Brief Communication

Effects of pharmacological concentration of melatonin on reperfusion injury in rats

Ayse S. Ilhan, Msc, *Eser O. Oyar,* MD, *Deniz Erbas,* PhD, *Ozlem Sivasli,* MD.

Cardiovascular diseases are considered as the number one cause of death in the world. It comprises its own set of pathologies, mostly are atherosclerosis, arteriosclerosis, hypertension, congestive heart failure, cardiomyopathy, coronary heart disease, hypertrophy, myocardial infarction, and stroke. It is worthwhile to mention that ischemic heart disease continues to be the major cause of cardiac death. Free radicals and oxidative stress play a crucial role in the pathophysiology of a broad spectrum of cardiovascular diseases including ischemic heart disease. Evidence gathered over the last years' shows that the pineal hormone melatonin participates in the regulation of the heart.[1] Melatoninergic receptors were found in the heart and vessels, and also in the higher centers involved in the regulation of cardiovascular system. Melatonin could be considered as a protective agent because of its ability to scavenge free radicals and its antioxidant properties.[2] The effect of melatonin on myocardial reperfusion injury has received attention only in recent years. These studies have emphasized the effect of melatonin on the incidence of reperfusion arrhythmias, stunning, and limitation of infarct size.[3-5] The objective of the present study was to examine the effects of melatonin on ischemia-reperfusion injury of the isolated perfused rat heart.

We conducted this study at the Department of Physiology, Gazi University, Ankara, Turkey. Twenty rats were used. The isolated rat hearts (n = 10 in each group), previously being perfused by oxygenated Krebs-Heinseleit solution were put in normothermic ischemic conditions. After 20 minutes of normothermic ischemia, the hearts were reperfused with Krebs-Heinseleit solution in the control group. The melatonin were administered to the heart (100 µM), 5 minutes before ischemia, and during reperfusion in the experimental group. We observed the heart rate and contractile force, as well as the perfusate malondialdehyde (MDA), glutathione (GSH), and nitrate levels, and were measured before and after the ischemic period, as well as at the end of the reperfusion period. The tissue MDA, GSH, and nitrate levels were measured at the end of the reperfusion period. Decreased tissue (23.74 ± 0.81; $p<0.05$) and

Table 1 - Effects of melatonin on ischemia-referfusion injury.*

Groups	Pre-ischemic	Post-ischemic	Post-reperfusion
Tissue MDA levels (nmol/g tissue)			
Control group			41.55 ± 1.22†
Experimental group			23.74 ± 0.81†
Perfusate MDA levels (nmol/g)			
Control group	0.187 ± 0.005	0.218 ± 0.004†	0.347 ± 0.007†
Experimental group	0.184 ± 0.003	0.172 ± 0.003†	0.170 ± 0.002†
Tissue GSH levels (µmol/g tissue)			
Control group			2.85 ± 0.06†
Experimental group			1.14 ± 0.02†
Perfusate GSH levels (mmol/ml)			
Control group	5.36 ± 0.22	5.94 ± 0.25†	4.92 ± 0.14
Experimental group	5.84 ± 0.17	7.84 ± 0.43†	5.71 ± 0.37
Tissue nitrate levels (µmol/g)			
Control group			63.36 ± 3.92
Experimental group			58.44 ± 1.60
Perfusate nitrate levels (µmol/l)			
Control group	4.93 ± 0.14	2.26 ± 0.10†	2.49 ± 0.15†
Experimental group	4.26 ± 0.11	4.93 ± 0.23†	3.32 ± 0.10†
Heart rate			
Control group	86.90 ± 3.1	66.60 ± 2.6†	82.20 ± 5.3†
Experimental group	84.90 ± 3.5	88.10 ± 5.0†	101.8 ± 3.1†
Contractile force			
Control group	8.70 ± 0.6	6.0 ± 0.6†	6.0 ± 0.4†
Experimental group	8.50 ± 0.5	12.50 ± 0.6†	22.10 ± 0.5†

*Values are mean ± SEM, MDA - malondialdehyde, GSH - glutathione, †$p<0.05$.

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perfusate MDA levels (0.170 ± 0.002; $p<0.05$), and increased perfusate nitrate levels (3.32 ± 0.10; $p<0.05$), were observed in melatonin added group. In the same group tissue, the GSH levels (1.14 ± 0.02; $p<0.05$) have decreased, but heart rate and contractile force have increased ($p<0.05$) (**Table 1**).

Heart ischemia-reperfusion injury is defined by a complex cascade of events including increased liberation of reactive oxygen species from a variety of cell types. The role of reactive oxygen species (ROS) in ischemia-reperfusion heart injury has been examined by detecting the by-products of target molecule oxidation (lipid peroxidation and protein oxidation), and by determining the consumption of tissue antioxidants, such as glutathione. Malondialdehyde is a relatively stable end-product of lipid peroxidation. In our study, in the experimental group, both tissue and perfusate MDA levels decreased significantly compared with the control group. Glutathione has been shown to be an important cellular antioxidant, protecting cells from the damaging effects of oxidation products (such as hydrogen peroxide, superoxide, and hydroxyl radicals) that are normally produced and destroyed by the cell during metabolism. The supply of glutathione may play a critical role in antioxidant defense. Under oxidant stress, the redox state of the cell could become oxidized, and as a result, the cell would have inadequate antioxidant defenses to prevent irreversible damage such as lipid peroxidation. In our study, in the experimental group, tissue GSH levels decreased significantly compared with the control group. The drop in GSH levels during ischemia-reperfusion was probably due to its consumption during oxidative stress. In the hearts subjected to ischemia, a burst of reactive oxygen species occurs early upon reperfusion, and there is considerable evidence that they are cytotoxic to the heart, and reduces contractile function. In this study, the beneficial effects of melatonin on contractile function and heart rate may be related to its antioxidant property. The direct measurement of nitric oxide (NO) *in-vivo* is difficult because of its short half-life in biological systems. The NO is endogenously synthesized from L-arginine by nitric oxide synthase (NOS), and rapidly metabolized to nitrite and nitrate due to rapidly metabolization of NO to nitrite and nitrate, these stable end-products in biological fluids have been measured as an index of *in-vivo* NOS activity. In our study, in the experimental group, we observed that nitrate was passed to perfusate. Both post-ischemic and post-reperfusion periods, perfusate nitrate levels were significantly higher ($p<0.05$) than those of the control group.

We conclude that ischemia-reperfusion injury is related to the increased tissue lipid peroxidation. Melatonin may provide protection against ischemia-reperfusion injury, and this protection was manifested as the reduced levels of product of lipid peroxidation.

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From the Department of Physiology, Faculty of Medicine, Gazi University, Ankara, Turkey. Address correspondence and reprint requests to: Dr. Eser O. Oyar, Istiklal Mahallesi 1106 sok., Erdogan Apt. Kat. 2, No. 3, Isparta, Turkey. Tel. +90 (246) 2113612. Fax. +90 (246) 2370240. E-mail: oze@gazi.edu.tr

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A comparison of sensitivities of the conventional and the real-time polymerase chain reaction methods for detection of *Treponema denticola* in periapical abscesses

Ahmet Ozbek, *MD, PhD,* ***Selcuk M. Ozbek,*** *RA,*
Elvan Ozbek, *MD, PhD.*

The periapical abscess is a collection of pus in the pulp, or around the root of the tooth. Most of the periapical abscesses can result from necrosis of the pulp (death), which usually originated from the progression of dental caries. The association of spirochetes with oral diseases has been known for many years. A variety of spirochetes inhabit supragingival and subgingival plaques in human, and only a small proportion of them have been cultured and characterized *in vitro*. The ones that have been cultivated and identified to the species level are within the genus *Treponema*. Because the identification of them on morphological grounds is generally not possible, the determination of genotypic characteristics and biochemical parameters, such as growth requirements and enzymatic activities

is necessary. Although oral spirochetes are difficult to isolate from healthy gingiva, these bacteria particularly *Treponema denticola* (*T. denticola*) and *Treponema pectinovorum* increase in both prevalence and number in patients with periodontal diseases. Recent studies utilizing 16S rRNA polymerase chain reaction (PCR) amplification of 16S rRNA gene sequences have revealed that oral spirochetes constitute a heterogeneous group. All of the oral spirochetes clearly fall under the genus *Treponema*. Although *T. denticola* is the best characterized of the currently cultivable spirochete species, it is usually difficult to grow. In the last decade, many advances in microbial molecular diagnosis rendered possible, the identification of previously unknown human pathogens, and recent molecular studies have demonstrated that *T. denticola* is among the most prevalent agents for endodontic infections. Some of the advantages of microbial molecular methods are higher sensitivity and specificity, less time consuming, rapid diagnosis, which is very important particularly in cases of life-threatening infectious diseases, or diseases caused by slow-growing microorganisms, does not need careful-controlled anaerobic conditions during sampling and transportation, to be feasible during antimicrobial therapy, and to be repetitive for epidemiological studies. The PCR is a very common molecular technique. There are several methods to check if the intended PCR product was generated. The most commonly used method for detecting PCR product is electrophoresis in an agarose gel using ethidium bromide staining, and ultraviolet transillumination. This method is known as conventional PCR. The real-time PCR, another PCR method, is characterized by the continuous measurement of amplification products throughout the reaction, of which several different applications are SYBR-Green, TaqMan, and molecular beacon. The TaqMan and molecular beacon use a specific labeled oligonucleotide probe along with the primers. Probes of real-time PCR, except molecular beacon probe with different structure, contain reporter and quencher dyes, at 5' and 3' on both ends of the probe. Each cycle of PCR amplification allows increasing fluorescence signal.[1] In the present study, we aimed to evaluate the prevalence of *T. denticola* in periapical abscesses using conventional and TaqMan real-time PCR methods, and to compare and analyze the results statistically for investigation of the sensitivities of 2 PCR methods used.

Pus samples were obtained from 26 adult patients with the symptoms of acute periapical abscess, who had been referred for root canal treatment to the Department of Endodontics, Faculty of Dentistry in Erzurum, Turkey. None of them had taken antibiotics within the 3 months before the study. All of the patients understood the nature of the research project, and provided their informed consent. Samples were collected via strict asepsis, and transferred to 2 mL cryotube containing 1 ml of 5% dimethyl sulfoxide in trypticase-soy broth, and immediately frozen at -20°C. To obtain the DNA from samples, the QIAamp® DNA Mini Kit (QIAGEN® GMBH, Germany) was used. Protocol for DNA extraction from tissue samples was applied. The conventional PCR with species-specific primers was carried out in 50 μL volume of the reaction mixture containing 5 μL of target DNA, 1 μL of each primer (40 pmol concentration) [*T. denticola* ATCC 35405; 5'-3' TAA TAc cgA ATg Tgc TcA TTT AcA T (base positions 17431-17455) and 5'-3' TcA AAg AAg cAT Tcc cTc TTc TTc TTA (base positions 17720-17746)], 5 μL 10X PCR buffer, 1.25 U Taq DNA polymerase and 0.2 mM/L of each deoxynocleoside triphosphate (dATP, dGTP, dCTP, and TTP) (Fermentas® GMBH, Germany). The magnesium chloride concentration in the mixture was 2.0 mM/L. The PCR thermocycler program was an initial denaturation step at 95°C for 2 minutes, 40 cycles of a denaturation step at 95°C for 30 seconds, a primer annealing step at 60°C for one minute, and extension at 72°C for 2 minutes. After PCR amplification, the product was imaged and analyzed by 1.5% agarose gel electrophoresis in Tris-Borate ethylenediamine tetraacetic acid buffer stained with 0.5 μg/ml of ethidium bromide, and was photographed under ultraviolet light.[2]

The amplification and detection of DNA with species-specific primers by real-time PCR were performed in totally 25 μL volume, consisting of 20 μl of a mixture that contained 1X QuantiTect Probe PCR buffer composing of Tris-hydrochloride, potassium chloride, ammonium sulfate, 8 mM $MgCl_2$, pH 8.7, deoxynucleotide 3 phosphate (QIAGEN® GMBH, Germany), 0.7 μM for each forward and reverse primers, and 0.24 μM for the dual labeled probe [forward primer; (5'-AgAgcAAgcTcTcccTTAccgT-3'), reverse primer; (5'-TAAgggcggcTTgAAATAATgA-3'), and a probe (5'-FAM-cAgcgTTcgTTCTgAgccAggATcA-TAMRA-3')], and 5 μl of target DNA. The DNA amplification condition was one cycle of 50°C for 2 minutes, one cycle of 95°C for 15 minutes, followed by 50 cycles of 95°C for 30 seconds, and 58°C for 90 seconds.[3] The results were analyzed by Kruskal Wallis test (Statistical Package for the Social Sciences, version 10.0).

All of the 26 samples contained bacteria that were demonstrated by conventional PCR amplification with ubiquitous primers, suggesting that all samples have bacteria and not significantly PCR inhibitors. The conventional PCR with species-specific primers for *T.*

denticola was detected with amplicon size predicted as 316 base pair in 15 of 26 samples (57.7%). Clinical samples that were positive for *T. denticola* denoted only one band of the predicted size. However, the samples that were negative for *T. denticola* were assigned as no band. The results of real-time PCR amplification with species-specific primers introduced 7 more *T. denticola*-positive samples in addition to the positive ones determined by conventional PCR with species-specific primers. Twenty-two positive results of real-time PCR (84.6%) were found. The difference between the results of the 2 PCR methods was statistically significant (significance is 0.013).

Generally, the bacterial products initially cause pulpal inflammation, either through a cytotoxic effect or indirectly by their antigenic properties. It has been widely known that the severe pulp injury, a localized necrotic area, facilitates ways of bacterial entry to the pulp cavity, and causes the establishment of colonies in necrotic tissue. Bacteria may well be present, both in the part of the necrotic side of the pulp, and in the superficial layers of the subjacent vital tissue. The presence of spirochetes belonging to the genus *Treponema* in the necrotic pulp of the non-vital teeth was evidenced by anaerobic culture, and scanning electron microscopy. Recently, molecular genetic analyses have confirmed the presence of oral treponemas in endodontic infections. The *T. denticola* is a gram-negative, anaerobic, helical shaped, highly motile bacterium. It has an assembly of virulence factor contributing its pathogenicity. This bacterium can adhere to diverse host cells and other tissue components, and it has also been demonstrated to invade cells and tissues. Some *T. denticola* surface-expressed proteins have adhesion, cytotoxic, and tissue destruction activities, including the major surface protein and the chymotrypsin-like protease complex.[4] In the present study, 16S rRNA with ubiquitous primers was targeted not only as a positive control of PCR amplification, but also a checker of the PCR inhibitors impeding the reaction. Conventional PCR with ubiquitous primers worked in all of the samples, which indicates that either the level of PCR inhibitors was undervalued or the inhibitors were absent. The rate of *T. denticola*-positive samples determined by conventional PCR amplification was 15 of the 26 samples (57.7%). This data is in accordance with other studies in which conventional PCR with same species-specific primers had been used. Results of other similar studies are between 50-53.3% for *T. denticola*. Rocas et al,[5] and Siqueira et al,[2] revealed the rate of *T. denticola* as 80% and 79% by using the nested PCR methods in symptomatic patients. The nested PCR is more sensitive than the conventional PCR, because of the dual amplification process using 2 sets of primers. One set of primers is used for the first round of the amplification, and the other, specific for an internal sequence amplified by the first primer pair, is used for second round of the amplification. In the present study, 22 positive samples (84.6%) were found with real-time PCR amplification. This data appeared as very near to the nested PCR results. The real-time PCR using the TaqMan system with a fluorogenic probe measures the accumulation of PCR products at the end of each cycle of the amplification. Such real-time chemistries also offer greater sensitivity than the traditional gel visualization, and can be used for quantification. This assay does not require post-sample handling. Our results revealed that the real-time PCR using the TaqMan system was more sensitive than the conventional PCR (significance is 0.013). Additionally, real-time PCR may be suggested as a more convenient method, than both conventional and nested PCRs, because of less time consumption, and the ability of avoiding the contaminations of post-sample-handling, and the false positive result due to carry-over from a previous experiment, such as while gel loading.

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From the Departments of Microbiology and Clinical Microbiology (A. Ozbek), Endodontics (S. Ozbek), and Histology and Embryology (E. Ozbek), Ataturk University, Erzurum, Turkey. Address correspondence and reprint requests to: Dr. Ahmet Ozbek, Department of Microbiology and Clinical Microbiology, Medical School, Ataturk University, TR-25100, Erzurum, Turkey. Tel. +90 (532) 3858623. Fax. +90 (442) 2360968. E-mail: aozbek@atauni.edu.tr/ahmetozbek1965@yahoo.com

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Motor vehicle accidents during pregnancy. *A review of maternal and fetal outcomes in Saudi Arabian population*

Hayfaa A. Wahabi, *FRCOG, FRCS,*
Ahmed T. Saleh, *MD, FRCSC,*
Abdelmonim A. Abdelrahman, *FRCS(Ed), MMedSci.*

Trauma during pregnancy has been recognized as an important cause of adverse maternal and fetal outcomes.[1] The ability to predict poor maternal and fetal outcome is important in the management of pregnant trauma victims to improve outcomes. This retrospective study done over a 10-year period was undertaken to identify the risk factors associated with poor fetal and maternal outcome, following motor vehicle accidents (MVA) during pregnancy, in a Saudi population.

We performed a retrospective chart review from January 1994 to January 2004, at King Abdulaziz Medical City (KAMC), of all pregnant patients who were admitted to the emergency room and who have sustained MVA. Severity of the patients' condition was assessed by Glasgow Coma Scale (GCS), Injury Severity Score (ISS) and the need for blood transfusion. The fetal condition was assessed by cardio-tocogram (CTG) and fetal ultrasound. Patients with minimal trauma, who were treated at the emergency department but did not need in-patient hospital treatment, were excluded from the analysis. A total of 45 patients were included, and were divided into 2 groups based on the pregnancy outcome: Group I (n=31) patients who were discharged home with an ongoing pregnancy and Group II (n=14), patients who had fetal death, miscarriage or emergency delivery as a result of MVA. There were 6 (13.3%) intrauterine fetal deaths (IUFD), 4 of them were associated with the maternal death and 5 were ≥28 week's gestation. Of the remaining 8 pregnant women, 6 needed emergency cesarean section for fetal distress, which was evident by CTG abnormalities due to placental abruption, all fetuses were delivered alive (gestation age 28 - 36 weeks). The remaining 2 patients had spontaneous miscarriage following MVA at 16 and 20 weeks. Data collected up to the day patients were discharge from the hospital. The 2 groups were compared according to GCS, ISS, blood transfusion need and abnormal fetal CTG, to evaluate the risk factors for poor fetal and maternal outcomes. Maternal mortality from obstetric causes in the hospital was obtained from hospital statistic records.

Continuous variables were compared using Student *t*-test, and dichotomous variables were compared using Fisher exact test. The mean difference between the groups were considered significant at $p<0.05$. Data expressed as mean ± SD. The high ISS, severe blood loss as indicated by the need for blood transfusion and abnormal CTG were significantly more frequent in Group II as compared to Group I. The mean GCS was significantly lower in Group II compared to Group I. The most common obstetric complication for all the 45 patients was placental abruption, which occurred in 8 (17.8%) patients. A CTG was performed in 15 of the 45 patients for a range of 30 minutes to 6 hours. Twenty-two patients were less than 24 weeks pregnant and all of them had ultrasound (US) scan to confirm fetal viability and gestation age. Seven patients (15.6%) had abnormal fetal heart tracing and, in 6 patients cesarean section was carried out to save the fetus. The most frequent fetal heart abnormality was persistent bradycardia and fetal heart deceleration. The reported maternal mortality from obstetrical causes in the hospital during the 10 years of study was on 2 patients only, both of whom died from complications of massive obstetric hemorrhage, based on hospital census.

This is the first study to investigate the effect of MVA on the pregnancy outcome in a Saudi population where women do not drive. The KAMC has level-I Trauma Center and a census of 190,000 admissions per year, of which 10% of those are for multiple trauma including MVA. In this study, we have compared the group of patients who were discharged from the hospital with an ongoing pregnancy following the MVA, with those who had either fetal death or emergency termination of pregnancy, as we believed that the factors most likely to cause fetal demise are the same factors causing severe fetal distress leading to iatrogenic termination of pregnancy. The fetal loss rate of 13% is similar to previous reports.[1] The ISS is an anatomical ordinal scoring system that provides an overall scoring for patients with multiple injuries. The score is 1 to 75, and the value correlates with mortality.[2] In this study, an ISS of ≥9, indicating moderate to severe maternal injuries, was associated with adverse fetal outcome as compared to the group of women with ISS of less than 9 (**Table 1**). A high ISS

Table 1 - Factors affecting fetal outcome in MVA victims.

Factor	Group I (n = 31)	Group II (n = 14)	*P*-value
GCS	14.5 ± 1.1	8.7 ± 4.7	0.0083
ISS	5.0 ± 4.8	34.3 ± 20	0.0030
Women needed blood transfusion (%)	1 (3.2)	6 (42.9)	0.0065
Abnormal fetal CTG (%)	1 (3.2)	6 (42.9)	0.0060

MVA - motor vehicle accidents, Values are mean ± SD, GCS - Glasgow Coma Scale, ISS - Injury Severity Score, CTG - Cardio-tocogram, Group I - patients who were discharged with an ongoing pregnancy, Group II - patients who had miscarriage, intrauterine death or emergency delivery as a result of MVA.

has been associated with a significant increase in the risk of adverse maternal and fetal outcome, demonstrated by over 500-fold increase in the risk of maternal death, and 17-fold increase in the risk of fetal death,[3] while minor trauma was associated with a 4.9-fold increase in maternal death and a 2.7-fold increase in fetal death, as compared to the controlled population.[3] However, the mechanism of fetal death might differ in patients with severe trauma from those with a minor one. Two patients in this study suffered fetal death despite an ISS of 1 and 4. The maternal mortality rate of 8.9% in this group of patients is similar to the rates reported by other investigators[1] and all 4 maternal deaths in this cohort were predictable by the severity of trauma as reflected by the high ISS. The CTG was recognized, in this cohort, as well as in other studies[4] to be a sensitive tool for screening for fetal compromise in patients with trauma. The CTG abnormalities were noted in over 46% of our patients who were monitored and in almost all of them, intervention in the appropriate time have saved the fetus. Fetal bradycardia and variable decelerations were the most frequent abnormalities noted in this group. Most of the patients in this cohort had fetal US examination. Despite the fact that the US examination is not sensitive in predicting fetal distress and placental abruption,[4] but it is a useful tool for determination of the gestational age, which is vital for the decision of emergency delivery if the fetus is at, or beyond the viability age of 24 completed weeks. Placental abruption in this study was the most frequent complication associated with fetal compromise occurring in 17.66% of the patients and second only to maternal death that causes fetal demise. This observation was found in all studies investigating the effect of trauma on the pregnancy outcome.[4] A 7.7-fold increase risk of placental abruption was reported in patients with minor trauma, and a 23-fold increase risk was reported with maternal severe trauma as compared to control.[3] The GCS is a neurological scoring scale that quantifies the level of consciousness in patients with traumatic brain injuries.[5] In this cohort of patients low GCS was associated with increase risk of fetal compromise as compared to patients with normal GCS (**Table 1**). The number of patients that needed blood transfusion in this study was significantly higher in Group II as compared to Group I. The association of maternal hemorrhage, indicated in this study by the need for blood transfusion, with fetal compromise was previously recognized.[1]

This study has some limitations that were based on a retrospective study design, and the use of chart review data, which are subject to a degree of error. However, our results are similar to other published work and prove that the factors which influence the fetal outcome in pregnant MVA victims in the Saudi Arabian population, are similar to those studied in other parts of the world, despite the fact that none of these women were in the driver's seat. The study has illustrated the high risk that the MVA is imposing on maternal health, as the maternal mortality from obstetric causes was 50% less than from MVA in the study period in KAMC.

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From the Departments of Obstetrics and Gynecology (Wahabi, Saleh), and Emergency Medicine (Abdelrahman), King Abdul-Aziz Medical City, Riyadh, Kingdom of Saudi Arabia. Address correspondence and reprint requests to: Dr. Hayfaa Wahabi, Department of Obstetrics and Gynecology (MC 1216), King Abdul-Aziz Medical City, PO Box 22490, Riyadh 11426, Kingdom of Saudi Arabia. Tel. +966 (1) 2520088 Ext. 1953. Fax. +966 (1) 4927987. E-mail: umlena@yahoo.com

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Epidemiology of atrial fibrillation among Qatari patients admitted with various cardiovascular disorder. *A population-based study*

Wafer A. Dabdoob, *EBSC, FESC,*
Abdulbari Bener, *MFPHM, FRSS,*
Dhabia Al-Mohannadi, *MBBS,*
Mohammad T. Numan, *FAAP, FACC,*
Hajar A. Al-Binali, *MD, FACC,*
Jassim Al-Suwaidi, *MD, FACC.*

Atrial fibrillation (AF) is an arrhythmia, commonly associated with systemic and organic heart diseases,[1] but in a significant proportion of patients (10-30%), detectable heart disease is not found. This arrhythmia is a major risk factor for cardiovascular events such as stroke, mortality, and coronary artery diseases.[2,3] The pattern of AF in the developing countries, especially in the Arabian Gulf, is not clear. The purpose of this retrospective cohort study was to characterize causes, and determine the pattern of all AF patients diagnosed and

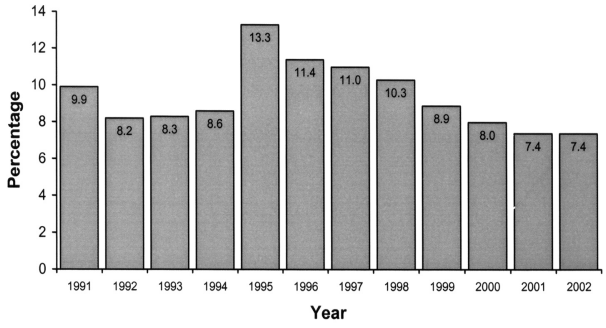

Figure 1 - Incidence of atrial fibrillation in Qatar from 1991-2002.

treated in Qatar over the period of 10 years. This study was conducted in the state of Qatar, with an estimated population of 616,138 in the year 2002. Approximately, 30% of the populations are Qatari nationals, and the others were expatriates mostly from the Middle East, southern Asia, and south east Asia. The state of Qatar, like many other developing countries, has witnessed a rapid development in many aspects of life during the last 2 decades. The database of the Coronary Care Unit (CCU) at Hamad Medical Corporation was used for this study. Data were collected from the clinical records taken by the physicians at the time of the patient's discharge from the hospital, according to predefined criteria for each data point. With the described database, all patients presenting with AF requiring hospitalization in the 10 year period, between 1991 and 2002, were retrospectively identified. The age of presentation, gender, cardiovascular risk factor profiles (hypertension, hypercholesterolemia, diabetes, and pre-existing coronary heart disease), were analyzed.

Definitions and statistics. Electrocardiographic diagnosis of AF was made according to Bellet's[4] and Levy's[5] definitions. Hypertension was diagnosed from a history of hypertension, or a diastolic blood pressure (≥95 mm Hg), or both were present. Student t-test, non-parametric Mann-Whitney test, and Chi-square analysis was performed to test the differences in proportions of categorical variables between 2 or more groups. The level of $p<0.05$ was considered the cut-off value of significance.

From the study period, 971 Qataris out of 1910 AF cases were admitted to the CCU and cardiology wards. Even though male proportion of AF was higher, AF was significantly more likely to be in females than males. When compared to non-AF patients, AF patients were older (mean age 55.6 ± 15.3 versus [vs] 52.5 ± 13.4 years). The incidence of AF in Qatari patients was higher than in expatriates (12% vs 8%), this is partly because hypertension (40.5% vs 22.7%, $p<0.001$) and diabetes mellitus (35.3% vs 19.7%, $p<0.001$) were more prevalent among Qatari patients, as well as in older age. History of angina and atypical chest pain were less common among AF cases (7.0% vs 35.1%, and 2.6% vs 5.1%, respectively, $p<0.001$). History of dizziness was significantly higher among AF cases (4.5% vs 2.9%), palpitation (37.3% vs 3.9%), and shortness of breath (23.7% vs 18.0%), with a p value of <0.001 in each mentioned symptom. Valvular heart disease was significantly higher among AF cases; mitral stenosis (6.8% vs 0.8%, $p<0.001$), mitral regurgitation (4.5% vs 1.1%, $p<0.001$), and aortic regurgitation (2.0% vs 1.2%, $p=0.004$).

This study is the largest report on the epidemiology of AF in a developing country. The findings in this community are consistent with previous reports in other communities, that AF is more common with older age, the presence of hypertension, heart failure, diabetes, and valvular heart disease.[2,3] The incidence of diabetes as a risk factor to develop AF in Qatari patients (35%) is significantly higher than what was reported in the literature. This can be attributed to the increased incidence of diabetes mellitus (DM) in the general population of Qatar (50%), which is mostly due to the stationary life style, secondary to the income increase in the last few decades, with the genetic predisposing factors and consanguinity in marriage. In the 10 years study period, we noted a significant high incidence of AF during the years 1993 - 1997 (**Figure 1**), with a decline in the overall incidence after 1997 - 2002. It might be attributed to the environmental factors and pollution. Hypertension was present in 31.7%, and DM in 27.6% of the AF patients. The incidence of congestive heart disease (19.5%) and old myocardial infarction (9.6%) was high among AF patients. Valvular heart diseases were a significant underlying diseases in AF patient in our study, particularly mitral stenosis (6.8%) and incompetence (4.5%). These findings are similar with the other literatures.[1,2]

In conclusion, long-standing AF is associated, in the majority of patients, with organic heart disease. Predictive factors of AF include diabetes, hypertension, hypercholesterolemia, congestive heart failure, old myocardial infarction, increasing age, and male gender.

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From the Departments of Cardiology and Cardiovascular Surgery (Dabdoob, Numan, Al-Binali, Al-Suwaidi), Epidemiology and Medical Statistics (Bener), and Internal Medicine (Mohannadi), Hamad General Hospital, Hamad Medical Corporation, Doha, Qatar. Address correspondence and reprint requests to: Dr. Jassim Al Suwaidi, Department of Cardiology & Cardiovascular Surgery, Hamad Medical Corporation, PO Box 3050, Doha, Qatar. Tel. +974 4392483/4883620. Fax. +974 4392454/4869427. E-mail: alsuwaidi.jassim@gmail.com

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Reducing the medical costs of urinary tract infections investigation in infants

Christos N. Karakos, *MD,*
Konstantinos N. Stamatiou, *PhD.*

Infants with a single episode of urinary tract infection are subject to radiological evaluation for vesico-ureteral reflux. Everyday practice revealed a respectful number of male infants presenting with vesico-ureteral reflux, whose radiological findings disappear after the lysis of balanopreputial adhesions. In such cases, balanopreputial adhesions and the resulting urinary obstruction were the most possible causative factor. It is well known that, circumcision practiced in Jewish and Muslim populations since antiquity, plays a protective role against genito-urinary infections. A brief review of the literature revealed that postneonatal circumcisions are increasing in frequency, while uncircumcised boys suffer from recurrent urinary tract infections and balanoposthitis.[1] In our country, as in the rest of Europe, circumcisions are not generally practiced. However, lysis of balanopreputial adhesions seems to guarantee similar benefits. Larsen and Williams,[2] reported that the "cost" of a postneonatal circumcision was 10 times that of a neonatal circumcision. We do believe that such procedures lead to a major decrease of the medical cost: an early lysis of balanopreputial adhesions could improve health outcomes in male neonates, while in the same time the medical expenditures (chemoprophylaxis, radiological evaluation, follow-up) could be critically reduced.

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From the Departments of Pediatrics (Karakos), and Urology (Stamatiou), General Hospital of Thebes, Piraeus, Greece. Address correspondence and reprint requests to: Dr. Stamatiou N. Konstantinos, 2 Salepoula Street, 18536 Piraeus, Greece. Tel./Fax. +30 2104539744. E-mail: stamatiouk@yahoo.com

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