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Editorial

Family Medicine in the Arab World: Is it a Luxury?

Faisal Abdul Latif Alnasir, FPC, FRCGP, MICGP, PhD[1]

Family medicine (FM) is a medical specialty that provides continuing and comprehensive health care for the individual and the family with a total health care responsibility from the first contact and initial assessment to the management of chronic problems. It includes prevention and early recognition of disease. Such services are provided by the Family Doctor (FD), a physician who is primarily responsible for providing primary, continuing, comprehensive, curative and preventive medical care in a personalized manner to patients and to their families, to all ages and both sexes, regardless of the presence of disease or the nature of the presenting complaint be it biological, behavioral, or social.

Since ancient times, doctors have been using the holistic approach while practicing medicine. Avicenna, Alrazi and several other Muslim doctors were implementing the concepts of family medicine while caring for their patients.

However, with the disintegration of medicine into various specialties and sub-specialties, FM as a discipline started re-emerging at the beginning of the 20th century. In 1923, Francis Peabody commented that modern medicine had markedly fragmented health care delivery. He also stated "the essence of the practice of medicine is that it is an intensely personal matter. The treatment of a disease maybe entirely impersonal; the care of a patient must be completely personal". Therefore, he called for the return of the generalist physician.[1]

While emphasizing the professional aspect of general practice, the Royal College of General Practitioners was founded in 1952 in the United Kingdom to be the professional body of the discipline of FDs.[2]

In the USA, the concept of a new specialty in primary care received official recognition in 1966 in two separate reports;

1. Report of the Citizens' Commission on Graduate Medical Education of the American Medical Association, which was known as the Millis Commission Report.[3]
2. The Ad Hoc Committee on Education for Family Practice of the Council of Medical Education of the American Medical Association, also called the Willard Committee. (4)

Three years later, in 1969, the American Board of Family Practice (ABFP) became the twentieth medical specialty board and in 1971, the American Academy of General Practice was renamed to be the American Academy of Family Physicians (AAFP).

Various studies have documented the importance of FM by advocating that the health of any nation is only developed and promoted by adequate and quality primary health care services provided to that nation. Such services usually formulate the base of the pyramid of all health services. Research in the West proved that people living in countries with an abundance of primary care physicians have a better quality of life.[5]

In this part of the world, the high prevalence of non-communicable diseases, communicable diseases and hereditary and genetic disorders, beside the cost burden, necessitate developing countries in general and the Arab countries in particular to implement Family Medicine. Therefore, FM should be the ultimate goal of health provision.

World-wide, the optimal doctor/patient ratio each FD should care for is 2000 people. With the realization that its population is over three hundred and fifty million, the Arab World now needs more than 175000 FD specialists, a number too far from reality.

Therefore, decisions are required and efforts need to be made in order to establish training programs which produce more skilled FDs if definitive care to undifferentiated patients is to be provided. But, such doctors must have unique attitudes, skills, and knowledge to qualify them to provide continuing and comprehensive medical care, health maintenance, and preventive services to each family member regardless of sex, age, or type of problem.

Training, if established should be effective and of high quality with the mission to produce medical doctors who are competent, community-oriented, and capable of taking full responsibility for the health of their patients within a family context. WONCA, in 1991, has also defined Family Physicians as those physicians who are primarily responsible for providing comprehensive health care to every individual seeking medical care.[6]

The Arab countries started reviewing their higher education policy for medicine which depended much on doctors' obtaining their medical specializations from foreign countries. This practice has led to very costly improper training in the majority of cases, and has caused losses in work productivity.

Therefore, in February 1978, the Arab Health Ministers, in their meeting in Kuwait decided to establish the Arab Board for Medical Specializations, a Board that aims to improve medical services in the Arab world by raising the level for professional skills of medical professionals working in various health disciplines in collaboration with the educational institutions concerned. It also aims to develop and institute guidelines for training within the different medical disciplines and to maintain the level of control and periodic review by keeping pace with the advances in medicine. Another important goal of the Arab Board is to accept responsibility

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to lay the foundation for assessing the scientific and technical characteristics of professional doctors who complete their training period accredited by the Arab Board.

Since its establishment more that twenty years ago, the Arab Board for Medical Specialization has been advocating for Family Medicine. It has offered assistance to any Arab state interested in establishing a FM discipline and training program. Despite that, and until the present time, unfortunately only a handful of programs accredited by the Board have been established in the Arab World. Very few FD, in comparison to the need, have been qualified by the Board. Only 2000 physicians have graduated since its foundation. Continuation at the current production rate of Board qualified FD, (100 per year); Arab countries would need 1750 years to have optimum FM services!!!

Taking Bahrain as an example, with its production of an average of 16 FD per year, and with its immediate need for more than 600 FD (with less than 250 currently available); it will require more than 20 years to reach to that goal.

FM has started in various countries of the Arab region at time. The first FM activity occurred in Turkey in 1961, followed by Bahrain in 1978 [7] Table 1.

Table 1 Family Medicine programs in various countries in Emro region.

Turkey	1961
Bahrain	1978
Lebanon	1979
Jordan	1981
Kuwait	1983
KSA	1987
Arab Board	1986
Qatar, UAE	1994
Oman	1994
Egyptian Board	2003
Libya	2006
Iraq	Recent
Yemen	To start

Such a decrease in the number of production of qualified FD is due mainly to the lack of commitment and political decision by the policy makers supporting this discipline in the various Arab countries.

In Saudi, the Ministry of Health, realizing the importance of FM, is seeking to recruit 13,000 FD to work at its newly established 150 primary health centers in various parts of the Kingdom. It has already hired 4,000 FDs and another 7,000 will be recruited in the next two years. These doctors will be recruited from Arab countries such as Syria, Jordan, Sudan and Egypt after they have gone through a tailor-made educational and training program. [8]

Again, to highlight the crucial importance of FM, the Gulf Cooperation Council participants who concluded three days of discussions on family medicine and primary health care in June, 2007, have recommended that 20 percent of all doctors in the six GCC member countries should be trained as specialists in family medicine over the next 10 years. However, there is still a drastic shortage in the training programs.

In conclusion, with no doubt, the health of the population of the Arab countries will be affected and may be in danger due to deficiencies in FD and, in a few countries, non-availability of FM service. Therefore a brave and immediate decision ought to be taken and efforts made in order to establish more training programs and to increase the capacity of the existing ones to produce more skilled Family Physicians to serve in maintaining and upgrading the health of the nations of the Arab world.

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Original

Penetrating Traumatic injuries of the duodenum; Experiences form Al-Yarmouk Teaching Hospital, Baghdad

Khalid Kareem Rajab, M.B.Ch.B. F.I.C.M.S.[1]

الملخص

خلفية البحث: تعتبر اصابات الاثني عشر النافذة واحدة من المشاكل التي تواجه الجراحين حيث لوحظ ازدياد نسبة الاصابات النافذة بصورة عامة خلال السنين الاخيرة مع ارتفاع نسبة الوفيات المصاحبة لها.

طريقة البحث: يشمل البحث 27 حالة اصابة نافذة للاثني خلال الفترة من سبتمبر 2005 لغاية نوفمبر 2007 تم تحليلها حسب العمر،الجنس ،نوع الاصابة،مكان الاصابة،درجة الاصابة،الاعضاء الاخرى المصابة اضافة الى الاثني عشري،الفترة بين الاصابة لغاية اجراء العملية، حالة جهاز الدوران،الطريقة الجراحية في العلاج،والمضاعفات مابعد العلمية مع نسبة الوفيات باستخدام دلالات حدة الاصابة ودلالات اصابات البطن النافذة.

النتائج: الاصابات الناتجة عن طريق الطلق الناري 23(85,2%) اما اصابات الانفجارات(الشظايا) كانت 4(14,8%)معدل اصابات البطن النافذة 30,2(15-90)، كانت المعدل الواطئ للاصابات 44,4% والمتوسط 37% والعالي 18,6%.كانت الاصابات في اكثر من عضو في 26 مريض وواحد كانت اصابته في الاثني عشر فقط.تم اصلاح الاصابة بالخياطة الاولية مع غلق فتحة بوابة المعدة او اجراء انواع اخرى من العمليات الجراحية.كانت نسبة الذكور للاناث هي 4الى 1علما ان معدل العمر كان 27,6 سنة(9-60 سنة) .تم تحليل المضاعفات وكانت نسبة الوفيات 11 (40,7%) حيث كانت مع معدل الوفيات في درجة حدة الاصابة الواطئ هو 2(16,6%) ومع المعدل المتوسط للاصابه 4(40%) وللاصابات الشديدة او العالية هو5(100%).

الاستنتاج: بالرغم من وجود خبرة كبيرة لدى اطباء الجراحة لازالت اصابة الاثني عشري تمثل نسبة عالية للوفيات والمشاكل لهؤلاء المرضى.ان استعمال قيمة الدلالات لاصابات البطن النافذة مع درجة حدة الاصابة تعتبر من الامور المهمة في المعلاجات وتقيم حالة المرضى.

Abstract

Background: Duodenal injury following penetrating trauma remains one of the most challenging problems confronting trauma surgeons. Experiance in trauma specially for penetrating injuries has increased in the last few years with accompanying increase in mortality.

Methods: Twenty seven patients with penetrating duodenum trauma, collecting from September 2005 to November 2007, evaluated according to the age, gender, types of injury, trauma location, severity of duodenal injury, associated injury, interval between trauma and definitive operation, hemodynamic status, surgical procedure, postoperative complication and mortality. Injuries according to Trauma and injury severity score (TRISS) and penetrating trauma abdominal index (PATI) were evaluated.

Result: Bullets injury were 23(85.2%) patients and blast injury (shell) 4(14.8%) patients. The mean PATI score was 30.2 (15-90); low score 44.4%, intermediate score 37% and high score 18.6%.Multiple organ injury in 26 patients and one with duodenum injured only. The mean TRISS was 11.55(1.5-90).Primary repair with pyloric exclusion (with or without by pass surgery) or other type of surgery were performed. Male to female incidence was 4:1 and mean age 27.6 year (9-60 yr.). Complications were evaluated and the mortality were 11(40.7%) with low score of PATI 2(16.6%), intermediate score is 4(40%) and high score5 (100%).

Conclusion: Experience suggests that duodenum injury still causing high morbidity and mortality in trauma. The predictive value of the PATI suggests that it should be included along with other injury severity indices in trauma data bases. Different surgical procedures needed to perform duodenum repair according to the type and site of injury.

Key word: Duodenum injury, Penetrating injury, duodenum trauma

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Introduction

Duodenal injuries are uncommon. About 75% of the patients in published reports of duodenal injury sustained penetrating rather than blunt trauma; however, this figure may primarily reflect the experience of urban trauma centers. Blunt duodenal injuries in adults are usually the result of a steering-wheel injury to an unrestrained driver and in children is usually the result of a direct blow from a bicycle handlebar or similar device.

Penetrating duodenal injuries can present a confusing picture for the surgeon. A variety of treatment modalities exist including primary repair alone, primary repair with pyloric exclusion, duodenal resection, duodenal diverticulization, and the Whipple procedure. [1]

Blunt duodenal injuries are relatively rare. Diagnosis is usually delayed resulting in significant morbidity and mortality.

The operative treatment of the duodenal trauma is subject of continuing controversy [2] Pancreatic and duodenal injuries are not common and their detection can be challenging both preoperatively and during explorative laparotomy. Their protected location in the retroperitoneal can give subtle symptoms and signs in isolated injuries leading to delayed diagnosis and management. [3] Depending on the institutional practice guidelines on managing penetrating and blunt abdominal injuries the indications for operative exploration vary.

Materials and Methods

Twenty seven patients with penetrating duodenum trauma, collected from September 2005 to November 2007, evaluated according to the age, gender, types of injury, trauma location, severity of duodenal injury, associated injury, interval between trauma and definitive operation, hemodynamic status, surgical procedure, postoperative complication and mortality. Injuries according to Trauma and injury severity score (TRISS) and according to the severity injuries to the duodenum and other organ was qualified by the penetrating trauma abdominal index (PATI) described by Moore et al. Different types of surgical procedures were done according to severity, type and associate injury. Surgical procedures like primary repair with or without drainage or with jejenostomy feeding tube, pyloric exclusions with gastro-jejenostomy or Roux-en-Y anastamosis, gastrojujenstomy with primary repair. The severity of injury seen in a particular patient is graded on scale of one to five for each organ. For the duodenum, the grading is as follows;1,single;2, ≤25%;3,>25%;4,duodenal wall and blood supply;5,injuries requiring pancreaticoduodenectomy.

During this period of study, the management of these patients consisted of initial stabilization in the emergency room followed by early laparotomy. All patients' received antibiotics before and during surgery. All patients had peritoneal drainage by closed tube drains placed in the vicinity of the duodenal suture line and others dependent parts or near by other organ injured.

Results

In twenty seven patients with penetrating duodenum trauma, male to female ratio 4:1,mean age group 27.6 year(9-60) Bullets injury were 23(85.2%) patients and blast injury (shell) 4(14.8%) patients table(1). The mean PATI score was 30.2 (15-90); low score12 (44.4%), intermediate score 10 (37%) and high score 5(18.6%). Total mortality were 11(40.7%) with low score of PATI, 2(16.6%), intermediate score 4(40%) and 5 with high score (100%).Multiples organ injury in 26 patients (twelve associated with one organ other than duedenum, 8 with two organs and four associated with three organ injured, the numbers of mortality related to associated organ injuries with mean TRISS,PATI illustrated in table(3). The most affected associated organ injury were small bowel 10(37%), kidney 9(33.3%), liver 6(22.2%), pancreas 5(18.5%), major vessels 4(14.8%), colon4 (14.8%), stomach 3(11%) and uterus 1table (4). Primary repair only done in 11(40.7%) patients, one of them died, pyloric exclusion with gastro jejenstomy 9, 8 of them dead and primary repair with jejenostomy in 4(14.8%) patients and Roux en Y 2(7.4%) patients. The mean TRISS was 13.5(1.5-90) and PATI

Table 1 - Aetiology of penetrating injuries

Bullets	23(85.2%)
Shells	4(14.8%)
Total	27

Table 2 - Aetiology of penetrating injuries

Score	low score	intermediate score	high score	Total
No. Of patients	12 (44.4%)	10 (37%)	5(18.6%)	27
Mortality	2(16.6%)	4(40%)	5(100%)	11

Table 3 - Types of surgery in relation to mortality

Type of Surgery	GJ+Pyloric exclusion	GJ+Primary repair	Primary repair (PR)	Roux en Y	Primary repair and Jejenostomy	Total
No. Surgery	9	1	11	2	4	27
No. Live	1	-	10	1	4	16
No. Dead	8	1	1	1	0	11
Total	9	1	11	2	4	27

Table 4 - Associated organs injury in relation to mortality and Mean TRISS,PATI.

duodenum	Only	+one	+Two	+Three	+four
No. Organ injury	1	12	8	4	2
No. Mortality	0	3(20%)	6(40%)	2(13.33%)	4(26.6%)
Mean TRISS	3	5.5	27.5	70.5	12.2
Mean PATI	15	22.3	35.6	23.5	31

Table 5 - Mortality in relation to TRISS, PATI, cause of injury,

	TRISS(mean)	PATI(mean)	Bullet	Shell
live	12.4	23.4	13	3
Dead	15.3	40.8	10	1
Total	13.5(mean)	30.5	23	4

Table 6 - Part of duodenum injury related to mortality

Duodenum	No.	live	Dead
First part	2	1	1
Second Part	12	8	4
Third Part	3	2	1
Forth Part	4	3	1
Multiple site	6	2	4

(30.5), in relation to cause of injury and mortality show in table (5). The most injured part of duodenum involved were the 2nd part 12(44.4%) and in more than one sites were 6(22.2%) patients Table 6.Two patients developed obstructive jaundice with injury was in the 2nd part and injury severity of third degree, all was referred to specialized center. Three patients developed duodenal fistula, two of them died (2 with grad III and one with grad IV injury severity. The other morbidity causes were pleural effusion 2, liver abscess 1, pneumonia 2, intra-abdominal abscess 2 and 5 wound infection the total numbers of death was 15 patients; Four patients died within the first 24hours one of them on table during surgery; the others died following days, 4 due to hemorrhagic shock, 4 due to multiorgan failure and 3 due to sepsis.

Discussion

The relatively low frequency of duodenal trauma compared to injuries of other abdominal organs and the high probability of serious complication causing morbidity such as fistula formation and sepsis after its repair has made this entity a challenging problem(4). In our hospital duodenal trauma does not exceed few cases per year in the last five years. Penetrating injuries most commonly followed gunshot wounds, particularly those where the bullet and shell tract travelled transversely across the peritoneal cavity.

Type of surgical procedures depend on the severity of duodenal injury,11 patients had primary repair, only one had died, but most

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Diabetic Retinopathy Screening Using Digital Retinal Camera: Experience in BAHRAIN, 2007

Dr. Noora Al- Kobaisi, MD,DO,CABS "Ophth" [1]

الملخص

الهدف من الدراسة : الكشف عن نتائج فحص العيون للمسح عن الاعتلال الشبكي لمرضى السكر في البحرين لسنة 2007

الطريقة : تم رصد و تدوين الصور الفوتوغرافية لجميع مرضى السكر المحولين بواسطة الكيمرا الرقمية لمدة سنة (2007)

النتائج : العدد الاجمالى للمرضى اللذين تم فحصهم كان في هذه السنة 3265 و72% منهم من لم يتم رصد اى تغيرات في الشبكية، 22% كانوا يعانون من اعتلال شبكي طفيف غير نابت، 3% كانوا يعانون من اعتلال شبكي متوسط الحدة غير نابت ، 0.3% كانوا يعانون من اعتلال شبكي شديد غير نابت. بينما 1% كانوا يعانون من اعتلال شبكي نابت. 4%من مجمل العدد كان الاعتلال مصحوب باعتلال في المقولة.

الاستنتاج: إن إدراج فحص قاع العين لمرضى السكر اثبت فعاليته في رصد الحالات بصورة آمنة و سريعة في تحديد من يستدعى وضعة التدخل السريع للعلاج

Abstract

AIM: To report the results of Bahrain diabetic retinopathy photo screening program during 2007

Methods: We audited the results of diabetic retinopathy photo screening program using digital retinal camera in Bahrain from the period January 2007 till December 2007

Results: A total of 3265 patients were screened by digital retinal camera 2359 patients (72 %) showed no diabetic retinal changes.
Mild nonproliferative changes were noticed in 711 patients (22%).
Moderate nonproliferative changes were noticed in 83 patients (3%)
Severe nonproliferative changes were noticed in 11 patients (0.3%).
Proliferative retinopathy changes were noticed in 44 patients (1 %).
Maculopathy was found in 123 patients (4%).

Conclusion: Digital retinal photo screening is practical in Health Centers and it can detect the normal retina from the retinopathy changes in diabetic patients accurately. Its implementation has been associated with a reduction in presentations with vision-threatening retinopathy within the total community. The normal eyes on initial photo screening yearly repeat photo screening schedule for this group.

Keywords: Diabetic retinopathy, diabetic retinopathy screening program, diabetic screening by digital camera, Proliferative retinopathy, nonproliferative retinopathy.

Introduction

Diabetic retinopathy is a highly specific micro vascular complication of both insulin dependant (type1) and non insulin dependant (type 2) diabetes. The prevalence of retinopathy is strongly linked to the duration of diabetes. After 20 years of diabetes nearly all patients with type 1diabetes and over 60% of patients with type 2 diabetes have some degree of retinopathy. Up to a fifth of newly diagnosed diabetics have been found to have some retinopathy. A diabetic is 25 times more likely to go blind than a person in the general population. Diabetic retinopathy poses a serious threat to vision.

Study Methods

Surveillance and treatment of diabetes-related complications should be part of routine care of all patients with diabetes. Since

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even advanced disease can be asymptomatic.The preferred method for screening is digital retinal photography. This technology has secondary advantages of easy storage and retrieval of images, which facilitates quality assurance, training, and patient education. Several studies have reported the cost effectiveness of screening for retinopathy. They have established that screening for diabetic retinopathy saves vision at a relatively low cost.

The Screening Process

The prevalence of diabetics in Bahrain is said to be 25-30 per cent among the nationals. The aim of diabetic retinopathy screening program in BAHRAIN is to develop an integrated screening program to prevent blindness caused from diabetic retinopathy. Main focus is on early detection and management of diabetic retinopathy.

In Bahrain there are 21 Health Centers at present and this program covers only 15 Health Centers. The fully digitalized screening clinic for diabetic retinopathy for diabetic patients is established and functioning at present and covers 15 Health Centers. Muharraq health center which covers 4 health centers and A'ali which covers 11 health centers. All the patients attending the health centers with diabetes are registered and the patients are directed to the two screening centers with an appointment system.

Screening Methods

Non mydriatic digital retinal camera Canon CR-6-45 NM single field fundus photography is used to take the digital fundus pictures of the diabetic patients. Patient's eyes were dilated with Mydryacyl 1 % drops. The digital photography is performed by ophthalmic technician trained in taking the digital fundus picture. The digital fundus pictures are electronically transmitted ophthalmology department in Salmaniya Medical Center. Consultant retina specialist routinely view the digital fundus pictures grade these images and plan the follow up or call them for direct visualization by ophthalmoscope examination and plan the modality of treatment.

Results

From January 2007 to December 2007, 3265 patients were screened for diabetic retinopathy. We found that 2359 (72%) didn't show any retinopathy changes therefore they are rescheduled for repeat photo screening in a year

There are two stages of diabetic retinopathy – nonproliferative and proliferative retinopathy:

Nonproliferative retinopathy is the earlier stage. In this stage there may be hemorrhages (bleeding) in the retina with leakage of blood causing a "wet retina" or protein deposits (exudates) in the retina. As a consequence, the retina does not receive enough oxygen. This early stage of diabetic retinopathy usually produces no visual symptoms but, if there is fluid in the central portion of the eye (macular edema), vision is diminished.

Diabetic retinopathy has four stages

1. Mild Nonproliferative Retinopathy. At this earliest stage, micro aneurysms occur. They are small areas of balloon-like swelling in the retina's tiny blood vessels. We found 711 patients (22%) showed mild nonproliferative retinopathy changes in the photo screening. (Fig-1)

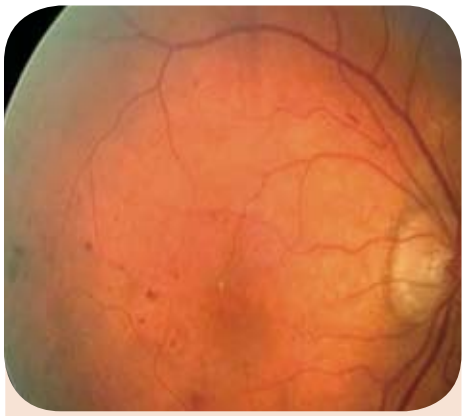

Fig-1 Mild Non proliferative retinopathy

2. Moderate Nonproliferative Retinopathy. As the disease progresses, some blood vessels that nourish the retina are blocked. We found 83 patients (3 %) showed moderate nonproliferative changes in photo screening. (Fig-2)

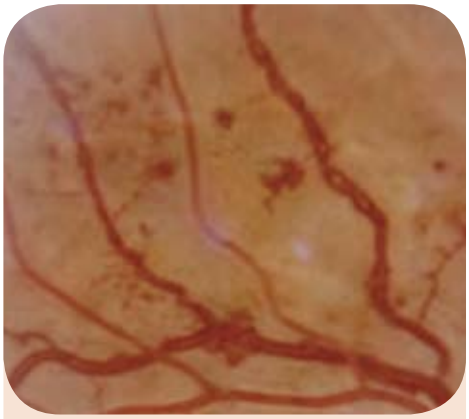

Fig-2 Moderate Nonproliferative retinopathy

3. Severe Nonproliferative Retinopathy. Many more blood vessels are blocked, depriving several areas of the retina with their blood supply. These areas of the retina send signals to the body to grow new blood vessels for nourishment. We found 11 patients (0.3%) showed sever nonproliferative changes in photo screening.(Fig-3)

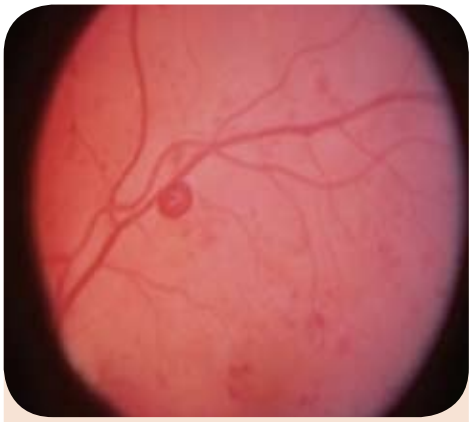

Fig-3 Severe Nonproliferative retinopathy

4. Proliferative Retinopathy. Proliferative retinopathy is the second stage. And more advanced stage of diabetic retinopathy,the abnormal cells rapidly spread - proliferative - across the inner surface of the retina. These weakened vessels can bleed into the vitreous. New abnormal vessels develop in the retina and grow towards the center of the eye. These vessels frequently bleed into the vitreous (the clear jelly in the center of the eye). Such bleeding episodes cause severe visual problems. Small bleeds may clear upon their own but larger bleeds need surgery. In addition, the connective scar tissue, which forms as a result of the ruptured blood vessels, can shrink, pulling the retina away from its underlying structure, causing it to detach. Severe loss of sight - even blindness - may result. We found 44 patients (1%) showed proliferative retinopathy in the photo screening. (Fig-4)

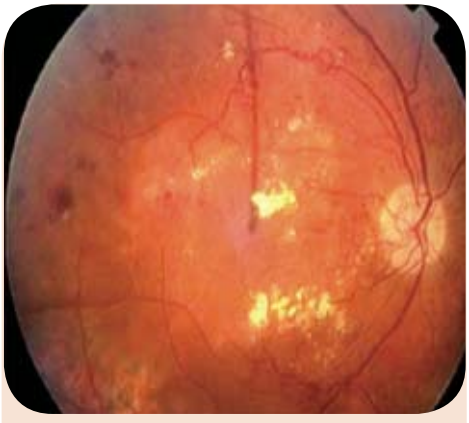

Fig-4 Proliferative Retinopathy

5. Maculopathy. Fluid can leak into the center of the macula, the part of the eye where sharp, ahead straight-vision occurs. The fluid makes the macula swell, blurring vision. This condition is called macular edema. It can occur at any stage of diabetic retinopathy, although it is more likely to occur as the disease progresses. About half of the people with proliferative retinopathy also have macular edema. We found 123 patients (4%) showed maculopathy in the photo screen. (Fig-5)

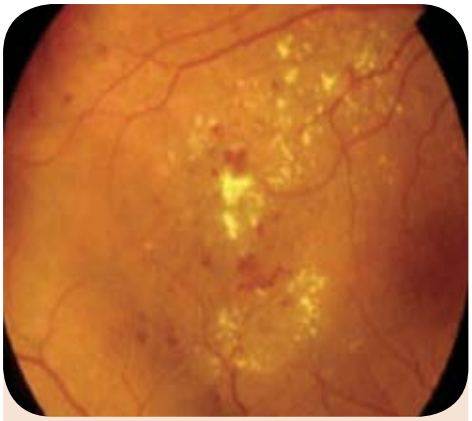

Fig-5 Maculopathy

Table 1

Final Finding of the Diabetic Retinopathy Screening

Nonproliferative	No: Cases	Percentage
Diabetic Retinopathy		
a) Mild	711	22
b) Moderate	83	3
c) Severe	11	0.3
Proliferative		
Diabetic Retinopathy		
Maculopathy	123	4
No clear view	57	2
Normal retina	2359	72
Total	3265	100

During the photo screening for diabetic retinopathy we found very significant retinal finding which are given in the following table

Table 2

Other retinal findings seen in the diabetic Screening

Findings	No: of cases	Percentage
Cataract	76	0.22
Myopia	87	0.25
Cupping of the disc	64	0.19
Drusen	68	0.19
Scars	8	0.02
RPE	7	0.02
Refractive errors	15	0.04
IOP	11	0.03
Myelinated	9	0.02
Total other findings	345	

Discussion

It has been estimated that the total number of people with diabetes in Bahrain is 20-25 %.The explosive growth of the diabetic population demands greater efficiencies in the management of our patients with potential or actual vision-threatening condition.

A screening programme should aim to detect patients at risk when they can still be effectively treated, and this can be achieved by regularly checking the patients' eyes. The service planning guidelines for diabetes recommended regular eye review for all patients with diabetes. This was not occurring due to the fact that comprehensive systematic review would put on the service. Our digital retinal

Photo screening program reduced the burden of normal eye screening on our ophthalmology service and allowed community-based capture of retinal images, ensuring coverage of those subjects who do not regularly attend hospital clinics. Images were then assessed centrally by specialist ophthalmologists.

Various methods of screening have been shown to be sufficiently sensitive and specific for the detection of sight -threatening eye disease (STED) [1, 2] at justifiable costs. [3, 4] However, the sensitivity and specificity of a screening program are not the only important considerations. The extent of the population coverage and the screening intervals are vital to the success of a screening program. The digital retina screening service makes the screening more accessible to a larger number of patients.

The Diabetic Retinopathy fundus digital camera screening in Bahrain is very accurate in differentiating from normal retina to abnormal diabetic retinopathy changes. Our digital retinal photo screening program has achieved good ascertainment of the estimated diabetic population for at least one photo screen. Approximately 72% of the diabetic population in Bahrain were screened one or more times.

The percentage of the non-assessable images was 52 patients 2 %. The British Diabetic Association recommends a maximum failure rate of 5% for any screening program to be acceptable. [5], It is important to differentiate between technical reasons for poor photography and physical causes such as cataract. The photograph should be repeated if possible if the reason is technical. Overall, the number of non-assessable images has been acceptable.

We found that 2359 eyes (72.0%) didn't show any retinal lesion and, therefore, these patients were rescheduled for repeat photo screening in one year, thus reducing the waiting list for a specialist ophthalmologist examination. The patients referred for specialist review Mild nonproliferative retinopathy 6 months, moderate at 4 months and sever at 2 monthly for direct ophthalmoscope examination with necessary treatment initiated as early as possible.

Proliferative retinopathy patients are called immediately for direct ophthalmoscopic examination and necessary treatments were initiated.

The true prevalence of sight-threatening diabetic retinopathy is unknown, current evidence suggests that the diabetic population have some diabetic retinopathy. Our data provide an estimate of the baseline prevalence of grades of diabetic retinopathy in Bahrain diabetic population, a community-based retinopathy screening program.

Significant retinopathy are followed in specialist ophthalmology clinics and do not appear on the photo screening register once they have been referred. We do not know precisely how many patients are in the specialist clinic program at the moment, but expect this to be a significant number. We intend to identify these patients to enable us to assess the percentage of expected diabetic patients in Bahrain.

In conclusion: The Diabetic Retinopathy digital retinal camera Photo screening Program has shown that digital retinal photography is a practical and effective method of screening for diabetic eye disease in Health Centers in Bahrain.

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Evaluation of the immune response to Hepatitis B vaccine in different age groups of the population of Sana'a - Yemen

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الملخص

الأهداف: هدفت هذه الدراسة إلى تقييم نسبة الاستجابة المناعية للقاح التهاب الكبد الفيروسي البائي، و كذا مستوى الأجسام المضادة بالنسبة للأفراد ذو الفئات العمرية المختلفة بعد استكمال جرعات اللقاح الثلاث. و هدفت الدراسة كذلك إلى تقييم نسبة الإصابة بفيروس التهاب الكبد البائي بين الأفراد الملقحين عن طريق قياس نسبة قشرة الفيروس (HBsAg) الموجودة في الدم.

الطرق: شملت الدراسة على 300 فرداً ممن استكملوا الجرعات الثلاث للقاح التهاب الكبد الفيروسي البائي. كانت نسبة الذكور فيها 47.7 % و نسبة الإناث 52.3 % حيث كان متوسط أعمارهم 26.67 سنوات أجريت هذه الدراسة خلال مدة تراوحت السنة من مارس 2004 إلى مارس 2005. جمعت عينات الدم من المستشفيات الرئيسية و بعض المراكز الصحية و العيادات الخاصة في مدينة صنعاء. تم فصل المصل وعمل الفحوصات المخبرية لفيروس التهاب الكبد البائي التي تضمنت قياس نسبة قشرة الفيروس (HBsAg)، الأجسام المضادة للب الفيروس (anti-HBc) و أيضا تحديد مستوى الأجسام المضادة لقشرة الفيروس النوعي (anti-HBs qualitative) و الكمي (anti-HBs quantitative) بواسطة فحص اليزا المتوفر تجارياً (ELISA)

النتائج: كانت الاستجابة المناعية للقاح مستوى الأجسام المضادة لقشرة الفيروس (anti-HBs) أكبر من أو يساوي 10 مل وحدة دولية (mIU/ml) أيجابية في مائتين و ستة عشر (81.2%) من إجمالي 266 فرداً (فاقدين كل من قشرة الفيروس و الأجسام المضادة للب الفيروس). كذا ثلاثة و أربعون (11.3%) من إجمالي 300 فرداً وجدت لديهم الأجسام المضادة للب الفيروس، بالإضافة إلى سبعة (2.3%) أفراد من إجمالي الملقحين وجدت لديهم قشرة الفيروس. سجل أعلى مستوى للأجسام المضادة لدى الفئة العمرية التي أعمارها أقل من15 سنة بنسبة 89.8%، كذلك ، بينما تناقص مستوى الأجسام المضادة تدريجياً لدى الفئة العمرية الأكبر من 35 سنة حتى وصل نسبة 66.7. أيضا تضمنت الدراسة الحالية على نوعين من برامج التحصين: البرنامج الأول يؤخذ فيه اللقاح شهرياً (0، 1، 2) و كانت نسبة الاستجابة المناعية فيه 62.2 %، بينما في البرنامج الثاني يؤخذ اللقاح بفرق شهر بين الجرعة الأولى والثانية و تعطى الثالثة بعد خمس أشهر من موعد الجرعة الثانية (0، 1، 6) و قد كانت نسبة الاستجابة المناعية فيه83.1%. أما بالنسبة لنوعية اللقاح، فقد وجد أن نسبة الاستجابة المناعية للقاح التهاب الكبد الفيروسي البائي المصنع (recombinant-yeast-derived vaccine) كانت 81.9%، بينما اللقاح المأخوذ من مصدر إنساني (plasma-derived vaccine) كانت نسبة الاستجابة فيه 79.8%. تبين من الدراسة أن الاستجابة المناعية لفيروس التهاب الكبد البائي بين العاملين في القطاع الصحي كانت 91.3% و هي نسبة عالية مقارنة بعامة الناس المتضمنين في الدراسة التي بلغت نسبة 78.3%. فئة المرضين و الأطباء كانت لهم النسبة الأكبر في الاستجابة المناعية للفيروس بنسبة 100% و 93.8 % على التوالي مقارنة بالفئات الوظيفية الأخرى. كما لوحظ أن نسبة قشرة الفيروس و الأجسام المضادة للب الفيروس كانت أكثر بين العاملين في القطاع الصحي مقارنة بعامة الناس المتضمنين في الدراسة و كانت نسبة قشرة الفيروس هي 3.1% و 1.8% لكل منهما على التوالي، بينما الأجسام المضادة للب الفيروس كانت 15.5% و 8.2% على التوالي. مثلت فئة المرضين النسبة الأعلى لكل من قشرة الفيروس والأجسام المضادة للب الفيروس حيث كانت النسبة 9.1% و 36.4 % لكل منهما على التوالي. لم يكن هناك فرق يذكر بالنسبة للاستجابة المناعية للقاح التهاب الكبد الفيروسي البائي فيما يخص الفترة الزمنية من 1-5 سنوات من استكمال الجرعات الثلاث للقاح.

الاستنتاج: إن نسبة الاستجابة المناعية للقاح التهاب الكبد الفيروسي البائي بين الأفراد الملقحين المتضمنين في الدراسة كانت فعالة، و لكن ظلت هناك نسبة معتبرة ممن لقحوا لم يستجيبوا للقاح و هؤلاء بحاجة إما إلى إعادة تلقيحهم أو إعطائهم جرعة تنشيطية. تناقص مستوى الأجسام المضادة و احتمالية الإصابة بالفيروس بتقدم العمر بحاجة إلى دراسة أوسع .

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Abstract

Objectives: The study was made to evaluate the immune response to HBV among individuals with different ages and sexes by measuring the level of circulating anti-HBs antibodies over an interval of 1 to 5 years after immunization with the three doses of hepatitis B vaccine.

Methods: A total of 300 individuals vaccinated against HBV prior to the study were included, of whom males represent 47.7% and females 52.3% with a mean age of 26.67 years. Sera were tested for HBsAg and anti-HBc by qualitative ELISA and anti-HBs by ELISA quantitative technique. The individual's data were collected in a pre-designed questionnaire including: vaccination date, number of doses of vaccine, sex, occupation and age at the time of the present study.

Results: Two hundred and sixteen (81.2%) of 266 individuals (lacking both HBsAg and anti-HBc) responded to the vaccine with anti-HBs antibody level ≥ 10 mIU/ml. Thirty-four (11.3%) of 300 individuals were reactive to anti-HBc, indicating an immune response due to previous infection rather than vaccination. Seven (2.3%) of all vaccinated individuals were reactive to HBsAg, indicating infection. Individuals having ages < 15 years had the highest immune response (89.8%) with antibody level ≥10 mIU/ml. There was no difference in response at ages from 16-35 (82.8%), while the lowest response was obtained at ages >36 years (66.7%). The present study included two vaccination schedules, the first one at 0, 1, 2 months, showing an immune response of 62.2%, while the second schedule at 0, 1, 6 months showed a greater immune response of 83.1%. Individuals immunized with a yeast-derived vaccine had higher anti-HBs levels (81.9%), than those immunized with a plasma-derived vaccine (79.8%). The year intervals (1-5 years) after primary immunization showed no difference in the immune response.

Conclusion: This study revealed a high response rate to the vaccine. However, a considerable proportion of vaccinated individuals remain to be reconsidered for either revaccination or booster doses due to non-existent, inadequate, or low response. The schedule of 0, 1, and 6 months was more efficient in inducing antibodies towards the vaccine than the 0, 1, 2 months schedule.

Key words: HBV, vaccine, evolution, Yemen.

Introduction

Hepatitis B is a human disease, caused by a virus that attacks the liver. The virus, which is called hepatitis B virus (HBV), can cause lifelong infection, cirrhosis of the liver, liver cancer, liver failure and death [1]. Hepatitis B infection is one of the world's most common and serious infectious diseases. It is estimated that more than one third of the world's population has been infected with the HBV [2]. About 5% of the population are chronic carriers of HBV, and nearly 25% of all carriers develop serious liver diseases such as chronic hepatitis, cirrhosis and primary heptocellular carcinoma (HCC) [3]. HBV infection causes more than one million deaths every year [4].

For long-term protection against HBV, there are two types of vaccines: plasma-derived hepatitis B surface antigen (HBsAg) vaccine, and yeast-derived HBsAg vaccine[5]. Hepatitis B immunization using either type of vaccine has been shown to eliminate HBV transmission and prevent HBV-related chronic liver disease [6].

Hepatitis B vaccine can be routinely given to children and high risk individuals, along with other commonly used vaccines in a variety of schedules that results in excellent immunogenicity and do not interfere with the immunogenicity of other vaccines [7]

The sero-conversion rate for vaccination is influenced by a number of factors, the most important ones are the age and sex. Rates in excess of 95% are seen in young women, whereas the rate may drop to 80% in older men. Immunosuppressed patients, smokers, and obese individuals show even lower rates [8].

According to the Yemeni National Infectious Viral Hepatitis Control Programme, Yemen was recognized as HBV-endemic area [9]. In 1998 the WHO recommended the entrance of hepatitis B vaccine in the national immunization programmes of Yemen [10], particularly among neonates, where vertical transmission is common, regardless of the HBsAg prevalence [11]. In Sana'a city, HBs antigen carrier rate is classified as intermediate, rather than high. The incidence of acute HBV has declined dramatically during the past decade after the vaccination programme, especially among young individuals [12, 13], although, it still may take several decades until the effect of vaccination will be translated into reduced transmission and morbidity in general.

The main aim of this study is to evaluate the immune response to HBV among individuals with different ages and sexes in Yemen by measuring the level of circulating anti-HB surface antibodies during a period of one year after one to five years of immunization with the three doses of HBV vaccine.

Materials and Methods

a- Study population

This cross sectional study was carried out during a period of one year, starting in March 2004 and ending in March 2005. Three hundred individuals (143 males and 157 females) were included, at their age groups ranged from <15 to >36 years and the mean age is 26.67 ± 6.88 SD years. All individuals received three doses of HBV vaccine, either plasma-derived vaccine or yeast-derived. The study subjects were selected from individuals attending the

National Centre of Public Health laboratories (NCPHL), Al-Kuwait University Hospital, Al-Jomhori Teaching Hospital, Al-Thawra Teaching Hospital, Al-Sabeen Hospital, Iranian Medical Center and some private clinics in the city of Sana'a.

b- Data collection

A full history was taken from each studied individual; and the findings were recorded in a predesigned questionnaire. The collected data included name, age at the time of the study, sex, residence, and occupational status, vaccination date according to the last dose of HBV vaccine, number of doses, intervals between the 3 doses and type of vaccine.

c- Laboratory methods

Four ml of whole blood was collected; then sera were separated and stored frozen at -20°C. HBsAg, total anti-HB core, qualitative and quantitative anti-HBs antibodies were determined by an Enzyme-linked immunosobent assay (ELISA) using a commercially available kit provided by Biokit, Spain. All individuals received less than three doses were excluded from the study.

In order to differentiate naturally occurring immunity to HBV infection, total anti-HB core antibodies were measured; all individuals with anti-HB core antibody positive were excluded. HBsAg was tested to determine the frequency of HBV positivity among the completely vaccinated individuals.

Results

The study included 300 individuals 143 (47.7%) males and 157 (52.3%) females. The mean age was 26.67 ± 6.88 SD years. From the whole studied group 266 (88.7%) individuals 127 (47.7%) males and 139 (52.3%) females were lacking both HBsAg and anti-HBc, thus were further examined for immune response to HBV vaccine by quantifying anti-HBs. Thirty four (11.3%) individuals were reactive to total anti-HBc indicating past infection, while 7 (2.3%) individuals were reactive to HBsAg indicating the presence of infection.

Table 1 shows the immune response to HBV vaccine by quantifying anti-HBs antibody level among males and females. A total of 50 (18.8%) individuals were non-responders in which 30 (23.6%) were males and 20 (14.4%) were females, 71 (26.7%) individuals were low-responders in which 27 (21.3%) were males and 44 (31.7%) were females, 26 (9.8%) individuals were adequate-responders in which 8 (6.3%) were males and 18 (12.9%) were females, 119 (44.7%) were high-responders in which 62 (48.8%) were males and 57 (41.0%) were females. In Addation table 1 shows that the protective rate among both sexes was 81.2%, being higher among females (85.6%) than males (76.4%). There was no statistical significant variation between both sexes.

Table 1 - The immune response to hepatitis B vaccine by quantifying anti-HBs antibody level and protective and non-protective level among males and females.

Antibody level	Male	%	Female	%	Total	%	χ^2	p*
Non-responders (< 10 mIU/ml)	30	23.6	20	14.4	50	18.8	3.71	0.050
Low-responders (10 – 100 mIU/ml)	27	21.3	44	31.7	71	26.7	3.66	0.0 55
Adequate responders (>100 - 1000 mIU/ml)	8	6.3	18	12.9	26	9.8	3.30	0. 600
High-responders (> 1000 mIU/ml)	62	48.8	57	41.0	119	44.7	1.64	0.200
Immune response								
Protective anti-HBs	97	76.4	119	85.6	216	81.2	3.7	0.05
Non-protective anti-HBs	30	23.6	20	14.4	50	18.8	3.7	0.05
Total								

** $\chi 2 \geq 3.84, P < 0.05$ (significant), - Protective anti-HBs ≥10 mIU/ml , Non-protective anti-HBs < 10 mIU*

Table 2- Immune response among vaccinated individuals with different age groups

Age groups	Protected		Non-protected		Total	%
	No	%	No	%		
<15	44	89.8	5	10.2	49	18.4
16-25	58	82.8	12	17.2	70	26.3
26-35	82	82.8	17	17.2	99	37.2
>36	32	66.7	16	33.3	48	18.1
Total	216	81.2	50	18.8	266	100.0

Protected (anti-HBs ≥10 mIU/ml) Non-protected (anti-HBs <10 mIU/ml)

Table 3 shows the comparison between the two schedules of vaccination and types of vaccine used in inducing immune response. In dose interval [0, 1, 2] 28 (62.2%) individuals were responders and 17 (37.8%) were non-responders. While in [0, 1, 6] a total of 188 (85.1%) were responders and 33 (14.9%) were non responders. In Yeast derived vaccine 149 (81.9%) individuals were responders, while in plasma-derived vaccine 67 (79.8%) were responders.

Table 3 - Comparison between the two schedules of vaccination and plasma and yeast-derived vaccines in inducing immune response.

Dose intervals	Responders		Non-responders		Total	%
	No.	%	No.	%		
0, 1, 2	28	62.2	17	37.8	45	16.9
0, 1, 6	188	85.1	33	14.9	221	83.1
Type of vaccine						
Yeast-derived vaccine	149	81.9	33	18.1	182	68.4
Plasma-derived vaccine.	67	798	17	20.2	84	31.6
Total	216	81.2	50	19.3	266	100.0

Responders (anti-HBs ≥10 mIU/ml) , Non responders (anti-HBs <10 mIU/ml)

Table 4 shows protection by year intervals after primary immunization against HBV. 32 (12.%) had got their primary immunization one year prior the study, 26 (81.3%) of them had protected levels, 22 (8.3%) individuals had got their primary immunization two years prior the study, 18 (81.8%) of them had protected levels, 26 (9.8%) individuals had got their primary immunization three years prior the study, 23 (88.5%) had protected levels, 78 (29.3%) had got their immunization four years prior the study, 61 (78.2%) had protected levels, while 108 (40.6%) individuals had got their primary immunization five years prior the study, 88 (81.5%) showed protected levels of antibodies.

Table 4 - Protected and non-protected vaccinated individuals according to period since vaccination

Year intervals	Protected		Non protected		Total No.	%
	No.	%	No.	%		
1 year prior the study	26	81.3	6	18.7	32	12.0
2 years prior the study	18	81.8	4	18.2	22	8.3
3 years prior the study	23	88.5	3	11.5	26	9.8
4 years prior the study	61	78.2	17	21.8	78	29.3
5 years prior the study	88	81.5	20	18.5	108	40.6
Total no.	216	81.2	50	18.8	266	100.0

Protected ≥10 mIU/ml, Non protected <10 mIU/ml

When different HBV markers were detected among the 300 vaccinated individuals 6 (2%) were HBsAg positive anti-HBc positive, 26(8.7%) were Anti-HBs positive anti-HBc positive, 1 (0.3%) was HBsAg positive anti-HBs positive anti- HBc positive, 233 (77.7%) were anti-HBs alone positive, and 1 (0.3%) was anti-HBc alone positive.

Discussion

The study findings showed that about 81.2% of all vaccinated individuals were regarded as protected (≥10 mIU/ml). The protective rate of HBs antibody was higher in females (85.6%), than in males (76.4%). Similar findings were reported in Iran among surgeons, where a higher anti-HBs response rate was found among females than males [14]. This difference could be attributed to a different response in the primary course of vaccination, different age groups, or to the different degrees of exposure to natural boosters [15].

Concerning the rest of the study group, 18.8% developed antibody amounts (<10 mIU/ml), indicating a poor anti-HBs response after receiving a full course of vaccine as shown in table 2. It can be guessed from this finding that these vaccinated individuals were hypo-responsive to the immunization and/or their antibodies may rapidly wane over time. Even in these instances, loss of antibody dose not necessarily imply loss of protection [16]. Since anti-HBs may disappear in a substantial proportion of vaccinees after initially successful vaccination, a booster dose of vaccine, following the administration of the primary course, is recommended by most national bodies. However, is it necessary to boost after initially successful vaccination. The results of long-term follow-up studies, together with assessment of the role of immunological memory among vaccinees, question the necessity of providing booster doses following a successful course of primary immunization [16,17]. Other studies showed that protection is still maintained among vaccinees, even in HBV-endemic countries, despite undetectable anti-HBs levels [18, 19]. The European Consensus Group on hepatitis B immunity recommend that following a complete course of vaccination, booster doses will be unnecessary in immunocompetent persons [20].

In this study, different HBV-markers were obtained among the completely studied vaccinated individuals, but due to the lack of serological data before vaccination, it was impossible to conclude whether these individuals were already infected at the time of vaccination or were infected subsequently. In the present study it was found that the frequency of HBsAg positivity among the whole group of vaccinated individuals was 2.3%, which was lower when compared with the rate of the non-vaccinated ones (7.4%) in Sana'a city in 1999[21], indicating the efficacy of hepatitis B vaccine in preventing chronic carriage of infection. In a long-term follow-up study (about 16 years) on hepatitis B vaccine in China, the positive rate of HBsAg for children born after the introduction of the immunization programme was much lower than those of the background group before vaccination, despite the fact that the rate of HBsAg positive and geometric mean titer declined (17). Lower results were found in Egypt (2003) among children of 6 years of age, where HBsAg positivity was 0.8% compared to 2.2% for the non-vaccinated group [22].

According to the present study, the positivity of anti-HBc was 11.3% indicating previous or ongoing infection with HBV in an undefined period. This result may indicate past infection, or that the infection was acquired just after getting the hepatitis B vaccine and before immune response took place. Since most vaccinated individuals who became infected did not develop a chronic carrier state, it could be speculated that vaccination might have partly protected these persons whose exposure to the hepatitis B virus resulted in a sub clinical infection. However, occasional break-through HBV infections among vaccinated individuals had occurred, due to s-gene mutants of hepatitis B virus, but at present, such mutants do not pose a public-health threat [23]. No clinically overt hepatitis has been reported so far among the studied vaccinated individuals. This finding was similar to those reported from elsewhere [24].

Host factors such as age may influence the immune response to the vaccine. Increasing age was shown to be correlated with a decreasing response to the vaccine (table 2). Response rate of anti-HBs declined from 89.8% in ages under 15 years to 66.7% in ages higher than 36 years. Similar findings were reported by Room et al. [25] showing that an age above 30 years correlated with a decreasing response to the vaccine. In addition, our results were similar to a study conducted in Saudi Arabia, where the older age groups show a decrease in the protection rate compared with the younger ones [26].

The importance of vaccination against hepatitis B is universally accepted [6]. However, the schedules of dose intervals are not yet determined [27]. At the beginning of the national immunization programme in Yemen in 1998, health centers all over the country decided to give the three doses of vaccine monthly (0, 1, 2) without boosters. After several months the strategy changed and immunization was given at 0, 1, and 6 months. Results in our study show low rates of HBs antibodies (62.2%) in 0, 1, 2 ; while HBs antibodies rates were higher (85.1%) in 0, 1, 6 (table 3). The study findings provided evidence that a strong immunological response is induced after immunization with the 0, 1, 6 schedule. Our result, support the findings of Scheiermann et al. [28].

Based on the careful comparative studies, the type of vaccine has proved to be a critical factor [7, 29]. In the present study, the immunization results showed that about 81.9% of individuals were protected (≥10mIU/ml) when immunized with a yeast-derived vaccine, versus 79.8%, when immunized with a plasma-derived vaccine as shown in table 3, indicating that there wasn>t a big difference in the protective rate. In addition, the yeast-derived vaccine is much safer when compared with the plasma-derived vaccine, the reason could be that the plasma-derived vaccine is no longer manufactured in the United States and other western countries [30].

In the present study, there was no difference in the protection rate at the various annual intervals (1-5 years) since vaccination (table 4). Floreani et al [31] reported that protective levels of antibodies remain in the healthy adults for at least 10 years after primary immunization.

Conclusion: This study revealed a high response rate to the vaccine. However, a considerable proportion of vaccinated individuals remain to be reconsidered for either revaccination or booster doses due to non-existent, inadequate, or low response. The schedule of 0, 1, and 6 months was more efficient in inducing antibodies to the vaccine than the 0, 1, 2 months schedule.

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Extraamniotic Versus Vaginal Misoprostol for Ripening the Unfavorable Cervix

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الملخص

الهدف: وجد ان الميزوبروستول له دور في نضوج عنق الرحم ومحفز لعملية الولادة ، هدف الدراسة مقارنة طريقتين مختلفتين في (مهبلي مقارنة بخارج السلى) استعمال الميزوبروستول في نضوج عنق الرحم الغير الملائم لعملية الولادة .

طريقة العمل : هي دراسة مقارنة – مستقبلية اجريت لمقارنة طريقتين مختلفتين في استعمال او أدخال الميزوبروستول لنضوج عنق الرحم الغير ملائم لعملية الولادة .

الطريقة الاولى (ميزوبرستول مهبلي) : هي عملية نضوج عنق الرحم بأستعمال (25 مايكروغرام) من مادة الميزوبرستول داخل المهبل .

الطريقة الثانية (ميزوبرستول خارج السلى) : هي عملية نضوج عنق الرحم بأستعمال قنطرة فولي لدفع 25 مايكروغرام من الميزوبرستول خارج السلى.

النتائج : اجريت الدراسة على مجموع 180 امرأة حامل في المجموعة الاولى (92) وفي المجموعة الثانية 98 وكانت نسبة النجاح في نضوج عنق الرحم 100% لكلتا الطريقتين .

وقد لوحظ من خلال هذه الدراسة ان الوقت اللازم لنضوج الرحم في الطريقة الثانية (للحوامل الخروس هي 05و6 ± 25و2 و للحوامل الولود 97و3 ± 1و1) وهو اقصر من الوقت في الطريقة الاولى حيث كان للحوامل الخروس (3و10 ± 3و1) وللحوامل الولود (22و9± 32 و1).

ووقت بدء الولادة مختلف قليلاً بين الطريقتين في الحوامل الخروس، بينما اقصر في الحوامل الولود في الطريقة الثانية.

معظم الحوامل في الدراسة حصل لهن ولادة طبيعية (100% في الطريقة الاولى و 97% بالطريقة الثانية)

الاستنتاجات : الميزو برستول خارج السلى يقلل من وقت نضوج عنق الرحم هذا يعود للحقيقة أن الميزوبرستول خارج السلى قد وضع مباشرة في مكان عمله.

Abstract

Objective: To compare the efficacy of two different routes of administration of misoprostol for ripening the unfavorable cervix.

Setting: Labor room in Basra Maternity (teaching) Hospital with 400 bed capacity.

Design: A prospective comparative study was conducted to compare two different routes of administration of misoprostol (Cytotec) for ripening the unfavorable cervix.

Group I (Vaginal misoprostol): The cervix was ripped using a 2cc of misoprostol solution (25µg) installed into the upper vagina.

Group II (Extramniotic misoprostol): The cervix was ripped using a Foley`s catheter, which was inserted into the extraamniotic space & 2cc misoprostol solution (25 µg) was infused through the catheter into the extraamniotic space.

Results: The clinical trial involved a total of 180 pregnant women, in method I (92), & method II (98), the success rates in achieving cervical ripening were 100% for both groups.

The ripening times in group II (primigravidae (6.05±2.25), multiparae (3.97 ± 1.1)) were significantly shorter than those in group I (primigravidae (10.3±1.3), multiparae (9.22±1.32). The induction delivery times were a slightly different in both groups in primigravidae; where as it was significantly shorter in multgravidae in group II.

The vast majority of the women (100% in group I & 97% in group II) had vaginal delivery.

Conclusions: This study confirms that vaginal and extra-amniotic misoprostol (which was evaluated for first time in this study) were effective in achieving cervical ripening but we recommend the use of vaginal misoprostol in stead of extraamniotic misoprostol because although it takes a longer priming time, it achieves a higher post ripening score, it is easily administered and do not requires special method for application as in the extraamniotic one. We also recommend that extraamniotic misoprostol is reserved for use in patient in whom quick cervical ripening is indicated.

Key words: Vaginal versus Extraamniotic Misoprostol & Unfavorable cervix.

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Introduction

Induction of labour is the initiation of labour by medical or surgical means prior to the spontaneous onset of labour for the purpose of accomplishing delivery of the fetal/placental unit.[1] To induce labour in a case with unripe cervix is frequently associated with maternal complications and induction failure.[2] The cervical effacement is an essential pre-requisite to its dilatation and one which depend on the softening and ripening of its connective tissue.[3]

Cervical ripening is the process of softening, shortening and partial dilatation of the cervix. It is usually takes place in the days or weeks prior to the onset of labour but the time of this process is variable.[4] The main factors involved in cervical ripening are invasion of leukocyte, remodeling of extracellular matrix and proteolytic enzyme activity.[5] Prostaglandin E2 is mainly responsible for vasodilatation of cervical capillaries and increasing permeability to circulating neutrophils which are captured by surface adhesion molecules and draw into the cervical stroma under the chemo attractant influence of IL-8.[3] Estrogen is known to stimulate PG synthesis in fetal membranes and the decidua, and the formation of gab-junction in the myometrium, and the synthesis of oxytocin receptors.[6]

Pharmaco-dynamic of misoprostol: Misoprostol is a synthetic PGE1 analogue.[7] Absorption is fast in all routes of administration ,when given vaginally or sublingually takes longer than oral route to start working and has a lower serum level (peak concentration after 60 min) but more sustained effect.[7] Plasma elimination half life is reported to be between 20-30min.[8] Vaginal bleeding and loss of amniotic fluid may have negative effect on absorption through the vagina.[7] Their efficacy depend on the number of PG receptors in the uterus which varies according to whether the women are pregnant or not and what stage of pregnancy she is [7].

Misoprostol is administered sublingually, orally, vaginally and rectally[7].

Dosage of Misoprostol: PG is well established for induction of labour.[8]. Using misoprostol tablet, doses employed have been 50µg orally every 4 hour until delivery or 25µg vaginally every 4 hour according to the patient response until delivery.[9]

Side effects of misoprostol: Adverse effects include Diarrhea (10), Abdominal pain, dyspepsia, flatulence, nausea and vomiting (10), uterine hyperstimulation, meconium stained liquor, PG crosses the placenta to stimulate fetal bowel smooth muscle and cause meconium passage , Precipitate delivery labour of less than 2 hour has been described as a complication of misoprostol, rupture of unscarred uterus , increase caesarean section rate & postpartum hemorrhage.[4]

This study aims at comparing the efficacy of two different routes of administration of Misoprostol (vaginal versus extraamniotic) for the ripening of the unfavorable cervix.

Materials and methods: A prospective comparative study which was conducted in Basrah maternity & children hospital during the period from January 2007 to of June 2008.

A total of 180 pregnant women (primigravidae and multigravidae (Para 1-4) were included in this study; they were admitted to the labour ward in Basrah maternity & children hospital with an indication for induction of labour.

The Inclusion criteria were gestational age 28-42 week, unfavorable cervix Bishop Score <6, singleton pregnancy, vertex presentation & intact membrane.

The exclusion criteria were known previous uterine surgery (myomectomy, caesarean section & post conization), multiple gestation, abnormal lie and presentation, uterine anomalies, placenta previa , documented episode of mid- trimester or 3rd trimester bleeding & grandmultiparity ≥ 5.

Indications for induction of labour were: prolong gestation ≥ 42 week and hypertensive disorders. Induction of labour was done at term unless added complication necessitated earlier intervention, Intrauterine growth restriction, Intrauterine death, diabetic patients with indications for induction.

After obtaining their consent women under study were randomly divided into two groups:

Group I (V. M.): This group consisted of 92 patients (primigravidae (42) & multigravidae (50)) , they were admitted at morning and preparation of misoprostol solution was done under aseptic technique as follow:-

Misoprostol (Cytotec) 200µg tablet was divided into 2 equal parts in an attempt to obtain 2 pieces each of them containing 100µg which was then dissolved in 8cc normal saline (as it was advice by the pharmacist) and the solution shacked until it become homogenous containing 100µg.

This solution divided into 4 portions each of them containing 2 cc (25µg).

Under aseptic technique, in dorsal position with a pillow under the left hip joint to elevate and lateral tilted the buttock to prevent release of the solution out side the vagina and avoid supine hypotension. A syringe which contains 2cc of misoprostol solution (25µg) was inserted into the vagina and the solution installed into the posterior fornix, after that the syringe was pulled out and the patient was advised to remain in left lateral position.

Uterine contractions were monitored by palpatory method and fetal heart was checked hourly, pelvic examination was done every 2 hrs to assess changes in Bishop`s score by the same examiner.

The dose was repeated every 6 hours until satisfactory result (priming of the cervix) was obtained. After ripening of the cervix, labour was managed by amniotomy if possible and oxytocin was given to augment uterine contractions whenever indicated in an escalating dose until efficient uterine contractions were obtained. Further management of labour were done in the usual way.

Group II (E.A.M.): This group consisted of 98 patients (primigravidae (40) & multigravidae (48)) , those patient were admitted to the hospital at morning and under aseptic technique in dorsal position with a pillow under the left hip joint as in first group, a 14 French gauge Foley>s catheter was inserted into the extra amniotic space and 2cc misoprostol solution (25µg) was injected through the catheter into the extraamniotic space, followed by injection of 4 cc of normal saline to wash any remnant of misoprostol solution inside the catheter.

The patient was advised to remain in left lateral position, monitoring was done every 2 hours to assess the response as in group I. Further management was as in the first group.

Data were analyzed using Z-test and the differences were considered to be significant only if Z-test value is > 1.96 i.e. (p-value < 0.05).

Results

Analysis of data revealed that the total number of the women in group I was 92, 42 of them were primigravidae and 50 were multigravidae and in group II was 88, 40 of them were primigravidae and 48 were multigravidae.

Table I shows the characteristics of the patients under study. There were no statistically significant differences in the mean gestational age and the mean initial Bishop's scores in the two groups in both primigravidae and multigravidae.

Table I - patient characteristic

Parameter		V.M* (n=88)	E.A. M** (n=92)
Primigravidae NO (%)		42 (33.33%)	40 (22.22%)
Multigravidae NO (%)		50 (27.77 %)	48 (26.66%)
Mean patient age ±SD	Primigravidae	22.73 ± 5.7	26.66 ± 4.1
	Multigravidae	23.7± 4.1	28.07 ± 6.7
Mean gestational age ± SD	Primigravidae	39.4± 3.1	39.025 ± 2.8
	Multigravidae	40.1± 2.5	39.85 ± 2.4
Mean Initial Bishop>s Score ± SD	Primigravidae	0.83±1.36	0.85 ±1.25
	Multigravidae	1.7± 1.2	1.22 ± 1.49

Two samples Z-test

Parameter		I vs n
Gestational age	Primigravidae	1.00 NS
Initial Bishop' score	Primigravidae	0.08 NS
	Multigravidae	1.126 NS

** vaginal Misoprostol. ** Extraamniotic Misoprostol.*

Table II shows the indications for induction of labour. Prolong pregnancy was the most frequent indication in both groups, followed by hypertensive disorder and pre-eclampsia. Two primigravidae in group I had induction for more than one reasons (reduction of fetal movement and oligohydramnios with history of primary infertility).

Table II - Indications for induction of labour

Parameter		Group I V.M NO(%)	Group II E.A.M NO(%)
Prolong pregnancy	Primigravidae	24 (57.1%)	14 (35%)
	Multigravidae	33 (66%)	23 (47%)
Hypertension	Primigravidae	0	0
	Multigravidae	9 (18%)	4 (8.3%)
Pre-eclampsia	Primigravidae	6 (14.3%)	12 (30%)
	Multigravidae	5 (10%)	9 (18.8%)
I.U.G.R.	Primigravidae	7 (16.7%)	9 (22.5%)
	Multigravidae	1 (2%)	9 (18.8%)
Intrauterine death	Primigravidae	3 (7.1%)	3 (7.5%)
	Multigravidae	2 (4%)	2 (4.2%)
Diabetes mellitus	Primigravidae	0	2 (5%)
	Multigravidae	0	1 (2.1%)
*Others	Primigravidae	2 (4.8%)	0
	Multigravidae	0	0

**(reduction of fetal movement & oligohydramnios with history of primary infertility).*

Table III shows pre and post ripening Bishop's scores and priming and induction-delivery times. The mean post-ripening Bishop's score was higher in group II in both primigravidae and multigravidae and the difference was statistically significant.

The mean priming times were shorter in group II compare to group I in both primigravidae and multigravidae and the differences were statistically highly significant.

With respect to mean induction-delivery time, it was shorter in primigravidae in group II compare to group I but vice versa was noticed in multigravidae (shorter in group I than in group II), the difference was significant only in multigravidae.

Both method (V.M and E.A.M) were successful in achieving cervical ripening in all cases (100% success rate).

The majority of cases had vaginal delivery (100% of women in vaginal Misoprostol group & 97% in extraamniotic Misoprostol group) there was no women required instrumental delivery and only one primigravida and one multigravida in group II had caesarian section delivery for failure to progress in cervical dilatation (primigravidae) and for fetal distress (multigravidae).

In all cases in both groups the placenta was delivered normally with no immediate postpartum complication (post partum bleeding or maternal pyrexia & in both groups there was no uterine hyper stimulation).

Table III - Pre and Post-ripening Bishop's scores and induction-delivery interval

Parameters		Group I V.M	Group II E.A.M
Mean initial Bishop's score ±SD	Primigravidae	0.88±1.36	O.85±1.25
	Multigravidae	1.7±1.2	1.22±1.49
Mean post ripening Bishop>s score ±SD	Primigravidae	8.45±1.2	7.77±1.47
	Multigravidae	8.78±1.39	8.06±1.43
Mean time between pre and post ripening score ±SD	Primigravidae	10.3±1.3	6.05±2.25
	Multigravidae	9.22±1.32	3.97±1.1
Mean induction delivery time after successful cervical ripening ±SD	Primigravidae	5.8±5.63	5.5±1.8
	Multigravidae	3.7±1.09	4.2±1.58

Two Samples Z- test

Parameter		I vs II	
Initial Bishop's score	Primigravidae	0.08	NS
	Multigravidae	1.186	NS
Post ripening Bishop's score	Primigravidae	2.64	S
	Multigravidae	2.98	S
Time between pre and post ripening score	Primigravidae	14.3	HS
	Multigravidae	23.43	HS
Induction- delivery time after successful cervical ripening	Primigravidae	0.7	NS
	Multigravidae	3.96	S

Table IV shows the neonatal outcome; all neonates were active immediately after delivery with a mean Apgar score at 5-minutes was equal to 8.5 and above and the differences were statistically not significant between all groups.

There was no statistically significant difference regarding the mean birth weight in all groups.

Table IV – Neonatal out come

Neonatal out come		Group I V.M	Group II E.A.M
Apgar score at 5 minutes	Primigravidae	8.88 ± 2.57	8.5 ± 2.9
Mean ± SD	Multigravidae	9.38 ± 1.56	9.41 ± 2.05
Birth weight	Primigravidae	2.88 ± 0.5	3.07 ± 0.58
Mean ± SD	Multigravidae	3.03 ± 0.35	3.004±0.40

Two sample Z-test

Parameter		I vs II	
Apgar score at 5 minute	Primigravidae	0.75	NS
	Multigravidae	0.1	NS
Birth weight	Primigravidae	1.16	NS
	Multigravidae	0.19	NS

Discussion

Misoprostol is a synthetic PGE1 analogue [4] and more effective than PGE2 vaginally for induction of labour.[11] It has been used widely in obstetrics and gynecological practice because of its effectiveness , low cost , stability in light and hot climate conditions and the ease of admistration.[12]

In this study we found that both vaginal and extra amniotic misoprostol were 100% successful in achieving cervical ripening and this finding is similar to that reported by Hofmeyr and Gulmezoglu[14] who found that a relative risk of unchanged cervix after vaginal misoprostol was 0.2 and Van-Gemund and Scherjon reported a relative risk of unchanged cervix.[14]

In this study the mean post ripening Bishop's score was significantly higher in patient with vaginal misoprostol compare to those with extraamniotic misoprostol in both primigravidae and multigravidae but extra amniotic misoprostol required a significantly shorter time to achieve cervical ripening than vaginal misoprostol in both primigravidae and multigravidae and this is could be due to the fact that in extra amniotic group misoprostol was applied directly to its site of action, and according to the pharmacokinetic vaginal misoprostol is the last one to achieve peak serum level (80 min to achieve peak value) [7], and for that reason it take longer time to produce its effect.

The post ripening Bishop's score was higher in vaginal misoprostol this could be due to the longer priming time it takes compare to extra amniotic misoprostol.

With respect to induction- delivery time there was a little difference between the two groups in primigravidae where as it was significantly shorter in multigravidae in group II.

The vast majority of the women in both groups (100% in group I & 97% in group II) had vaginal delivery and this is similar to that reported by Van-Gemunud and Scherjon [14] (relative risk of Caesarean section rate was lower than 0.8).

In this study we reported no serious neonatal complications with a mean Apgar score at 5 min was above 8 in both groups (I & II) and this is also similar to that reported by Van-Gemund and Scherjon [15] who reported a relative risk of serious neonatal complication of 0.7.

No maternal complications, including maternal pyrexia, postpartum haemorrhage & uterine hyper stimulation, where reported with the use of 25 µg misoprostol vaginally or extra amniotically in both primigravidae & multigravidae and this is similar to that reported by Hofmeyr & Gulmezoglu.[11]

During our work we found that extraamniotic misoprostol took a much shorter priming time than vaginal misoprostol but it required special method of application and achieve less post ripening score compare to vaginal misoprostol and although it was not documented patients included in extra amniotic group were anxious about the method of application and catheter insertion.

Conclusions

Our study confirm that vaginal & extra amniotic misoprostol were effective in achieving cervical ripening but we recommend the use of vaginal misoprostol instead of extraamniotic Misoprostol because of the following facts:-

Vaginal Misoprostol although takes a longer priming time, it achieve a higher post ripening score in comparison to the extraamniotic Misoprostol.

Vaginal Misoprostol is easily administered & do not requires special method for application as in the extraamniotic one.

By adding the cost of Foley's catheter to that of the drug, vaginal Misoprostol method was cheaper than extraamniotic.

Patients subjectively felt more comfortable with vaginal compared to those with extra amniotic misoprostol.

We also recommend that extraamniotic Misoprostol is preserved for use in patient in whom quick cervical ripening is indicated

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Effect Of L-Carnitine On Serum Lipid Profile In Iraqi Diabetics

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الملخص

الأهداف: دراسة تأثير مادة الكارنتين كماده دوائية اضافيه لمرضى البول السكري على طلعة جانب الشحميد لمرضى البول السكري من النوع الثاني (غير المعتمد على الأنسولين) مع أو بدون وجود اعتلال كلوي.

المرضى والطرق: شارك في هذه الدراسة 54 من المرضى المتطوعين (32من الذكور و22من الإناث) من الفئات العمرية بين 25-70 سنه من المرضى المراجعين لعيادة الوفاء لعلاج مرضى السكري في مدينة الموصل في الفترة بين الأول من تشرين الأول 2005، و لغاية الحادي و الثلاثون من آذار 2006. تم إعطاء (550) ملغم من الكارنتين بشكل حبوب عن طريق الفم بجرعتين يوميا ولمدة 45 يوما مع الاستمرار في استخدام علاجات السكري التي يستعملها المريض و بنفس جرعها.

تضمنت هذه الدراسة المتغيرات في طلعة جانب الشحميد في مصل الدم:- الكولسترول الكلي، كولسترول البروتين عالي الكثافة، الدهون الثلاثية، كولسترول البروتين واطئ الكثافة، الكولسترول الكلي غير المتضمن كولسترول البروتين عالي الكثافة، دليل التصلب الشرياني و أخذت هذه القياسات جميعها في حالة الصيام الليلي. تمت هذه الدراسة بأخذ أربع عينات من الدم لكل مريض، الأولى قبل أخذ الجرعة الأولى من الكارنتين مباشره ثم بعد 15. 30. و45 يوما من سحب ألعينه الأولى. تم جمع العينات صباحا بعد صيام 12 ساعة تقريبا.

النتائج: انخفض الكولسترول الكلي بشكل معنوي ((p<0.001و حيث كان (8.55 ملمول /لتر) قبل إعطاء الكارنتين ثم (6.47ملمول /لتر) بعد 15 يوما من استمرار العلاج و (5.99ملمول/لتر) بعد شهر من بدء استخدام الكارنتين و (5.5ملمول/لتر) بعد 45 يوم من ذلك. كما وجد انخفاض معنوي للدهون الثلاثية في المصل ((p<0.001للفترات الاربعة المذكورة حيث كان (2.17 ملمول /لتر) قبل إعطاء الكارنتين ثم (1.81ملمول /لتر) بعد 15 يوما من استمرار العلاج و (1.55 ملمول/لتر) بعد شهر من بدء استخدام الكارنتين و (1.41ملمول/لتر) بعد 45 يوم من ذلك. إضافة إلى حصول زيادة معنوية في كولسترول البروتين ألدهني عالي الكثافة ((p<0.001 بين الفترات الأربعة حجيث كان (1.25ملمول /لتر) قبل إعطاء الكارنتين ثم (1.44 ملمول /لتر) بعد 15 يوما من استمرار تناول العلاج و (1.71 ملمول/لتر) بعد 30 يوم من بدء استخدام الكارنتين و (1.56 ملمول/لتر) بعد 45 يوم من ذلك.

و انخفض دليل التصلب الشرياني بشكل معنوي (p<0.001) حيث كان ((7.72قبل إضافة تناول الكارنتين ثم ((3.6 بعد الانتهاء من فترة (45) يوما من تناول الكارنتين.

إلى جانب ذلك انخفض كولسترول البروتين ألدهني واطئ الكثافة وبشكل معنوي (p<0.001) حيث كان (6.88 ملمول/لتر) قبل إعطاء الكارنتين ثم (4.21 ملمول/لتر) بعد 15 يوما مع استمرار العلاج و (3.73 ملمول/لتر) بعد شهر من بدء استخدام الكارنتين و (3.45 ملمول/لتر) بعد 45 يوما من ذلك. كذلك انخفض الكولسترول الكلي غير كولسترول البروتين عالي الكثافة بشكل معنوي (p<0.001) حيث كان (177. ملمول/لتر) قبل البدء بتناول الكارنتين ثم (3.83ملمول/لتر) بعد 45 يوما من تناول الكارنتين مع بقية علاجات السكري

الاستنتاج : يستنتج من هذه النتائج أن الكارنتين يمكن أن يكون مفيدا كماده غذائية اضافيه أو ماده دوائية والتي تتكامل مع بقية الأدوية ألمخفضه للسكر في علاج مرض البول السكري من النوع الثاني بدلالة تحسن نتائج فحوصات طلعة جانب الشحميد.

Abstract

Objective: To assess the effect of L-carnitine administration, as an additional useful supplement, on serum lipid profile in type 2 diabetics.

Patients and Methods: Fifty-four patients (32 males, 22 females) aged 25-70 years, with type 2 diabetes mellitus who were attending Al-Waffa Diabetic Clinic, Mosul, Iraq; during the period from 1st October 2005 to 31st March 2006, were included in this study. L-carnitine was given to each of these diabetics for 45 days in a dose of 550 mg, in form of tablets in two doses orally, in addition to their other hypoglycaemic drugs. Blood samples were taken from each patient for the measurement of serum triglyceride (TG), total cholesterol

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(TC), high density lipoprotein-cholesterol (HDL-C), and calculation of low density lipoprotein-cholesterol (LDL-C), Non-HDL-C and TC: HDL-C (atherogenic index, AI). Four measurements were taken: before the first administration of L-carnitine, then after 15, 30 and 45 days from the commencement of the study.

Results: Mean TC showed a significant decrease ($p<0.001$) between the four intervals with a mean of 8.55 mmol/L before starting L-carnitine administration, and 6.47, 5.99 and 5.5 mmol/L after 15, 30 and 45 days respectively from the commencement of the study. There is also a significant decrease ($p<0.001$) in TG between these four intervals with means of 2.17 mmol/L before administrating L-carnitine, and 1.81, 1.55 and 1.41 mmol/L after 15, 30 and 45 days from the commencement of the study respectively. In addition, a significant increase ($p<0.001$) in HDL-C was found between these four intervals with means of 1.25 mmol/L before administrating L-carnitine, and 1.44, 1.71 and 1.56 mmol/L after 15, 30 and 45 days from starting carnitine administration respectively. The AI was also significantly decreased ($p<0.001$) with a mean of 7.72 before the administration of carnitine and 3.6 after finishing the period of 45 days of carnitine administration. The LDL-C was significantly decrease ($p<0.001$) with a mean of 6.88 mmol/L before administering L-carnitine, and 4.21, 3.73 and 3.45 mmol/L after 15, 30, and 45 days from the commencement of the study respectively. The Non-HDL-C was significantly decreased ($p<0.001$) with a mean of 7.17 mmol/L before starting carnitine administration and 3.83 mmol/L after 45 day from starting carnitine administration.

Conclusion: L-carnitine can be useful as an additional dietary supplement and pharmaceutical agent that has an improving effect on serum lipid profile in type 2 diabetics.

Key words: Diabetes mellitus, L-carnitine, triglyceride, total cholesterol, HDL-C, LDL-C, Non-HDL-C, atherogenic index.

Introduction

Carnitine is one of the dietary supplements, synthesized from the amino acids methionine and lysine [1]. It is β-hydroxy γ-trimethyl ammonium butyrate, a naturally occurring compound inside the body that facilitates the transport of fatty acid inside the mitochondria. L-carnitine or so-called levo carnitine is one of the important derivatives for mitochondrial β-oxidation system of fatty acids [2]. It increases the production of energy through stimulating fats oxidation. This will result in the reduction of total fat mass and serum lipid with increase in the percentage of total muscle mass. Hence, carnitine can improve the nutritional state and body mass index, and promote a positive protein balance [3]. Moreover, carnitine can decrease the oxidative stress and inhibit apoptosis (programmed cell death) by preventing ceramide formation (4). It also plays a role in membrane repairing process especially in the erythrocytes [5]. Carnitine can stimulate the immune response [6], promote maturation of the fetus and sperm [7], and correct receptors abnormalities in aging brain, and heart [8].

Diabetes mellitus is a common disease that is characterized by disturbed metabolism of carbohydrates and fats, which leads to the development of long-term microvascular and macrovascular complications [9, 10]. As carnitine contributes in the metabolism of fat and glucose, therefore any deficiency may cause a defect in their metabolism [11]. Decreased plasma carnitine level has been reported in type 2 diabetics (12) and it has some correlation with the development of complications [13]. This may be attributed to insulin deficiency and to unopposed glucagons excess (14). It may be recommended that plasma free carnitine should be determined in diabetics, even if they have good metabolic control [15]. In addition, carnitine has many effects on serum lipids, and it has been reported that when L-carnitine is given, in a dose of 2-3 g daily, to patients with hyperlipidemia, the lipid profile will be improved significantly with reduction in total and LDL-cholesterol and increase in apolipoprotien A-1 and B levels [16].

Dyslipidaemia is an independent predictor of coronary heart disease in type 1 and type 2 diabetics [17, 18]. Reduced level of HDL-cholesterol (HDL-C) is observed in type 2 diabetics which is correlated to the degree of insulin resistance (19), and may coexist with hypertriglycerdemia (20). This combination may be caused by lipoprotein lipase (LPL) deficiency particularly in those with poor glycemic control. These lipid components together with total and LDL cholesterol (LDL-C) usually improve with the improvement of glycemic control [21]. Also, diabetics treated with insulin, usually show an elevation in HDL-C which can be accounted to the improvement in LPL activity induced by insulin[22]. Hypertriglycerdemia is also common in a diabetic which occurs in the form of hyperchylomicronemia and as altered composition of the VLDL subfraction, which becomes more atherogenic [23, 24]. Non-HDL-C, which represents cholesterol carried on all of potentially proatherogenic apo-B containing particles (VLDL, IDL, LDL, chylomicrons remnants and lipoproteins a), is also increased in diabetics and it is an additional index for risk assessment in diabetics with dyslipidaemia[25, 26, 27].

The objective of this work was to assess the effect of L-carnitine administration in type 2 diabetics as an additional useful supplement with its possible pharmaceutical therapy as lipid modifying agent as reflected by serum lipid profile.

Patients And Methods

Patients: Fifty-four diabetic patients (32 males and 22 females) were volunteered in this study. Their ages were ranged from 25-70 years with a mean of 45 years. All of them were known to have type 2 diabetes mellitus and were regularly consulting Al-Wafaa Diabetic Clinic, Al-Zahrawi Hospital, Mosul, Iraq; during the period from 1st October 2005 to 31st March 2006. All of them have already been diagnosed to have type 2 diabetes mellitus by a specialist/consultant physician, and have developed certain complications of diabetes. Ethically, all these diabetics agreed to cooperate

in this study by taking orally 550 mg of L-carnitine twice daily for 45 days, and to give blood samples every 15 days from the commencement of the treatment.This form of medicine is produced under the name of Health Aid, L-carnitine is manufactured by PHARMADASS Limited, health aid house company (UK). The patients continued the use of other oral hypoglycemic drugs such as Glibenclamide or/and Metformine or any other drug such as antihypertensive, which have already been prescribed to them before starting this study.

Specimens and methods: Fasting blood samples were obtained by antecubital venepuncture between 9 am and 1 pm, from all subjects included in this study. About 3 ml of venous blood specimen was collected from each subject and transferred into a plain tube, allowed to clot for 15 min in a water bath at 37°C, and then serum was separated by centrifugation and followed by the determination of serum lipid profile.

Serum total cholesterol (TC) and triglycerides (TG) were measured by enzymatic method [28] using kits supplied by Biomerieux (France). HDL-C was measured according to Lopez-Virella [29] by a kit supplied from Biomerieux (France). LDL-C was calculated as follows:

LDL-C (mg/dl) = total cholesterol – HDL-C – (TG × 0.2)
or LDL-C (mmol/L) = total cholesterol – HDL-C – (TG × 0.455) (30)

Non-HDL-C was calculated as (Non-HDL-C = TC – HDL-C (25) and TC/HDL-C ratio (atherogenic index, AI) as the ratio of the two lipid components (31) (recommended cut-off ≤ 5).

Statistical analysis:The experimental data were subjected to Analysis of Variance, Duncan Multiple Range Tests, and Trend Analysis using Statistical Analysis System (SAS) according to Littlell et al., [32].

Results

The values of serum lipid profile for all patients before and following L-carnitine administration are shown in Tables 1 and 2. Mean TC showed a significant decrease ($p<0.001$) between the four intervals with a mean of 8.55 mmol/L before starting L-carnitine administration, and 6.47, 5.99 and 5.5 mmol/L after 15, 30 and 45 days respectively from the commencement of the study.There is also a significant decrease ($p<0.001$) in TG between these four intervals with means of 2.17 mmol/L before administrating L-carnitine, and 1.81, 1.55 and 1.41 mmol/L after 15, 30 and 45 days from the commencement of the study. In addition, a significant increase

Table 1 - Values of serum lipid profile for all patients before starting L-carnitine therapy.

Biochemical parameter	Means	Standard deviation	Range mg/dl (mmol/L)
Total Cholesterol mg/dl (mmol/L)	330.24 5 8.5)	127.86 3.31))	114-620 2.96-16.05))
Triglycerides mg/dl (mmol/L)	186.42 (2.12)	86.82 (0.99)	42.6-376 (0.39-4.28)
HDL-C mg/dl (mmol/L)	48.88 (1.25)	20.67 (0.54)	17.5-115 (0.45-2.97)
LDL-C mg/dl (mmol/L)	244.08 (6.88)	99.89 (2.82)	67.97-413.82 (1.91-11.68)
Non-HDL-C mg/dl (mmol/L)	277.21 (7.17)	113.455 (2.94)	77.2-470 (1.99-12.17)
TC: HDL-C	9.32	4.50	6.14-9.32

Table 2 - Means of serum lipid profile at different intervals/periods from the commencement of the administration of L-carnitine.

Biochemical Parameter	Intervals/periods of measurements			
	Before	After 15 day	After 30 day	After 45 day
Total Cholesterol mg/dl (mmol/L)	330.24 (8.55)	250 (6.47)	231.37 (5.99)	212.37 (5.5)
Triglycerides mg/dl (mmol/L)	186.42 (2.17)	158.69 (1.81)	135.93 (1.55)	123.78 1.41))
HDL-C mg/dl (mmol/L)	48.88 1.25))	55.57 (1.44)	65.94 (1.71)	64.32 (1.56)
LDL-C mg/dl (mmol/L)	244.08 (6.88)	162.67 (4.21)	138.24 (3.73)	123.29 (3.45)
Non-HDL-C mg/dl (mmol/L)	277.21 (7.17)	-	-	148.08 (3.83)
TC:HDL-C	7.72	-	-	3.6

(p<0.001) in HDL-C was found between these four intervals with means of 1.25 mmol/L before administrating L-carnitine, and 1.44, 1.71 and 1.56 mmol/L after 15,30 and 45 days from starting carnitine administration. There is also a significant decrease (p<0.001) in LDL-C between the four intervals with mean of 6.88 mmol/L before administering L-carnitine and 4.21, 3.73, and 3.45 mmol/L after 15, 30, and 45 days from starting carnitine administration. The Non-HDL-C was significantly decreased (p<0.001) with a mean of 7.17 mmol/L before starting carnitine administration and 3.83 mmol/L after 45 day from starting carnitine administration. The AI was also significantly decreased (p<0.001) with a mean of 7.72 before the administration of carnitine and 3.6 after finishing the period of 45 days of carnitine administration.

Discussion

The major key for prevention and slowing the progression of diabetic complications is by achieving good metabolic control that aids proper management [33]. In the follow-up, frequent assessment of glycemic state and its consequences on organs and tissues functions, should be regularly done [34].

The present study showed significant decrease in serum triglycerides (p<0.001) with means of 2.17 mmol/L before administrating L-carnitine, and 1.81, 1.55 and 1.41 mmol/L at 15, 30 and 45 days respectively following the commencement of L-carnitine treatment (550 mg twice daily). This finding is in agreement with the result reported by Argani et al (35) , who observed significant reduction in triglycerides in hyperlipidemic hemodialyzed uraemic patients following L-carnitine (500 mg daily for 2 months). Also, Digiesi et al (36) observed significant decrease in triglycerides after the administration of L-carnitine in hypertensive patients (in a dose of 2 g daily). In addition, Piston et al (3) reported significant decrease in triglycerides, and other lipid parameters as well as increase in HDL-C in healthy elderly subjects following L.carnitine (2 g daily in two doses).

The change in lipid profile reported in this study as well as others', may be accounted to that, the administration of L-carnitine can increase β-oxidation of the fatty acids especially in carnitine deficient patients[37]. The lower dose of L-carnitine increases β-oxidation to an extent, that the resultant acetyl-coA enters Kreb>s cycle and result in an increase in the production of energy by burning fats. This in turn, results in a decrease in fatty acids and possibly in serum triglycerides concentration. Carnitine deficiency and hypertriglycerdemia are common in diabetics, and reversal of the deficiency state may improve the lipid abnormalities [9]. Also in the aforementioned studies, secondary carnitine deficiency status is expected in uraemics [35], hypertensives [36] and elderly subjects[3] and contributing in explaining the response to L-carnitine therapy, as also in this study.

The results of this study, on the other hand, disagree with that of Rahbar et. al., [38] who showed a significant increase in triglycerides, after giving L-carnitine (3 g daily for 3 months) to type 2 diabetics with complications. This may be explained by the high dose administered, as this may result in an over production of acetyl-coA which becomes a substrate for the synthesis of malonyl-CoA that is required for fatty acid synthesis in the extra mitochondrial pathway, and which is a potent inhibitor for carnitine palmitoyl transferase I, that may inhibit the effect of L-carnitine in the transportation of fatty acid in diabetic patients [39]. Moreover, the results of the present study disagree with the study of Derosa et al. [40] who found no significant decrease in triglycerides after giving L-carnitine (1 gm twice daily for 3-6 months) to newly diagnosed diabetics without complications and who were treated with diet alone. As these patients, had not yet developed complications, and so L-carnitine may still within the normal range, and so no change was found in their lipid parameters after L-carnitine administration.

The results of the present study showed a significant increase in HDL-C which also agree with other studies, those of Argani et al. [35] and Piston et al. [3]. These results can be explained by that, L-carnitine increases β-oxidation, utilization of cellular fatty acids, and removal of abnormal fat on cellular membrane. Hence, there is an increase in the metabolism of lipoprotein, including LDL by apo-B receptors which may account for the significant decrease in both LDL-C and Non-HDL-C (16). This may result in an increase in HDL-C concentration (41). However, Derosa et al., in their study [40] in diabetics with metabolic complications, showed no significant effect on HDL-C after 3 months of L-carnitine administration (1 gm twice daily). These patients may have no carnitine deficiency status; therefore, administration of L-carnitine gave no further increase in β-oxidation. In addition, the study of Rahabr et al, [38] showed no increase in HDL-C which may be due to that, the high dose of L-carnitine in complicated diabetics may increase serum triglycerides. This may cause inhibition of LPL, with its consequence on lipoprotein metabolism which results in insulin resistance state [42]. However, the small dose of L-carnitine used in complicated diabetics may increase insulin sensitivity with activation of LPL, which is consequent effect on other lipids including an increase in HDL-C [43].

However, the overall improvement in lipid profile may be accounted due to the improvement in the glycemic state of the patients [19, 21].

Conclusion

L-carnitine can be useful as an additional dietary supplement and pharmaceutical agent that complete other hypoglycemic drugs for the management of type 2 diabetes . It has an improving effects on lipid profile as it lower the level of serum; TC, TG, LDL-C, Non-HDL-C an AI and increasing the level of serum HDL-C.

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Outcome of premarital counseling of hemoglobinopathy carrier couples attending premarital services in Bahrain

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الملخص

تمهيد: لقد تم العمل بفحص قبل الزواج في عام 1993م للراغبين فقط ، وفي عام 2003م تم مراجعة إحصائيات العشر سنوات السابقة وأتضح إن نسبة الحضور للفحص لا تتعدى 25% التي لم تكن مرضية. تم تطبيق المرسوم الملكي بخصوص إلزامية فحص المقبلين على الزواج قبل صدور الشهادة الطبية في عام 2005م وذلك بهدف الحد من انتشار أمراض الدم الوراثية لفقر الدم المنجلي والثلاسيميا.

الهدف: لمعرفة نسبة الأشخاص الذين تم زواجهم بعد حصولهم على المشورة الطبية الخاصة بأمراض الدم الوراثية.

الطرق: دراسة مقطعية وصفية شملت 1070 شخصا من المقبلين على فحص و مشورة ما قبل الزواج في البحرين في الفترة ما بين 1 أبريل 15 مايو 2006م.

النتائج: نسبة انتشار المصابين بمرض فقر الدم المنجلي 14 (1.3%)، حاملي فقر الدم المنجلي 175 (16.4%) ، منهم 22 زوج حاملين للمرض، نسبة المصابين بنقص الخميرة 268 (24%)، شخص واحد فقط (0.09)% مصاب بالثلاسيميا ب ، 30 (2.8%) حاملي الثلاسيميا ب، منهم 3 أزواج. 365 (34%) لديهم صغر في حجم خلايا الدم الحمراء، منهم خمس أزواج.

مجموع الأزواج المصابين و الحاملين لإمراض الدم الوراثية 30 زوج (60 شخص) تم تحويلهم لقسم أمراض الدم الوراثية لتقديم المشورة الطبية اللازمة، متوسط أعمارهم 25.7 عاما. تزوج منهم 17 زوج (56.7%) بعد تقديم المشورة الطبية.

الاستنتاج: من هذه الدراسة تم استنتاج أن السياسة المتبعة حاليا في الفحص وتقديم المشورة للمقبلين على الفحص قبل الزواج ليست فاعلة في الحد من زواج أغلب المصابين أو حاملي أمراض الدم الوراثية.

مفتاح الكلمات: أمراض الدم الوراثية، مشورة قبل الزواج.

Abstract

Background: Premarital screening was introduced in 1993 as an optional service. Evaluation of 10 years statistics in 2003, showed only 25 % attendance. Therefore, a Royal decree of compulsory testing before issuing marriage health certificate was introduced in 2005 in order to improve attendance aiming to decrease the prevalence of hereditary blood diseases.

Objective: To determine the frequency of marriage among couples referred for hereditary blood diseases genetic counselling.

Methods: A cross sectional study involving 1070 individuals attending premarital screening in Bahrain during the period of 1st April and 15th May 2006.

Results: The frequency of sickle cell disease (SCD); 14 (1.3%), sickle cell trait (SCT); 175 (16.4%), 22 couples were both SCT. The frequency of G6PD was 268 (24%). One candidate (0.09%) was β thalassemia major, 30(2.8%) β thalassemia trait, 3 couples were carriers. 365(34%) individuals with low RBC indices indicating possible α-thalassemia including 5 couples. Thirty couples (60 individuals) were referred for genetic counseling with a mean age of 25.7 years. 17 couples (56.7%) got married in spite of counseling.

Conclusion: Based on this study; the current policy of premarital screening and counseling do not seem to be successful in discouraging most of the couples with high-risk for hereditary blood diseases from getting married.

Key words: Hereditary blood diseases, Premarital counseling.

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Introduction

The world health organization estimated that about 5% of the world's population carries genes responsible for haemoglobinopathies. The burden of genetic blood disorders has long been recognized as a major public health problem in Bahrain, since the first neonatal screening in 1984 that showed the birth rate of sickle cell disease (SCD) of 2.1%, and the sickle cell trait 11.2%. The incidence of α-thalassemia was 24.3% in these neonates. [1]

In an attempt to increase awareness about these diseases among the public, the first genetic clinic was established in 1984,and the Bahrain Hereditary Anemia Society was formed in 1991. In 1992, the national committee for the prevention of genetic diseases in Bahrain was formed. In the same year screening of all pregnant women began, and in the following year 1993 premarital screening was introduced as an optional service in all primary health services. A review of the service in 2003 (Annual Health Statistics 2003-Ministry of Health); showed only 25% of the married couples attended such screening.

There was an overall decline in the prevalence of SCD, in 2003; the birth rate was 0.9%, which indicates a 60% decline [1]. The latest data from genetic department in 2008 showed incidence of 0.65% only.

Screening is defined as a public health service in which members of a defined population, who do not necessarily perceive that they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of disease or its complication (NSC 2000) [2]

While Counseling has been defined as a process of helping a person/couple learn how to solve decisional problems, it is an interactive, collaborative and respectful process, Client- or couples centered, directing towards developing autonomy to make wise and realistic decisions, considering interpersonal situation, social/ cultural context, and readiness to change through providing information and altering their own behavior to produce desirable consequences.

1993 premarital counseling (PMC) service began in the kingdom of Bahrain; all nationals were encouraged to undergo such screening as an optional service.

In 2003, a review of the statistics showed poor attendance (25%). In January 2005; Royal decree of compulsory premarital screening for hereditary blood diseases for all nationals was implemented. Several countries have adopted such measures that resulted in marked reduction in the prevalence of such diseases (Cyprus, Iran, Gaza strip-Palestine). In Saudi Arabia, the royal decree was implemented in February 2004.

A premarital screening study was conducted in one of the southern cities of Turkey found the frequency of HbS 4.6% and β thalassemia 2.3%. In 1.65% both partners were carriers. [3]

Another study of candidates attending premarital screening program in Al-Hassa -Saudi Arabia, found a prevalence of β-thalssemia trait to be 3.4%. (4)While in Iran a country with high prevalence of β -thalassemia trait (5-10%), the prevalence has declined from 11.6 to 7.2 per 10000 population in a five-year period due to premarital screening program.[5]

In Cyprus screening high-risk families for β thalassemia was introduced in 1979 and made compulsory in 1980. In 1984, prenatal diagnosis was started, affected birth rates showed a sharp decrease from 18-20 cases per year before the implementation of the Programme to only five thalassemic babies born per annum» Between 1991 to 2001, the number further fell to one in every 2-3 years. No thalassemic babies have been born between 2002 and 2007. [6]

A premarital screening program was implemented for β -thalassemia in 1995 in the city of Denizli in the Aegean region of Turkey, couples at risk were counseled and offered prenatal diagnosis and termination of pregnancy in case of an affected fetus. The 4-year results found the prevalence of β -thalassemia trait to be 2.6%, sickle trait 0.11%. After genetic counseling, 13% planned carrier marriages were canceled, 47% declared that they do not intend to have a child. Prenatal diagnosis was sought by 40%, one had β thalassemia major; this pregnancy was terminated by elective abortion. [7]

Gaza Strip, Palestine adopted obligatory premarital testing for β -thalassaemia in September 2000; a study was conducted among candidates for premarital screening between 2003-2005 showed 25% carriers. Since implementation, there has been a reduction in the birth of children with β -thalassaemia major. [8]

In Jordan; consanguineous marriages declined from 28.5% between 1950 and 1979 to 19.5% after 1980. In the overall population, carrier rates for β -thalassemia, α-thalassemia and sickle cell anemia are in the range of 2-4% and 3.2-12% of males for glucose-6-phosphate dehydrogenase deficiency. A mandatory premarital screening program for β -thalassemia carriers commenced in June 2004.[9]

In Konya urban area of Turkey, the thalassemia trait was detected in 2%, and the sickle cell trait in 0.05%. These results are very similar to Turkey>s beta-thalassemia and sickle cell trait averages. [10]

Materials and Methods

This is a cross-sectional descriptive study conducted to find out the marriage outcome after counseling couples at risk for hemoglobino-pathies during the premarital screening program.

All couples attended premarital screening services including non-Bahraini partners during the period of April 1st to May 15th 2006 in twenty-two maternal and child health units based in the local health centres in Kingdom of Bahrain.

A convenience sample previously selected for the purpose of conducting a study on hepatitis C virus (HCV) prevalence among couples attending premarital screening as well as for hemoglobinopathies was used in this study.

The sample was calculated according to HCV prevalence in the previous studies. The sample size was 1070 and was over six week>s period.

Blood testing for hemoglobin pattern using chromatography (HPLC) was performed for all candidates. Couples returned in 10-14 days for the results, and those at risk of sickle cell disease or β thalaessemia (both partners sickle cell trait or one or both with

β thalaessemia trait), α thalaessemia (if both partners with Hb< 11gm, low indices MCV, MCH, and or HbA2 [3.4-3.7]) were referred for further genetic counseling to explains the risk of getting affected children, and options of pre-conceptional and prenatal diagnosis using chorionic villous sampling(CVS) or aminiocentesis if the couples choose to continue the process of marriage and possibly further investigations such as DNA testing for couples with low indices to rule out α-thalassemia.

Couples referred for genetic counseling were contacted by telephone one and two months later to verify their decision.

The statistical methods for the analysis: (SPSS version 14) was used to study frequency for categorical variables and means with standard deviation (SD) for quantitative variables.

Results

Of the 1,070 candidates screened. 93.8% were Bahraini and 6.1% were non Bahraini. The age of the total sample ranged between 14 and 74, with a mean age 25.9±7.1 years.

Out of the 1070 individuals screened with HPLC, 869 (81.2%) were normal, 14 (1.3%) had sickle cell disease (SCD), 175 (16.4%) were sickle cell trait (SCT) of which 22 couples were both carrier. One candidate (0.09%) had β thalassemia major and 30(2.8%) were β thalassemia trait , of which 3 couples were both carriers. 365(34%) individuals with low indices and or HBA2 (3.4-3.7), and 5 couples both with low indices.

Total of 30 couples (60 individuals) were referred for genetic counseling with a mean age of 25.7, out of which 17 couples (56.7%) got married in spite of counseling.

Twenty two couples had both SCT: 2 refused referral to genetic counseling and choose not to continue the marriage certificate procedure. Twenty couples were referred to counseling, thirteen couples were advised against, but finished their marriage procedures in spite of the facts given regarding the genetic risk. Seven couples were convinced of the risk of having affected babies and choose not to continue, among them three couples have family history of affected individuals.

Five couples referred with low indices, HBA2 (3.4-3.7): advised to wait for DNA testing to rule out α-Thalassemia; 3 got married without being tested, one cancelled and one delayed their marriage. Non of them has family history of affected person .

Three couples with β thalassemia trait; one of whom were both carriers, cancelled their marriage; the second couple one with low indices cancelled their marriage; the third couple with SCT got married. None of them have family history of affected person. (Table 1)

Discussion

Total of 30 couples (60 individuals) were referred for genetic counseling, 17 couples (56.7%) got married in spite of counseling, which is in our opinion considered high. Similar findings were reported in Iran in the Mazandaran Province where 51% of couples at-risk, who received genetic counseling, decided not to marry. [11]

In a screening study for SCD and β thalassemia in Saudi Arabia during the period February 2004 to January 2005; 4.20% had sickle cell trait, 0.26% had SCD, 3.2% had β thalassemia trait, and 0.07% had β thalassemia disease. The couples considered as high risk comprised 2.14% of the screened population. Among the 2,375 high-risk couples contacted by telephone, 89.6% married each other, despite the known high-risk status. [12]

While another study assessing the 10-year results of the premarital screening programme for β-thalassemia, in Southern Iran, which offered counseling for carrier couples, prenatal diagnosis and termination of pregnancy since 1995, showed the prevalence of (2.53%) in 1995, (1.07%) in 1999 and 0.82 patients per 1000 births in 2004. It was concluded that the programe has decreased the birth rate of β- thalasemia but has not eliminated the disease due to cultural and religious causes. [13]

Our study showed that counseling given to couples at risk did not discourage many of them from getting married. On questioning many of them for the reasons behind their decision, they stated that the risk of having affected child is very low, that it is not a very bad disease, or have not seen any case before and people can live until late age with the disease, and that it is all in God>s hand, while others were convinced of the ability of prenatal identification and termination of affected fetuses as they were informed during the counseling. Many admitted that they have no choice except taking the risk because of family, cultural and some social commitment such as arranged marriages.

Table 1 - Marriage outcome of groups at risk of hemoglobinopathies:

Socio-demography of the abnormal HPLCfindings	Couples with SCT	Couples with red blood cell low indices	Couples with β Thalasemia Trait
Education:			
- Read and write.	1 (2.3%)	0	0
- Primary, intermediate	4 (9%)	0	0
- Secondary.	27(61.3%)	5 (50%)	3 (50%)
- University and higher	12(27.3%)	5 (50%)	3 (50%)
Total -	44 (100%)	10 (100%)	6 (100%)
Age range (Mean age)	17-45 (25.8)	18-28 (23.7)	17-36 (27.5)
Number, Percentage of those got married in spite of counseling	13 couples (59.1%)	3 couples (60%)	One couple (33.3%)

In a cohort of 74 sickle trait-carrying couples in Virginia- USA, who were counseled concerning the disease and their risk, majority of the pregnancies after counseling occurred in the group who had no children or had no affected child before counseling. The author stated that in young couples, concern for producing a child with sickle cell anemia is often offset by a strong desire to have children regardless of risk. [14]

There are many reasons for ineffective counseling in this study: the short time between screening and marriage, the short time given for consultation and counseling, lack of physicians training in counseling, family interference or pressure, misinformation given that indirectly ease the decision of marriage, lack of knowledge about the disease especially among couples with no background or affected relatives, the inadequate facts about risk of prenatal diagnosis such as chorionic villous sampling (CVS), amniocentesis, fetal blood sampling, as well as the issue of legality of abortion in the Kingdom of Bahrain.

Conclusion:

The prevalence of hereditary blood diseases among couples attending premarital screening program at primary care corresponding to the results of other local studies is a common health problem, and the effect of counseling in discouraging affected couples from getting married does not seem to be very effective.

In the absence of the law preventing marriage of affected couples, efforts should be concentrated on developing the counseling skills of the counselors, and increase public awareness

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Medical Education

Use of OSCE in undergraduate assessment of Psychiatry at the College of Medicine and Medical Sciences – Arabian Gulf University, Bahrain

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ملخص

إن كلية الطب والعلوم الطبية في جامعة الخليج العربي قد تكون أول كلية طب في العالم العربي تطبق امتحان الـ OSCE في تقييم طلبة كلية الطب في مستوى البكالوريوس.

تتضمن الورقة وصف لطرق تقييم أداء الطلبة في كلية الطب بجامعة الخليج العربي مع التركيز على استخدام امتحان الـ OSCE وشرح محتواه ونتائج تطبيقه وتخلص الدراسة إلى امتحان الـ OSCE هو امتحان مناسب لفحص القدرات العملية والعلمية اللازمة لمستقبل الطلبة في ممارسة الطب.

Abstract

The college of Medicine and Medical Sciences (CMMS) at the Arabian Gulf University (AGU) is amongst the first Medical Schools in the Arab World to implement OSCE in Undergraduate assessment of Psychiatry. Despite the matured implementation of OSCE, as a valuable assessment tool, in other medical fields it remains a novelty in terms of its application in Psychiatry.

This paper provides a description of assessment methods at CMMS with particular emphasis on the use of OSCE, its content, examination structure, and learning outcomes and conclusions derived from implementation and application of the program. Overarching results indicate that OSCE is a valid and fair test of the immediately relevant abilities relevant to their future careers within the medical field of pratice.

Key words: CMMS, AGU, OSCE, Assessment.

Introduction

Amidst the Arab world, the college of Medicine and Medical Sciences (CMMS) at the Arabian Gulf University (AGU) was amongst the first institutes to implement a problem-based curriculum within the faculty of Medicine. The total objectives of the problem-based curriculum are structured to cover a thorough and wide-ranging span of medical disciplines divided into two distinct phases. Phase I of the program covers the study of Health Sciences based on simulated health problems and phase II addresses rotation within clinical clerkship. Within the overall program, the Psychiatric objectives constitute approximately 3.5% of the total objectives of the curriculum[1]. It is expected that with this, students will be equipped to achieve a level of competence in the general objectives and studies relevant to Psychiatry.

Through-out the course of the program, examination of the curriculum is conducted via integrated forms of assessment, which engage students in cross-disciplinary evaluations rather than segregated exams. Moreover, the division of the curriculum into problem blocks, associated with medical issues, allows for end of block assessments conducted on both written and clinical levels. Summative examinations are also conducted at the end of each year with written and clinical examinations. Individual disciplines are assessed in the final qualifying examinations within Phase II, where clinical examinations are conducted in accordance to separate disciplines.

The Objective Structured Clinical Examination (OSCE) consists of approximately 20 stations. Various clinical specialties are accounted for within these stations, including Psychiatry and basic Sciences, represented in various appraisal formats including slide analysis, specimens, and diagnostic records amongst others.

The OSCE has long become a respected and widely used tool for the assessment of clinical competence in Psychiatry. Its validity and reliability has been reported and proven by numerous researches [2,3,4,5]. Amongst other tools, the Watched Structure Clinical Examination (WASCE) has also been used and validated as an assessment tool in various Behavioral Sciences and end of Clinical rotations in the CMMS, AGU[6,7].

The OSCE in Psychiatry

Of the 20 noted stations within the noted curriculum, no less than two are allocated to the discipline of Psychiatry, whilst the rest cover various disciplines such as General Medicine, Surgery, Pediatrics, Obstetrics and Gynecology, Radiology, Opthalmology, ENT, and Dermatology. The design and setup of the 20 stations requires each student to rotate amongst stations at five minute intervals. Each of the two psychiatric stations necessitates students to attend to a simulated patient (usually a psychiatric nurse).

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The Content

Within the examinations, scenarios are drawn up for students with storylines based on real clinical cases inclusive of investigation of items such as orientation, memory and concentration, and mini-mental state examination of depressed or psychotic patients, and the elicitation of symptoms such as types of delusions, hallucinations and depressive symptoms. Also amongst the tested subjects is the skill of breaking bad news to patients with cancer or HIV+Ve status. In evaluation, the examiner is provided with a score sheet (containing the correct answers) and is expected to mark each of the designated items of the interview examination separately. The evaluative aspects include communications skills (e.g student introducing himself/herself to the patient, greeting the patient, eye contact, empathy etc) in addition to eliciting the correct required symptoms. An example of such a typical station is included within the associated appendix.

The Outcome

There is a notable learning curve for both staff and students in the organization, application and associated use of the OSCE in Psychiatry, as reflected in the learning affiliated with conducting the exam in general, with the specific details of each station, as well as in training the psychiatric nurses to act as simulated patients. Most notably, it has been found that there should be sufficient space to run the exam accounting for the segregation of students to prevent them from meeting between stations. Additionally, an average of two hours is needed to teach the simulated patient the clinical case scenario and ensure that he/she does not deviate from the examination objectives. Clear instructions are provided on the score sheet for the examiners as well the means by which to partition the exam into individual segments with a relevant mark against each tested item. Finally, it is necessary to prepare the examiners well before the exam via mock trials in order to avoid major discrepancies in examiner scoring techniques and to reach an agreeable inter-rater reliability score.

The preparation of the OSCE in general and in psychiatry in particular is taxing both in time and resources, however its functional capacity in furnishing students with a blend of blending theory and practical clinical experience as well as its objective means of learning and grading are tangible advantages. At the student level, OSCE is usually welcomed by students; feedback suggesting that they feel it is a fair and comprehensive exam that prepares them for a practical future within the medical field.

Conclusion

The introduction of OSCE in testing psychiatric knowledge and clinical skills reflects the orientation of the examinations towards the fulfillment of objectives set by the curriculum committee at the beginning of the program. These same objectives are set as a reflection of the capabilities immediately relevant to the future career requirements of a medical student. This is in line with the recommendations of the Royal College of Psychiatrists on competency based curriculum training in psychiatry[8]. Continuing to question and improve on the assessment methods at the CMMS, AGU may produce further changes in the application of OSCE. At present, OSCE remains an innovative examination of medical knowledge, clinical skills, and attitude.

Appendix

I. OSCE station: actor playing the role of a severely depressed 45 years old School teacher. He has a two months history of depressive illness resulting in loss of six kilograms of weight and suicidal ideations but he did not act upon them. His responses to questions are delayed zas a result of his motor retardation, he is unshaven, untidy and looks disparate and severely depressed.

II. Instructions to the student: please interview this patient with the aim of eliciting one feature of psychotic depression and four other biological symptoms of depression. Explain to the patient the nature of his condition and his treatment.

III. Score sheet (Examiner)

Objective not met	0
Partially met	1
Fully met and appropriate rapport and empathy achieved	2

IV. Items to be scored

• Introducing oneself and making the patient feel at ease	0	1
• Explanation of the purpose of the interview	0	1
• good communication Skills and empathy	0	1
• discussing the management with the patient	0	1
• Ending interview and thanking the patient	0	1

5 marks

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Case Report

Management Dilemma of Cervicofacial Necrotizing Fasciitis

Ghassan Dhaif FFDRCSI[1], Ameen Al-Saati, FRCS DLO[2], Bassim M Ashoor Cabs, FRCSI[3]

الملخص

إن التآكل الناتج عن الالتهاب الميكروبي في الأنسجة التي تحت الجلد من الأمور النادر حدوثها. وإذا حدث ذلك فإن العواقب قد تكون وخيمة وتؤدي إلى انتشار التآكل في الجلد والأغشية التي تحت الجلد والعضلات والأوعية الدموية.

ويمثل التشخيص المرحلة المهمة لتفادي انتشار المرض وعلاجه. وعادة ما يكون العلاج باستخدام المضادات الحيوية إضافة إلى التدخل الجراحي.

وسوف نستعرض في هذا التقرير حالات تم علاجها في مجمع السلمانية الطبي في الفترة مابين 1999-2006 مع التطرق إلى التدخلات المختلفة للعلاج.

Abstract

Cervicofacial necrotizing fasciitis is a rare polymicroibial infection, which carries high morbidity as well as mortality rate. It is usually the result of rapid spread of infection along the fascial planes, causing necrosis of the fascia and overlying skin, which eventually involve the blood vessels and muscles. Early diagnosis is crucial in limiting the fatal consequences of the disease process and the establishment of the appropriate line of management. We discuss the management dilemma in selected cases treated at the Department of Oral & Maxillofacial Surgery, Salmaniya Medical Complex, Bahrain during the period 1999-2006 and outline briefly the medical as well as the surgical management.

Key words: Necrotizing, fasciitis, neck, cervicofacial, infection, necrosis.

Introduction

Necrotizing fasciitis (NF) is a severe life threatening, potentially fatal and rapidly spreading infection that involves the superficial subcutaneous fascia1,2. It is characterized by an extensive diffuse necrosis of the fascial planes and subcutaneous tissues. The nature of the disease is progressive, and if treatment is not prompt and aggressive may result in widespread undermining of the surrounding tissues and deep spaces of the neck, and extensive systemic toxicity. Cervicofacial necrotizing fasciitis is rare but usually caused by dental infection, infection secondary to trauma, throat abscess, osteoradionecrosis or, rarely, salivary gland infection[2,3].

There are several predisposing factors, which may help in the development of the disease process, and this includes association with diabetes mellitus, peripheral vascular disease, atherosclerosis, intravenous drug abuse and alcoholism1,4,5. However, necrotizing fasciitis can also strikes young and healthy individuals. The mortality rate varies significantly from 10% to 40%, though figures as high as 80% have been reported without an early surgical or medical intervention2. This mandates accurate diagnosis, fluid and electrolyte replacement, early and aggressive surgical debridement and appropriate antibiotic therapy.

Originally, this was to be caused by Haemolytic streptococcus organisms or Staphylococcus aureus, but recent advancements in microbial culturing have shown it to be a poly-microbial infection caused by synergy between aerobic and anaerobic organisms [6,7,8]. This disease usually starts similar to an abscess or cellulitis, but in contrary to these infections, which usually responds promptly to antibiotic therapy or incision and drainage, treatment of NF generally requires thorough surgical debridement of the necrotic tissues4. It is imperative that appropriate broad spectrum antibiotic therapy should be used in the early stages in order to ensure wide coverage. Later, this can be organisms-specific upon obtaining culture results.

Recent studies have suggested an adjunctive therapy in order to improve surgical outcomes and reduce the mortality rates. This includes hyperbaric oxygen therapy and intravenous immunoglobulin G (IVIGG)[9].

Airway compression will be inevitable if the disease is not discovered early and treated promptly. Further spread into the mediastinum may carry grave consequences with this life threatening infection[10,11,12].

We are reporting four cases of cervicofacial necrotizing fasciitis and discuss their management.

Case 1

A-68-year-old Bahraini female was referred to Salmaniya Medical Complex, Bahrain for the treatment of right submandibular abscess of dental origin. The patient had toothache one week earlier and was seen by her general dental practitioner at the health center who prescribed her antibiotics treatment. Her past medical history includes uncontrolled diabetes and hypertension without current treatment. On admission, the patient was in a toxic condition, temperature was 38.7°C and blood pressure 135/85 mmHg. Clinical

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examination revealed extensive erythema and fluctuance of the right side of the neck crossing the midline and extending to the nipple line of the right side of the chest. There was swelling of the left submandibular region extending to the postauricular region, indurations and fluctuance in the right submental area. Intraoral examination showed neglected mouth with remaining roots in both jaws and food debris covering the oral mucosa. The patient had a White blood cell count of 26,900/µL, the random blood sugar was 25.5 mmol/L, the Red blood cell count, haematocrit and serum electrolytes were normal. Chest radiograph was normal. Panoramic radiograph showed multiple remaining roots in both jaws. A medical consultation was sought to control the patient>s diabetes and hypertension. The patient was kept on the sliding scale to control the high blood sugar, Tenormin 50mg and intravenous amoxicillin antibiotics (Augmentin 1.2gm, three times daily). The patient>s condition started to deteriorate 24 hours after admission with necrosis of the skin at the right submandibular region, the anterior chest wall and the breast (Figure 1). This was covered with a thick

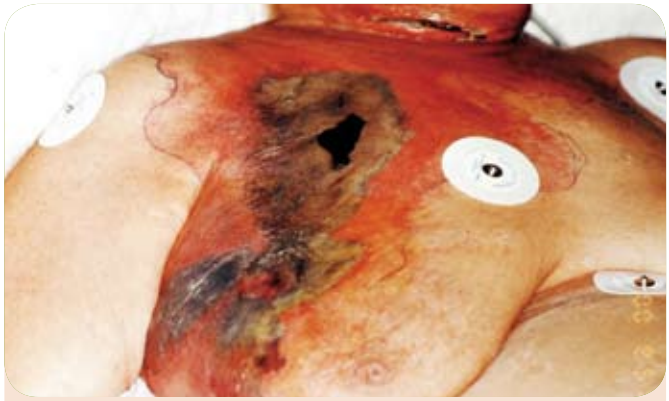

Figure 1. Case 1 showing extension of the edema and necrosis to the anterior chest wall and the right breast. Note the extension of this to cross the midline.

layer of brown exudates. There was an extensive foetid odor.

The patient was taken to operating theatre, under general anesthesia, the patient underwent an incision and drainage of the right submandibular and submental space abscess and complete excision of the necrotic skin of the right neck. Deep in the neck, there were necrotic muscles, glands and vessels. The wound was extensively and promptly debrided and the residual wound packed with Bisthmus Iodine Paraffin Paste (BIPP) gauze. The remaining roots were extracted.

The general surgeon decided to perform a complete right mastectomy and excision of the skin and the deep muscles of the anterior chest wall including the right axillary region because he found the skin and its underlying tissues were extremely necrotic (Figure 2). Complete debridement of all necrotic tissues was performed until bleeding was encountered. The areas of debridement had to be extended throughout the operating areas and crossing beyond. The chest wound was irrigated with hydrogen peroxide and normal saline, and covered with BIPP gauze. All the excised tissues were sent for tissue culture. Intravenous Clindamycin (900 mg, three times daily) was started. The patient was transferred to the intensive care unit intubated and ventilated. She had regular

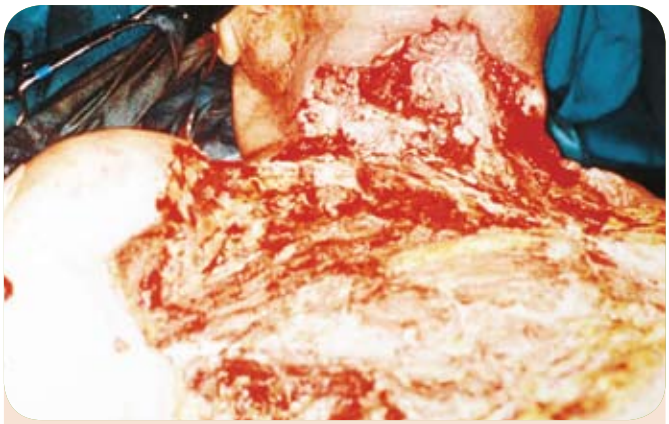

Figure 2. Case 1 following debridement and excision of the necrotic skin and deep tissues leaving raw bleeding areas.

change of dressing with wound coverage using Povidone-soaked gauze and regular irrigation using hydrogen peroxide (H2O2). Two days later, the patient's condition improved significantly, all the drains were removed and the patient was extubated and transferred to the ward. The residual neck and chest wounds remained and were treated with daily dressing changes of H2O2/ Saline. The patient was transferred to the plastic surgery division for the management of neck and chest wounds. She underwent wound coverage with split-thickness skin grafts at different settings. The patient was discharged from the hospital and subsequently was on regular follow-up for three years uneventful.

Case 2

A-37-year-old Indian man presented with a rapidly progressive left neck swelling of 10 days duration. He was seen earlier by his general dental practitioner with pericoronitis related to the lower left wisdom tooth and was kept on Metronidazole tablets 400 mg, three times daily. His medical history was not contributory. On admission, the patient appeared acutely ill and toxic with temperature of 39°C and blood pressure of 120/80 mmHg. Examination showed a diffuse firm and tender swelling on the left side crossing neck midline involving submandibular and submental areas extending to the left clavicle inferiorly. The neck skin was red, edematous and tender (Figure 3). The mouth was open with the tongue pushed outside the oral cavity. There was an extensive edema in the floor of the mouth and the left pharyngeal walls. The operculum overlying the lower left wisdom tooth was inflamed and there was obliteration of the buccal vestibule. Blood tests showed leukocytosis of 24,400 and Erythrocyte Sedimentation Rate (ESR) of 100mm/hr and glucose level of 3.5 mmol/L. Chest radiograph was normal. The clinical diagnosis was soft tissue infection of the submandibular, submental and parapharyngeal spaces (Ludwig's angina). A computed tomography (CT scan) revealed "gas pockets" in the right submandibular, submental and parapharyngeal spaces (Figure 4). This picture raised the suspicion of cervicofacial necrotizing fasciitis. Under general anesthesia, incision and drainage was performed by two incisions in the submandibular and submental regions bilaterally. A large amount of pus was drained. The superficial fascia and subcutaneous tissues including the deep muscles appeared necrotic. The necrotic tissues were meticulously

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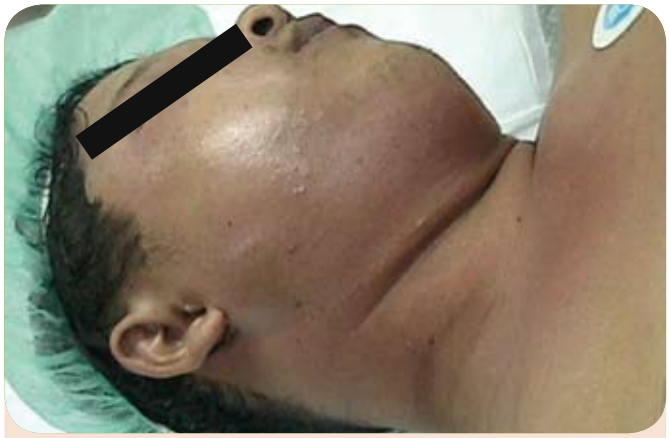

Figure 3. Case 2 showing right side neck edema with extension down to the chest wall.

excised and submitted for culture and histology. The wisdom tooth was surgically removed and the wound was sutured. The patient was transferred to the ICU intubated and sedated. He was kept on intravenous amoxicillin/clavulanate potassium (Augmentin) 1.2 gm three times daily and metronidazole 400mg three times daily. Gram-stained smears showed the presence of beta Hemolytic streptococci, bacteroides and proteus organisms. The patient's condition improved and was extubated and transferred to the surgical ward. The wounds healed spontaneously within 7 days and she was discharged from the hospital. Routine follow-up for 1 year

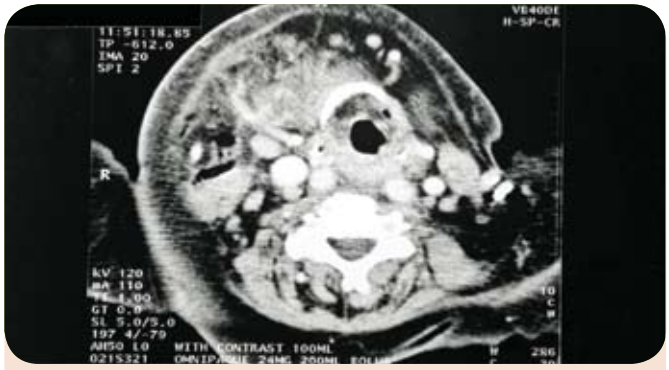

Figure 4. CT scan for case 2 showing massive necrosis of the deep fascia and other structures in the neck with multiple lymph nodes enlargement and deviation of the trachea to the left side and significant narrowing.

was uneventful.

Case 3

A-68-year-old Bahraini woman was admitted into the hospital because of dysphagia. On admission, there were bilateral puffy and tender red swellings of both submental and submandibular regions. Her symptoms started 4 days earlier with difficulties in swallowing and breathing. Due to the severity of dysphagia and reduced PO2 and increased PCO2, it was decided to perform urgent tracheostomy by ENT surgeon in order to secure the airway. The patient was sedated and ventilated upon admission in the ICU. CT scan of the neck demonstrated gas accumulation in the face, neck and parapharyngeal spaces. There was an extensive necrosis of the soft tissues in these spaces (Figure 5). She was kept on intravenous amoxicillin/clavulanate potassium (Augmentin) 1.2gm, three times daily. The patient's condition deteriorated 24 hours following tracheostomy. Under general anesthesia, surgical exploration of the cervical region was performed via long submandibular neck crease incision. Necrosis of the superficial fascia, deep investing fascia, submandibular gland and a portion of suprahyoid and infrahyoid musculature was noted. Meticulous debridement of the necrotic tissues and excision of the necrotic submandibular gland was contemplated (Figure 6). Irrigation of the wound with

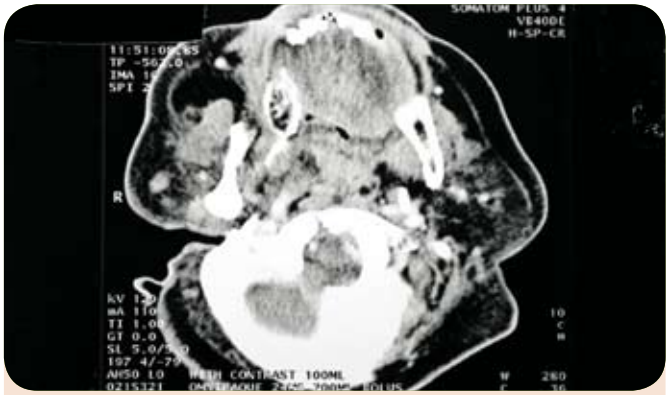

Figure 5. CT scan of case 3 showing extensive necrosis of the neck tissues and deviation of the trachea to the left side.

betadine/normal saline was done vigorously and two vacuum drains were inserted. The patient's condition improved significantly with normal vital signs within 48 hours. The tracheostomy tube was removed four days later with complete closer of the tracheostomy wound. The patient was discharged from the hospital after 1 week and post-operative follow-up was uneventful.

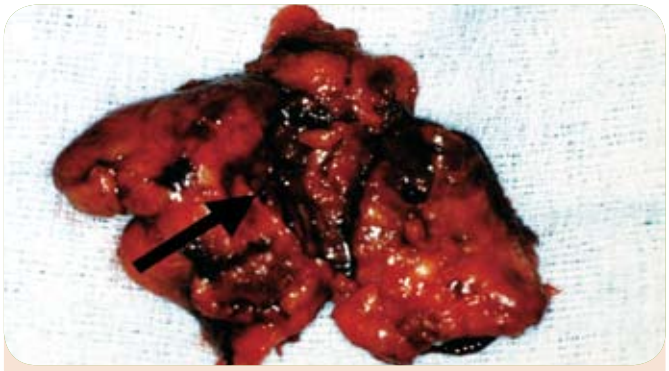

Figure 6. The excised necrotic neck tissues including submandibular gland for case 3 submitted for histology examination.

Case 4

A-45-year-old female patient was referred from a local health center with a 6-days history of a painful upper lip swelling. This had been treated by her dentist by oral metronidazole and ibuprofen but the symptoms continued (Figure 7). The patient was febrile, toxic and

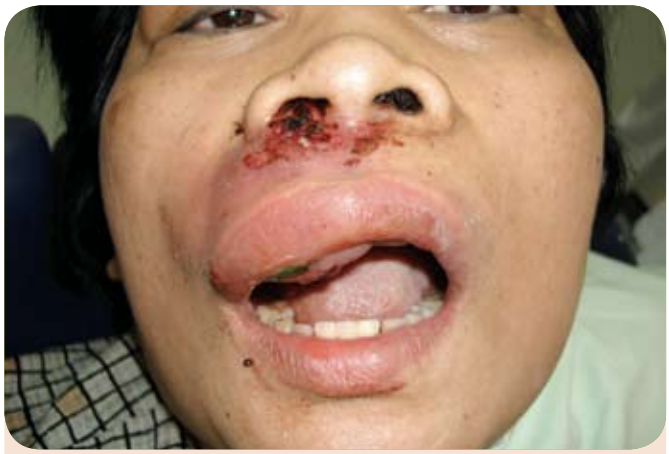

Figure 7. Case 4 Step by step management of NF with large defect reconstruction using nasolabial musculocutaneous pedicled flap.

tachycardic. She gave a history of Non-Insulin Dependent Diabetes Mellitus (NIDDM) and hypertension. Clinical examination revealed a firm and painful swelling on the right side of the upper lip creating double-lip appearance. The skin appeared to be stretched, covered with multiple bullae and necrotic. There was a breach in the skin communicating the right side of the nose with the mouth. Intraoral examination showed crowned upper central incisors which were non-tender to percussion and the labial vestibule was clear. Intraoral periapical radiograph showed a root canal treated upper central incisors but with a suboptimal seal.

The patient was admitted to the hospital and started on empirical intravenous antibiotics and analgesia. CT scan of the facial bones was obtained which showed extensive necrosis of the muscles of the upper lip and the overlying skin. The infection spreads to the nose and the surrounding structures. Next day, the patient>s condition started to deteriorate with fever and hypotension and difficulties in breathing all suggestive of septic shock.

She was taken to operating room where extensive complete debridement of all the necrotic tissues done until area of fresh bleeding and healthy tissues reached. An attempt was made to decompress all the focal infection in the region and the entire neighboring fascial spaces. Swab for culture and sensitivity was taken as well as tissue samples were submitted for culture. The wound promptly irrigated with hydrogen peroxide and bovidone iodine solution. The wound was covered with gauze soaked in iodine and the patient was shifted to the ICU. The patient>s condition started to improve and haemodynamically was stable.

The patient was shifted to the ward after 2 days and continued on intravenous gentamycin and metronidazole. Later, she was taken to operating room for definitive reconstructive surgery. She had bilateral nasolabial flap for ablating the surgical defect.

The patient was discharged from the hospital one week later and was reviewed in the outpatient clinic. She had a root canal retreatment for the upper central incisors.

Disscussion

Necrotizing fasciitis (NF) is a rare bacterial infection but potentially fatal and life-threatening in nature. This potentially fatal infection affects the superficial subcutaneous fascia and may mimic an abscess or cellulitis1.It is caused by aerobic and anaerobic microorganisms that spread rapidly along fascial planes, causing necrosis of the fascia, overlying skin, muscles and blood vessels. In the initial stages prior to the establishment of the necrosis, the infection usually spreads in the subcutaneous tissues and may appear similar to dental infection, but with the disease progression, the overlying skin becomes more dusky and stretched. The underlying destruction of the subcutaneous tissues provides an ideal culture medium for the bacterial growth. Later, the skin becomes gangrenous and necrotic.

This infection necessitates rapid diagnosis, early and aggressive surgical debridement and appropriate antibiotic therapy[1,4,5]. NF most frequently affects the abdominal wall, perineum and lower extremities following surgical interventions or any traumatic injuries but in a favorable host [6,7]. The term "hospital gangrene" was first used by Joseph Jones in 1871 while Pfanner in 1918 used the term "necrotizing erysipelas" for a similar condition caused by hemolytic streptococcus[8]. Wilson in 1952 was the first to use the term "necrotizing fasciitis" to embrace widespread necrosis of the superficial fascia which later has gained wide acceptance[10].

Cervicofacial necrotizing fasciitis (CNF), however, considered polymicrobial infection often involving group A ß-Haemolytic streptococcus acting in synergy with obligate anaerobic organisms[11]. Most of the cases originating in the head and neck were the result of complications of dental and pharyngeal sepsis with rapid progression to the adjoining sites including the chest wall and mediastinum[1,2,7,8,10]. It is usually caused by group A β Haemolytic streptococci, Staphylococcus aureus and anaerobes. However, improved culture techniques have isolated a broader spectrum of microbes including obligate anaerobes.The aggressive behavior of CNF is linked to the synergy of the mixture of aerobes and anaerobes. The hallmark of the disease is fast progress of the infection along fascial planes and necrosis of the fascia and subcutaneous tissues including the skin and muscles[12,13,14]. The routes of introducing these organisms are iatrogenic, burns, trauma, tonsillar or pharyngeal abscess and dental infection[3,4,15]. In the four cases we are reporting, three cases appeared to be caused by dental infection, while only one case appeared to be a complication of pharyngeal infection. CNF is most commonly affecting immunocompromised hosts including small vessel disease such as diabetes mellitus[12,13]. Diabetes mellitus was present in three cases but also poor oral hygiene with neglected mouth was apparent as predisposing factors in the development of this complication. Patients with diabetes mellitus usually have worse prognosis than the otherwise healthy ones. Tung-Yiu et al reported 11 cases of CNF of Odontogenic origin with 7 patients having immunocompromised host including diabetes mellitus[13,16,17,18]. On the other hand, Balcerak et al reviewed 25 cases of NF of the head and neck region and found 10 patients had diabetes mellitus, 2 had atherosclerosis and 1 patient had myxoedema1.

Moreover, Obiechina et al have reported 8 cases of CNF of dental origin but found none of them had any associated medical condition15. Therefore, they suggested that the underlying medical condition may not have a direct influence in the etiology of CNF of Odontogenic origin. They have isolated normal oral commensals of the oral mucosa from these patients.

In our series however, it was clearly evident that the superficial cervical fascia and the subcutaneous tissues were found necrotic in all the cases, but the skin was involved only in one case and partially

necrosed in another. Deep cervical fascia and muscles necrosis was found in all the cases but the submandibular gland was necrotic in two cases only. Neurovascular bundles in the neck involving the facial vessels and nerves were necrotic in two cases. In one case, there was an extension of the necrosis to the chest and breast. Grayish or brownish fluid material could be seen spreading along fascial with foul odor. In addition, yellowish pus accumulation was found in all but one case. Our strategy mandates excision of the non-viable tissues until healthy tissues are reached as evident by bleeding edges. However, all efforts were made to avoid radical debridement and conservation of healthy tissues and normal viable structures.

The importance of early recognition of this life-threatening disease is crucial in the initiation of successful treatment. However, this may not always be possible due to the close resemblance to an acute abscess or celluitis[11,16,17]. There are several clinical features which might be indicative of CNF including: the affected skin may turn dusky or purplish in color with irregularities at its border, skin and subcutaneous tissue hyperemia, subcutaneous crepitation caused by the accumulation of gas in the tissues and the rapid progression of the dental infection to the neck and chest wall. Gas accumulation in the cervical tissues which is the main reason for enhancing the spread and necrosis of the skin and subcutaneous tissues is believed to be caused by the production of tissue destructive enzymes and host-defensive suppressive endotoxins by the anaerobes[1,2,14].

The severity and rapid progression of this form of infection mandates an aggressive form of surgical drainage and debridement of the necrotic tissues as a sole line of treatment. This should be coupled with coverage with broad spectrum antimicrobial drug therapy. In order to minimize the vast consequences and the morbidity as well as mortality of this infection, it should be started immediately. However, it is imperative to determine the appropriate antibiotic therapy and the modification of the regimen by culture and sensitivity tests.

In our series, all patients have received high dose of parenteral metronidazole, cefuroxime, co-amoxiclav. Two cases have received gentamycin coupled with amoxicillin/clavulanate potassium. Some modifications were necessary following the results of the culture and sensitivity tests. In all patients, local application of tetracycline antibiotic powder was contemplated following appropriate debridement and irrigation with hydrogen peroxide and bovidone iodine[7,10,15,17]. It is postulated that this is very likely will increase the alkalinity of the infection site and leads to fibrosis and elimination of dead space7. But it should always bear in our mind that the keystone for the success of the treatment is surgical excision of the necrotic fascia alongside with adjacent soft tissues coupled with proper antibiotic therapy. This prevents the establishment of septicemia and further auscultation of the disease process.

The mortality rate for CNF even with appropriate therapy remains high ranging from 20% to 80%[1,2,3,16,17]. Several factors play a vital role including the associated medical illnesses, improper or late medical and surgical intervention, and distant extension of the infection i.e. mediastinum or thoracic.

The outcome of treating CNF can be improved significantly by the addition of hyperbaric oxygen therapy and intravenous immunoglobulin G19. The mechanism of action of both is not clearly known but it has been suggested that hyperbaric oxygen therapy can improve the oxygenation and perfusion of the adjacent viable tissues and limit the spread of the infection. The use of intravenous immunoglobulin G, on the other hand, can neutralize the antigens and limit the production of tissue necrosis factors[vz].

Conclusion

Early recognition and aggressive surgical maneuvers are highly recommended in the management of cervicofacial necrotizing fasciitis to ensure reduction of the associated morbidity and mortality rates. However, antimicrobial therapy remains an adjunctive therapy in order to control the underlying infection. Further improvement can be gained by addition of hyperbaric oxygen therapy and intravenous immunoglobulin G.

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A 24 Year Old Pregnant Lady With Skin Rash over her Body

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Clinical History

A 24 year old lady who was pregnant at 5 months, presented with one month history of painful and itchy rash all over her body. On examination, there were generalized erythematous plagues with blistering on the surface involving chest, abdomen and upper and lower extremities. Excoriation marks and crusted papules were also found (Figure 1 & 2). The laboratory examination for CBC, liver function test, thyroid function test, urea and electrolytes were all within normal limits. The patient underwent skin biopsy which shown is in the (figure 3). Direct immunofluorescence showed a linear deposition of C3 along the basement membrane zone. The patient delivered a normal baby girl.

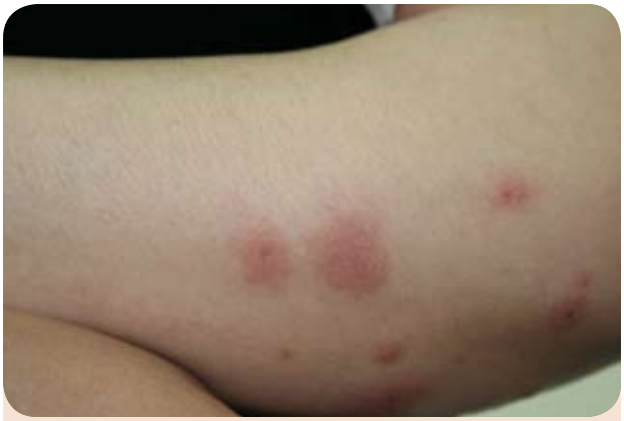

Figure 1: shows the pattern of skin rash on the extensor surface of the left forearm.

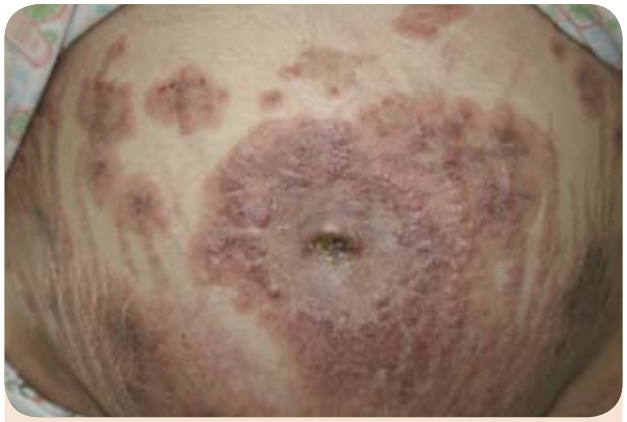

Figure 2: note the presence of erythematous plagues on the abdominal area.

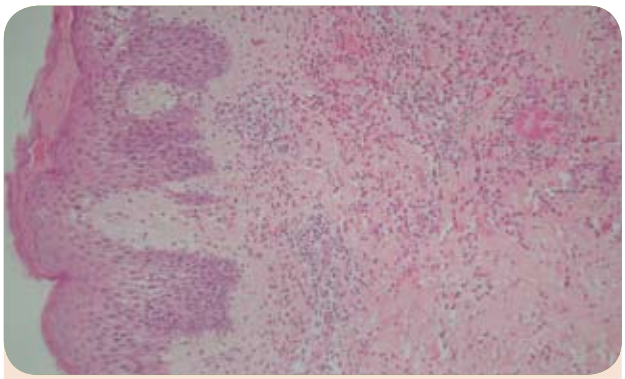

Figure 3: skin biopsy showing spongiosis of the epidermis and edema of papillary dermis. Note the presence of mixed inflammatory cells including eosinophils, lymphocytes and histiocytes in the dermis

Questions

1. What is your diagnosis? What is the differential diagnosis?
2. What is the etiology and pathogenesis of this condition?
3. What is management of this disorder?

Answer

1 This is a case of pemphigoid gestationis (herpes gestationis). Pemphigoid gestationis (PG) is a rare, autoimmune polymorphic, blistering skin disease which occurs in pregnancy and the post partum period. It has an estimated prevalence of 1 case in 50,000 pregnancies. PG usually presents as extremely pruritic papulovesicular eruption on the abdomen but may involve other area, including the palms, soles, chest, back and face. Mucosal lesions occur in less than 20% of the cases. Lesions vary from erythematous, edematous papule to large tense bullae with many intermediate forms, including small vesicles, papules and urticaria like plaques with and without grouped vesicles, bullae, erosion and crusts.

PG usually develops at the second and third trimesters, but the skin rash may appear at any time during pregnancy and immediate post-

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partum period. Although the disease is self-limited, it may or may not recur in subsequent pregnancies. PG may be exacerbated by use of estrogen or progesterone containing medication. Intrauterine fetal death, premature deliveries and small for gestational age are among the complications of this condition. The lesions almost always resolved spontaneously during the first several weeks. The differential diagnoses include the following disorders:

- Pruritic urticarial papules of pregnancy (PUPPP): eruptions begin in the abdomen, as papules and plagues in late pregnancy and are severely pruritic.
- Erythema multiformis: Immunoglobulin and complement may be seen in the superficial blood vessels.
- Dermatitis herpetiformis: IgA deposition along basement membrane.
- Others like bullous pemphigoid, cicatricial pemphigoid, linear IgA dermatosis, acute urticaria, papular dermatitis of pregnancy, pruritic folliculitis of pregnancy and drug-induced bullous disorders.

Skin biopsy is required to confirm the diagnosis of PG. The classical microscopic picture is shown in the figure 3. However, direct immunofluorescence usually supports the diagnosis of PG, which shows deposition of C3 and, sometimes, IgG in a linear pattern along the basement membrane zone.

2. PG is a pregnancy associated autoimmune disease. However, hormonal and immunological factors may play an important role in the pathogenesis of this disease. PG has been reported in association with other autoimmune diseases and occurs in patients with the HLA antigens DR3-DR4. Aberrant expression of the class II molecules of the major histocompatibility complex in the placenta is the major initiating process in PG. Circulating IgG antibodies are initiated in response to antigen stimulus amnion which crossreacts with an antigen in the basement membrane of the skin. Antibodies against 2 hemidesmosomal proteins are found. The antigen mostly found is glycoprotein of 180 kd which is identical to the bullous pemphigoid antigen (BP180) and less frequently is BP230.

The examination of peribullous and urticarial lesions of normal appearing skin in PG demonstrated heavy, homogenous linear deposit of C3 along the basement membrane with IgG despotion in 80% of patients. The heavy deposition of C3 at basement membrane is the diagnostic hall mark in patients with PG. The C3 deposition has been noted in clinically normal as well as affected infants> skin.

3. The aim of the treatment is to suppress blister formation and to relieve the intense pruritis. Patients with mild disease can be treated with antihistamines and tropical or intralesional steroids. In sever cases systemic steroids can be used. Prednisone is given 20-40 mg per day. Exacerbation of pruritis and blistering occur at parturition may require increase in prednisolone. The prednisone is tapered gradually during the post-partum period. Few patients don>t require oral prednisone and can be managed with antihistamine, topical steroids or emollient.

Some individuals after parturition require azathioprine, dapsone, methotexate, plamapheresis and others in addition to prednisone to control their disease. Infant born of affected mother who received high doses of prednisone should be examined by neonatologist for evidence of adrenal insufficiency. The cutaneous lesions noted in such infant are transient nature requiring no therapy.

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Conference News

Alsalama Hospital 1st International Congress MEDICAL CHALLENGES BEYOND THE MILLENEUM

5 to 6 February 2009
Abu Dhabi, United Arab Emirates
Website: http://www.alsalama-congress.com
Organized by: Alsalama Hospital

Chronic heart failure and hypertension: risks, diagnosis and management

12 to 13 February 2009
London, United Kingdom
Website: http://www.mahealthcareevents.co.uk
Organized by: MA Healthcare Ltd

International Conference Trauma Management, Critical Care and Prevention

16 to 17 February 2009
Al Ain, Abu Dhabi, United Arab Emirates
Website: http://www.traumaconf.uaeu.ac.ae
Organized by: FMHS, UAE University

Clinical Outcomes and the Quality of Nursing Care

4 March 2009
London, United Kingdom
Website: http://www.healthcare-events.co.uk
Organized by: Healthcare Events

32 Ain Shams International Medical Congress

19 to 22 March 2009
Cairo, Egypt
Website: http://www.ainshams32.org
Organized by: Faculty of Medicine, Ain Shams University

Joint Oncology Symposium

26 to 27 March 2009
ISTANBUL, Turkey
Website: http://www.jointoncology2009.org
Organized by: YEDITEPE UNIVERSITY AND MD ANDERSON CANCER CENTER

Ethical Issues and Cancer. From the Bench to the Bedside

20 to 21 March 2009
Milan, MI, Italy
Website: http://www.semm.it/meeting/ethical
Organized by: SEMM Foundation (European School of Molecular Medicine)

Family Medicine: Focus on Dermatology

10 to 20 April 2009
Sail from Ft. Lauderdale, Spain
Website: http://www.continuingeducation.net
Organized by: Continuing Education, Inc.

Internal Medicine: Urology

25 April 2009 to 2 May 2009
Sail from Venice, Italy
Website: http://www.continuingeducation.net
Organized by: Continuing Education, Inc.

Fourth Regional Conference on Medical Journals in the Eastern Mediterranean Region

5–7 November 2008 - Manama, Bahrain

Introduction

The conference was organized by the Journal of the Bahrain Medical Society and the WHO Regional Office for the Eastern Mediterranean, in collaboration with the Ministry of Health, Bahrain, and the Eastern Mediterranean Association of Medical Editors (EMAME) under the patronage of H.E. Dr Faisal Bin Yaqoub Al-Hamer, Minister of Health, Kingdom of Bahrain.

The conference was preceded by pre-conference workshops on medical writing and medical statistics. The conference comprised keynote presentations, parallel sessions and parallel workshops. It was attended by around 200 participants.

Conference and workshop sessions

The conference sessions were held in parallel and comprised the following topics: editorship, medical research publication, peer review, publication ethics, open access, indexing, e-journalism and statistics. More than 50 oral presentations and one poster were presented. Keynote speeches were given on "The craft of editing", "Reaching out to mainstream science" and "Plagiarism and copyright. Parallel workshops were held on two afternoons focusing on publishing a journal in a small community and strategies to increase quality and visibility, publication ethics, Cochrane Library, the principles of evidence-based medicine and the 'hierarchy of evidence' and how to search the library, peer review, statistics for medical editors and a workshop on electronic publishing and open access.

Conference recommendations

1. Participants, in particular EMAME members, to develop a list of individual action points based on what they have learned in the conference to implement in regard to their journals.
2. EMAME members to plan local, national and sub-regional activities together for networking, information sharing and educating editors of medical journals in the Region.
3. WHO to continue to support networking and information sharing activities between editors in the Region.

The second EMAME General Assembly

The second EMAME General Assembly was held in Bahrain. The General Assembly was attended by 45 EMAME members. Ahmed Jamal, EMAME interim president welcomed the Assembly.

The list of new Executive Council members was announced by Ahmed Jamal and endorsed by the General Assembly.

President: **Ahmed Jamal** (Bahrain)

Post-President: **Basim Yaqub** (Saudi Arabia)

President-Elect: **Maqbool Jafary** (Pakistan)

Vice-Presidents: **Farrokh Habibzadeh** (Islamic Republic of Iran)

Fatema Jawad (Pakistan)

Hassan Bella (Sudan)

Secretary-General/ Treasurer: **Farhad Handjani** (Islamic Republic of Iran)

Vice-Presidents-at-large:

Region 1: **Diaa Rizk** (Egypt)

Region 2: **Yusef Abdulrazzaq** (United Arab Emirates)

Region 3: **Mohammad Tarwaneh** (Jordan)

Region 4: **Mohammad Baher Rokni** (Islamic Republic of Iran)

It was confirmed that the next EMAME conference would be held in Karachi, Pakistan in 2010

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محتويات العدد

Vol. 21, No: 1 January –March 2009

مجلة جمعية الأطبـاء البحرينيـة

مجلة جمعية الأطباء البحرينية هي المجلة الرسمية لجمعية الأطباء البحرينية.تصدر كل ثلاثة أشهر وهي من مسئولية رئيس جمعية الأطباء البحرينية.

تقوم مجلة جمعية الأطباء البحرينية بنشر المقالات الطبية والصحية الشاملة لجميع فروع الطب والمهن الطبية. الآراء التي ترد بالمقالات المنشورة تعبر عن رأي أصحابها فقط ولا تعبر عن رأي الجمعية.

ترسل جميع المراسلات على العنوان الآتي:
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مجلة جمعية الأطباء البحرينية
مملكة البحرين
ص.ب ٢٦١٣٦ – المنامة
هاتف: ١٧٨٢٧٨١٨-٩٧٣ (٤-٩ مساء)
هاتف: ١٧٧٢٧٨١٨-٩٧٣
فاكس: ١٧٨٢٧٨١٤-٩٧٣
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Ministry of Health
Kingdom of Bahrain

Bahrain Medical Society

The Education Centre at Bahrain Medical Society
in collaboration with the Education Departments of the Ministry of Health Announces:

BASIC RESEARCH METHODOLOGY
FOR DOCTORS AND HEALTH PROFESSIONALS

16 - 17 June 2009
8am - 2pm

Venue:
Arabian Gulf University, Manama.

Registration fees BD30
(includes coffee breaks, workshop documents & certificate of attendance)
Registration form overleaf

Topics:

- Introduction to medical research
- Basic elements of research
- Various methods of research
- Ethical principles in medical research
- Use of scientific resources e.g medline etc
- Introduction to Cochrane library
- How to read /write a scientific paper
- Introduction to medical statistics used in research
- Principles of referencing

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