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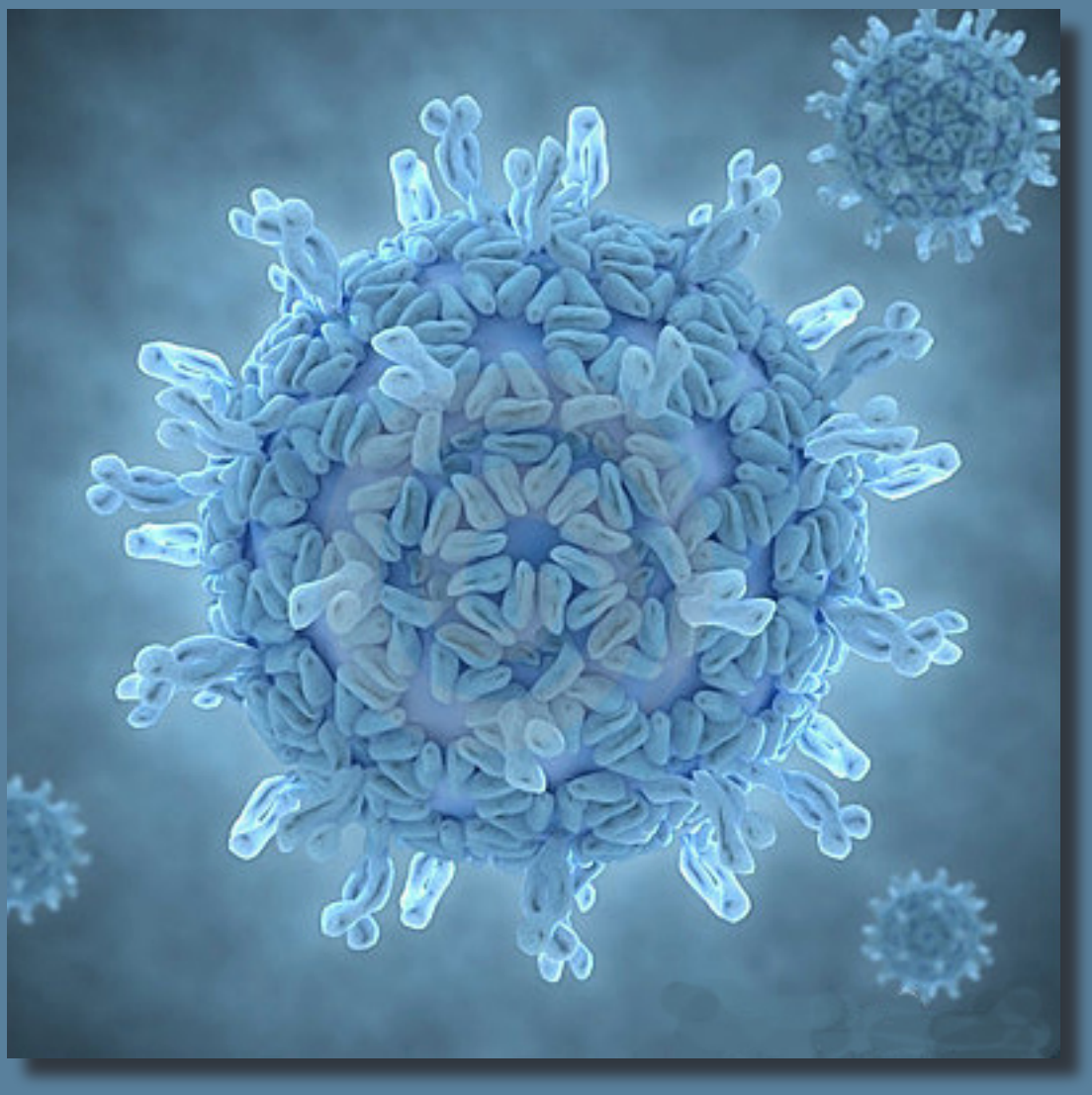

Rota virus vaccine- induced intussusception: A case report study

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From the Editor

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This issue of the journal has a number of research papers from the region. A paper from Saudi Arabia evaluates the sensitivity of urine dipstick analysis as a screening test in predicting UTI in symptomatic adults in the primary care setting. Urinary tract infection (UTI) is a common clinical problem in the primary care. Urine dipstick analysis is a quick, cheap and a widely used test to predict UTI in clinically suspected patients. A total of 420 culture-positive urine samples from patients with symptomatic UTI, and had dipstick urinalysis in a primary care center were the subjects of this study. The sensitivity of urine dipstick nitrites (NT), leukocyte esterase (LE) and blood was calculated and compared with positive culture samples either individually or in combination. The sensitivity of dipstick NT alone was the lowest of all tests (20.7%), while LE alone was little higher than NT (31.42%), whereas dipstick blood test when considered alone was the highest sensitive (61.9%). On combination, NT and/or LE were marginally higher than either test alone (41.2%), while NT and/or blood were (64.5%).The highest sensitivity of dipstick is obtained when all the three parameters are considered together (81.4%). The authors concluded that Dipstick NT, LE, and blood are poor screening tests when used individually. Dipstick sensitivity significantly increases, and it could be considered a good screening test to predict UTI in symptomatic adults in the setting of primary care when its three components are considered together. However, negative dipstick analysis should not rule out UTI in symptomatic adults, and urine culture is necessary for accurate diagnosis.

Intussusception. The authors stressed that Intussusception is a rare potential adverse effect of oral rotavirus vaccination, estimated to occur in approximately 1 in 100,000 vaccine recipients. The patient is a six-months old boy presented with vomiting for 3 days, colicky abdominal pain, and did not pass stool for one day prior the admission. No seizure, no cough, no jaundice, no skin/joint/ bone complications. History of similar condition 2 months ago at age of 4 months (one week following his scheduled vaccination which contains Rota vaccine). Physical examination; lethargic, afebrile with stable vital signs, abdomen was soft lax and not distended and no palpable mass. Per rectal (PR) examination was blood stained. He was diagnosed with intussusception. Laparotomy resection of 6 CM of terminal ileum 15CM away from ileocaecal valve with appendectomy. The authors concluded that although the reported vaccine-induced intussusception every now and then , The overall risk benefit balance of vaccines remains positive So World Health Organization (WHO) and the Australian Technical Advisory Group on Immunization (ATAGI) have recommended the continued use of rotavirus vaccine for infants as it reduce annual hospital admissions in children under 5 years due to rotavirus gastroenteritis.

A paper from Turkey looked at Accelerated atherosclerosis and digital clubbing in sickle cell diseases. The authors stressed that Sickle cell diseases (SCDs) are chronic destructive processes mainly on the capillary endothelium. We tried to understand significance of digital clubbing in severity of SCDs. All patients with SCDs were taken into the study. The study included 397 patients (193 females). There were 36 cases (9.0%) with digital clubbing. Male ratio was significantly higher in the digital clubbing group (66.6% versus 49.8%, $p<0.05$). The mean white blood cell counts of peripheric blood were similar in both groups ($p<0.05$). On the other hand, the mean hematocrit value and platelet count of peripheric blood were lower in the digital clubbing group, significantly ($p= 0.001$ and $p= 0.012$, respectively). Beside that, prevalence of leg ulcers, pulmonary hypertension, chronic obstructive pulmonary disease, coronary heart disease, cirrhosis, and stroke were significantly higher in the digital clubbing group ($p<0.01$ for all). There were 25 mortalities during the period, and 13 of them were males. The authors concluded that SCDs are chronic destructive processes on endothelium particularly at the capillary level, and terminate with accelerated atherosclerosis induced end-organ failures in early years of life. Probably digital clubbing is one of the terminal consequences of the SCDs indicating significantly shortened survival in such patients.

A Cross sectional study from Dubai and Saudi Arabia assessed the components of self monitoring blood glucose among patients with type 2 diabetes attending primary health care service and its relation to glycemic control. One hundred and seventy eight (178; male 72, female 106) were randomly selected from our diabetic registry. All selected patients were having type 2 diabetes. Data was collected through designed questionnaire. The three components of the glucose self monitoring system was assessed. One hundred and seventy eight – 178; (40.04% male vs 59.56% female). Eighty eight (88 subjects) were illiterate (49.4%) and most of them were female (38.9% male vs 56.6% female). In the male group only 77.7% had glucometers while In female group only 52.8% had glucometers (P value <0.0001). in male group only 61.1% know how to operate the SMBG while only 39.6% of female group can do (P value <0.00001).In male group only 33.3% stated that they knew the targets of glucose monitoring while it was 68.8% in female group (P value <0.00001) . Only 55.5% of male subjects had the three components of proper home glucose self monitoring while 56.1% (P value 0.036). The authors concluded that Lack of proper structured education presented by educators and illiteracy may explain the bad glycemic control in our study sample. Further large studies were recommended

A double blind study from Lebanon examined the efficacy and safety intramuscular vitamin B12 (Tricortin 1000) in the treatment of low back pain in patients with mechanical lumbago. A total of 120 patients aged between 18 and 65 years with lumbago or sciatic neuritis of mechanical origin without need for surgical procedures were enrolled. Patients had to present with a proven medical history for back pain (lasting from 6 months to 5 years). Both treatment groups experienced a sharp decrease in pain and disability. However, comparison between groups at the end of the treatment period showed a statistically significant difference in favour of the active treatment). In addition the use of paracetamol proved significantly higher in the placebo group than in the active treatment ($p < 0.0001$). The author concluded that the efficacy and safety of parenteral Vitamin B12 in alleviating low back pain and related disability and in decreasing the consumption of paracetamol was confirmed in patients with no signs of nutritional deficiency.

2 Editorial

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How Sensitive is Urine Dipstick Analysis in Predicting Urinary Tract Infections in Symptomatic Adults in a Primary Care Setting?

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Abstract

Background: Urinary tract infection (UTI) is a common clinical problem in the primary care setting. Urine dipstick analysis is a quick, cheap and widely used test to predict UTI in clinically suspected patients.

Objective: To evaluate the sensitivity of urine dipstick analysis as a screening test in predicting UTI in symptomatic adults in the primary care setting.

Methods: A total of 420 culture-positive urine samples from patients with symptomatic UTI, who had dipstick urinalysis in a primary care center were the materials of this study from March to October 2015. The sensitivity of urine dipstick nitrites (NT), leukocyte esterase (LE) and blood was calculated and compared with positive culture samples either individually or in combination.

Results: The sensitivity of dipstick NT alone was the lowest of all tests (20.7%), while LE alone was marginally higher than NT (31.42%), whereas dipstick blood test when considered alone was the highest sensitive (61.9%). In combination, NT and/or LE were marginally higher than either test alone (41.2%), while NT and/or blood were (64.5%). The highest sensitivity of dipstick is obtained when all the three parameters were considered together (NT and/or LE and/or Blood, sensitivity 81.4%).

Conclusion: Dipstick NT, LE, and blood are poor screening tests when used individually. Dipstick sensitivity significantly increases, and it could be considered a good screening test to predict UTI in symptomatic adults in the primary care setting when its three components are considered together. However, negative dipstick analysis should not rule out UTI in symptomatic adults, and urine culture is necessary for accurate diagnosis.

Key words: Urinary tract infection, dipstick analysis, screening, urine culture, nitrites, leukocyte esterase, blood.

Introduction

Overall, urinary tract infections (UTI) are the second most common infectious complaint in outpatient primary care clinics, and the most common outpatient complaint caused by bacteria. [1]It is estimated that, 2-3% of all consultations, and even 6% in the case of women, are due to symptoms suggesting UTI. [2]According to one estimate, 1 out of every 2 women will experience a UTI in her lifetime. [3]Almost 20% of UTIs are found in men especially the elderly due to prostatomegaly and distorted anatomy of the urinary tract. [4]

Symptoms of uncomplicated UTI include frequency, burning, straining, urgency, and pain with voiding. Patients may also experience hematuria, suprapubic pain or tenderness, and a change in the odor of the urine. [5]

Early diagnosis of uncomplicated UTI could significantly improve patient management in addition to providing optimum cost-effectiveness. [6,7] Urine culture is the gold standard for the diagnosis of UTI but is expensive and time consuming, requiring at least 24 hours to produce results. These limitations have made urine analysis including dipstick a preferred first-step investigation among primary care clinicians. [8]

The urine dipstick is a standard diagnostic tool of UTI, but there is much debate about its utility and role. There is doubt that this test is rapid, cheap, quick, and easy to administer. [9] Leukocyte esterase (LE, an enzyme produced by neutrophils) and nitrite (NT, the end product of bacterial nitrate reductase acting on nitrate in the urine), two important parameters of dipstick urinalysis, have been frequently used to predict UTI. Positive results of LE and NT are often used as a reflex to confirm diagnosis by urine culture (both in the presence and absence of clinical symptoms of UTI), or start of empiric antimicrobials. [10] Dipstick detection of blood in urine has been reported to possess a high sensitivity but poor specificity to detect UTI. [11]

There is much debate about the utility and role of Dipstick screening in predicting UTI. [9]Some studies have found negative urine dipstick analysis to be valuable in ruling out UTI. [12]However, other studies have shown a lack of sensitivity and specificity of these tests as indicators of UTI. [13]
So, there is marked heterogenicity in interpretation of results of dipstick analysis. The purpose of this study was to evaluate the sensitivity of dipstick urine analysis with emphasis on NT, LE and blood test, in predicting UTI in symptomatic patients in a primary care setting.

Materials and Methods

This study evaluated the urine dipstick analysis of 420 culture-positive urine samples of patients who attended the family medicine and internal medicine outpatient clinics of Umm Alqura University Medical Center, Makkah, Saudi Arabia, from March to October 2015. The center provides primary health care to the university employees and their families.

Urine samples from patients of both sexes and complaining of symptoms suggestive of UTI were included. Samples of patients less than 16 years of age, and pregnant women were excluded. The study was approved by the Research and Ethics Committee of Umm Alqura Faculty of Medicine.

Samples were collected by the patients themselves where they were asked to provide a midstream clean catch urine sample in the same day of the test. Dipstick urine analysis was done using multistix 10 SG (Siemens) and clinitek advantus analyzer. The reagent strip contains test pads for NT, LE, blood, glucose, protein, ketone, pH, specific gravity, bilirubin and urobilinogen. In this study, urine parameters considered in dipstick analysis were NT, LE, and blood. Reading time for NT and blood was one minute, and two minutes for LE. Cut-off values for a positive result was trace or more of LE, nitrite (+) and blood (+).

The presence of infection in this study was determined by quantitative urine culture. This is the gold standard criterion against which the three dipstick tests were compared. The cultures were done using blood agar and MacConkey agar plates. The cultures were read after 24 hours of incubation at 37°C. A colony count of more than 104 organisms/ml (for one organism) was defined as a positive urine culture for clean catch specimens. Full bacterial identification and antimicrobial susceptibility testing were performed for all positive specimens.[14] Specimens that contained more than two isolates (with any quantitation) were considered contaminated and were not included in the analysis. Dipstick urinalysis data as regards NT, LE, and blood were compared with positive culture results. The comparison was made for every individual test alone, then in combinations.

Results

In this study, the urine dipstick analyses of 420 culture-positive urine samples of symptomatic adults were studied. Age of included patients ranged from 21 to 64 years. The mean age of the patients was 39 years. Among 420 patients, 77.6% were females (n=326), and 22.4% were males (n=94).

Of the 420 culture positives samples, E. coli (62.1%) was the predominant isolate followed by Enterococcus species, Klebsiella, Proteus, Pseudomonas, Streptococcus species, Candida, and staphylococcus aureus, and others [Table 1].

Table 1: Number and percentage of the isolated organisms on the culture positive specimens

Organism	Number of Isolates	Percentage (%)
Escherichia Coli	261	62.14%
Enterococcus aeruginosa	52	12.4%
Klebsiella pneumoniae	30	7.14%
Proteus mirabilis	22	5.23%
Pseudomonas aeruginosa	15	3.6%
Streptococcus pyogenes	13	3%
Candida species	9	2.14%
Staphylococcus aureus	7	1.66%
Streptococcus saprophyticus	5	1.2%
Streptococcus agalactiae	3	0.72%
Miscellaneous	3	0.72
Total	420	100%

The sensitivity of dipstick NT alone was the lowest of all tests (20.7%), while LE alone was a little higher than NT (31.42%), whereas dipstick blood test when considered alone was the highest sensitive (61.9%). In combination, NT and/or LE were marginally higher than either test alone (41.2%), while NT and/or blood were (64.5%). The sensitivity increases when LE and/or blood were considered (69.7%). The highest sensitivity of dipstick screening is obtained when all the three test parameters are considered together (81.4%) [Table 2].

Table 2: Sensitivity of the urine Dipstick analysis used for screening UTI

Parameter	Sensitivity
Nitrite test	20.7% (n=87)
Leukocyte esterase test	31.42% 132
Blood test	61.9% 260
Nitrite and/or leukocyte esterase	41.2% 173
Leukocyte esterase and/or blood	69.7% 293
Nitrite and/or blood	64.5 271
Nitrite and/or blood and/or leukocyte esterase	81.4% (342)

UTI: urinary tract infections

Discussion

Urinary tract infection is the second common bacterial infection in the primary care setting. It is more common in females especially during their reproductive age. In this study, most patients diagnosed with UTI were females. This coincides with many studies which reported higher prevalence of UTI in adult women compared to men mainly due to the anatomy of the female genito-urinary tract.[3]

Diagnosis of UTI is based on clinical symptoms, together with positive urine culture.[15] However, the concerns of cost-effectiveness and lengthy processing time in urine culture have stimulated the use of other rapid diagnostic tools to predict UTI.[16] Dipstick analysis is a common rapid laboratory screening tool used by many primary care clinicians to predict UTI in symptomatic patients. It assesses presence of bacteriuria, pyuria, and hematuria associated with UTI. Notably, several studies have demonstrated significant heterogenicity in interpretation of dipstick results.[17]

Dipstick nitrite test (NT) is used to detect bacteriuria. Normally, nitrites are not found in urine but result when bacteria reduce urinary nitrates to nitrites. Many gram-negative bacteria including E. Coli, and some gram-positive bacteria are capable of this conversion, and a positive dipstick nitrite test indicates that these bacteria are present in significant numbers (i.e., more than 10,000 per mL). [18] However, non-nitrate-reducing organisms

e.g. Candida and Streptococci including Enterococci do not reduce nitrates, and may cause false-negative results. Although E. coli was the predominantly isolated organism in this study (62.1%), similar to other studies,[19-21] almost 20% of the isolates were Enterococci, Candida, and Streptococcus species, which do not produce nitrites.

Also, for bacteria to be able to reduce nitrates and produce nitrites, urine should contain sufficient dietary nitrates and have been retained in the bladder for more than 4 hours before voiding.[22,23] Performing this test on dilute urine may contribute to false-negative findings.[24] In patients who urinate frequently, dilution of NT may result in negative results. The first voided urine morning specimen has been proven to be accurate for nitrate, but such sample collection was not possible in all patients in this study. [25]Also, NT may be affected by common antibiotics e.g. nitrofurantoin, cephalexin, doxycycline, as well as vitamin C and phenazoperidine leading to suboptimal detection of bacteria. [26] Hence, an absence of urinary nitrite cannot rule out UTI.

All mentioned above may be the likely explanations for the low sensitivity of nitrite test in this study when done alone. This has been supported by findings from other similar studies. [27, 28] However, the sensitivity of nitrites in other studies varied between 39% and 81%. [19, 25, 29]

The leukocyte esterase (LE) test detects esterase, an enzyme released by neutrophils and may indicate white cells in urine (pyuria) associated with UTI. [22] Normally, urine is negative for LE. Positive value of the test correlates with the number of WBC/hpf urine sediment, and can vary from trace to many. [30] However, there are many conditions other than UTI causing pyuria and subsequent positive LE test results e.g. chlamydial urethritis, analgesic nephropathy and bladder tumors. False positives are seen in conditions when the urine is contaminated with bacteria, eosinophils or trichomonas. These reasons cause the positive predictive value of the LE test to vary from 19% to 88%. [31, 32]

False negative results may occur in the presence of significant levels of protein or glucose and in urines with high specific gravity which can crenate the white blood cells, leaving them unable to release esterases. [26, 33]

Similar to NT, LE results may be affected by common antibiotics mentioned above, as well as vitamin C, phenazoperidine, glycosuria, and urobilinogen. Also, high proteinuria has been shown to inhibit LE test. [26,34,35]

Hence, LE when considered alone as a parameter for diagnosing UTI is not as sensitive as when it is combined with nitrites in urine. A similar finding by Bhavsar et al., [36] found only substantial improvement of sensitivity when NT and LE are combined together to predict UTI in urine culture positive patients. This finding was different from other studies where the sensitivity of LE alone was high and varied between 61.7% and 77%. [29, 37, 38]

The explanation for low sensitivity of LE in this study may be attributed to some patients' self-initiation of common antibiotics to treat their condition. These medications are given over-the-counter in Saudi Arabia. Moreover, false negative LE test may be attributed to glycosuria and proteinuria, a common association of a prevalent medical problems in Saudi Arabia, diabetes mellitus.

The dipstick test for blood detects the peroxidase activity of erythrocytes in case of hematuria with UTI. However, myoglobin and hemoglobin also will catalyze this reaction, so a false positive test result may occur with conditions other than UTI including hematuria and myoglobinuria e.g. ureteric calculus, glomerular diseases, menstrual blood, malignancy, medications, concentrated urine, and strenuous exercise. [34] False negative results occur if pH of urine is less than 5.1, high specific gravity, and ascorbic acid (vitamin C) is present in the urine. [22] Blood test was the highest sensitive single test in this study. It has been reported that dipstick sensitivity for blood ranges from 91-100%.[22,39,40]

In this study, the sensitivity of dipstick was highest (81.4%) when its three parameters (NT/LE/blood) were all considered together, where any positive dipstick test results for detection of bacteruria by NT and/or detection of pyuria by LE and/or detection of blood improves sensitivity significantly, a finding comparable with that of Mambatta et al. with sensitivity 74%,[40] and Memişoğullari et al. with a sensitivity of 80%, [41]. However, in almost one fifth of the patients, there will be no positive dipstick test results and the patient's diagnosis might be missed. Hence, correlation of the dipstick test results with the patient's clinical condition is essential for accurate diagnosis.

Conclusion

Dipstick NT, LE, and blood are poor screening tests when used individually. However, Dipstick sensitivity significantly increases, and it could be considered a good screening test to predict UTI in symptomatic adults in the setting of primary care when its three components are considered together. However, negative dipstick analysis should not rule out UTI in adult patients with symptoms suggestive of UTI, and urine culture is recommended for these patients for proper diagnosis and management.

Recommendations

Primary care and family physicians are encouraged to utilize the quick, cheap, sensitive dipstick screening to predict UTI in symptomatic adults in primary care centers, and to delegate the expensive, time consuming urine culture for highly suggestive conditions of UTI with negative dipstick screening. Larger studies are recommended for larger samples from multiple primary care centers for more data generalizability.

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Accelerated atherosclerosis and digital clubbing in sickle cell diseases

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Abstract

Background: Sickle cell diseases (SCDs) are chronic destructive processes mainly on the capillary endothelium. We tried to understand the significance of digital clubbing in severity of SCDs.

Methods: All patients with SCDs were taken into the study.

Results: The study included 397 patients (193 females). There were 36 cases (9.0%) with digital clubbing. Male ratio was significantly higher in the digital clubbing group (66.6% versus 49.8%, $p<0.05$). The mean age was significantly higher in the digital clubbing group, too (36.5 versus 29.0 years, $p=0.000$). Additionally, smoking was also higher in the digital clubbing group, significantly (30.5% versus 11.0%, $p<0.001$). The mean white blood cell counts of peripheric blood were similar in both groups ($p<0.05$). On the other hand, the mean hematocrit value and platelet count of peripheric blood were lower in the digital clubbing group, significantly ($p= 0.001$ and $p= 0.012$, respectively). Beside that, prevalence of leg ulcers, pulmonary hypertension, chronic obstructive pulmonary disease, coronary heart disease, cirrhosis, and stroke were significantly higher in the digital clubbing group ($p<0.01$ for all). There were 25 mortalities during the period, and 13 of them were males. The mean ages of mortality were 33.0 ± 9.6 (range 19-47) in females and 30.0 ± 8.6 years (range 19-50) in males.

Conclusion: SCDs are chronic destructive processes on endothelium particularly at the capillary level, and terminate with accelerated atherosclerosis induced end-organ failures in early years of life. Probably digital clubbing is one of the terminal consequences of the SCDs indicating significantly shortened survival in such patients.

Key words: Sickle cell diseases, digital clubbing, chronic capillary damage, accelerated atherosclerosis, metabolic syndrome

Introduction

Chronic endothelial damage induced atherosclerosis may be the major cause of aging by inducing prolonged cellular hypoxia all over the body. For example, cardiac cirrhosis develops due to the disseminated hepatic hypoxia in patients with pulmonary and/or cardiac diseases. Probably whole afferent vasculature including capillaries are involved in the process. Some of the currently known accelerator factors of the destructive process are physical inactivity, overweight and smoking, for the development of irreversible consequences including obesity, hypertension, diabetes mellitus (DM), peripheric artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary heart disease (CHD), cirrhosis, mesenteric ischemia, osteoporosis and stroke, all of which terminate with early aging and death. They were researched under the title of metabolic syndrome in the literature, extensively (1-5). Similarly, sickle cell diseases (SCDs) are chronic destructive processes on endothelium mainly at the capillary level. Hemoglobin S (HbS) causes loss of elastic and biconcave disc shaped structures of red blood cells (RBCs). Probably, loss of elasticity instead of shapes of RBCs is the major problem, since sickling is very rare in the peripheric blood sample of the SCDs patients with associated thalassemia minors, and human survival is not so affected in hereditary elliptocytosis or spherocytosis. Loss of elasticity is probably present in the whole lifespan, but it is exaggerated with increased metabolic rate of the body. The hard cells induced prolonged endothelial inflammation, edema, remodeling, and fibrosis mainly at the capillary level and terminate with disseminated tissue infarcts all over the body (6,7). On the other hand, obvious vascular occlusions may not develop in greater vasculature due to the transport instead of distribution function of them. We tried to understand significance of digital clubbing in severity of SCDs in the present study.

Materials and Methods

The study was performed in the Medical Faculty of the Mustafa Kemal University between March 2007 and March 2015. All patients with SCDs were taken into the study. The SCDs are diagnosed with hemoglobin electrophoresis performed via high performance liquid chromatography (HPLC) method. Medical histories including smoking habit, regular alcohol consumption, painful crises per year, surgical operations, priapism, leg ulcers, and stroke were learnt. Patients with a history of one pack-year were accepted as smokers, and one drink-year were accepted as drinkers. A check up procedure including serum iron, iron binding capacity, ferritin, creatinine, liver function tests, markers of hepatitis viruses A, B, and C and human immunodeficiency virus, a posterior-anterior chest x-ray film, an electrocardiogram, a Doppler echocardiogram both to evaluate cardiac walls and valves and to measure the systolic blood pressure (BP) of pulmonary artery, an abdominal ultrasonography, a computed tomography of brain, and a magnetic resonance imaging (MRI) of hips, was performed. Other bones for avascular necrosis were scanned according to the patients' complaints. So avascular necrosis of bones was diagnosed by means of MRI (8). Cases with acute painful crises or any other inflammatory event were treated at first, and then the laboratory tests and clinical measurements were performed on the silent phase. Stroke is diagnosed by the computed tomography of brain. Acute chest syndrome (ACS) is diagnosed clinically with the presence of new infiltrates on chest x-ray film, fever, cough, sputum production, dyspnea, or hypoxia in the patients (9). An x-ray film of abdomen in upright position was taken just in patients with abdominal distention and discomfort, vomiting, obstipation, and lack of bowel movement. The criterion for diagnosis of COPD is post-bronchodilator forced expiratory volume in one second/forced vital capacity of less than 70% (10). Systolic BP of the pulmonary artery of 40 mmHg or higher during the silent period is accepted as pulmonary hypertension (11). CRD is diagnosed with a serum creatinine level of 1.3 mg/dL or higher in males and 1.2 mg/dL or higher in females during the silent period. Cirrhosis is diagnosed with liver function tests, ultrasonographic findings, and histologic procedure in case of indication. Digital clubbing is diagnosed with the ratio of distal phalangeal diameter to interphalangeal diameter which is greater than 1.0 and with the presence of Schamroth's sign (12,13). Associated thalassemia minors are detected with serum iron, iron binding capacity, ferritin, and hemoglobin electrophoresis performed via HPLC method. Stress electrocardiography is just performed in cases with an abnormal electrocardiogram and/or angina pectoris. Coronary angiography is taken just for the stress electrocardiography positive cases. So CHD was diagnosed either angiographically or with the Doppler echocardiographic findings as the movement disorders in the cardiac walls. Rheumatic heart disease is diagnosed with the echocardiographic findings, too. Ileus is diagnosed with gaseous distention of isolated segments of bowel, vomiting, obstipation, cramps, and with the absence of peristaltic activity of the abdomen. Eventually, cases with digital clubbing and without were collected into the two groups, and they were compared in between. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 397 patients with the SCDs (193 females and 204 males). There were 36 cases (9.0%) with digital clubbing. Mean age of patients was significantly higher in the digital clubbing group (36.5 versus 29.0 years, $p=0.000$). The male ratio was significantly higher in the clubbing group, too (66.6% versus 49.8%, $p<0.05$). Parallel to the male ratio, smoking was also higher in the digital clubbing group, significantly (30.5% versus 11.0%, $p<0.001$). Prevalence of associated thalassemia minors were similar in both groups (58.3% versus 66.2% in the clubbing group and other, respectively, $p>0.05$) (Table 1). The mean white blood cell (WBC) counts of the peripheric blood were similar in both groups ($p<0.05$). The mean hematocrit (Hct) value and platelet (PLT) count of peripheric blood were lower in the digital clubbing group, significantly

Table 1: Characteristic features of the study cases

Variables	Cases with digital clubbing	*p*-value	Cases without digital clubbing
Prevalence	9.0% (36)		90.9% (361)
Male ratio	***66.6% (24)***	***<0.05***	***49.8% (180)***
Mean age (year)	***36.5 ± 10.9 (16-56)***	***0.000***	***29.0 ± 9.7 (5-59)***
Thalassemia minors	58.3% (21)	Ns*	66.2% (239)
Smoking	***30.5% (11)***	***<0.001***	***11.0% (40)***

*Nonsignificant (p>0.05)

Table 2: Peripheric blood values of the study cases

Variables	Cases with digital clubbing	*p*-value	Cases without digital clubbing
Mean WBC* counts (/µL)	15.329 ±4.801 (7.000-26.600)	Ns†	15.114 ±6.756 (1.580-48.500)
Mean Hct‡ values (%)	***21.0 ± 4.3 (12-32)***	***0.001***	***23.9 ± 5.1 (8-42)***
Mean PLT§ counts (/µL)	***378.916 ± 184.460 (114.000-1.142.000)***	***0.012***	***461.116 ± 231.611 (48.800-1.827.000)***

*White blood cell †Nonsignificant (p>0.05) ‡Hematocrit §Platelet

Table 3: Associated pathologies of the study cases

Variables	Cases with digital clubbing	*p*-value	Cases without digital clubbing
Painful crises per year	5.0 ± 9.1 (0-36)	Ns*	5.2 ± 8.1 (0-52)
Tonsilectomy	2.7% (1)	Ns	8.0% (29)
Priapism	2.7% (1)	Ns	2.7% (10)
Ileus	8.3% (3)	Ns	3.3% (12)
Leg ulcers	***33.3% (12)***	***<0.001***	***11.9% (43)***
Pulmonary hypertension	***27.7% (10)***	***<0.001***	***9.6% (35)***
COPD†	***38.8% (14)***	***<0.001***	***12.1% (44)***
CHD‡	***27.7% (10)***	***<0.01***	***12.1% (44)***
CRD§	11.1% (4)	Ns	7.2% (26)
Rheumatic heart disease	5.5% (2)	Ns	6.0% (22)
Avascular necrosis of bones	13.8% (5)	Ns	22.9% (83)
Cirrhosis	***25.0% (9)***	***<0.001***	***1.6% (6)***
ACS¶	8.3% (3)	Ns	3.3% (12)
Stroke	***27.7% (10)***	***<0.001***	***6.9% (25)***
Mortality	8.3% (3)	Ns	6.0% (22)

*Nonsignificant (p>0.05)
†Chronic obstructive pulmonary disease
‡Coronary heart disease
§Chronic renal disease Acute chest syndrome

(p= 0.001 and p= 0.012, respectively) (Table 2). On the other hand, the prevalence of leg ulcers, pulmonary hypertension, COPD, CHD, cirrhosis, and stroke were significantly higher in the clubbing group (p<0.01 for all) (Table 3). Beside that there were 25 mortalities during the eight-year follow up period, and 13 of them were males. The mean ages of mortality were 33.0 ± 9.6 (range 19-47) in females and 30.0 ± 8.6 years (range 19-50) in males (p>0.05). Additionally, there were five patients with regular alcohol consumption who are not cirrhotic at the moment. Although antiHCV was positive in eight of the cirrhotics, HCV RNA was detected as positive just in two, by polymerase chain reaction method.

Discussion

Chronic endothelial damage induced atherosclerosis is the most common type of vasculitis, and it is the leading cause of morbidity and mortality in the elderly. Probably whole afferent vasculature including capillaries are involved in the body. Much higher BP of the afferent vasculature may be the major underlying cause, and efferent vessels are probably protected due to the much lower BP in them. Secondary to the prolonged endothelial damage and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic natures that can reduce the blood flow and increase BP further. Although early withdrawal of the causative factors including smoking, physical inactivity, excess weight, increased serum glucose and lipids, and elevated arterial BP may prevent terminal consequences, after development of COPD, cirrhosis, CRD, CHD, PAD, or stroke, the endothelial changes may not be reversed completely due to the fibrotic nature of them (14).

SCDs are life-threatening genetic disorders affecting nearly 100,000 individuals in the United States (15). As a difference from other causes of atherosclerosis, the SCDs probably keep vascular endothelium mainly at the capillary level (16), since the capillary system is the main distributor of the hard RBCs to tissues. The hard RBCs induced chronic endothelial damage, inflammation, edema, and fibrosis mainly at the capillary level and build up an advanced atherosclerosis in much younger ages of the patients. In other words, SCDs are mainly chronic inflammatory disorders, and probably the main problem is endothelial damage, inflammation, edema, and fibrosis induced occlusions in the vascular walls rather than the vascular lumens all over the body. As a result, the lifespans of patients with the SCDs were 48 years in females and 42 years in males in the literature (17), whereas they were 33.0 and 30.0 years in the present study, respectively. The great differences may be secondary to delayed initiation of hydroxyurea therapy and inadequate RBC transfusions in emergencies in our country. On the other hand, longer lifespan of females with the SCDs and longer overall survival of females in the world cannot be explained by the atherosclerotic effects of smoking alone, instead it may be explained by more physical power requiring role of male sex in life (18,19), since physical power induced increased metabolic rate may terminate with an exaggerated sickling and atherosclerosis in human body.

Digital clubbing is probably an indicator of disseminated atherosclerosis even at the capillary level, and it is characterized by bulbous enlargement of distal phalanges because of the increased soft tissue. Digital clubbing develops in the following steps; fluctuation and softening of the nailbed, loss of normal <165° angle between the nailbed and fold, increased convexity of the nail fold, thickening of the whole distal finger, and shiny aspect and striation of the nail and skin (20). Schamroth's window test is a well-known test for the diagnosis of clubbing (13). When the distal phalanges of corresponding fingers of opposite hands are directly opposed, a diamond-shaped 'window' is normally apparent between the nailbeds. If this window is obliterated, the test is positive. Digital clubbing is seen with pulmonary, cardiac, and hepatic disorders that are featuring with chronic tissue hypoxia (12,14), since lungs, heart, and liver are closely related organs that affect their functions in a short period of time. Similarly, hematologic disorders that are featuring with chronic tissue hypoxia may also terminate with digital clubbing. For example, we observed digital clubbing in 9.0% of patients with the SCDs in the present study and leg ulcers, pulmonary hypertension, COPD, CHD, cirrhosis, and stroke like other atherosclerotic disorders were significantly higher among them (p<0.01 for all). Similar to some other studies, there was a male predominance in the digital clubbing cases (66.6% versus 49.8%, p<0.05) that may also indicate roles of smoking on digital clubbing (12,14).

Smoking has a major role in systemic atherosclerotic processes such as COPD, cirrhosis, CRD, PAD, CHD, stroke, and cancers, too (21,22). Its atherosclerotic effects are the most obvious in Buerger's disease and COPD. Buerger's disease is an inflammatory process terminating with obliterative changes in small and medium-sized vessels and capillaries, and it has never been reported without smoking. COPD may also be a capillary endothelial inflammation terminating with disseminated pulmonary destruction, and it may be accepted as Buerger's disease of the lungs. Although it has strong atherosclerotic effects, smoking in human beings and nicotine administration in animals may be associated with weight loss (23). There may be an increased energy expenditure during smoking (24), and nicotine may decrease caloric intake in a dose-related manner after cessation of smoking (25). Nicotine may lengthen inter-meal time, and decrease amount of meal eaten in animals (26). Body weight seems to be the highest in former, lowest in current, and medium in never smokers (27). Since smoking may also show the weakness of volition to control eating, prevalences of HT, DM, and smoking were the highest in the highest triglyceride having group as a significant indicator of metabolic syndrome (28). Additionally, although CHD were detected with a similar prevalence in both sexes (22), smoking and COPD were higher in males against the higher prevalences of body mass index and its consequences including dyslipidemia, HT, and DM, in females.

COPD is an inflammatory disease that may mainly affect the pulmonary vasculature, and aging, smoking, and excess weight may be major causes of the inflammation. The inflammatory process of endothelium is enhanced by

release of various chemical factors by lymphocytes, and it terminates with fibrosis and atherosclerosis. Probably the accelerated atherscerotic process is the main structural background of the functional changes characteristic of the disease. Although COPD may mainly be an accelerated atherosclerotic process of the pulmonary vasculature, there are several reports about existence of an associated endothelial inflammation all over the body (29-30). For example, there may be a close relationship between COPD and CHD, PAD, and stroke (31). In a multi-center study performed on 5.887 smokers aged between 35 and 60 years, two-thirds of mortality cases were caused by cardiovascular diseases and lung cancers, and CHD was the most common cardiovascular complication among them (32). When the hospitalizations were searched, the most common causes were the cardiovascular diseases again (32). In another study, 27% of all mortality cases were due to the cardiovascular causes in the moderate and severe COPD patients (33). Similarly, beside digital clubbing, pulmonary hypertension, leg ulcers, and stroke, COPD may be one of the final consequences of the SCDs (34).

Leg ulcers are seen in 10 to 20% of patients with the SCDs (35), and the ratio was 13.8% in the present study. The incidence increases with age and they are rare under the age of 10 years (35). Leg ulcers are also more common in males and sickle cell anemia (HbSS) cases (35). They have an intractable nature, and around 97% of healed ulcers return in less than one year (36). The ulcers occur in distal areas with less collateral blood flow in the body (36). They are mostly seen just above the medial malleolus. The lateral malleoli are involved, secondly. Venous insufficiency is not a primary cause, but chronic endothelial damage at the microcirculation of the skin due to the hard RBCs may be the major cause in the SCDs (35). Prolonged exposure to the causative factors due to the blood pooling in the lower extremities by the effect of gravity may also explain the leg but not arm ulcers in the SCDs. Probably the same mechanism is also significant for the diabetic ulcers, Buerger's disease, and varicose veins. Smoking may also have an additional role for the ulcers (37), since both of them are more common in males (35), and atherosclerotic effects of smoking are well-known in COPD, CHD, PAD, and Buerger's disease (21,22).

Probably cirrhosis is also a systemic atherosclerotic process prominently affecting the hepatic vasculature, and aging, smoking, regular alcohol consumption, local and systemic inflammatory or infectious processes, excess weight, elevated BP, dyslipidemia, hyperglycemia, and insulin resistance may be the major causes of inflammation (38). The inflammation is enhanced by the release of various chemical factors by lymphocytes to repair the damaged endothelium of hepatic vasculature (39), and the chronic inflammatory process terminates with an advanced atherosclerosis and tissue hypoxia and infarcts. Although cirrhosis is mainly an accelerated atherosclerotic process of the hepatic vasculature, there may be a close relationship between cirrhosis and CHD, COPD, PAD, CRD, and stroke probably due to the underlying systemic atherosclerotic process (40). For example, most of the mortality cases in cirrhosis may actually be caused by cardiovascular diseases, and CHD may be the most common one among them (41). Similarly, beside digital clubbing, pulmonary hypertension, leg ulcers, stroke, and COPD like other atherosclerotic end-points, cirrhosis may be one of the final consequences of the SCDs (42).

Stroke is an important cause of death, and thromboembolism in the background of atherosclerosis is the most common cause of it. Aging, male sex, smoking, increased serum glucose and lipids, elevated arterial BP, and excess weight may be the major accelerator factors of it. Stroke is also a common complication of the SCDs (43,44). Similar to the leg ulcers, stroke is higher in HbSS cases (45). Additionally, a higher WBC count is associated with a higher incidence of stroke (46). Sickling induced endothelial injury, activations of WBC, PLT, and coagulation system, and hemolysis may terminate with chronic endothelial inflammation, edema, remodeling, and fibrosis (47). Probably, stroke is a complex and terminal event in the SCDs, and it may not have a macrovascular origin, instead disseminated capillary inflammation induced endothelial edema may be much more important. Infections and other stressful conditions may precipitate stroke, since increased metabolic rate during such episodes may accelerate sickling. A significant reduction of stroke with hydroxyurea may also suggest that a significant proportion of strokes are secondary to the increased WBC and PLT counts induced disseminated capillary inflammation and edema (16,48).

As a conclusion, SCDs are chronic destructive processes on endothelium particularly at the capillary level, and terminate with accelerated atherosclerosis induced end-organ failure in early years of life. Probably digital clubbing is one of the terminal consequences of the SCDs indicating significantly shortened survival in such patients.

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Assessment of home glucose monitoring system in primary health care system; where are we?

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Abstract

Introduction: Self Monitoring Blood Glucose system is one of the glycemic control assessment tools. There are many barriers limiting its proper usage. This system is based on three components; availability of the glucometers system, operating skills and knowledge to interpretate its results.

Objectives: To assess the components of self monitoring blood glucose among patients with type 2 diabetes attending primary health care service and its relation to glycemic control.

Methodology: Cross sectional study was designed; one hundred and seventy eight (178; male 72, female 106) were randomly selected from our diabetic registry. All selected patients had type 2 diabetes. Data was collected through a designed questionnaire. The three components of the glucose self monitoring system were assessed. Selected nurses were trained to help patients who could not fill out the questionnaire by themselves. Data was collected and analyzed by SPSS Vers 14.

Results: One hundred and seventy eight (178) subjects ; (40.04% male vs 59.56% female). Eighty eight (88 subjects) were illiterate (49.4%) and most of them were female (38.9% male vs 56.6% female). In the male group only 77.7% had glucometers while in the female group only 52.8% had glucometers (P value <0.0001). In the male group only 61.1% knew how to operate the SMBG while only 39.6% of female group could (P value <0.00001). In the male group only 33.3% stated that they knew the targets of glucose monitoring while it was 68.8% in the female group (P value <0.00001). Only 55.5% of male subjects had the three components of proper home glucose self monitoring compared with 56.1% of female subjects (P value 0.036). Among males with full SMBG components HbA1c was 9.4(+/-)1.9% and 8.1(+/-)1.7 among females with full SMBG components (P value 0.002) .

Conclusion: Lack of proper structured education presented by educators and illiteracy may explain the bad glycemic control in our study sample. Further large studies were recommended.

Key words: Diabetes, glucose monitoring

Introduction

The measurement technology of measuring real time blood glucose has passed through many generation of development. The first self-testing kit for measuring glucose in urine was developed in the 1940s. The advent of capillary blood test strips followed in 1956 and glucose meters in the 1970s and early 1980s. (1) These advances facilitated the adoption of self-monitoring of blood glucose levels as part of the routine diabetes care especially for those on insulin therapy.

The self-monitoring blood glucose is one of the tools used to assess glycemic control and it can contribute to the control process by allowing for adjustments in diet, physical activity and pharmacotherapy in response to test results. The effect of self monitoring in patients taking insulin was well established (2) but its effect on those not on insulin is still controversial (3) but it is still the standard method for glucose assessment. Factors such as economic costs of strips used for tests and patient discomfort and inconvenience may be some of the limitations that have decreased the use of this tool.

Literature review showed some systematic reviews reported marginal advantage of self-monitoring blood glucose levels in terms of controlling HbA1c; interestingly these studies usually did not assess other outcomes such as hypoglycemia, long-term complications of diabetes or quality of life. (4-7)
It was very interesting that many studies did not account for the degree to which participants were educated on how to interpret and act on test results of self-monitoring. This is one of the three components of proper self-monitoring blood glucose systems, since people using test strips must be able to act properly in response to abnormal readings if the system is to be effective. One systematic review and meta analysis showed that self monitoring of blood glucose levels was associated with a modest, statistically significant reduction in hemoglobin A1c concentration (weighted mean difference - 0.25% , confidence interval 0.36% - 0.15%) regardless of whether patients were provided with education on how to interpret and use the test results (weighted mean difference - 0.28% , 95% CI 0.47 - 0.08%) . (8)

The proper self-glucose monitoring needs the availability of a glucose measurement device, skills to operate the device and knowledge to interpret the results. In our study we try to find answers whether, these components are available among our patients and if their presence will affect glycemic control (HbA1c level).

Methodology

Cross sectional study was designed .One hundred and seventy-six (176 subjects) were randomly selected from the diabetic patient registry. Only patients with type 2 diabetes who did two or more HbA1c tests during the year 2014 were included. We select the one that comes each with three components .Questionnaire was designed and distributed to all selected participants after their verbal acceptance to fill out the questionnaires. Two nurses were trained to help participants if they needed help in filling the questionnaire. Each questionnaire-contained questions covering the three components of glucose self-monitoring system; availability of device system, capability to operate the device system and knowledge to interpret results. One hundred and seventy six questionnaires were collected. Patients' medical records were reviewed and mean HbA1c for each patient was calculated. Data was analyzed using SPSS ver 14. One-way ANOVA test analysis was used to find any statistically significant differences between means.

We defined high blood glucose as blood glucose >= 250mg/dl and define low blood glucose as blood glucose =< 70mg/dl.

Results

One hundred and seventy eight (178; 72 male and 102 female) subjects with type 2 diabetes were randomly selected with main age 56.13(+/-) 12.95 and mean HbA1c 8.6(+/-) 2.12 (mean male HbA1c 9.76(+/-) 2.05, female mean HbA1c 8.3(+/-) 1.8) (Table 1).

Eighty eight (88) subjects (50%) were illiterate and most of them were female (57% female vs 38.9% male P value <0.00001) (Table 1). Majority of our subjects receive oral hypoglycemic medication (71.6%; male 66.6% while female 73.5% P value <0.00001) (Table 1).

In the male group only 56 subjects had glucometers while 16 subjects had not (77.7% vs 22.2%, P value <0.00001). In female group 56 subjects had glucometers while 56 had not (52.8% vs 47.1%, P value <0.0001) (Table 2). It was interesting to notice that 44 male subjects could operate their glucometers while 12 could not (61.1% vs 16.6%, P value <0.00001). In the female group, 42 of subjects could operate their glucometers while 32 could not (39.6% vs 30.1%, P value 0.00001) (Table 2). In the male group we noticed 12 patients had glucometers but they cannot operate them while in the female group we found 16 subjects had glucometers but they could not operate them (16.6% vs 15.1% , P value <0.00001) (Table 2) (Figure 1).

In the male group 52 subjects use their glucometers frequently at home while 12 subjects did not (72.2% vs 16.7% ,P value <0.00001). In the female group 48 subjects did frequent use of their glucometers while 28 subjects did not (45.2% vs 26.4% ,P value <0.00001) (Table 3). It was very interesting to note that only 32 male subjects had a glucose test results diary while only 8 females had (42.1% vs 7.5% , P value <0.00001).

In the male group only 24 subjects stated that they knew the targets of glucose monitoring while 20 subjects stated they did not know (33.3% vs 22.2% , P value <0.00001) (Table 4). In the female group 74 stated they knew the targets while 22 did not (68.8% vs 20.7%, P value <0.00001) (Table 4).

Table 1: Bibliography of subjects

	Male N= 72	Female N=106	P value
Age	59.07(+/-)14.13	55.4(+/-)12.4	0.044
Duration of diabetes	11.3(+/-) 4.2 years	10.9(+/-) 5.8 years	0.284339
HbA1c (mean)	9.76(+/-)2.05	8.3(+/-)1.8	<0.00001
Educational level			
Illiterate	38.9% (n=28)	57% (n=60)	<0.00001
Primary	5.5% (n=4)	24.5%(n=26)	<0.0001
Intermediate	22.2% (n=16)	5.7% (n=6)	<0.00001
Secondary	27.7%(n=20)	5.7% (n=6)	<0.00001
University	5.5%(n=4)	7.5% (n=8)	<0.00001
Type of medication			
Oral	66.6% (n=48)	73.5% (n=78)	<0.00001
Insulin	11.1% (n=8)	5.6% (n=6)	<0.00001
Oral + insulin	22.2% (n=16)	20.7% (n=22)	<0.00001

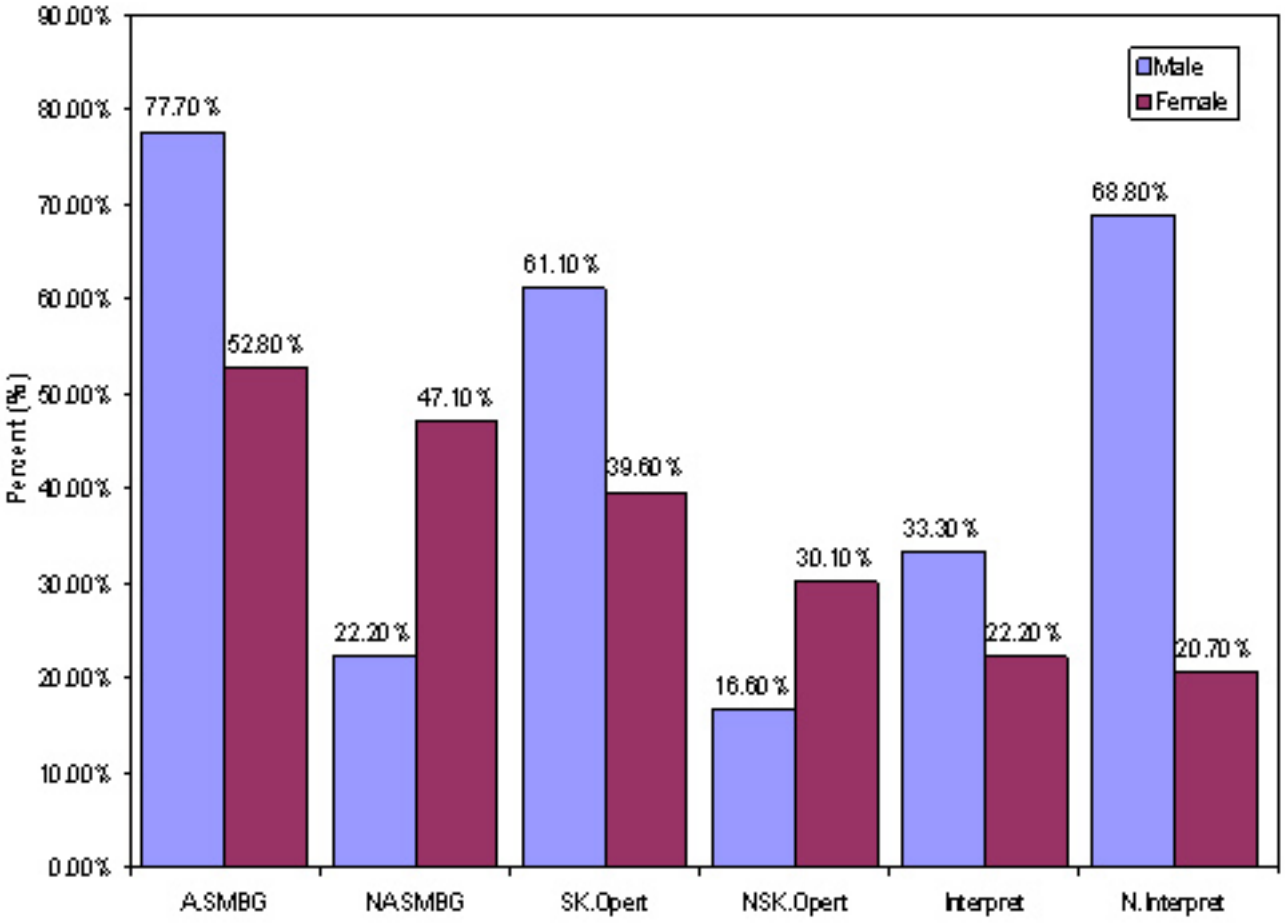
Table 2: Availability of glucometers and operation skills

	Male	Female	P value
Available % (subjects)	77.7% (n=56)	52.8% (n=56)	<0.00001
Not available % (subjects)	22.2% (n=16)	47.1% (n=50)	<0.00001
Can operate % (subjects)	61.1% (n=44)	39.6% (n=42)	<0.00001
Cannot operate % (subjects)	16.6% (n=12)	30.1% (n=32)	<0.00001
Available but cannot operate% (subjects)	16.6% (n=12)	15.1(n=16)	<0.00001

Table 3: Frequency of glucose test at home

	Male	Female	P value
Use glucometer frequently % (subjects)	72.2% (n=52)	45.2% (n=48)	<0.00001
Do not use glucometer frequently % (subjects)	16.7%(n=12)	26.4% (n=28)	<0.00001
Frequency of test (56.8% n=100)			
Daily % (subjects)	46.6% (n=24)	33.3% (n=16)	<0.00001
Weekly % (subjects)	38.4% (n=20)	45.8% (n=22)	<0.00001
Monthly % (subjects)	15.3% (n=8)	20.8% (n=10)	<0.00001
Had glucose test results diary			
Yes % (subjects)	42.1% (n=32)	7.5% (n=8)	<0.00001
No % (subjects)	57.8% (n=44)	93.3% (n=99)	<0.00001

Figure 1: Components of SMBG



A.SMBG = Availability of self-monitoring blood glucose
NA.SMBG = No availability of self-monitoring blood glucose
SK.Opert = Skills to operate glucometer
NSK-Opert = No Skills to operate glucometer
Interpret = interpretation glucometer result
N.Interpret = No interpretation glucometer result

Only 24 male subjects can take action in case of high blood glucose results (> 250mg/dl) while 12 stated they did not know what to do (47.2% vs 30.5% , P value <0.00001). In the female group 60 subjects can take action while 32 subjects did not know what to do (58.8% vs 31.3% , P value <0.00001) (Table 4).

When we compared the male group to female group ,we found that 47.2% male vs 58.8% female can take action if their blood glucose > 250mg/dl (P value 0.00001)

In case of low blood glucose (< 70mg/dl), 50 male subjects can take action and only 14 did not know (55.5% vs 5.6%, P value <0.00001). In the female group 90 subjects can take action while six subjects cannot take action (88.2% vs 5.8%, P value <0.00001) (Table 4). When we compared the male group to female group, we found that 55.5% male vs 88.2% female can take action if their blood glucose <70mg/dl (P value 0.00001).

Only 40 male subjects had the three components of proper home glucose self monitoring while 60 female subjects had them (55.5% vs 56.5%, P value 0.036) (Table 5).

Table 6 explains the relation between the components of SMBG and glycemic control among male and female groups. The differences were statistically different between male and female groups. Neither component was associated with good glycemic control (mean HbA1c <7%).

In (Table 7) we discussed the relation between those with full SMBG components and the type of medication they received. Interestingly HbA1c was 7.6(+/-) 0.75 among females with full SMBG components treated with insulin in comparison with 10.9 (+/-) 1.1 in the male group (P value <0.00001) and there is no statistically difference between male and female groups with full SMBG monitoring components treated with oral medication plus basal insulin (HbA1c 9.8(+/-) 0.4 vs 9.5(+/-)2.11 , P value 0.3085).

Table 4: Knowledge of glucose targets

	Male	Female	P value
Know the targets of home monitoring:			
Yes % (subjects)	33.3% (n=24)	68.8%(n=74)	<0.00001
No % (subjects)	22.2%(n=20)	20.7%(n=22)	<0.00001
Who told you the targets:			
Doctor % (subjects)	83.3% (n=20)	86.4% (n=64)	<0.00001
Educator % (subjects)	0% (n=0)	5.4% (n=4)	<0.00001
Relative(s) % (subjects)	16.7% (n=4)	8.1%(n=6)	<0.00001
Can take action in high blood glucose (> 250mg/dl):			
Yes % (subjects)	47.2% (n=34)	58.8%(n=60)	<0.00001
No % (subjects)	30.5%(n=22)	31.3%(n=32)	<0.022
Can take action in low blood glucose (<70mg/dl):			
Yes % (subjects)	55.5%(n=40)	88.2% (n=90)	<0.00001
No % (subjects)	5.6% (n=4)	5.8% (n=6)	0.119
Did you refer to diabetes educators:			
Yes % (subjects)	8.3% (n=6)	11.7% (n=12)	<0.0001
No % (subjects)	91.6% (n=66)	88.2% (n=90)	<0.0001

Table 5: Subjects who had all components of home glucose self monitoring

Gender	Availability of glucometer	Availability of operation skills	Availability of knowledge to interpret	Subjects	Mean HbA1c
Male	yes	yes	yes	55.5% (n=40	9.4(+/-)1.9%
Female	yes	yes	yes	56.4% (n=60)	8.1(+/-)1.7%
P value				<0.036	0.002

Table 6: Relation of SMG components to HbA1c

SMG component	Mean Male HbA1c	Mean Female HbA1c	P value
System available			
Yes	9.6(+/-)2.25%	8.2(+/-)0.6%	<0.00001
No	9.9(+/-)1.15%	7.7(+/-)2.48%	0.002
P value	0.227	0.0546	
Operation skills			
Yes	9.8(+/-)2.04%	8.4(+/-)1.7%	0.00023
No	9.97(+/-)2.16%	7.7(+/-)1.6%	0.00069
P value	0.421	0.04	
Knowledge to action			
Yes	10.03(+/-)1.8%	8.05(+/-)1.6%	<0.00001
No	7.3(+/-)1.7	8.26(+/-)1.7%	0.027
P value	<0.00001	0.29979	

Table 7: Comparison between subjects with full SMBG based on their type of treatment

	Mean Male HbA1c	Mean Female HbA1c	P value
Oral medications	8.7(+/-)1.8	7.5(+/-)1.4	0.00135
Oral medication+ Basal insulin	9.8(+/-)0.4	9.5(+/-)2.11	0.3085
Insulin only	10.9(+/-)1.1	7.6(+/-)0.75	<0.00001

Table 8: Relation between mean HbA1c and referred patients to structured education by nurse educators among all subjects

	Mean Male HbA1c	Mean Female HbA1c	P value
Not referred to structured education by nurse educators	9.9(+/-)1.97	8.5(+/-)1.6	0.00001
Referred to structured education by nurse educators	8.97(+/-) 1.56	8.24(+/-)1.43	0.000762
P value	<0.0001	<0.00001	

Table 9: Relation between referral to structured education by educators and mean HbA1c in subjects with full SMBG components

	Mean Male HbA1c	Mean Female HbA1c	P value
Referred to structured education by nurse educators	9.58(+/-)1.49	8.43(+/-)1.42	0.041
Not referred to structured education by nurse educators	9.7(+/-)2.18	8.22(+/-)1.84	0.022
P value	0.797	0.719	

Table 10 : Relation with full SMBG components and frequency of SMBG to mean HbA1c

Frequency	Mean Male HbA1c	Mean Female HbA1c	P value
Daily	9.69(+/-)2.05	8.3(+/-)0.45	0.011
Weekly	10(+/-)2.44	8.25(+/-)1.68	<0.00001
Monthly	9.2(+/-)1.13	7.62(+/-)1.25	0.005
P value	0.544	0.445	

In (Table 8) we discussed the effect of referral to structured diabetes education. Interestingly, our results showed that there is no effect of referral to structured education programs by nurse educators on bringing HbA1c towards the target (<7%) . Interestingly there is statistical difference between male and female groups who either referred or not referred; those not referred (9.9(+/-)1,97 vs 8.5(+/-)1.6 , P value 0.00001) and those referred (8.97(+/-)1.56 vs 8.24(+/-)1.43 ,P value 0.000762). When we compared male to male not referred to referred the difference was statistically significant (9.9(+/-)1.97 vs 8.97(+/-)1.56 ,P value < 0.0001) and female to female also the difference was found to be statistically significant (8.5(+/-) 1.6 vs 8.24(+/-)1.43 , P value <0.00001); but all did not drop to the target level (<7%).

In (Table 9) we compared those with full component of SMBG regarding referral or not referral to structured training programs by nurse educators. Among those who referred, there is statistically significant difference (male mean HbA1c 9.58(+/-) 1.49 vs female mean HbA1c 8.43(+/-) 1.42, P value 0.041). Interestingly it was not a statistically significantly difference when we compared the same gender groups; male group (mean HbA1c 9.58(+/-) 1.49 vs 9.7(+/-) 2.18, P value 0.797) vs female group (mean HbA1c 8.43(+/-) 1.42 vs 8.22 (+/-) 1.84, P value 0.719).

In (Table 10) we showed comparison between those with full SMBG components regarding their frequency of SMBG use and their mean HbA1c. Results showed that there are no statistically significant differences in male or female groups regarding the frequency of use and HbA1c; in male group daily, weekly and monthly frequency of test showed HbA1c 9.69(+/-) 2.05, 10(+/-) 2.44 and 9.2(+/-) 1.13 respectively with P value 0.544. While in the female group, it was 8.3(+/-) 0.45, 8.25(+/-) 1.68 and 7.62(+/) 1.25 with P value 0.445. When we compared male to female groups it was significantly statistically different for daily, weekly and monthly frequency (P value 0.001 ,P value <00001 and P value 0.005).

Discussion

Diabetes mellitus is a chronic disease that necessitates continuing treatment and patient self-care education. Monitoring of blood glucose to near normal level without hypoglycemia becomes a challenge in the management of diabetes. The global prevalence of diabetes by International Diabetes Federation (IDF) estimation shows that there are 366 million people with diabetes in 2011, and this is expected to rise to 552 million by 2030. (9)

Self-monitoring of blood glucose (SMBG) has been shown to be as effective in insulin-treated type 1 and type 2 diabetes. Although the effect of SMBG is already demonstrated in some meta-analysis (10-11), it is not recommended as regular use in non-insulin treated type 2 diabetes. SMBG fails to detect nocturnal hypoglycemia and asymptomatic hypoglycemia even in patients with good control of HbA1c values and it needs multiple blood samples throughout the day. In addition, SMBG gives a single instant reading without any information on glucose trends and thus may miss important and significant glucose fluctuations. (12-14)

In our study, we tried to answer some questions related to SMBG. Firstly, we raised the question whether the availability of a SMBG system will affect the glycemic control. Our results showed that availability of the system did not lead to good glycemic control either among male or female groups. The mean HbA1c during the year 2014 did not drop to below 7%, which we considered as good glycemic control, but it was much better among the female group who had a SMBG system (8.2 (+/-) 0.6% vs 9.6(+/-) 2.25%, P value 0.00001). In a randomized control trial done by Wing RR et al (15) the authors also found no statistical difference in HbA1c between those who had SMBG or not. Interestingly this study was done among patients treated with insulin.

On the other hand, another randomized clinical trial (16) in subjects treated with insulin reached a conclusion that presence of SMBG significantly improved HbA1c.

Guerci et al in their randomized control trial (17) concluded that availability of a SMBG system significantly improved HbA1c while Davidson et al (18) did not find any statistically difference in HbA1c. Interestingly Guerci et al was a large trial that included 689 participants while Davidson et al's trial included 88 participants. In sub analysis of our participants we noticed that females with SMBG system treated with insulin have better mean HbA1c than the male group treated with insulin (7.6(+/-)0.75 vs 10(+/-)1.1 , P value <0.00001) . When we work to find an explanation for this result we noticed that compliance to insulin therapy was better among female subjects treated with insulin than male subjects treated with insulin (P value <0.00001).

Then we raised a second question whether the capability to operate the SMBG will affect glycemic control? Our results showed that these skills did not take participants to good glycemic control whether they are male or female (mean HbA1c 9.8(+/-)2.04 vs 8.4(+/-)1.7 , P value 0.00023), but when skills are available with other components mean HbA1c improved (male mean HbA1c 9.4(+/-)1.9 vs female mean HbA1c 8.1(+/-)1.7 , P value 0.002). Brendan M et al (19) found in their systematic review and meta analysis that provided patients with education on how to interpret and apply SMBG system, results were similar to those from RCTs that did not.

Among those who were referred, the male group mean HbA1c was 8.97(+/-)1.56 while in female group mean HbA1c was 8.24(+/-)1.43 with statistically significant difference between the two groups (P value 0.000762). In subjects who were not referred to the structured education program by nurse educator the results showed a statistically significant difference between male and female groups (9.9(+/-) 1.97 vs 8.5(+/-) 1.6, P value 0.00001) with better mean HbA1c in the female group. This finding can be explained by that female patients were more adherent

to educational data and advice. Female patients usually implement more what they learn from educational sessions to their daily life, than male patients.

When we do sub-analysis no those who have the full components of appropriate SMBG and look to their mean HbA1c based on their referral or not referral to structured diabetes program, we found that mean HbA1c dropped more in the male group. It was 9.58(+/-)1.49 vs 8.97(+/-)1.56 P value 0.00001). Interestingly it was not improved in the female group (8.24(+/-)1.43 vs 8.43(+/-)1.42, P value 0.382). This data can be explained by that female patients with full components of SMBG were more reliant on the system itself and did not think that they need multiple structured education sessions. Also the power of culture and the restriction on female movement in the community forces those with full components to hold any participation in such continuous education programs as long as they have the components. Among male patients, the presence of full components of SMBG was a motivation to join a structured educational program, which reflected positively on their mean HbA1c (Table 8-9).

Then we ask ourself if the frequency of SMBG among those with full criteria of appropriate SMBG affected their mean HbA1c? Our results showed no statistically significant difference between male to male and female to female groups who did tests on a daily base, weekly base and monthly base (P value 0.544 vs P value 0.445), but when we compared male to female groups, the difference was statistically significant (daily base, weekly base and monthly base with correspondent P values 0.005, <0.00001 and 0.11) (Table 10). We did not find an effect on frequency of SMBG and mean HbA1 in patients receiving oral, oral plus insulin or insulin only. Schutt M et al (20) did not find effect of frequency of SMBG and level of HbA1c among patients on oral anti-hyperglycemic medications but they found effect among those who use insulin.

Conclusion

The use of SMBG in patients with type 2 diabetes is a complex issue with no clear findings supporting clear recommendations. There are many papers that support its use in patients with type 2 diabetes mellitus especially in the first year of diabetes where its significance starts to decline after 12 months. On the other hand, there are studies that concluded on not to use SMBG in patients with type 2 diabetes due to insignificant effect on glycemic control indicators such as HbA1c as well as the cost of these systems.

In our opinion, the SMBG when individually recommended to selected patients such as type 2 patients on insulin or with add on insulin or on their first year after diagnosis will help these patients very well to improve their HbA1c and the long term metabolic complications. (21)

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Abbreviations:

SMBG = Self Monitoring Blood Glucose
HbA1c = Glycated Haemoglobin

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Cobalamin Injection: Is it Useful in Lumbosacral Diseases?

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Abstract

Background: Low back pain is an everyday problem worldwide. It can lead to a great financial burden to society due to absenteeism or having work limitations.

Back pain is one of the most common symptoms for seeing primary care physicians and one of the top 5 causes of surgery.

Objectives: The purpose of this study is to examine the usefulness of cobolamin injection in lumbosacral disc disease in patients with mechanical or irritative lumbago.

Methods: Over 4 years hundred and twenty patients with Lumbosacrol disease were enrolled in the study. Patients' ages ranged between 18 to 65 years. The patients were divided randomly into treatment and control group. Both groups received relative bed rest, NSAID's and daily injection of vitamin B12 for the treatment group and sterile water for the control group. The duration of treatment lasted for three weeks, and the concentration of vitamin B12 was 1000 mg/ml. Patients were seen initially and at the end of treatment.

Results: Both treatment groups experienced a sharp decrease in pain and disability. However, comparison between groups at the end of the treatment period showed a statistically significant difference in favour of the active treatment both for pain, paraesthesia, and nocturnal pain. Consumption of paracetamol proved significantly higher in the placebo group than in the active treatment ($p < 0.0001$).

Conclusions: Intramuscular vitamin B12 injections seem to be effective at ameliorating nonspecific chronic low back pain as compared to placebo. Vitamin B12 injections also have exhibited only minimal side effects. There is a need for a larger study with longer duration that spans several years to assess the long term side effects, especially as long term effects can possibly be serious.

Key words : Vitamin B12, low back pain, paracetamol

Introduction

For decades B12 injection, has been given to patients with a variety of symptoms without documented cobalamin deficiency(1). Vitamin B12 is essential for the health of our nervous system and blood cells, and vitamin B12 replacement is known for its role in the treatment of peripheral neuropathy and megaloblastic anemia (1).

Vitamin B12 is one of the body's main building blocks, assisting it to make DNA and keep nerves and blood tissue vigorous. Vitamin B12 is present in animal products, including beef, seafood, milk and cheese. Therefore, vegetarians run the risk of having vitamin B12 deficiencies. Vitamin B12 is essential for prime health. Even in the absence of deficiency, shots of the vitamin have been considered recently as an alternative therapy for chronic conditions, including back pain.

Traditionally vitamin B12 had been used to treat anemic elderly patients and as an adjuvant in sport nutrition. It was considered as a painkiller since 1950 in some countries. Lately studies have shown that vitamin B12 plays a major part in the normal functioning of the brain and nervous system and the formation of blood. Vitamin B12 is generally implicated in several metabolisms such as DNA synthesis and regulation, fatty acid synthesis, and energy production. Vitamin B12 has some analogs including cyanocobalamin (CNCbl), methylcobalamin (MeCbl), hydroxocobalamin (OHCbl), and adenosylcobalamin (AdoCbl). In mammalian cells, CNCbl and OHCbl are inactive forms and AdoCbl acts as a coenzyme of methylmalonyl Co-A mutase in mitochondria. However, vitamin B12 was not used directly in the human body, and it should be translated into activating forms such as MeCbl or AdoCbl. MeCbl differs from vitamin B12 in that the cyanide is replaced by a methyl group (2). It is a coenzyme of methionine synthase, which is needed for the formation of methionine from homocysteine in the methylation cycle which includes methylation of DNA or proteins (3-6). Compared with other analogs, MeCbl is the most effective one in being uptaken by subcellular organelles of neurons. Therefore, MeCbl can provide better treatments for nervous disorders through effective systemic or local delivery.

Multiple Clinical Studies reported improvement of patients with vertebral pain to Intramuscular injection of vitamin B12 (7-9). The purpose of this study is to examine the usefulness of cobolamin injection in lumbosacral disc disease.

Methods

Over 4 years hundred and twenty patients with Lumbosacrol disease were enrolled in the study. A routine medical work up showed that none of the patients had other medical diagnosis. Patients' ages ranged between 18 to 65 years. The patients were divided randomly into treatment and control group. Both groups received relative bed rest, NSAID's and daily injection of vitamin B12 for the treatment group and sterile water for the control group. The duration of treatment lasted for three weeks, and the concentration of vitamin B12 was 1000 mg/ml. Patients were seen initially and at the end of treatment. A research assistant blinded to the hypothesis of the study assessed patients using their reports of improvement in their symptoms.

Setting

The study was performed in the Abyad Medical Center, a model multispeciality group with 15,000 thousand registered patients. The group is located in the North of Lebanon.

Results

The mean age of the patients was 55 years. Fourty percent of the patients were male. Both treatment groups noted a marked improvement (Table 1). Howver good improvement was statistically more significant in the treatment group.

Both the treatment and placebo group reported decrease in spontaneous pain (Table 2).

Again both moderate and good improvement was statistically more significant in the active treatment group.

As for pain provoked by movement the treatment group was statistically better on the moderate and good improvement category (Table 3).

The comaprison of the group at the end of treatment period revealed that nocturnal pain showed a statistical significant difference in favor of the active treatment (Table 4).

At the end of treatment both the control and treatment group report a reduction in nocturnal paraesthesia (Table 5).

Mean consumption of paracetamol was significantly higher in the placebo group than in the active treatment group (45.7+-10.32 vs 14 +-9/21 days; $p<0.0001$). Fifteen patients in the treatment group did not take any paracetamol tablets vs only 2 subjects in the placebo groups.

Safety was good in both groups. No change in their medical conditions, vital signs, nor any adverse effects at the end of treatment.

Discussion

Chronic pain is a usual complaint, leading the sufferer to be up to five times more likely to pursue medical attention as compared to those people without chronic pain (10). Lumbago, is a main cause of chronic pain. Within a year period one third of patients with this pain will experience lumbago (11). It has also been projected that around 80% of people will have low back pain at some point during their life (12). The bulk of low back pain (90%) without related neurological symptoms improves within 3 months (13).

Table 1: Global Result treatment as reported by patients

	Treatment group	Control group	P
No improvement	6	14	0.2
Modest improvement	10	16	0.4
Moderate improvement	16	18	0.8
Good improvement	28	12	0.03

Table 2: Spontaneous Pain as reported by patients at the end of treatment period

	Treatment group	Control group	P
No improvement	4	12	0.3
Modest improvement	4	18	0.05
Moderate improvement	28	20	0.4
Good improvement	24	10	0.05

Table 3: Pain provoked by movement as reported by patients at the end of treatment period

	Treatment group	Control group	P
No improvement	2	18	0.02
Modest improvement	6	22	0.03
Moderate improvement	28	12	0.03
Good improvement	24	8	0.04

Table 4: Nocturnal Pain as reported by patients at the end of treatment period

	Treatment group	Control group	P
No improvement	2	18	0.02
Modest improvement	18	10	0.2
Moderate improvement	12	20	0.4
Good improvement	28	12	0.03

Table 5: Nocturnal Paraesthesia as reported by patients at the end of treatment period

	Treatment group	Control group	P
No improvement	4	14	0.1
Modest improvement	4	18	0.05
Moderate improvement	20	12	0.3
Good improvement	32	16	0.04

The remaining 10% are a challenge to many healthcare providers, not only because chronic low back pain is challenging to manage, and normally linked to anxiety, depression, job dissatisfaction, poor body image and somatization (11).

Back pain is one of the most frequent health complaints. It is a common complaint affecting 70-85% of people worldwide at some point during their life (14). The differential is extensive including cancer, infection, inflammatory disorders, structural disorders of the spine itself and disk herniation, are somewhat more common, and together account for back pain.

According to the WHO (World Health Organization), low back pain leads to a high economic burden due to the effects this often chronic problem has on work productivity (15). It is one of the most frequent causes behind visiting a primary care provider, and in the top five of the most common reasons for having surgery(12).

Initially, low back pain is usually managed with anti-inflammatories including non-steroidal, muscle relaxants, and narcotics. Persistent back pain is further treated with physical therapy, TENS units, massage, epidural steroid injections, and surgery. Treatment varies depending on the patient. The majority of patients recover within 12 weeks, while 10 to 20% endure low back pain past this time period, even with treatment (11,12).

It emerges that vitamin B12 might be one of those additional treatment options. This study clearly showed the beneficial

effects of the vitamin in low back pain. The advantage of using B12 shots included decreasing the amount of non-steroidal anti-inflammatory drugs (NSAID), such as aspirin and ibuprofen. Vitamin B12 has no known side effects, according to the National Institutes of Health Office of Dietary Supplements, rivaled to long-term NSAID use, which may harm the gastrointestinal system and probably lead to heart attacks and strokes. Vitamin B12 helps nerves repair and regenerate in the back. Additional benefits to treating back pain with B12 shots include the vitamin's low cost, minimal side effects, and ability to get patients back to work and enjoying their lives.

Studies have shown that vitamin B12 shots can successfully decrease back pain (16,17).

One study conducted in 2000 by Italian researchers at the University of Palermo found that vitamin B12 helped to alleviate lower back pain. The study evaluated 60 patients aged between 18 and 65 with proven back pain lasting anywhere from six months to five years.

Study participants were divided into two groups and received either a B12 shot or a placebo. Results showed injections alleviated back pain in patients even if they entered the study with adequate blood levels of vitamin B12 (17).

The therapeutic options for low back pain include NSAIDs, tramadol acetaminophen combinations, non-SSRI antidepressants, and glucocorticoids or local anesthetic to the spine (18). These medications may lead to serious side effects, particularly when used for a long time. NSAIDS, for example can lead to kidney dysfunction, acetaminophen can cause liver dysfunction and glucocorticoids can cause weight gain, insomnia, and Cushing syndrome. Studies revealed that out of the available treatments only NSAIDs seem to ameliorate function (18). Recent studies including this study (16,17) have shown that injectable cobalamin might also be a promising treatment option for lumbago.

Several studies (19-25), have suggested that large doses of vitamin B12 in combination with NSAIDs may lead to heightening effect on the analgesic properties of NSAIDs, therefore possibly decreasing NSAID dosing.

Vitamin B12 is mostly used for treatment of deficiency, which is often due to malabsorption, insufficient dietary intake, pernicious anemia, gastric surgery, GI disease, and particular medications (26). If long term effects of vitamin B12 injection show to be safe, vitamin B12 might be a precious treatment alternative for low back pain. This will be particularly important for the elderly, for patients prone to liver or kidney disease or people interested in natural substances. This study revealed that vitamin B12 compared to placebo, decreases low back pain and improves function significantly.

However there are certain limitations, including small size that leads to large confidence intervals that the possibility that treatment effect was not precise. In addition none of the studies investigated the long term effects of injectable vitamin B12.

Although vitamin B12 seems to have significant benefit in the treatment of chronic low back pain, further research, with elimination of some of these limiting factors, is needed to study whether the intramuscular vitamin B12 injection doses are indeed harmful in the long run.

Conclusion

Intramuscular vitamin B12 injections seem to be effective at ameliorating nonspecific chronic low back pain as compared to placebo. Vitamin B12 injections also have exhibited only minimal side effects, which include hematoma and pain at the injection site.

There is a need for a larger study with longer duration that spans several years to assess the long term side effects, especially that long term effects can be possibly serious.

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Rota virus vaccine-induced intussusception: A case report study

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Abstract

Introduction: **Intussusception is a rare potential adverse effect of oral rotavirus vaccination, estimated to occur in approximately 1:100,000 vaccine recipients.**

Case presentation: **Six-months old boy presented with vomiting for 3 days, colicky abdominal pain, and did not pass stool for one day prior to the admission. Passage of a reddish soft jelly like motion was reported by his mother. No seizure, no cough, no jaundice, no skin/joint/ bone complications. History of similar condition 2 months ago at age of 4 months (one week following his scheduled vaccination which contains Rota vaccine). Physical examination; lethargic, afebrile with stable vital signs, abdomen was soft, lax with no distension or palpable mass. Per rectal (PR) examination was blood stained. He was diagnosed with intussusception. Hydrostatic reduction was failed. Laparotomy resection of 6 CM of terminal ileum 15CM away from ileocaecal valve with appendectomy. Patient underwent uneventful postoperative course and discharged in good condition.**

Conclusion: **Although the reported vaccine-induced intussusception occurs every now and then, the overall risk benefit balance of vaccines remains positive So World Health Organization (WHO) and the Australian Technical Advisory Group on Immunization (ATAGI) have recommended the continued use of rotavirus vaccine for infants as it reduces annual hospital admissions in children under 5 years due to rotavirus gastroenteritis.**

Key words: **Intussusception, Rota virus, Vaccination**

Introduction

Rotavirus is the leading cause of severe diarrhea in infants and children worldwide, leading to more than half a million deaths each year in children under the age of five years. The first rotavirus vaccine, Rotashield, was introduced in 1999. It was voluntarily withdrawn from the market within a year because post-marketing surveillance found 1-2 excess cases of intussusception per 10,000 recipients [1]. Two newer vaccines, Rotateq and Rotarix, were thought not to carry that risk, but two new trials have shown that they do. Still, the risk is small and the benefits of the vaccines are great. Newer vaccines, Rotateq and Rotarix, were licensed only after testing (in over 60,000 infants for each) failed to find any association with intussusception [2]. Those trials were designed to have enough statistical power to detect a risk similar to that of RotaShield. Both new vaccines contain live, attenuated strains of the virus and are given orally. Rotateq is a pentavalent (prepared from 5 strains) vaccine given in 3 doses at age 2, 4, and 6 months. Rotarix is monovalent (prepared from 1 strain) and is given in 2 doses at age 2 and 4 months. Either is recommended, but about 10 times more doses of the pentavalent vaccine have been administered. After the new vaccines came into common use, studies in other countries pointed to a small increase in intussusception with the newer vaccines, but still at a much lower rate than with Rotashield[3].

Intussusceptions after administration of Rota vaccine is a very rare serious complication that could be easily missed. Intussusception is a “telescoping” of the intestine where one section slides inside another section. This can cut off the blood supply, block the intestine, and cause tears, infections, and death. Most cases are in young children [4]. The baseline incidence of intussusception in children is 1-4 per 1,000. Most cases have no identified cause, but the most plausible candidate is hypertrophied lymphoid tissue resulting from viral illnesses, especially rotavirus infections. They have severe abdominal pain (intermittent at first), and pass blood in the stool, typically mixed with mucus and having the appearance of currant jelly [5]. A barium enema can confirm the diagnosis and simultaneously treat it. Sometimes surgery is needed[6].

Case presentation

Six months old boy presented to emergency room complaining of vomiting for 3 days, colicky abdominal pain, and he did not pass stool for 1 day prior to the admission. The patient developed fever and decreased feeding. He developed vomiting of large amount of undigested food, non- bilious passage of reddish soft jelly like motion as reported by the mother. He suffered from decreased activates. No seizure, no cough, no jaundice, no skin/ joint/bone complication. History of similar condition 2 months ago at the age of 4 months (one week following his scheduled vaccination which contains Rota vaccine). On physical examination he looks lethargic afebrile with stable vital signs, abdomen was soft, lax, not distended with no palpable mass. Per rectal (PR) examination was blood stained.

Investigations

Complete blood picture showed **:** Hemoglobin 11.3g/dl, White Blood Cell count 21.5/cc, Platelet count 367/cc

Chemistry and coagulation profile results were within normal.

Radiology; A-P erect X-ray film showed dilated bowl loops.

Abdominal ultrasound (U/S) showed intussusception with minimal free fluid.

Management

Hydrostatic reduction was done initially and confirmed by contrast enema .After 12 hours , he developed vomiting and redcurrant jelly stool. Repeated abdomen ultrasound showed ileo-ileal intussusception with failed hydrostatic reduction. Laparotomy proceeded and revealed ileo-ileal intussusception with intraluminal polyp. Resection of 6 Cm of terminal ileum 15Cm away from ileocaecal valve with appendectomy was carried out. The patient underwent uneventful postoperative course and was discharged in good condition.

Discussion

Risk with RRV-TV:

In 1999, just over a year after human-rhesus rotavirus reassortant vaccine (RRV-TV, RotaShield) was licensed, it was withdrawn from the market because of an epidemiologic link to intussusception[4]. The increased risk was estimated to be approximately 22-fold over the background risk within five to seven days of vaccination and overall approximately one excess case for every 10,000 to 12,000 vaccinated infants [5,6]. The mechanism of this association is unclear. One hypothesis is that; vaccination triggered intussusception in infants who were likely to develop intussusception with any enteric infection, based upon the observation that rates of intussusception were actually lower among vaccine recipients than non-vaccinees in the period of 4 to 12 weeks after vaccination [7] .Thus, RRV-TV may have caused intussusception in infants who otherwise would not have experienced intussusception, but it also may have protected against natural rotavirus infection-induced intussusception in others.

Risk with RV5 and RV1:

Intussusception is a rare potential adverse effect of oral rotavirus vaccination, estimated to occur in approximately 1 in 20,000 to 1 in 100,000 vaccine recipients [8-13]. A history of intussusception is a contraindication to rotavirus vaccination [14,15], but for infants without a history of intussusception, the risk of intussusception after rotavirus vaccination is much lower than the risk of severe rotavirus gastroenteritis in children who do not receive rotavirus vaccine [16-18].

Figure 1: A-P erect X-Ray film showed: Dilated bowl loops

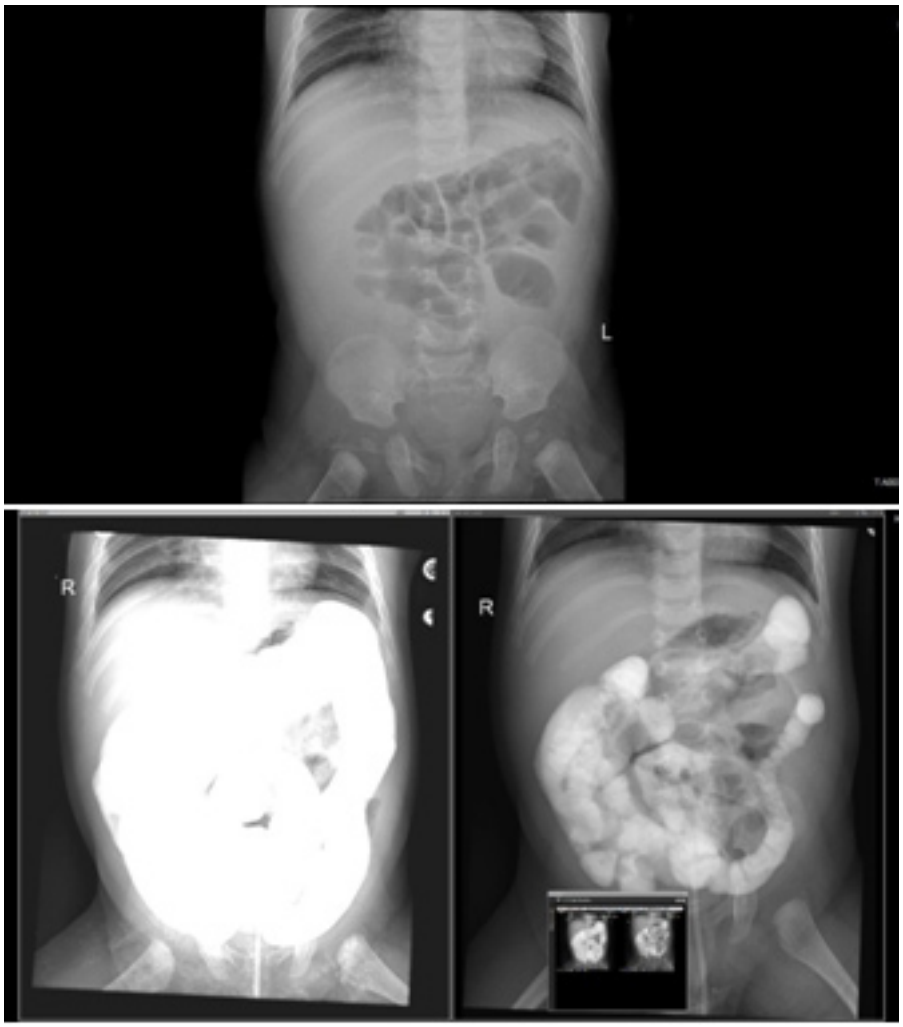
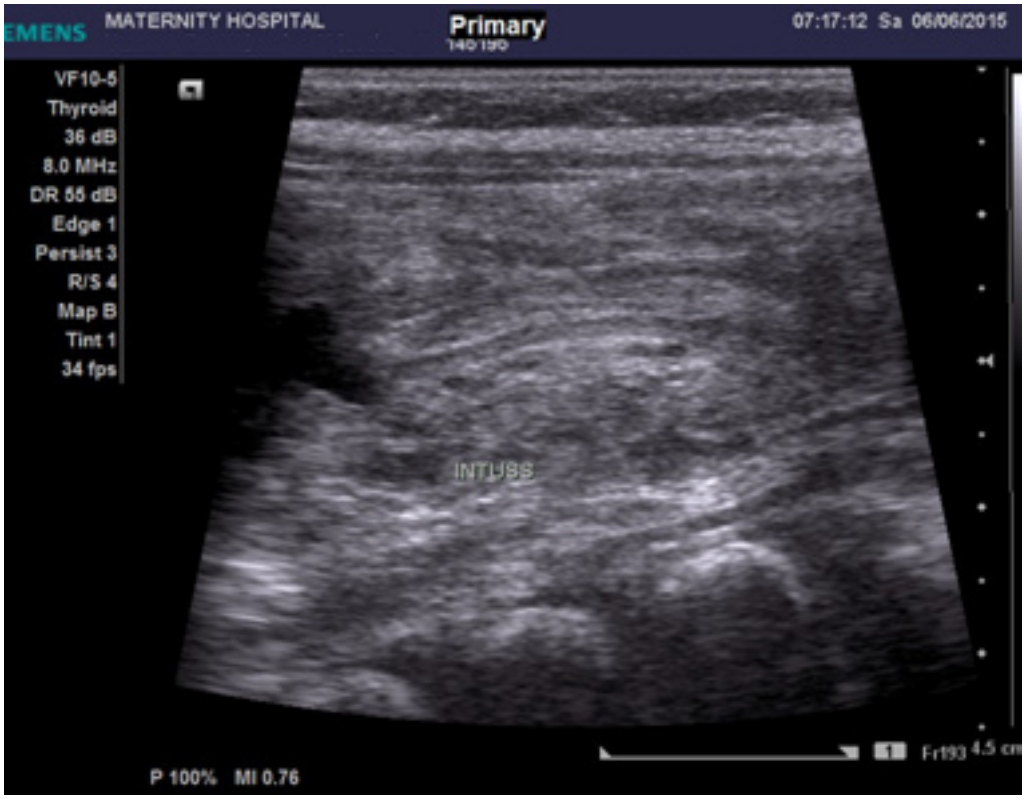


Figure 2: Abdominal ultrasound showed intussusception with minimal free



Parents should contact their child's healthcare provider if the child develops signs of intussusception (ie, stomach pain, vomiting, diarrhea, blood in the stool, or change in bowel habits) at any time after vaccination, especially within the first 14 days after a dose was given.

Pre-licensure studies of pentavalent human-bovine rotavirus reassortant vaccine (RV5) and attenuated human rotavirus vaccine (RV1), found no increased risk of intussusception among vaccine recipients compared with placebo recipients [19.20], however, post-licensure studies conducted by the Centers for Disease Control and Prevention (CDC), the Vaccine Safety Data link investigation group, the US Food and Drug Administration (Post-licensure Rapid Immunization Safety Monitoring), vaccine manufacturers, and others suggest a rare association between RV5 and RV1 vaccination and intussusception within 21 days of the first dose [8-13,21]. The absolute number of estimated rotavirus hospitalizations prevented by rotavirus vaccines far exceeds that of cases of intussusception associated with rotavirus vaccine (eg, 65,000 hospitalizations prevented and 40 to 120 cases of intussusception per year in the United States) [16]. The CDC continues to recommend universal rotavirus vaccination for infants in the United States.

Conclusion

A rotavirus vaccine (either one) is recommended by the CDC, the American Pediatric Association, and other professional groups as a part of the routine immunization schedule in the United States. Parents should be informed of the signs of intussusception and should monitor their infants especially in the first 7 days after vaccination; and since intussusception can recur, caution is advised in children who have a history of intussusception. A rotavirus vaccine (either one) is recommended by the CDC, the American Pediatric Association, and other professional groups as part of the routine immunization schedule in the United States. Parents should be informed of the signs of intussusception and should monitor their infants especially in the first 7 days after vaccination; and since intussusception can recur, caution is advised in children who have a history of intussusception.

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