Efficacy of Species Specific Anti-scorpion Venom Serum (AScVS) against Severe, Serious Scorpion Stings (Mesobuthus tamulus concanesis Pocock) — An Experience from Rural Hospital in Western Maharashtra

VS Natu*, RKK Murthy**, KP Deodhar***

Abstract

Background: Death caused by scorpion envenoming is a common event in the tropical and subtropical countries including many regions in India. Severe scorpion envenoming causes an autonomic storm producing multi-system organ-failure (MSOF) and death.

Objectives: To determine the efficacy of Anti-scorpion venom serum (AScVS) in patients stung by scorpions (Mesobuthus tamulus concanesis Pocock – earlier called Buthus tamulus); to compare it with other modalities of therapy and to detect complications, if any, arising out of AScVS treatment.

Methods: Total 48 patients of severe, serious scorpion envenoming syndrome were studied during the period from 1992 to 2002. In 17 patients AScVS was the only mode of treatment. Others had received adjunctive therapy along with AScVS.

Results: 47 patients out of 48 scorpion sting victims recovered completely. Recovery period in patients given AScVS (10 hours) was faster than those who received alpha blockers (16-42 hours). No anaphylactic reaction with AScVS was observed.

Conclusions: AScVS is effective and safe method of therapy in severe scorpion envenoming syndrome.

INTRODUCTION

Death due to severe scorpion envenoming syndrome is a common event in the developing tropical and sub-tropical countries of Africa, Latin America, China, India and the Middle East. All over the world there are about 650 species of scorpions that belong to 6 families. Buthidae is the largest family of the scorpions with the most toxic species such as the Androctonus, the Buthus, the Centruroides, the Leiurus quinquestriatus and the Tityus.

India harbors 99 scorpion species from six families, of which 45 species belong to Buthidae family. The venomous scorpions of Buthidae are responsible for a number of deaths in infants, children and adults. These killer scorpions are geographically distributed all over the length and breadth of India. In spite of zoological differences resulting in venoms of differing chemical structure, the signs and symptoms following stings by scorpions of Buthidae from all over the world are remarkably similar.

Severe scorpion envenoming causes an autonomic storm with massive release of catecholamines. The symptoms and signs are vomiting, profuse sweating, absence of pain to severe excruciating pain at the site of the sting, increased salivation, generalized tingling & numbness, priapism, tachycardia, tachypnoea, transient hypertension followed by hypotension and pulmonary edema.

The earlier experimental studies on scorpion (Mesobuthus tamulus concanesis Pocock) envenoming demonstrated cardiac sarclemmal defects displayed by alterations in Na’-K’ ATPase, Mg++ ATPase and Ca++ ATPase activities. Initial transient hypertension followed by hypotension and shock, glycoenolysis in atria, ventricle, liver and skeletal muscle, hyperglycemia, increased free fatty acid levels and reduction in...
triglyceride levels, altered erythrocyte Na⁺-K⁺ ATPase activities resulting in osmotic fragility changes of red blood cells, involvement of exocrine pancreas causing acute pancreatitis, changes in insulin levels (hypoinsulinemia followed by hyperinsulinemia), increased glucagon, thyroid hormones (T₃, T₄), cortisol, angiotensin II levels; increased clotting time, Prothrombin time, thrombin time, partial thromboplastin time with kaolin, decrease in fibrinogen and acute reduction in platelet count, absence of factors V, VII and VIII in envenomed animals indicative of DIC, reduced partial pressure of oxygen, bicarbonate, changes in PH (acidosis), increased lactic acid and ketoacid levels, are also demonstrated. All these changes in scorpion envenoming indicate the involvement of multiple systems and organs and their failure along with cardiogenic pulmonary edema and Adult Respiratory Distress Syndrome (ARDS).

Experimental study shows that antivenom administration resulted in reversal of ECG changes and reduction in LDH, SGOT, SGPT, CK-MB and alpha HBDH enzyme levels. AScVS without any adjunctive therapy caused the return of normal blood pressure from hypertensive levels, prevented a further rise in blood pressure; maintained blood pressure and prevented the occurrence of hypotension. Additionally, AScVS caused the return of normal blood pressure from hypotension, maintained blood pressure and prevented the occurrence of hypotension and hypertension. If the antivenom did not inhibit the catecholamine-mediated toxicity, which in turn suppressed the release of insulin secretion it would have resulted only the arrest of a further rise in hyperglycemia and FFA concentration. The attainment of normal blood glucose level and lipogenesis following antivenom therapy in the experimental animals indicated that the antivenom effectively neutralized the inhibiting action of catecholamines on insulin secretion. This resulted in physiologically active insulin secretion.

AScVS was available in few countries. Haffkine Biopharmaceutical Corporation Ltd. (Mumbai) manufactured AScVS, conducted clinical field trials in 1992 and marketed it in 1997. Now with the free availability of antivenom, more rational treatment is use of AScVS to neutralize the venom present in the circulation and body fluids.

AScVS is lyophilized monovalent enzyme refined immunoglobulins specific for the scorpion Mesobuthus tamulus concanensis Pocock. 1 ml. of AScVS neutralizes 1 mg. of dried scorpion venom. Usual mode of AScVS administration is either by i.v. or i.m route. Scorpion antivenins are rather species specific.

The toxicity of venom, collected from a scorpion, depends on age of the offending scorpion, season of the year; and the age, sex and weight of the scorpion stung victim. The amount of venom injected in to a victim is variable in scorpion stung patients. Therefore the dose of AScVS has to be increased till the symptoms are abolished. If the sufficient dose of antivenom is used, adjunctive therapy is seldom required. Previously mortality rate following scorpion envenoming syndrome was 25-30%, with the use of alpha blocker therapy the mortality has reduced to 2-5%, but recovery time varies from 16-42 hours and close monitoring for 48 hours is necessary as patient may develop pulmonary edema even after administration of alpha blocker (Prazocin). The long stay of the venom in the body explains the development of pulmonary edema even after administration of alpha blockers and indicates the importance of neutralization of scorpion venom by AScVS. This study assessed the use of AScVS in 48 severe scorpion sting cases.

**MATERIAL AND METHODS**

48 patients of scorpion sting treated with AScVS were studied prospectively. Confirmation of the species of the killer scorpion was made by identification of the preserved specimen. It was diagnosed on clinical presentation in one case of unknown sting. An adult male gave a history of passing of thick secretions like ejaculation, before the act of passing urine.

Blood pressure, temperature, pulse and respiratory rate were recorded on admission and after completing the dose of AScVS. ECG was recorded in 15 cases at 4 and 8 hours after AScVS. All cases were given AScVS developed by Haffkine Biopharmaceutical Corporation Ltd; Mumbai (Batch no-110, 402-1, 403-1). 10 ml. Sterile Water for injection was used for reconstitution of one vial of AScVS. Informed consent was taken for AScVS treatment.

AScVS test dose was given on forearm. Patient was observed for hypersensitivity reaction to antivenom for 15 minutes. 3 ml of reconstituted AScVS was injected i.m. every 15minutes and the contents in one AScVS vial were given in an hour. AScVS was given as slow i.v. bolus in severe cases of pulmonary edema with haemoptysis and cardiac arrhythmias. Patient was assessed clinically again after administration of one vial of AScVS. 2nd, 3rd and 4th vials of AScVS were injected depending upon severity of envenomation.

Inj. antihistamines and steroids were given along with AScVS (10 cases) till the year 2000. AScVS alone was given in 17 cases out of which 4 cases were before 2000, but after the year 2000, AScVS alone was used to start the treatment and 2-3 vials were injected one after another in critically ill victims, and was found to be sufficient in 13 cases.

Adjunctive supportive therapy like inj. lasix, inj. Aminophylline with glucose, steroids and oxygen were used along with AScVS in another 10 patients of pulmonary edema.
In 11 cases, Prazosin was already given at peripheral primary health centre, and these patients were referred here as early improvement was not seen. These patients were then given AScVS and adjunctive treatment of inj. lasix, aminophylline and glucose. Prazosin was not repeated in our study.

Local anesthesia at the site of sting was necessary in 3 pediatric cases. These patients complained of severe pain after systemic recovery.

Attainment of normal pulse rate from tachycardia; warm extremities in cases of perspiration and cold clammy skin; blood pressure reaching normal levels in scorpion stung patients in whom the earlier blood pressure at the time of admission was low and sometimes not recordable; blood pressure reaching normal levels in whom there was hypertension; normal respiratory rate in patients with tachypnoea; and increasing pain at the site of the sting were considered as signs of improvement.

**RESULTS**

Total 48 cases were studied. 24 patients of scorpion sting reported within 2 hours, 14 patients reported within 4 hours and rest 10 patients within 4 to 8 hours. Pulse, respiratory rate, blood pressure and coldness of extremities were recorded on admission (Table 1).

Blood pressure was not recordable in 12 pediatric patients. Priapism was seen in 6 cases, (adults as well as in pediatric age group). Complete improvement was seen in 2 hours in pediatric age group. Overall 41 out of 48 patients recovered completely within 12 hours (Table 1).

In the present study one vial of AScVS (one vial of lyophilized AScVS was reconstituted with 10 ml. Sterile water) was sufficient in 28 cases. 20 ml. were required to neutralize the venom in 9 cases. 30 ml. in 9 cases, 60 ml. and 80 ml. were required in one case each.

**Table 1 : Year-wise distribution of scorpion sting victims**

<table>
<thead>
<tr>
<th>Year</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991-92</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>1997-2002</td>
<td>21</td>
<td>22</td>
</tr>
</tbody>
</table>

**Age-wise distribution of scorpion sting victims.**

<table>
<thead>
<tr>
<th>Age</th>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td>Upto 12 years</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>12-30 years</td>
<td>07</td>
<td>09</td>
</tr>
<tr>
<td>Above 30 years</td>
<td>08</td>
<td>03</td>
</tr>
</tbody>
</table>

ECG showed improving pattern 4 hours after AScVS. Ectopics disappeared within 2 hours of AScVS in an 11 year old female patient.

Patient with severe perspiration with cold extremities started showing improvement within 4 hours.

Eight out of 11 patients of severe tachycardia (H.R>120/min) had normal heart rate at the end of 12 hours after AScVS. 4 out of 11 patients had received prazocin before coming to this hospital.

There were 8 patients with severe hypertension (B.P.>160/100 mm of Hg). Out of these, two young patients showed early recovery within 6 hours. Five patients improved within 12 hours and one after 16 hours. One patient out of these 8 patients had received prazocin at periphery.

Most of the tachypnoea patients with fine crepitations had normal respiratory rate within 12 hours. Four patients had severe pulmonary edema with frothing. Two out of these 4 cases of pediatric age group showed early improvement within 6 hours.

None of the patients had anaphylactic reaction. One Patient had rash behind left ear and back. Other Patient had allergic rash all over the body and itching. None had severe, rash which subsided after injecting dexamethasone and antihistaminic drugs.
DISCUSSION

Scorpion envenoming causes release of massive amount of catecholamines, (epinephrine and norepinephrine) and suppresses insulin secretion. This causes lipolysis and results in increased FFA levels, which are arrhythmogenic in nature. Excessive sympathetic and parasympathetic stimulation causes severe perspiration, severe vasoconstriction of medium sized arterioles, myocardial dysfunction and pulmonary edema.

About 20 years ago treatment of scorpion sting was symptomatic and consisted of inj. Atropine for perspiration and inj. lasix and steroids for pulmonary edema. In the last 15 years, with better understanding of pathophysiology, the treatment is now directed towards correcting hormonal imbalance.

Insulin allows the incorporation of fatty acids into triglycerides in the liver and in adipose tissues. Glucose infusion along with insulin suppresses fat mobilization by favoring re-esterification.

The alpha blocker treatment is directed towards neutralizing the effects of over-stimulated autonomic nervous system. Prazosin is an alpha adrenoreceptor antagonist and stimulates insulin secretion.

The results in this study confirm that scorpion antivenom directly neutralizes the venom in the circulation as well as present at the other body compartments.

In an experimental study after administration of intravenous Tc-99m labeled venom, the venom was found in the blood (28%), muscle (30%), bone (13%), kidney (12%), and liver (11%) within 5 minutes. The labeled venom was excreted through renal and hepatobiliary pathways. The maximum renal uptake of 32% at 30 minutes dropped to 22% at 3 hours, indicating that clearance of labeled venom from the kidney is slow. The scorpion venom has a half-life of 24 hours, indicating that clearance of labeled venom from the kidney is slow. The alpha blocker treatment is directed towards neutralizing the effects of over-stimulated autonomic nervous system. Prazosin is an alpha adrenoreceptor antagonist and stimulates insulin secretion.

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It is concluded that AScVS therapy directly neutralizes the venom in the circulation and other body compartments. Anaphylactic reaction is not seen and seems unlikely. It is rational, effective and safe method of therapy in severe scorpion envenoming syndrome. Further multicentre randomized clinical trials are necessary to confirm the superiority of AScVS therapy.
REFERENCES


18. Freire-Maia L, De Matos IM. Heparin or PAF antagonist (BN-52021) prevents the acute pulmonary edema induced by Tityus Serrulatus scorpion venom in the rat. Toxicon 1993;31: 1207-10.

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Announcement

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