Association between angiographic evidence of coronary artery disease and seropositivity for *Helicobacter pylori* and *Chlamydia pneumoniae* infection

Mohammad B. Sharif Kazemi, MD, Vahid Emad Marvasti, MD, Ehsan Hoseini, MD, Reza Mohammadian, MD, Sharareh Roshanzamir, MD, Sara Ekramzadeh, MD, Vafa Rezayee, MD, Mohammad M. Samim, MD.

In 1970, experimental infection of gram-free chickens with an avian herpes virus was found to produce arterial disease that resembled human atherosclerosis. From that time several studies were done on *Helicobacter pylori* (*H. pylori*), *Chlamydia pneumoniae* (*Ch. Pneumoniae*), cytomegalovirus and periodontal infections, which had different results. In 1994, Mendall et al.² reported for the first time an association between *H. pylori* infection and coronary artery disease (CAD). After that, several studies were performed which confirmed Mendall's theory³ while some rejected the theory.⁴ Several studies have provided evidence for a causal relationship between *H. pylori* and CAD. It has been hypothesized that *H. pylori*-associated chronic inflammation of the gastric mucosa leads to elevated plasma levels of fibrinogen, C-reactive protein and leukocytes. Other hypotheses include gastritis induced vitamin B-12 deficiency, leading to hyperhomocysteinemia. The suggested mechanism for *Ch. pneumoniae* is the direct effect of this microorganism on the intima of vessels.⁵ Despite many studies, which have been performed to prove the association between the causative role of *H. pylori* and *Ch. pneumoniae* in atherosclerosis, there are still many controversies which remain. Two problems are observed in many of the studies, which has been carried out up to now. Firstly, only half of the studies, CAD was proved by angiography while in the other half, CAD was diagnosed by other means such as history, electrocardiogram or other non-reliable diagnostic tests. The other problem was the lack of homogeneity in the population selected for the studies. Socioeconomic level is one of the important factors that is related to both CAD risk factors and the incidence of *H. pylori* and *Ch. pneumoniae* infection and this factor was not foreseen in many of the studies.

In this study, we investigated the seroprevalence of *H. pylori* and *Ch. pneumoniae* infection in patients with proved CAD and in normal population. The population selected for the study were 207 males and females between 20-80 years old (mean age of 56 years old) who were referred to the angiography division of Namazi Hospital and Saadi Hospital (2 major hospitals) in Shiraz, Southern Iran. These patients were divided into 66 normal patients and 141 patients with CAD according to angiography results. Patients with CAD were defined as having one, 2 or 3 vessels disease, according to the number of arteries affected. Letter of consent was filled by the patients for blood sampling and all were interviewed by means of a structured questionnaire including age, educational status, family history of myocardial infarction, history of cigarette smoking, history of alcohol consumption, history of hypertension, history of hyperlipidemia, history of diabetes, history of gastrointestinal symptoms and history of drugs. From the patients, 10 cc of non-fasting blood sample were drawn from each patient and centrifuged. Sera were stored in -70°C. After collection of the samples, the frozen sera of the patients and controls were simultaneously investigated for *H. pylori* specific immunoglobulin G (IgG) by an enzyme linked immunosorbent assay (ELISA) (Genesis HpG screen ELISA kit). Manufacturer’s recommended cut-off point is 6.25 µg/ml, which in a Caucasian population provides a sensitivity of 91% and a specificity of 100%. *Chlamydia pneumoniae* IgG titer was measured by ELISA (IBL). Manufacturer’s recommended cut-off point is 10 U, which in Caucasian population provides a sensitivity of 96% and a specificity of 97.1%.

Two hundred and seven patients participated in the study including 130 males (62.8%) and 77 females (37.2%). The mean age of the participants was 56 years old (maximum age was 80 years old and minimum age was 20 years old). Out of the 207 patients who participated in this study, 66 patients (31.9%) had normal angiography without evidence of CAD and 141 patients (68.1%) had CAD. Of the 141 patients with CAD, 45 patients (31.9%) had one vessel disease, 37 patients (26.2%) had 2 vessels disease, 53 patients (37.6%) had 3 vessels disease and 6 patients (4.3%) had 4 vessels disease. Out of the 207 patients who participated in this study, 25 patients (12.1%) were *H. pylori* seronegative and 182 patients (87.9%) were *H. pylori* seropositive. Fifty-eight out of 66 patients (87.9%) with normal angiogram and 124 of 141 patients (87.9%) with abnormal angiogram were *H. pylori* seropositive (odds ratio (OR) of 1.006, 95% confidence interval (CI) of 0.411 - 2.465, p value with fisher’s exact test = 1]. Comparing the extent of CAD with *H. pylori* seropositivity showed that, 42 of 45 patients (93.3%) with one vessel disease, 33 of 37 patients (89.2%) with 2 vessels disease, 44 of 53 patients (83.0%) with 3 vessels disease and 5 of 6 patients (83.3%) with 4 vessels disease had *H. pylori* seropositivity.
(83.3%) with 4 vessels disease were *H. pylori* seropositive. ($\chi^2 = 2.616$, df = 4, $p = 0.624$). There was no association between *H. pylori* infection and angiographic evidence of CAD. Out of the 207 patients who participated in this study, 166 patients (80.2%) were *Ch. pneumoniae* seronegative and 41 patients (19.8%) were *Ch. pneumoniae* seropositive. Fourteen of 66 patients (21.2%) with normal angiogram and 27 of 141 patients (19.1%) with abnormal angiogram were *Ch. pneumoniae* seropositive ($p$ value with Fisher’s exact test = 0.713, $\chi^2 = 0.120$ df = 1, chi-square $p = 0.729$). Comparing the extent of CAD with *Ch. pneumoniae* showed that 5 of 45 patients (11.1%) with one vessel disease, 15 of 37 patients (40.5%) with 2 vessels disease, 6 of 53 patients (11.3%) with 3 vessels disease and 1 of 6 patients (16.7%) with 4 vessels disease were *Ch. pneumoniae* seropositive. ($\chi^2 = 14.678$, df = 4, $p = 0.005$). There was no association between *Ch. pneumoniae* infection and angiographic evidence of CAD. In contrast to other studies we have not demonstrated an association between *H. pylori* and *Ch. pneumoniae* seropositivity and angiographic evidence of CAD.

Mendall et al° in a general practice-based case control study demonstrated an OR of 2.28 (95% CI =1.25 - 4.15). In contrast, one meta-analysis of 18 studies involving more than 10000 people ,which was performed by Danesh and Peto,° showed no significant evidence of correlation between *H. pylori* infection and CAD. In addition, atherosclerosis risk in communities, who studied 15792 patients between 45-64 year-old ,after adjustment for age, gender and race demonstrated adjusted hazard ratio of 0.97 (95% CI =0.52 - 1.78), which did not show any correlation between this infection and CAD.

This present study has 2 important advantages to other studies; one is the sufficient homogeneity of the social status of the patients. Most of the patients who participated in this study were from a low socioeconomic class with similar hygiene level. Their daily diets were also very similar. Another point in this study is that atherosclerosis was proven in the case group and rejected in the control group by angiography, which is a sensitive and specific technique in diagnosing CAD. There is no significant association between CAD and *H. pylori* and *Ch. pneumoniae* infection.

Received 28th July 2004. Accepted for publication in final form 11th November 2004.

From the Department of Internal Medicine, Shiraz University of Medical Sciences, Fars, Iran. Address correspondence and reprint requests to Dr. Mohammad B. Sharifkazemi, Cardiologist, Department of Internal Medicine, Namazee Hospital, Namazee Square, Shiraz, Iran. Tel/Fax: +987 (11) 6261089. E-mail: msharifkazemi@hotmail.com

References


Screening for glucose-6-phoshate dehydrogenase deficiency in Behçet’s disease

Rafid A. Najim, PhD, DDV, Khalifa E. Sharquie, MBChB, PhD, Mahmood H. Al-Janabi, MBChB, MSc.

Glucose-6-phosphate dehydrogenase deficiency occurs with high frequency in the Middle East.° Iraq lies at the center of the Middle East and is well known to have relatively a high frequency of G6PD deficiency. Previous reports from Iraq have estimated the frequency of G6PD deficiency to be 8.9% or 12.4%.° However a more recent report using the methemoglobin reduction test has put the frequency at 6.3%.°

Another disease, which occurs in the Middle East and particularly in Iraq, is Behçet’s disease.° Behçet’s disease has a well-known association with certain genetic characteristics. Thus, the association between human leukocyte antigen (HLA) B51 and Behçet’s disease is well known.° More recently an association with genetically controlled slow acetylator status was reported and this was found to be related to the disease severity and HLA B51.° Thus in this report we try to answer the question if there is any association between G6PD deficiency and Behçet’s disease.

Forty-one Behçet’s disease patients, 25 males and 16 females, with ages ranging from 19-46 years, were recruited in the study. Patients were registered...
at Behçet’s disease Clinic at Medical City Teaching Hospital, Baghdad, Iraq. All Behçet’s disease patients fulfilled the International Study Group Criteria (ISGC) for the diagnosis of Behçet’s disease. Their informed consent was obtained. The ethical committee approved the study. Thirty-seven healthy individuals, 19 males and 18 females, with ages ranging from 25-38 years, participated in the study. None of the participants had a history of serious illness and the findings of the physical examinations were normal. Written informed consent was obtained from all patients. Two ml of blood were withdrawn and put in a tube containing 0.3 ml of acid citrate dextrose from each subject or Behçet’s disease patient. The methemoglobin reduction test was used to screen for G6PD deficiency. Screening for G6PD deficiency in both Behçet’s disease patients and normal control subjects using methemoglobin reduction test did not detect any case of G6PD deficiency. Therefore, we can conclude that there is no association between Behçet’s disease and the genetic abnormality, which leads to G6PD deficiency. It may be argued that the sample of Behçet’s disease patients is small. But we have to take into consideration that this number represents an adequate number for this uncommon disorder. In addition, the same number of patients was used to determine the 2 other genetically controlled traits, which are the frequency of HLA B51 and acetylation. Results of that parallel study showed that the frequency of patients with positive HLA B51 was 68.2%. Another genetically controlled trait studied in the same population was acetylation. It is well established that acetylation demonstrates genetic polymorphism; slow acetylators being homozygous for an autosomal recessive gene. Results of the previous study showed that all Behçet’s disease patients were slow acetylators. In addition there was an association between the frequency of slow acetylators, positive HLA B51, and severity of Behçet’s disease. Therefore, the fact that this study failed to show an association between Behçet’s disease and G6PD deficiency is significant. The frequency of G6PD deficiency in a large sample reported in a recent study using the methemoglobin reduction test was 6.3%. The present report does not rule out that the frequency of G6PD deficiency in Behçet’s disease is similar to that reported in the general population.

Dapsone is a drug well known to cause hemolysis in G6PD deficient patients. Dapsone has been used successfully in our department for the last 20 years in treatment of Behçet’s disease with no incidence of major reported hemolysis. This observation has been subsequently confirmed in a double blind controlled study. The fact that Behçet’s disease has no association with G6PD deficiency, it helps to explain why dapsone has been used safely.

Received 31st July 2004. Accepted for publication in final form 30th November 2004.

From the Department of Pharmacology (Najim, Al-Janabi) and the Department of Dermatology (Sharquie), College of Medicine, University of Baghdad, Baghdad, Iraq. Address correspondence and reprint requests to: Prof. Rafid A. Najim, Chairman, Department of Pharmacology, College of Medicine, University of Baghdad, PO Box 61208, Baghdad 12114, Baghdad, Iraq. E-mail: rafidnajim@yahoo.com

References


Abruptio placentae following snake bite in a Sudanese woman

Ishag Adam, MD, Abdul-Salam Gerais, MD, FRCOG.

The fact that venomous snake bites during pregnancy result in a high fetal wastage and may cause maternal mortality makes this an important, albeit uncommonly encountered, entity in obstetrics. Thus, it is essential that all emergency physicians become familiar with the recognition and treatment of venomous snake bites.

A 29-year-old Sudanese woman, gravida 4 para 3, full term with normal spontaneous vaginal deliveries at home were presented to the New Halfa Teaching Hospital, Sudan with snake bite in her right leg for 8 hours. She was in her 32 weeks gestation. The patient’s pulse rate was 90 beats/minute, the blood pressure was 110/70 mm Hg and her temperature was 37.2°C. No complain of abdominal pain; vaginal bleeding or hematuria and urine examination was free of microscopic hematuria. The patient’s renal function’s tests were within normal values. Ultrasound confirmed the gestational age and the fetal activity. The patient...
was admitted to the hospital where she received polyclonal antivenom serum by intravenous infusion and whole blood clotting time (5 minutes and 20 seconds) was carried out initially and repeated daily until she was discharged form the hospital. Sixteen hours later, she developed severe abdominal pain and profuse vaginal bleeding and her cervix was found opened 4 cm and the membranes were bulging. The diagnosis of abruptio placentae was suspected and confirmed by ultrasound and the cessation of fetal heart pulsation was confirmed. The patient was managed accordingly (morphine, fresh blood, artificial rupture of the membranes and oxytocin infusion). Six hours later she delivered vaginally, there was no postpartum bleeding and her clotting time was 5 minutes and 35 seconds and renal functions tests were within normal values. The patient was kept in the hospital for 5 days and discharged on folic acid tablets, 0.5 mg daily for 6 months.

Abruptio placentae with an evidence of fibrin deposition and microthrombus formation in the spongy layer which lead to placental cleavage and separation following snake bite was reported before. The venom of the snake contains a procoagulant that defibrinates the blood and leads to bleeding throughout the body and this might cause the placental separation. There are several mechanisms, which lead to fetal wastage following snake bite during pregnancy; they include direct effect of the venom on the fetus, fetal hypoxia due to maternal hypotension, venom induced uterine contraction, pyrexia and cytokine released following tissue damage.

The patient received polyclonal antivenom serum by intravenous infusion, which is the mainstay of treatment for poisonous bites to neutralize the effects of the venom. Techniques such as the use of tourniquets, incision and suction should no longer be practiced. The use of antivenom serum during pregnancy should balance its risk benefit and it may be life saving. However, anaphylaxis that may follow its administration as well as its treatment with adrenaline may jeopardize the placental circulation.

References

Prevalence of smoking and frequency of visits to primary health care clinics
Dhafer A. Al-Qahtani, ABFM, SBFM, Osman M. Abdalla, MBBS, Mohammed L. Imtiaz, MBBS.

The prevalence of cigarette smoking is declining in some of the western countries. In the United States, it decreased from 42.4% in 1965 to 25% in 1993 and 23.3% in year 2000 due to awareness of the harm caused by cigarette smoking. In Saudi Arabia, different studies have shown a prevalence varying between 20-47%. Smoking has become a major health problem in Saudi Arabia, contributing to national morbidity and mortality. In contrast to the situation in the western countries, the trend is towards an increase in prevalence of this habit over the past decade. The aim of the present study is to assess the prevalence of smoking among the adult male soldiers residing in King Khalid Military City (KKMC) situated near Hafr Al-Batin, Saudi Arabia.

Nine primary care clinics are attached to the Northern Area Armed Forces Hospital at KKMC. The present study included subjects from 4 of these clinics catering to the military personnel. A total of 25,000 soldiers who have their medical files in these clinics constituted our target population. Even if the patient is seen in other clinics or at the emergency room, the follow-up sheet is transferred to his permanent file at his clinic. Hence, the file of each subject reflects the total number of visits paid by him to the primary care clinics. A random sample of 1411 was drawn using computerized randomization. The number of cases chosen was according to the statistical table for sampling numbers with 5% level of significance. Medical record (MR) numbers were obtained for all the subjects included in the sample. Telephone numbers of these subjects were retrieved from the medical records. Subsequently, the subjects were contacted over the phone and their answers were filled into a pre-structured
Table 1 - Prevalence of smoking and frequency of visits to the primary care clinics.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Respondents n (%)</th>
<th>N of visits to primary care clinics</th>
<th>N of clinic visits annually per person</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2001</td>
<td>2002</td>
</tr>
<tr>
<td>Smokers</td>
<td>368 (30.5)</td>
<td>780</td>
<td>704</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>840 (69.5)</td>
<td>1640</td>
<td>1978</td>
</tr>
<tr>
<td>Total</td>
<td>1208</td>
<td>2420</td>
<td>2682</td>
</tr>
</tbody>
</table>

Prevalence of smoking in KKMC

The questionnaire consisted of 8 simple questions including age, smoking status, number of cigarettes smoked per day, duration of smoking, and so forth. The questionnaire was answered by a total of 1208 subjects with a response rate of 85.6%. Subsequently, we scanned the files of the subjects to estimate the number of visits paid by them to the primary care clinics during the period from 1st January 2001 to 31st December 2002. The frequency of visits per person per year was obtained from these figures. The number of current smokers was found to be 368 out of a total of 1208 respondents with a prevalence of 30.5% (Table 1). Approximately half the smokers (46.7%) smoke between 10-20 cigarettes/day. Of the remaining, 18.5% smoke more than 20 cigarettes per day, and 34.8% smoke less than 10 cigarettes per day. The number of visits paid to primary care clinics by non-smokers was found to be 1640 visits for 2001, and 1978 visits during 2002 with a total of 3618 visits for 2 years and a mean of 2.15 visits per person per year. For smokers, the number of visits was found to be 780 and 704 for 2001 and 2002, with a total of 1484 for the 2 years and a mean of 2.02 visits per person per year. The difference between the visits paid by the smokers and non-smokers to their clinics is statistically not significant at 95% confidence interval (4.08, 3.868) with a p value of 0.953. The mean age for smokers was found to be 35 years and for non-smokers 36 years. The difference is not statistically significant (p value 0.308). The number of smokers who have smoked for less than 10 years was 122 (33.15%). The number who smoke between 10-20 cigarettes per day was 194 (52.7%) whereas 52 smokers were found to smoke more than 20 cigarettes per day.

This is the first study of its type performed at KKMC for estimation of the prevalence of smoking in the male population, and its correlation with general morbidity using the frequency of visits to primary care clinics as an index of morbidity. The prevalence of smoking among Saudi male soldiers has been estimated by this study to be 30.5%. This exceeds the prevalence of smoking in some developed countries such as the USA where the prevalence was estimated at 23.3% in 2000. The prevalence estimated in this study correlates well with some other studies performed elsewhere in the Kingdom. Al-Shahri et al found a prevalence of 34.4% for current smokers. Al-Damegh et al found a prevalence of smoking of 29.8% among male secondary school students in Al-Qassim. Hasim found a prevalence of 29% current smokers among the students of College of Applied Medical Sciences in Riyadh. However, Jarallah et al, who studied the prevalence of cigarette smoking among Saudi nationals in 3 regions of Saudi Arabia using a pre-structured questionnaire and interviews by primary care physicians, found a prevalence of 21.1% current smokers among males. They found that the rate for certain groups, including army officers, was significantly higher. Similarly, Al-Shahri et al found a prevalence of 17% among the primary care physicians in Riyadh. However, this rate cannot be applied to the general population in this country since the subjects of this study were highly educated and Saudis constituted <5% of the participants.

No significant difference was found between the number of visits made by smokers and non-smokers to their primary care clinics. Non-smokers may be more conscious of health issues and may pay more frequent visits to the primary care clinics for minor complaints.

Ex-smokers were not included in the study as it was thought that this would inflate the prevalence rate. While counting the number of visits made by the subjects to their primary care clinics, the diagnosis and the "reason for encounter" or "problem" were not considered. The visits paid by the subjects to the hospital specialty clinics were not included in the study. Subjects with chronic conditions such as hypertension and diabetes mellitus are likely to have regular follow-up visits at the Consultant clinics. These visits were ignored.

In conclusion, cigarette smoking is an important public health problem in Saudi Arabia. Estimates of prevalence of smoking show that one in every 3 adult male Saudi is addicted to tobacco. This is likely to lead to a heavy burden on the healthcare resources of this country in the future. Efforts must be made to avoid this calamity by means of a multidisciplinary approach that should include public education campaigns, publicity through the
mass media and legislation to make cigarette smoking expensive for the consumer and unprofitable for the manufacturer.

Received 27th October 2004. Accepted for publication in final form 2nd January 2005.

From the Department of Primary Care and Emergency Medicine, Northern Area Armed Forces Hospital, Hafir Al-Batin, Kingdom of Saudi Arabia. Address correspondence and reprint requests to Dr. Dhafer A. Al-Qahtani, Family Medicine Consultant, Chief of Primary Care and Emergency Medicine, Director of Education, Training and Research, Northern Area Armed Forces Hospital, PO Box 10018, Hafir Al-Batin 31991, Kingdom of Saudi Arabia. Tel., +966 (3) 7873422, Fax. +966 (3) 7871382. E-mail: hateemco@hotmail.com

References


Surgical beds in neonatal intensive care unit

Shabi Manzar, MD, FAAP, Arun K. Nair, MD, FRCPCH, Mangalore G. Pai, DCH, MD, SALEH M. AL-KHUSAIBY, FRCPCH, PhD.

Tertiary health centers with centralized neonatal intensive care units (NICU) provide finest care to the sick neonates. However, these units are often full to capacity with reversal of infant-bed ratio. The increased proportion of surgical beds is blamed to be one of the reasons for over-occupancy of the NICU. Although, there is no allocated quota for surgical beds and babies admission is on first come first served bases but it has been observed that surgical infants occupy a major portion of the NICU at any given time. Further that many of these neonates for example: the clinically stable cases of delayed passage of meconium with suspected diagnosis of Hirschsprung’s disease requiring rectal washes, do not even meet the arbitrary admission criteria of intensive care unit. Thus, there arises a need to look and document the real status of bed consumption by the surgical cases in the NICU. For this purpose, we carried out the present study.

Neonatal intensive care units at Royal Hospital in Muscat, Oman has 30 beds providing centralized care to all high-risk neonates admitted from different regions of the country. It is one of the main tertiary care centers of the capital; the only one with the facility of neonatal surgery. Records of all admission and discharges to and from the NICU are kept as medical files, computer database and NICU register. For this study, we utilized the NICU register. Our aim was to look at the number of beds occupied by surgical cases as compared to medical cases. A cross-sectional survey of bed occupancy was carried out for 2 consecutive months from January 2004 to February 2004. Data were collected from the admitting register of the NICU. The surgical cases were short-listed from the total admissions.

The medical cases were then separately counted for bed days. Total admitted days (from date of admission to the day of discharge or death) were counted as occupied bed days. In cases of death on the same day, the stay was counted as one day (one occupied bed day). One day of stay in NICU cost ranges from 10-30 Omani Riyal (approximately 28-79 US dollar or 16-48 Sterling pound). After counting the total surgical and medical admission with the occupied bed days, the proportion was calculated by dividing the surgical bed days and the medical bed days by the total bed days. Results

Table 1 - Bed occupancy in neonatal intensive care units by the Surgical and Medical cases.

<table>
<thead>
<tr>
<th></th>
<th>January 2004</th>
<th>February 2004</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total admissions</td>
<td>52</td>
<td>51</td>
<td>103</td>
</tr>
<tr>
<td>Surgical admissions</td>
<td>9</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Medical admissions</td>
<td>43</td>
<td>45</td>
<td>88</td>
</tr>
<tr>
<td>Total bed days occupied by all cases</td>
<td>763</td>
<td>554</td>
<td>1317</td>
</tr>
<tr>
<td>Total bed days occupied by surgical cases (%)</td>
<td>73 (9.5)</td>
<td>81 (14.6)</td>
<td>154 (11.6)</td>
</tr>
<tr>
<td>Total bed days occupied by medical cases (%)</td>
<td>690 (90.5)</td>
<td>473 (85.4)</td>
<td>1163 (88.4)</td>
</tr>
</tbody>
</table>
Surgical beds in neonatal intensive care unit

were expressed in number and percentages. One hundred and three infants were admitted to the NICU during the study period representing 1317 consecutive patient bed days, 52 cases in January (763 bed days) and 51 (554 bed days) in February. The comparison between the surgical and medical bed occupancy is depicted in Table 1. Total NICU beds occupied by surgical cases during 2 months period were 154 (11.6%) in comparison to 1163 (88.4%) by medical cases. Contrary to the common assumption, we noted that the surgical bed occupancy in our NICU is roughly one tenth of the total admission proving the allegation of ‘no space’ for admission in NICU. It was made clear that medical cases comprised the main bulk of NICU admission and beds. Thus, despite centralization of surgical care to one unit, bed occupancy remained unaffected putting the question of quota and rationing for surgical cases out of context. Neonatal intensive care unit beds are seldom vacant. Suggestion has been made earlier regarding strict admission criteria. Others have advocated the need for increased in the NICU beds. Some have shown that decentralization of NICU care is as effective as centralized care, taking care of bed problems in single tertiary unit. The finding of our study provided answer to all these alternatives. Firstly, it has shown that bed occupancy from surgical cases is not high, proving that the increased need for the NICU beds relates to medical rather than surgical cases. Secondly, it clearly indicated that centralized care for surgical cases is still a valid option and no great benefits could be achieved or expected by deferring surgical transfers and managing them at regional centers (decentralized approach), as the proportion of these cases were noted to be small. In conclusion, we have demonstrated that only small amounts of resources were consumed by the surgical cases admitted to the NICU. Expecting cost savings from further limiting surgical beds is thus not warranted.

Acknowledgment. We would like to thank the Pediatric Surgical team of Royal Hospital, Muscat, Sultanate of Oman for providing their expertise in managing all the surgical cases in the NICU and limiting the hospital stay of these infants.

References


Which local anesthesia should be used in neonatal circumcision in newborns?

Ercan Sivasli, MD.
Tugba Gursoy, MD.
Murat Yurdakok, MD.

Methemoglobinemia results from oxidation of ferrous iron (Fe2+) to ferric iron (Fe3+), and renders the hemoglobin molecule unavailable for oxygen transport, resulting in potentially life-threatening hypoxemia. Under physiological conditions, methemoglobin reduction is accomplished mainly by red cell NADH-cytochrome b5 reductase (NADH-methemoglobin reductase) thus, efficiently that there are insignificant amounts of methemoglobin in the circulating blood. These enzyme pathway is immature in the neonate, therefore this disorder may be triggered by oxidation agents such as topical anesthetics used in minor surgical procedures such as circumcision. The local anesthetic prilocaine is a popular choice for penile blockade in circumcision owing to its short onset time and low incidence of cardiac and central nervous system toxicity. However, prilocaine is the most potent methemoglobin forming local anesthetic.

Circumcision was performed in 15 and 3-day-old neonates in other medical centers using the standard surgical technique. Prilocaine was administered subcutaneously in a dose of 5 mg/kg around the radix of the penis and no complication was observed in both patients. They developed perioral cyanosis one and a half hour and 3 hours after the circumcision respectively and succeeding central cyanosis was seen. The pregnancies and deliveries were unremarkable. The physical examinations revealed no other abnormality. Their cyanosis persisted and transcutaneous oxygen saturations were 89% and 91% with supplemental oxygen. Complete blood cell counts, arterial blood gases and chest x-rays were all normal. Electrophoresis revealed methemoglobin levels of 9.9% and 13%
respectively. Methylene blue was infused intravenously in a dose of 1 mg/kg diluted to 1% in normal saline in both patients. The symptoms resolved completely in an hour and methemoglobin levels returned to normal (2.4% and 1.4%) in 12 hours.

Methemoglobinemia is a condition characterized by increased quantities of hemoglobin in which the iron of heme is oxidized to the ferric (Fe3+) form. This disorder may be triggered by topical anesthetics used in circumcision, especially prilocain.1,3-5 Newborn babies are particularly susceptible as methemoglobinemia is related to high levels of fetal hemoglobin, which is more readily oxidized to the ferric state than is hemoglobin A. Also, the transient deficiency of cytochrome b5 reductase enzyme activity that persists for the first 3–4 months of life favors the development of methemoglobinemia in neonates. Cyanosis is first clinical evident when methemoglobin levels of ≥10%, but symptoms of hypoxemia and diminished oxygen transport do not appear until levels increase to 30-40%. Levels >70% may cause death.2 In our patients, cyanosis occurred approximately 10% levels of methemoglobin, and they did not show signs of tissue hypoxia (mottled appearance, paleness, decreased peripheral perfusion, increased negative base excess).

O-toluidine which is prilocaine’s main metabolites is responsible for methemoglobinemia. In neonate, methemoglobinemia has been reported after prilocaine penile ring blocks in circumcision. Methemoglobinemia after the use of EMLA® cream (a eutectic mixture of lignocaine and prilocaine) has been reported in previously.4 However, in a double-blind, randomized, placebo controlled trial; no change has been found in blood methemoglobin concentrations after the use of EMLA cream.3

Circumcision is widely used in many countries due to religious tradition. Therefore in conclusion, during the process of circumcision performed after the first 3–4 months, the use of EMLA® cream as local anesthetic instead of penile blockade with prilocaine reduces the risk of methemoglobinemia and favors its outcome.

References