ORIGINAL ARTICLE

Impact of scorpion stings on electrocardiographic changes and relationship with body oxidant and antioxidant status

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Abstract

Objecive: To investigate electrocardiogram changes due to scorpion stings and association between oxidative stress index, body oxidant/antioxidant system and the electrocardiogram changes.

Methods: The study was conducted at the Faculty of Medicine, Gaziantep University, Turkey, between May 2009 and October 2010. It comprised 44 patients admitted to the emergency department for scorpion sting, and a control group of matched age and gender of 20 persons. Electrocardiograms were taken promptly in the most painful phases of the patients. Cardiac parametres were measured. Erythrocyte packages were prepared to detect toxin/antioxidant levels. SPSS 18 was used for statistical analysis.

Results: Of the 44 patients, 22 (50%) were male. Overall average age of the patients was 45.22±17.99 years. None of the patients required intensive care and none of them had limb losses. Cardiac parametres of the patients in electrocardiogram were higher ($p<0.05$). Difference between those with changed electrocardiogram and unchanged electrocardiogram in terms of the values of total antioxidant status, total oxidant status, and oxidative stress index, were not statistically significant ($p> 0.05$).

Conclusion: Scorpion stings associated with electrocardiogram changes. The mechanism of this relationship is not related with the status of body oxidative stress index and body oxidant and antioxidant capacity. Some parametres warrant further study in terms of potential serious arrhythmias in scorpionism.

Keywords: Scorpion sting, Electrocardiography, Oxidative stress. (JPMA 64: 423; 2014)

Introduction

Scorpionism and its consequences are an actual public health problem in several parts of the world; especially in north-Saharan Africa, Sahelian Africa, South Africa, Near and Middle-East, South India, Mexico and South Latin America, east of the Andes.[1] The effects of the sting depend on the delivery dose of the scorpion poisoning, the age of the offender, the season, and the size of the victim.[2] The severity of envenomation is related to haemodynamic and cardio-respiratory changes, with cardiogenic shock and pulmonary oedema being the main causes of death.[3-6]

The pathogenesis of cardiac dysfunction and myocardial damage secondary to scorpion envenomation had largely been the subject of debate in the past. The most accepted hypothesis was the increased catecholamine circulating secondary to a direct stimulatory effect of the venom on the adrenals and on sympathetic nerve endings. This hypothesis was confirmed by some clinical and experimental studies.[7] In effect, it is possible that the venom affected the myocardial cell membranes directly, altering its permeability as well as electrical properties, and through abnormal electrolytes fluxes and shifts, causes functional damages. However, the myocardial dysfunction may be due to myocardial ischaemia.[8] This hypothesis was advanced on some clinical, electrocardiographic, echocardiographic and radionuclide studies.[9,10] All of these proposed mechanisms may act separately or simultaneously. Catecholamine-mediated cardiac injury appears to be multifactorial and may be attributed to the relative hypoxia that occurs due to increased heart rate, coronary spasm and vasoconstriction of the microcirculation and due to direct toxic effects on myocardial cells brought about by increased intracellular calcium concentration.[11] All these paradigms cause electrocardiogram abnormalities.

In the present study, we tried to determine the electrocardiographic (ECG) abnormalities in scorpion envenomation and to evaluate the relationship between these ECG abnormalities and oxidant-antioxsidant system.

Patients and Methods

The study, performed in compliance with the resolutions of Helsinki Decisions, Regulation on Patient Rights and

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ethical rules, and after the approval of institutional Ethics Committee, was carried out at the Faculty of Medicine, Gaziantep University, Turkey. Forty-four patients admitted to the emergency department (ED) with scorpion sting between May 2009 and October 2010, were included. Those with heart failure, renal failure, chronic obstructive pulmonary disease, diabetes mellitus, malignancy or history of drug use were included. An age and gender matched control group of 20 persons were also included.

Twelve-lead ECG was performed on arrival and every 6 hours following the admission of the patients to the ED due to scorpionism. ECGs taken in the most painful phase of patients were used for analysis. The studied parametres were: age, gender, location of scorpion sting in the body, symptoms, and findings and treatment; and the heart rate (HR), PR interval, QRS, prolonged Corrected QT interval (UQTc), corrected shortened QT interval (KQTc), QT dispersion (QTd), corrected QpT value (QpTc), minimum P wave duration (Pmin), maximum P wave duration (Pmax), and P wave dispersion (PWd) were computed and ECG changes were recorded. QT dispersion was computed as the difference between maximum QT and minimum QT. The difference between Pmax and Pmin outlined the P-wave prolongation. Corrected QT was calculated by dividing the time measured in milliseconds of the interval from the beginning of QRS wave until the end of the T wave by the square root of the value in milliseconds of the interval of two successive R waves. QpTc was computed by dividing the interval between the begining of the QRS wave to the peak of the T-wave by the square root of the time in milliseconds of the interval of two successive R-waves. Further, 2cc of blood samples were placed in two tubes; one heparinised and the other unheparinised for the total antioxidant status (TAS), and total oxidant status (TOS) investigation. The samples taken were centrifuged at 5000 rpm for 5 minutes and serum in the unheparinised was separated while plasma in the heparinised tube was separated. Blood sample remaining in the heparinised tube was washed three times with 0.15 mL 0.9% isotonic saline and then centrifuged again for 30 minutes at 10000rpm. Plasma on the tube was again removed and disposed of. Thus, red blood cell packages were prepared. Same processes were applied also for the control group. Serum, plasma and erythrocyte packages were stored in a freezer at -80oC.

TAS and TOS levels automated and colorimetric were measured by the published methods.[12,13] TAS measurement method is based on the bleaching of the characteristic colour of a more stable 2,20-azino-bis (3-ethylbenz-thiazoline-6-sulfonic acid) radical cation by antioxidants.[14] TOS method is based on the oxidation of ferrous ion to ferric ion in the presence of various oxidant species in acidic medium and the measurement of the ferric ion by xylenol orange. Results were evaluated in μmol Trolox equivalent (equiv)/L, mmol H_2O_2/L and mg/dL, respectively, and the precision of this assay is very good (< 3%).[15] The per cent ratio of TOS to TAS yields the oxidative stress index (OSI): OSI (arbitrary unit) = TOS (μmol H_2O_2 equiv/L)/TAS (mmol Trolox equiv/L).

SPSS 18.0 used for statistical analysis, and all data was expressed as mean ± standard deviation (SD). The distribution of the permanent data was examined graphically, using a Kolmogorov-Smirnov test. For data that was normally distributed and independent, groups were compared using independent t-test, while for the data that was not normally distributed and independent, groups were compared using a Mann-Whitney U test. In all comparisons, $p<0.05$ was considered statistically significant.

Results

Of the 44 patients, 22 (50%) were male, while the overall average age of the patients was 45.22±17.99. The location of stings in 18 (40.9%) patients was on the upper extremities stung by one scorpion, and in 14 (31.8%) it was on the lower extremities by one scorpion. Twelve (27.3%) patients had been stung by more than one scorpion and on more than one location. Some patients applied directly to the ED, while others had been sent from other centres. For this reason, ECG of 30 (68.2%) patients was taken within the first 4 hours on arrival, and ECG of 14 (31.8%) was taken after the second four hours and in the following hours thereafter. Twenty-six (59%) patients were treated with scorpion serum therapy, while 18 (41%) were treated without scorpion serum. On admission, all patients had clear consciousness, 19

Table-1: Comparison of ECG level between scopionism and control group.

	Scorpionism group (n=44)	Control group (n=20)	p
HR/min	82±17.37	84.48±0.18	0.26
PR/sec	0.16±0.003	0.13±0.02	0.001*
QRS/sec	0.850±0.012	0.12±0.1	0.5
UQTc	0.46±0.4	0.41±0.03	0.001*
KQTc	0.40±0.04	0.38±0.04	0.93
QTd	0.06±0.04	0.038±0.04	0.022*
QpTc	0.33±0.03	0.31±0.34	0.034*
Pmin	0.06±0.05	0.04±0.01	0.04*
Pmax	0.08±0.01	0.07±0.014	0.129
PWd	0.03±0.01	0.032±0.017	0.687

HR: heart Rate. PR: PR interval. UQTc: Prolonged corrected QT interval. KQTc: Corrected shortened QT interval. QTd: QT dispersion, QpTc: Corrected QpT value, Pmin: Minimum P wave duration. Pmax: Maximum P wave duration, and PWd: P wave dispersion. ECG: electrocardiogram.

Table-2: Comparison of TAS, TOS and OSI levels in scorpionism with and without ECG changes.

	Scorpionism without ECG Changes (n=25)	Scorpionism with ECG Changes (n=19)	P
TAS	1.81±0.37	1.78±0.27	0.823
TOS	9.39±8.29	8.42±6	0.942
OSI	0.58±0.45	0.55±0.33	0.923

TAS: Total Antioxidant Status. TOS: Total Oxidant Status. OSI: Oxidative Stress Index. ECG: Electrocardiogram.

(43.18%) did not have any relevant symptoms; but in the rest of the patients nausea 4 (9.09%), vomiting 4 (9.09%), dizziness 1 (2.2%), abdominal pain 1 (2.2%), nausea-vomiting, dizziness 10 (22.72%) and dizziness-nausea-vomiting-chest pain (11.36%) were observed. Of the patients, 32 (72.72%) were complaining about pain in the extremity due to scorpionism, while 10 (22.72%) had severe pain and numbness in limbs, and 2 (4.5%) were admitted with leg oedema and severe pain. All patients were observed in the emergency observation room. Grade 1 group patients received analgesia and fluid support (0.9% isotonic saline). Grade 2 group were given scorpion serum in addition to previous treatments. No patients were established in Grade 3 group. None of the patients required intensive care and none of them had limb losses.

PR interval in electrocardiography, UQTc, QTd, QpTc, Pmin values were higher in scorpion stings than those of the ECGs of the control group, and the cited highness was statistically significant. The other parametres were also higher in patients than the controls except HR and the PWd. However, highness of these parametres was not statistically significant (Table-1).

TAS, TOS levels of the patients whose blood samples were obtained was studied and OSI of each patient was computed. When TAS, TOS, OSI admission values were compared between those with ECG changes and without ECG changes, a statistically significant difference was not detected (Table-2).

Discussion

Scorpionism may cause clinical manifestations ranging from local effects to systemic poisoning symptoms. The sting may cause symptoms such as widespread pain at location of sting, redness, tingling, paraesthesia, fever, sweating, tachycardia, nausea, myocarditis, rhythm disorders and respiratory distress. In our locality the majority of scorpion species are yellow scorpions. Especially, Androctonus crassicauda and Leiurus quinquestriatus are more common and they may cause myocardial injury.[16] In this study we sought to determine the impact of scorpion stings on ECG changes and investigate the association of ECG changes with oxidant and antioxidant status.

Antioxidants are classified into enzymmatic (superoxide dismutase, catalase, glutathione peroxidase, glutathione-s-transferase, etc.)[17] and non-enzymmatic (ascorbic acid, α-tocopherol, carotenoids, melatonin, etc.).[18] They decrease local oxygen concentration, prevent the initiation of lipid peroxidation by cleansing hydroxyl radicals, bind and deactivate transition metal ions, play an active role in conversion of peroxides into non-radical products such as alcohol, and break the chain by reacting with all of the radicals that cause chain reactions. As a result, radical metabolite production is prevented, radicals produced are cleansed, cell damage is repaired, chain reactions that produce secondary radicals are stopped, and endogen antioxidant capacity is increased.[19]

We found that scorpion stings are significantly associated with important parametres of ECG changes. However, this relationship is independent of oxidant and antioxidant status. Further study should focus on other mechanisms rather than body oxidation system.

On admission, all patients were fully conscious in our study. Symptoms, including nausea, vomiting, dizziness, chest pain, abdominal pain and paralysis were identified in 56.82% of the patients. No patient had major systemic findings such as severe cardiac symptoms and pulmonary oedema. The most common finding in a prospective study of disease in 120 patients was localised pain.[20] Serious systemic effects in patients had not been found and these results are similar to the the present study. Bouaziz et al made a classification in patients according to presence or absence of systemic symptoms as localised pain in location of scorpion stings to be within Grade 1, systemic symptoms to be within Grade 2 and cardiac symptoms such as cardiogenic shock, pulmonary oedema or severe neurological findings such as convulsions, coma to be within Grade 3.[21] Grade 3 findings were not encountered in our study. However, 26 patients were evaluated as Grade 2 and 18 patients were Grade 1. Scorpion serum therapy was used in 26 patients. Only symptomatic treatment was sufficient in patients for whom scorpion serum was not used. HR, PR interval, QRS, UQTc, KQTc, QTd, QpTc, Pmin, Pmax, PWd were calculated in patients who were admitted. PR interval, UQTc, QTd, QpTc, Pmin values in the patient group were statistically higher than the values found in the control group ($p<0.05$). Mostly sinus tachycardia and T wave changes, 1° AV block, sinus arrhythmia, ST elevation in leads V1-V4

and ventricular extra beats were identified in patients in terms of ECG changes. Our results are similar to the case results of 76 cases of scorpion stings which was determined by an earlier study.[22] ECGs of the patients were evaluated in this study and the PR, QRS, HR, QTc, QTd, PWd, Pmin values thereof were computed. Sinus tachycardia, atrial ectopic beats, ST changes, ventricular extrasystoles, sinus arrhythmia, 1° AV block, left bundle branch block, right bundle branch block were found in cited cases. Unlike the present study, the control group was not included in the earlier study. QT intervals on the 12-lead ECG are not stable and can be different. Day et al and Higham et al stated that the clinical importance of the evaluation of these differences between the derivations in QT interval is due to the non-homogeneous repolarisation measurement between the derivations and this difference is the QT dispersion.[23,24] The diversity of QT intervals has importance in heart rate dissimilarities. Corrected QTd indirectly measures ventricular repolarisation and this has an effect on ventricular arrhythmias.[20] In our study, UQTc, QTd values of the patients were established to be statistically higher than and those of the healthy control group which confirms a high risk of arrhythmia in scorpionism.

There is no direct evidence that scorpion venom has toxic effect on myocardium. It has been reported that autopsy findings of pulmonary oedema and myocardial necrosis were observed in the case of a 4-year-old who died after admission and who was admitted due to being stung by a serrulatus, a species of scorpion, causing a direct effect on the adrenal and the sympathetic nervous system due to venom in the circulation system thereof.[25] This shows that myocardial necrosis is due to sympathetic and adrenal discharge and the increase of catecholamines. Another complication of scorpionism is myocarditis and pulmonary oedema and these complications were specified in two scorpionism cases of adults reported by Karakurt et al.[26] In our study, serious conditions such as fatal arrhythmia, cardiogenic shock, cardiac tamponade, and pulmonary oedema did not occur.

In our study, a significant correlation between TAS, TOS, and OSI blood values of patients with and without ECG changes was not established. This case shows that toxic effects of scorpion venom on heart are independent of the oxidant-antioxidant system. It has been indicated by Petricevich et al in a compilation study that the effects on myocardia depend on catecholamines and cytokines.[27] Accordingly, long-chain toxins separate as alpha (leads to prolongation of action potential in nerves and muscles) and beta (leads to the formation of negative membrane potential) toxins affecting sodium channels. Voltage-gated potassium channels take a role in immune response and lead to T cell proliferation and IL-2 production. In addition, opening of the voltage-gated potassium channels increases the passage of calcium. Blockade of calcium-activated potassium channels lead to relative hyperkalaemia and the release of catecholamines. Petricevich et al,[28] in another study, have stressed that the amount of released pro-inflammatory and inflammatory cytokines has a direct proportion with the severity of symptoms.[28] Annane et al. similarly expressed that immune response in scorpionism is initiated by nitric oxide (NO) and the complement system.[29] Oxidant-antioxidant levels disrupt the function and integrity of membrane lipids, cellular proteins, nucleic acids, and lead to production of signals in the immune cells and gene expression. Complement activation causes tissue damages directly.

Our study had its limitations. The differences in ECG changes between patients who received scorpion serum and those who did not could not be analysed. Absence of Grade 3 patients caused failure in clarification of potential serious ECG changes. For this, it is required to conduct studies involving severe cases.

Conclusion

Scorpion sting is associated with ECG changes, including increased PR interval, QT dispersion, corrected QpT value and Pmin. The mechanism of this relationship is not related with OSI and the status of body oxidant and antioxidant capacity. Increased QT dispersion warrants further study in terms of potential serious arrhythmias in scorpionism.

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