Original Article

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Community Section

Retrospective Analysis of Cardiotoxic Scorpion Envenomation in Konkan Region of Western India with Special Reference to Echocardiography

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ABSTRACT

Introduction: Mortality due to scorpion sting is high in rural India as preference is given to traditional healers above hospitalisation. In rural Indian settings where there is a lack of diagnostic facilities Electrocardiogram (ECG) was supposed to be the only test to diagnose cardiotoxicity. However, we proposed to study Echocardiography (ECHO) serially in scorpion sting cases for classifying them into mild, moderate and severe envenomation.

Aim: To study serial changes of cardiac dimensions on ECHO in cardiotoxic scorpion sting patients.

Materials and Methods: This study was a retrospective and cross-sectional analysis of 925 patients stung by scorpion, admitted from January 2011 to December 2017 at BKL Walawalkar Hospital, Chiplun, Maharashtra, India. All patients were classified into mild, moderate and severe envenomation based on clinical findings and electrocardiography. All patients had ECHO done on admission but only 81 severely or moderately envenomed had complete records of ECHO readings. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 21.0 (SPSS Inc., Chicago, USA). Data has been presented as mean and Standard Deviation (SD) for all the ECHO measurements.

Results: In 81 patients, ECHO on admission showed severe Left Ventricular (LV) dilatation. There was significant reduction in LV size (3.69 cm to 3.025 cm for systolic and 4.19 cm to 3.82 cm for diastolic, p-value <0.001 for both) in subsequent ECHOs, showing improvement in cardiac status and LV function {Ejection Fraction (EF) 28.17% to 43.31%, p-value=0.002} with normal coronary angiography.

Conclusion: Diagnosis of cardiotoxicity, following scorpion sting, is challenging on ECG. In present study, LV dimensions on serial 2D ECHO were studied. After the sting, LV dysfunction occurs initially and it is completely reversible on subsequent serial ECHO.

Keywords: Echocardiography, Ejection fraction, Left ventricular dysfunction

INTRODUCTION

Scorpion sting is prevalent globally but it is more common in villages. Morbidity and mortality of scorpion sting is a major occupational health problem for farmers in rural India. Annual number of worldwide scorpion stings is estimated to be 1.2 million [1]. In rural Indian settings there is a lack of diagnostic facilities so ECG was supposed to be the only test to diagnose cardiotoxicity. Pathophysiology of scorpion sting is still not clearly understood. In few studies the pathophysiology of scorpion sting envenomation has been studied using neurotransmitters studies, radioisotope studies, and ECHO and haemodynamic patterns [2-6].

Few researchers have used Electrocardiogram (ECG) which showed tachycardia, bradycardia or ventricular premature beats [7], pulmonary angiography or cardiac Magnetic Resonance Imaging (MRI) to study the events after envenomation which showed toxic myocarditis and pulmonary oedema [8]. It must be noted that MRI and angiography were presented as case studies. Very few researchers have performed Echocardiography (ECHO) as a part of their routine investigations where they found few patients with reduced Ejection Fraction (EF) [9]. It must be noted that earlier ECHO or MRI reports on scorpion envenomation are cross sectional and there are no serial ECHO reports to measure the cardiac recovery. Earlier report in the same region of Konkan has documented cardiotoxicity in the form of reduced EF responding to inotropic drugs [3,10]. Researchers have tried various ways of investigations to unfold the pathophysiology in scorpion sting patients. A 2017 report [11], repeated Cardiac Magnetic Resonance (CMR) assessments done among subjects with scorpion sting induced toxic myocarditis, found a possible irreversible and subclinical myocardial damage. Cardiotoxicity has been observed by Bawaskar HS and Bawaskar PH by tracing ECG in these patients [2]. Karnad DR, measured pulmonary artery wedge pressures [4]. Since the advent of scorpion antivenom, vasodilators, dobutamine and intensive care facilities, the fatality due to severe scorpion sting has been significantly reduced in areas where these treatment modalities are available. But inspite of advances in pathophysiology and therapy, the mortality remains high in rural areas due to lack of access to medical facilities and superstitious beliefs [12]. Moreover, the medical attendees from developing, tropical countries may not be aware of the advances in the treatment of scorpion sting [2]. Hence, study was done on pathophysiology of envenomation using serial 2D ECHO on day 1, 3 and 5 of hospitalisation to measure LV function and dimensions in patients with scorpion sting. A 2D ECHO was performed as it is a comparatively simple and non-invasive method to document the cardiotoxicity even in rural areas. On a small subset coronary angiography was performed to know the status of coronary vasculature. Cardiotoxicity progression or recovery on serial findings were studied.

BKL Walawalkar hospital is a charitable hospital, run by Shree Vithalrao Joshi Charitable Trust. It is located at Dervan village situated about 250 km from Mumbai. The area falls in the coastal region of Konkan. The tertiary care hospital was established in 1996. It caters to almost 25 lakhs population. Incidence of scorpion sting is high in this region with prevalence of prazosin-resistant cardiotoxicity [3]. The aim was to study serial changes of cardiac dimensions on ECHO in cardiotoxic scorpion sting patients.

MATERIALS AND METHODS

This study was a retrospective and cross-sectional analysis of 925 patients stung by scorpion, admitted from January 2011 to December 2017. Permission from Institute Ethics Committee (IEC) was obtained to extract the data from hospital records (IEC Letter no: 091/EC/755/INST/MH/2017/RR-18).

Inclusion and Exclusion criteria: All patients aged between 2 to 80 years admitted after being stung by scorpion were enrolled for the study. Patients not having ECHO record were excluded from study.

Methodology

All the patients had ECG recorded on the day of admission. As the hospital is located in a rural area having high prevalence of scorpion stings, It is a routine protocol to perform ECG and 2D ECHO of all patients admitted to the hospital with scorpion stings. A 2D ECHO was repeated to check improvement in cardiotoxicity on day 3 and day 5 if the first ECHO showed cardiotoxicity. For the data analysis, all the patients were classified into three groups [3] based on their clinical manifestations and ECHO findings:

Mild envenomation: Those with local pain, tingling, sweating and vomiting with no cardiovascular symptoms.

Moderate envenomation: Signs of mild envenomation with profuse sinus tachycardia, tall 'T' waves on ECG, reduced Left Ventricular (LV) function on 2D ECHO/global hypokinesia, hypertension, hypotension, Left Ventricular Failure (LVF) (Killip's class I and II) [10].

Severe envenomation: Signs of moderate envenomation with pulmonary oedema, severe LV dysfunction.

Each patient from moderate and severe envenomation group also underwent 2D ECHO on day 3 and day 5, if found to have cardiotoxicity on first ECHO. All patients were treated in Intensive Care Unit (ICU) with oxygen, dobutamine, diuretics, ventilation as per the requirement. In a few patients, coronary angiography was performed to study the status of coronary circulation.

STATISTICAL ANALYSIS

Statistical analysis was performed using Statistical Package for the Social Science (SPSS) version 21.0 (SPSS Inc., Chicago, USA). Data has been presented as mean and standard deviation for all the ECHO measurements. All the ECHO variables (Left ventricular systolic, Left ventricular diastolic, EF) measured on 2 or 3 occasions (day of admission or day 1, day 3 and day 5) were tested for normality using Shapiro-Wilk test. The difference between two successive measurements was tested by paired t-test. Generalised Linear Model (GLM) command was used for repeated measurements. In case of three repeated measurements Bonferrroni adjustment for multiple comparisons was done. Age was used as a covariate in all the analysis. The p-values ≤0.05 were used as a cut-off for statistical significance.

RESULTS

Total 925 patients with scorpion sting were admitted to the hospital during the year January 2011 to December 2017. Total 11 patients died after admission. Remaining 914 patients underwent various investigations such as ECG, 2D ECHO as a part of routine check-up as a protocol of the hospital. There were 245 moderate and severely envenomated patients. Out of them 81 patients had a complete record of 2 serial echocardiograms done on admission and on day 3. Out of these 34, were moderate and 47 were severely envenomed patients. Twenty patients had 3rd ECHO done on day 5. Median age of the patients was 16 years with a range (2-80 years). There were 53 female and 28 male patients. The median age and range were 20 years (3-80) for females and 14 years (2-67) for males.

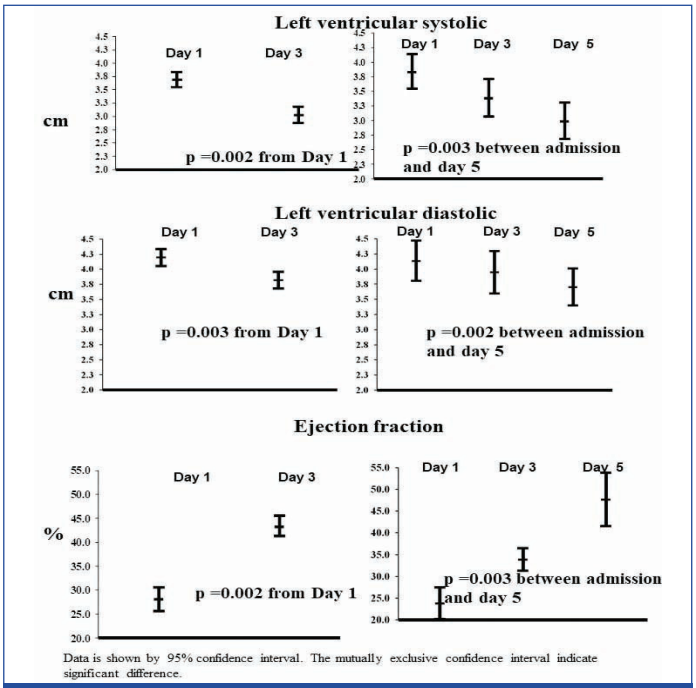
Left Ventricular (LV) dimensions were increased with global hypokinesia, mild to moderate mitral regurgitation and reduction in EF was observed in cardiotoxic scorpion sting patients on admission. However, on subsequent ECHO on day 2, 3 and day 5 there was significant reduction in LV size (3.69 cm to 3.025 cm for systolic and 4.19 cm to 3.82 cm for diastolic, p-value <0.001 for both). This was accompanied by improvement in LV function (EF 28.17 % to 43.31%, p-value=0.002). In a small set of 20 patients with subsequent ECHO on day 5, there was further statistically significant reduction in LV size and improvement in LV function [Table/Fig-1-3].

ECHO	Left ventricular systolic (cm)	Left ventricular diastolic (cm)	Ejection fraction %
Admission	3.69 (3.55, 3.83)	4.19 (4.05, 4.34)	28.17 (25.85, 30.49)
Day 3	3.025 (2.88, 3.18)	3.82 (3.68, 3.96)	43.31 (41.21, 45.42)
p-value for difference adjusted for age	0.002	0.003	0.002

[Table/Fig-1]: Comparison of ECHO measurements (n=81).
Statistical difference was tested using paired t-test. Mean (95% confidence interval); p-values <0.05 was considered statistically significant

ECHO	Left ventricular systolic (cm)	Left ventricular diastolic (cm)	Ejection fraction %
Admission	3.84 (3.54, 4.13)	4.14 (3.80, 4.47)	23.82 (20.21, 27.43)
Day 3	3.38 (3.07, 3.70)	3.95 (3.59, 4.30)	33.88 (31.31, 36.44)
Day 5	2.99 (2.68, 3.31)	3.70 (3.40, 4.01)	47.62 (41.51, 53.74)
p-value for difference between admission and day 5 adjusted for age	0.003	0.002	0.003

[Table/Fig-2]: Comparison of ECHO measurements (n=20) on day 5.
Statistical difference was tested using generalised linear model taking into account multiple comparisons; Mean (95% confidence interval); p-values <0.05 was considered statistically significant

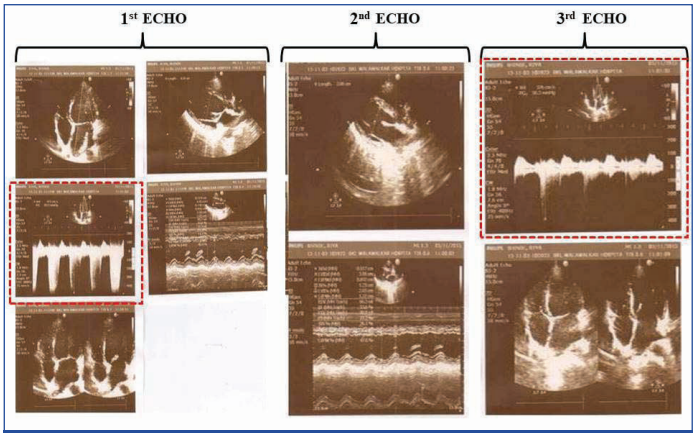


[Table/Fig-3]: Graphical representations of ECHO measurements.

There was gradual improvement in LV dimensions; gradient of mitral regurgitation in three consecutive ECHOs images in a case of cardiotoxic scorpion sting [Table/Fig-4]. Coronary angiography was performed before discharge in six severely envenomed patients and no abnormalities were detected.

DISCUSSION

Scorpion sting is a public health hazard in western Maharashtra, with 30 to 40% mortality in the past [7]. The people rely more on traditional healers. Only those who have symptoms, not relieved by traditional healers are referred to hospitals. Availability of ECHO and cardiac catheter laboratory is also challenging but the study centre has these facilities. Scorpion stings also have seasonal variability [3].



[Table/Fig-4]: The subsequent ECHO cardiograms showing significant reduction in Left Ventricular (LV) dimensions and mitral regurgitation.

Scorpion envenomation by the Indian red scorpion, Mesobuthus tumulus is a common sight in rural India [7]. This venomous scorpion belongs to the Buthidae family and is distributed in warmer parts of the world. Majority of deaths following scorpion envenomation occur due to cardiovascular dysfunction [13].

Mild envenomation results in severe vasoconstriction leading to hypertension [14], while the severe ones show LV dysfunction, with increased pulmonary wedge pressure and pulmonary oedema [13-15]. This leads to persistent depolarisation of autonomic nerves with release of neurotransmitters from the adrenal medulla and parasympathetic and sympathetic nerve endings (the autonomic storm). These neurotransmitters are largely responsible for the toxic cardiovascular manifestations [5]. Effect of excess catecholamine can be documented on 2D ECHO [3]. In a Turkish child, it was noticed that excessive catecholamine release led to impairment in LV contractility which was persistent for a few hours and LV function became normal after a few weeks [16]. Mishra OP and Prasad R, also emphasises the role of ECHO in all patients with moderate to severe envenomation to forecast outcome and decision about discharge policy [17].

In the present study, all of the cardiotoxic patients had dilated LV, global hypokinesia with reduced EF and mild to moderate mitral regurgitation on day 1. The size of the LV reduced gradually from day 3 to day 5 on serial echocardiograms. Mitral regurgitation disappeared and the EF improved in the last ECHO. These findings are consistent with the report of the Turkish child [16] and the study by Mishra OP and Prasad R [17]. There are a few case reports where abnormal angiographic findings were documented as patients developed acute myocardial infarction post-envenomation [18,19]. In the present study, only six patients underwent coronary angiography before discharge and they had normal angiograms. Authors were unable to perform coronary angiography on admission in cardiotoxic envenomated patients as they were critically ill and had hypotension.

As per the study by Bawaskar HS and Bawaskar PH due to continuous prolonged stimulation of sodium neuronal channels by Mesobutus Tamulus venom there was down regulation of cardiac neuronal sodium channels thus manifesting into Brugada syndrome in scorpion sting cases [2]. Karnad DR demonstrated haemodynamic patterns in severe envenomation [20]. More severe cases showed LV dysfunction, with increased pulmonary wedge pressure and pulmonary oedema. Sodium and potassium channel toxins of scorpion venom are responsible for depolarisation of autonomic nerves and causing release of autonomic neuromuscular neurotransmitter evoking an autonomic storm [6,21]. In an experimental study, sustained catecholamine decrease was recorded despite re-envenomation. Prolonged or repeated sympathetic stimulation is blunted because of exhaustion of the catecholamine store [22]. In a young Italian woman CMR assessments performed on (11 days; 3, 9 and 15 months), revealed a possible irreversible and subclinical myocardial damage [11].

The present study reveals ECHO findings of scorpion envenomation in cardiotoxic scorpion stings. This study documented that severely envenomated patients have severe tachycardia and tall T-waves on ECG, severe LV dysfunction (global hypokinesia) on 2D ECHO with mild to moderate mitral regurgitation. There was gradual improvement in EF of left ventricle on serial ECHO recordings after dobutamine infusion. Exhaustion of catecholamines due to excessive beta stimulation is documented by reduced EF with preserved cardiac muscle thickness. Coronary blood flow on angiography was normal without any myocarditis or coronary spasm. Gradual improvement in LV dimensions and EF with preserved cardiac muscle thickness on ECHO observed in our study reveals that effect of venom is only at the receptor level and cardiotoxicity is completely reversible.

Limitation(s)

It was a retrospective and cross-sectional study and was not hypothesis driven. Only 2 serial echocardiographs measurements were available for 81 patients, and 3 serial measurements for 20. Thus, there has been survival as well as selection bias while analysing such small numbers. Also, Generalised Linear Modeling (GLM) with repeat measurements enables us to do multiple time point comparisons with appropriate corrections. Parametric analysis approach was used considering the wide age range of patients so that age could be used as a covariate.

CONCLUSION(S)

In rural areas, cardiotoxicity due to scorpion sting is usually diagnosed on ECG. But in the present study ECHO was found to confirm the cardiotoxcity on the basis of increased LV dimensions and reduced EF. Subsequent repeat echocardiograms were also found to be beneficial in knowing the improvement in cardiac status. It was also revealed that there is complete reversal of LV dysfunction on subsequent ECHO performed during treatment. A 2D ECHO can diagnose cardiotoxic scorpion stings and it can be repeated many times thus giving information about the current cardiac status, EF and recovery. This will enable the treating physician to plan the treatment protocol, ambulation policy in critically ill patients and will also help to design the discharge policy.

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