped lights as on full beam.	0.23	0.78	Lapse	Average	0.774
11	Turn left onto a main road into the path of an oncoming vehicle that you hadn't seen, or whose speed you had misjudged.	0.88	1.09	Lapse	Average	0.753
12	Misjudge your gap in a car park and nearly (or actually) hit the adjoining vehicle	0.59	0.88	Lapse	Average	0.746
31	Hit something when reversing that you had not previously seen	0.51	0.82	Lapse	High	0.753
33	Plan your route badly, so that you meet traffic congestion you could have avoided	0.83	0.94	Lapse	Low	0.772
34	Overtake a single line of stationary or slow-moving vehicles, only to discover that they were queuing to get through a one-lane gap.	0.77	0.96	Lapse	Low	0.750
37	Get into the wrong lane at a roundabout or approaching a road junction.	0.67	0.98	Lapse	Low	0.743
49	Brake too quickly on a slippery road and/or steer the wrong way in a skid	0.53	0.96	Lapse	High	0.756
50	Misjudge your crossing interval when turning right and narrowly miss a collision.	0.50	0.87	Lapse	High	0.737

Table 7: The Statistical Indexes of the Fourth Factor (Unintentional Violations)

Row	Items	Mean	STDEV	Type of Behavior	Possibility of risk	Reliability after removing the question
2	Check your speedometer and discover that you are unknowingly travelling faster than the legal limit.	1.88	1.43	Unintentional Violation	Average	0.495
22	Forget to pay/renew your statutory insurance and discover that you are driving illegally.	0.59	1	Unintentional Violation	Low	0.239
28	Lost in thought or distracted, you fail to notice someone waiting at a zebra crossing, or a pelican crossing light that has just turned red	0.60	1.03	Unintentional Violation	High	0.214

Discussion

In today's world, car accidents are one of the the leading causes of death of human beings. In Iran, the first fatal car accident was reported in 1926 which has witnessed a progressively ascending trend ever since, so that one of the major causes of three hundred thousand annual deaths occurring in the country, except the cardiovascular diseases, has been car accidents (2). Driving offences, as one of the causes of traffic problems, obstacles and accidents in societies, have different forms depending on the cultural, social, economic and geographical contexts of societies (16,17). Notwithstanding the environmental, controlling and executive factors as well as the disproportion of road structures to the number of vehicles and traffic units and other factors contributing to driving violations, the human factors, as the leading cause, constitute the highest percentage of violations (18,19,20).

The results of the present study demonstrated that with the increase of the age of the subjects under study, the rates of the unintentional violations and average risks were on the rise. This finding was consistent with the results of a study conducted by Lucidi et al. (2006). To further explicate this finding, it can be expressed that with the increase of one's age, one would have a false confidence in one's driving skills, thereby leading to risky behaviors in driving patterns (21). On the other hand, the growing consumption of alcohol and other mind-altering drugs among older drivers has been reported as the cause of risky driving behaviors (22). It should be noted that various studies have addressed the emergence of risky behaviors in the driving patterns at young ages, for example, having less control over stress and losing temper easily (23 & 24). Given this finding, it seems essential that the significance of safe driving be stressed in training programs aimed at strengthening the driving skills of the emergency personnel, regardless of age.

In the driving profession, one should be able to show more distinct driving behaviors than those adopted by other drivers. There have been various reports on the difference between the professional and amateur drivers in terms of risky driving and response to stress, so that the training needs of professional drivers about driving behaviors are very different from those of amateur drivers, for example, the speed limit and destination (25). The results of the present study also indicated that the rate of the average risk in driving increased in line with greater work experience, which can be caused by the abundant stress in the profession.

Given this finding, it is suggested that further studies be conducted in this respect. Although there have been reports about the higher rates of overtaking and exceeding the speed limit among drivers with higher education, the results of the present study demonstrated that the rates of lapses and unintentional violations were higher among drivers holding education under high school diploma (26). This remarkable finding should be taken into consideration in choosing the interurban taxi drivers, and further studies are suggested to be undertaken in this regard.

Compared to other drivers, it seemed that the taxi drivers under study acted more in compliance with the basic principles of preventing accidents such as fastening seat belts and not using mobile phones during driving. In the present study, the rate of fastening seat belts upon riding or driving a car measured 86.8%, while the same rate measured 63.1% in a study done by Bener et al. (2011) (27). In terms of abiding by driving tips, such as not talking on cellphones while driving, not eating and drinking while driving and observing the speed limit, the participants of the present study were in better condition in comparison with those studied by Bener et al. (2011) (27). In Iran, after conducting some research into the causes of driving fatalities, it was found out that not using seat belts was the number one cause, thereby leading to the enactment of a rule in this respect in 2005 which made fastening seat belts compulsory (28), so that the institutionalization of this rule and its growing use have been reported in recent studies (29). However, it should be noted that there were more driving lapses among the samples who used seat belts. It is noteworthy that the primary goal of fastening seat belts is to reduce driving fatalities and injuries with this assumption that it prevents initial hits. Given the interurban driving profession and the importance of the health of victims and the fact that safe driving is one of the main pillars of this profession, it is essential that the driving skills of interurban drivers across Kermanshah be boosted through holding safe driving courses.

Talking on cellphones while driving is another example of unsafe driving, which is more dangerous than other distractors like eating and drinking while driving. Sending and receiving SMS while driving distract the driver's attention from paying close attention to the road ahead, thereby leading to dangerous consequences. Moreover, the results of the present study revealed that there was a significant negative relationship between risky driving behaviors and history of accidents leading to injury and death, thereby confirming reports in this regard in Iran (30).

The present study had several limitations. Firstly, the data were collected through the self-reporting methods, possibly affecting the accuracy of the results and social desirability bias, but various studies have reported that the questionnaire has weak effects on the responses of the subjects in terms of the social desirability bias nevertheless (17 & 10). Secondly, the type and the make of cars were not considered in the present study, and no comparisons were made in this respect. There are some studies that have reported that the drivers of new, more powerful and luxurious cars commit the offense of exceeding the speed limit (31 & 32).

The results of examining the structure of the Manchester driving behavior questionnaire showed that the highest risks were related to deliberate violations and slips, while in a study performed by OREYZI (2011), the highest risks were related to unintentional violations and slips (11). This finding was indicative of the fact that the patterns of taking risks among the interurban taxi drivers residing in Kermanshah were not similar to those adopted by other

drivers in other cities and even other countries. This finding was consistent with the point mentioned by Özkan et al. (2006), stating that 'the Manchester driving behavior questionnaire is regarded as a valid instrument for assessing the driving behaviors. It should be noted that, in addition to the national traffic problems in any society, the regional and local problems and the indigenous and cultural contexts of cities should be taken into consideration, not to mention, training positive driving behaviors may be seen as the best way to improve driving behaviors (9).

Conclusion

Driving is one of the necessary skills of interurban taxi drivers residing in Kermanshah. With the increase of age and work experience, it is likely that the incidence of driving accidents rises, and this skill should not be considered trivial for the sake of age and work experience by any means. In addition, it should be noted that young drivers may not have enough experience in these skills and may have more slips and unintentional violations in their driving behaviors. More to the point, fastening seat belts is no guarantee for safe driving and making driving mistakes. Hence, it is necessary that safe driving workshops and low-risk driving programs be considered for interurban taxi drivers and their driving skills be enhanced.

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Comparison of Standard Triple Therapy Regimen with Sequential Therapy Regimen Containing Levofloxacin Used for The Eradication of Helicobacter Pylori in Patients with Gastrointestinal Infection Caused by Helicobacter Pylori

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Abstract

Objectives: The aim of this study was to compare standard triple therapy regimen with sequential therapy regimen containing levofloxacin used for the eradication of *H. pylori* in patients with gastrointestinal infection caused by *H. pylori*.

Methods: This single blind clinical trial study was conducted on 96 patients with positive Rapid Urease Test (RUT) who were referred to the Endoscopy center of Hajar Hospital in Shahrekord city, located in southwest of Iran. The patients were randomly assigned into two treatment groups: sequential therapy regimen and triple therapy regimen. The patients in the first group received sequential therapy regimen including omeprazole, amoxicillin, levofloxacin, and tinidazole; the second group of patients received a triple therapy regimen consisting of omeprazole, amoxicillin, and clarithromycin. Four weeks after the end of the treatment, using *H. pylori* Stool Antigen (HpSA), a test was performed to prove the eradication of *H. pylori*. The influences of patients' age, gender and eradication level were also investigated.

Results: There were significant differences between the two groups in terms of age and education. While *H. pylori* eradication rate was 67.3% in the sequential therapy regimen, it was 66% in standard triple therapy regimen. In addition, among patients receiving triple therapy regimen, being aged older than 40 years had a significant relationship with eradication. Moreover, in patients receiving sequential therapy regimen, education level had a significant relationship with eradication.

Conclusion: There was no statistically significant difference between the two therapy groups in terms of *H. pylori* eradication rate. However, given the low rates of *H. pylori* eradication in both sequential and triple therapy regimens observed in the present study, it seems that it is necessary to conduct further research on the bacterial resistance to the prescribed antibiotics.

Key words: *H. pylori*, standard triple therapy, sequential therapy, Eradication

Introduction

H. pylori is a microaerophilic gram-negative bacterium which has affected more than half of the world population [1-6]. Infections caused by *H. pylori* are known as the main cause of chronic gastritis disease type B, peptic ulcer, and mucosa associated lymphoid tissue (MALT) lymphoma; in addition, the treatment of related infections are recommended to prevent adenocarcinoma gastric cancers [7-14]. The guidelines proposed for the treatment of *H. pylori* infection have emphasized on the eradication of the bacteria using multiple medication regimens [15]. Nevertheless, treatment success rate depends on several factors including type of antibiotic, dosage, formulation, duration of treatment, patient compliance, smoking, and bacterial resistance to one or more antibiotics [16]. Resistance to antibiotics is the most common cause of failure in achieving an eradication rate of higher than 80% [12, 17, and 18]. Moreover, using the same regimens, the rates of relapse and re-infection in developing countries are higher than those in other countries [19].

According to studies conducted in Iran, the prevalence of *H. pylori* resistance to clarithromycin, furazolidone, and metronidazole is remarkably increasing and the level of resistance to amoxicillin is much higher than that in other countries [20, 21]. Hence, as the result of the increase in bacterial resistance to common antibiotic regimes and differences in resistance patterns in different regions, there have been some differences in therapy regimens and techniques used in different areas [22-24]. Quadruple therapy is a conventional therapy regimen which consists of a proton pump inhibitor drug, amoxicillin, metronidazole, and clarithromycin [15,25-27]. Resistance to clarithromycin and metronidazole has increased in recent years. Resistance to metronidazole has also been observed in 40-50% of people in developed countries and 80% of people in developing countries [12]. In Iran, the prevalence of resistance to clarithromycin and metronidazole are about 16.7% and 57.5%, respectively [21].

Sequential therapy is one of the methods which have had promising outcomes in recent years. Using sequential therapy, an eradication rate of more than 80% has been achieved and patients have tolerated it well [12]. Vaira and colleagues compared two regimens of triple therapy and sequential therapy for 10 days; According to their findings, using triple therapy and sequential therapy regimens, eradication rates of 77% and 89%, respectively, were achieved. It shows that sequential therapy had resulted in higher eradication rate, in comparison with the standard triple therapy [28]. In Polat 's study, *H. pylori* eradication rate was significantly higher in the group undergoing sequential therapy, compared to the group undergoing triple therapy [29].

To avoid treatment failure and the development of secondary resistance to antibiotics, it is necessary to select an appropriate treatment regimen as the first line treatment; hence, it is of great value to conduct research to evaluate the effectiveness of common therapy regimens

for the eradication of the bacteria, compare these methods and finally identify the most effective and the safest treatment regimen. Moreover, Levofloxacin is a medication that is commonly used in such therapy regimens and it has been introduced into the pharmacopoeia of Iran in recent years. Therefore, to identify an effective treatment regimen to reduce antibiotic resistance and to achieve bacteria eradication, this study aimed to compare standard triple therapy regimen with sequential therapy regimen containing levofloxacin used for the eradication of *H. pylori* in patients with gastrointestinal infection caused by *H. pylori*.

Materials and Methods

Study population

This single blind clinical trial was conducted on 96 patients with dyspepsia and positive Rapid Urease Test (RUT) who were referred to the endoscopy center of Hajar Hospital in Shahrekord city, located in southwest of Iran, from May to August 2015. This study was approved by the Ethics Committee of Shahrekord University of Medical Sciences, Shahrekord, Iran. Eligible patients were selected in the study period. Patients with drug resistance and drug intolerance or other complications and those unwilling to continue the study were excluded. To determine the sample size, we considered the quantitative changing condition of the sample size and took into account the Type I error (α) of 0.05 and Type II error (β) of 0.20 (power of 80%); accordingly, the sample size was determined as 50 patients per group.

The patients with dyspepsia and positive RUT who were referred for outpatient services and admitted to endoscopy center were randomly assigned to one of the two groups. To maximize the randomization process and assign patients to the groups, the necessary medications for each group were taken out of their packages and were placed in opaque envelopes whose content was not visible. The envelopes were titled by the letters A and B; each letter represented a particular treatment group. Patients were not aware of the type of treatment group. Each patient received a piece of paper on which type of therapy regimen was determined by the letters A (triple therapy regimen) or B (sequential therapy regimen containing levofloxacin). All the patients were trained about how to take the drugs; then, the patients were asked to visit their physician whenever they experienced any problems during treatment, especially when facing drug complications or being forced to discontinue the treatment.

After assigning the patients to the groups, the patients in Group A who were under triple therapy for 10 days, received omeprazole 20 mg twice a day, amoxicillin 1 g twice a day, and clarithromycin 500 mg twice a day. The patients in group B, who were under sequential therapy regimen, for five days received omeprazole 20 mg twice a day and amoxicillin 1 g twice a day; in the next five days, they received levofloxacin 250 mg twice a day, omeprazole 20 mg twice a day, and tinidazole 500 mg twice a day. Four weeks after the end of the therapy regimen, the patients

were visited by a doctor and using H. pylori Stool Antigen (HpSA), a test was performed to prove the eradication of H. pylori. The patients were informed about the time of HpSA test in advance and they were warned not to take proton-pump inhibitors (25-27), antibiotics, and bismuth before the test. If the patients were forced to take any medication within two weeks before the test, the patient would have been asked to notify the research team to schedule a new date for performing HpSA test.

Ethical issues

1) The research followed the tenets of the Declaration of Helsinki; 2) informed consent was obtained, and 3) the research was approved by the ethical committee of Shahrekord University of Medical Sciences (Ethical code#IR.SKUMS.REC.1394.71).

Statistical analysis

Data collection was conducted through using a questionnaire which collected demographic data including age, sex, and education level and recorded the results of HpSA test. Analysis of the data was performed using SPSS version 18. Continuous quantitative variables were analyzed using T test and qualitative variables were analyzed using chi-square test.

Results

Of all the patients, three patients in group A and one patient in group B were excluded from the study; as a result, the remaining 96 patients were randomly assigned to the two groups receiving sequential therapy regimen with levofloxacin (49 patients) and triple therapy regimen (47 patients). The mean age of the patients in the sequential therapy group and triple therapy group was 33.29 ± 1.54 years and 45.53 ± 2.17 years, respectively. There was a significant difference between the two treatment groups in terms of the mean age ($p = 0.00$). However, there was no significant difference between the two treatment groups in terms of patients' sex distribution ($p = 0.57$). Moreover, there was also a significant difference between the two treatment groups in terms of the distribution of patients in different education groups ($p = 0.00$). Table 1 presents the data on patients' age, sex, and education level.

Of the patients in the two groups, 67.3% of the patients in the sequential therapy group and 66% of the patients in the triple therapy group had negative HpSA (H. pylori Stool Antigen); there was no significant difference between the two treatment groups in terms of the eradication of H. pylori ($p = 0.99$) (Table 2). In addition, concerning the side effects of the medications, one person (2%) in the sequential therapy group (because of the nausea caused

Table 1: Demographic data of patients in the two treatment groups receiving triple therapy regimen and sequential therapy regimen to eradicate H. pylori

Treatment Group	Sex	Number	Percentage		P value
Sequential	Male	23	46.9		0.57
	Female	26	53.1		
Triple	Male	22	46.8		
	Female	25	53.2		
Sequential	40 years and younger	37	75.5	33.29 ± 10.7	0.00
	Over 40 years	12	24.5		
Triple	40 years and younger	18	38.3	45.53 ± 14.9	
	Over 40 years	29	61.7		
Sequential	Lower than high school diploma	16	32.7		0.00
	High school Diploma	18	36.7		
	Academic education	15	30.6		
Triple	Lower than high school diploma	34	72.3		
	High school Diploma	9	19.1		
	Academic education	4	8.5		

* $P < 0.05$ is considered as significant.

by amoxicillin) and one person (2.1%) in the triple therapy group (because of the cramps caused by clarithromycin) were unable to tolerate the drug. However, the rest of the participants in this study did not report any treatment-specific complaints.

The results of stool antigen test were used to assess the effects of patients' age on the efficacy of sequential therapy and triple therapy for the eradication of *H. pylori*. The results showed that when comparing the patients aged 40 years and younger between the two treatment groups, there was no significant difference between them in terms of the treatment outcome ($p = 0.32$); however, when comparing patients aged over 40 years, there was a significant difference between the two treatment groups in terms of response to treatment. Accordingly, the response to treatment was better in the triple therapy group ($p = 0.045$) (Table 3).

The effects of education levels on eradication of *H. pylori* were assessed; according to the results, the responses to the treatment in sequential therapy group were significantly different between different education groups ($p = 0.01$), but in the triple therapy group there was no significant difference between different education groups in terms of the response to treatment ($p = 0.46$) (Table 4). There was a significant difference between the two groups of patients with education levels lower than high-school diploma and academic education in terms of response to treatment ($p = 0.048$). There was also a slightly significant difference between the two groups of patients with high-school diploma and academic education in terms of response to treatment ($p = 0.063$). However, there was no significant difference between the two groups of patients with an education level lower than high school diploma and with high school diploma in terms of response to treatment ($p = 0.89$).

Table 2: Comparison of the results of stool antigen test between the two treatment groups receiving triple therapy regimen and sequential therapy regimen to eradicate *H. pylori*

Group Therapy	Stool antigen test (Stool Ag)	Number	Percent	P value
Sequential	Positive	15	30.6	0.99
	Negative	33	67.3	
	Drug intolerance	1	2	
Triple	Positive	15	31.9	
	Negative	31	66	
	Drug intolerance	1	2.1	

* $p < 0.05$ is considered as significant.

Table 3: Comparison of the effects of patients' age on the efficacy of treatment (based on the results of stool antigen test) between the two groups receiving triple therapy regimen and sequential therapy regimen to eradicate *H. pylori*

Group Classification	Group Therapy	Stool antigen test		Drug intolerance	P value
		Positive	Negative		
40 years and younger	Sequential	7	29	1	0.32
		18.9%	78.4%	2.7%	
	Triple	6	11	1	
		33.3%	61.1%	5.6%	
Over 40 years	Sequential	8	4		0.045
		66.7%	33.3%		
	Triple	9	20		
		31%	69%		

* $p < 0.05$ is considered as significant.

Table 4: Comparison of the effects of patients' education on the efficacy of treatment (based on the results of stool antigen test) between the two groups receiving triple therapy regimen and sequential therapy regimen to eradicate H. pylori

Treatment Group	Education level	Stool antigen test (stool Ag)		Drug intolerance	P value
		Positive	Negative		
Sequential	Lower than high school diploma	9	17	0	0.01
		56.3%	43.8%	0%	
	High school diploma	5	12	1	
		27.8%	66.7%	5.6%	
	Academic education	1	14	0	
		6.7%	93.3%	0%	
Triple	Lower than high school diploma	9	24	1	0.46
		26.5%	70.6%	2.9%	
	High school diploma	5	4	0	
		55.6%	44.4%	0%	
	Academic education	1	3	0	
		25%	75%	0%	

* $p < 0.05$ is considered as significant

Table 5: Comparison of the effects of patients' sex on the efficacy of treatment (based on the results of stool antigen test) between the two groups receiving triple therapy regimen and sequential therapy regimen to eradicate H. pylori

Treatment Group	Sex	Number	Percentage	P value
Sequential	Male	23	46.9	0.009
	Female	26	53.1	
Triple	Male	22	46.8	0.64
	Female	25	53.2	

The effect of sex on eradication of H. pylori was also assessed. In the triple therapy group, there was no significant difference between females and males in terms of response to treatment ($p = 0.64$); however, in the sequential therapy group, a significant difference was observed between females and males in terms of response to treatment ($p = 0.009$). Accordingly, the response to treatment was better in males than females in the sequential therapy group (Table 5).

Discussion

This study was conducted to compare standard triple therapy regimen with sequential therapy regimen containing levofloxacin used for the eradication of H. pylori in patients with gastrointestinal infection caused by H. pylori. H. pylori eradication rate was 67.3% in the sequential therapy regimen and 66% in standard triple therapy regimen. As the main goal of treatment is to eradicate the infection in

85-95% of the patients; however, because of the lower treatment success rates observed in this research, hence, these two regimens in this study is not recommended. Several studies have been conducted on standard triple therapy in Iran. In a study by Aminian and colleagues, the regimen consisted of omeprazole 20 mg twice a day, amoxicillin 1 g twice a day, and clarithromycin 500 mg twice a day which had been administered for 10 days with the eradication rate of 90.7% [30]. Moreover, Keshavarz and colleagues used the above-mentioned treatment regimen for seven days and reported an eradication rate of about 87.5% [31].

Furthermore, one of the most common causes of treatment failures could be the emergence of new antibiotic-resistant bacterial strains [32]. In this study, the emergence of H. pylori strains resistant to the antibiotics might have been a cause of treatment failure. In a similar study conducted by Polat and colleagues, of a total of 72 patients receiving

sequential regimen containing levofloxacin, 65 patients were affected by gram-negative bacteria, while of a total of 67 patients receiving standard triple therapy regimen, only 34 patients were affected by gram-negative bacteria [29], which may refer to the fact that in different geographic areas, bacterial resistance to antibiotics might be different.

Because of the common complication of furazolidone and high cost of clarithromycin, many Iranian physicians routinely prefer to use metronidazole, amoxicillin, bismuth, and omeprazole for *H. pylori* eradication [4]. In this study, the patients in triple therapy for ten days received omeprazole 20 mg twice a day, amoxicillin 1 g twice a day, and clarithromycin 500 mg twice a day; however, the patients in the sequential therapy group for five days received omeprazole 20 mg twice a day and amoxicillin 1 g twice a day; in the next five days, they received levofloxacin 250 mg twice a day, omeprazole 20 mg twice a day, and tinidazole 500 mg twice a day. In fact, *H. pylori* resistance to these antibiotics might have been a reason for reduced efficacy of the regimens in eradication of the bacterial infection in this research. Long-term clarithromycin monotherapy for the treatment of respiratory tract diseases could indeed lead to the increased resistance to this antibiotic. *H. pylori* resistance to clarithromycin might also be the most important factor explaining the failure of treatment regimens, particularly triple therapy, used for the eradication of infection [33-36]. Moreover, it is reported that the optimal efficacy of metronidazole-based triple and quadruple drug regimens in western countries is about 80-95% [5, 15]. However, due to the high rates of resistance to metronidazole in Iran [37,38], the eradication rate is usually not optimal [4, 39]. In this study, the use of the mentioned treatment regimens may have resulted in low rates of *H. pylori* eradication which is consistent with the findings of Zhou and colleagues' study (in 2014) who reported the *H. pylori* resistance to sequential and triple therapy regimens [40].

Studies which have compared sequential and triple therapy regimens have reported different results, as some of them reported the superiority of sequential treatment regimen while other others have reported the superiority of triple therapy regimen [32, 41-44]. In a study conducted by Khaleghi and colleagues, the patients with chronic dyspepsia were classified into two groups each consisting of 80 people [45]. One of the groups received omeprazole and amoxicillin for the first five days and then omeprazole, furazolidone, and clarithromycin for the next nine days; the other group received quadruple regimen for 14 days consisting of omeprazole, amoxicillin, clarithromycin, and bismuth. Of all, 50.9% of the patients in the sequential therapy group and 49.1% of the patients in the second group were cured, and the difference was not statistically significant [45]. In another study, Kaboli and colleagues investigated 140 patients with dyspepsia and classified them into two groups; the first group received omeprazole, amoxicillin, and clarithromycin for 14 days and the second group (sequential group) first received omeprazole and amoxicillin for five days, and then omeprazole, clarithromycin, Tinidazole for the next five days; there was

no significant difference between the two groups in terms of *H. Pylori* eradication [46]. Zullo and colleagues studied 36 patients who received rabeprazole 20 mg twice a day, levofloxacin 250 mg twice a day, and amoxicillin 1 g twice a day. According to the results, *H. pylori* was successfully treated in 30 patients [47]. In fact, comparing with the sequential regimen used in this study and the obtained results, it can be concluded that the *H. pylori* strains resistant to levofloxacin might have been caused by the indiscriminate use of antibiotics in this region.

In the present study, considering people in the age group over 40 years, the eradication rate in the triple therapy group (69%) was higher than the eradication rate in the sequential therapy group (33.3%) ($p = 0.045$). To justify these results, it can be concluded that the use of sequential therapy regime, especially for older people, is more difficult than that of triple therapy regimen. The more complex schedule for taking sequential therapy regimen, especially in people over 40 years of age, may increase the risk of treatment failure in this study. Nevertheless, Hashemi and colleagues (in 2007) reported that patients' age had no significant relationship with the eradication of *H. pylori* [4]. Higher education level is reported as a factor influencing the eradication of *H. pylori* infection. In this study, the highest level of eradication was observed in people with an academic degree. These findings are in line with other studies in this field that have proven *H. pylori* infection is lower among people with higher education levels [48-50]. People with lower education level are indeed at a higher risk of infection than those with higher education levels; such a negative relationship is also observed between parents' education and infection [51,52].

The results of this study showed that men had a better response to treatments than women. It is inconsistent with the results of studies by Misattari and Hashemi which reported no statistically significant difference between men and women in terms of the response to treatments; however, in this study in patients in the triple therapy group, there was no significant difference between the two sexes in terms of response to treatments [4, 32, 53].

Given the low rate of *H. Pylori* eradication by the sequential and triple therapy regimens observed in this study, further research must be conducted to study the resistance of the bacteria to the studied treatment lines and antibiotics in Iran. Considering the results of this study, it is also recommended to utilize other treatment regimens to achieve higher rates of eradication. It is also suggested to use more effective and simple treatment regimens for older people and those with lower education levels.

Conclusion

The use of sequential therapy regimen containing levofloxacin for the eradication of *H. pylori* results in outcomes which are less than the optimal levels. However, further studies in this field are needed to be carried out with larger sample size in different places.

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Risk Factors of Resistance to Intravenous Immunoglobulin in patients with Kawasaki: A Cross-Sectional Study Over a 10 Year Period (2006-2016)

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Abstract

Introduction: Kawasaki is an acute vasculitis and is the most common cause of acquired heart disease in children. About 25% of patients remain infected and febrile despite receiving intravenous immunoglobulin and aspirin. The aim of this study was to investigate the clinical and laboratory predictive resistance factors for intravenous immunoglobulin in patients with Kawasaki hospitalized in Khorramabad Shahid Madani Hospital.

Materials and Methods: Patients were divided into two groups: a) responders to IVIG treatment, consisting of 47 patients (90/4 %); and b) resistant to treatment, consisting of 5 patients (9.6%), and the difference between clinical manifestations and laboratory findings of the two groups were examined and the results were statistically analyzed.

Results: 52 patients with Kawasaki diagnosis were gauged. In the treatment-resistant group (9.6%), the number of clinical symptoms was lower than that of KAU diagnosis criteria, but this difference was not statistically significant between the two groups. Laboratory tests evaluation showed that the mean of ESR and CRP were higher in the treatment-resistant group and the mean of serum sodium in this group was lower than that of the responder group.

Discussion and Conclusion: High ESR and CRP and lower serum sodium levels can be considered as predictors of resistance to intravenous immunoglobulin therapy in patients with Kawasaki.

Key words: Kawasaki disease, immunoglobulin resistance, acute vasculitis

Introduction

Kawasaki disease is a self-limiting acute vasculitis with unknown etiology and is more predominant in children younger than 4 years, which was first described in 1967 by Tomisacu Kawasaki (1).

Diagnosis of the disease is based on the presence of at least 5 findings out of the six following clinical findings: 1. Stable fever 2. Cutaneous rash 3. Organ changes including erythema, edema and flatulence, 4. Bilateral non-viral conjunctivitis 5. Oral mucosa and lips changes including redness and lips fissure 6. Lymphadenopathy (2). Although some sources characterize this disease by continuous fever for at least 5 days and 4 signs out of 5 other symptoms (3). Occasionally, patients do not have all the diagnostic criteria or they appear later which is known as Kawasaki latent or incomplete Kawasaki. These patients are about 15 to 36.2 percent of the infected and are beyond the defined age range (less than one year and more than 5 years) (5, 4). Kawasaki disease is the main cause of childhood acquired cardiac disease in developed countries (6).

Coronary artery aneurysm is the most important problem of the disease that occurs in 15-25% of untreated patients and can lead to myocardial infarction, sudden death, or ischemic heart disease in children (7,8). The risk in case of early onset of treatment by Intravenous immunoglobulin and aspirin will be reduced to 5% (9). Although this treatment reduces the fever and risk of cardiac problems, about 10-20% of the patients remain febrile even after receiving the suitable treatment (11) and these patients are most at risk for coronary arteries problems (11). Late cardiac manifestations are reported with Kawasaki cases, with symptoms other than fever not yet improving for more than a month from the onset of the disease (12).

Recent studies have described some of the demographic characteristics links and laboratory findings with a variety of resistant Kawasaki treatments. These factors include age, sex, duration of disease before treatment, abnormal Primary echocardiography, ESR, CRP, sodium, lactate dehydrogenase, hemoglobin, eosinophil, neutrophil, lymphocyte, liver transaminases and serum albumin (13, 14). Kobayashi et al. calculated 13 variables in patients with Kawasaki, including the duration of the disease before treatment, gender, age, the percentage of neutrophils, platelet count, transaminase (ALT, AST), total bilirubin, sodium, chlorine, total protein, albumin, and CRP. This retrospective study was performed on 546 patients to confirm the predictive accuracy of resistant cases in a prospective study conducted on 204 cases. Primary treatment of IVIG (2 g / kg) was prescribed aspirin and dipyridamole for two consecutive days, and patients who remained febrile after 24 hours were considered as resistant to treatment. In this study, IVIG resistance was considered interrelated to serum sodium less than 133 mmol / L, the duration of the disease before treatment less than 4 days, AST > 133, neutrophil < 80%, CRP < 10mg / dl, age less than 12 months and platelets less than 300,000

(15). In Japan, Kobayashi grading is used to predict drug-resistant cases and initiate oral prednisone with IVIG from the very beginning of the diagnosis (3). Although the study of Davis et al. stated that Kobayashi grading has not been promising in the prediction of resistant cases (16). The aim of this study was identifying the demographic, clinical and laboratory factors of Kawasaki resistant to treatment and to use alternative remedies or additional therapies to reduce the cost of treatment and lethal and enervating problems of the disease.

Materials and Methods

This cross-sectional study included all the patients admitted to Shahid Madani Hospital of Khorramabad (West of Iran) with the diagnosis of Kawasaki over a ten year period from 2006 to 2016. The sampling method was census-based and at that time all patients were hospitalized with full Kawasaki (fever and 4 signs out of 5 disease symptoms), as well as atypical or incomplete cases of fever less than 5 days or with fewer symptoms were examined. Patients who did not register their demographic information, clinical findings during hospitalizing, the desired tests, or the course of the disease in their records were excluded. The patients were then divided into two groups, (A) responding to the first dose of intravenous immunoglobulin and aspirin, and (b) not responding to the first dose of intravenous immunoglobulin and aspirin, and demographic characteristics, clinical signs, laboratory findings such as complete blood cell count, liver transaminases (ALT, AST), serum sodium level, ESR and CRP and problems related to each of them were recorded and compared in two groups. The criterion for treatment response was fever breakdown at 48 hours after treatment. Data were examined using t-test and chi-square tests. To determine the severity of the relationship, the odds ratio (OR) was calculated with a confidence interval of 90%.

Findings

In total, 52 patients with final Kawasaki diagnosis were observed. 26 (50%) patients had the fever for more than 5 days and 17 patients (32.7%) with fever had 4 out of 5 signs of Kawasaki, and the other 35 patients (3 / 67%) were considered as incomplete or atypical Kawasaki. Out of 52 children with Kawasaki, 47 (90.4%) responded to the first dose of intravenous immunoglobulin (group A) and 5 children (9.6%) did not respond to initial treatment (group B).

35 (67.3%) patients were male and 17 (32.7%) were female. 30 male patients (85.7%) and all female patients responded to the first dose of intravenous immunoglobulin, but the frequency of gender distribution in the two groups was not statistically significant ($P = 0.1$).

Most children responded to the first dose of intravenous immunoglobulin and all single-dose resistant children were in the age of 12-60 months. The age distribution of the two groups was not statistically significant ($P = 0.29$) (Table 1)

Table 1: Frequency Distribution of age in two groups

Studied groups	Age				P-Value
	Under 12 months	60-12 months	over 60 months	Total	
	N (%)	N (%)	N (%)	N (%)	
Receiving 1 dose of IVIG	7 (14.9)	31 (66)	9 (19.1)	47 (100)	0.29
Receiving more than 1 dose of IVIG	0 (0)	5 (100)	0 (0)	5 (100)	

The mean weight of children receiving the intravenous immunoglobulin dose was between 15.5 ± 5.2 Kg and the mean weight of children resistant to treatment was 14.2 ± 1.48 kg and based on t-test the difference was not statistically significant ($P = 0/59$)

Differences in the distribution of oral lesions, conjunctivitis, neck lymphadenopathy, edema and cutaneous rash were not statistically significant. (Table 2)

Table 2: Frequency distribution of clinical symptoms on admission in two studied groups

Clinical symptoms	Group A	Group B	P-Value
	Responding to treatment	No response to treatment	
	N (%)	N (%)	
Skin rash	27 (57.4)	4 (80)	0.32
Terminal lesions	19 (40.9)	33 (60)	0.4
Neck lymphadenopathy	21 (44)	2 (40)	0.84
Mucosal lesions	37 (78.7)	4 (80)	0.94
Conjunctivitis	33 (70.2)	4 (80)	0.66

33.3% of the respondents to the initial treatment with IV immunoglobulin had fever along with 4 other disease signs, while most of the resistant children to the treatment had 3 symptoms, but according to Fisher's exact test, the difference in the number of symptoms associated with fever on admission between the two groups was not statistically significant ($P = 0.04$) (Table 3)

Table 3: Frequency distribution of the number of symptoms associated with fever on admission in studied groups

Studied groups	The number of symptoms associated with the fever on admission					P-Value
	1 sign	2 signs	3 signs	4 signs	Total	
	N (%)	N (%)	N (%)	N (%)	N (%)	
Receiving 1 dose of IVIG	2 (4.4)	14 (31.1)	14 (31.1)	15 (33.3)	45 (100)	0.4
Receiving more than 1 dose of IVIG	0 (0)	0 (0)	3 (60)	2 (40)	5 (100)	

Indicator type	Hb (g/dl) $\mu \pm SD$	Hct (%) $\mu \pm SD$	ESR (mm/hr) $\mu \pm SD$	CRP (g/dl) $\mu \pm SD$	ALT (IU/L) $\mu \pm SD$	AST (IU/L) $\mu \pm SD$	WBC ($\times 10^3/\mu$) $\mu \pm SD$	Pit ($\times 10^3/\mu$) $\mu \pm SD$	Na (meq/l) $\mu \pm SD$	PMN (%) $\mu \pm SD$	Lymph (%) $\mu \pm SD$
Responding to 1 dose of IVIG	10.6 \pm 1.39	31.4 \pm 3.6	82.5 \pm 31.2	1.26 \pm 0.99	48.2 \pm 65.97	45.3 \pm 53.1	487149 \pm 16167	487149 \pm 185344	13.9 \pm 5.2	59.1 \pm 15.1	40.1 \pm 15.2
Resistance to 1 dose of IVIG	10.3 \pm 0.72	31.2 \pm 1.8	10.3 \pm 10.3	2.25 \pm 0.5	31.8 \pm 18.3	30.4 \pm 6.7	30860 \pm 36910	483600 \pm 126074	129.2 \pm 3.5	62.4 \pm 13.8	37 \pm 14.4
T statistics	0.45	0.12	-3.18	-3.44	0.55	0.62	-0.95	0.042	3.26	0.46	0.43
P Value	0.65	0.89	0.002	0.017	0.2	0.079	0.39	0.95	0.017	0.63	0.66

Table 4: The Comparison of mean and standard deviation of laboratory indices in the two groups

In comparing the laboratory indices between the two groups, the results showed that there was no significant difference between the mean values of hemoglobin and hematocrit percentage, liver enzymes, the number of leukocytes, the percentage of polymorphonuclears and lymphocytes and the number of platelets in the two groups.

Nevertheless, the mean values of ESR (P = 0.002) and CRP (P = 0.011) in the group resistant to the first dose of intravenous immunoglobulin was higher than that of the responder group, and this difference was statistically significant based on t-test. Also, the difference in serum sodium levels was statistically significant on the basis of t-test between the two groups (p = 0.017) (Table 4 - left).

In four responder patients (8.9%) to the first dose of intravenous immunoglobulin a heart disease was recorded; this rate was 60% in children who were resistant to treatment and this difference was statistically significant based on t-test (P = 0/002) (Table 5).

Table 5: Frequency Distribution of cardiac complication possibility in the studied groups

Studied group	Cardiac Complication			P-Value
	Has	Has not	Total	
	N (%)	N (%)	N (%)	
Receiving 1 dose IVIG	4 (8.9)	41 (91.1)	45 (100)	0.002
Receiving more than 1 dose IVIG	3 (60)	2 (40)	5 (100)	

* Type of test: T test

Discussion and Conclusion

Kawasaki disease is an engaging vasculitis in multiple organs, of unknown etiology and the main cause of acquired heart disease in developed countries (9).

Diagnosis is based on fever for more than 5 days and at least 4 out of the five main symptoms of the disease such as cutaneous rash, non-puerperal bilateral conjunctivitis, neck lymphadenopathy, oral mucosal lesions, and edema or scaling of the organs (8). Some patients may not have the necessary diagnostic criteria from the beginning, which are recognized as atypical or, preferably, incomplete Kawasaki, since many patients' symptoms will appear in the course of the disease or echocardiographic findings confirm the disease (3). Incomplete types are more common in children of lesser age, and their timely identification and treatment to prevent cardiac problems are essential. Distinct differential diagnoses include streptococcal infections, measles, rheumatoid arthritis, and drug reactions (16). Prescribing of an intravenous immunoglobulin dose (2 g / kg) plus oral aspirin leads to improved symptoms and signs of disease and reduces the risk of cardiac problems from 20% to about 5% (17). Unfortunately, about 10-20% of patients do not respond to classical treatment and need recurrence doses or other treatments (18).

These patients are classified as resistant to intravenous immunoglobulins. These patients are at greater risk for heart problems (19). Identifying predictive factors for treatment-resistant types, considering other treatments or the probability of problems occurrence will allow them to be treated in a timely manner. Therefore, this study was conducted to identify these factors.

In this study, demographic factors including age, sex, weight, and laboratory and clinical symptoms were compared in the two groups of responders to the first dose of intravenous immunoglobulin (A) and non-responders to the first dose of intravenous immunoglobulin (B).

A total of 52 patients were diagnosed with Kawasaki's final diagnosis. 47 (90.4%) patients responded to intravenous immunoglobulin (group A), and 5 patients (9.6%) remained febrile 48 hours after receiving treatment and were classified as resistant (group B). There was no significant difference in age, sex, and weight between the two groups A and B.

In a study conducted by Sungho et al., 51 patients were evaluated, 33 of whom responded to treatment with IVIG (64.7%) and 13 patients (35.3%) classified in the treatment-resistant group. The percentage of people resistant to treatment in this study was higher than our study. In the study of Sungho et al., there was no significant difference between the two groups in terms of gender and age (10). In another study conducted by Young and colleagues on 82 Kawasaki patients, 16 (19.5%) patients were resistant to treatment, and here as well there was no difference in terms of sex, age and weight between the responders and those who were resistant to treatment (9).

In our study, due to the low number of patients, especially the cases resistant to treatment comparing to Sungho et al. and Tremoulet et al. were lack of high sensitivity concerning other studies (10, 11).

In our study, there was no significant difference in the amount of hemoglobin, hematocrit, liver transaminases, and the number of leukocytes and neutrophils and lymphocytes in the liver.

In the study of Sundel et al. and Wallace et al., there was no difference in the demographic characteristics and clinical manifestations in the two groups while hospitalized (20, 23). In the Sungho study, laboratory tests were administered on two groups and compared to the time of admission and after IVIG. Hemoglobin, hematocrit, albumin, ESR, and the number of blood leukocytes were not significantly different between the two groups, while the percentage of polymorphonuclears (PMNs) and bilirubin and AST in the resistant group were significantly higher, and albumin and platelet count in the resistant group were significantly low. After prescription of IVIG, hemoglobin and hematocrit values, total protein and albumin were lower in the resistant group, and the number of leukocytes, the percentage of PMNs, ESR and total and direct bilirubin in the resistant group were higher and there was not a significant difference in the levels of transaminases and CRP (10).

In our study, the mean values of hemoglobin, hematocrit, liver transaminases, the number of leukocytes and platelets, and the percentage of poly-Moreno cells and blood lymphocytes were not significantly different in the two groups.

Though, the mean values of ESR ($P = 0.002$) and CRP ($P = 0.017$) were significantly higher in the treatment-resistant group. Correspondingly, mean serum sodium was lower in the treatment-resistant group ($P = 0.017$). Serum albumin and bilirubin value were not included in our study due to the lack of record values in the files. Also in our study, laboratory tests were considered when the patients were hospitalized since none of the patients had not undergone laboratory tests again after receiving IVIG. In the study of Uehara et al., the relationship between high hepatic transaminases and the incidence of cardiac problems in patients with Kawasaki has been described (22). In the study of Sungho et al., the high levels of transaminases were associated with resistant varieties and Kawasaki referral, but in our study, there was no relationship between the level of liver transaminases and treatment resistance.

Tetsuya et al. have reported high levels of bilirubin, transaminases of the liver, and CRP as independent predictors of resistance to IVIG (25). In our study, there was a correlation between high CRP level and treatment resistance. Bilirubin values were not recorded in the files and liver transaminases were not included in predictor factors. In our study, the percentage of cardiac problems in the treatment-resistant group was significantly higher than the response group ($p = 0.002$) (Table 5).

In a study conducted by Uehara et al., the incidence of cardiac problems was significantly higher in the IVIG-resistant group. In this study, male gender, the onset of treatment before the fifth day of the disease and recurrence of the disease were also known as factors related to resistance to IVIG (26). Although in the study of Taraguchi et al., there was no significant difference in the incidence of cardiac problems in patients who were resistant to primary treatment with IVIG and prednisolone treatment (24). In sum, in a large number of studies, some of the demographic and laboratory factors such as low age, the onset of treatment before the fifth day of the disease (which may indicate the severity of the disease), low platelet levels, sodium and albumin levels, raised liver transaminases, and Neutrophils were also associated with resistance to treatment and the incidence of cardiac problems (25). Further studies are needed to define the diagnostic criteria for incomplete Kawasaki type to initiate timely treatment (25). Currently, the recommended dose for Kawasaki disease is high doses of intravenous immunoglobulin and aspirin, but in the case of primary resistance cases, a second dose of intravenous immunoglobulin is also prescribed. Considering the predictive factors for treatment resistance, the second dose of intravenous immunoglobulin may be avoided due to its high cost and other adjunctive treatments.

Sonoda et al. have considered plasma replacement with infliximab prescription as effective factors in reducing the symptoms of patients who have been resistant to the second dose of intravenous administration of IVIG (28). In our study, high levels of ESR and CRP and low sodium levels were recognized as predictive factors for treatment resistance. Among the limitations of this study, we can point out the inadequacies of the records, which led to the elimination of a number of patients from the study and consequently the small size of samples. These deficiencies included the incompleteness of the cases' summary, the miscarriage to record the results of experiments, the absence of infection course, and the lack of patients' following up in terms of echocardiographic findings.

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Evaluation of hematological indices of workers exposed to benzene

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Abstract

Purpose: Benzene is a clear, colorless, flammable liquid that can be steamed and flowing. Benzene is a by-product of incomplete combustion of many materials. Due to its high utilization in the industry, it is one of the 20 major chemical products in the world. Benzene-induced industrial poisoning occurs almost entirely by inhalation of benzene vapors in the air. The goal of this study is to answer the questions about whether exposure to benzene is associated with changes in the level of human blood parameters under normal conditions.

Materials and Methods: This is a comparative and analytical cross-sectional study. In this study we examined 40 workers exposed to benzene compared with 40 healthy subjects with no history of being exposed to benzene as a control group with the same sex and age (26-40), with a work record of 5 to 15 years and an exposure of 8 hours. It was measured using standard methods for concentration of benzene in air. Blood samples were taken from humans for evaluation of hematological factors. An impedance method by cell counter device was used for measurement.

Results: The average concentration of benzene in workshops was 1.68 ppm. The results of blood tests showed that the mean concentration of red blood cells (MCHC) in the control group was higher and Erythrocyte sedimentation rate (ESR) in exposed benzene workers was higher than control group. However, in other parameters there was no meaningful difference between the two groups.

Conclusion: The average exposure of workers at different workshops with benzene vapors is not greater than the exposure limit values of these compounds. In the results of this study, other factors such as alcohol consumption, smoking, non-vegetarian diet and exposure to benzene are effective.

Key words: Benzene, Hematologic factors, Cell counter device, Impedance method

Introduction

Coke is a coal derivative and coal is a mixture of carbon, hydrogen, and sulfur-containing oxygen. Coke plays an important role in oxidative reactions. Workers in coking are exposed to pneumoconiosis in the presence of coke, which is a disease of the parenchyma tissue of the lung. It is caused by inhalation of coke and coal dust. Coke has a harmful effect on the liver, including cirrhosis of the liver. Liver diseases are generally classified into both acute and chronic types, in which liver cirrhosis is included as a chronic disease (1).

Benzene is produced during the process of coal-to-coke conversion; benzene is a coke derivative and is caused by the coke's heat and coke gas purification. Michael Faraday discovered benzene in 1825. Benzene was previously obtained by heating coal tar and then converting vapor into liquid, but today benzene is extracted from high amounts of crude oil (2).

A very low amount of benzene is found in oil and coal. This is a by-product of incomplete combustion of many materials. For commercial use, benzene was obtained as a coke or lightweight coke furnace product for the steel industry until the Second World War (3).

Benzene is a clear, colorless, flammable liquid, with a gas like smell that can be steamed and flowing. Benzene is an organic compound found in the air most of all due to the burning of coal and oil, gasoline vapors, vehicle smoke, smoke, fire from wood and other sources. The major cause of environmental pollution is by industry benzene. Urban weather is becoming more polluted with benzene due to transportation systems. Benzene is a pollutant that is everywhere, like the workplace and the environment. It categorizes risks for humans and animals due to its carcinogenic effects in the first group of carcinogenic substances (4).

The two main sources of exposure to benzene include the following:

1. Synthesis and construction activities.
2. Its use in the production of other chemical materials.

Other businesses may also be exposed to benzene, such as jobs that use petroleum products or solvents. The routes of contact with benzene in the workplace are usually breathable and absorption through the skin, and the assessment of the exposure is relatively easy. Human contact with benzene does not occur solely through breathing and absorption of the skin. Swallowing food or drinking water can be another way. High levels of accumulation of benzene in groundwater can be dangerous to human health and change the diversity and structure of ecosystems (4). Benzene is one of 20 major chemical products in the world due to its high utilization in industry. In many industries, benzene is used for the production of styrene, plastics and nylon and rubber, synthetic fibers, various resins, paints, reagents, drugs, insecticides, glues, solvents, explosives, inks, glosses and lubricants. The use

of benzene in vehicles is to increase fuel consumption and octane number. Environmental Protection Agency (EPA) has classified benzene as a carcinogenic category A, and the International Agency for Research on Cancer (IARC) has identified benzene as a carcinogen for humans (5).

Absorption and excretion of benzene and disease

Industrial benzene-induced poisoning occurs almost entirely by inhalation of benzene vapors in the air. Blood flow in the human body is quickly saturated with this substance and after half an hour, the saturation of the blood will be 70% to 80%; it will take several days for all body fluids and tissues to saturate with benzene. Benzene is almost insoluble in the blood, and its balance is in mg benzene per liter of blood, divided by mg of benzene per liter of air. This means that the average concentration of benzene in the blood in balance is about 1.2 mg per 100 ppm of benzene in the inhaled air. Benzene in the circulating blood enters the tissue and fat tissue stores some of it. Excretion of this substance is also done vice versa, this means it is transmitted to the lungs by blood and through the capillaries, and placed in the balance with air inside the lung cavities and thus repelled. Some benzene is excreted intact in the urine and a portion of it is oxidized in the form of phenols and diphenols, which, in turn, are combined in liver with sulfate ions and excreted in the urine (6).

Benzene enters the liver, where it converts to toxic metabolites like benzene oxide, phenol, hydroquinone (HQ), muconic acid. The tendency of benzene toxin to the hematopoietic tissue is probably related to the capacity of these liver metabolites in their own community in bone marrow. Some evidence suggests that benzene may be cause of the following:

1. Acute and chronic lymphocytic leukemia
2. Non-Hodgkin's Lymphoma
3. Multiple myeloma
4. Anemia due to hematopoietic organs dysfunction (4).

The effects of benzene on body organs: Leukemia, particularly acute bone marrow leukemia and benzene exposure, are closely related. Additionally, exposure to benzene can have devastating effects on the body's immune system, nerves, and reproduction. Benzene can directly damage bloodstream cells, which in turn leads to the death of some cells or may reduce the response to cytokines and cellular adhesion molecules. Poisoning of bone marrow cells or mature blood cells by benzene can disrupt the process of hematopoiesis (4).

Benzene increases the risk of cancer and other diseases. Benzene causes aplastic anemia, acute leukemia and bone marrow disorders (7).

In cases where contact with benzene is relatively high but its duration is short, there is a significant reduction in white blood cell count. If the contact is relatively less intense,

but its duration is somewhat long, various changes will occur in blood. If benzene adsorption continues, an infectious poisoning occurs in the blood-forming generator and leads to death. In acute osmomethania, benzene has a sleeping and opiate effect. Excessive inhalation of benzene vapors may initially cause a rise in joy, resulting in confusion, drowsiness, fatigue, nausea, and headache. If the concentration is higher or the duration of contact is longer, seizure and then loss of sensation will eventually occur, and death may eventually occur by paralysis of the respiratory system. In chronic benzene poisoning, bone marrow testing may sometimes be normal, and in some cases be aplastic or hyperplastic. Symptoms and side effects include headaches, dizziness, fatigue, loss of appetite, feeling unwell, anger, nose bleeding, and other forms of bleeding (6).

Benzene has been used as a common solvent in laboratories in the past, but when scientists have found their carcinogenic identity, its use as a solvent has been very limited and have tried to use similar solvents such as acetone and others. Side effects of chronic exposure to benzene include the reduction of hematopoiesis, the inability of the immune system, as well as leukemia, disorders of the respiratory system, delay on embryonic skeletal system, damage to the reproductive system of humans, infertility, production of lymph node tumors and liver damage. Several institutes, including the World Cancer Research Association, the American Society for the Protection of the Environment, the US Department of Health, have identified benzene as a cause of leukemia and carcinogenicity level A. The secret period of leukemia usually occurs 5 to 15 years after the first contact with benzene. The acute effects of benzene include drowsiness, dizziness, headache, anesthesia and tremors, nausea, seizure, insomnia, stomach stimulation, and increased heart rate and coma (5).

However, in most cases deadly benzene poisoning occurs if the concentration of this substance is 200 parts or more in million. However, many cases have been reported that exposure to benzene is much lower and even reported deaths with an average concentration of 100 to 105 parts per million. In addition, some reports, suggests that concentrations below 100 ppm are also dangerous. As noted, the maximum allowable benzene concentration is 10ppm, and this is the extent to which the average and normal person has the necessary safety against the dangers of this substance. Blood tests are far more valuable than other tests for determining the amount of urinary sulfate. It is therefore logical that continuous hematologic tests and cellular counting should be carried out at all intervals of every thirty days for all workers who deal with benzene vapors, as well as a test for sulfate amount per week. In addition, determination of the amount of benzene from the air of the workshop environment is also required at different intervals (6).

Materials and Methods

This study is a comparative and cross-sectional analytical study, in which 40 benzene exposed workers are compared to 40 healthy subjects with no exposure to benzene as the control group with the same sex and age (26-40). The number of people working in benzene refining and biochemical energy was about 200 people who were randomly assigned to one day of the week and a special shift based on the willingness and satisfaction of the person. The number of people was 80, 40 people selected based on entry criteria: lack of exposure to metals such as plumbum and zinc, lack of alcohol consumption, supplemental antioxidants and psychotropic drugs, lack of chronic disease and mental illness, lack of radiation therapy background, surgery and anesthesia over the past year, work experience, and ability to answer questions. 40 people who did not have entry criteria were excluded from the study. It should be noted that all 80 people filled out clinical symptoms and inclusion criteria questionnaires, and an expert interviewed all of them. Then, 40 cases were examined for blood samples at 8:30 am in the morning and immediately transferred to the hospital. Then, according to age, sex, entry criteria, and place of residence, 40 healthy people from the sales office (office jobs) 50 kilometers away from the factory, were matched to the group. The blood samples of these individuals after clinical interviews and entry criteria were taken at 8:30 am and immediately transferred to the hospital laboratory and factors of hematologic evaluation was performed in both groups. Impedance method was used to measure blood factors using cell counter.

CBC measurement with Cell Counter method

The KX-21 delivers decomposing eighteen blood parameter quickly and accurately, and reveals abnormal samples. In order to facilitate the sampling of abnormal samples in the laboratory, the device displays the information associated with abnormal analysis with unusual symptoms on the monitor screen. Therefore, abnormal specimens are exposed to further analysis and review. The KX-21 is used for separation of blood by three separators and two types of reagents. The number of white blood cells (WBCs) is calculated by using the DC discovery method in WBC explorer container. The RBC and platelets are stopped in the RBC explorer container, and they are measured using the DC discovery method. In hemoglobin (HGB) explorer container (HGB), using the non-cyanid e method carried out hemoglobin analyzer and measured hemoglobin concentration (8).

Detection method via DC (Direct Current)

We take the blood sample to a predetermined amount, dilute it to a certain degree, and then enter into the energy converter. The energy converter enclosure has a small hole that is called an aperture. On both sides of the aperture, there are electrodes through which passes direct flow. The blood cells stored in the diluted sample pass through the aperture and cause the direct current resistance (i.e., the opposite current) change between the electrodes. With this change and by the pulse of electricity (showing itself)

the size of the blood cell is discovered. The number of blood cells is calculated by counting the pulses, and by specifying the size of the pulse, a blood cell size chart is plotted. In addition, the analysis of the graph can be used to obtain various analytical data (8).

Analysis Parameters

This device analyzes and decomposes the following parameters using three explorer containers and two types of reactants.

1. Total WBC (White Blood Cell) (Analysis Law: Using the Discovery Method via DC)

Unit: The ratio of the number of WBCs in 1 μL to the whole blood, the WBC unit 10 to power 3 on millimeters square ($10^3 / \text{Cumm}$).

2. Lymphocyte percentage (white blood cells and small cell volume)

Unit: ratio (because it is uncountable with percentage). The ratio (percentage) of lymphocytes (small cells) to the total WBC.

3. MXD% (WBC and middle cell volume)

Unit: Ratio (percentage total sum of basophils, isinophils and monocytes (middle cells) to total WBC)

4. Neutrophil percentage (WBC and large cell volume)

Unit: ratio (%) of neutrophils (large cells) to the whole WBC

5. Lymphocyte count (WBC and small cell count)

Unit: The ratio of the absolute number of lymphocytes (small cells) in 1 μL of the total blood (8).

6. MXD% (WBC and middle cell count)

Unit: ratio of absolute number of basophils, isinophils and monocytes (middle cells) in 1 μL of total blood

7. Number of neutrophils (WBC and large cell count)

Unit: The ratio of absolute number of neutrophils (large cells) in 1 μL of the total blood

8. RBC (red blood cell) (Analysis Law: Using Discovery Method via DC)

Unit: The ratio of RBC to 1 μL of the total blood. The RBC unit is million / Cumm.

9. ESR is the erythrocyte sedimentation rate. Sedimentation rate is total amount of RBC in a saline or plasma solution at a given time, which is nonspecific. The ESR unit is millimeter per hour (mm / hr).

10. RDW The distribution of the red blood cells represents the amplitude of the dispersion of the total volume of the RBC.

Unit of measurement: percentage (%).

11. MCV is the average volume of red blood cells.

Unit is femtolite (fl).

12. HGB (Hemoglobin) (Analysis Law: Using “non-cyanide analysis of hemoglobin”)

The proportion of hemoglobin in 1 dL of the total blood.

Unit of measurement: gram-per-decilitre (gr / dl).

13. HCT (hematocrit values) (Analysis Law: Using the Red blood cell pulse rate detection method)

Ratio (percentage) of total RBC volume in the whole blood

14. Average red blood cell volume

The average volume of RBC (fL) in total blood, measured by hematocrit / RBC

15. Average hemoglobin red blood cell

The average volume of hemoglobin (pg) in RBC, which is measured by hemoglobin / RBC

Unit of measurement: picogram (pg) (8).

16. Average hemoglobin concentration of red blood cells

The average hemoglobin concentration in RBC, which is measured by hemoglobin / hematocrit.

Unit of measurement: gram-per-decilitre (gr / dl).

17. Platelet (Analysis Law: Using “Discovery Method via DC”)

The number of platelets in 1 μL of the total blood

Platelet distribution width

The distribution width (fL) with a height of 20% of the floor, when the peak in the distribution of platelet particles is assumed to be 100%.

18. The average platelet volume of the MPV in a platelet similar to MCV is for RBCs (8).

Unit of measurement: The femtoliter (fl)

Results

Data from the studied subjects were analyzed by KS test for normalization. Then, normal data were analyzed by t-test and non-normal by Mann Whitney U test. p value less than 0.05 was significant. In our study 80 subjects participated (40 experimental and 40 control).

Table 1: Frequency tables

Groups	Frequency	Frequency percentage
Test (benzene)	40	40 %
Control	40	40 %

Table 2: Age of test and control group

Variable (age)	N	The least	The most	Average	The standard deviation
Test (benzene)	40	26	40	31/55	4/662
Control	40	26	40	32/4	4/447

Table 3: Default Testing Normality of Data Distribution

	K-S test	
	Z	P-value
WBC(10^3 /Cumm)	1/293	0/071
RBC(Mil/Cumm)	0/852	0/462
HB(gr/dl)	0/636	0/813
HEM(%)	5/221	0/001
MCV(fl)	1/077	0/196
MCH(pgr)	1/25	0/088
MCHC(gr/dl)	1/142	0/148
RDW(%)	1/571	0/014
MPV(fl)	1/226	0/099
ESR(mm/hr)	0/706	0/009

Default Testing Normality of Data Distribution using the K-S test shows that most variables have a normal distribution (the significant level of most variables is higher than 5%).

Table 4: Red blood cell count (RBC Mil / Cumm) of exposed workers to benzene with control group

Indicator	Standard deviation \pm Mean	Standard mean error	Significant level (P-value)
Test (benzene)	5/298 \pm 0/426	0/0603	0/903
Control	5/338 \pm 0/465	0/065	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of data analysis, there was no significant difference between the levels of red blood cells (RBC) of workers exposed to benzene with the control group ($P > 0/05$).

Table 5: The white blood cell (WBC 10^3 / Cumm) of workers exposed to benzene with control group

Indicator	Standard deviation \pm Mean	Standard mean error	Significant level (P-value)
Test (benzene)	6/576 \pm 1/437	0/203	0/914
Control	6/648 \pm 1/402	0/198	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of data analysis, there was no significant difference between the levels of white blood cells (WBC) of workers exposed to benzene with the control group ($P > 0/05$).

Table 6: The average volume of red blood cells (MCV fl) of workers exposed to benzene and a control group

Indicator	Standard deviation ± Mean	Standard mean error	Significant level (P-value)
Test (benzene)	88/858±4/997	0/706	0/431
Control	87/728±5/718	0/808	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of data analysis, there was no significant difference between the average volumes of red blood cells (MCV) of workers exposed to benzene with the control group ($P > 0/05$).

Table 7: Distribution of red blood cells (RDW %) of workers exposed to benzene and control group.

	RDW		RDW
Mann-Whitney	1094/5	Test (benzene)	12/636±0/806
Wilcoxon	2369/5	Control	12/922±1/196
Z	-1/073		
Significant level of p-value	0/283		

Due to the unusual nature of the data in the RDW distribution, Mann-Whitney test was used to compare the study parameters. Based on the results of the data analysis between the red blood cell distribution (RDW) there was no significant difference between subjects exposed to benzene and control group ($P > 0.05$).

Table 8: Average hemoglobin in each cell (MCH pgr) of exposed workers to benzene with control group

Indicator	Standard deviation ± Mean	Standard mean error	Significant level (P-value)
Test (benzene)	29/796±2/175	0/307	0/104
Control	29/334±2/641	0/373	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of data analysis, there was no significant difference between the Average hemoglobin in each cell (MCH) of workers exposed to benzene with the control group ($P > 0/05$).

Table 9: Mean red blood cell concentration (MCHC gr / dl) of workers exposed to benzene and a control group

Indicator	Standard deviation ± Mean	Standard mean error	Significant level (P-value)
Test (benzene)	33/508±1/046	0/147	0/011
Control	33/604±1/586	0/224	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of the data analysis, there is a significant difference between the mean concentration of MRC in red blood cells (MCHC) of workers exposed to benzene and the control group ($P < 0.05$). According to the mean of the two groups, the mean concentration of red blood cell (MCHC) in the control group is more than exposed group of benzene.

Table 10: The mean platelets volume (MPV fl) of workers exposed to benzene and control group

Indicator	Standard deviation ± Mean	Standard mean error	Significant level (P-value)
Test (benzene)	9/85±1/057	0/149	0/902
Control	9/81±1/687	0/238	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of data analysis, there was no significant difference between the mean volumes of platelets (MPV) of workers exposed to benzene with the control group ($P > 0/05$).

Table 11: Hemoglobin (HBg / dl) of workers exposed to benzene and control group

Indicator	Standard deviation ± Mean	Standard mean error	Significant level (P-value)
Test (benzene)	15/674±1/169	0/165	0/557
Control	15/514±1/053	0/149	

Due to the normal distribution of data, independent t-test was used to compare the mean of two groups. According to the results of data analysis, there was no significant difference between hemoglobin levels of workers exposed to benzene with the control group ($P > 0/05$).

Table 12: Hematocrit (HEM %) of workers exposed to benzene and control group

	HEM (%)		HEM (%)
Mann-Whitney	1130/5	Test (benzene)	31/78±19/661
Wilcoxon	2405/5	Control	30/68±14/2305
Z	-0/824		
Significant level (P-value)	0/410		

Due to the lack of normal Hematocrit data (HEM), Mann-Whitney test was used to compare the study parameters. According to the results of the data analysis, there was no significant difference between the hematocrit (HEM) subjects exposed to benzene and the control group ($P > 0.05$).

Table 13: Red blood cell sedimentation rate (ESR mm / hr) of workers exposed to benzene and control group

	ESR(mm/hr)		ESR(mm/hr)
Mann-Whitney	715/5	Test (benzene)	8/72±4/0519
Wilcoxon	1990/5	Control	5/86±2/835
Z	-3/706		
Significant level (P-value)	0/001		

Due to the non-normalization of the ESR data, the Mann-Whitney test was used to compare the study parameters. According to the results of the data analysis between the sedimentation rate of red blood cells (ESR) there was a significant difference between subjects exposed to benzene and the control group ($P < 0/05$).

Discussion

The results of this study showed that blood parameters (RBC, WBC, MCV, RDW, MCH, MPV, HB, HEM) were not significantly different in the exposed group compared to the control group; only MCHC had a significant difference. Due to Normal distribution of data, independent t-test was used to compare the means of the two groups. According to the results of the data analysis, there is a significant difference between the mean concentration of red blood cells (MCHC) exposed to benzene and the control group ($P < 0.05$). Regarding the mean of the two groups, the mean concentration of red blood cells (MCHCs) in the control group was higher than the benzene group. Based on the results of the data analysis, there was a significant difference between the sedimentation rates of red blood cells (ESR) in the benzene-exposed group with the control group. In studies of blood factor changes such as anemia, aplastic anemia and leukemia caused by exposure to benzene, there are conflicting results that require data from long-term studies (9).

Parts of the studies in this regard are in line with the findings of this study. For example, Mow and Fow (2004) concluded in their studies that there was a negative correlation between exposure levels of benzene and red blood cell count (10). In addition, Keh et al. (2015) in a study conducted between 2005 and 2008 on a group of Korean workers, it is stated that the number of RBCs in the exposed workers with low levels of benzene has a significant negative relationship

(11). Posotori et al. (2009) also in their research concluded that benzene had no effect on examined blood factors the 153 Bulgarian petrochemical workers (239 ppm - 0/01) (12). Rajia and Hall (2014) in their study on 60 gasoline workers, of which 40 were exposed to benzene, compared to 20 controls concluded that exposure to benzene with concentrations of less than 1 ppm has no relevance with the reduction of red blood cells (9). Drummond et al. (1988), in their study on the bioavailability of workers exposed to benzene, stated that hematotoxic effects were found at high concentrations of 300 ppm and leukemogenetic effects at concentrations above 100 ppm (13). Kirkliet et al. (2008) examined the effect of benzene on human blood and stated benzene altered the gene expression and caused hematological disorders (14). In numerous studies, the blood-induced effects of exposure to benzene have been shown in low concentrations. Here can be pointed out blood toxicity especially in sensitive individuals exposed to concentrations of 1 ppm or less (15) changes in red blood cells, white blood cells and neutrophils in concentrations of less than 0.2 ppm (16), increased hemoglobin concentration in less than ppm 5 (17) reduction of lymphocytes, platelets, white blood cells and increase of average cellular mass of red blood cells in the presence of concentrations of 10-1ppm (18). A number of studies have also pointed to the lack of observation of abnormal blood parameters in exposure to benzene at low concentrations in occupational environments (19, 20). In concentrations of ppm of 0/01 - 1/4 benzene has no detectable blood abnormalities, and there are no significant abnormalities in the periodic observation of workers in the presence of

benzene 1 to 30 ppm concentrations, except temporary reduction in the number of red blood cells (21). In addition, in the study, Neqab et al. (2011), at a concentration of 0.24-ppm benzene in a gas station in Shiraz examined 400 people, 200 exposed to benzene and 200 controls. According to the findings, average number of white cells blood, red blood cells, hemoglobin, platelets, mean cellular RBC, average cell hemoglobin, mean hemoglobin concentration, lymphocytes, monocytes, neutrophils and eosinophils were similar in both control and exposure groups (22). A similar study during the years 1981 and 2007 Sevan et al. (2010) was conducted on 701 workers exposed to concentrations of 0/1-0/85 ppm benzene, compared to 1059 administrative staff. There were no significant differences in the blood factors between the two groups (it should be noted that hemoglobin, hematocrit, white blood cell, lymphocyte, monocytes, neutrophils, basophils were studied in this study) (19). Zamanpour et al. (2003) examined 400 workers with an average exposure of 3.99-ppm benzene and 40 employees. The average number of white blood cells, red cells, the average cell hemoglobin, mean hemoglobin concentration had no significant difference in the two groups of exposure and control (23). Of course, there are conflicting results for example, Ward et al. (1996) study in a 35-year on tyre manufacturing factory workers indicated that there is a significant relationship between exposure to benzene and anemia, and this result is dependent on exposure to 34-ppm benzene (24). Many cases of anemia have been reported for years, when benzene was used as a solvent in the workshops, including shoe manufacturing and tyre manufacturing workshops in high concentrations (hundreds of milligrams of benzene per m³) of benzene. When according to the past, the examination of workers' blood tests was done, the effect of reduction over time was observed parallel to the level of benzene reduction in the workshop air from 240 mg/m³ to 64-48 mg/m³ (25). In addition, it was found that workers exposed to benzene (above 120 mg/m³) had a high concentration of average levels, and their red and white blood cells were significantly lower than those exposed to benzene in the concentration below the average levels (20). Reduced red and white blood cell count has been reported at a concentration above the benzene average level (120 mg / m³), and below 32 mg/m³ was observed weak effect, and at concentrations of 0/03-4/5 mg/M³ have no effect (26). Hepatotoxicity studies of benzene show its myelotoxic effects (27, 28, and 29). Also, several studies on mice exposed to a minimum of 320 mg/m³ of benzene for several weeks showed that a decrease in the number of blood cells and bone marrow cells occurs as a result of exposure to benzene, some of which effects of benzene have been reported at lower concentrations. For example, in the amount of 32 mg/m³ or 10 ppm for 25 weeks, there is a decrease in the number of red blood cells and blood lymphocytes. Other evidence of adverse effects of benzene on blood-forming units on animals are reported at concentrations ranging from 10 to 300 ppm and above (25).

Miaw and Faw (2004) in their studies showed using multiple regression analysis that there is a negative correlation between the levels of exposure to benzene and

the number of white blood cells (10). Posotori et al. (2009) also concluded that benzene had no effect on the blood factors of 153 Bulgarian petrochemical workers exposed to benzene (ppm 0.01- 239). Only eosinophils numbers were influenced by benzene, which was only reported among smokers, in studies by Yishun Dera and Rana (2001) that confirmed this and stated that alcohol, tobacco and Non-vegetarian diet increases benzene's absorption and metabolism in the human body. In particular, excessive alcohol consumption can alter the sensitivity of the human body to benzene (12). In addition, the immunological effects of benzene are probably due to its effect on bone marrow. In this study, he reported a decrease in the ability to proliferate lymphocyte B week after inhalation of benzene at a low concentration of 32 mg/m³; this response developed for benzene inhalation of lymphocyte T at 96 mg/m³ concentration. Different types of blood diseases such as aplastic anemia, thrombocytopenia, granulocytes, lymphocytopenia are caused by exposure to benzene. As observed in laboratory animals, the organ that is the primary target of benzene, which causes blood disorders, is bone marrow (25). The results of this study indicated that minor leukopenia would occur after inhalation of 150 mg/m³ of benzene for 32 weeks. However, in another study, the reduction in the number of white blood cells in the 2 to 13 weeks was shown, or the reduction in bone marrow cells will occur in the amount of 960 mg/m³ or higher (25). Studies per year on 105 workers of an oil company between 1994 and 1997, exposed to benzene in concentrations between 0.14 and 2.08 parts per million benzenes indicate that time and duration of exposure to benzene is associated with changes in MCV and platelet count. Decline in MCV is only noticeable among workers who have worked for more than 10 years at this company. The findings of this study showed that low levels of benzene may affect CBC levels, and CBC can be a useful tool for biological monitoring for exposure to low benzene levels (30).

Studies of 928 workers in five factories in and around Shanghai, China have achieved a wide range of benzene concentrations, in which benzene-sensitive parameters have been introduced as neutrophils and mean platelet volume (MPV) in which effective benzene concentrations in the air is expressed from 7.8 to 8.2 in ppm (18).

The process of benzene poisoning occurs when benzene converts via metabolism into a number of metabolites that bind into the bone marrow, and are then converted by peroxidases into active and reactive species that, in turn, form reactive oxygen species (ROS) (31).

Conclusion

The average benzene concentration in the air of the studied workshops was 1.68 ppm. The results of blood tests showed that there was a significant difference between the mean concentration of red blood cell and the red blood cell sedimentation rate of workers exposed to benzene compared to the control group. So that the mean concentration of red blood cells (MCHC) in the control group is higher, and the rate of sedimentation of red blood

cells (ESR) of workers exposed to benzene is higher than control group. Moreover, in other parameters there is no significant difference between the two groups. The average exposure of workers at different workshops with benzene fumes is not exceeded from the permissible limits occupational exposure to these compounds. In addition, it seems that in the results of the study, other factors such as alcohol consumption, smoking, non-herbal diet and exposure to benzene are effective.

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The Effect of Internet Usage on Relations between Members of the Iranian Family in Tehran City

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Abstract

Iran has a society which is highly driven by religious cultural values. Religion and culture have both been apparent sustenance to shape every area of Iranian's daily life at individual, familial and societal levels. The instituting of modern technology, particularly the internet, has a decisive impact on the traditional and structural nature of Iranian's family life. This study has examined such impact on families. This is an exploratory study employing quantitative data. Around 50 families from different parts of Tehran (such as Saadat Abaad, Gheytaarieh, Shahriar, Dibagy and Shahrak Gharb) have been recruited by purposive sampling, and their views and experiences on how the use of modern technology influences their life, were collected. The findings suggested that internet use has produced a low husband-wife relationship in family life. Findings also suggest that there was a low relationship between siblings in a family. The internet use had also effects on Iranian families' traditional culture and beliefs.

Key words: internet usage, Iran, family, relationship, culture

Introduction

Societies in the Persian Gulf have been undergoing radical changes in various aspects of people's lives. Families are passing through a rapid transition that affects functions and relationships among members. The internet is a powerful tool that has shaped the performance of various fields including communication, business, politics, and education. There is no doubt that the Internet is virtually everywhere and has dramatically altered the way we live. It is rapidly growing not only in the industrialized countries but also in the developing world. As a result, the role of the internet in our daily lives has expanded rapidly to the degree that many of us have become dependent on it, if not addicted to it (1). As is the case elsewhere in the world, the use of the Internet has become an important element of life in Iran, opening doors to allow people to interact freely. While any technology can be put to good or bad use depending on the user, many Iranian's families use their computers for multiple purposes in an effort to search out materials they need or are interested in without major challenges. Because relationships among family members are essential to the maintenance of kinship family ties and reflect respect, compassion, and love, it will become increasingly important to re-examine the impact of the internet usage on Iranian families. This study delves into the effect of Internet usage on the family relationships in Tehran city, focusing on relationships between spouses, parents, children, and between the children themselves.

The statement of the Problem

The family is a dynamic social system that has structure, functions, roles and authority patterns. The way the system operates and adapts to change affects the relationships within it, and it is affected by external and internal factors. The Internet is one of several important factors that affect relationships among the family members. Hence, this study attempts to highlight this new technology that has entered most households in order to study the effect of internet usage on relationships among the members of Iranian families.

The Aim of the study

This study aims to study the effect of internet usage on relationships among the members of Iranian families including relations between spouses, their children, and the children themselves. It also will provide through recommendations, optimal ways to deal with this new technology.

Objectives

This study will determine the effect of internet usage on the family relationships, family's budget and children's educational achievement, incorporating its positive and negative effects, religiously, morally, and socially. This can be done through the recognition of certain social and economical characteristics of the research group, studying the nature of internet usage in Iranian families' place, time, period of usage, within individual or collective applications, reasons for usage, and most-visited websites on the net, identifying the level of organizing the internet's usage and the amount of monitoring imposed by the user and members of his family.

Research Questions

The study has the following three research questions to derive answers to satisfy its objectives

1. What is the nature of using internet by members of the family?
2. What are the effects of internet usage in shaping relations of members of family?
3. What are the effects of internet usage on other areas of daily life of family members?

Review of Literature

The family is a social system that has "a collective identity," which is the "result of shared recollections of togetherness that are created as family members spend time together in shared meals, games, and chatting" (2). Communication is "a symbolic, transactional process or the process of creating and sharing meanings" (3) and it plays a significant role in the relationship between individuals for the functioning of a family or household. Families that spend time together "in common activities enjoy a higher quality of communication" (2). Family communication is essential to any family and household as it "plays a significant role in the relationship between family leisure and family functioning" (3).

The internet is a new form of online interaction that enhances "offline relationships" (4). Furthermore, Smith et al. (2009) found that the internet is a way of increasing "interaction with family members and closeness to friends." In saying this, however, the frequency of daily internet use by adolescents plays a vital role in the quality of their relationships with parents and friends (5). Mesch (2006) found that adolescents who have low internet usage had better relationships with parents and friends than those who have high internet use (2). A great number of studies on internet Usage have handled and recycled factors like time and age. Studies of (6) and (7) analysed such factors respectively. The Social context and how its variables impact family relations have been less seldom analysed.

Family life with an eye to internet Use over a two-year period was screened by Kraut R et al (8). It was found that interaction was the main purpose both mothers and fathers and their children opted for. This had happened less often before the people had the facility available at home. Although the outcome might show an impact on familial relationships in a subsequent study, this concern didn't continue to persist (8). In another study of Orleans and Laney (7), at the age of 8-17, 32 children were observed with their parents. They scarcely communicated as they used their computers three times with sessions of no less than one hour of time. Children communicated together in as much as 65% of the time they went online. Different sexes used the computers differently: females used the computer instrumentally while use by males was more integrative (7).

In a study by Livingstone (9), it was found that only 6% of parents were concerned with their children's use of computers and the internet. Parents were far more concerned with other concerns and standards. Findings show that parents were more concerned with other threats to their children's well-being than with computer and internet use; 6% but around 50% of the parents were reported to have rules for internet use. Differently, children have only around half of those restrictions. This signifies the necessity for closer observation and data to explain the behavior of both parties inside the households.

The contextual nature of parent's internet concerns compared with their concerns with other aspects of life illustrates the importance of studying the Internet in context to provide a more complete understanding of how the technology fits with other aspects of family life. When the Internet is studied in isolation, it is easy to misunderstand how it fits with other aspects of family life and might distort its significance and influence. These studies provide a glimpse into the variety of ways that the internet may affect relationships in families. Whether they have a positive or negative impact on family interactions is a complicated question that requires more research and the consideration of what and how household technologies, namely, the internet might affect issues such as family communication, and socialization in general.

Social actualities of family life lend themselves to having better understanding of whether or not internet use can have any impact on family relations, and if any, whether similar impact(s) have certain trends and if they influence family communication and socialization in general. Another important research trend is whether this facility can help family members; communication between members, distant or inbound members, order generations, social problems such as divorce, doing office work or even household education.

It's time to start to explore questions relevant to household relationships such as maintaining relationships with distant and inbound family members, doing family work and education for a better understanding of modern family socialization. It is time to consider the ways family members

employ the internet in all family affairs. New internet users seem to confirm that the internet might be relevant to withdrawal from socialization (10). This actuality returned to normal after a period of 2-3 years of use.

In another study with a different sample, the same researchers added more variables and a wider spectrum of social measures. This time, findings showed that the number of close and distant social contacts as well as the in-person communication with family and friends increased. The result fostered the assumption that the facility had a positive impact on the maintenance of social networks.

In support of this, other researchers have concluded that the internet does maintain social relations. Internet users at home were reported to use it for friend and family communication. Moreover, and in another study, interpersonal relationships were reported to be the why behind sending and receiving e-mail messages (11). The number of those who used this facility for this end was twice as many as those who used it for business or information. Franzen (12) reported social relations were better maintained due to the same application. Nearly two thirds had more friend and family communication once they had their e-mails functioning (6). The internet fostered familial communication (13).

Overall, these findings suggest that the internet has positive effects on family members' ability to maintain socialization outside the parameter of people's own families.

Methodology

This is an exploratory study that embarked using quantitative data. To garner rich data, to meet the research objectives and answer the research questions viably, this research design is essential for this study. The basic aspects pertaining to the methodology of this study are: research population, research area, sampling, data collection and data analysis, as described in this chapter.

Research population

The research population of this study is families living in Tehran. These families are structured in a basically tradition manner. However, they are today increasingly becoming users of modern technology to fulfill their needs. This use of technology has been apparently impacting their oldest traditional family life today in the region.

Sampling

Some two hundred (200) families were included in this study. They were recruited from Tehran. A purposive sampling was employed to recruit them. Apart from this, separate recruitment criteria were also applied during their selection. The criteria were one or both members of a spouses unit (husband or wife) must use the Internet and at least one of their children (if they had any) must also use the internet.

Rational for sample

The researchers found that the purposive sampling was sufficiently viable for this study. This is because this sampling was widely recognized in social sciences as a most efficient tool to derive reliable and rich data and articulate the real picture and gravity of any issue/phenomenon in the society (Dolores & Tongco, 2007).

Data collection

Data were collected from all 200 participants in the study by questionnaires. Three types of questionnaires were set by the researchers themselves. Type 1 was for the husband, Type 2 for the wife and Type 3 for the children. All three types of questionnaires were distributed to respective participants and data was collected. Participants were asked to freely share their experience of internet usage in daily life. Type one questionnaires found 178 of 200 husbands to be internet users. Type two questionnaires showed that 133 of 200 wives were internet users. Meanwhile, Type 3 questionnaires suggested that out of 200 children in families, 187 were serious internet users.

Data analysis

The data were analysed with a computer-guided analytical system. The Statistical Package of Social Science (SPSS) program was applied to ensure descriptive statistics (such as arithmetic mean, standard deviation, frequency distribution and percentages as a method to display basic variables. Apart from this, Berelson's coefficient of correlation and Chi-square test were also applied to present, manage, and protect data in the study.

Findings and Discussion

The findings of the study were split into five major categories based on data derived from all participants. They include: socio-economic demographic characteristics of participants, the nature of internet usage, the internet's influence on families, advantages and disadvantages of internet usage for families and the statistical correlation between the research variables.

Social and Economical characteristics of the Research Group

- 54.5% of the fathers were between the ages of 40-50, and 45.5% of mothers were between the ages of 30-40. Children were aged between 15 and 20; they represented 42% of the total participants.
- Regarding the education status of participants, 52% of fathers, 49% of mothers, and 47.7% of children were holders of a degree.
- Among participants, 65% of fathers and 48.5% mothers were public employees.
- Regarding their income level, 31% of families had a monthly income of RO 1,000-1,500, while 39% of them received above RO 1,500 monthly.

The Data Related to the Internet

- 78.5% of families had at least one computer connected to the internet. All families had a unique place for the computer in their homes.

- 92.1% of fathers, 98.5% of mothers, and 97.9% of children listed the home as their prime internet access point.
- 35.4% of fathers, 18% of mothers, and 32.6% of children had a private computer connected to the internet. Meanwhile, the findings showed that 78.6% of fathers, 85.7% of mothers, and 80.3% of children used the internet in the company of others.
- The findings suggested 77.5% of fathers, 88% of mothers, and 68.4% of children used the internet 3 hours per a day, while the usage among 73.6% of fathers, 75.2% of mothers, and 75.9% of children was an unspecified period of time.
- Findings also indicated that most respondents just surf the web jumping from one page to another. Using e-mail came next. It became clear that the primary reason for the internet usage was entertainment, and secondly education. The most visited web sites by our research group were news sites, following online forums.
- According to findings, half of families were organizing the usage of the internet and monitor the user enough.

Influence of the Internet on the Family

Findings suggested:

- 92.4% of husbands reported low relations with their wives and this inadequate relation was experienced by 69.1% of wives with their husbands. Meanwhile, 6.8% of husbands and 23.6% of wives felt that the influence of the internet is average. And on the other side, 0.7% of husbands and 7.3% of wives thought that the influence was high.
- When it came to parents-child relations, the report from 78.6% of the parents and 89.8% of children was that the internet had not influenced their relationships in any way. However, 17.1% of the parents and 8.9% of children felt its influence to be significant. Findings showed that a low percentage of subjects felt the internet impacted the relationships between the parents and children, with just 4.2% of parents and 1.2% of children responding in this manner.
- For the relationships between children and the family, 84.8% of children responded that the internet's effect on their relationships with siblings was low. Meanwhile, 12.4% of them felt that the effect was average. A high level of internet use was reported among just 2.7% of them.
- Financially, 39% of husbands, 38.5% of wives, and 44.5% of children felt that internet usage had no effect on the family budget.
- For the impact of internet usage on their children's education, 67.9% of fathers, and 63.1% of mothers found neither positive nor negative influence.

Advantages and Disadvantages of the Internet

Advantages

Findings of the study showed that the internet granted better access to educational information. However, such information was mostly unrelated to curriculum. Many of the respondents claimed the internet provided them with good opportunities to interact with other people around the world who have the same interest of communicating. Respondents also stated that the internet was a vehicle for them to purchase what they wanted and sell what they had. It was, according to respondents, serving them to acquire

further knowledge on multiple aspects in their daily life, such as religion, culture, tourism, important locations, and different people around the world. For respondents, the internet has been a powerful tool to disseminate important information and circulate different media news and reports on every area of life. Most respondents completely agreed that the internet gives its users the ability to find information without any supervision.

Disadvantages

About half of the respondents (46% husbands, 49% wives, and 52.5% children) complained that the internet was being used to access unpopular or unethical things like pornography. Another half of respondents (55.5% husbands, 63.5% wives, and 67% children) on the other hand reported that some people employ the internet to have relations with the opposite sex. In both cases, the percentages are comparatively high in society which is driven by religious values, beliefs, social norms, and people's behaviours.

A relatively high number of respondents viewed the internet as influencing Iranian society's religious values and ethical principles negatively. According to a considerable number of respondents (24.7% husbands, 15.8% wives, and 35.8% children), the internet use was discouraging people from performing their religious obligation on time. For example, as a result of internet use, people were forgoing their prayers at their local mosque, which is an obligation in Islam.

The Statistical Correlation between the Research Variables

Although studying the relations between some independent variables and the effect of internet usage on family relations as dependent variables, the findings showed:

- There was a spiritual correlated relation between the sex of the couple and the effect of internet usage on the relationship.
- There was a correlation between the period of time the husbands spend online and the effect of internet usage on the relationship between the couple.
- There was a correlation relation between the period of time children spend online and the effect of internet usage on relations between parents and children from the parents' point of view.
- There was an inverse correlation between the level of organizing the usage of the internet and the amount of monitoring imposed on the children from the parents' point of view.

Through investigating the relation between some independent variables and the period of time spent online as dependant variables, results show:

- There was a correlation between the users' sex and the period of time they spend online.
- There is an inverse correlation between the age of fathers and mothers and the period of time they spend online.
- There was a direct correlation between the children's age and the time they spend online.
- There was an inverse correlation between fathers' educational level and the period of time they spend online.

- There was a direct correlation between children's educational statuses and the period of time they spend online.
- There was a direct correlation between the family's monthly income and the period of time the fathers spent online.
- There was a correlation between the level of organizing the usage of the internet and the amount of monitoring imposed on the children and the period of time they spend online.

By studying the correlations between the level the family's monthly income as an independent variable and the level of organizing the usage of the internet and the amount of imposed monitoring as a dependent variable, the following result emerged.

- There was inverse correlation between the family's monthly income and the level of organizing the children's usage of the internet and the amount of monitoring imposed on them.

Conclusion

Since the emergence of the internet, the effect of the internet for Iranians has become apparent. This study reveals some of the effects of internet usage on relations between members of the Iranian family, focusing on relationships between spouses, parents, children, and the children themselves. Overall, findings from the study show that half of the families had at least one computer connected to the internet. Findings also indicated that most respondents just surf the web, jumping from one page to another. Using e-mail came next. It became clear that the primary reason for the Internet usage was entertainment, and secondly education. The most visited web sites by our research group were news sites, following online forums. Findings of the study showed that the internet granted better access to educational information. However, such information was mostly unrelated to curriculum. The respondents claimed the internet provided them with good opportunities to interact with other people around the world who have the same interest of communicating. Respondents also stated that the internet was a vehicle for them to purchase what they wanted and sell what they had. It was, according to respondents, serving them to acquire further knowledge on multiple aspects of their daily life, such as religion, culture, tourism, important locations, and different people around the world. For respondents, the internet has been a powerful tool to disseminate important information and circulate different media news and reports on every area of life. Most respondents completely agreed that the internet gives its users the ability to find information without any supervision.

About half of the respondents complained that the internet was being used to access unpopular or unethical things like pornography. Another half of respondents on the other hand reported that some people employ the internet to have relations with the opposite sex. In both cases, the percentages are comparatively high in a society which is driven by religious values, beliefs, social norms, and people's behaviours.

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Investigate the Relationship between Information Technology and Employees' Productivity with Mediating Role of Knowledge Management (Case study: Imam Reza Hospital of Sirjan)

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Abstract

The purpose of this study was to investigate the relationship between information technology and employees' productivity with mediating the role of knowledge management. A descriptive, quantitative, co-relational design was used. The statistic population of research consisted of all employees of Imam Reza Hospital in Sirjan. The population consisted of 250 employees. The data collection instrument included demographic questionnaire, questionnaire of information technology, employees' productivity and knowledge management. Data analysis included descriptive statistics, and structural equation by software of Lisrel. There is a significant relationship between information technology and employees' productivity with mediating role of knowledge management. According to the results, there is a significant relationship between knowledge management and productivity.

Key words: Information technology, Productivity, Knowledge Management, Sirjan

Introduction

Nowadays some issues are presented that we can't solve with past strategies. The main characteristics of today's issues is the vast amount of data and information that needs to be collected, preserved, processed, retrieved and analyzed. This property, which is considered as the creator of organizational complexities, caused a move toward modern technology, called Information Technology (IT) that helps to facilitate the work with data and information (Abzari et al., 2007). Despite the short life of IT and its rapid development, different definitions and perceptions are presented about it that through careful observation we can find some internal inconsistencies. (Sarfazari, 2006). These definitions cover the broad range of concepts that sometimes are quite limited in the computer processing of operations and sometimes are remembered broadly as a technology that organized life is dependent on. According to Mantel (2006), information technology is to collect, store, organize, process and disseminate information including audio, image, text or numbers that is done by computer and telecommunication tools (Eshlaghi and et al., 2011).

Today, the importance of information is discussed either as an important tactical and strategic source in an organization and it has been known as a major source of value adding as well. Information has always been regarded in the business environment as a competitive advantage. But the important point is that real changes can increase the potential value of information, the organizations' ability in using of this important resource is through the application of new technology. Information technology with features like storage, processing, marketing and data transfer can assist

managers in improving the organizations' performance. On the other hand, the importance of productivity and the necessity to review it with regard to expanding of competition levels, technological complexity, and variety of tastes, lack of resources and the data transfer speed is not hidden for anyone. The impact of information technology on productivity has been discussed as the arguable major issue in the economy in the 1990s. In terms of theoretical and experimental, many studies have been conducted in developed countries and developing countries (Mahmoodzadeh, 2011). The main features of the present age, is information and turning it into knowledge. Such features will have a large impact on the social and economic institutions; if a social institution also uses it as a base it , changes their structure and rebuilds it. In fact, it can be stated that information technology has increased the ability of organizations and with knowledge and human rationalism of ideas, in order to exploit it and assign repetitive affairs and non-creative activities to machines, as well as increasing efficiency and releasing of human skills, much attention has been paid to it in recent years (Eshlaghi and et al., 2011). The aim of this study to was examine and investigate the relationship between information technology and employees' productivity with the mediating role of knowledge management.

Principal Hypothesis

There is a significant relationship between information technology and employees' productivity with mediating role of knowledge management.

Secondary Hypotheses

- (1) There is a significant relationship between information technology and employees' productivity.
- (2) There is a significant relationship between information technology and knowledge management.
- (3) There is a significant relationship between knowledge management and employees' productivity.

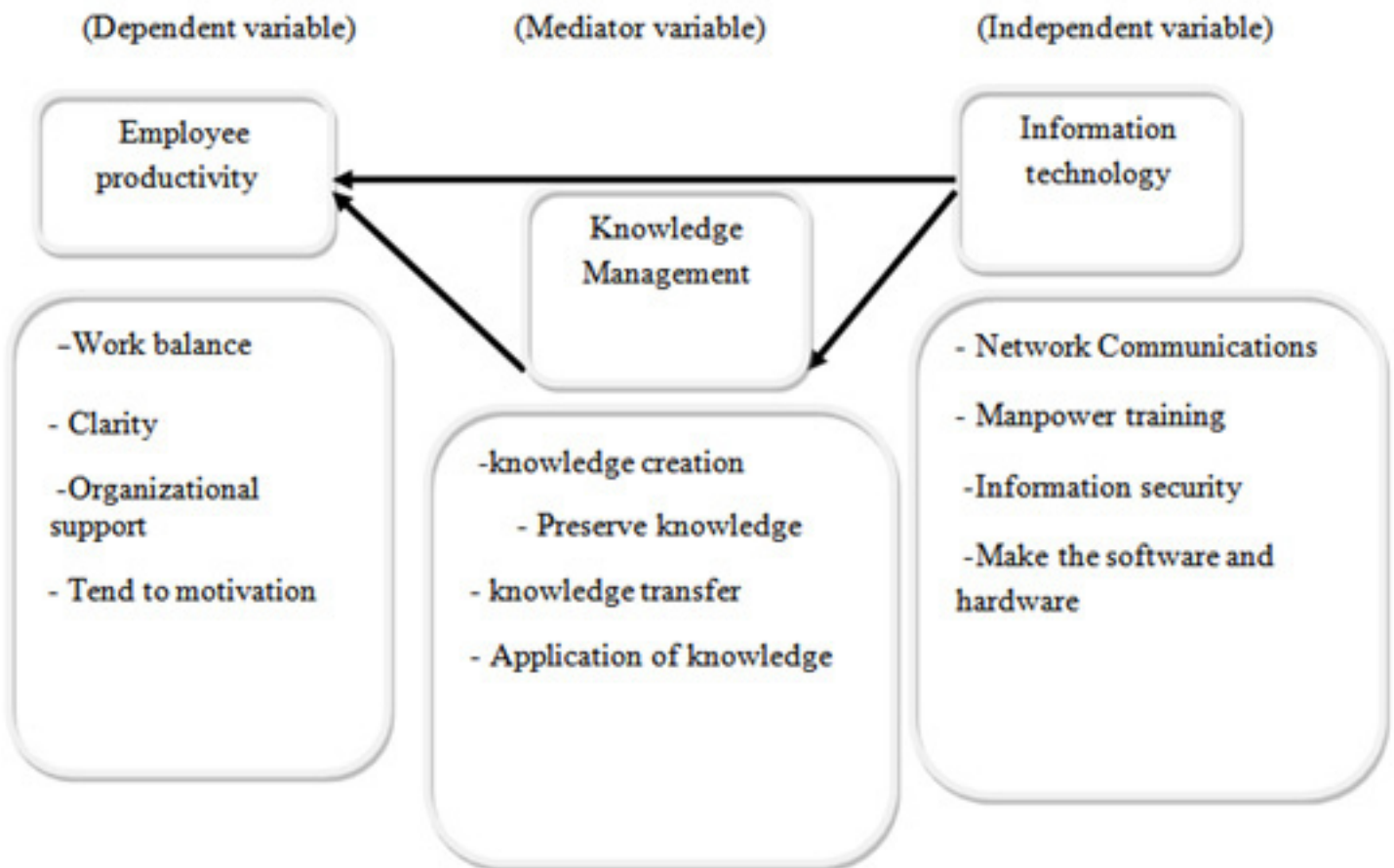
Research methods

A descriptive, quantitative, co-relational design was used. The statistic population of research consisted of all employees of Imam Reza Hospital in Sirjan. The population consisted of 250 employees. The data collection instrument i included demographic questionnaire, questionnaire of information technology, employees' productivity and knowledge management. The staff answered the same questionnaire including information technology (20 questions), employees' productivity (28 questions) and knowledge management (i=25 questions). Cronbach's alpha that was obtained from the pilot data was 0.8 for information technology, 0.86 for employees' productivity and 0.79 for knowledge management (Treadway et al., 2004; Harris & Harris, 2007). Data analysis included descriptive statistics, structural equation by software of Lisrel.

Demographics Results

Of the 250 subjects enrolled in the study, 39.7 % were male and 60.3% were female. Among respondents those aged 31 to 40 years were most frequent and least frequent in the age group were 30 and lower.

Conceptual Model



Results

Principal Hypotheses

[1] There is a significant relationship between information technology and employees' productivity with mediating role of knowledge management.

H0: There is a not a significant relationship between information technology and employees productivity with mediating role of knowledge management.

H1: There is a significant relationship between information technology and employees productivity with mediating role of knowledge management.

The results of this study show there is a significant relationship between information technology and employees' productivity with mediating role of knowledge management. Thus H0 is rejected and research hypothesis is approved. According to the results, numbers significant between IT and knowledge management is 7.23. So there is a significant relationship between information technology and knowledge management. According to the results, standard coefficient between information technology and knowledge management is 0.66 . This reflects the strong relationship between information technology and knowledge management. The results of this study show the numbers significant between employees productivity and knowledge management is 6.62 .So there is a significant relationship between productivity and knowledge management. According to the results, standard coefficient between employees productivity and knowledge management is 0.59. This reflects the strong relationship between productivity and knowledge management (Chart 1 and 2).

Chart 1: Values significant of structural equation modeling

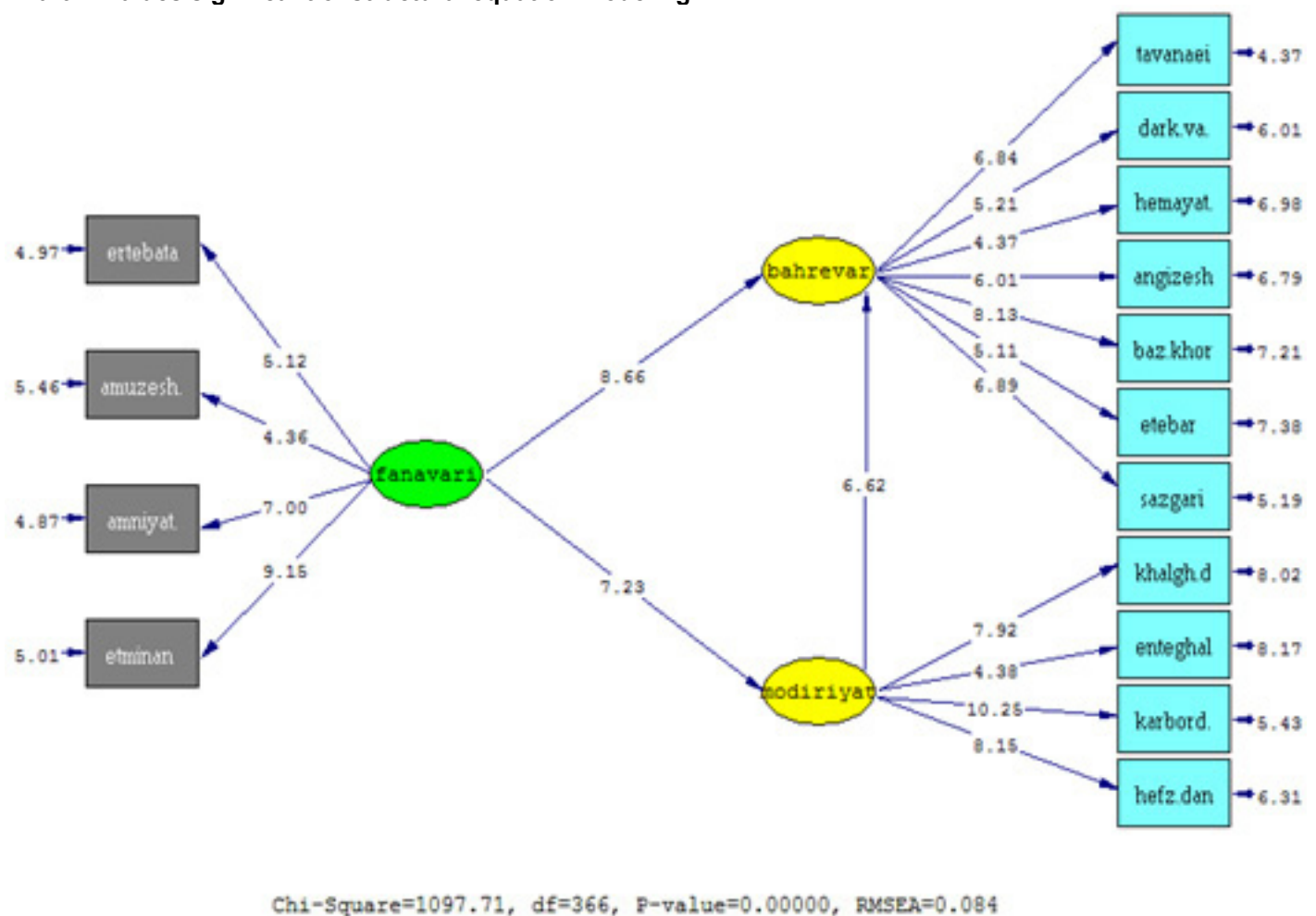
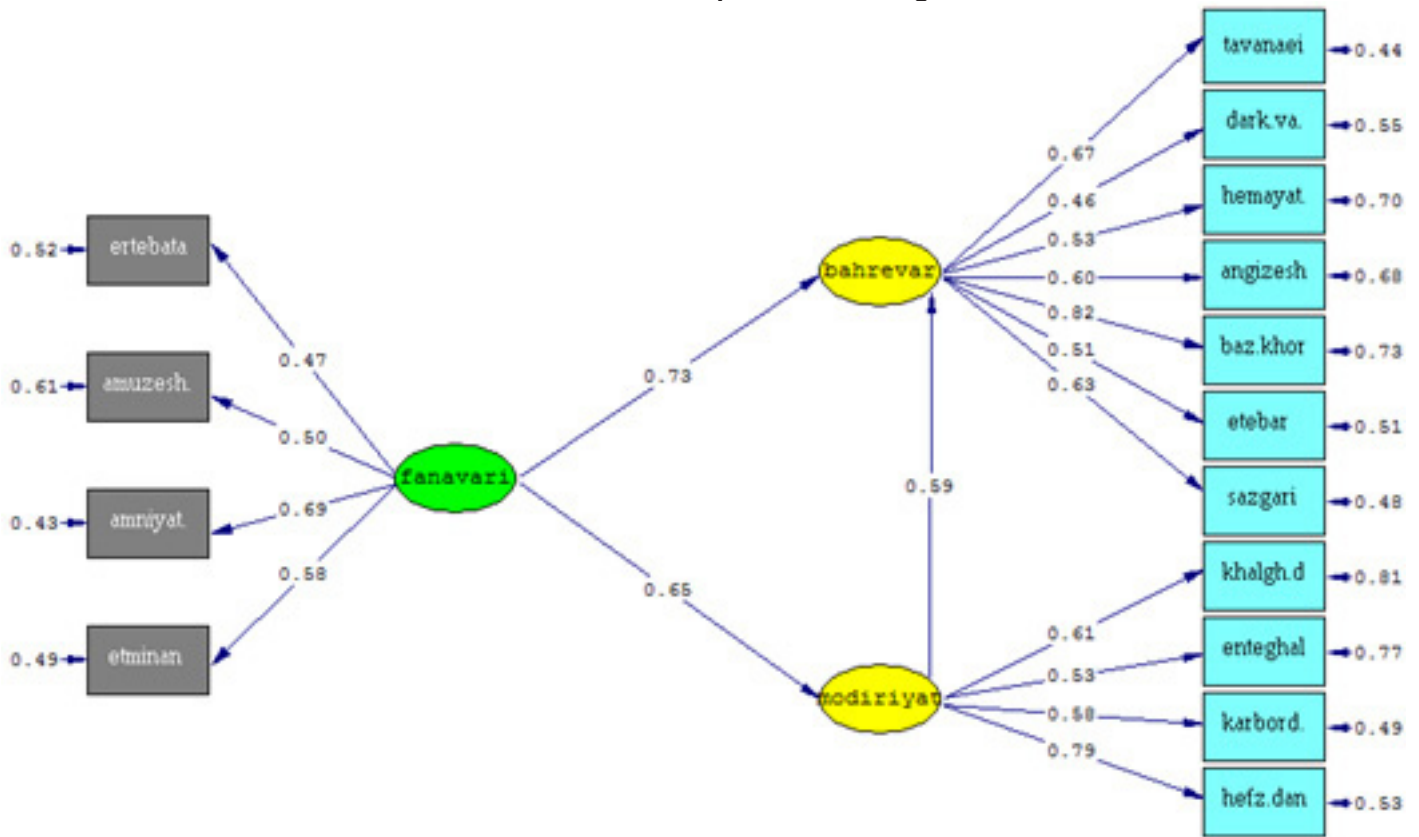


Chart 2: Values standardized coefficients of structural equation modeling



Chi-Square=1097.71, df=366, P-value=0.00000, RMSEA=0.084

Table 1: The results of the implementation of structural equation modeling

Relation between variables	Value of t	Direct effect (R)	Relation between variables	Value of t	Direct effect (R)	Result	Relation
IT - knowledge management	7.23	0.66	Knowledge management - productivity	6.62	0.59	Accepted	direct

Table 2: Fitting indexes for Model

Index	χ^2/df	RMSEA	GFI	AGFI	CFI	NFI	IFI
Calculated value	2.99	0.084	0.91	0.74	0.95	0.92	0.95
Acceptable level	<5	<0/1	>0/90	>0/90	>0/90	>0/90	>0/90
Result	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate

RMSEA: Root- mean- square error of approximation **GFI:** Goodness- of-fit index **AGFI:** Adjusted goodness -of-fit index **CFI:** Comparative fit index **NFI:** Normed fit index **IFI:** Incremental fit index

- [1] There is a significant relationship between information technology and employees' productivity.
- H0: There is not a significant relationship between information technology and employees' productivity.
- H1: There is a significant relationship between information technology and employees' productivity

The results of this study show there is a significant relationship between information technology and employees' productivity. Thus H0 is rejected and the research hypothesis is approved. According to the result, numbers significant between IT and productivity is 8.02. So there is a significant relationship between information technology and productivity. According to the result, standard coefficient between information technology and productivity is 0.76. This reflects the strong relationship between information technology and productivity (Chart 3 and 4).

Chart 3: Values significant of structural equation modeling

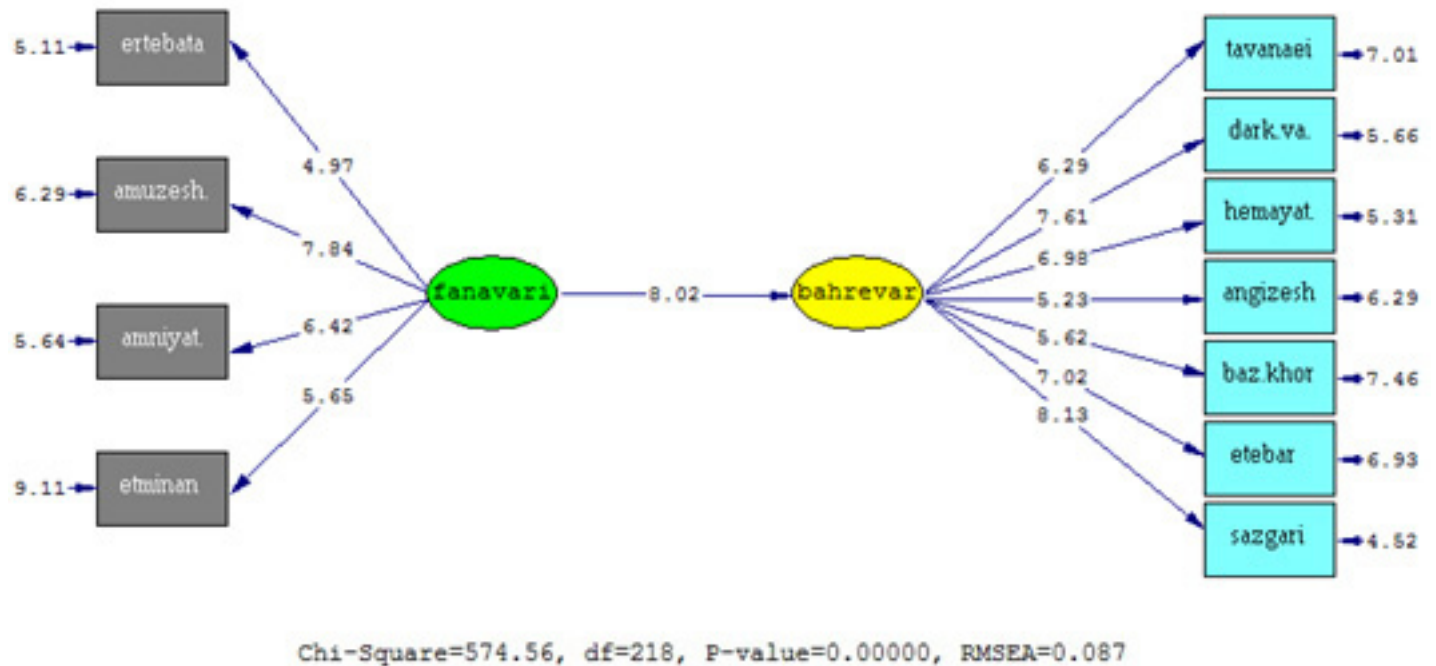


Chart 4: Values standardized coefficients of structural equation modeling

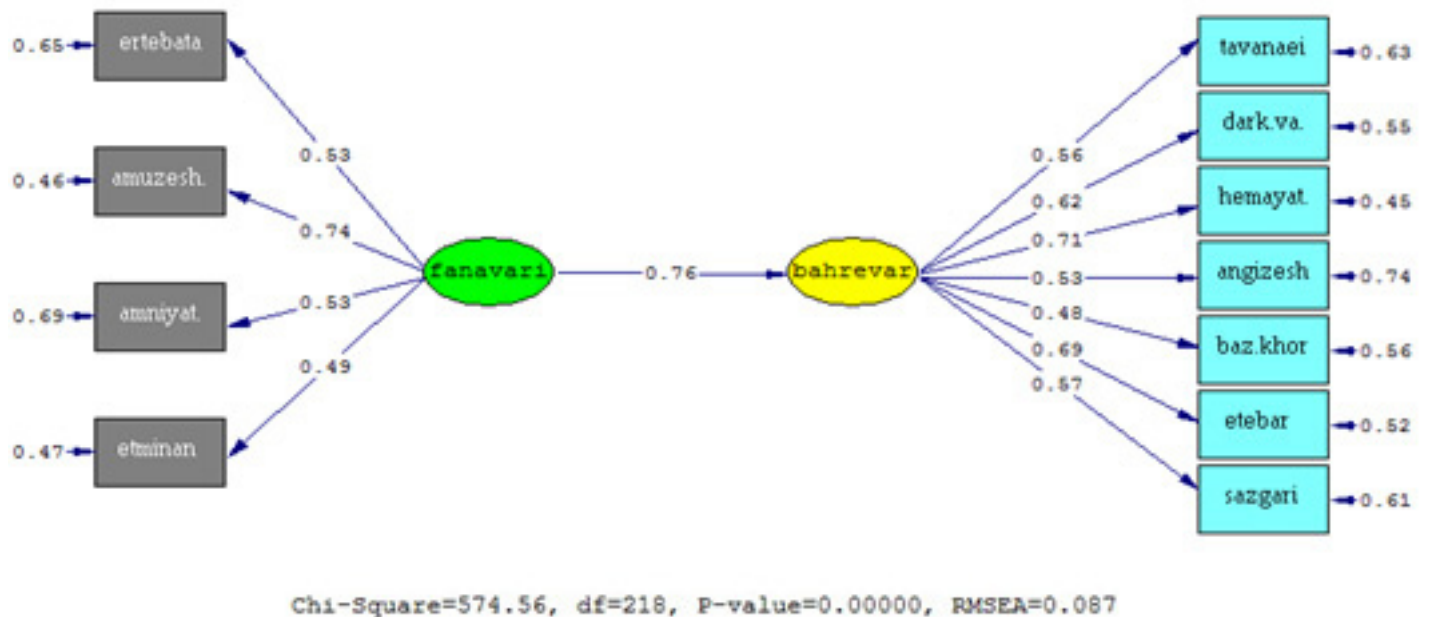


Table 3: The results of the implementation of structural equation modeling

Relation between variables	Value of t	Direct effect (R)	Total effect	Result	Relation
IT - productivity	8.02	0.76	0.76	Accepted	Direct

Table 4: Fitting indexes for Model

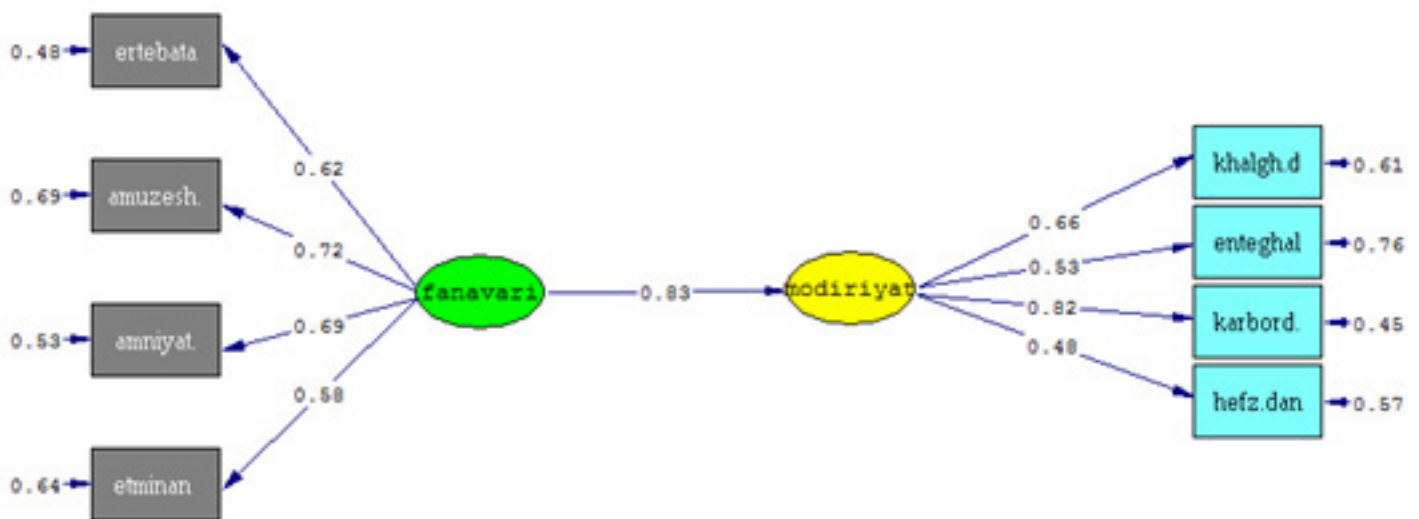
Index	χ^2/df	RMSEA	GFI	AGFI	CFI	NFI	IFI
Calculated value	2.63	0.087	0.94	0.71	0.91	0.91	0.91
Acceptable level	<5	<0/1	>0/90	>0/90	>0/90	>0/90	>0/90
Result	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate

RMSEA: Root- mean- square error of approximation **GFI:** Goodness- of-fit index **AGFI:** Adjusted goodness -of-fit index **CFI:** Comparative fit index **NFI:** Normed fit index **IFI:** Incremental fit index

- (2): There is a significant relationship between information technology and knowledge management.
- H0: There is not a significant relationship between information technology and knowledge management.
- H1: There is a significant relationship between information technology and knowledge management.

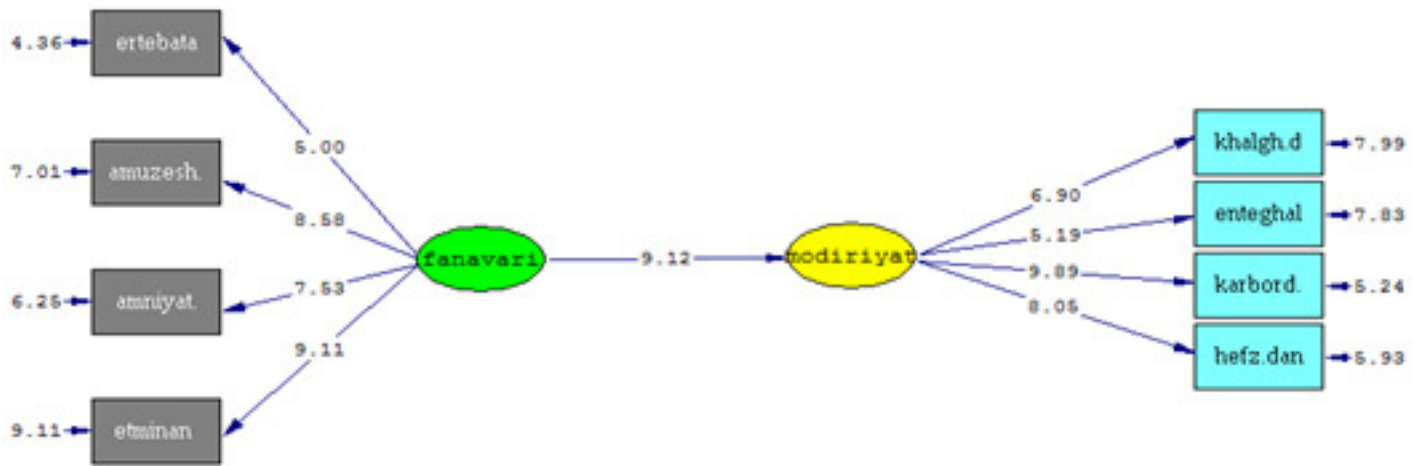
The results of this study show there is a significant relationship between information technology and knowledge management. Thus H0 is rejected and research hypothesis is approved. According to the result, numbers significant between IT and knowledge management is 9.12. So there is a significant relationship between information technology and knowledge management. According to the results, standard coefficient between information technology and knowledge management is 0.83. This reflects the strong relationship between information technology and knowledge management (Chart 5 and 6).

Chart 5: Values significant of structural equation modeling



Chi-Square=573.49, df=278, P-value=0.00000, RMSEA=0.088

Chart 6: Values standardized coefficients of structural equation modeling



Chi-Square=573.49, df=278, P-value=0.00000, RMSEA=0.088

Table 5: The results of the implementation of structural equation modeling

Relation between variables	Value of t	Direct effect (R)	Total effect	Result	Relation
IT - productivity	9.12	0.83	0.83	Accepted	Direct

Table 6: Fitting indexes for Model

Index	χ^2/df	RMSEA	GFI	AGFI	CFI	NFI	IFI
Calculated value	2.06	0.088	0.94	0.71	0.91	0.91	0.91
Acceptable level	<5	<0/1	>0/90	>0/90	>0/90	>0/90	>0/90
Result	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate

RMSEA: Root- mean- square error of approximation **GFI:** Goodness- of-fit index **AGFI:** Adjusted goodness -of-fit index **CFI:** Comparative fit index **NFI:** Normed fit index **IFI:** Incremental fit index

- (3): There is a significant relationship between knowledge management and productivity.
- H0: There is not a significant relationship between knowledge management and productivity.
- H1: There is a significant relationship between knowledge management and productivity.

The results of this study show there is a significant relationship between knowledge management and productivity. Thus H0 is rejected and research hypotheses is approved. According to the results, numbers significant between knowledge management and productivity is 9.82 so there is a significant relationship between knowledge management and productivity. According to the results, standard coefficient between knowledge management and productivity is 0.83. This reflects the strong relationship between knowledge management and productivity (Chart 7 and 8).

Chart 7: Values significant of structural equation modeling

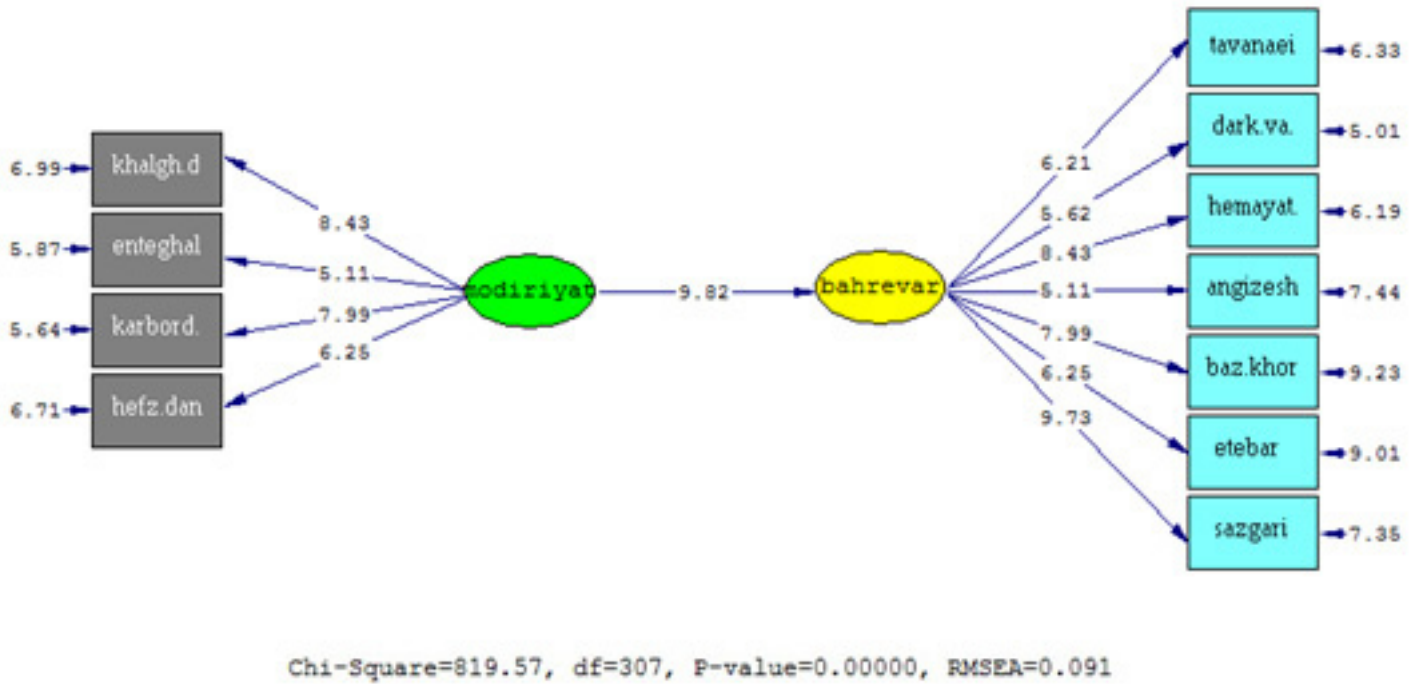


Chart 8: Values standardized coefficients of structural equation modeling

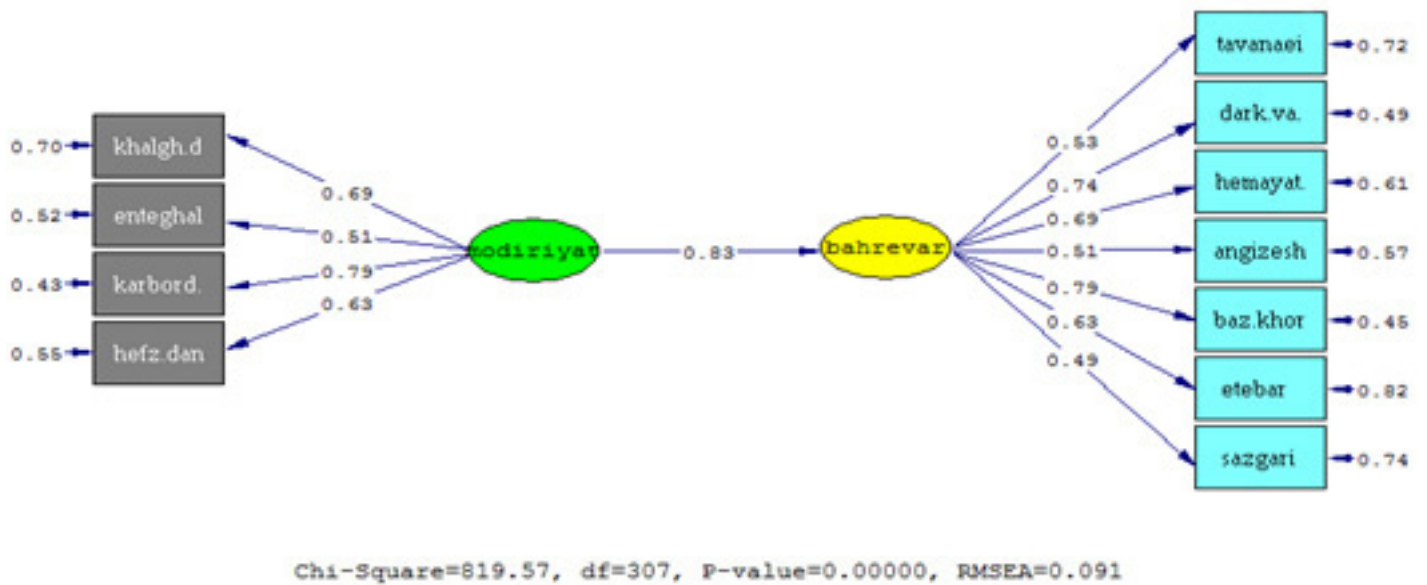


Table 7: The results of the implementation of structural equation modeling

Relation between variables	Value of t	Direct effect (R)	Total effect	Result	Relation
IT - productivity	9.82	0.83	0.83	Accepted	Direct

Table 8: Fitting indexes for Model

Index	χ^2/df	RMSEA	GFI	AGFI	CFI	NFI	IFI
Calculated value	2.66	0.091	0.84	0.75	0.95	0.90	0.93
Acceptable level	<5	<0/1	>0/90	>0/90	>0/90	>0/90	>0/90
Result	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate	Appropriate

RMSEA: Root-mean-square error of approximation GFI: Goodness-of-fit index AGFI: Adjusted goodness-of-fit index CFI: Comparative fit index NFI: Normed fit index IFI: Incremental fit index

Discussion and Conclusion

The purpose of this study was to examine the relationship between information technology and employees productivity with mediating role of knowledge management. The results of this study show there is a significant relationship between information technology and employees productivity with mediating role of knowledge management. This means that information technology affects on productivity through knowledge management. These results are in agreement with results Rotena and Kovar (2016) and Hasanzadeh and Ghahremani (2016). The results of this study show there is a significant relationship between information technology and employees productivity. This means that if the Employees in the organization use of information technology to increase their productivity. These results are in agreement with results Rotena and Kovar (2016) and Hasanzadeh and Ghahremani (2016). According to the results, there is a significant relationship between information technology and knowledge management. This means that if employees were used of facilities, programs, services and basic technologies in knowledge management will be more successful. These results are in agreement with results Meres (1999). The results of this study show there is a significant relationship between knowledge management and productivity. This means that if there is collection of appropriate information in organization and used of knowledge employees, finally will be increased employees productivity. These results are in agreement with results Hossini (2012). Hasanzadeh and Ghahremani (2016) in a study entitled investigate the relationship between IT and employees productivity reports there is a significant relationship between IT and employees productivity. Hossini (2012) in a study entitled investigate the relationship between knowledge management and employees productivity reports there is a significant relationship between knowledge management and employees productivity.

Goodarziand (2008) showed that there is a significant positive relationship between knowledge creation and knowledge transfer. In the traditional model, organizations and individuals are often unwilling to transfer and exchange their knowledge. Since instead of looking at knowledge as an organizational resource, consider knowledge as a source of power and a guarantee for the continuity of their jobs and are not willing to share it with others because they are afraid to lose the control of their organization knowledge. In fact, a knowledge that is not circulated in organization won't be developed and eventually will be obsolete and will be changed into an obstacle. In short, knowledge circulation through sharing, business and trade will lead to the production of new knowledge that would seem impossible without the use of information technologies. An organization that supports information sharing and knowledge creation among its employees can define efficient and effective processes and improve its organizational performance and productivity.

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Pre-competition anxiety score among Elite Boy Swimmers in Iran

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Abstract

Introduction: The present study was performed to measure the precompetitive anxiety and its two subcomponents (somatic and cognitive) and its relationship with age, weight, height and body mass index. **Methods:** This is a descriptive study performed using a demographic questionnaire and sport competition anxiety test (SCAT) designed by Martens consisting of 15 questions. The study population consisted of 14 elite boy swimmers. The questionnaires were filled out by swimmers 30 minutes before competition. The data were analyzed by SPSS software, using pair t-test, student t-test and linear regression test. **Results:** The mean score of precompetitive, somatic and cognitive anxiety was 17.93 ± 3.25 , 14.71 ± 2.95 , 3.21 ± 0.97 , respectively. The percent of somatic and cognitive competitive anxiety was not significantly different. The results showed no significant relationship between precompetitive, somatic and cognitive anxiety with age, weight, height and body mass index of swimmers ($p > 0.05$). **Conclusions:** Our study suggests that the swimming competition equally effects on somatic and cognitive components of anxiety.

Key words: precompetitive anxiety, cognitive, somatic, male, swimmer

Introduction

Anxiety is defined as a significant negative effect (1) and is a common fact of everyday life that plays an important role in human life. Anxiety in athletes is common and is a physiological response to a real or imagined threat. According to Murphy over 50 percent of consultations in athletes at an Olympic festival were related to stress (2). The findings of Katkat in male Judo, Karate and Taekwondo athletes (3), Raglan et al in high school swimmers (4), Parnabas and Yahaya in Malaysian athletes (5), Serhat and Yildiz in Turkey elders wrestling national team (6), Matsumoto et al in male elite judo athletes (7), Singh et al among male inter-collegiate badminton players (8), Mottaghi et al in the futsal players (9) and Esfahani and Softlu among volleyball players (10) suggest the existence of sport anxiety in athletes.

Anxiety includes two subcomponent, cognitive and somatic (11, 12). The somatic component is often accompanied by physiological aspect, which is related to negative symptoms such as nervousness, elevated blood pressure, dry throat and mouth, muscle tension, rapid heart rate and sweaty palms (11-13). This type of anxiety had no role in decreasing the performance (11, 14). But, the mental component of anxiety is cognitive which is characteristic of fears about performance, failure image, failure to concentrate and disturbed consideration (11, 12).

The mean score of cognitive anxiety among runners of different skills were 12.41 for national, 14.73 for state, 17.39 for district and 21.45 for university (15). The results of a study showed that cognitive and somatic anxiety score were 16.6 ± 3.7 and 15.4 ± 3.2 in 18 elite male basketball

players, respectively (16). According to Cooper, the somatic and cognitive anxiety level was 14.08 ± 3.87 and 17.95 ± 4.16 among 37 youth classic soccer players with CSAI-2 questionnaire (17).

A positive amount of anxiety is required to achieve a desirable task. Higher level of anxiety physically inhibits performance by causing muscular tension and disturbing coordination of the movements.

Recent research has shown that athletes suffer stress which significantly affects mental health (18). Nowadays one of the most challenging tasks for athletes is how they improve psychological behavior and performance in competitive sports. It has been previously accepted that psycho-physiological conditioning programs and traditionally skill practices are of fundamental prominence in high-level competitive sports, which highly affects an athlete's performance. Researchers showed a significantly negative correlation between anxiety scores and sport performance, that higher anxiety levels impair sporting performance (15, 19, 20). Also, competition anxiety is negatively correlated with sport experience, sport ability and general physical competence (21).

Remco et al detected that cognitive state anxiety but not somatic state anxiety was associated with swimming performance in child swimmers during competition (22). Also, Parnabas et al showed that higher cognitive anxiety lowered the sport performance (23). Even, Hatzigeorgiadis and Chromi et al showed that intensity of cognitive anxiety had low to moderate negative correlations with approach coping strategies (24). Also, Vosloo et al showed that compatible groups of swimmers had a more facilitative clarification of somatic anxiety and high levels of self-confidence (25). Cognitive anxiety had a linear relationship with performance, and somatic anxiety had an inverted-U relationship with performance (26).

The aim of the study was to measure sport anxiety and to examine the difference of subcomponents of sport anxiety. Also the present study aimed to determine the relationship of competitive anxiety (cognitive and somatic) between some variables (age, weight, height and Body Mass Index) among elite boy swimmers.

Methods and Materials

The subjects for the present study included 14 elite boy swimmers with ages ranging from 10 to 13 years. A questionnaire to record some data such as age, weight and height was used by the researcher. The investigator used the Sport Competition Anxiety Test (SCAT) questionnaire for assessing sport competition anxiety approximately 30 minutes before competition. The SCAT questionnaire consists of fifteen items of which five items, including first, fourth, seventh, tenth and thirteenth items are neutral questions and are not scored. All items are rated on 3-points Likert-type scale that varies from 1 (hardly ever), 2 (sometimes) and 3 (often). The items number 6 and 11 are scoring reversed, 1 (often), 2 (sometimes) and 3 (hardly

ever). The competitive anxiety score is computed by summing ten items with 10 for low anxiety and 30 for high anxiety. The questions 2, 6, 8, 9, 11, 12, 14, and 15 were related to evaluation of physical or somatic competitive anxiety level, and questions 3 and 5 were for cognitive competitive anxiety evaluation (27). To compare the cognitive and physical anxiety scores, the score obtained was expressed as a percentage. The competitive score less than 17 said low level of, 17-24 an average level of and more than 24 a high level of anxiety. The SCAT has also been extensively used in sports research and shown to be both reliable and valid (28, 29).

The athletes who met the selection criteria were included and convinced that the information provided by himself would be kept confidential and would be used for research purposes only. All the participants were informed of the study objectives and how to complete the questionnaires. Before the interview, written informed consent was obtained from all of their parents, who were assured that the information would remain private, and they were told that they would be allowed to leave the study at any stage if they did not wish to continue. The athletes were asked to read all instructions carefully and give the answer of questions as exactly as possible. All data were collected 30 minutes before competition.

Subjects diagnosed with systemic diseases and who had performed any intense exercise or consumed alcohol for two weeks before competition were excluded from the study.

The present study was approved by the Ethics Committee of Jahrom University of Medical Sciences. The participants received oral information about the study.

The data were analyzed by SPSS for Windows (version 15; SPSS Inc., Chicago, IL., USA), and distribution of data was expressed in mean and standard deviation. Pair (dependent) t statistical test was used to examine difference of cognitive and somatic score and student (independent) t test was used for difference of anxiety subcomponents and age, weight, height and BMI groups. Linear regression test was used for relationship anxiety components with age, weight, height and BMI. Statistical significance was set at $P < 0.05$ for all comparisons.

Results

Fourteen young elite male swimmers participated in our study. Table 1 provides some data of participants such as age, height, and weight and body mass index.

The majority of the boys were 12 years old (50.0%) and age varied from 10-13 years with mean age of 11.71 ± 0.82 years. The result showed that 57.1% participants had BMI ≥ 19.5 .

The response of subjects to Sport Competition Anxiety Test is shown in Table 2.

Table 1: Demographic data of youth swimmer players

Data	Number (n=14)	Percent (%)
Age (year), 10	1	7.1
11	4	28.6
12	7	50.0
13	2	14.3
Height (cm), <155	7	50.0
≥155	7	50.0
Weight (kg), ≤45	7	50.0
>45	7	50.0
Body Mass Index, <19.5	8	57.1
≥19.5	6	42.9
Continues variables	Mean	SD*
Mean of age	11.71	0.82
Height (cm)	155.64	8.09
Weight (kg)	47.00	6.66
Body Mass Index	19.55	1.29

* Standard Deviation

Table 2: Participants response to the Sport Competition Anxiety Test

Item	Hardly ever, No (%)	Someti me No (%)	Often No (%)	Mean	Median	Standard Deviation
2. Before I compete I feel uneasy	0 (0.0)	6 (42.9)	8 (57.1)	2.57	3	0.51
3. Before I compete I worry about not performing well	5 (35.7)	4 (28.6)	5 (35.7)	2	2	0.88
5. When I compete, I worry about making mistakes	11 (78.6)	3 (21.4)	0 (0.0)	1.21	1	0.43
6. Before I compete I am calm	3 (21.4)	7 (50.0)	4 (28.6)	2.07	2	0.73
8. Before I compete I get a queasy feeling in my stomach	9 (64.3)	4 (28.6)	1 (7.1)	1.43	1	0.65
9. Just before competing, I notice my heart beats faster than usual	5 (35.7)	6 (42.9)	3 (21.4)	1.86	2	0.77
11. Before I compete I feel relaxed	1 (7.1)	7 (50.0)	6 (42.9)	2.36	2	0.63
12. Before I compete I am nervous	9 (64.3)	2 (14.3)	3 (21.4)	1.57	1	0.85
14. I get nervous wanting to start the game	9 (64.3)	2 (14.3)	3 (21.4)	1.57	1	0.85
15. Before I compete I usually get uptight	12(85.7)	0 (0.0)	2 (14.3)	1.29	1	0.73

Table 3: Mean competitive anxiety scores by some variables

	Somatic, Mean (SD)	Cognitive, Mean (SD)
All swimmers	14.71 (2.95)	3.21 (0.97)
Age (year), 10-11	13.20 (1.10)	3.20 (1.30)
12-13	15.50 (3.36)	3.22 (0.83)
p-value	0.081	0.969
Height (cm), <155	13.14 (0.69)	3.00 (1.16)
≥155	16.29 (3.55)	3.43 (0.79)
p-value	0.058	0.433
Weight (kg), ≤45	13.57 (1.62)	3.29 (1.11)
>45	15.86 (3.62)	3.14 (0.90)
p-value	0.165	0.796
BMI, <19.5	13.75 (1.39)	3.38 (1.06)
≥19.5	16.00 (4.05)	3.00 (0.89)
p-value	0.241	0.498

With regard to the cognitive subscale, high-percentage responses were identified when participants were asked specific questions related to experiencing cognitive anxiety previous to a competition. When responding to "Before I compete I worry about not performing well" 35.7% and 28.6% of the participants responded hardly ever or sometimes. Near 79% of participants responded hardly ever or sometimes to the item "When I compete, I worry about making mistakes."

With regard to the somatic subscale, high-percentage responses were identified when participants were asked particular questions related to experiencing somatic anxiety before competition. When responding "Before I compete I usually get uptight" about 86% of participants stated hardly ever. When responding to "Before I compete I am nervous" approximately 64% responded hardly ever. Over 64% participants responded hardly ever to the item "I get nervous wanting to start the game". Also, over 85% participants responded hardly ever to the item "Before I compete, I usually get uptight".

The overall mean score of sport anxiety was 17.93 ± 3.25 among swimmers, that was higher than 50% of total score (30 score). According to classification of anxiety, 35.7% (5), 57.1% (8) and 7.1% (1) of elite boy swimmers had low, average and high level of sport anxiety 30 minutes before competition, respectively.

Our result showed that the percentage of somatic sport anxiety (61.31 ± 12.28) is not significantly different to cognitive component (53.51 ± 16.25) among male elite swimmers (Table 3). Also, our results revealed that the average somatic and cognitive anxiety score was not significantly different for the boy swimmers aged 10-11 years over boys aged 12-13 years, with a difference of 2.30 ($p=0.081$). Our results revealed that, although the average somatic anxiety score appeared to be slightly higher for

the participants with height less than 155 cm, weight ≤ 45 kg and BMI < 19.5 over than other groups, height ≥ 155 cm, weight > 45 kg and BMI ≥ 19.5 , scores between the two groups were not significantly different. Based on the results we found no significant differences between the cognitive anxiety with age, height, weight and BMI groups.

The linear regression test revealed that the somatic and cognitive anxiety scores were not significantly related to age, weight, height and BMI.

Discussion

The study was designed to measure and compare the level of cognitive anxiety and somatic anxiety in a sample of 14 elite male swimmers.

Our result found that the precompetitive anxiety score was at an average level (17.93 ± 3.25) and 59.77% of total score in swimmers. As stated by SCAT scale score (17-24), individuals have an average level of anxiety which is good in psychological terms. The precompetitive score was higher than in a study conducted by Sahu ((30) in 20 male batsmen (16.35 ± 2.03) and 20 male bowlers (16.20 ± 2.95), Sil (31) in 23 male basketball players (17.13 ± 2.83), Kerketta (32) in 30 volleyball male players (18.66 ± 2.82) and 30 soccer male players (17.85 ± 3.74), Mottaghi et al (9) in soccer players (16.79 ± 2.10), Schaefer et al (33) in 164 male golfers (15.57 ± 3.96).

But the results of Saxena and Sathe (34) in 30 urban school state level male players (18.63 ± 3.71), Kumar (35) in 30 male basketball players (20.79 ± 0.64) and Matsumoto et al (7) in 43 male judo athletes (22.05 ± 3.77), were higher than our result.

Precompetitive anxiety is dependent upon factors such as skill level, experience and general level of arousal in daily activities. Avramidou et al found that the competitive

environment increased the intensity of somatic anxiety and decreased the level of self-confidence in the twenty swimmers, whereas cognitive-anxiety intensity was not significantly different (36). Parnabas et al identified the negative correlation between cognitive anxiety and sport performance in swimmers (37).

Although, the percentage of somatic anxiety score was higher than percentage of cognitive score, there is no significant different. This result is similar to reports by Halilaj et al (38) and Agaoglu (39). Adversely, Mehdipoor et al (40) suggested more cognitive anxiety score than somatic component of anxiety among college athletes. Also, Soltani et al indicated that cognitive sport anxiety was significantly higher than somatic anxiety among team sport and individual sport athletes.(41).

The cognitive anxiety score in a study conducted by Parnabas et al (37) was lower (16.34 of 36) in 15 district swimmers, than in our finding.

However, according to Drive theory, the presence of audience for low skilled athletes, during the sport competition could increase their cognitive anxiety. Cognitive anxiety is the extent to which an athlete worries or has negative thoughts, and the negative thoughts may include fear of failure, loss of self-esteem and self-confidence. It could lead to poor performance of an athlete in competition. It may start before a competition in the form of pre-competitive anxiety that might affect performance throughout the competition.

The relationship between cognitive anxiety and performance was explained best in Multidimensional Anxiety Theory. This theory explains that cognitive anxiety effects performance. The relationship between cognitive anxiety, where an athlete experiences worries, negative thoughts and fear of failure, will affect the performance (42).

According to Martens and researchers (14), somatic A-state anxiety may be classified as a common response to competition and can cause no necessary harm to performance. Unfortunately, an increase in cognitive A-state anxiety in an athlete can cause concentration and focus disruption and a mental development of worry and self-doubt. A lack of focus and concentration while participating in sports can negatively affect overall performance. Possible causes of cognitive A-state are negative verbal feedback, lack of readiness for competition, a negative attitude towards a previous poor performance, or negative expectations from other individuals such as team members, coaches, and family members.

Significant differences are not noticed between the precompetitive, somatic and cognitive anxiety with age, weight, height and BMI. Also, Schaefer et al found that the age of golfers did not effect on their competitive anxiety (33). Inversely, Modrono and Guillen (43) reported a significant relationship between age and cognitive anxiety. Also, the results of the Taner et al study (21) pointed out that age is

a one of the important factors in determining competition anxiety. Das and Ghosh (44) show that middle adolescent and late adolescent players differ significantly from each other and late adolescents are found more anxious than middle adolescents. Ferreira et al (45), Agurre-loaiza and Bermudez (46) and Mottaghi et al (9) showed that there was a significant inverse (negative) relationship between the competitive anxiety levels and age. This may have been the result of the older athletes having had more experience than their younger counterparts.

Conclusion

As a conclusion of the study, the somatic and cognitive anxiety is equal in the elite male swimmers 30 minutes before competition, and the factors of age, weight, height and body mass index have no effect on somatic and cognitive anxiety.

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Assessment of the Presence or Absence of Palmaris Longus and the Fifth Superficial Flexor Tendon in the Iranian Population: Are these tendons evolutionary?

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Abstract

Introduction: The lack of a Palmaris longus tendon and the absence of a fifth superficial flexor function are normal variations found in the human wrist and hand. The purpose of our study was to assess the incidence of both of these variations and also to answer the question of whether they are evolutionarily conserved muscles.

Methods: The study population was volunteers (or informed consent from parents) from preschools, grammar schools, high schools and universities, offices, and nursing homes who were examined for the presence of the Palmaris longus tendon and for variations of the fifth superficial flexor.

Results: By the end of the study, 1180 individuals were enrolled and their data were recorded. Of the total 2,360 hands studied, 1,688 had a Palmaris longus tendon (71.4%) and 1,284 had a functional fifth superficial flexor (54.4%). In 886 hands fourth flexor-dependent function was found (37.5%) and ultimately in 190 (8%) the function was absent.

Presence, dependent function, or absence of fifth flexor or Palmaris was not related to age, hand side or dominance. Fifth flexor variations were not related to sex, but unilateral absence of Palmaris longus was 1.5 times more common in women. No difference was found between the sexes regarding variations of the superficial flexor. No correlation was found among the variations between one tendon and the other within one hand and/or that individual's other hand.

Conclusion: The findings of the present study are similar to those found in some other similar reports related to variations in these tendons. It seems that Palmaris longus and the fifth superficial flexor function are not evolutionarily determined, at least in the studied population.

Key words: Palmaris longus, fifth superficial flexor, variation, evolution.

Introduction

The Palmaris longus is one of the most variable muscles of the body and may be absent in some individuals (1). The fifth superficial flexor of fifth finger is also among the variations of the human body, and in some individuals it is not detectable or not present. This claim is controversial: some studies have concluded that this tendon is absent in certain individuals (2, 3) while others have concluded that the absence is functional rather than anatomical (4). Both of these tendons have been considered to have evolved (5). In the present study our main purpose was to assess the frequency of these variations in relation to an Iranian sample population and to answer the question of whether they are evolutionarily determined.

Materials and Methods

This prospective study was performed on a population comprised of volunteers from preschools, primary schools, high schools, universities, offices and nursing homes in the city of Kerman, Kerman province, Iran. Institutional ethics committee permission was granted. In each case, if informed consent was given by the individual, s/he was examined by an examiner trained for that purpose. At first the classic test for the presence of Palmaris was performed, in which the individual would place his or her fifth and first fingers in opposition to each other while flexing the wrist. If the Palmaris longus tendon was visually detected and palpated, the individual was assumed to possess the tendon (6). If this visual examination and palpation test was negative, then the other tests were performed to confirm the absence of the tendon, and if the results were negative for all tests, the individual was assumed to be without the tendon. Contradictory or suspicious cases were excluded from the study.

The fifth superficial flexor was assessed by asking the volunteer to flex the Proximal interphalangeal joint (PIP) at least 90 degrees while the examiner kept the second, third, and fourth fingers fully extended. The individual was considered to have a functional Flexor Digitorum Superficialis (FDS), if s/he could. If the test result was negative, then the examiner would release the fourth finger and repeat the examination. If this time the PIP was bent to 90 degrees, it was a dependent tendon, and if not, the individual had a nonfunctional or completely deficient fifth FDS (4).

Results

By the end of the study, 1,180 individuals and thus 2,360 hands were enrolled, comprising 433 males and 747 females. The mean age of the individuals was 26.64 ± 17.94 , with a range of 5 to 91. 1,132 individuals were right-handed (95.9%), 414 men and 718 women.

The Palmaris Longus tendon was present bilaterally in 730 (62%) and absent bilaterally in 222 (19%). In 228 individuals the tendon was present on one side, 101 in the right hand and 117 in the left. Of the total 2,360 hands, the tendon was present in 1,688 (71.4%) and absent in 672 (28.6%). Of the male hands studied, 679 (78.4%) possessed the tendon and in women's hands, the tendon was present in 1,005 (67.3%). Of the right hands studied, 831 (70.5%) possessed the tendon, and of the left hands, the tendon was found in 853 (72.2%). Of the total dominant hands, 1,624 of 2,264 dominant right hands (71.7%) and 65 of 96 dominant left hands (67.5%) featured the Palmaris longus tendon. These results are shown in Table 1.

480 individuals had functional FDS bilaterally (40.4%); in 273 individuals it was dependent on the fourth FDS bilaterally (23.2%), and in 32 individuals the fifth FDS was bilaterally nonfunctional (2.7%). Of the remaining 391 individuals, in 134 the right hand had a dependent and the left a functional FDS; in 135, the left side had a dependent tendon and the right a functional one; in 33, the right had a functional and the left a nonfunctional tendon; and ultimately, in 24 the left was dependent and right was nonfunctional (Table 2). Of the total 2,360 hands, 1,284 had functional FDS (54.4%), 886 had dependent FDS (37.5%) and 190 had nonfunctional FDS (8%). Table 3 shows FDS incidence in dominant hands.

Twenty-three right and 31 left hands had neither the Palmaris longus nor fifth flexor tendon. Twenty-three individuals had absent Palmaris and nonfunctional flexors bilaterally.

The results were analyzed with a generalized estimation equation and the conclusion was reached that the variations in the Palmaris longus and the fifth superficial flexor tendons' presence or absence were not related to age, side, or dominance. The fifth FDS variations were not affected by sex, but bilateral lack of Palmaris longus was 1.8 times more frequent in females, while there was no difference between the sexes with regard to the unilateral absence or presence of Palmaris. Again there were no correlations among the variations of Palmaris and the fifth flexor tendon.

Table 1. Palmaris longus situation regarding side and sex (p>0.05 in all)

Palmaris	male		female	
	right	left	right	left
present	324 (77/7%)	329 (78/9%)	486 (65/9%)	505 (68/3%)
absent	93 (22/3%)	88 (21/1%)	251 (34/1%)	234 (31/7%)

Table 2. Palmaris longus situation regarding bilateral absence or presence

	female	male	sum	p-value
Bilaterally present	431 (59/9%)	299 (69/2%)	730	<0/001
Bilaterally absent	170 (22/8)	52 (12%)	222	<0/001

Table 3. Fifth FDS situation regarding side and sex (p>0.05 in all)

Fifth FDS	Male		Female	
	right	left	right	left
Present	229	229	419	412
dependent	182	170	272	308
absent	22	34	56	27

Table 4. Fifth FDS situation regarding dominant side

Fifth FDS	Present	Dependent	Absent
Right dominant hand	1244 (54/9%)	885 (39/1%)	135 (6%)
Left dominant hand	46 (47/9%)	46 (47/9%)	4 (4/1%)
p-value	0/106	0/053	0/302

Discussion

In the present study we assessed the variations in the Palmaris longus and the fifth superficial flexor in an Iranian population, and also considered their presence or absence in relation to age and to each other; ultimately we found no correlations.

The variations in Palmaris longus have been studied extensively in different populations and very different findings have been reported, from the absence of the tendon in more than 50% (6) to its presence in more than 96% (7). In one study of an Iranian population, the 23% absence of the Palmaris longus tendon was the result that is closest to ours (8). For the fifth superficial flexor we could find only one epidemiologic study with results comparable to ours: about 6% absolute deficiency and 40% dependency on the fourth flexor. Another study found an absence of the tendon in 33% of the population, which is a lower incidence than in our findings (10).

As previously reported, Palmaris and fifth FDS are commonly considered evolutionary developments, disappearing with time over generations. This hypothesis has been examined in a study on an African population by assessing the difference of variations in different age groups and it was concluded that no obvious evolutionary trend was present (11). Another study with the same method reached the conclusion that the tendon was evolutionarily

determined (12). Our study assessed variations in the detection of these tendons with age, which we think is statistically more meaningful. We could not find any study that assessed an evolutionary trend for FDS.

Are the variations affected by the dominance of the hand? To the best of our knowledge only one study has tried to address this topic directly, and only regarding Palmaris longus. It concluded that the nondominant hand had a higher incidence of an absent Palmaris longus (13). Another study noticed this too, but not as its primary conclusion, and it noted that Palmaris was more frequently absent in the left-dominant hand (8). Again, we used the relation instead of difference and did not find a correlation, either for Palmaris or for the flexor. Our findings for flexor independence in relation to sex, age, and dominance are comparable to at least one previous study (14).

Another point to be noted is the correlation among variations in the tendons, as they have a common origin from the medial epicondyle and similar innervations. So, it may seem logical that variations are found together or at least that there is a relationship. To our knowledge, only one study has been performed to answer this question and has found no correlation (15). It considered the absence of presence (functional, non-functional) of the tendon, in contrast to the present study in which dependency on the fourth flexor was considered too, though the result was similar as no correlation was found.

Studies of Palmaris longus variations and their relationship with sex have reached different conclusions. In some, the absence of these tendons has been reported more frequently in females (16, 17, and 18). In others, no difference was reported (19 and 20) and at least one study found more frequent absence of the tendons in men (21). It is interesting to note the finding of a more frequent bilateral absence in women, and the equal incidence of a unilateral absence in men and women (22).

The last point is the fact that different statistics about variations in Palmaris longus are related to the studied race and location, but is it possible that different observers have different interpretations of a test on a single person? To the best of our knowledge no study has noted the interobserver and interobserver reliability of different tests performed for assessing these variations and this may be a good topic for further research. At least one study observed that different tests may give different results in one person (23), at least in relation to this topic.

The most important limitation of the present study is the fact that due to several considerations we included a larger population of young people than the elderly; the most obvious was their availability. The very sensitive tests that we used for statistical analysis, would have compensated for this, but of course not completely.

Based upon the findings of the present study, it seems that the tendons that are the subject of this paper, at least in the population studied, are not evolutionary and, in other words, are not related to age.

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Moral challenges in the provision of care for Infant and Family: a qualitative study

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Abstract

Introduction: Today, nurses are faced with many problems in their workplace that could cause them stress. The stress associated with moral problems is commonly called moral distress. The aim of this study has been to explore nurses' live experiences of the moral challenges in the NICU.

Method: This study is a qualitative study. Sampling was conducted by purposeful sampling method until reaching data saturation with a choice of 12 nurses. The method of collecting data was deep semi-structured interview. Total of interviews were transcribed verbatim. A qualitative content analysis with conventional approach based on Graneheim and Lundman approach was used.

Results: Results of this study revealed three main themes: the challenge of proper care with love, the challenge of understanding and proper dealing with families of newborns, and the challenge of professional skills and nursing ethics.

Conclusion: The first mentioned challenge was connected with issues such as nursing workforce shortage or lack of facilities and equipment as a factor in defects of neonatal care that implicitly affect nurses' performance and were beyond the control of the nurse. The second mentioned challenge was due to the lack of attention to family-centered care.

The last mentioned challenge can be associated with individual and professional characteristics of the nurse. Thus, it is suggested that by providing necessary facilities and equipment, emphasis on the importance of family-centered care, considering appropriate educational programs, and changing attitudes of nurses, special attention be given to the moral challenges faced by nurses in order to prevent moral distress and to increase quality of neonatal care in the NICU.

Key words: Moral challenges, End-of-life care, ethical issues, Infant; Family, Iran

Introduction

Moral distress has been named and discussed in nursing at least since 1980. In this era, Jameton defined moral distress. In 1995, Corley developed a moral distress measuring scale to measure nurses' moral distress. Moral distress is different from moral dilemmas. Moral distress is a mental instability where the right action is clear, but the individual is not able to do it, but in moral dilemma, correctness of doing it is doubtful (1). Typically, moral distress is in a form of experienced mental imbalance or stress in situations in which a person sees something that is morally accepted but unable to do in terms of the laws in the workplace. In the new amended definition, stress occurs in situations where providers of health care feel that they are unable to keep all interests at risk of the patients (2, 3). According to recent studies, moral dilemmas may cause stress among the health care team. Stress associated with moral dilemmas is commonly called moral distress. Moral distress occurs when the person knows doing something is correct but the organization or other restrictions make it hard for him to do that. Studies have shown moral dilemmas are important and common among nurses (2). Moral distress is defined as a painful sensation when the nurse considers doing something morally correct and required, but due to the organization, is unable to do it. (3, 4).

Moral uncertainty occurs when the nurse does not know whether there is a moral dilemma or not, and if there is, she does not know what principles or values to adopt to deal with it. Moral dilemmas are created when two or more than two values or principles are in conflict. Distress usually occurs due to moral dilemmas. Over the past decade, the impact of moral issues in nursing practice in the United States has dramatically increased. Nurses in performing nursing care, spend a large amount of their time on solving moral dilemmas that may result in moral distress. Moral distress can be a component of occupational stress in nursing (3).

The nursing profession has occupied a significant role in the application of professional moral concepts. Every nurse should maintain her deeds within the moral framework and promote them. The nurses are expected to adopt appropriate moral decisions on behalf of patients (5). Individual factors such as personality, values, lack of knowledge, lack of sensitivity on the rights of patients, dissatisfaction with working conditions, and limited powers may have negative effects on decisions and moral practice of the nurses (6).

The hospital environment itself causes stress in different levels. Death as an inherent reality causes doctors and nurses when communicating with patients to have emotional control at the hospital. These staff, especially when involved in emergency departments and intensive care units, are more vulnerable to mental stress (7).

Moral distress is a major problem for nurses, which can lead to physical and emotional problems, job retention, job

satisfaction, and the quality of care. In nurses, increasing the level of moral distress could lead to medical errors, burnout, fatigue, weakness, and avoidance of the patient. In addition, frustration and job dissatisfaction may lead to unhealthy workplace violence =. Distress can lead to physical symptoms such as anxiety and sadness. Moral distress is not often recognized in nurses, which itself can lead to disappointment, anger, and leave negative effects on staying in the job (4).

Moral distress can have important consequences such as stress, burnout, job dissatisfaction, and separation from nursing. Complete information on the impact of moral distress on the quality of nursing care is not available (1).

In a study, Rathert et al. studied moral distress predictors and interventions in acute care units. More than half of respondents reported that they have experienced moral dilemmas and moral conflicts a few times a month (8).

In another study, the highest source of moral distress experienced by nurses in the oncology ward was pain control and issues related to the cost of treatment. Moral issues that could cause moral distress in nurses' were issues of prolonging life, doing unnecessary tests, and telling the truth. When nurses failed to fulfill their moral obligation, they felt anger, frustration, and grief (3).

NICU is an emotional, moral environment and nurses face moral challenges, and nurses' moral distress in these wards may be unique. Newborns are vulnerable and caring for them can create a new dimension of moral distress. Moral distress among nurses working in NICUs is a significant problem. Moral distress has physical, emotional, and psychosocial symptoms and negative impact on the quality and quantity of the newborn's care. Moral distress leads to loss of moral integrity and is an important factor in job satisfaction, burnout, and leaving job by nurses (9).

Prentice et al, (2016) conducted a systematic review of the literature on the moral distress in working with newborns in neonatal intensive care units. They analyzed 13 studies. In these studies, they noted that inappropriate use of technology is not suitable for the patient and reduces the power of nursing. The concepts of moral distress have been expressed in different ways in nursing and medical literature. Nurses considered themselves as victims who are forced to perform aggressive care for the patients. In medical texts, moral distress is described as facing moral dilemmas or moral confrontation. In Neonatal Intensive Care Units, moral distress had an impact on patient care (10).

Despite the rise in demand in the field of moral judgment, health care organizations lack policies, standards, and systematic training guidelines in the field of morality and moral support structures for staff. Thus, it is not surprising that many health care workers suffer from stress related to this issue (3).

Given the importance of this issue, and that little attention is paid to moral challenges by nurses in NICUs, conducting research in this field becomes necessary. This research was conducted by qualitative research, because there is little knowledge about this issue and qualitative research tends to deeply search a phenomenon about which there is little knowledge. Thus, this study was conducted to "Explore Moral challenges in the provision of care in NICU in Isfahan."

Methods and Participants

This study was conducted by qualitative method and qualitative content analysis with conventional approach (11). The participants of this study were nurses working in NICU of Al-Zahra in 2015. Sampling in this study continued until reaching information saturation, and data saturation was achieved after 12 interviews. To ensure data saturation, two follow-up interviews were also conducted, but more categories and data not obtained.

Data collection

Method of data collection was individual interviews of semi-structured type. After getting permission from the hospital head, the researcher introduced himself to the NICU head and qualified nurses for the study were identified. One day before the interview, a half-hour session was held to explain the objectives of the study, to get oral and written informed consent, and to determine the time and place of the interview with the agreement of participants. The study started on July 6, 2015 and lasted until December 6, 2015. In this study, 12 interviews were conducted, all of which were in the break room of nurses in NICU of Al-Zahra hospital. All interviews were recorded with MP3. Press interview duration was from 40 to 60 minutes based on the willingness of participants to continue the interview. Before the interview, the participants were asked for consent to record, and they were assured of confidentiality of data and their voice. The researcher did all the interviews. The interview started with a general question: "Please explain your experience about the challenges in taking care of newborns and their families in NICU." Then the next questions were asked based on the answers given to this questions and were oriented towards moral challenges.

Data Analysis

Data analysis was carried out in line with the purpose of this study that is an exploration of the moral challenges faced by nurses in NICUs. All interviews were transcribed verbatim at the end of each day. The researcher read the interviews several times to find out the meaning of words and phrases and to find an overall sense. Two researchers independently analyzed the data. Meaning units were read several times. Then the similar codes were classified into Category and sub-Category categories.

Themes were identified and entitled separately by each individual researcher and minor disagreements discussed and evaluated. Qualitative content analysis with conventional approach in inductive method with Graneheim and Lundman approach was used, since there were only

limited theories and data in this regard, especially in Iranian context and culture. The following steps were used to obtain a deep understanding and describe this phenomenon: Step 1) determining the content of analysis and analysis unit, 2) determining meaning unit or coding unit, 3) condensation and abstraction of codes, 4) Classification of codes into subcategories 5) the formation of Category from sub-Category, 6) the formation of themes from categories, 7) and the final report.

To ensure the validity of the data in this study, stability was achieved when participants gave consistent and similar answers to similar questions that had been raised in a different format. In this study, after extracting information, to validate data, the researcher referred to available participants and assessed their approval of the content extracted, and the final agreement and confirmation was achieved. In this study, about generalizability, the researchers tried to choose the participants from a relatively wide age and cultural backgrounds to achieve this goal.

Morality

This study is the result of findings of a thesis approved by the University of Isfahan and Isfahan University of Medical Sciences Ethics Committee. In order to comply with moral issues, informed consent was obtained from all participants after explaining the purpose of this study and the confidentiality of the participants' names were taken into consideration.

Findings

In the 12 interviews with nurses working in NICUs, the average age of the subjects was equal to 33.5 years. Of the nurses studied, 10 had bachelor's degree in nursing and 2 had a master's degree in nursing. Seven were single and five were married. Moreover, the average work experience of the nurses was 9 years and average work experience of nurses in NICU was 6 years, which is shown in Table 1 (next page).

As shown in Table 2) moral challenges have three themes: "the challenge of proper care with love," "the challenge of understanding and proper dealing with families of newborns," and "the challenge of professional skills and nursing ethics." The challenge of proper care with love is composed of two categories of proper care for the newborn and care with love.

The challenge of understanding and proper dealing with families of newborns is composed of two categories of understanding and sympathy for the families of the newborns and conflict in dealing with newborns' families consists of four sub-categories. Moreover, based on the analysis conducted, the challenge of professional and moral skills of nurses, as the third moral challenge of the nurses, is composed of two categories of nursing skills and nurses' moral features with four sub-categories.

Table 1: Distribution of demographic characteristics of nurses

NICU work experience (years)	Marital status	Work experience in years	Degree of education	Age	Participants	Row
6	single	6	nursing expert	29	1PN1	1
7	single	8	nursing expert	32	PN2	2
5	single	5	master of nursing	32	PN3	3
5	single	8	nursing expert	32	PN4	4
7	single	13	master of nursing	38	PN5	5
4	single	11	nursing expert	34	PN6	6
15	married	15	nursing expert	37	PN7	7
1	single	8	nursing expert	32	PN8	8
20	married	22	nursing expert	45	PN9	9
1	married	6	nursing expert	34	PN10	10
1	married	2	nursing expert	29	PN11	11
2	married	4	nursing expert	28	PN12	12

Table 2: Moral challenges

Themes	category	sub-category
Challenge of proper care with love	Proper care of the newborn	Challenge of proper care of the newborn
		Challenge of failure of care of newborn
		Attention to soothing the newborn
	Care with love	Challenge of understanding pain in newborn
		The challenge of having affectionate behavior with love in working with newborns
		Having a newborn attachment and dependency
The challenge of understanding and proper dealing with family of the newborn	Understanding and empathy for the families of the newborns	Good sense of the nurses in giving good news to the family of the newborn
		The importance of understanding the newborn's mother
	A conflict in dealing with the newborn's family	Having a bad sense of guilt in bad communication with newborn's mother
		The challenge of having proper dealing with family of the newborn
Challenge of professional and moral skills of nurses	Professional nursing skills	Challenge of having experience and expertise in working with newborns
		The importance of accuracy and speed in working with newborns
	Moral features of the nurse	A work morality in newborn care
		Challenge of conscience for nurse during a painful procedure for the newborn

1. The challenges of proper care with love

The first theme from the above study is "The challenge of proper care with love" that is composed of two Categories: "proper care of the newborn" and "taking care with love." In general, this theme includes issues such as the importance of a commitment to revive the newborn, lack of resources and equipment in failure to care for newborn, attention to medical relief of the newborn, good sense of the nurse in working with newborns, and challenges such as knowing the newborn like one's own newborn.

1.1. Proper care of the newborn

The category is composed of three sub-Categories: the challenge of proper care of the newborn, the challenge of defects in care of the newborn, and attention to relieving pain of the newborn.

According to nurses, proper nursing care, attention to relieving the newborn's pain, and defects in taking care of were the main challenges. Nurses were sensitive to infant care, or in other words, infant care was highly sensitive.

One of the participants (nurse # 2) stated:

"Massaging the newborn or lubricating the skin is not ordered by the doctor, but we occasionally do it when we see kid's skin is dry: for example, we wash the newborn when he is hospitalized for a long time and has dirty odor, or we wash, dry, and place them in their place if they do not have IV. We do things of this kind, even though they might not be in our job description. However, we do them because they are important for the newborn."

Another participant (nurse # 12) about relieving the pain of the newborn stated:

Usually, when a newborn has pain, I do some things to relieve him, for example, I swaddle them or put some mellitus to their mouth, and for the ones who are under the device and have pain, we ask the doctor to order fentanyl or phenobarbital to relieve them."

Experiences stated by the participants show that caring for newborns always needs accuracy and high sensitivity and this creates challenges related to care for newborns. On the other hand, it is necessary to pay special attention to relieve newborn pain.

1.2. Care with love

This category is composed of two sub-Categories of the challenge of affectionate behavior with love in working with newborns and having attachment and dependency to newborn. In general, the nurses stated that, it is necessary to feel good and have loved while caring for the newborns, and some believed that, one should consider the newborn as own child.

One of the participants (Nurse # 7) stated:

"Some say that working with newborns is hard but it is not difficult for me, so I would love to work with interest, although sometimes working pressure is so high and we do not even have a second opportunity to sit down. Working

in ICUs is generally difficult, but I love it. If I have a break for some days I miss my job."

One of the participants (Nurse # 1) stated:

You have to be very gentle with the newborn. You should think of it as your own kid. You should give its milk on time, you should not let its blood sugar drop, do not let pressure drop, skin care especially for premature infants, they should not be exposed to light, we usually make here dark because when the lamps are on they get shocked and jump up and it makes us sad.

Nurses in NICUs considered the infant like their own child and after some time working with them, they became dependent on them that challenges their taking care of newborns.

One of the participants (Nurse # 2) in this regard stated:

For about one month, it was difficult to work with them, but later, it became normal, so that if I am on break for some days I call and ask how the newborns are in the unit (with a smile). I love working with newborns with all its difficulties. This is so that if in rotation, they send me to work somewhere else I resign; I just can work with newborns.

2. The challenge to understand and deal properly with families of newborns:

The second theme of moral challenges of nurses is the challenge of understanding and dealing properly with families of newborns. The theme is composed of two categories of the conflict in dealing with newborns' families understanding and empathizing with the family of the newborn.

2.1. Having contradiction in dealing with the newborn's family

Nurses felt bad in dealing badly with the newborn's family and had even a sense of guilt. They have sometimes challenged due to dealing with unenforceable requests from the family of the newborn, but they knew that they should have proper treatment with their families.

One of the participants (nurse # 5) stated:

It rarely happens that I might even disagree with many of the things that mothers do, but I tell them that as here NICU and infection control is very important and they should not bring anything from outside. We sometimes even ask the mothers to be with the newborn or if they want to give something to the newborn, we oppose even if they insist we do not let them. It rarely happens that they bring something and ask us to give it to the newborn even when they know we do not lie, but again we explain so that they are convinced that it is for their own benefit. However, if they are not convinced at all, we ask them to put it in the closet or near the newborn but not touch the newborn.

One of the participants (nurse # 11) stated:

I feel sad myself, but I tell them not to be upset with me. However, it is not correct you cannot give them anything

even a drop of water. You cannot do it to yourself. If you want the health of your newborn, this is what you should do. Now, she has to decide whether to listen or not. I have seen some mothers that in a hidden way.... For example, you say your newborn cannot drink milk, but when they see another mother is feeding the newborn, they go and do it in a hidden way. Moreover, when you say why? She says because she did, and when you explain, they are convinced.

One of the participants (nurse # 8) stated:
See, for example some people bring Zamzam water. The truth is that we oppose that, because it is a newborn anyway, you cannot give anything you do not know what it is, and we do not accept responsibility. Some bring Koran and prayer and put them over their head. Some of our colleagues say take them away we do not let you put them here. However, I myself say there is no problem. Put it near his sheet so that it is not around because we want to change the sheets and do other things, but placed over the sheet there is no problem.

2.2. Understanding and Empathy for the families of newborns

Nurses believed that the family and the conditions of the infant should be understood, but due to the crowding of the unit and inconsistency of newborns' status and the number of nurses, sometimes they could not establish proper communication with the family. The nurses liked to give the newborn's good news of recovery and have a good treatment with the family, but sometimes the newborn's condition did not improve and it was a challenge to the nurses.

One of the participants (nurse # 4) stated:
Well, since I am myself an emotional person and I have a small kid, I sympathise with the families. Well, when someone is sick and in the hospital yard, there is a lot of stress on it. Now, imagine a mother that after birth is in the hospital instead of house for one or two months, you know what feeling she gets. Instead of going home and being cared for, you have to stay in the hospital. This is no good feeling.

One of the participants (nurse # 8) stated:
It happens that for example, a mother says something that is difficult to accept, but I myself control myself as far as possible. I may get sad but I do not want to make the mother sad. This is my behavior; I try not to make mothers sad even if I am myself because their condition is special.

3. Challenges of professional skills and nursing morals:

This theme is composed of two categories of professional skills of nurses and nursing moral properties with four sub-categories. Participants in this study believed that nurses need knowledge and experience to work with the newborn. Moreover, they believed that each of these skills (knowledge and experience) alone cannot guarantee the success of nurses in neonatal care, and moral principles should be considered.

3.1. Professional nursing skills

This category is composed of two sub-categories: the challenge of having experience and expertise in working with newborns and the importance of accuracy and speed in working with newborns.

Participants believed that working with newborns primarily requires high precision in the care of the newborn and then having a high speed in dealing with this sensitive segment. On the other hand, newborn care requires knowledge, experience, and work experience in working with children. One of the participants (nurse # 6) stated:

Having knowledge and experience are both important. We have colleagues who are masters of neonatal intensive care and some others like Ms....with experience and good knowledge and it rarely happens that someone is like this, for example, our experienced veterans only have 15 years of work. I can surely say that many of our nurses do not have enough experience. I mean they do something routine for 15 or 20 years and their experience is just the years they have done something. But there was a nurse who was very knowledgeable and she studies a lot. She loves to learn and train new things, and we have the ones with high degrees but not enough experience, so both knowledge and experience are important.

One of the participants (nurse # 1) stated:
"I think a man should be calm and sedate to work with the newborn and for reducing challenges, accuracy should go up. Accuracy should go higher, and you should think the newborn is your own. This newborn you are working with needs love and your accuracy should be fairly good."

One of the participants (nurse # 1) stated:
"Speed of a nurse working in NICU is very important because, for example, a moment of ignorance leads to hypoxia of the newborn and finds thousands complications."

3.2. Moral characteristics of a nurse

This class is composed of two sub-categories: conscience in taking care of newborns feeling guilty while doing a painful procedure for the newborn. Results showed that the participants believed that their conscience in infant care is of paramount importance.

One of the participants (nurse # 3) stated:
Infant nurse should have good conscience, be caring and compassionate as features that all nurses have plus the features nurses working in NICU have.

One of the participants (nurse # 12) stated:
"There are many times that things depend on your own conscience, for example, to change the newborns' position once or ten times in your shift, many places' symptoms show what you have done? But not in many places, sensitivity of newborns are high because a newborn is an oppressed defenseless creature and our conscience is so much involved in working with newborns."

Participants believed that while performing painful procedures for infants and unintentional injuries, they severely feel guilty.

One of the participants (nurse # 2) stated:

Yes, well while venepuncture and blood sampling I try once or eventually twice if not possible, I call a more experienced colleague, because I really take punishment with a newborn suffering.

As participants' statements showed, nurses in the care of newborns in NICU face many challenges and to improve the quality of care of the newborn and reduce the potential distress of nurses in the above units, special attention should be paid to these challenges.

Discussion

The findings of this study showed that nurses in NICU are faced with different moral challenges. These moral challenges are in three categories: the challenge of proper care with love, challenge of understanding and dealing properly with newborns' families, and challenge of professional and moral skills of nurses.

The first theme of the above study was "the challenge of proper care with love," which is composed of two categories: "proper care of the newborn" and "taking care with love."

Nurses see newborn care as very sensitive and emphasize that proper care of the newborn should be done and any nursing care for newborn should be done with love and if proper care was not done with love, they were morally challenged. Impairment in nursing care of the newborn due to nursing labor shortages and lack of resources and equipment impairment is a factor contributing to newborn care defect, which is one of the most frequent challenges in the care of newborns. In one study, it was cited that nurses of infant care unit have high levels of moral distress during treatment and loss of newborn. This distress worsens when nurses feel the care provided for the newborn has not been the best care. Providing palliative care at the end of life may reduce some of this distress. There are a few barriers to palliative care. The first obstacle is lack of NICU staff training in the correct definition and use of comfort care at end of life. The existence of a palliative care program is essential because it leads to kind communication with family and reduction of moral distress for nurses and providing quality care for newborns (12). In a study in the field of life dilemmas and moral distress in care system, it mentioned that many moral dilemmas could be because of shortage of nurses' time. Nurses noted that while they want to devote more time to patients, they do not have enough time to do it. On the other hand, the work of nurses is so much (3).

In this study, when caring for infants, nurses had good feelings and cared for the newborns with love. They preferred working in the neonatal unit to other units, and although most of the participants were single and thus had

no newborns, they were interested in taking care of infants. However, in several studies, it is suggested that moral distress may have negative effects on job satisfaction and lead to job burnout and intention to leave the job by the treatment team (2, 3) and nurses working in intensive care units have moderate to severe levels of moral distress (1). In the present study, despite the moral challenges, nurses did care of the newborn with love. A basic premise is that health-staff preserve work values and when faced with moral dilemmas try to solve them (3).

The second theme of moral challenges of nurses is the challenge of understanding and proper dealing with the family of the infant. This theme includes two categories: conflict in how to deal with the family of the newborn and understanding with newborn family. This challenge means that nurses feel bad about dealing badly with families in coping with the demands of the family of the newborns, which were contrary to the newborn's health and caused challenged the nurses and they believed that the family of the newborn should be dealt with appropriately. The existence of these challenges in nurses studied showed to what extent they try to act Patients' Bill of Rights.

In the study by Cavaliere, one of the moral distresses faced by nurses in NICU was continuing infant treatment at the request of the family even when not in favor of newborn (9). NICU is an environment with a lot of moral challenges and the issues related to resuscitation and treatment of very premature newborns. The philosophy of care of such infants is different in different countries among physicians and medical centers and can cause challenges in the care of newborns (13). In the study by Brosig, parents referred to the importance of care of the employees of them such as taking care of their newborns (14). Relationship with empathy can be pivotal for effective communication between nurse, newborn, and his family (15). The findings of the present study are in line with the findings of these studies.

The third theme of our research was professional and moral skills of nurses. This theme includes has two categories of professional skills and moral skills of the nurses. These challenges show that nurses in this study believed that to work with newborns, nurses need enough knowledge and experience. This is while they believe that each of these skills (knowledge and experience) alone cannot guarantee success of nurse in dealing with and caring for the newborns. Moreover, according to the nurses, fear and stress at the beginning of working with newborns has always been there, but with the passage of time, one can gain the skills and experience of working with newborns and with greater work experience, one can be more compatible with the environment. However, seeing the agony of a newborn when performing invasive procedures and lack of palliative care guide of nurses in terms of whether what they do is correct or not is a challenge. In a study conducted on the moral challenges experienced in providing nursing care at the end of life in nursing homes in Norway, the lack of competence in the care of the patient has been referred to as one of the moral challenges.

Unnecessary medical orders for testing and treating in newborn, such as increasing the dose of a sedative by doctors for fear of death of the newborn, not relieving the suffering of newborns, preparing a child dependent on ventilator for placing gastrostomy tube, extensive measures to save the patient while only prolonging death, prescriptions for unnecessary tests, and treatment for a terminally ill child were of the moral challenges reported in a study (9).

In the study by Elpern et al. conducted on 28 nurses working in intensive care units, the results showed that nurses often experience moral distress. The greatest source of moral distress among nurses was providing aggressive care for patients in whom they did not expect recovery was regarded as futile care. Moral distress was associated with years of experience in nursing. Nurses argued that moral distress could have negative effects on job satisfaction, psychological and physical well-being, body image of self, and spirituality. The nurses who worked in intensive care units had moderate to severe levels of moral distress. Situations with the greatest distress were when life was long, or at the time of aggressive actions (1). As the results of various studies show, moral challenges of nurses are different in the care of patients in different situations. It should be noted that most cases referred to in research were obtained through quantitative research, but the results of the present study have been achieved through qualitative method, so it is recommended that in studying moral challenges, NICUs must be considered.

Conclusion

Results of this study showed that nurses working in NICUs face challenges in the care of newborns. Overall, the challenge of defects in newborn care were due to nursing workforce shortage, lack of facilities and equipment, caring for newborns with love, good feeling of nurse in working with newborns, the importance of empathy with the newborn mother and family, the challenge of coping with the request of the family of the newborn while in violation of infant health, the importance of conscientiousness in caring for newborn, and creating feeling of guilt in the nurse when performing painful procedures for the newborn are the most important moral challenges nurses face in the face of newborns admitted to the intensive care unit.

In general, it can be concluded some of the challenges mentioned like "moral characteristics of nursing" can be associated with individual and professional features of the nurse and others like "the challenge of defects due to labor shortages in nursing care" or "lack of resources and equipment in impairment for infant care," which implicitly affect performance in nurses, are beyond the control of nurses. Challenges such as "challenge of understanding and proper dealing with family of the newborn" are due to the lack of attention to family-centered care.

Thus, we suggest that special attention should be paid to moral challenges faced by nurses in order to prevent moral distress by taking into account the appropriate educational

program, change of attitudes of nurses, providing facilities and equipment needed, and emphasis on family-centered care facilities and equipment.

Limitations of the study

One limitation of this study is conducting the research in a particular area. Another limitation is all participants were female.

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A Study of the Effects of Factors Related to Food Consumption in Health Workers of Najaf Abad-based Healthcare Centers, Isfahan, Iran

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Abstract

Introduction & Objective: The present study aimed to investigate the effects of factors related to food consumption (demographic, culture and customs, awareness, and attitudes) in health workers of Najaf Abad-based healthcare centers, Isfahan, Iran, in 2012.

Methodology: In this cross-sectional study, 167 health workers participated. The sampling method was simple random sampling, which was conducted through tables of random numbers. The acceptable inclusion and exclusion criteria were the interest of all healthcare personnel working in Najaf Abad-based healthcare centers to participate in the study, and there were no other criteria. For data analysis, the descriptive statistics and regression analysis were used. Additionally, the SPSS Statistics Software Version 18.0 was utilized.

Findings: The results of the present study revealed that the bread and cereal group had the highest mean of consumption in employees (4.4 ± 9.1). Moreover, it was demonstrated that the factors affecting the consumption of bread and cereals were as follows: attitudes, and customs, spouse employment, monthly income, head of the household, age, marital status, and family size ($p < 0.05$).

Conclusion: Nowadays, multiple data sources publish and educate on nutrition in which unscientific and contradictory nature of the sources causes confusion, thereby leading to making wrong decisions. Education was also a factor influencing food choices in employees. Therefore, coordinating training with the level of education is a major factor that should be considered for proper planning. Therefore, it is suggested that the underlying factors be recognized before education in advance to improve nutrition and prevent diseases caused by malnutrition.

Key words: Food Consumption, Health Workers, Health Network.

Introduction

In today's world, people's lifestyles have undergone massive changes, from traditional to industrial modes of living. In addition, due to various developments in food supply, people's access to a variety of industrial and processed foods has increased. These foods are usually high in calories and low in nutritional value, not to mention, a significant percentage of women and men are employed, and this situation has not allowed them enough time to prepare their own food at home, thereby having a propensity for fast foods and processed foods.

On the other hand, the statistics reported in nutritional studies indicate that obesity, overweight and their related diseases, such as cardiovascular diseases and diabetes, are highly prevalent in societies. For example, the results of a study conducted by Tadayan (2008) revealed that 40% of the population under study had obesity and overweight problems in Najaf Abad County, Isfahan, Iran. The results also demonstrated that 45-50% of workers and employees were overweight or fat (1).

Overweight and obesity-related illnesses are prevalent, too. According to the statistics collected in 2011, the cardiovascular, cancerous and metabolic diseases were the first, second and fourth causes of death in Najaf Abad County, Isfahan, Iran (2).

According to the reports presented by the department of non-communicable diseases of Najaf Abad-based healthcare centers in 2011, there were 418 and 915 patients with diabetes and blood pressure, respectively (3).

Additionally, the results of a study done by Dastanpour et al. (2006) revealed that 30% of the inhabitants of Isfahan Province, Iran, were overweight, 10.4% were fat, and 3.1% were obese. According to the same survey, 5.5% of the population under study had high blood pressure and 17% had a history of diabetes. The results of this study also demonstrated that the average cholesterol measured 190, and 62.7% of the population

under study had cholesterol levels equal to or greater than 200 (4), which were caused by obesity, overweight and related diseases (e.g., diabetes, high blood pressure, increased blood fat, cardiovascular diseases, and cancer), sedentary lifestyle and poor intake of food groups.

Therefore, many factors play efficacious roles in food choices. More to the point, the results of various studies in this respect are indicative of the fact that people do not follow suitable patterns in food consumption, and employees are among the groups in which the prevalence of malnutrition is significantly high and their food patterns are not suitable.

In a study performed by Afrouzian et al. (2006), the knowledge of cardiovascular patients and the employees of Arak-based healthcare centers, Markazi, Iran, about healthy nutrition was investigated, and the results revealed that doctors and nurses' knowledge about the oil consumption measured 86.7% as opposed to 74.2% in health experts. Further, the results indicated that the percentage of the consumption of protein sources and oilseeds, fruits and vegetables were as follows respectively: doctors (81%, 48%, and 98%), nurses (73%, 30%, and 75%), and health experts (83%, 45%, and 98%) (22).

In another study on the knowledge and performance of female health workers in Flaverjan County, Isfahan, Iran, the results showed that 61% of the employees did not know how much they had to eat, and 27%, 33% and 65% of them did not eat breakfast, dinner and snacks, respectively. Furthermore, the results revealed that 44.4% and 59% of the participants in the study did not eat main courses and snacks, respectively (23).

In a study conducted about the food consumption patterns of employees at Tabriz University of Medical Sciences, Rastibrojani et al. (2008) found out that the patterns were not appropriate, and there were significant differences between the male and female employees in terms of the consumption of grains, liver, biscuits, pasta, ice cream, milk, walnuts, pepper, pomegranate, and peach. In this study, it was suggested that necessary measures be employed to improve the eating habits of the male population (24).

Compared to other groups in society, health workers had better nutritional information because they took training courses on this issue every year. Thus, according to the observations and interviews that I had with health workers and given the prevalence of problems and concerns for nutrition in this group and the role of nutrition in the development of chronic diseases, we decided to study food groups in health care workers because employees are the custodians of public health. Therefore, the present study aimed to investigate the effects of factors related to food consumption (demographic, culture and customs, knowledge, and attitude) in health workers of Najaf Abad-based healthcare centers, Isfahan, Iran, in 2012.

Methodology

In this cross-sectional study, 167 health workers participated. The sampling method was simple random sampling, which was conducted through tables of random numbers. The acceptable inclusion and exclusion criteria were the interest of all healthcare personnel working in Najaf Abad-based healthcare centers to participate in the study, and there were no other criteria. The sample size was calculated through the following formula, in which the confidence coefficient measured $s=1.96=96\%$, and $s=0.18=d$.

The data collection tool was a self-made questionnaire that included the following sections: 1) demographic characteristics, 2) culture and customs, 3) awareness, 4) attitudes, and 5) information on food intake. To assess the validity of the questionnaire, a group of five nutrition experts was consulted. Moreover, to assess the reliability of the questionnaire, it was distributed among 30 members of the target population and their information was collected. Further, the reliability of the questionnaire was confirmed using the Cronbach's alpha coefficient ($\alpha=0.75$). For data analysis, the descriptive statistics and regression analysis were used. Additionally, the SPSS Statistics Software Version 18.0 was utilized.

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Findings

Table 1: Consumption of Food Groups by the Health Workers of Najaf Abad-based Healthcare Center in 2012 Based on the Consumed Units per Day

Row	Food groups	Maximum Consumption by Employees	The Maximum Recommended Intake	Mean \pm STDEV	Confidence Interval of 95%	Number of Participants
1	Bread and cereals	28.8	12	9.1 \pm 4.4	8/4 – 9/8	167
2	Milk and dairy	15.1	3	1.8 \pm 1.6	1.6– 2	167
3	Fruit	20.8	3	3 \pm 3.4	3– 3.7	167
4	Vegetable	6.1	5	0.9 \pm 1	0.9– 1	167
5	Meat	38.9	3	6.2 \pm 4.7	5.5– 6.9	167
6	Oil	61.7	10	7.3 \pm 7.6	6.3– 8.5	167
7	Sugar	114.6	5	9.0 \pm 14	7.4– 11.4	167
8	Fast Foods (Consumption per Month)	28.6	1	4.6 \pm 5.6	3.9– 4.7	167
9	Restaurant Foods (Consumption per Month)	4	1– 4	0.6 \pm 0.7	0.6– 0.69	167

Table 2: The Major Factors Influencing the Consumption of Bread and Cereals in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.1	0.24	0.049
2	Gender	0.2	0.02	0.9
3	Marital status	1.5	0.20	0.08
4	Place of residence	1.5	0.08	0.47
5	Family size	0.3	0.03	0.002
6	The head of the household	0.2	0.12	0.57
7	Monthly income	0.4	0.04	0.68
8	Education	0.3	0.09	0.43
9	Spouse Employment	0.2	0.04	0.73
10	Ranking of nutrition in household budget	0.3	0.10	0.33
11	Nutrition budget	0.1	0.06	0.55
12	Source of nutritional information	1.2	0.09	0.34
13	Employment of the person in charge of cooking	0.2	0.11	0.45
14	Culture	1.2	0.03	0.049
15	Awareness	5	0.11	0.9
16	Attitude	0.3	0.003	0.08

The five primary factors that were effective in the consumption of bread and cereals were as follows: attitudes, culture, spouse employment, monthly income, head of the household, age, marital status and family size. These factors significantly correlated with the consumption of bread and cereals.

Table 3: The Major Factors Influencing the Consumption of Milk and Dairy in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.018	0.49	0.084
2	Gender	0.60	0.43	0.16
3	Marital status	0.040	0.72	0.04
4	Place of residence	0.11	0.89	0.01
5	Family size	0.27	0.16	0.16
6	The head of the household	0.03	0.91	0.02
7	Monthly income	0.13	0.57	0.06
8	Education	0.34	0.16	0.17
9	Employment of the wife	0.12	0.78	0.03
10	Ranking of nutrition in household budget	0.01	0.90	0.01
11	Nutrition budget	0.12	0.54	0.07
12	Source of nutritional information	0.06	0.25	0.11
13	Employment of the person in charge of cooking	0.78	0.21	0.18
14	Culture	0.25	0.47	0.07
15	Awareness	0.20	0.64	0.05
16	Attitude	0.91	0.81	0.02

The five primary factors that were effective in the consumption of milk and dairy were as follows: employment of the person in charge of cooking, education, gender, family size, and source of nutritional information. These factors significantly correlated with the consumption of milk and dairy.

Table 4: The Major Factors Influencing the Consumption of Sugar in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.079	0.65	0.05
2	Gender	4.6	0.36	0.19
3	Marital status	12.7	0.12	0.19
4	Place of residence	7.1	0.20	0.14
5	Family size	0.54	0.68	0.04
6	The head of the household	1.11	0.52	0.14
7	Monthly income	0.30	0.85	0.02
8	Education	1.45	0.37	0.109
9	Employment of the wife	0.52	0.86	0.023
10	Ranking of nutrition in household budget	0.19	0.73	0.037
11	Nutrition budget	1.26	0.34	0.11
12	Source of nutritional information	0.39	0.27	0.11
13	Employment of the person in charge of cooking	1.06	0.80	0.038
14	Culture	0.18	0.93	0.008
15	Awareness	2.22	0.44	0.82
16	Attitude	2.33	0.37	0.97

The five primary factors that were effective in the consumption of sugar were as follows: attitudes, awareness, marital status, gender, place of residence, and the head of the household. These factors significantly correlated with the consumption of sugar.

Table 5: The Major Factors Influencing the Consumption of Fruits in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.10	0.009	0.30
2	Gender	1.66	0.16	0.27
3	Marital status	0.80	0.67	0.04
4	Place of residence	0.73	0.57	0.06
5	Family size	0.83	0.007	0.29
6	The head of the household	0.40	0.31	0.20
7	Monthly income	0.46	0.90	0.01
8	Education	0.67	0.86	0.02
9	Employment of the wife	0.03	0.96	0.006
10	Ranking of nutrition in household budget	0.17	0.18	0.13
11	Nutrition budget	0.39	0.20	0.13
12	Source of nutritional information	0.08	0.29	0.09
13	Employment of the person in charge of cooking	0.80	0.41	0.11
14	Culture	0.41	0.45	0.07
15	Awareness	1.13	0.09	0.16
16	Attitude	0.31	0.59	0.05

The five primary factors that were effective in the consumption of fruits were as follows: age, family size, gender, the head of the household, and awareness. These factors significantly correlated with the consumption of fruits.

Table 6: The Major Factors Influencing the Consumption of Vegetables in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.024	0.122	0.18
2	Gender	0.29	0.52	0.13
3	Marital status	0.41	0.56	0.06
4	Place of residence	0.007	0.98	0.002
5	Family size	0.16	0.16	0.16
6	The head of the household	0.09	0.56	0.12
7	Monthly income	0.25	0.07	0.20
8	Education	0.20	0.16	0.16
9	Employment of the wife	0.13	0.61	0.06
10	Ranking of nutrition in household budget	0.11	0.82	0.02
11	Nutrition budget	0.24	0.04	0.23
12	Source of nutritional information	0.004	0.90	0.01
13	Employment of the person in charge of cooking	0.07	0.84	0.02
14	Culture	0.14	0.49	0.06
15	Awareness	0.15	0.56	0.06
16	Attitude	0.056	0.81	0.02

The five primary factors that were effective in the consumption of vegetables were as follows: nutrition budget, monthly income, age, family size, and education. These factors significantly correlated with the consumption of vegetables.

Table 7: The Major Factors Influencing the Consumption of Fast Foods in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.07	0.42	0.09
2	Gender	2.61	0.33	0.20
3	Marital status	6.19	0.15	0.17
4	Place of residence	2.32	0.43	0.09
5	Family size	0.38	0.57	0.06
6	The head of the household	0.29	0.75	0.07
7	Monthly income	0.86	0.30	0.12
8	Education	0.15	0.85	0.023
9	Employment of the wife	0.53	0.73	0.04
10	Ranking of nutrition in household budget	0.05	0.85	0.02
11	Nutrition budget	0.41	0.55	0.07
12	Source of nutritional information	0.04	0.83	0.02
13	Employment of the person in charge of cooking	0.42	0.84	0.029
14	Culture	0.82	0.94	0.007
15	Awareness	1.72	0.26	0.12
16	Attitude	1.63	0.23	0.13

The five primary factors that were effective in the consumption of fast foods were as follows: education, gender, marital status, monthly income, and awareness. These factors significantly correlated with the consumption of fast foods.

Table 8: The Major Factors Influencing the Consumption of Restaurant Foods in Health Workers of Najaf Abad-based Healthcare Center in 2012.

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.009	0.39	0.09
2	Gender	0.33	0.26	0.22
3	Marital status	0.08	0.86	0.02
4	Place of residence	0.28	0.38	0.09
5	Family size	0.06	0.38	0.09
6	The head of the household	0.08	0.40	0.17
7	Monthly income	0.12	0.18	0.14
8	Education	0.02	0.82	0.02
9	Employment of the wife	0.12	0.50	0.08
10	Ranking of nutrition in household budget	0.03	0.25	0.11
11	Nutrition budget	0.11	0.12	0.17
12	Source of nutritional information	0.027	0.20	0.12
13	Employment of the person in charge of cooking	1.21	0.22	0.17
14	Culture	1.32	0.18	0.13
15	Awareness	1.60	0.11	0.16
16	Attitude	0.42	0.67	0.04

The five primary factors that were effective in the consumption of restaurant foods were as follows: gender, the head of the household, nutrition budget, employment of the person in charge of cooking, and awareness. These factors significantly correlated with the consumption of restaurant foods.

Table 9: The Major Factors Influencing the Consumption of Meat in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.10	0.009	0.30
2	Gender	1.66	0.16	0.27
3	Marital status	0.80	0.67	0.04
4	Place of residence	0.73	0.57	0.06
5	Family size	0.83	0.007	0.29
6	The head of the household	0.40	0.31	0.20
7	Monthly income	0.46	0.90	0.01
8	Education	0.67	0.86	0.02
9	Employment of the wife	0.03	0.96	0.006
10	Ranking of nutrition in household budget	0.17	0.18	0.13
11	Nutrition budget	0.39	0.20	0.13
12	Source of nutritional information	0.08	0.29	0.09
13	Employment of the person in charge of cooking	0.80	0.41	0.11
14	Culture	0.41	0.45	0.07
15	Awareness	1.13	0.09	0.16
16	Attitude	0.31	0.59	0.05

The five primary factors that were effective in the consumption of meat were as follows: family size, age, culture, awareness, and education. These factors significantly correlated with the consumption of meat.

Table 10: The Major Factors Influencing the Consumption of Oil in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	0.02	0.83	0.024
2	Gender	2.6	0.41	0.16
3	Marital status	2.4	0.63	0.05
4	Place of residence	2.8	0.42	0.08
5	Family size	1.4	0.08	0.19
6	The head of the household	0.69	0.53	0.13
7	Monthly income	0.81	0.41	0.09
8	Education	1.80	0.83	0.20
9	Employment of the wife	1.42	0.45	0.09
10	Ranking of nutrition in household budget	0.16	0.63	0.04
11	Nutrition budget	1.77	0.03	0.23
12	Source of nutritional information	0.49	0.03	0.21
13	Employment of the person in charge of cooking	4.46	0.09	0.23
14	Culture	2.17	0.15	0.14
15	Awareness	1.86	0.31	0.10
16	Attitude	0.73	0.65	0.04

The five primary factors that were effective in the consumption of oil were as follows: employment of the person in charge of cooking, nutrition budget, source of nutritional information, education, and family size. These factors significantly correlated with the consumption of oil.

Table 11: The Major Factors Influencing the Consumption of Foods (Total Calorie) in Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Factors	Non-standard Regression Coefficient	Sig.	Standardized Regression Coefficients
1	Age	23.2	0.096	0.20
2	Gender	45.2	0.913	0.023
3	Marital status	746.06	0.325	0.11
4	Place of residence	123.59	0.785	0.029
5	Family size	347.48	0.002	0.371
6	The head of the household	25.7	0.856	0.04
7	Monthly income	47.10	0.711	0.04
8	Education	52.76	0.688	0.048
9	Employment of the wife	89.8	0.711	0.049
10	Ranking of nutrition in household budget	7.07	0.875	0.016
11	Nutrition budget	7.00	0.488	0.08
12	Source of nutritional information	29.3	0.312	0.103
13	Employment of the person in charge of cooking	183.22	0.599	0.078
14	Culture	215.31	0.266	0.116
15	Awareness	132.76	0.571	0.06
16	Attitude	16.91	0.936	0.009

The five primary factors that were effective in the consumption of foods (total calorie) were as follows: family size, age, marital status, culture, and source of nutritional information. These factors significantly correlated with the consumption of foods (total calorie).

Table 12: The Role of Culture and Customs in Food Choice by Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Influence	Frequency	Percentage
1	Very much	85	50.9
2	Much	70	41.9
3	Average	2	1.2
4	Little	-	-

Table 13: Awareness of the Amount of Food Groups Consumed by Health Workers of Najaf Abad-based Healthcare Center in 2012

Row	Food Groups	True		False	
		Frequency	Percentage	Frequency	Percentage
1	Vegetables	104	61.2	63	38.8
2	Fruits	14	8.2	153	91.8
3	Meat	90	52.9	77	47.1
4	Bread And Cereals	64	37.6	103	62.4
5	Milk and Dairy	115	67.6	52	32.4
6	Fat and Oil	28	16.5	139	83.5

Discussion and Conclusion

The statistics announced by Iran's Institute of Industrial Research, Food and Nutrition have shown that the intake of fruits, vegetables, milk and meat in Iranian families is lower than the recommended limits, while the consumption of bread and cereals exceeds the recommended limits. For example, the intake of the following items exceeds the recommended amounts by the mentioned values: vegetables (2.8 units), fruits (one unit), milk and dairy (0.7 units), meat (1.8 units), bread and cereals (14 units), and other items (40%) (5).

Studying the risk factors of non-communicable diseases across Isfahan Province, Iran, in 2006 showed that the residents of this province ate one unit of fruit and 1.2 units of vegetables on average, and 90% of the population ate lower than five units of fruits and vegetables per day, while the minimum recommended intakes of fruits and vegetables were two and three units, respectively.

The results also indicated that 68.2% of the inhabitants of this province ate fish fewer than once per month. The results also revealed that 56.4% used vegetable oil as opposed to liquid oil consumed by 42% of the participants in the study (6). In another study, the relationships between awareness, attitudes and performance with fields of study and academic terms of students staying at the dormitories of Shahid Beheshti University of Medical Sciences were investigated. The results of this study demonstrated that all medical students had appropriate awareness about milk and dairy products, but their attitudes and other factors affected their consumption (9).

The availability of food can play effective roles in food choices. For example, in a study done by Jafari et al.

(2008), the results indicated that the availability of dairy products at home could be effective in their consumption (10). Rasti et al. (2008) showed that having enough time to prepare and consume foods was a major factor in choosing foods. In addition, it was shown that 44% and 59% of the health workers under study did not eat main courses and snacks, respectively (11).

In another study conducted by Rezazadeh et al. (2006), the results showed that unhealthy food patterns correlated with place of residence (North or South), ethnicity, age, education, monthly income, and the area of the house (12). In a study conducted by Shakerinejad et al. (2006), the results revealed that the food consumption patterns of students were dependent on family budget (13). In another study done by Peneaus et al. (2009), the effects of environmental factors on food intake and choice of beverage during meals were investigated in teenagers. The results of this study indicated that the monthly income, gender, parents' employment and men's participation in preparing meals played effective roles in this regard (14). The results of a study performed by Jilcott et al. (2009) revealed that watching T.V., listening to music when one is hungry and thirsty and eating alone or in a group were effective in food choices (15). In a study performed by Delvaj et al. (2007), it was shown that the availability of healthy and unhealthy foods in American schools and their economic, social and ethnic status played major roles in their food choices (16). Moreover, the social customs were reported as a major factor in food choices by the London Department of Health (17).

In a study done by Mckie et al. (1998), it was found out that food choices were different in urban and rural areas because there were more fast food restaurants and supermarkets in cities, and the circle of friends and colleagues as well as environmental factors were among

the effective factors (18). Additionally, lack of coordination between the nutritional education and available foods was also an important factor affecting food choices (19). The results of a study done by Waq & Mavoia (2006) revealed that lack of time management and friends and family members were among the most important factors influencing food choices (20). Afrouzian et al. (2006) found out that 60% of the population under study had adequate information about the consumption of fish, but due to lack of suitable groundwork to use their information, they did not have a desirable performance (21).

The results of the present study indicated that family size, age, marital status, culture and customs and sources of nutritional information were among the most important factors in choosing foods.

Awareness and attitudes have been reported as effective factors in food consumption in many studies. However, these two factors had trifling effects on food consumption because this group had better awareness and attitudes compared with other groups.

Rezazadeh et al. (2006) showed that unhealthy food patterns correlated with place of residence, ethnicity, age, education, monthly income and the area of the house (12). The results of the present study were consistent with this study in terms of the correlations between unhealthy food patterns and each of age, education, and culture and customs.

In many studies, it has been shown that social and ethnic status correlates with food intake. This finding is consistent with the results of the present study in which culture and customs correlated with food consumption. Moreover, the results of the present study showed that sources of nutritional information, marital status, employment of the person in charge of cooking and nutrition budget were among the factors that correlated with the consumption of certain food groups.

In households where both husband and wife work outside the home, access to healthy and fresh food items, such as vegetables and dairy products, become difficult. As the results of the present study indicates dairy and vegetable consumption in this group is lower than what is recommended because they do not have enough time to prepare their own healthy meals. Hence, the forgoing items should be taken into consideration to improve the food consumption pattern in this group, and appropriate planning should be made in this respect.

Culture and ethnic and local customs and inadequate financial and economic conditions in crowded and densely populated families, poorly planned and insufficient household budgets are some of the factors that should be taken into account in interventions and improving the nutritional patterns. Increasing age and declining physical and financial power are other major factors that affect the food consumption of health workers.

The results of the present study showed that the consumption of meat, fast foods, sugar and oil was higher than the recommended limits. The results of the present study was consistent with the results of other studies in terms of the consumption of fast foods, sugar and oil, while these results were inconsistent with the results of other studies in terms of the consumption of meat because those who do not have the opportunity to cook food and do not have access to healthy food are forced to eat fatty and sugary foods which are easy to make. These foods usually have better appearance, tastes and shapes, and that is why they are chosen first. In this regard, the results of the present study demonstrated that one's culture and customs are major factors involved in choosing foods.

The source of nutritional information was another factor that was felt to be associated with food choices. In addition, the circle of friends and colleagues and rumors were other important factors in choosing foods. Nowadays, multiple data sources publish and educate nutrition whose unscientific and contradictory nature of the sources cause confusion, thereby leading to making wrong decisions. Education was also a factor influencing food choices in employees. Therefore, coordinating training with the level of education is a major factor that should be considered for proper planning. Therefore, it is recommended that the underlying factors be recognized before education in advance to improve nutrition and prevent diseases caused by malnutrition.

To improve the feeding pattern of Employees, the problems and issues that lead to the wrong selection of foods should be taken into consideration. To do so, careful planning is important, and the required interventions can be put into action based on the presented plans and solutions, thereby laying the groundwork for honing their performance in this respect. Further, it is suggested that similar studies be performed in other populations in order to avoid parallel work that causes confusion and discourages officials. If the foregoing items are considered in planning and interventions, achieving the ultimate goal, i.e., reforming the patterns of food consumption and reducing diseases caused by malnutrition, will be easier and faster.

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Restoration of Let-7: a possible approach for increased sensitivity to paclitaxel in ovarian cancer

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Abstract

Ovarian cancer is one of the common cancers of the female reproductive system. Paclitaxel is the first-line treatment of ovarian cancer and the second-line treatment of advanced ovarian cancer. Unfortunately, many patients cannot be treated because of drug resistance. miRNAs comprise a group of small non-coding RNAs 18-25 nucleotides in length that specifically interact with their own mRNAs. Many miRNAs that have so far been identified play a role in cancer. miRNAs regulate formation of cancer stem cells (CSCc) and drug resistance-associated epithelial-mesenchymal transition (EMT) phenotype. The let-7 miRNA is a founding member of the miRNA family and is conserved in invertebrates and vertebrates. In this review paper we have tried to describe a possible approach for increased sensitivity to paclitaxel in ovarian cancer by restoration of Let-7. In addition to suppressing tumorigenic activities and negatively regulating a number of oncogenes (Kras-Hras-HMGA2-c-myc-BF2), let-7 affects the main regulators of cell cycle, cell differentiation, and apoptosis pathway. Let-7 via RNA decomposition of the IMP-1 gene increased sensitivity to paclitaxel drug. Various compounds such as Isoflavone specifically can affect expression of

Let-7. Although let-7 is a potential therapeutic target for therapy resistant ovarian cancer, further studies should be conducted to investigate clinical use of let-7 to treat or suppress ovarian cancer.

Key words: miRNA, Ovarian cancer, Drug resistance, Let-7

Introduction

Today cancer as a deadly disease causes many problems for all of the people in the world. Ovarian cancer is one of the common cancers of the female reproductive system and one of the most life-threatening cancers such that it is the cause of over 50% of deaths due to gynecological cancers. At early stages, ovarian cancer is asymptomatic or its symptoms may be so vague that they cannot be detected by physician or the patient (1). There are many drugs for prevention and treatment of cancers such as ovarian cancer. Natural products such as medicinal plants have been used as one of the main resources for production of anticancer drugs (2-7). Paclitaxel as a natural compound is the first-line treatment of ovarian cancer and the second-line treatment of advanced ovarian cancer that prevents microtubule depolymerization in the process of cell proliferation. Hence, paclitaxel inhibits cell cycle. If ovarian cancer is diagnosed at early stages, treatment consists of surgery and chemotherapy. At advanced stages, chemotherapy is started as well, but unfortunately treatment may not be successful in many cases because of drug resistance (8) such that following surgery, combination chemotherapy (paclitaxel+carboplatin) is also used with an 80% response rate.

However, in most patients, unfortunately, recurrent cancer develops and the disease becomes resistant to chemotherapy after 18 months. Currently, the cell line NCI/ADR-RES, which has become resistant to paclitaxel, and the cell line OVCAR8, as control, are used to investigate resistance to ovarian cancer drugs in vitro. In this review paper we have tried to describe a possible approach for increased sensitivity to paclitaxel in ovarian cancer by restoration of Let-7.

miRNAs

miRNAs comprise a group of small non-coding RNAs approximately 18-25 nucleotides in length that cause destruction of mRNA and inhibition of its translation. miRNA genes comprise approximately 1% of the genome of different species. Each miRNA gene has hundreds of target genes. Over 2500 miRNAs have been identified in the human genome that regulate 30% of protein-coding genes. Most of these small regulatory molecules that were first identified in 1983 are located on Chromosomal fragile regions that are predisposed to removal, addition, chromosomal replacements, and epigenetic changes in different diseases such as cancer. miRNAs target several genes simultaneously such that the number of target genes may exceed 100 (9, 10). Since 2002, disruption of miRNA regulation has been found to be associated with cancer (11, 12).

miRNA biogenesis

miRNA in the nucleus transcribes the gene and produces primary miRNA (pri-miRNA). Then, Drosha creates a precursor called pre-miRNA under RNase III (endonuclease), and pre-miRNA is transferred to cytoplasm by exportin-5. This molecule is cleaved by an enzyme called

Dicer and produces a double-stranded sequence 20-22 nucleotides in length. One of the strands is degraded and the miRNA's, another strand, is loaded into RNA-induced silencing complex (RISC). This active complex targets the mRNA of interest and binds to the end of 3'-UTR mRNA, and exerts inhibitory effect. miRNA induces its effect in regulating gene expression through inhibiting the protein translation and decomposing the target mRNA (13).

miRNA and Cancer

Many miRNAs that have so far been identified play a role in cancer. Comparing tumor tissues with healthy tissues has indicated that miRNAs are located at fragile sites of the human genome and are likely to face gene deletion or duplication at chromosomal rearrangement. Besides that, it is possible that epigenetic mechanisms lead to inappropriate expression of miRNA genes and cause abnormal expression of miRNAs in tumor tissues leading to numerous changes in regulation of the target miRNA expression. Many miRNAs play no part in development of cancer. In contrast, certain miRNAs play an oncogenic role in cancer phenotype, and dysregulation of these miRNAs has been reported in a wide spectrum of cancers (14). Oncogenic miRNAs include miR-10b, miR-155, miR-21, and miR-17-92 (15), and out of repressive miRNAs, miR-26a, miR-335, and members of the families let-7 and miR-34 can be mentioned. Different miRNAs affect different stages of cancer. For example, miR-10b regulates metastasis and is highly expressed in advanced malignancies. Inhibition of miR-10b can prevent metastasis of cancer cells but has no effect on already developed metastases. Expression of miR-335 can prevent metastasis but cannot prevent proliferation of tumor cells and has no effect on cell apoptosis rate. However, some miRNAs can prevent proliferation of tumor cells and metastasis (16). miRNA expression has been reported to change (increase or decrease) in different human cancers (17, 18).

miRNA and chemotherapy resistance

Recently, some studies have found miRNA and chemotherapy resistance to be associated (19, 20). In recent years, considerable advancements have been made to figure out drug resistance mechanism in ovarian cancer consisting of drug efflux, changes in DNA repair pathway, apoptosis suppression, and epithelial-mesenchymal transition and cancer stem cells. However, more effective therapeutic purposes are still needed to improve overall survival rate and therapeutic strategies for ovarian cancer patients. miRNAs play a critical role in cell processes such as cellular differentiation, proliferation, and apoptosis. The recent discovery of miRNAs in cancer has offered new paths for research on basic mechanisms of response to chemotherapy. Besides that, several studies have demonstrated that certain miRNAs such as let-7 and miR-34a can affect response to chemotherapy in different types of tumors including ovarian cancer. Use of miRNAs to overcome resistance to treatment is being studied. This study investigated the role of let-7 in overcoming resistance to treatment through several molecular mechanisms and with emphasis on potential therapeutic uses.

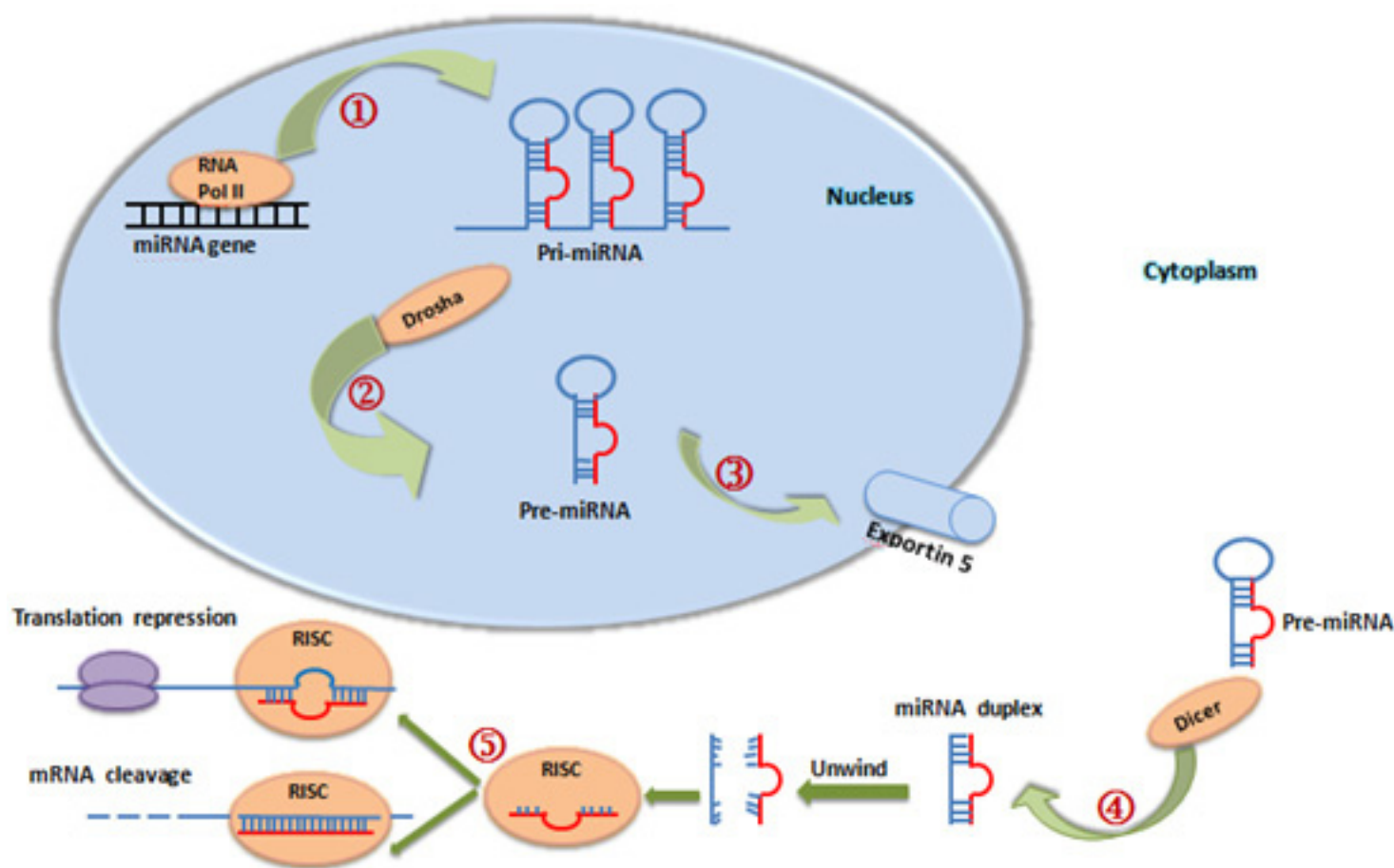


Figure 1: Biogenesis of miRNA: miRNA biogenesis is a multistep process. First, miRNA genes are transcribed by RNA polymerase II in the nucleus. The resulting primary transcript is cleaved by Drosha and DGCR8 to produce pre-miRNA. After exportin-5- and RanGTP-mediated transport to the cytoplasm, the pre-miRNA undergoes its final processing step, which consists of Dicer-dependent cleavage just below the stem loop to produce a duplex molecule. The duplex is then separated and usually one strand is selected as the mature miRNA and directed to target-specific mRNAs

miRNA Let-7

Let-7 is from a 13-member family localized on nine different chromosomes. An association between let-7 and drug resistance has been demonstrated. Recent studies have demonstrated that let-7 specifically affects 3-Urt-BCL-XL in hepatocellular cell line and let-7 high expression makes the cells susceptible to sorafenib (21). Since let-7 expression has been reported to decrease in many cancers, the changes in the expression of this miRNA are likely to be associated with chemotherapy resistance, but the data are scant in this field. Igf2 mRNA binding protein1 (IMP-1) is a drug resistance-associated protein and it has recently been demonstrated that IMP-1 level is associated with let-7 level. In fact, let-7 negatively regulates IMP-1 which in turn exerts protective effect on multi-drug resistance (MDR-1). Measuring let-7 in different cell lines indicated that the members of this family were co-regulated and co-expressed. Let-7 expression has been demonstrated to decrease before and after treatment with chemotherapy drugs, which is associated with increased production of IMP-1 and MDR-1.

Molecular mechanisms of chemotherapy resistance in cancer

Chemotherapy resistance develops molecularly via two pathways consisting of de novo or internal pathway through CSCs, and external or acquired pathways including genetic and epigenetic changes. However, the precise mechanisms of chemotherapy resistance generally have not yet been identified. In de novo pathway, limited drug absorption, increased efflux, and activated detoxification and in the second pathway, epigenetic changes such as DNA methylation-histone modification and mRNA regulation play part in drug resistance. For example, in colorectal cancer, the transcription factors AP2E and DKK4 undergo methylation changes that cause them to become resistant to fluorouracil. In ovarian cancer, the gene MLH1-TAP73 is hypermethylated and predisposed to acquiring resistance to d-azacitidine-hydralazine. miRNA deregulation has been demonstrated to be associated with cancer drug resistance. For example, in breast cancer, increased expression of miR-21 leads to trastuzumab resistance. In case of resistance to cisplatin in ovarian cancer, the expression rates of miR 376 and miR-214 increase and therefore it is necessary to study miRNAs so

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Potential mechanisms of let-7 action on ovarian cancer

Let-7 regulates CSCs and EMT formation which is associated with drug resistance (23, 24). Let-7 exerts regulatory effects on p53 (25). Let-7 negatively regulates MDR and indeed exerts effect on MDR1 indirectly through IMP1. Let-7 causes decomposition of mRNA related to IMP-1 which is both a target of let-7 and inhibits endolithic activity of MDR1 (26). In experimental studies, silencing the gene EZH2 has been demonstrated to cause decrease in cell proliferation, M-G2 arrest, and cell drug susceptibility. Increased expression of let-7 causes the expression of the gene EZH2 to decrease but it has not yet been discovered how this occurs. Let-7a, let-7b, and let-7c exert inhibitory effects on EZH2. Let-7 can also exert inhibitory or down-regulatory effect on CCND1. CCND1 is a member of the family of cyclins that affects cell cycle and its expression in tumors increases in cisplatin resistance (26). Studies have demonstrated that the expression of the common miRNAs that exist in most paclitaxel-resistant cell lines is associated with ovarian cancer. These miRNAs include miR: pre218-let-7e-130a-130b-pre204-0c-335-106-pre106, and let-7 (27). MS-PCR results have indicated that in chemotherapy drug-resistant cell lines, let-7-related CPG hypermethylation occurs in DNA in most cancers including ovarian cancer, and since one of the mechanisms of disrupted expression (deregulation) and decreased expression of let-7 is hypermethylation, then hypermethylation is likely to occur in ovarian cancer as well.

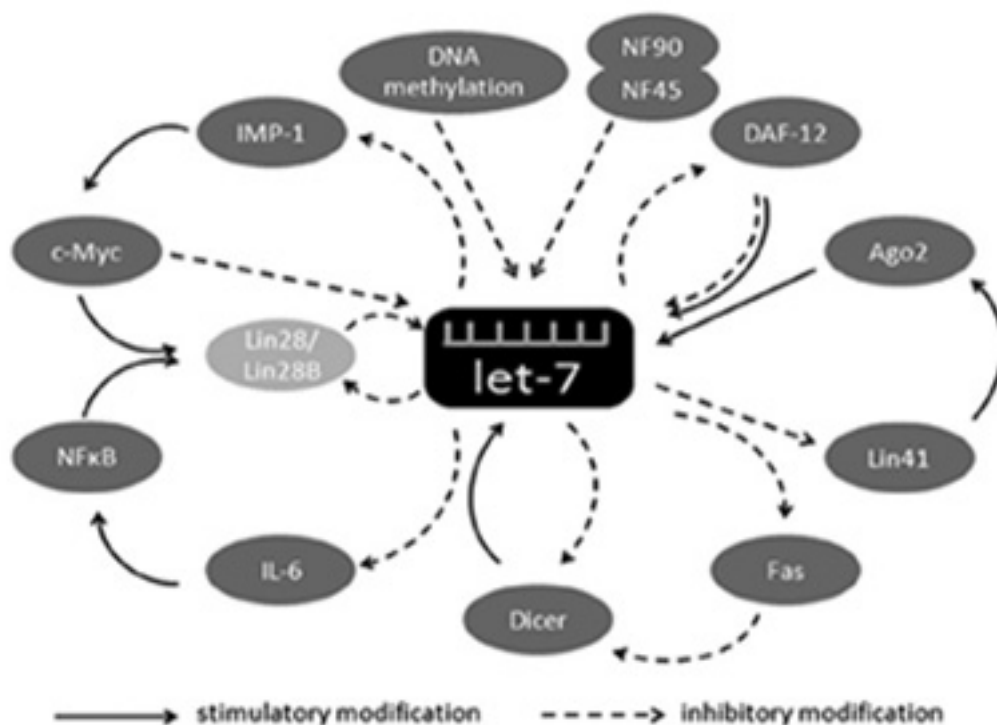


Figure 2: illustrates the mechanisms and factors that affect let-7. IMP-1 plays a role in drug resistance and inhibits its let-7. DNA methylation exerts inhibitory effect on let-7 (28).

Flavonoid's effect on let-7 expression

Recently, nature-based compounds such as isoflavone and DIM have been demonstrated to affect the expression of miRNAs including let-7 and can induce its expression; therefore, flavonoid's effect on paclitaxel transporters can be investigated in a resistant cell line, termed NCI/ADR-RES. Flavonoids affects miR-21 expression and increases its production, and causes increase in production of the molecules PTEN-PDCD4-RECK that progress the cell mainly toward apoptosis. Although no study has yet reported clinical use of these compounds, clinical trials at different phases are being conducted (25). Synthetic and/or nature-based compounds derived from plant flavonoids mainly target malignant cells. In neuroblastoma, the flavonoid and retinoid compound, called cyclincyc, can exert effect on miRNA with oncogenic role and miRNA with tumor-suppressing role (23). Since synthetic let-7 has limited use and is easily degraded, use of flavonoids to increase let-7 expression seems appropriate.

Conclusion

Introduction of miRNAs and their role represents a new level of controlling gene expression. Studies have demonstrated that disrupted regulation of miRNAs can be an important stage of progression in most cancers. Dysregulation of miRNAs can be due to genetic mutations or regulation at transcription level which are important mechanisms of increased expression of the target genes causing tumorigenesis. miRNA-based treatments are based on two bases; use of mimics miRNAs that is mainly conducted by miRNA replacement therapy and causes the expression levels of tumor-suppressing miRNAs (undergoing decrease in expression) to reach normal levels. The second approach is use of their antagonists which are mainly used to inhibit function of oncogenic miRNAs. A drug called AS1411 is from a group of compounds called G-rich aptamer. This drug acts via blocking production of oncogenic miRNAs in the cell whose expression levels increase in cancer. AS1411 inhibits a protein called nucleolin that plays an important role in miRNA maturation (29). In studies miRNA microarray, decreased expression of miR30C-miR130a-let7 was demonstrated to cause paclitaxel resistance and cisplatin. Moreover, let-7 inhibits certain oncogenic proteins such as Kras-Hras-HMGA2-c-myc-NF2. Studies have demonstrated that the removal rate of DNA in ovarian cancer is over 44% for Let-7a-3 and let-7b (30). In the near future, use of nanoparticle technology, particularly in cancer drug resistance, will facilitate use of let-7 and other miRNAs in treatment. Let-7 nanoparticle is being used In vitro (31).

Taken together, regarding the potential role of let-7 in paclitaxel resistance in ovarian cancer and that let-7 can suppress the expression of the genes involved in this cancer, let-7 has attracted attention as a potential therapeutic target in therapy resistant ovarian cancer. In addition to suppressing tumorigenic activities and negatively regulating a number of oncogenes (Kras-Hras-HMGA2-c-myc-BF2), let-7 affects the main regulators

of cell cycle, cell differentiation, and apoptosis pathway. Therefore, let-7 can be used to inhibit the expression of these genes and therefore therapy resistant cancer. Regarding the findings of recent studies, we can use increase in expression of let-7 using medicinal plants, or mimic production of it as a synthetic and transporting it into the cell to enhance treatment and control the growth of ovarian cancer, and mimic let-7 most probably can be used as an adjuvant drug in the treatment protocol for patients with paclitaxel resistance. However, this issue requires further investigation. Increase in Let-7 expression is expected to serve as an effective treatment for therapy resistant cancer. Although acceptable advancements have been made to figure out regulation of let-7 synthesis and role in signalling pathways, its regulation in cancer and normal cells, and mechanism of cell proliferation control and cell survival need further investigation. Further studies are needed to use let-7 in clinical settings to treat or suppress therapy resistant cancer.

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The First Electronic Immunization Registry System in Iran, Iranian Immunization Registry (IIR)

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Abstract

Introduction: A national immunization electronic registry system could improve Immunization levels. This system of immunization coverage facilitates shared experiences, information and specialized consultation. The aim of this study is to establish an immunization registry system in the Health- Therapeutic center in Shiraz city.

Method: The study type is to set up a method or academic-implementation system. The immunization software design and implementation was done in 2016 at one of the health centers in Shiraz city. The study population is the area covered by the health-Therapeutic center. The research tool, flow chart design and development of a data collection form were developed prior to making the immunization software.

Results: The main and important result of this research is construction and Setting up of electronic immunization registry software in accordance with country guidelines in 2016 (the latest guidelines). The software has three phases and stages including initial and daily actions by the vaccinator (cold chain control) before starting the process of

immunization, immunization registration of children under 18 years of age and immunization registration of adults (over 18 years), pregnant women and women of childbearing age.

Conclusion: The results showed that this web-based system includes the following attributes - timely immunization registration ability, report of vaccine adverse events, report of delayed cases, stocks of vaccine, requests and appropriate distribution of vaccine, ease of use of immunization and reducing parents' failure to follow the immunization and by the adoption of a coordinated and comprehensive system in the province and the country, the possibility to compare immunization coverage, report of shortcomings, problems and risks of immunization program are prepared.

Key words: Immunization, Electronic registry of immunization, Complications of immunization, Immunization coverage, Registry

Introduction

The expanded immunization program of WHO (World Health Organization) was considered to eradicate smallpox in 1974 (Katz, 1993). At that time, in accordance with the immunization program and time schedule of EPI (Expanded Program of Immunization) less than 5% of the world's children were vaccinated against diseases like tuberculosis, polio, diphtheria, tetanus, whooping cough and measles. By 1984, this figure rose to 25 percent (Hueston et al, 1994 and Kelley, 2006).

Vaccines are the greatest successes and achievements of biomedical sciences and public health, and represent one of the most effective means for the prevention of diseases (John, 2010). Continuous efforts to improve the effectiveness and safety of vaccines and vaccine coverage among all age groups will provide overall benefit of public health (Roush et al, 2007 and Zhou et al, 2001).

There are major and significant gaps in scientific research for a complete description of how the registers facilitate the most accurate effectiveness of the vaccine studies based on population. In addition, immunization information systems preparation of IIS (Immunization Information System) is a new field and it is under development and major restrictions such as the disappearance or loss of data, inaccurate data or the potential inability of unrealistic data have not been studied and explored fully (Adams et al, 2000 and Danovaro-Holliday et al, 2014).

However, without detailed information about immunization coverage, we lack the data for placing and initiating necessary systemic and programmatic changes to achieve national Immunization objectives (Morris et al, 2015, Lieu et al, 2015, Bates et al, 2003).

A computer and computer-based system is reliable for maintaining immunization records and a register presenting immunization dates and its reports are printable for parents and schools and they provide guidance for the time being and implementation of immunization program (Young et al, 2015). It provides clinically useful reports for children, teens and adults like report of vaccination coverage and next forecast immunization program of people is possible (Garrido et al, 2016, MacDonald et al, 2014).

All vaccines are registered and collected in the form of a system. Immunization records, and providing safe, accurate and updated immunizations are for children who have been referred to the service supply (Badgett and Mulrow, 2005). It provides a reminder list and tags to people who are delayed in keeping to the schedule. For children and patients who are overdue in their immunization, a reminder is sent and registration and reminders, keeps their immunization schedule up to date.

According to the above criteria we tried to implement the outlook for childhood immunization supply at public and private health centers in the form of electronic data registration based on immunization implementation authenticity with the benefit of new and updated information and

communication technologies with high accuracy at the individual level and the monitoring of data accuracy, facilitate immunization coverage and by developing of an immunization electronic system and shared experiences and information and expert advice, expand dramatically the immunization program and develop an important step in data management and implementation of health interventions at the local and national level and also an opportunity for education and research in this field. Therefore, the aim of this study is to establish an immunization registry system in selective health-therapeutic centers of Shiraz city.

Method

In this research, study type is to set up a method or academic-implementation system. The immunization software design and implementation was done in 2016 at one of the health centers in Shiraz city that is a subsidiary of the city health center (Engelab). It has the ability to expand to other health-therapeutic centers, health homes, public and private hospitals and link with headquarters of health center of the city and other provinces and cities of the country.

The method in the project consists of two phases. To start the process, first the flowcharts and guidelines were provided that were based on a program and immunization guide approved by the National Committee in 2016. The first stage started with the vaccinator, health workers or social workers who have responsibility for inoculation and injection of vaccine, and by controlling the cold chain, temperature of vaccine refrigerator and charting temperature, decide whether vaccine is to be kept at refrigerator temperature or not? Subsequent decisions would be taken (based on VVM and cold chain monitoring indicators) and entered into the beginning of immunization stages.

To initiate and carry out immunization, refrigerator vaccine inventory should control with full specifications of vaccines, including vaccine types, the number of vials, serial numbers, expiration date, factory or company of manufacture. Registration and layout of vaccine was conducted according to the National Committee and accordance with the type of person (children or adults), (new or duplicate), date of birth, gender, disease history, effect of the vaccine, an appropriate form is designed, selected and immunization process starts.

In this regard if the visitors have complications or adverse reactions to the vaccine, it can design and select an appropriate form in accordance with the drawn flowchart and based on the immunization process, which will continue. If the child is a delayed visitor, delayed forms would be designed according to child's age and national Committee guidelines, and the selection and immunization program continues. Also for patients older than 18 years (male or female), the form will be designed according to the immunization guidelines of the National Committee and having qualification, standard of selection and immunization will be done (hepatitis, Diphtheria-tetanus, MMR).

Thus, according to a steps summary of the outlined flowcharts, the data collection form was designed and developed. This form that was designed by the researcher, included variables such as vaccinator profile, vaccines important features, visitor specifications, information relating to child immunization, immunization of people over 18 years of age, pregnant women and women of childbearing age. This form was designed for age groups under 18 and over 18 years under the National Immunization Program Committee.

Our target registry population, is the area covered by the health center and people with the age group mentioned, Iranian and non-Iranian nationality and all the people who have moved to this area who have no immunization prohibition and are referred to health center with satisfaction (including children, adults of both genders, pregnant women and women of childbearing age). Explanations were given before completing the form for collecting data in compliance with health research ethics and informed consent of the visitor or parents to register their full details.

It should be noted that for design of the software, it is used first by searching for articles and resources of various databases from the countries which have electronic immunization registry program, because Iran has not have an electronic immunization registry program. The data collection form, collection samples form were separated and from target population until the initiation and progression stages of software development, at least 50 samples were collected for software testing (images as sample of the data collection form).

Table 1: Properties of vaccine

Table 2: Daily actions of vaccinator (Vaccine stock)

Table 3: Visited people Profile

Table 4: Type of visit

Figure 1: Visit due date and on time

The second step (build software) was based on the technical specifications of the registry immunization system. Registry System of the software is Web-based and it is designed and developed based on PHP server technology Version 5.6, MySQL database and HTML 5 world standard and Ajax technology. In this software, minimum hardware requirements are processor: 2x2GHZ, Memory: 4GB, storage space: 20GB for the OS + 500 KB for each data item.

Results

A major result of this research project was construction and setting up of electronic immunizations registry software according to the National Committee in 2016. The immunization data from 50 individuals were collected and developed in accordance with the data collection form, and entered into the software as a pilot and test. Entering data into the software was according to different criteria like the cold chain control, daily actions of vaccinator of refrigerator temperature controlled vaccine, full registration of vaccines information, and the immunization data of children under

18 years of age, their gender, the type of vaccine and also registration information of adults (over 18 years of age), pregnant women and women of childbearing age in terms of the type of vaccine used and information gathering. The software has three phases and stages: initial and daily actions of vaccinator, immunization registration of children under 18 years of age, immunization registration of adults (over 18 years), pregnant women and women of childbearing age.

Images of application performance: Figure 2, Figure 3, Figure 4.

Discussion

The collected data was entered into the software. During data entry we have concluded that, as data entry to the software is needed to complete information, this is contrary to the manuscript notes and paper, which can be changed at any time and line correction and the noted information, is not complete (Kolasa MS et al, 2006). On the other hand, with the lack of a coherent system, each person's immunization program had an immunization registration record in various health units in each immunization time and through improvement of design of the form of data collection, items were very complete that is background of data entry to the software and the software also confirmed its authenticity.

A system of simulated immunization registry of immunization status of children was conducted in county of Olmsted in 1995 for children up to the age of 24 months (Rousseau et al, 2014). Immunization records taken from a population-based sample in this county are secure by summarizing Immunization data, collected from provincial health care centers and they were analyzed by the software system (Rousseau et al, 2014). The results show that 9.1 percent of all children were updated until to the age of 20 months and this increased to 74.2 percent until 24 months of life (Rousseau et al, 2014). The 24-month-old child immunization rates registered in the health care system were changed from 24.3 to 79.5 percent. Added data from health care centers to simulated registry immunization system has increased rate of immunization in each location.

An increase of 27.7 percent while they had the lowest rates of registered immunization had an increase of 6.9% when the immunization rate was the highest. (Rousseau et al, 2014). Setting up of a software system in medical centers and health care facilities can report only immunization within the scope of the health unit and this is only one step of the immunization improvement process (Rousseau et al, 2014, Des Roches et al, 2010).

The availability of a population-based registry system is a solution to the health service provider's data uncertainty and a guide to strengthen the immunization program to Immunization Information Systems (IIS) (Rousseau et al, 2014, Des Roches et al, 2010). Immunization data should be collected ultimately in a central electronic database that

Table 1: Properties of vaccine

Needles Number	Prescription rate	Prescription method	Injection site	The minimum age of receiving	Maintenance time after opening the vial by mobile teams of vaccination	Storage time after opening the vial in service centers	Place of registration and doing immunization	The location of the placing refrigerator	Nature of vaccine	Vaccine name
26 or 27	0.05 ml.	Intradermal	Left side	at Birth time	By the end of working day	4 hours	Defined health unit	The upper floor of Refrigerator	Attenuated live basil	B.C.G
	2 drops	oral		at Birth time	By the end of working day	By the end of the expiration time, it should not be crossed by observance of cold chain conditions and more than a month since the opening of the vial.	It is registered according to the most basic form completed by the system.	upper floor	Attenuated live virus	Opv
23	0.5 ml.	Subcutaneous or intramuscular (preferably muscle)	Right side	6 weeks of age	By the end of working day	By the end of the expiration time, it should not be crossed by observance of cold chain conditions and more than a month since the opening of the vial.		upper floor	Inactivated virus	IPV
26 or 27	10 years and under, 5.0 ml and above 10 years, 1 ml (in adult hemodialysis and adult patients with immune deficiency and thalassemia double dose injected)	intramuscular	Left side	at Birth time	By the end of working day	By the end of the expiration time, it should not be crossed by observance of cold chain conditions and more than a month since the opening of the vial.		upper or middle floor	Virus surface antigen	Hepatitis B
23	0.5 ml.	Subcutaneous	Right side	12 months of age	By the end of working day	6 hours		upper floor	attenuated live virus	Measles, rubella, mumps, MMR
23	0.5 ml.	intramuscular	Left side	6 weeks of age	By the end of working day	By the end of the expiration time, it should		lower or middle floor	Tetanus toxoid,	Conjugate

Table 2: Daily actions of vaccinator (Vaccine stock)

The Daily print capability with vaccine stock situation

Edits	Short age of vaccine (type)	Date and hours of vaccine opening	vaccinator Education	vaccinator genders	vaccinator Name	The number of doses removed from inventory	Expiration date registered by serial number	The serial number removed from inventory	The number of total dose	manufacturing factory	Dose number according to serial number	The number of vials by serial number	vaccine Serial	The overall number of vials	English name of vaccine	Symbol	Vaccine name
Edit / Delete necessary serial number of vaccine			Cycle Diploma Diploma Bachelor's Degree or higher	Female Male	Defined users	Registration by system 1 - 2 - 3 - - 4 -	Registration by system	registration of the relevant number	1 - 2 - 3 - 4 -	1 - single dose 2 - two doses 3 - Five doses 4 - Ten doses 5 - Twenty doses 6 - Other	1 - 2 - 3 - 4 -	1 - 2 - 3 - 4 -	registration of the relevant number	Bacille Calmette-Guérin	BCG	BCG	
														Bivalent oral polio	bOPV	Bivalent oral polio	
														Trivalent oral polio	tOPV	Trivalent oral polio	
														Injectable polio	IPV	Injectable polio	
														Measles, rubella, mumps	MMR	Measles, rubella, mumps	
														Hepatitis	HepB	hepatitis B	

1 - fracture of vaccine vial.
 2 - suspected contamination of vaccine vial.
 3 - Keeping more than one month from the date of opening of vaccine
 4 - Change of Index

In case of lack of vaccine or vaccines, option of compensation vaccination for next and delayed injection is activated

If the expiration date is Expire, it should be reported by the system

Choosing right of the relevant serial number should be given to vaccinator

Table 3: Visited people profile

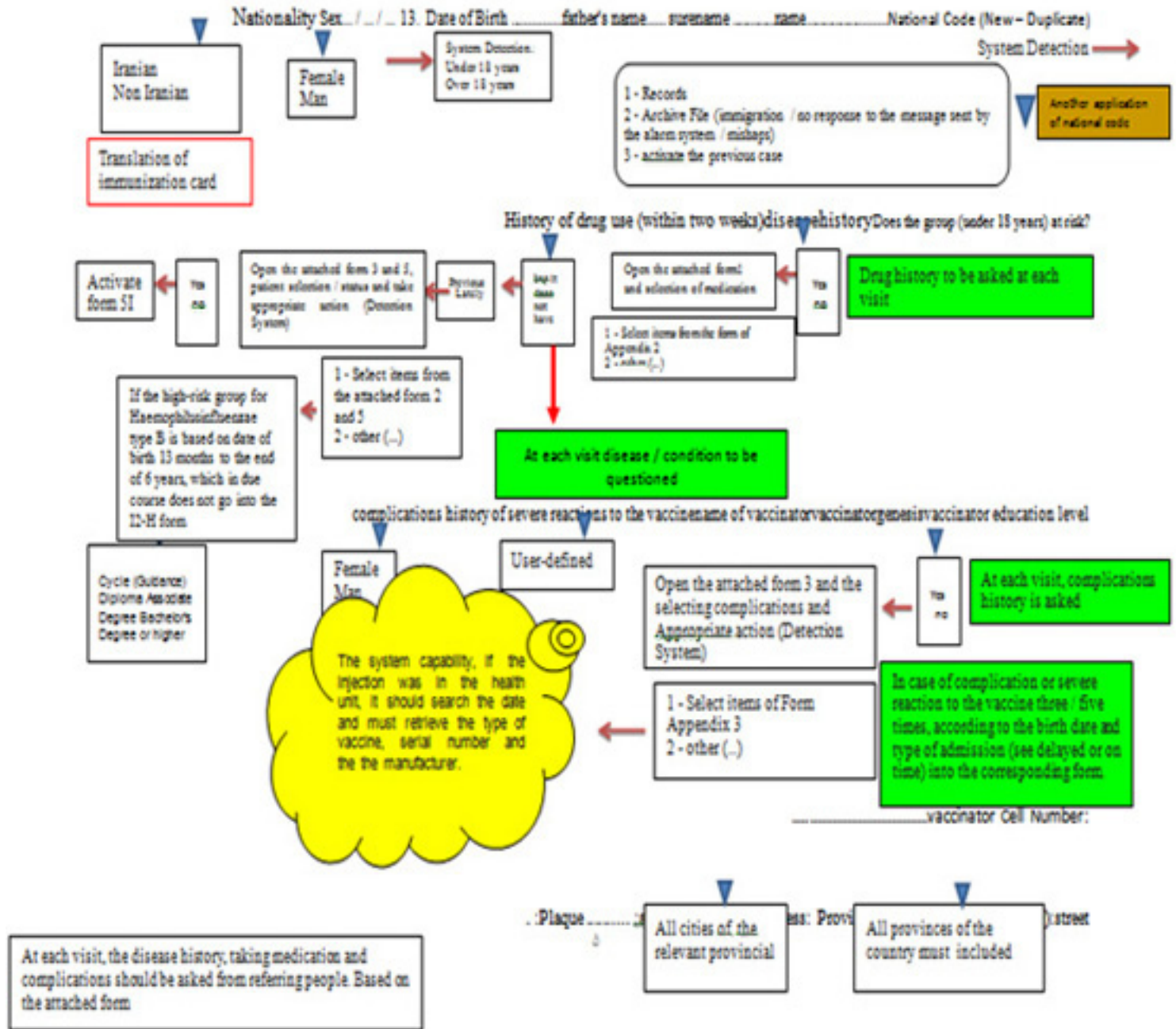


Figure 1: Type of visit

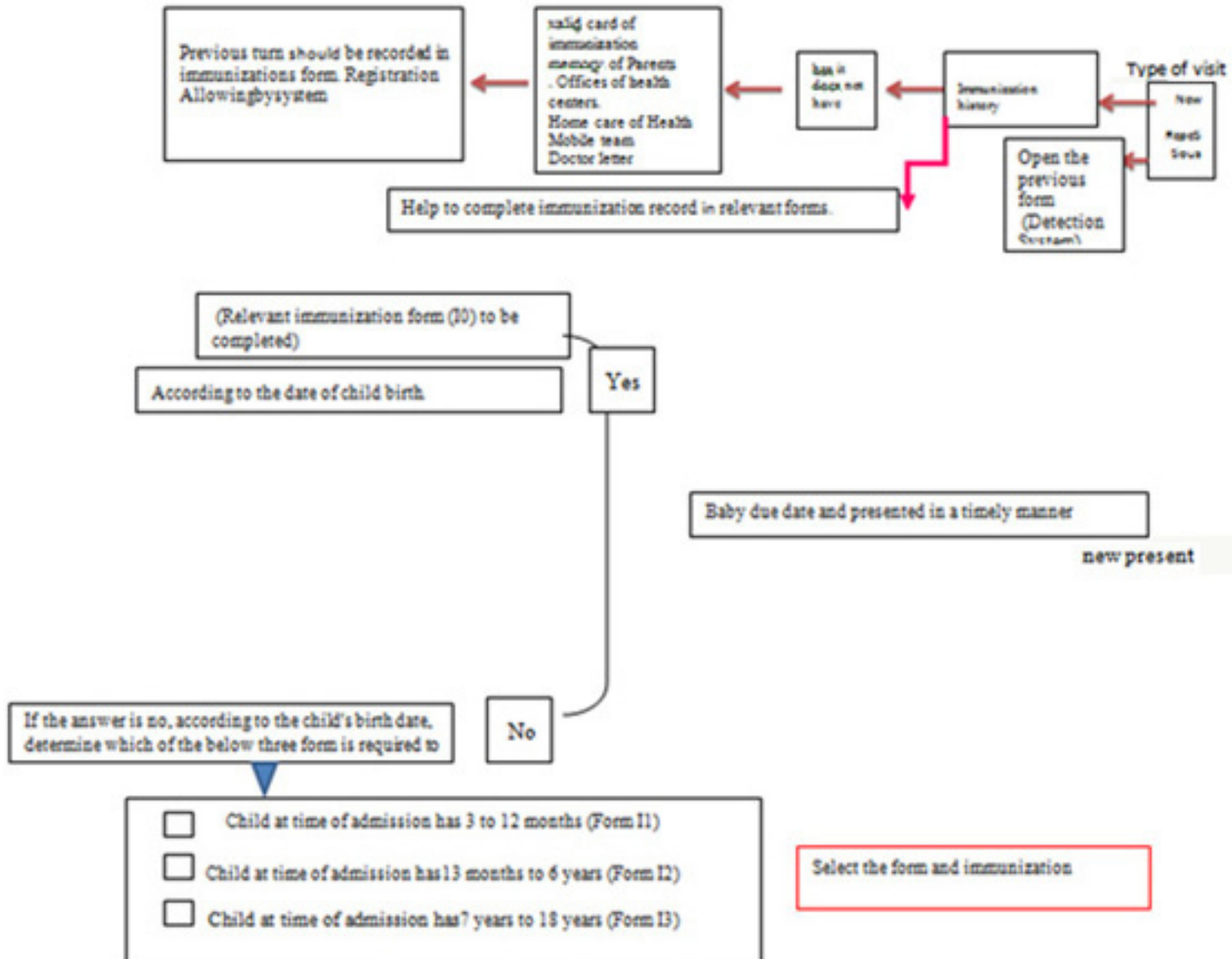


Figure 2. Demographic information

اطلاعات دموگرافیک

نظام ثبت داده واکسیناسیون کودکان

محمد رضا هاشمی Online

1395/12/13 تاریخ ثبت

2282251063 کد ملی

هاشمی زاده نام خانوادگی

محمد رضا نام

جنسیت: مرد زن

نام پدر: هاشمی

میت: ایران

شهرستان: قزوین

شماره: خ زند - ساختمان منتخب - طبقه 2

نشانی: 7146765595

کدپستی: 09173087527

تلفن همراه پدر: 09171069656

تلفن همراه مادر: info@sums.ac.ir

پست الکترونیک

1

انصراف اطلاعات واکسیناسیون ذخیره

Figure 3: Record vaccine information

ثبت اطلاعات واکسیناسیون

نام واکسیناسیون

نام خانوادگی واکسیناسیون

نام خانوادگی واکسیناسیون

جنسیت: مرد زن

کد ملی واکسیناسیون

تاریخ ثبت واکسیناسیون

مکان واکسیناسیون

انتخاب کنید

انصراف ذخیره

Figure 4: Referral at due time

has capabilities of storage, retrieval and analysis, because parents are not good sources for a centralized database and they are often unable to report even basic information, such as number and timing of immunizations and their information and report accuracy is not more than 50 to 60 percent (Rousseau et al, 2014).

However, short-term and long-term potential benefits of an immunization registry system should be weighed against the costs, because it requires the purchase and installation of hardware and software and networking capabilities and requires planning and development of a series of standardized data and privacy rights of individuals should be considered (Rousseau et al, 2014, Des Roches et al, 2010, Janet et al, 2015). Creating a system of immunization registry does not change the immunization rate in a community, but it allows authorities to collect gradually immunization report cards and prevent the extreme and excessive effects of missed opportunities to (Rousseau et al, 2014).

Conclusion

The advantages of this web-based system are on-time registration, reports of adverse events, stock of vaccine, requests and appropriate distribution of vaccines, ease of immunization and reducing the failure of parents. In the case of employing a coordinated and comprehensive system at province and country level it is possible to compare immunization coverage, report shortcomings, problems and risks of the immunization program which can be helpful in policy-making and getting the final decision for the process of immunization. It is proposed to improve the immunization program; this web-based system expanded first in Fars province and then other provinces, so that ultimate data collection could be made available to the Ministry of Health and be considered by policy-makers, managers and practitioners.

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Comparison of Dyspepsia Symptoms from the Viewpoints of Persian Traditional and Modern Medicine: A Qualitative Study using Content Analysis approach

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Abstract

Background: Dyspepsia is one of the most common reasons for outpatient referrals. In Persian traditional medicine, dyspepsia is discussed as a basic gastrointestinal problem. Considering the prevalence of this disease and its diagnostic and therapeutic approaches in Persian traditional and conventional medicine, the current study aimed to compare dyspepsia based on the viewpoint of these two medical systems and provide an integrated approach to diagnose and treat this condition.

Methods: The current comparative study was conducted based on a content analysis method. The symptoms of dyspepsia were collected from literature of modern and Persian traditional medicine by note taking methods based on library research strategies, and then data were analyzed using directed content analysis.

Results: Etiologic agents of dyspepsia were more than 68% similar in the two medical doctrines. Epigastric pain, nausea, and vomiting were the most common symptoms, followed by heartburn, bloating, early satiety, decreased appetite, burping, and weight loss. In the Persian traditional medicine system, dyspepsia is discussed as gastric indigestion and its causes, symptoms, and treatments are also discussed.

Conclusion: Diseases causing dyspepsia are very similar from the viewpoint of Persian traditional and modern medicines. Some conditions, such as gastric dysfunction, are thought to be the most common causes of dyspepsia in Persian traditional medicine, and some of them can be categorized as functional disorders. Therapeutic approaches from Persian traditional medicine can be used to treat such conditions as an adjuvant treatment along with routine methods, and give new ideas for clinical trials.

Key words: Dyspepsia Symptoms, Traditional Medicine, Qualitative Study, content analysis

Introduction

Dyspepsia is a permanent or recurring discomfort in the upper abdomen [1]. Generally, pain associated with dyspepsia is localized in the central part of the upper abdomen and is naturally different from that of other gastrointestinal syndromes, such as gastric reflux and irritable bowel syndrome [2].

Dyspepsia is one of the most common reasons for outpatient referrals to clinics. Different studies conducted worldwide showed that about 1.8–57% of people experience dyspepsia during their lifetimes [3, 4]. The prevalence of dyspepsia has been reported to be 19–41% in European countries [4], 8–14% in Asian countries [5], and about 3–30% in Iran [6].

The difference in the prevalence of dyspepsia among countries may be the result of a real difference in the incidence, diagnostic indices, or degree of accuracy in the identification of gastrointestinal tract lesions (3). Dyspepsia is diagnosed based on the latest criteria of Rome III in modern medicine. The criteria for dyspepsia diagnosis are as follows: 1. bothersome postprandial fullness, 2. early satiation, 3. Epigastric pain, 4. Epigastric burning, a criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis [7]. However, many other symptoms can indicate dyspepsia; for example, some researchers used the Leeds dyspepsia questionnaire to evaluate the prevalence of dyspepsia. Its shortened form (SF-LDQ) with eight items is also used in some studies [8].

Complementary and alternative medicine is a medical approach that is different from conventional medicine, which currently attracts more attention. The World Health Organization (WHO) and legislative bodies focused on the capacity of different countries in traditional medicine and asked for information on low cost and low risk methods for managing medical complications [9]. Persian traditional medicine, with a history of more than a thousand years, and reliable books and physicians, could be considered as a medical doctrine for development of health and hygiene.

According to literature of Persian traditional medicine, the gastrointestinal function is of great importance. Dyspepsia is among the disorders discussed and evaluated in Persian traditional medicine. According to this doctrine, dyspepsia is defined as, “incompatible and abnormal digestion” [10]. Dyspepsia is diagnosed based on the etiology and symptoms, and the principles of treatment should rely on the proper understanding of them [11]. Dyspepsia symptoms in both the Persian traditional and modern medicines can be assessed. The current comparative study helps to better understand the high prevalence of dyspepsia in different populations and provide new ideas for researchers to complete the available diagnostic criteria around the world.

A comparative study is an understanding of a phenomenon or theory along with comparisons based on descriptions and explanations of similar and opposite positions, aimed at understanding the phenomenon better and finding new ideas through the provided description and explanations [12]. In medical research, comparative studies help researchers look beyond personal limits and understand hidden aspects of many health-related difficulties, when viewed through the perspective of classical medicine, and understand the potential of complementary medicines, especially traditional Persian medicine. Considering the profound scientific and technological developments, performing a comparative study on the pathophysiology of diseases from the viewpoint of traditional and modern medicine is difficult, and possibly even impossible. Despite the significant developments in medical science during recent centuries, the diagnostic model of many diseases is not stable or consistent.

A comparison between classical and modern medicine will help to identify the similarities and differences of the disease, in definition, symptoms, diagnosis, treatment, and prevention. The current study aimed to compare and explain the symptoms of dyspepsia, based on the directed content analysis approach.

Methods

The current comparative study employed content analysis methodology. First, the symptoms and diagnosis of dyspepsia were extracted from classical medicine references. Subsequently, the gastric diseases along with their symptoms and diagnoses were extracted from “the Canon” of Avicenna. Accordingly, other reliable books on traditional medicine were also evaluated. Data, including symptoms and the equivalent words in the traditional medicine references, were provided in text tags. To analyze the data based on the content analysis, the gist of each tag was extracted and the gist that belonged to each category was collected in a new tag. In order to achieve the study aims, the extracted gist, including all symptoms and etiologies associated and related to the gastric diseases were collected in text and tables. These findings were discussed in different sessions in the researchers’ team from the viewpoint of accuracy and degree of compliance. They were then analyzed and explained after the final approval.

To increase the validity and reliability of findings, some methods, such as the review of tags by the research team, evaluation of reliable and numerous traditional medicine references, and a panel of experts were integrated. To increase the reliability of the data, the accuracy of explanations and the codifying process were evaluated by the research team. For the final consensus, the tags and codes were reviewed by the researchers’ team; cases with no consensus were discussed to make the final decision.

The inclusion criteria for the Persian traditional references were as follows:

- The author of the book should have sufficient credibility in Persian Traditional Medicine.
- The references should be gathered from different historic eras.
- The original version of Arabic texts should be available.
- The dictionaries used in the current study should cover Farsi and Arabic words.
- A panel of experts should approve the inclusion criteria and selected books.

Accordingly, 8 books were selected: *Ferdows-ul-Hikmah* by Ali ibn Tabari (236 A.H.), *Kamel-al-Sanatate Tabiat* by Ali ibn Abbas Majousi Ahwazi (4th century A.H.) [13], *Hedayat-ul-Moteallemin fi-tebb* by Rabie ibn Ahad Akhveini Bokhari (4th century A.H.) [14], *Zakhireye Khwarazmshahi* and *Aghraz-al-Tabiat* by Seyed Esmaeil Jorjani (5th and 6th centuries A.H.) [11], and *Tib-e-Akbari* by Akbar Arzani (12th century A.H.) [15].

Results

In modern medicine, dyspepsia is divided into two categories, organic and functional. The organic causes of lesions are: peptic ulcers (15%–25%), gastroesophageal reflux (5%–15%), gastric cancers (less than 3%), biliary tract diseases (rare), abdominal wall pain (rare), pancreatitis (rare), gastroparesis (rare), carbohydrate malabsorption (rare), medicines, stress, alcoholic drinks, and pregnancy; functional causes include: gastric motor function, visceral sensitivity, mental, and social causes [1, 4].

Today, the most common index to confirm the diagnosis of dyspepsia in Rome III is the continuation of each of the following symptoms for at least 3 months within the last 6 months. According to the references of classic medicine, epigastric, nausea, and vomiting are the main symptoms of dyspepsia, followed by heartburn, bloating, early satiety, decreased appetite, burping, and weight loss [7].

According to the provided definitions, it can be concluded that the definition of dyspepsia is based on the symptoms, most of which are nonspecific and can be observed associated with gastric ulcers, reflux, and gastric cancer.

From the viewpoint of Persian traditional medicine, if the digestion is incompatible and does not proceed normally, the condition is called dyspepsia. Complications associated with digestion are explained as poor digestion, indigestion, and no digestion (*Tekhmeh* in the Persian traditional references) and include a wide spectrum of dyspepsia. Hence, in case of poor digestion, food remains in the stomach longer than normal. Although the stomach delivers its contents to the small intestine in a delayed manner, the stomach contents are qualitatively normal and the food is digested sufficiently, and is useful for the body. In dyspepsia, the quality of digestion changes and the stomach contents do not have a normal quality; therefore, the food cannot be used by the body, and it is recognized as waste materials, which are excreted in different ways via

the excretory mechanisms and organs. No digestion refers to the status in which the eaten food cannot be digested and is not affected by gastrointestinal secretions; in other words, the eaten food cannot be absorbed and accordingly, the body excretes it through vomiting or diarrhea.

From the viewpoint of Persian traditional medicine, dyspepsia has different causes and one of the most important ones is associated with food (qualitatively and quantitatively). The style of eating and drinking refers to the following points: insufficient chewing, lack of sufficient time intervals between meals, eating snacks, taking different types of food during a meal, drinking plenty of fluids during a meal, eating hot and cold food simultaneously, eating slow-digesting and fast-digesting foodstuff during a meal, sleeping after a meal, eating food while one is angry or in a rage, taking a bath, exercising or having intercourse after a meal, drinking water while fasting, eating food when one is not hungry, and overeating. Other causes of dyspepsia are as follows: weakness of stomach, abnormal humors in the stomach, mental disorders, obesity, pregnancy, sleeplessness, abnormal and extensive sleeping, gastric ulcer, gastritis, weakness of the stomach muscles, stomach tissue damage, and a congenital small stomach.

According to Persian traditional medicine, symptoms of dyspepsia are as follows: heartburn, bloating, early satiety, decreased appetite, and burping (*Jeshaa*); according to the aforementioned results and evaluating the symptoms of dyspepsia based on modern medicine, it can be concluded that epigastric, nausea, and vomiting are the main symptoms of dyspepsia, followed by heartburn, bloating, early satiety, decreased appetite, burping, and weight loss. The most important symptoms of the disease based on Persian traditional medicine are stomachache, nausea, and vomiting followed by burping (*Jeshaa*), bloating, decreased appetite, early satiety, stomach heaviness, heartburn, and thirst.

Discussion

Definition of dyspepsia: According to modern medicine, "Dyspepsia is a permanent or recurring discomfort in the upper abdomen," which explains, "how the disease is" and provides a "description," and explains dyspepsia based on some symptoms. According to Persian traditional medicine, dyspepsia is, "If the digestion is incompatible and does not go on its normal way," which is different from the definition provided by modern medicine. The definition in traditional medicine explains "the quiddity" of the disease and provides an image of its nature [1, 10].

Symptoms of dyspepsia

By evaluating and comparing the symptoms of the disease between the two medical doctrines, many symptoms of dyspepsia in the Persian traditional medicine are similar to those of modern medicine, such as epigastric, which refers to stomachache in Persian traditional medicine. In addition, nausea, vomiting, bloating, early satiety, heartburn, and burping are other symptoms. In contrast, some symptoms in traditional medicine that are not mentioned in modern

medicine include thirst (intensity of thirst) and stomach heaviness. However, some symptoms in modern medicine that are not mentioned in Persian traditional medicine include weight loss [1, 10, 11, 13, 14, 15].

Among the symptoms of the disease, epigastric, nausea, and vomiting are the most frequent ones followed by heartburn, bloating, early satiety, decreased appetite, burping, and weight loss. From the viewpoint of Persian traditional medicine, some symptoms cause dyspepsia, among which stomach ache, nausea, and vomiting had the highest frequency followed by bloating, decreased appetite, burping, heartburn, stomach heaviness, early satiety, and thirst. When comparing the symptoms between modern and traditional medicine, it becomes clear that the frequency of diseases causing dyspepsia is almost similar between the two doctrines. Some symptoms, such as burping, had a higher frequency in Persian traditional medicine compared with modern medicine, and heartburn was more frequent in modern medicine compared to traditional medicine.

Diseases causing dyspepsia are similar in both medical doctrines; however, there are also some differences. The most common causes of dyspepsia were evaluated in the current study and accordingly, out of 16 main causes from the viewpoint of modern medicine, 11 (75.68%) causes were mentioned in traditional medicine. Conversely, there were some causes for the disease in traditional medicine, which were not available in modern medicine, such as stomach dysfunction, loss of eaten food humors, and retropharyngeal secretions [7, 1, and 10].

Stomach dysfunction is among the diseases that should be diagnosed by para-clinical assessments and it seems that a major part of functional disorders can be placed in this category. In the Persian traditional medicine, stomach dysfunctions were discussed; for example, there were 12 dysfunctions for the stomach and some of them were similar to those of Rome III, such as cool and wet temperaments. Weakness and looseness in the stomach wall and tissue is another disease mentioned in traditional medicine, but not available in modern medicine. Since disorders of the tonicity of stomach muscles are the most common para-clinical finding, conducting more qualitative and quantitative studies is recommended.

Conclusion

Diseases causing dyspepsia are similar in modern and Persian traditional medicine. Some of them, such as stomach dysfunction, are common in dyspepsia and most of them can be categorized as functional diseases. Using Persian traditional therapeutic approaches can be used along with routine treatments, in addition to providing interesting ideas for clinical trials.

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Comparison of the effect of Salvizan Gel with Teriident in patients with minor aphthous ulcers

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Abstract

Background and objective: Recurrent Aphthous Stomatitis (RAS) is the most common inflammatory ulcer of the mouth that has involved humans throughout history. Relieving the pain and shrinking the ulcer size is of great importance for the patient. Finding an appropriate drug is of particular importance in relieving these sores.

Materials and methods: In this clinical trial study, the study population was 30 patients referred to the Department of Oral Disease of Faculty of Dentistry of Ahvaz Jundishapur University of Medical Sciences with the diagnosis of minor oral aphthous in the academic year 2015-2016. The participants were divided randomly into two groups of 15 persons. Each group was given one of the two drugs: salvizan gel or teriident ointment. The amount of pain was evaluated by VAS scale and ulcer size was measured in millimeters. The results were analyzed by using Mann-Whitney and Friedman tests. ($P < 0/05$ was considered significant).

Results: No significant difference was seen between the two groups in the amount of pain and the ulcer size before use of drugs; however, there was a significant difference between the two groups in terms of the amount of pain and the ulcer size after use of drug on the second and sixth days ($P \leq 0.05$); so, salvizan gel with a lower average rating has significantly better performance in reducing the ulcer size.

Conclusion: The results indicate the both medicines, have a significant effect on reducing the pain and the oral aphthous ulcer size; so, salvizan gel and teriident ointment are markedly effective respectively in the control of pain and in reducing the ulcer size.

Key words: Oral Aphthous; Pain, Salviza Gel; Teri-ident; Ulcer size

Introduction

Recurrent Aphthous Stomatitis (RAS) is the most common inflammatory ulcers of the mouth (1) that has involved humans throughout human history (1). The Greek word "Aphtha" was used by Hippocrates for the first time for the definition of these oral ulcers (2).

RAS is a disease with unknown cause, but factors such as local trauma, systemic, genetic, immunological, and nutritional problems as well as allergy and microbial factors are suggested as its predisposing factors (3).

Sometimes the patient feels prodromal symptoms such as itching or burning feeling 2-48 hours before the advent of the ulcer in the place that turns gradually Erythematous and eventually turns into a small white papule that gets bigger during 48- 72 hours (3). The prevalence of RAS in a society is over 25% and its three-month recurrence reaches to 50% (4). The first occurrence of the disease is commonly in the second decade of life (3) but the faster incidence of the disease may be seen by slight trauma, menstruation, upper respiratory tract infection, or associated with certain foods (3). The percentage of incidence of RAS in children may be higher (approximately 39%) and influenced by the incidence of RAS in the parents (5). In this case in children with parents affected by the RAS, its incidence chance is 90% and in children whose parents have not been affected by RAS so far, this level is reduced to 20% (6).

The most important issue in the diagnosis and management of aphthous in dental science is that diagnosis of it is totally based on description and clinical symptoms and there is no laboratory test to prove any diagnosis (7).

The correct treatment of RAS depends on repeat (s), size, and the number of sores (8). The best treatment for aphthous, is a therapy where the wound is controlled over a long time and there are few risky side effects (9). In patients with a history of repeated courses of RAS the topical treatments reduce the risk of the disease (8). The use of topical antiseptics, topical antibiotics and topical corticosteroids are some therapies that are prescribed for patients with aphthous stomatitis (10).

Among the corticosteroids used for the aphthous patients in Iran is triamcinolone acetonide with a brand of teriident. Due to the loss of defensive mucous barrier of oral mucosa in aphthous disease, this drug is well absorbed and also due to the antiinflammatory features of the corticosteroids, it causes earlier regeneration of tissue (11). But since corticosteroids have systemic effects such as hypothalamic-pituitary-adrenal axis suppression, Cushing's syndrome, epithelial atrophy, hyperpigmentation, candidiasis, and acne, it is better that a drug with less complications is used (12, 13).

In the twenty-first century which is named as century of back to nature and the use of herbs in treatment, we see the increasing expansion of the research in the field of medicinal herbs and we see the supply of new

herbal medicines in the broader dimensions (14). One of the medicinal plants that is said to have many healing properties, is a plant known as *Salvia officinalis* (Common sage).

The leaves of the *Salvia officinalis* are very famous because of their antioxidant effect. This plant has a variety of properties such as antimicrobial, antifungal, antiviral, astringent effects and it reduces secretion of sweat and saliva and it is effective in the treatment of RAS (15). The extract of this plant HAS its antimicrobial effects more on gram negative bacteria and IT also HAS anti-fungal effects on *Candida albicans*. These effects are attributed to the active substance of β -thujone that the leaves of the *Salvia officinalis* contain. Active substances of β -thujone because of their antifungal and antimicrobial effects, remove the resulting inflammation of pathogens; on the other hand, ursolic acid contained in the herb has a powerful anti-inflammatory and antiphlogistic effect (16).

Salvizan gel in addition to β -thujone has tannins, phenolic acid, ursolic acid and so on, and reduce the inflammation through these substances and their effect on the lymph tissues (16). A pharmaceutical company called the Gol daru in Isfahan has prepared a therapeutic product from the herb *Salvia officinalis* for the treatment of aphthous, which is distributed under the commercial brand name of salvizan gel and is marketed as there is 28% of the hydro-alcoholic extract of *Salvia officinalis* per 15 g of gel (16) and according to the manufacturer's claims, it has been prepared and marketed in order to treat canker sores.

With regard to this point the policy of the Ministry of Health, Treatment, and Medical Education focuses on finding and using effective herbal drugs in the treatment of disease. (17), given the side effects of corticosteroids and to verify the claims of the manufacturer, this study was designed and conducted scientifically and practically to evaluate the hydro-alcoholic extract of a *Salvia officinalis* (Sage) compared with teriident ointment in the treatment of canker sores.

Materials and Methods

In this clinical trial study, 30 patients, diagnosed as having minor oral aphthous, were referred to the department of oral diseases of Faculty of Dentistry of Ahvaz Jundishapur University of Medical Sciences, and were investigated in the academic year 2015-2016. This study was conducted in a pilot form, and a final sample size of 30 people was determined using random sampling and on the basis of the results of the initial pilot study.

In this study the inclusion criteria were: 1) patients referred to the Department of the oral diseases of the dental school; 2) patients who had a willingness to collaborate on this research; 3) People who were perfectly healthy and without systemic problems; 4) people with a maximum 24- hour history of minor RAS since the incidence of ulcers. Exclusion criteria were: 1) any sensitivity to NSAID drugs; 2) asthma patients; 3) a history of heart disease;

4) pregnant women; 5) people with gastrointestinal tract diseases such as peptic ulcers; 6) people with liver and kidney diseases; 7) patients with any periodontal surgery in the last six months; 8) the presence of systemic diseases such as diabetes. Participants were randomly divided into two groups of 15 people. Age, sex and features of minor RAS and ulcer size and amount of pain were recorded before treatment and matched at each group.

After a full explanation of the terms and methods, the basic situation of pain in patients was measured with the use of the scale VAS (Visual Analogue Scale). This scale is used to measure the amount of pain, and patients were asked to rate their pain to a number between zero to 10. The number zero represents the absence of pain and the number 10 represents the greatest amount of pain. Furthermore, the initial size of the ulcer was calculated and recorded using a disposable paper ruler by mm square (mm^2) at baseline.

In the control group, 0.1% teriaderent ointment (Raha , Isfahan, Iran) was used and in the case group, salvizan gel (Goldaru, Isfahan, Iran) containing an amount of 28% of the hydroalcoholic extract of *Salvia officinalis* per 15 g of gel, was used. Before beginning the design, tubes of both drugs were covered completely by a third party, so that type of medication was not identified for the patient and the investigator. Then, the tubes were marked with "a" and "b" marks, and were randomly given to patients.

For every drug use in each group, people were trained to impregnate a small piece of health cotton of about 3 to 5 cm in size, in the drug and hold it in the sore's location for 30 seconds. People were asked to repeat this operation three times daily and refuse eating and drinking or washing the mouth at least 30 minutes after doing this for the better impact of the medication. Patients also were prohibited to use any oral anti-inflammation and pain medication during treatment. Patients were asked to refer in the second and sixth days after receiving the drug and to be examined again and the amount of pain was recorded based on VAS and ulcer size was measured with a disposable paper ruler. The collected data were given to a statistics expert to analyze statistics.

Statistical methods of analysis of the results

to compare the three groups, the Friedman- Whitney test was used. The results of this research were analyzed using SPSS version 22. A significance level of $P \leq 0.05$ for was considered for all statistical tests.

Results

After providing data to the statistical consultant, they were evaluated and the following results were achieved; the number of patients participating in the study was 30 people; of these 15 persons were men (50%) and 15 were females (50%). The overall average age of the patients participating in the study was 30.62 ± 0.515 for men it was 559.0 ± 2.31 and for women it was 57.29 ± 913.0 . The average amount of pain in patients receiving teriaderent

ointment and salvizan gel along with details is shown in Table 1 and the average size of the ulcer in Table 2.

In this study, it was shown that there are significant differences between the amount of pain in the patients before using teriaderent ointment and salvizan gel with the amount of pain after use of medications ($P \leq 0.05$). Also, no significant differences were seen between the amounts of pain before the use of drugs between the two groups however, there were significant differences between the amount of pain after use of drugs in the two groups on the second and the sixth days ($P \leq 0.05$). As it was shown, salvizan gel with a lower rank average has significantly better performance in the control of pain.

In this study, it was shown that there were significant differences between the size of the ulcer in patients before using teriaderent ointment and salvizan gel with the size of the ulcer after the use of medications ($P \leq 0.05$). Also, this study showed that there was not a significant difference between the size of the ulcer prior to the use of drugs in the two groups but there was no significant difference between the two groups in the size of the ulcer after the use of drugs on the second day and the sixth day .

As it was shown that teriaderent ointment with a lower rank average has significantly better performance in reducing the size of the ulcer.

Discussion

RAS is a recurrent inflammatory disease of the oral mucosa that can be seen as single or multiple or painful sores in patients without systemic disease. These sores are one of the most common oral diseases that are seen in 20% of the world's population (18, 19).

Diagnosis of RAS disease is based on history and clinical profile and there is no specific test for RAS (63). Several factors are discussed in the etiology of RAS. Heredity, blood factors and immunity are the three main factors in the incidence of aphthous ulcers (64). In addition to these various factors, such as local trauma, cigarette smoking, viruses, stress, medication and allergy are very involved in the creation of the RAS (20-24).

This study showed that there is a significant difference between the amount of pain and the size of the ulcer in the patients before the use of teriaderent ointment and gel salvizan with the amount of pain after the use of the medications.

In this study, it was shown that there is no significant difference between the groups in the amount of pain and the size of the ulcer in the patients before the use of the medications ($P \geq 0.05$); however, there is no significant difference between the two groups in the amount of pain and ulcer size after the use of medicines on the second day and the sixth day ($P \leq 0.05$).

Table 1: The amount of pain in patients with oral aphthous by day and the type of gel

The amount of pain in the days off Gel type	At the visiting day	On the second day after treatment	On the sixth day after the treatment	Test results
Teriident ointment	5.73±0.358	4.20±0.416	1.80±0.327	0.0001
Salvizan Gel	6.40±0.335	2.13±0.215	0.27±0.118	0.0001
Test results	0.206	0.0001	0.0001	

Table 2: The extent of oral aphthous by the following time and the gel type

Amount of pain in the days off Gel type	At the visiting day	On the second day after treatment	On the sixth day after the treatment	Test results
Teriident ointment	4.4±0.349	2.33±0.287	0.933±0.118	0.0001
Salvizan Gel	3.933±0.462	1.150±0.123	0.2±0.106	0.0001
Test's result	0.478	0.001	0.0001	

It was shown that salvizan gel with a lower rank average has significantly better performance in reducing the size of the ulcer.

Farokh Rad et al. (25) have compared the medical effect of topical intraoral triamcinolone ointments and herbal solution of myrtus in the treatment of minor oral aphthous ulcers. Contrary to the results obtained in the present study, they found that there is no significant difference between topical intraoral triamcinolone ointment and herbal solution of myrtus in the response rate to treatment. However, in this study it became clear that there was a significant difference between the teriident ointment and salvizan gel in the response rate to treatment, as salvizan gel has significantly better performance in reducing the pain of RAS and teriident ointment has significantly better performance in reducing the size of the ulcer. Perhaps the differences in the results achieved are in the higher number of patients under investigation (100 patients) compared with the present study (30 patients).

MM Fani et al. (26) have compared the effect of phenytoin syrup and triamcinolone acetonide ointment on aphthous ulcers. They found that the rate of the effectiveness of triamcinolone acetonide ointment in the treatment of aphthous ulcers is more than phenytoin syrup. However, in this study it became clear that salvizan gel has significantly better performance in reducing pain induced by aphthous, and teriident ointment has significantly better performance in reducing the size of the ulcer. Perhaps the differences in the results achieved is in the higher number of patients under investigation (60 patient) compared with the present study (30 patients) as well as differences in the used drugs. They also investigated patients with Behcet's syndrome to evaluate the impact of drugs on aphthous ulcers, but in this study, the subjects were completely healthy and lack any systemic disease and syndrome.

Jahanshahi et al. (27) conducted an introductory study of the effectiveness of triamcinolone in treatment of the minor oral aphthous ulcer. Similar to the present study, they found that triamcinolone has significant effect in relieving pain and reducing the sizes of the ulcers and it can be used in accelerating the improvement of aphthous ulcers. A difference between their study compared to the present study is less people under investigation (23 patients) and the methods in their study so that they have compared the effect of triamcinolone with placebo. But in the present study, the therapeutic effect of teriident ointment was compared to the salvizan gel. So it can be said that the results obtained from this study was more comprehensive and more accurate than their study.

Abbasi et al. (28) compared the effect of triamcinolone acetonide 0.1% and diclofenac 1% in patients with minor oral aphthous. This study showed teriident ointment and salvizan gel significantly are effective in reducing pain and the size of the ulcers. They also found that the amount of pain and the size of the ulcers has a significant decrease in triamcinolone gel and diclofenac gel. Contrary to the results obtained in the present study that showed the salvizan gel with a lower rank average, had significantly better performance in controlling the pain and teriident ointment with a lower rank average, had significantly better performance in reducing the size of the ulcer. In their study, they did not find significant differences between the two groups in the reduction of pain and the size of the sore. Perhaps because of the differences in the results achieved is in the lower number of patients undergoing their study (25 patients) compared with the present study (30 patient) as well as differences in the used drugs.

Conclusions

Both teriudent ointment and salvizan gel have a significant effect on reducing the amount of pain and the size of the oral aphthous, so salvizan gel has significantly better performance in the control of pain, and teriudent ointment has significantly better performance in reducing the size of the ulcer.

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Radiological and clinical evaluation of maxillofacial cysts and tumors in patients referred to Hospitals in Kermanshah during 2008-2012

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Abstract

Background: Maxillofacial cysts and tumors are major causes of jawbone destruction; and may occasionally result in early mortality of patients. This study purposed to radiologically and clinically evaluate maxillofacial cysts and tumors among Iranian patients.

Methods: A retrospective study was conducted on medical records of patients referred to surgical departments of two hospitals (Bisotun and Imam Khomeini) in Kermanshah, Iran, from 2008 to 2012. Totally, 347 records were reviewed and 85 cases with intraosseously maxillofacial lesions were selected. The information including age, gender, type of lesion and its characteristics (number of lesions, anatomic location, radiolucency, and lesion border) were collected. Data were presented by descriptive statistics using SPSS 20 software.

Results: Overall occurrence of maxillofacial lesions was 24.5% (85/347) including 41 cysts, 14 benign tumors, 10 malignant tumors, and 20 bone diseases in jaws. The most common cysts, benign tumor, malignant tumor, and jawbone disease was radicular cyst (41.5%), ameloblastoma (57.1%), squamous cell carcinoma (75%), and central giant

cell granuloma (65%), respectively. The posterior region of mandible and anterior part of maxilla were respectively identified as the first and second most common anatomic locations for development of the maxillofacial lesions. The peak age of patients was third and fourth decade for the majority of lesions but seventh and eighth decade for squamous cell carcinoma.

Conclusions: Our findings are generally consistent with those reported in the literature. However, there are a few dissimilarities that may be due to racial and/or environmental differences.

Key words: Maxillofacial, cysts, benign tumor, malignant tumor

Introduction

Jawbones as the main hard tissue of orofacial region can be the sites for development of various conditions such as cysts, neoplasms, or systemic bone diseases. Approximately, 90% of metastatic tumors of the orofacial region occur in jaw bones, especially the mandible [1].

Jaw cyst is described as a pathological cavity that contains fluid, semi-fluid, or gaseous substance. Its frequency has been reported from 7.8% to 36% of jawbone biopsies [2]. Radicular cyst, dentigerous cyst, and odontogenic keratocyst (OKC) are the three most common cysts in jawbones [3].

Odontogenic tumors are a heterogeneous group of tumors with specific location in the mandible and maxilla. These tumors are benign (e.g. ameloblastoma, myxoma, odontoma, and fibroma) or malignant such as squamous cell carcinoma (SCC). SCC has been reported as the most prevalent malignant tumor in jaw-bones of adult patients. While, Burkitt's lymphoma and rhabdomyosarcoma are common among children and adolescents[4].

Cystic and tumoral lesions in mandible and maxilla are important because of resulting in morbidities such as jaw swelling, pain and sensory disturbances [5]; displacement of tooth [6]; occlusal alterations; and failure of eruption of teeth [7]. Moreover, a large portion of primary intraosseous malignancies of the jaws are originated from pre-existing cysts more commonly odontogenic cysts [8]. Aggressive lesions of jaws may also invade and destroy the walls of maxillary sinus, floor of the orbit and nasal wall[9]. Early death of patients with mandibular and maxillary malignancies may occur from infection or metastatic spread [10].

The overall and relative frequency of cystic and tumoral lesions in jawbones differs among various populations that may be attributed to variations in geographic or cultural settings. The aim of this study was to evaluate maxillofacial cysts and tumors among Iranian patients according to age, gender, anatomic area, and radiological features.

Materials and Methods

This descriptive cross-sectional study was performed by using medical records of patients referred to the surgical department of two hospitals (Bisotun and Imam Khomeini) in Kermanshah city, Iran, from 1 January 2008 to 31 December 2012.

A total of 367 records were reviewed and 85 cases with intraosseously maxillofacial lesions confirmed by histopathology diagnosis were selected. An oral-maxillofacial radiologist examined all associated radiographs. Demographic information (age and gender) as well as type of lesion and its characteristics (number of lesions, anatomic location, radiolucency, and lesion border) were collected.

The data were analyzed by SPSS 20 (SPSS Inc., Chicago, IL, USA). Descriptive statistics (frequency and percentage) were used to represent the results.

Results

A total of 85 patients had intraosseously maxillofacial lesions including 41 cysts, 14 benign tumors, 10 malignant tumors, and 20 bone diseases presented in jaws. Therefore, overall occurrence of maxillofacial lesions was 24.5% (85/347).

Radicular cyst was the most frequent cystic lesion (41.5%; 9 males, 8 females), followed by OKC (29.3%) and dentigerous cyst (14.6%). The most common benign and malignant tumor was ameloblastoma (57.1%; 5 males, 3 females) and SCC (80%; 5 males, 3 females), respectively. The first and second most common bone diseases in jaws was CGCG (65%; 5 males, 8 females) and cement-ossifying fibroma (25%). (Table - next page)

The peak age of presentation was third and fourth decade for radicular cyst, OKC, ameloblastoma, and osteosarcoma; but seventh and eighth decade for SCC. Of 17 patients with radicular cyst, 14 patients had one cyst and three patients had 2 cysts including a total of 20 cysts. Twelve patients with OKC included 16 cysts (8 patients with 1 cyst and 4 patients with 2 cysts). The other patients presented with one lesion.

Radicular cysts commonly occurred in the anterior region of the maxilla (45%). Posterior part of mandible was detected as the most frequent anatomic location for OKC (68.8%), dentigerous cyst (66.6%), ameloblastoma (75%), SCC (75%), and bone diseases (75%). (Table)

Most cysts were typically observed as radiolucent areas with well-defined borders. Of benign tumors, ameloblastoma and myxoma were radiolucent, but odontoma and osteoma were radio-opaque. Hemangioma presented a mix of radiolucency and opacity. Benign tumors commonly showed well-defined borders. All malignant tumors presented with undefined borders. SCC was radiolucent and osteosarcoma had a mixed radiolucent/radio-opaque view. Most jawbone diseases were characterized with radiolucent areas and well-defined borders.

Discussion

Studies of jawbone cystic and tumoral lesions among the population are essential for identification of individuals at risk, possible factors of development, and for accurate differential diagnosis. Therefore, we aimed to determine clinical and radiographic pattern of maxillofacial cystic and tumoral lesions among patients in Kermanshah, a city in west of Iran.

In this study, the most common cystic lesions were radicular cyst(41.5%), followed by OKC (29.3%) and dentigerous cyst (14.6%) that is consistent with results of other studies[11,12]. However, Rezvani et al reported oral cystic

Table: Frequency distribution of maxillofacial lesions

Maxillofacial lesions	Frequency of patients (%)	Peak age (decade)	location			
			Maxilla		Mandible	
			Anterior	Posterior	Anterior	Posterior
Cysts:						
Radicular cyst*	17 (41.5%)	3rd and 4th	9 (45%)	2 (10%)	4 (20%)	5 (25%)
Odontogenic keratocyst**	12 (29.3%)	3rd and 4th	1 (6.2%)	3 (18.8%)	1 (6.2%)	11 (68.8%)
Dentigerous cyst	6 (14.6%)	< 5th	1 (16.7%)	1 (16.7%)	0	4 (66.6%)
Nasolabial cyst	2 (4.9%)	-	2	0	0	0
Simple bone cyst	2 (4.9%)	-	0	0	0	2
Residual cyst	2 (4.9%)	-	1	0	0	1
Total	41 (100%)	3rd and 4th	14	6	5	23
Benign tumors:						
Ameloblastoma	8 (57.1%)	3rd and 4th	1 (12.5%)	1 (12.5%)	0	6 (75%)
Odontoma	3 (21.4%)	1st and 2nd	0	1	2	0
Myxoma	1 (7.1%)	-	0	1	0	0
Hemangioma	1 (7.1%)	-	0	0	0	1
Osteoma	1 (7.1%)	-	0	1	0	0
Total	14 (100%)	-	1	4	2	7
Malignant tumors:						
Squamous cell carcinoma	8 (80%)	7th and 8th	0	1	1	6 (75%)
Osteosarcoma	2 (20%)	3rd and 4th	1	0	0	1
Total	10 (100%)	-	1	1	1	7
Bone diseases:						
Central giant cell granuloma	13 (65%)	-	-	-	-	-
Cement-ossifying fibroma	5 (25%)	-	-	-	-	-
Periapical cemental dysplasia	1 (5%)	-	-	-	-	-
Fibrous dysplasia	1 (5%)	-	-	-	-	-
Total	20 (100%)	3rd	-	-	-	75%

* 14 patients with 1 cyst and 3 patients with 2 cysts

** 8 patients with 1 cyst and 4 patients with 2 cysts

lesions in decreasing frequency as radicular cyst (32.83%), dentigerous cyst (31.34%), and OKC (26.12%) [13]. The study by Baghaei et al showed prevalence of dentigerous cysts 27.2%, radicular cysts 18.6% and OKC 18.6% [14]. This variation indicates that the racial and environmental factors probably influence on development of these lesions.

Radicular cysts were more common among patients in the third and fourth decade of life. This finding is consistent with a study in Italy [3]. Arotiba et al indicated that mean age of occurrence was 26.5 years for radicular cyst [15]. In a study by Meningaud et al, patients with radicular cyst were 38.4 ± 17.9 years [16]. Nevertheless, Fomete et al reported second decade as peak age for radicular cysts among Nigerian patients [17]. Radicular cysts occurred most frequently in the anterior part of the maxilla (45%) as

reported previously by Tortorici et al [3], Ramachandra et al [11], and Koseoglu et al [12].

Peak age incidence of OKC was third and fourth decade of life which agrees with the study on Iranian patients in Mashhad city [18] as well as studies on Indians [11] and Turkish populations [12]. OKC was chiefly located in the posterior part of the mandible (68.8%). This finding is similar to previous studies indicating posterior region of mandible as the main location of OKC [11,19]. Goteti reported OKC location with a mandible-to-maxilla ratio of 1.6:1 [20]. OKC occurs most often intraosseously in the third molar region, angle, and ramus of mandible but rarely in soft tissues such as gum, oral mucosa, or lateral facial deep region [21].

Peak age incidence of dentigerous cysts was third and fourth decade. This is concomitant to most studies in the literature. Contrarily, Fomete et al showed common occurrence of dentigerous cysts in younger patients in second and third decades [17]. Dentigerous cyst was more frequent in the posterior part of mandible (66.6%). This is comparable to a study by Ramchandra et al [11].

The most frequent benign tumors were ameloblastoma (33.4%) followed by odontoma (12.5%). Consistently, ameloblastoma has been reported as the most common benign maxillofacial tumor among patients in Nigeria[22], China [23], and Egypt[24]. However, Tamme et al[25], Santos et al [26], and Ochsenius et al [27] demonstrated the first and second most common benign tumors were odontoma and ameloblastoma, respectively.

The peak age of ameloblastoma was the third and fourth decade of life. Peak incidence of ameloblastoma has been reported third decade in Indians [19] and Libyans [20], and fourth decade in Nigerians [22]. A review of 3677 cases of ameloblastoma by Reichart et al indicated that ameloblastoma tumors occur 10 to 15 years earlier in developing countries (average 27.7 years) than industrialized countries (average 39.1 years) [28]. Ameloblastoma was located more often in the posterior region of mandible (75%) followed by maxilla (25%). A similar, study on Iranian population in Mashhad city by Saghravani et al revealed that the most frequent location of the tumor was the posterior part of mandible (66/88)[29]. Ameloblastoma occurrence with a predilection for mandible has been noted in previous studies [30,31]. Reichart et al reported that ameloblastoma tumors are seen more frequently in the anterior region of the jaws among Blacks (21.6%) compared to Caucasians (12.6%) and Asians (11.9%)[28]. According to Siar et al, unicystic and solid/multicystic ameloblastoma tumors involve predominantly the body and posterior region of mandible, whereas desmoplastic ameloblastoma preferentially involves the anterior part[32].

In the present study, the second most common benign tumor was odontoma (12.5%) with peak age of incidence in the first and second decade. Taghavi et al indicated peak age occurrence of second decade for odontoma[33]. Odontoma was located in anterior region of mandible (two cases) and posterior region of maxilla (one case). The study by Isola et al reported that odontoma more likely occurred in mandible than maxilla with ratio about 2:1 [34]. However, Taghavi et al showed a predilection of odontoma for maxilla (59.3%) than mandible [33].

The most common malignant tumor was SCC detected in eight patients (80%). Parkins et al reported that SCC was present in 64% of orofacial malignant tumors from Ghana patients[35]. Similarly, SCC was reported as the most common malignant orofacial tumor among populations in Nigeria[36] and Portugal [37]. The present study showed that SCC commonly presented in patients aged 60+ years. In previous studies conducted by Monteiro et al[37] and Bassey et al[4], oral and maxillofacial SCC was often

found among patients aged 50+ years. SCC was mostly located in posterior part of mandible (75%). Bassey et al found 9 and 6 SCC tumors in mandible and maxilla, respectively [4].

In our study, osteosarcoma was identified in two patients (20%). Peak age of osteosarcoma was third and fourth decades of life that is consistent with a previous report [4]. This is comparable to Ajayi et al that found patients with sarcomas in orofacial region were younger than those with carcinomas [36].

The most systemic bone disease with involvement of jaws was CGCG. This condition is an intraosseous lesion that rarely occurs in the Head and Neck region[38], involves the mandible more than the maxilla and is more common in second and third decade of life [39].

Other conditions in our study sample were nasolabial cyst, simple bone cyst, residual cyst (2 cases each one), myxoma, hemangioma, osteoma (1 case each one), cement-ossifying fibroma (5 cases), periapical cemental dysplasia, and fibrous dysplasia (1 case each). Simple Bone Cyst also known as Traumatic Bone Cyst is a non-neoplastic osseous lesion that appears as a rare pathology, representing approximately 1% of all jaw cysts [40,41]. Hemangioma is a benign neoplasm with endothelial origin that is usually located in soft tissues but rarely develops in bones such as mandible [42].

Conclusion

This study showed that cysts were the most common lesions in the maxillofacial region followed by benign and malignant tumors. The most common cyst, benign tumor, malignant tumor, and jawbone disease was radicular cyst, ameloblastoma, squamous cell carcinoma, and central giant cell granuloma, respectively. The findings are generally consistent with reports in the literature; and some variations may be attributable to racial and/or environmental factors.

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The effects of *Matricaria Chamomilla* extract during neonatal period of rats on pituitary-gonadal hormone axis and changes in testicular tissue of male progenies

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Abstract

German Chamomile (*Matricaria Chamomilla*) is from the *Astraceae* family. This plant has been used in traditional medicine such as analgesic, antispasmodic and anti-inflammatory drugs and for treating skin diseases and so on. In this study, the effects of using German chamomile's hydroalcoholic extract during the neonatal period were evaluated on pituitary-gonadal hormone axis and changes in testicular tissue of male rat progenies. Forty female mature virgin rats from the Wistar race, in the weight range of 180-200g and age range of 90-100 days, were used. After childbirth, samples were divided into four groups (ten mice per group) including control, placebo, and two experimental groups. Control group did not receive injections. Placebo group was injected with 0.5cc of normal saline daily during the lactation period. Experimental groups received 50mg/kg and 100mg/kg of hydroalcoholic extract obtained by soaking method. Injections were done intraperitoneally every day during the lactation period. At the end of the period (24 days), blood samples were taken from heart, serum was separated and the amount of testosterone, FSH, and LH were measured. Also, testis tissue slides were prepared and colored using eosin-hematoxylin method and studied histologically. Results showed that the extract increased FSH not significantly whereas increased LH, testosterone and also male sexual cells including spermatogonia, spermatocytes,

spermatids, Sertoli cells, and Leydig cells significantly ($P < 0.05$).

Key words: Chamomile, hydroalcoholic extract, neonatal, pituitary gonadal axis, testis tissue, testosterone, LH, FSH

Introduction

The use of herbs is as old as human creation. By studying the ancient tribes, we find that medicinal plants have been used as medicine, pesticides, detergents, paints and so on. Some extant chemical compounds in plants have a complex structure that it is impossible to synthesize in the laboratory or is possible only by spending a lot of time and money. After facing problems such as water, air and soil pollution which have been caused by chemical factors and also side effects of chemical drugs which often appear after a few generations, the use of nondestructive matters was proposed so that herbal drugs were used more than 7% in industrialized countries (Zargari, 2008, Zaman 1989).

Due to adverse effects and side effects of chemical drugs, using medicinal plants has been considered of late. Many studies have been conducted about the effects of various plants on fertility of laboratory mammals which have presented valuable results (Parandin et al. 2011).

Fertility is one of the most important issues in medicine. The most common reason for men's infertility is their inability in producing male sexual hormones and sufficient active healthy sperms (Kumar and Kant Singh. 2015). Spermatogenesis in the testis is carried out under the control of secreted testosterone and secretion action of testes is controlled itself by hypothalamic-pituitary-testicular axis (Ramaswamy and Weinbauer. 2014).

Chamomile (*Matricaria Chamomilla*) from *Astraea* family has been proposed in traditional medicine because of its different properties. It is a fragrant plant which grows in lawns and gravel courts. Chamomile has a green white stem, and small hairy leaves with narrow irregular cuts (Esmaeili et al. 2007). The origin of this plant is from different parts surrounding the Mediterranean Sea but is now found in Europe, Moderate regions of Asia, and even in America. Chamomile is used in traditional medicine as a pain reliever and anti-depression drug (Viapiana et al. 2016). Chamomile is also used for treating many human diseases such as hay fever, inflammation, muscle spasms, menstrual disorders, insomnia, ulcers, digestive disorders, rheumatic pain, and hemorrhoids (Srivastava et al. 2010). Also, scientists have reported positive effects of chamomile on clinical and laboratory symptoms of polycystic ovaries (Zafari Zangeneh et al. 2010).

Chamomile contains flavonoids such as apigenin and luteolin, volatile oils such as bisabolol chamazulene, and sesquiterpene, lactones including matricarin, mucilage contains polysaccharides, capric and nonilik ethers amino acids, fatty acids, phenolic acids, and other compounds (Johari et al. 2015). Previous studies have shown that extant compounds in chamomile's extract have anti-bacterial, anti-inflammatory properties and anti-oxidant activity. This plant is full of flavonoids which have effective anti-oxidants for neutralizing oxygen radicals (Hatami and Estakhr. 2013).

Free oxygen species are capable of lipid peroxidation in sperm membrane which is followed by reduced mobility and damages to membrane parts of sperm. Anti-oxidants are compounds which prevent formation of free radicals and peroxidation of lipids, protect sperm cells from free radicals and improve sperm quality and fertility parameters (Maneesh and Jayalskhmi. 2006). Medicinal plants have positive effects on fertility increment, hormonal imbalances, sexual dysfunction and have been considered from ancient times.

Chamomile is dry and warm according to traditional medicine of Iran, and has been used as a sexual stimulant. Chemical studies on this plant have shown large amounts of anti-oxidants (Hatami and Estakhr. 2013).

Since the efficacy of herbal medicines must be proven in clinical trials, and because few have studied the effects of chamomile's extract on male reproductive activity and testicular function, this study was carried out to investigate the effects of German chamomile's extract during the neonatal period of rats on pituitary-gonadal hormone axis and changes in testicular tissue of male progenies.

Materials and Methods

The study was conducted in the animal nest of Islamic Azad University- Falavarjan Branch (2016). Forty virgin mature female rats from Wistar race, in the weight range of 180-200g and age range of 90-100 days were used as parents. To adapt to the environment, samples were kept under 22 to 26 ° C, 40-60% humidity and natural photo period with free access to water. Also, 10 adult male Wistar rats were used for mating.

At first, 100 micrograms of estradiol valerate was dissolved in olive oil and injected intramuscularly to synchronize the ovulation time of rats. After 42 hours, 50 micrograms of progesterone was injected intramuscularly (Hosseini et al. 2013). Six hours later, vaginal smears were taken from rats using swab moistened with saline. Immediately after spreading the sample on a slide, 96% ethanol was added to stabilize them and they were dried in the air. Then, slides were colored using Gimsa solution which was diluted at a ratio of 1 to 20 (Jamil et al. 2013).

According to the proportions and morphology of leukocytes and epithelial cells, estrus cycle stages were determined. So that in proestrus stage nucleated epithelial cells were dominant, in estrous phase, horn cells without nuclei and during the next stage Metestrus, the same percentage of horn cells, epithelial cells and leukocytes were observed. In diestrus stage leucocytes were dominant (Hubscher et al. 2005, Marcondes et al. 2002).

Microscopic observations showed that rats had been synchronized at Estrous stage. Rats were divided into four members' groups with a male rate for mating and kept for one night. By observing vaginal plug day zero of pregnancy was designated and then male rats were separated and samples were divided into four groups (10

rats in each group) including control, placebo, and two experimental groups. Control group received no treatment. Placebo group received 0.5 cc of normal saline for 24 days as injection stress. Experimental groups received 50 and 100 mg/kg weight of hydroalcoholic extract intraperitoneal every day during location.

Herbal samples were prepared from Isfahan Agricultural Research Center and the extract was prepared using soaking method.

Male and female progenies were separated from day 24 which is the end of lactation and were kept until maturity (two months). After that, male progenies were anesthetized by intraperitoneal injection of 0.7 mg/kg ketamine 10 % and blood samples were taken from the heart. For separation of serum, special test tubes were used. Samples were centrifuged for 15 minutes (300 cycles/ minute).

Then, serum was separated from clot and the amount of FSH and LH hormones were measured using electrochemiluminescence (ECC- SIMENS) whereas testosterone was measured using Elisa method (state fax 2100). Also, testis tissues were placed in formalin 10%. Then, some slides were taken from every tissue sample and after dehydration, clarification, paraffinization, molding and preparation of tissue sections by microtome stages, slides with 5 micrometer thickness were prepared, colored by eosin-hematoxylin method and studied using light microscopy.

Obtained data were analyzed using SPSS. One-way analysis of variance and Tukey's mean comparison test were used at 5% probability level.

Results

Pituitary- gonadal axis hormones

Variance analysis results showed that Follicle stimulating hormone (FSH) of experimental groups (50 and 100 mg/kg of extract) were increased in proportion to control and placebo groups during neonatal period but not significantly (Table 1).

Luteinizing hormone (LH) of experimental groups (50 and 100 mg/kg of extract) were increased in proportion to control and placebo groups during neonatal period. The increment was not significant for 50 mg/kg but was significant for 100 mg/kg (Table 1).

Testosterone was increased significantly (P<0.05) by experimental groups during neonatal period (Table 1).

Testis tissue

Microscopic studies of testis sides did not show significant differences between various groups. In these samples, tissue appearance was normal with somniferous tubules which had spermatogenesis cells and tubular connective tissue. It must be mentioned that better appearance of experimental groups shows stimulating effect of chamomile on spermatogenesis.

Average and standard deviation of spermatogonia are presented in Table 2 (page 122). Statistical analysis showed significant increases in experimental groups in proportion to control group.

Statistical analysis showed significant increases in the number of spermatocytes in the experimental groups in proportion to control group. (Table 2)

Table 2 shows significant increase in spermatid number of experimental groups in proportion to control group during neonatal period (P<0.05).

The number of Sertoli cells was increased significantly in experimental groups (Table 2)

The number of Leydig cells showed significant increases in experimental groups in proportion to control group. (Table 2)

Table 1: Comparison the mean serum level of LH, FSH hormones and testosterone in the groups treated with HEG

Hormones	FSH(mIU/dl)	LH(mIU/dl)	Testosterone (ng/dl)
Groups	Mean ±SD	Mean ±SD	Mean ±SD
Control	0.927 ± 0.0356	0.858 ± 0.0476	0.402 ± 0.0447
Placebo	0.894 ± 0.0222	0.858 ± .0518	0.381 ± 0.0446
experimental group1	0.959 ± 0.0517	0.908 ± 0.0567	0.699 ± 0.0886*
experimental group2	1.002 ± 0.1023	1.011 ± 0.0543*	0.869 ± 0.0384*

*Shows significant difference from control group (P<0.05)

Figure 1: Cross-section of testis, control group (10X)

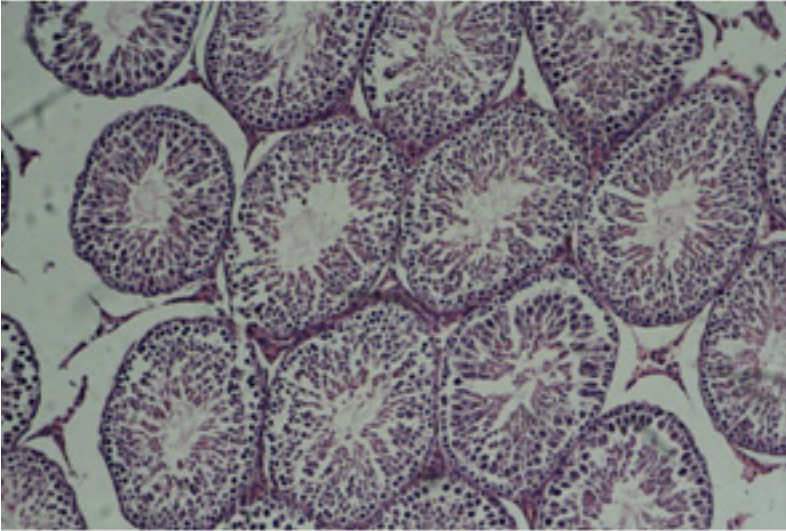


Figure 2: Cross-section of testis, placebo group (10X)

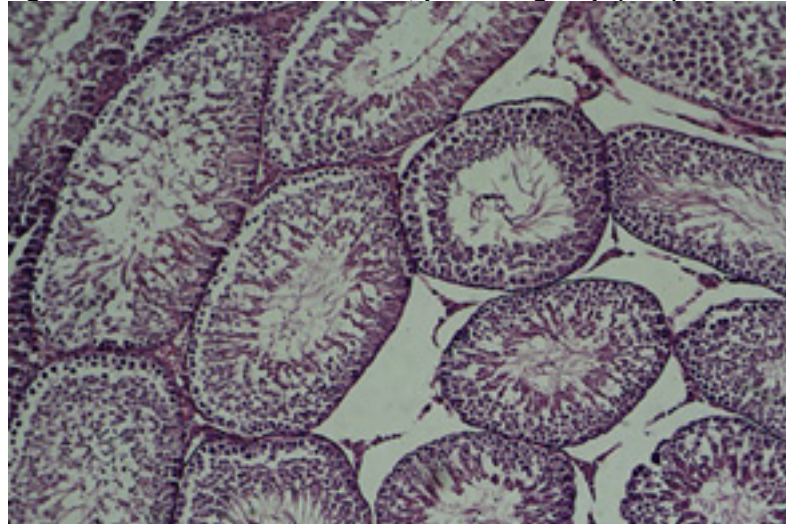


Figure 3: Cross-section of testis, first experimental group (10X)

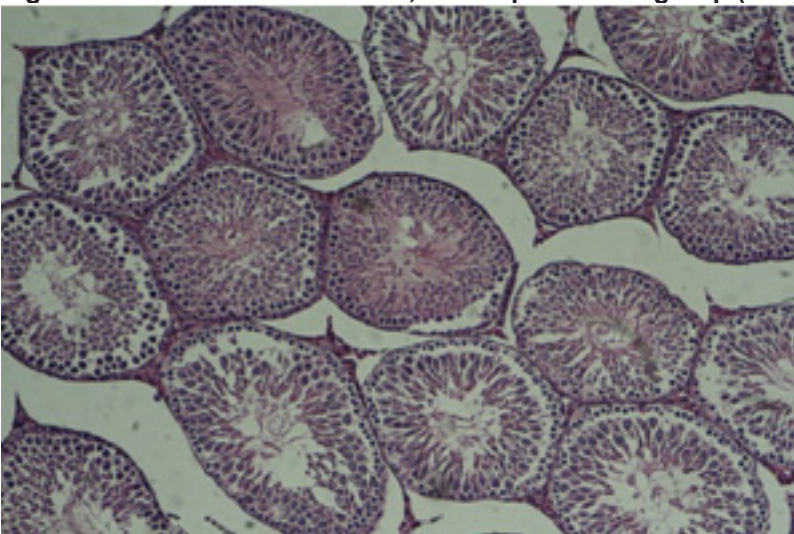
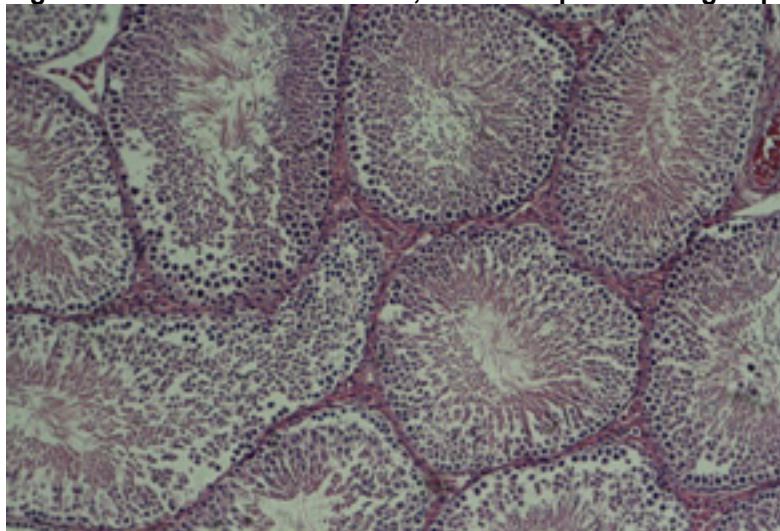


Figure 4: Cross-section of testis, second experimental group (10X)**Table 2: the number of lineage sex cells in the groups treated with HEG in comparison to control**

Cells Groups	Spermatogonia cells	Spermatocytes cells	Spermatid cells	Sertoli cells	Leydig cells
Control	67.740 ± 3.1081	80.280 ± 2.5503	162.21 ± 3.626	16.330 ± 0.3466	26.970 ± 0.4762
Placebo	65.700 ± 4.0393	84.520 ± 2.6448	166.16 ± 3.795	17.280 ± 0.8561	27.270 ± 0.8820
experimental group1	78.790 ± 3.6309*	93.710 ± 3.0090*	182.74 ± 5.591*	18.920 ± 0.7843*	29.060 ± 1.2686*
experimental group2	85.520 ± 3.1818*	98.450 ± 3.0222*	192.47 ± 6.444*	20.310 ± 1.0203*	30.720 ± 1.3522*

*Shows significant difference from control group (P<0.05)

Discussion

Results of this study showed that hydro alcoholic extract of chamomile did not change testis structure of rats. However, the amount of spermatogonia, spermatocytes, spermatids, Sertoli and Leydig cells were significantly increased by the extract. Also, FSH amount was increased but not significantly and LH was significantly increased by 100 mg/kg group. Testosterone was increased significantly in both experimental groups.

Also, the number of spermatogonia, spermatocytes, spermatids, Sertoli and Leydig cells were increased in experimental groups dose dependently.

The increment may be because of extant compounds in chamomile which affect hypothalamic-pituitary- testis axis and increased mentioned hormones. This axis itself can be affected by various controlling factors (negative and positive). Previous studies have shown that testosterone plays an improvement role in nourishing the dividing sexual cells by direct effect on Sertoli cells, secretion of seminiferous tubules liquid and various proteins such as growth factor and transferrin (Carlson. 2012).

In Hatami and Estakhr's study (2013), the number of spermatogonia, spermatocytes and spermatids were

increased by chamomile extract. In that study, FSH amount of the treatment group was not significantly different from the control group and LH and testosterone hormones were significantly increased by the extract which is in agreement with our results.

Capuzzoa et al. (2014) reported that anti-oxidant power chamazulene in chamomile was much more than ascorbic acid (vitamin C).

Chamomile is rich of flavonoids and phenolic compounds which are effective antioxidants for neutralizing oxygen free radicals (Pekka et al. 1996). Antioxidants are probable mechanisms of chamomile's effects on sperm increment.

Crocetin comes from phenolic compounds of chamomile's extract (Karbalaydoust. 2009). This matter is used for storing sperm under very low temperatures because of its anti-oxidant effects (Henkel. 2005). Also, anti-oxidant properties of phenolic compounds eliminate free radicals and affect sperm relating factors (Gill-Guzman et al. 2001).

Acharya et al. (2008) showed that reduced activity of antioxidant enzymes decreased the number of sperm but following administration of antioxidants total number of sperm was increased.

Chamomile extract contains phytoestrogen compounds which are from prolactin secretion stimulating factors. Prolactin increment causes down-regulation of luteinizing hormone (LH) in Leydig cells, reduction in enzymes involved in steroidogenesis and finally testosterone reduction which cholesterol is its synthesis prerequisite. Also, phytosterols of chamomile's extract reduce steroidal hormones such as testosterone by reducing cholesterol amount (Wilson and Foster. 2003, Hannana et al. 2003, Shingo et al. 2015).

Johari et al. (2015) studied the effects of chamomile's extract on serum concentrations of testosterone and gonadotropins in male rats and reported that chamomile reduced the amount of testosterone but didn't affect gonadotropins and announced that phytoestrogen existence was the reason for testosterone reduction. These results are opposed to our results which can be due to dose difference or consumption time of extract at maturity or neonatal periods.

Since free radicals are produced in daily reactions of body and affect reduction of sperm number and its mobility (Gill-Gursman et al. 2001) and due to the fact that laboratory animals experience stress because of living in closed spaces, chamomile has probably had positive effects on spermatogenesis because of its anti-oxidants including chamazulene (a powerful anti-oxidant).

Chamomile with its anti-oxidant properties can improve the process of making sperm plus increase in sexual hormones.

Conclusion

According to results, existence of antioxidant reduces negative effects of phytoestrogens on performance of pituitary-gonadal axis and spermatogenesis process but more studies are needed.

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In Vitro Effects of Ascorbic Acid on Corneal Collagen Cross-Linking in Keratoconus

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Abstract

Purpose: To assess the efficacy and safety of ascorbic acid in the treatment of keratoconus by increasing the number of “anchors” that bond collagen fibers together in human in vitro cornea using electron microscopy.

Methods: In this semi experimental study keratoconus cornea is divided into six equal parts after keratoplasty. Two doses of ascorbic acid (10-3 mg/ml and 10-4 mg/ml) in two time ranges of 4 hours and one week after the treatment are applied to analyze the deviations of cross-linking. A part of the cornea is considered as control sample (without ascorbic acid) for different times. Various parts are randomly assigned to different studied doses. Each section of cornea is evaluated using electron microscopy. Friedman and Wilcoxon tests are used for data analysis. The value of significance level was set at 0.05.

Results: The average distance between collagen fibrils are measured after the treatment with two different doses of ascorbic acid for two different time ranges. These results showed that higher doses

of ascorbic acid and longer treatment time led to lower distance between collagen fibrils of cornea ($p < 0.001$). This implies the better strength of the cornea. Apoptosis and vacuolization were not observed in keratocytes by electron microscopy after treatment with ascorbic acid.

Conclusions: Results showed that ascorbic acid strengthens the cornea and decreases the distance between collagen fibrils (consequently increase cross-linking). Therefore, the efficacy of ascorbic acid is observed by more recovery through increasing its doses and passing time.

Key words: Ascorbic acid, Cross-linking, Cornea, Keratoconus, Keratocytes

Introduction

Cornea is the anterior and transparent segment of the eyeball. There are five layers from anterior to posterior of cornea: epithelium, bowman, stroma, Descemet's membrane and the endothelium. Stroma, constitutes 90% of corneal thickness, and consists of collagen fibrils blades intussusception (anchors). Keratocytes, as important formation cells of stroma, produce collagens and their apoptosis and necrosis cause structural weakness of corneal tissues (1).

Keratoconus (KC) is a bilateral, progressive, degenerative and non-inflammatory pathology of corneal ectasia(2). It usually starts at puberty. Irregular astigmatism, corneal thinning and progressive myopia and protrusion are characteristics of keratoconus that lead to decreased visual acuity(3). The prevalence of KC in the general population is reported to be around 1/2000 often affecting young patients(4). The etiopathogenesis and pathogenesis of keratoconus is unknown but it is likely a multifactorial disease (5). There are changes observed in corneal collagen organization (6), structure (7), intercellular matrix, necrosis and apoptosis of keratinocytes (8). Furthermore, a reduction is observed in cross-linking chemical bonds between collagen fibers inside the stroma for keratoconic corneas as compared to normal ones (9). This implies structurally weakened keratoconus corneal tissue (8).

There was not any effective way to stop progressive keratoconus so that about 21% of keratoconus patients need corneal transplantation (10). Conventional methods only improve the refractive errors and the loss of vision of corneal ectasia such as spectacles, rigid contact lenses, scleral, mini scleral and hybrid lenses, photorefractive keratectomy, intrastromal corneal ring, epikeratoplasty, phakic intraocular lens, keratophakia, keraflex (11) and penetrating keratoplasty. It should be noted that these methods do not remedy keratoconus and cannot stop the progression of this disease (2, 12).

Corneal collagen cross-linking is introduced for the treatment of progressive keratoconus(13). The first research of photobiology was conducted to increase the resistance of stromal collagen in the 1990s (14). The procedure of corneal collagen cross-linking is a combined action of chemical and physical factors which consisted of UVA ray at 370 nm (15) and a photosensitizing substance (riboflavin or vitamin B2) (8). Corneal rigidity is increased by corneal collagen cross-linking (16). This treatment is based on the changes of biomechanical properties of stromal collagen and cause pathogenesis of keratoconus (10).

Investigations show that oxidative stress is effective in KC (5, 17). Oxidative stress leads to disorder in the normal state of the cell and destruction of all cellular components including proteins and collagens resulted in a toxic effect by free radicals (18). Vitamin C (ascorbic acid) and vitamin E (α -tocopherol) react with free radicals. It is strongly accepted that the antioxidant virtues of these vitamins

are responsible for their biological activity (18). Ascorbic acid is a basis for normal collagen formation (19). It is a main component in the synthesis of hydroxylysine and hydroxyproline in collagen (20). Hydroxylysine is important for formation of the intermolecular collagen cross-linking (21). Furthermore, ascorbic acid plays an important role in collagen biosynthesis (22, 23).

In this study, the distance between collagen fibrils are measured because of the study of cross-linking was qualitative and there were no plans or software to count cross-linking. The consistency of cornea is increased by reducing the distance between collagen fibrils. The purpose of this pilot study was to assess the efficacy and safety of ascorbic acid in the treatment of keratoconus by increasing the number of "anchors" that bond collagen fibers together (the corneal cross-linking strengthen the cornea). This study can be considered as a basis for the future conservative treatment of keratoconus.

Materials and Methods

This semi experimental study was performed on patients attending the cornea clinic at Negah hospital in Tehran, Iran. The participants of this study were patients with confirmed diagnosis of progressive keratoconus who had an operation of penetrating keratoplasty. Two keratoconus corneal buttons (7-8.5mm) were obtained from 25 and 26-year-old patients treated with 10-3 and 10-4 mg/ml ascorbic acid (chemical formula: C₆H₈O₆, molecular weight (MW): 176.13 gr/mol and Art No: F413727). Two corneal buttons were sliced individually with a microtome to six equal sections. One section was stored in optisol and 10-3 mg/ml ascorbic acid. Another section was stored in optisol and 10-4 mg/ml ascorbic acid for 4 hours. Furthermore, one randomized section was just soaked in optisol as a control sample. Three samples of cornea were considered to be examined after one week as witness groups: one at optisol with 10-3 mg/ml ascorbic acid, one at optisol with 10-4 mg/ml ascorbic acid and the last one at optisol.

Transmission Electron Microscopy

After the treatment with ascorbic acid, corneal buttons with their controls were prepared for transmission electron microscopy (TEM) (Zeiss EM 900). All sections were immersed in 2% glutaraldehyde. Sections of corneal button were embedded in hard resin after being fixed and dehydrated for transmission electron microscopy. 50–70-nm ultrathin sections were prepared and mounted on copper grids when the semithin sections stained with toluidine blue were observed.

Grids containing color samples were prepared to observe by transmission electron microscopy. EMC software V.16.8 was applied to study respective areas. In order to select images: magnifications of 7000 and 12000 were used to assess keratocytes (vacuolization and evaluation keratocyte membrane), the magnification of 30,000 was applied to assess the distance between collagen fibrils. 150000 sections of each sample were prepared by microkeratome and about 30 images of each section was taken. Finally,

10 images were selected to analyze keratocytes, cross-linking and the distance between collagen fibrils.

The distance between collagen fibrils was measured by AutoCAD 2007 software. In each case, the distance between the fibrils was randomly measured at 100 points to obtain an average. The average of different 100 points were randomly obtained for three cases which were almost same without any considerable difference. Images were passed to two medical geneticists to study keratocytes according to apoptosis, necrosis, the existence of vacuolization in them, shrinkage and freshness. They separately commented on freshness and keratocytes apoptosis rate in different doses of ascorbic acid at different times of treatments. It should be mentioned that the mean comments of these two medical geneticists are reported.

Considering that the control and treated groups were prepared from two corneas and comparisons between samples relevant only to each of these two corneas, there was no difference between comparisons in terms of clinical and demographic parameters (normalized). Studied variables did not follow a normal distribution based on the result of Kolmogorov-Smirnov test. Therefore, non-parametric tests were used for data analysis. Wilcoxon test was applied to compare the interrelated variables. Furthermore, Friedman test was used to assess deviations over time. The first type of error was considered about 0.05 to make decisions about significant deviations. All statistical analyzes were performed using SPSS v.16.

Results

Measurements of the average distance between collagen fibrils of two corneas after the treatment with two different doses of ascorbic acid at 4 hours after treatment and one week after treatment showed that increasing the dose and passing time, reduce the gap between collagen fibrils (Table 1 - next page). It should be noted that the changes in the measurement of control samples showed the reverse trend. Friedman test showed a significant effect of time on the change in distance between collagen fibrils according to the comparison of repeated measurements for the following conditions: without intervention over three times, intervention with 10^{-3} mg/ml ascorbic acid at fourth hour, intervention with 10^{-3} mg/ml ascorbic acid in one week, intervention with 10^{-4} mg/ml ascorbic acid at fourth hour and intervention with 10^{-4} mg/ml ascorbic acid in one week (Table 2 - page 129). All comparisons are statistically significant in case of mutual conditions for changes in maintenance dose and time and also in comparison with witness group for both corneas (Table 3- page 130). In the first cornea, 98% and 95% of keratocytes were healthy and unchanged with 10^{-3} mg/ml and 10^{-4} mg/ml ascorbic acid after 4 hours, respectively. 87% of keratocytes were healthy and unchanged in the control sample after 4 hours. 78% and 79% of keratocytes were healthy and unchanged with 10^{-3} mg/ml and 10^{-4} mg/ml ascorbic acid after one week, respectively. 72% of keratocytes were healthy and unchanged in the control sample after one week. In the second cornea, 88% and 92% of keratocytes

were healthy and unchanged with 10^{-3} mg/ml and 10^{-4} mg/ml ascorbic acid after 4 hours, respectively. 83% of keratocytes were healthy and unchanged in the control sample after 4 hours. 75% and 78% of keratocytes were healthy and unchanged with 10^{-3} mg/ml and 10^{-4} mg/ml ascorbic acid after one week, respectively. 78% of keratocytes were healthy and unchanged in the control sample after one week.

Discussion

In the present study, we investigated the effect of ascorbic acid on the increase of corneal strength.

Significant changes in the distance between collagen fibrils were found for the samples by doses of 10^{-3} and 10^{-4} mg/ml ascorbic acid in 4 hours. Both samples showed greater changes for mentioned doses in one week. This indicated the impact of ascorbic acid and longer time of treatment on the strength of cornea and the reduction of distance between collagen fibrils (consequently the increase of cross-linking). The dose of 10^{-3} mg/ml ascorbic acid had a greater effect in comparison with 10^{-4} mg/ml ascorbic acid in one week.

Collagen cross-linking leads to new covalent bonds between the collagen strings. These bonds affect the biomechanical strength and stiffness of cornea. Furthermore, they also change the corneal refractive index at multiple locations in cornea and reduce its adverse effects on vision. The gradual increase of visual acuity implies the efficacy of collagen cross-linking in cornea and its modifying factors. Wollensak et al. (24) studied the effects of riboflavin and UVA rays on 23 eyes with advanced keratoconus. They showed the best corrected vision was raised by 1.65 ± 1.5 lines in vision chart for 65% of patients (24).

Sander et al. (25) also conducted a study on the corneal collagen cross-linking in 60 eyes with advanced keratoconus. They concluded that the best corrected vision was increased about 2.04 ± 1.4 lines in eye chart (25). Caporossi et al. (26) reported the increase of 6 3.6 and 1.66 lines of eye chart in corrected and uncorrected visual acuity for 10 patients at 6 months after treatment, respectively (26). Pinelli (27) showed that uncorrected and corrected visual acuity has been increased by 2 and 1.8 lines in the eye chart at nine months after collagen cross-linking on 10 patients with advanced keratoconus (27). Raiskup et al. (28) studied 272 patients with advanced keratoconus. They showed that the best corrected vision in 53 % of patients was increased more than one line in the eye chart at the first year after collagen cross-linking while it did not change for 20 % of patients (28).

Our results showed that ascorbic acid with different doses and at different times was very less destructive at keratocyte in comparison with optisol. These were inconsistent with cell cultures derived from keratocyte of pigs, the damage threshold for UVA ray in combination with riboflavin 0.0025 was determined 0.4 mw/cm² which was 10 times lower than the threshold of UVA ray alone (29). In another study

	Cornea1						Cornea2					
	10 ⁻³ AA+ 4hours	10 ⁻⁴ AA 4hours	Control 4hours	10 ⁻³ AA 7 days	10 ⁻⁴ AA 7 days	Control 7 days	10 ⁻³ AA 4hours	10 ⁻⁴ AA 4hours	Control 4hours	10 ⁻³ AA 7 days	10 ⁻⁴ AA 7 days	Control 7 days
Mean	24.67	26.61	61.86	13.84	14.68	74.73	19.70	19.84	50.94	10.06	11.76	79.65
SD (mean)	.56	.66	.80	.43	.53	.88	.68	.96	.85	.74	.80	1.26
Median	24.85	26.65	61.78	13.91	14.72	74.65	19.48	19.87	51.07	10.14	11.75	79.69
Minimum	23.00	25.13	60.17	12.75	13.78	72.64	18.18	17.69	48.26	7.95	9.30	76.95
Maximum	25.71	28.11	63.89	15.04	17.78	77.28	21.72	21.71	52.86	12.07	13.85	82.46
Percentiles	25	24.42	26.00	13.59	14.28	74.43	19.28	19.27	50.25	9.73	11.28	78.91
	50	24.85	26.65	61.78	13.91	74.65	19.48	19.87	51.07	10.14	11.75	79.69
	75	25.01	27.05	62.46	14.03	74.97	20.16	20.46	51.46	10.40	12.25	80.34

• Ascorbic Acid

Table 1: The distance between collagen fibrils of cornea for two distinct patients at different time and treatments

Cornea1						Cornea2					
	Number	Average	Standard deviation	P-value of Friedman		Number	Average	Standard deviation	P-value of Friedman		
Control/ 4 hours	100	61.86	.80	<0.001	Control/ 4 hours	100	50.94	.85	<0.001		
10 ⁻³ AA/4hours	100	24.67	.56		10 ⁻³ AA/4 hours	100	19.70	.684			
10 ⁻³ AA/ 7 days	100	13.84	.430		10 ⁻³ AA/ 7 days	100	10.06	.74			
Control/ 4 hours	100	61.86	.80	<0.001	Control/ 4 hours	100	50.94	.85	<0.001		
10 ⁻⁴ AA/ 4 hours	100	26.60	.66		10 ⁻⁴ AA/ 4 hours	100	19.84	.96			
10 ⁻⁴ AA/ 7 days	100	14.68	.53		10 ⁻⁴ AA/ 7 days	100	11.74	.80			

* Ascorbic Acid

Table 2: Comparison of changes in measurements during different times based on Friedman's nonparametric test between the two corneas

Cornea1						Cornea 2					
	Number	Average	Standard deviation	P-value		Number	Average	Standard deviation	P-value		
Control/ 4 hours	100	61.86	.80	<0.001	Control/ 4 hours	100	50.94	.85	<0.001	Control/ 4 hours	
10 ⁻³ AA* / 4 hours	100	24.67	.56		10 ⁻³ AA/ 4 hours	100	19.70	.68			
Control/ 4 hours	100	61.86	.80	<0.001	Control/ 4 hours	100	50.94	.85	<0.001	Control/ 4 hours	
10 ⁻⁴ AA/ 4 hours	100	26.60	.66		10 ⁻⁴ AA/ 4 hours	100	19.84	.96			
Control/ 4 hours	100	61.86	.80	<0.001	Control/ 4 hours	100	50.94	.85	<0.001	Control/ 4 hours	
Control 7 days	100	74.73	.88		Control/ 7 days	100	79.65	1.26			
10 ⁻³ AA/ 7 days	100	13.84	.43	<0.001	10 ⁻³ AA/ 7 days	100	10.06	.74	<0.001	10 ⁻³ AA/ 7 days	
10 ⁻⁴ AA/ 7 days	100	14.68	.53		10 ⁻⁴ AA/ 7 days	100	11.76	.80			
Control/ 7 days	100	74.73	.88	<0.001	Control/ 7 days	100	79.65	1.26	<0.001	Control/ 7 days	
10 ⁻⁴ AA/ 7 days	100	14.68	.53		10 ⁻⁴ AA/ 7 days	100	11.76	.80			
Control/ 7 days	100	74.73	.88	<0.001	Control 7 days	100	79.65	1.26	<0.001	Control 7 days	
10 ⁻³ AA/ 7 days	100	13.84	.43		10 ⁻³ AA/ 7 days	100	10.06	.74			
10 ⁻³ AA/ 7 days	100	13.84	.43	<0.001	10 ⁻³ AA/ 7 days	100	10.06	.74	<0.001	10 ⁻³ AA/ 7 days	
10 ⁻⁵ AA/ 4 hours	100	24.67	.56		10 ⁻⁵ AA/ 4 hours	100	19.70	.68			
10 ⁻⁴ AA/ 4 hours	100	26.61	.66	<0.001	10 ⁻⁴ AA/ 4 hours	100	19.84	.96	<0.001	10 ⁻⁴ AA/ 4 hours	
10 ⁻⁴ AA/ 7 days	100	14.68	.53		10 ⁻⁴ AA/ 7 days	100	11.76	.80			
10 ⁻³ AA/ 4 hours	100	24.67	.56	<0.001	10 ⁻³ AA/ 4 hours	100	19.70	.68	<0.001	10 ⁻³ AA/ 4 hours	
10 ⁻⁴ AA/ 4 hours	100	26.61	.66		10 ⁻⁴ AA/ 4 hours	100	19.84	.96			

* Ascorbic acid

Table 3: Comparison of various average measurements of distance between collagen fibrils based on nonparametric Wilcoxon test for two corneas

on keratocytes in pigs, Wollensak et al. (30) showed that the threshold of cellular damage of keratocytes were 0.5 mw/cm² and 5 mw/cm² for a combination of UVA ray and riboflavin 0.1% and UVA ray, respectively (30). The reduction in keratocytes for the depth of 270-350 micron inside stroma were observed by clinical investigations with the help of confocal microscopy on 10 corneal cross-linking. However, it was completely restored by the adjacent cell mobilization after 6 months (26, 31).

The low number of samples and different measurements of the distance between collagen fibrils were the weaknesses of our study. The novelty of this work was to study the effects of ascorbic acid on the increase of corneal collagen cross-linking.

Conclusion

The purpose of the current study was to determine the effects of ascorbic acid on corneal collagen cross-linking in keratoconus in vitro. Corneal collagen cross-linking is explained as the most promising novelty in the treatment of progressive keratoconus in recent years. We found statistically significant increasing in the resistance of stromal collagen. Results showed that ascorbic acid can strengthen the cornea and decrease the distance between collagen fibrils (consequently increase cross-linking). Therefore, the efficacy of ascorbic acid is observed by more recovery through increasing its doses and passing time. It is noteworthy that this study can be a useful preliminary to future researches.

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Investigating the prenatal exposure of hydro-alcoholic extract of ginger on the function of Pituitary – Gonad axis in male mature offspring rats

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Abstract

Background and Objective: Ginger has been used for a long time as a spice in food as well as pharmaceuticals in a wide variety of diseases. Ginger has been shown to prevent the nausea in pregnant women. The aim of the present study was to examine the effect of hydro-alcoholic extract of ginger (HEG) on function of pituitary – gonad axis in mature male rats exposed to HEG in the prenatal period.

Method: In this experimental study, 40 pregnant female rats were divided into four groups. Groups contained control, placebo (daily received 0.5 ml normal saline), and treatment groups receiving 50 mg/kg and 100 mg/kg of HEG in pregnancy period. At the end of the infancy period, males of groups were separated and 10 rats out of each group were randomly chosen in maturity.

Upon the time of maturity of chosen male rats, blood samples were drawn for measurement of the levels of sex hormones in male rats. Also the number of Leydig, Sertoli, spermatogonia, spermatocytes and spermatide cells were counted.

Results: Administration of HEG in groups received 50mg/kg and 100 mg/kg which resulted in a significant increase in concentration of testosterone, LH and FSH hormones in male progenies. HEG administration also significantly increased the number of Leydig and Sertoli cells, spermatogonia, spermatocytes and spermatid.

Conclusion: With regard to the results of this research, consumption of HEG in the perinatal period results in increase in function of Pituitary – Gonad axis in born male adult rats.

Key words: Ginger; testosterone; Luteinizing Hormone; Follicle Stimulator Hormone; Spermatocyte,

Introduction

Despite many achievements in modern medicine, the main problem is still the usage of synthetic chemical drugs for the treatment of diseases causing serious side effects in patients receiving them (1). Nowadays traditional medicine has been revisited as the use of herbal medicine is markedly increasing due to it possessing lower side effects (2). So the current approach is to apply herbal medicine to obtain a high standard of therapy for the treatment of myriad diseases with minimum side/adverse effects.

Ginger (*Zingiber officinale*) belongs to the *Zingiberaceae* family. As spice, ginger has been used in the diet and pharmaceutical components. Historically medicine has shown that ginger has been widely used in China, Japan and India for the treatment of nausea and vomiting in women during pregnancy (3).

The ingredients of ginger contain water, protein, fat, minerals (including iron, calcium and phosphorus), vitamins (such as thiamine, riboflavin, niacin and vitamin C), fiber and carbohydrate. These compounds may be different as a result of variation in agricultural, drying and storage conditions. In the rhizome of fresh ginger, gingerols are the main components. Special aroma and the taste of ginger come from the mixture of gingerols, shogaol and zingerone which are found in ginger (4 and 5).

Until now, more than 50 types of antioxidants have been isolated from the rhizome of ginger. Gingerols are the most important components of ginger that have significant antioxidant properties. In addition, they have a high antioxidant activity due to containing vitamins such as A, B, C and E as well as flavonoids and glutathione (6). Ginger has a wide variety of pharmaceutical properties to treat many health problems over the years, including stomach ache and intestinal problems. Because of possessing cholinergic and anti-histamine properties, ginger has desirable effects on reducing the nausea and vomiting in women during pregnancy (7). Ginger is able to stimulate blood circulation, increase cell activity and metabolism. It also can have anti-cancer property because of antioxidant activity and ability in inactivating the effective factors on carcinogenesis (8). Regular intake of ginger in the dietary regimen can improve the activity of heart and circulation system (9). Ginger causes a significant decrease in the physical signs of initial dysmenorrhoea (10). Studies indicate that the extract of ginger stimulates menstruation, eliminates the irregularities in the menstruation cycle, increases spermatogenesis and enhances sperm fertility factors (11, 12). Furthermore, ginger is used to treat fever, rheumatism, neuronal diseases, gingivitis, tooth pain, asthma and coughing (13).

There are many concerns about using chemical drugs in women during pregnancy for the nausea and vomiting owing to possible deformities in fetus. Hence, using herbal components paves the way for alternative treatment in pregnant women. Based on the above evidence, having less side effects for ginger usage has opened a new

horizon to treat such complications in women during pregnancy (14).

Research has shown that ginger increases spermatogenesis and effectiveness of sperm fertility parameters. Regarding high prevalence of men's infertility in the world which is resulting from the production of damaged sperm and malfunction of the cells responsible for spermatogenesis, there is a need for an alternative therapy for the treatment of infertility due to the high cost of therapeutic agents and severe side effects. Several lines of evidence suggest ginger has a beneficial role in spermatogenesis and sperm parameters because of the antioxidant properties of ginger. In light of the effectiveness of ginger on spermatogenesis, the present study was established to examine the effect of prenatal exposure to HEG on pituitary – gonad axis hormones and spermatozoa of young adult male rats.

Materials and Methods

In this study, 40 Wistar adult female rats weighing between 200-220 gr were grouped into 4 groups (10 per group) including control, placebo and two treatment groups. In addition, 8 Wistar adult male rats were used for crossbreeding.

Rats were kept in Animal House of Azad Islamic University of Falavarjan in a 12 hour light/12 hour dark cycle in 25 ° c and relative humidity ranging from 40-60% in order to be acclimatized in their new place. Also, water and food were provided *ad libitum*.

To prepare the HEG, the rhizome of ginger was obtained from the Agricultural Research Center of Isfahan. For this purpose, fresh and intact plants were used. Then herbarium no.128/3/001/001 was approved by the plant specialists of Islamic Azad University of Falavarjan. After that, ginger rhizome was dried and then ground and finally the resulting powder was extracted by maceration.

Before crossbreeding the female rats with males, in order to synchronize the menstrual cycles of female rats, 100 mg estradiol valerate was dissolved into 0.2 ml olive oil and then was injected into the rat muscles using insulin syringes. After 42 hours of the first injection 50 mg of progesterone was injected into the muscles of rats. After 6 hours of the second injection, a vaginal smear was obtained from the rats. Marcondes' method was used for recognizing the steps of estrous cycle. In this method, each step of the cycle is recognized based on the proportion among three cell populations including epithelial, horny and leukocytes observed in the vaginal smear (15).

Microscopic observations showed that synchronizing the cycle of rats had occurred in the estrous s step. Then, for crossbreeding, 8 adult male rats were co-caged with female rats (16). Upon observing sperm in vaginal smears the day 0 of pregnancy was defined. During pregnancy for two treatment groups 50 mg/kg and 100 mg /kg HEG were intraperitoneally injected every day. The control group received no treatment. The placebo group daily

received 0.5ml normal saline. At the end of the infancy period, male and female offspring were separated and kept without any treatment for up to 2 months. Then, 10 male rats of each four groups were randomly selected for analysis of hormones. To do that, blood was obtained from their hearts after being anesthetized. Blood samples were centrifuged at 300 rpm for 5 minutes and kept in -20° C until usage.

The levels of FSH, and LH hormones were measured by electro-chemiluminescence luminescence method (ECL) and the levels of testosterone hormones were measured by enzyme linked immunosorbent assay (ELISA). Kits used for measuring FSH and LH were purchased from (Cusabio, USA) and one for testosterone with mark IBL, GmbH made in Germany, respectively.

In order to count the number of sexual dynastic cells, at first, right testicles of male rats were removed and placed in a 10% solution of formalin. Soon after, dehydration by ethanol, clearing by xylene alcohol and tissue embedding were done. Next, using Rotary Microtome (LEIYZ Australian model 1512) 5 micron thickness tissue sections were provided. Then, the obtained sections were stained by hematoxylin and eosin. The number of Leydig, Sertoli, spermatogonia, spermatocytes and spermatide cells were counted using light microscopy. Finally, data were analyzed by SPSS software by one-way analysis of variance (ANOVA) and Tukey HSD test. Significance level was considered if p value was less than 0.05.

Results

Results obtained from data analysis showed that there wasn't any significant difference between serum mean of LH, FSH and testosterone hormones and sex lineage cells, while HEG in both used doses resulted in significant increase in serum mean of LH and testosterone hormones and also in serum mean of FSH hormones in $P \leq 0.01$ in the groups receiving a high dose of HEG (Table 1).

In addition, results obtained from counting lineage cells showed that administration of HEG in both doses resulted in significant increase in the number of Leydig, spermatogonia, Sertoli, spermatocytes and spermatide cells in these groups in comparison to controls in $P \leq 0.01$ level (Table 2 and Figure 1).

Table 1. Comparison of the mean serum level of LH, FSH hormones and testosterone in the groups treated with HEG

Hormones	N	LH (IU/dl)Mean \pm SD	FSH (IU/dl)Mean \pm SD	testosterone(ng/ml)Mean \pm SD
Control	10	0.841 \pm 0.04	0.950 \pm 0.09	0.292 \pm 0.03
Experimental	10	0.866 \pm 0.04	1.06 \pm 0.32	0.270 \pm 0.04
Ginger extract 50 mg/kg	10	0.958 \pm 0.07**	1.10 \pm 0.13	0.600 \pm 0.08**
Ginger extract 100 mg/kg	10	1.140 \pm 0.09**	1.27 \pm 0.07**	0.780 \pm 0.07**

* Shows the significant difference in level ($P < 0.05$) in comparison to control

** Shows the significant difference in level ($P < 0.01$) in comparison to control

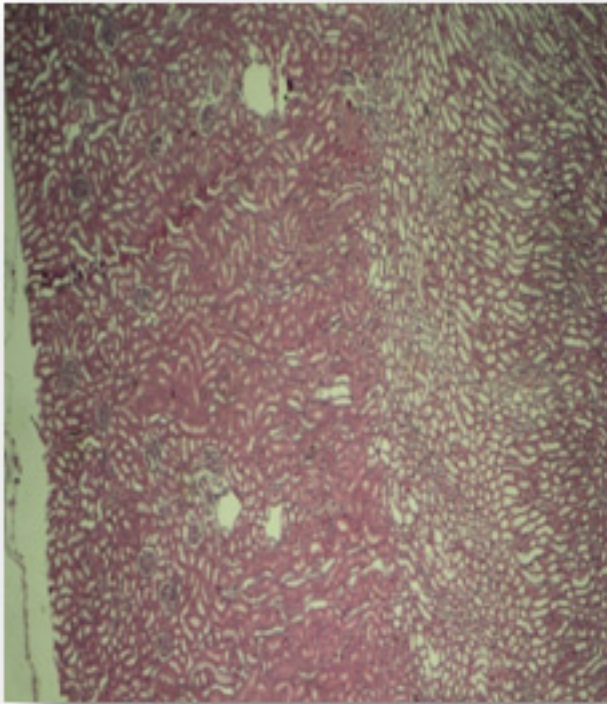
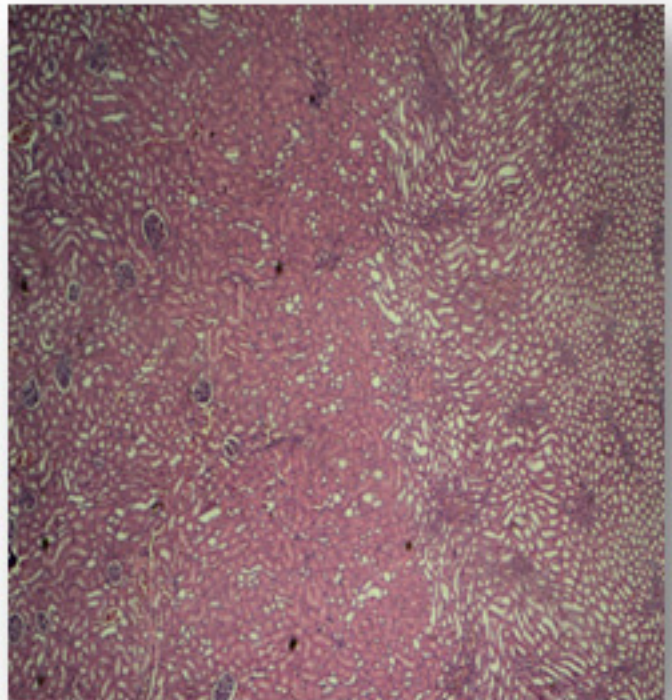
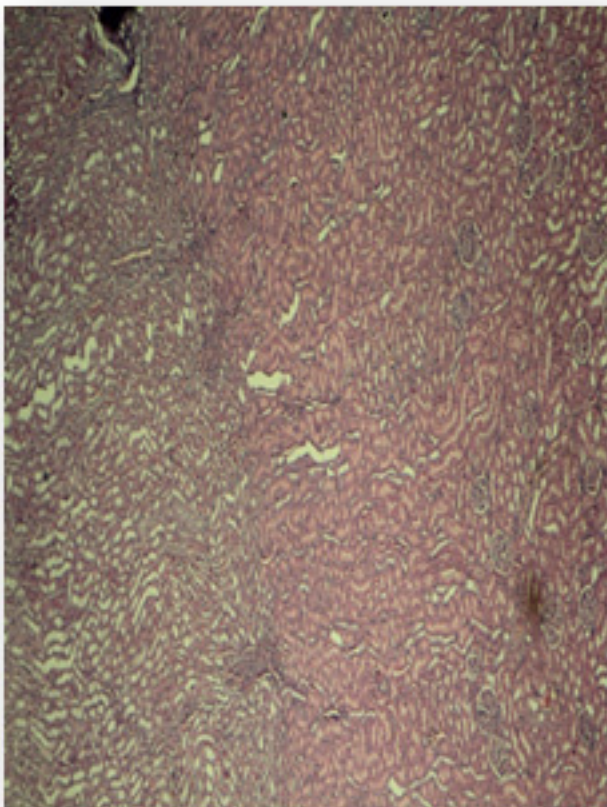
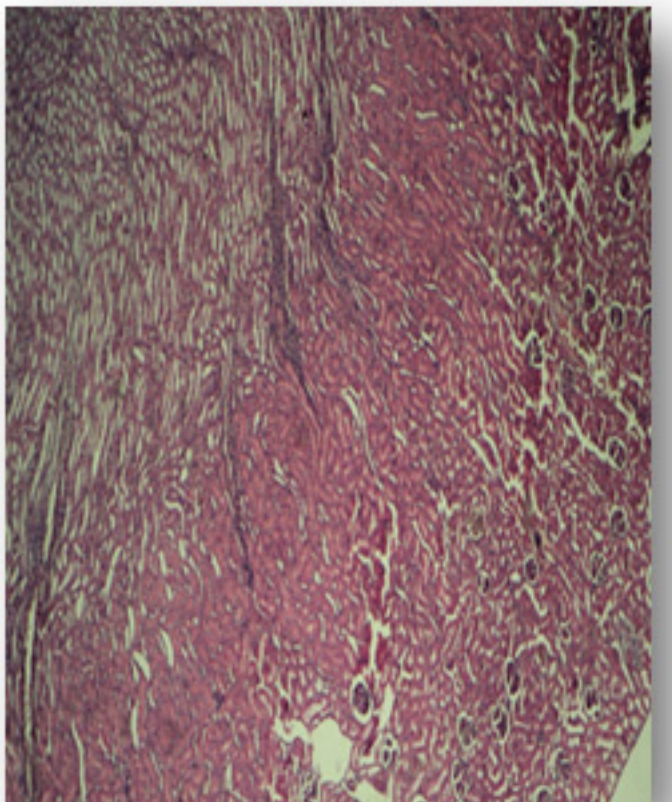
Table 2: the number of lineage sex cells in the groups treated with HEG in comparison to control

Follicles Groups	The total number of spermatogenic cells Mean \pm SD	The total number of spermatocyte Mean \pm SD	The total number of spermatid cells Mean \pm SD	The total number of Sertolic cells Mean \pm SD	The total number of Leydig, cells Mean \pm SD
Control	67.74 \pm 3.10	80.28 \pm 2.55	109.19 \pm 1.73	16.33 \pm 0.34	26.97 \pm 0.47
Experimental groups	64.99 \pm 3.94	83.67 \pm 2.58	110.39 \pm 1.83	17.37 \pm 0.35	28.02 \pm 0.415
Ginger extract 50 mg/kg	78.00 \pm 3.23**	93.06 \pm 2.73**	124.05 \pm 3.51**	18.53 \pm 0.35**	29.01 \pm 0.70**
Ginger extract 100 mg/kg	84.77 \pm 3.33**	97.98 \pm 2.82**	133.66 \pm 3.24**	19.99 \pm 0.76**	30.48 \pm 1.22**

* Shows significant difference in level (P <0.05) in comparison to control

** Shows significant difference in level (P <0.01) in comparison to control

Figure 1: Light photomicrograph of thyroid tissue in group 1(control), Placebo group (2) (3) group received the extract of HEG with dose 50 mg/kg (4) group received HEG with dose 100 mg/kg H & E was used for staining the tissues.

**1****2****3****4**

Discussion

Results of this study showed that administration of HEG in both doses resulted in significant increase in the levels of testosterone, LH and FSH hormones. HEG also increased the number of germ cell lineage. In view of increase in number of Leydig, spermatogonia, spermatocytes and spermatid cells along with increase in testosterone hormone, it seems that testosterone hormone plays an important role in division of Gametes, nourishing the dividing gametes. HEG could have a beneficial role in sperm through direct effect on Sertoli cells and excretion of tube fluid and various proteins including growth factor and transferrin (17). Subsequently, given the important role of testosterone in spermatogenesis, it is obvious that increasing the levels of this hormone could increase the number of sperm. Our findings show a significant increase in the count of sperm after treatment with ginger.

In similar studies, the concentration of testosterone and LH in groups receiving ginger extract was significantly increased in comparison to controls. Since the testosterone is an androgenic hormone produced by Leydig cells which belong to testis stimulated by the excretion LH from pituitary gland, it would be plausible that the mechanism underlying this phenomenon might be due to the direct effect of HEG on luteotropic cells of anterior pituitary increased levels of LH (17).

Ginger has many types of antioxidants. Among these compounds, gingerols are of note. Gingerols possess anti-oxidant, anti-serotonergic and anti-inflammatory properties. (18) In line with the results of this study, Khaki et al in an experimental study have shown that ginger can increase the number of sperm and their motility which may be attributed to gingerols and shogaol. They stimulate the androgens especially the testosterone (19).

In addition to the above properties, ginger has a high anti-oxidant activity because of the vitamins including vitamin A, B, C and E also flavonoids and glutathione (18). Vitamin E is considered as a strong non-enzyme antioxidant which can inhibit the peroxidation lipids of the cell membrane through scavenging the free radicals (20). In the male genital system, the antioxidant activity of vitamins has been reported and is thought to be a result of inhibition the destructive effects of free radicals in the testis (21) and sperm (22 and 23). Moreover, vitamin E can strengthen the antioxidant defense system of testis and sperm cells (24).

Studies have shown that ROS are produced by two different sources in sperm fluid containing damaged spermatozoa cells and active white blood cells whereby a high amount of them results in male infertility through breakage in the DNA structure, decrease in live sperm percentage and dissociation of sperm from ovule surface (25 and 26). These compounds increase the amount of malone-di-aldehyde. Malone-di-aldehyde leads to distortion in distribution of lipid in cell membrane through penetration of the structure of cell membrane. Furthermore, ROS can

cause chromosome disintegration by intercalating into the DNA. Vitamin E can make a breakage between two peroxide lipid bonds thereby the inhibition producing free radical (27). Another crucial vitamin in ginger is vitamin C that acts as a neutralizing antioxidant scavenging the free radicals produced by ROS. It has been demonstrated that it would facilitate the entrance of other antioxidants such as vitamin E and uric acid to the cycle (28).

Glutathione peroxidase (GPx) enzyme plays an important role in protecting the sperm and epididymis in which the reduction of GPx results in infertility. Extract of ginger increases the activity and expression of GPx enzyme cells of liver, kidney, breast, testis, etc. Studies show that antioxidant enzymes including GPx and superoxide dismutase protect the cell through hindrance of the formation of the peroxide and oxidative reactions. (29) Therefore, GPx prevents the deleterious effects of DNA breakage consequences in the sperm and sperm-producing cells. It also protects the sperm nuclei and epididyme fluid against free radicals, resulting in correct maturation of sperm.

Consistent with these results, Mohammadi et al studied the effect of ginger on testicles of rats by treating the cells with Cyclophosphamide. They found that ginger had protective effect on the testis of rats because of high antioxidant content (30).

In a study conducted by Hafez in Greece on the effect of a ginger and cinnamon combination on infertile diabetic rats, a significant increase was observed in sperm parameters and reproductive behavior in terms of sperm parameters including count, motility and viability (31). Another study was conducted by Abo-Ghanema et al using the combination of ginger and L-carnitine to treat infertile rats. The authors showed that this combination increased the weight of testicles and seminal vesicles, improved the quality and quantity of semen (32).

Selenium is another antioxidant found in ginger. Selenium is a quasi-metal micro-nutrient which is requisite for the dietary regimen of mammals found in plant and animal products. Various reports of research implies that the positive effect of selenium on male health is by reducing the signs and symptoms of diseases such as infertility, viral infections, cancer and cardiovascular diseases. Selenium is an essential antioxidant for spermatogenesis and male fertility (33, 34). Investigation carried out in this regard showed that selenium stimulates the motility of sperm (35).

Conclusion

Tantalizing evidence suggests a key role for oxidative stress in the development of infertility in men implying that further studies are warranted to unravel the role of oxidative stress in the progression of male infertility (36). Regarding the protective role of ginger on sperm through antioxidant properties and deleterious effects of oxidative agents on them, it is suggested that antioxidants found in

ginger could be used as a potential therapeutic agent for the treatment and alleviation of infertility in men.

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