Severe envenoming by the Indian red scorpion Mesobuthus tamulus: the use of prazosin therapy

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Summary
We describe the clinical course and outcome in 46 victims of severe scorpion envenoming treated with prazosin (P), and compare them with earlier patients treated with conventional therapy (C) (n = 45) and nifedipine (N) (n = 28). The incidence of complicating left ventricular failure was 29% for C, 35% for N and 6.5% for P; that of acute pulmonary oedema was 46% for C, 14% for N and zero for P; mortality was 25% for C, 3.5% for N and zero for P. Although this is a historical study, prazosin appears to significantly reduce morbidity and shorten recovery time. Experience in other countries suggests that antivenom is helpful in controlling many of these problems, but in rural India serotherapy remains largely unavailable, and prazosin is a mainstay of treatment.

Introduction
Scorpion envenoming is common in many parts of the world, inducing an autonomic storm and hypercatecholaemia. In the Mahad region of India, envenoming is usually from the Indian red scorpion Mesobuthus tamulus, and mortality was once as high as 30%. Our clinic has treated envenoming and its complications since 1976, and has used prazosin, a post-synaptic alpha blocker, since 1984. Serotherapy, although established in Brazil and Saudia Arabia, is still experimental in India.

Methods
Our clinic is the sole referral centre for the Mahad region. The town (pop. 20,000) is 210 km south of Bombay, and some 500 villages are also served by the clinic. We retrospectively analysed the records of severely envenomed victims admitted from 1976 to 1995. Severe envenoming was characterized by features of an autonomic storm with vomiting, profuse sweating, hypersalivation, priapism in males, puffy face, parasternal lift, cardiac arrhythmias, cool extremities, limited local pain at sting site, and ECG changes suggestive of myocardial infarction. All treatment groups were given oral rehydration solution to correct the hypovolaemia induced by sweating, salivation and vomiting, and diazepam to relieve anxiety where necessary.

Results
All victims exhibited the above signs soon after envenoming. Reappearance of pain at the sting site was accompanied by improved tissue perfusion, reduced cardiovascular symptoms and a rise in skin temperature as vasoconstriction eased. The clinical data are summarized in Tables 1 and 2.

Conventional treatment
Conventional treatment was with digoxin, frusemide, hydrocortisone i.v., antihistamines and subcutaneous atropine 0.3 mg. Of 45 patients (28 male, 17 female), 39 (86%) were hypertensive on arrival, 38 (85%) had tachycardia with a loud gallop, 32 (71%) had grade 2/6 systolic murmur. Within 12 h, all had marked tachycardia, cool extremities, grey pallor, low-volume fast thready pulse, peripheral cyanosis.

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Table 1  Patient characteristics on admission

<table>
<thead>
<tr>
<th>Treatment...</th>
<th>Conventional</th>
<th>Nifedipine</th>
<th>Prazosin</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>45</td>
<td>28</td>
<td>46</td>
</tr>
<tr>
<td>Males</td>
<td>28 (62%)</td>
<td>19 (68%)</td>
<td>30 (65%)</td>
</tr>
<tr>
<td>Setting</td>
<td>Intensive care</td>
<td>General</td>
<td>General</td>
</tr>
<tr>
<td>Age (years)</td>
<td>20 (2.5–6.7)</td>
<td>23 (2–70)</td>
<td>21 (3–70)</td>
</tr>
<tr>
<td>Time from sting to admission (h)</td>
<td>4.5 (1–20)</td>
<td>3 (1–10)</td>
<td>4.5 (1–19)</td>
</tr>
<tr>
<td>Blood pressure*</td>
<td>122 (97–163)</td>
<td>129 (97–167)</td>
<td>118 (97–137)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>39 (86%)</td>
<td>28 (100%)</td>
<td>40 (87%)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>7 (16%)</td>
<td>10 (36%)</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>38 (85%)</td>
<td>18 (64%)</td>
<td>35 (79%)</td>
</tr>
<tr>
<td>Heart murmur</td>
<td>32 (71%)</td>
<td>16 (57%)</td>
<td>31 (67%)</td>
</tr>
<tr>
<td>Priapism (in males)</td>
<td>24 (85%)</td>
<td>19 (100%)</td>
<td>25 (83%)</td>
</tr>
</tbody>
</table>

* Diastolic plus one-third systolic.
Data are medians (range) where appropriate.

Table 2  Complications and outcome

<table>
<thead>
<tr>
<th>Treatment...</th>
<th>Conventional</th>
<th>Nifedipine</th>
<th>Prazosin</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>45</td>
<td>28</td>
<td>46</td>
</tr>
<tr>
<td>Left ventricular failure</td>
<td>13 (29%)</td>
<td>10 (35%)</td>
<td>3 (6.5%)</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>21 (46%)</td>
<td>4 (14%)</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>11 (25%)</td>
<td>1 (3.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Full recovery</td>
<td>34 (75%)</td>
<td>27 (96%)</td>
<td>46 (100%)</td>
</tr>
<tr>
<td>Recovery time (h)*</td>
<td>37 (10–72)</td>
<td>18.5 (10–36)</td>
<td>11 (6–20)</td>
</tr>
</tbody>
</table>

* Medians (range).

and tachypnoea. Acute left ventricular failure developed in 13, of whom 12 recovered with aminophylline i.v., frusemide, sublingual isosorbide dinitrate and 2.5 mg chlorpromazine i.v. Massive pulmonary oedema with haemoptysis developed in 21, and was treated with sodium nitroprusside i.v., successfully in 11. Eleven (25%) patients with persistent pulmonary oedema died (one with left ventricular failure, ten with pulmonary oedema), generally from ventricular arrhythmias and cardiac arrest, with evidence of progressive myocardial injury, fascicular block, left bundle branch block, low voltage pattern, widened QRS, ventricular tachycardia and fibrillation. None responded to DC cardioversion.

Nifedipine

These patients (n=28, 19 males) were given 5 mg oral nifedipine in liquid form on admission. Eighteen (64%) had tachycardia, of whom 16 (57%) had gallops or systolic murmur grade 2/6. Blood pressure and heart rate were monitored every 5 min for 30 min, then every 30 min for 3 h. Irrespective of blood pressure control, 13 recovered uneventfully, and 15 patients remained tachycardic. Ten of these developed left ventricular failure, five acute pulmonary oedema. They were treated with aminophylline i.v., oxygen and oral prazosin. Only one died.

Prazosin

These 46 patients (30 males) were given 500 µg prazosin (250 µg for children) on admission, repeated six-hourly until symptoms of tissue perfusion and cardiovascular signs improved. Clinical parameters were monitored every 30 min for 4 h. On admission, 40 (87%) were hypertensive, 35 (76%) had tachycardia, and 31 (67%) had systolic murmur or gallops. After 2 h, only two patients were still in tachycardia, with breathing difficulties and low-volume pulse. They were given i.v. aminophylline and another dose of prazosin, and recovered. The return of pain at the sting site is much greater with prazosin than with the other two treatments, and may require local anaesthetic or oral analgesic.

Discussion

The severity of envenoming in our three treatment groups was similar, and although our study is historical, the results suggest that prazosin therapy may...
have real advantages in treatment of red scorpion envenoming, the cardiovascular complications of which often produce medical emergencies in the Mahad region of India. Similar modes of scorpion poisoning have been reported in Israel, Brazil, Saudi Arabia and Mexico. Scorpion venom activates sodium channels, causing excessive neurone activity.\(^8\) Charybdothins, a blocker of calcium-activated potassium channels, is found in the venom of the Israeli scorpion *Leirus quinquemaculatus,\(^9\) and iberiotoxin from *M. tamulus* venom may have similar effects.\(^10\)

The pathogenesis of cardiac involvement is poorly understood,\(^11\) but may result from a hypercatabolic state causing increased myocardial oxygen demand.\(^12,13\) Drugs such as digoxin, atropine, diuretics, dopamine and antihistamines may therefore increase myocardial oxygen consumption and worsen the situation. The limited use of such drugs in the prazosin group may have contributed to improved outcome.

Nifedipine, a slow calcium-channel blocker, causes reflex tachycardia and has a negative inotropic effect, and for this reason is no longer used to control blood pressure where there is risk of acute cardiac failure. This is particularly important in a rural setting without intensive care facilities. It may however have some use in treating hypertensive encephalopathy following scorpion sting.\(^14\)

Prazosin is an alpha-1 blocker. Alpha adrenergic receptors are important in the pathogenesis of pulmonary oedema due to scorpion sting.\(^15\) Prazosin reduces preload and left ventricular impedance without raising heart rate or renal secretion.\(^16\) It also counters the action of angiotensin II liberated in the myocardium,\(^17\) and the vasoconstriction caused by endotoxins.\(^18,19,20\) In rabbits, prazosin pretreatment reduced histological damage from noradrenaline i.v. where alpha-2 blockers did not.\(^21,22\) Prazosin also counteracts the suppression of insulin excretion by scorpion venom,\(^23\) thus helping to reverse the metabolic changes (hyperkalaemia, hyperglycaemia,\(^24,25\) energy deficit\(^26\) which are associated with cardiac arrhythmias.\(^27,28\) Thus prazosin is both cardioprotective and an antagonist to the toxicological effects of scorpion venom.

Although there is evidence from Brazil\(^29,30\) and Saudi Arabia\(^31,32\) that antivenom can reduce pain and vomiting, and the incidence of cardiorespiratory complications, this treatment is not presently available to our clinic. It may also be argued that antivenom is not directly cardioprotective, and that in cases where its administration has been delayed and some haemodynamic disturbance has already occurred, prazosin may be useful in speeding recovery. In view of the advantages of prazosin over the earlier treatments we have described, we believe a placebo-controlled trial to be unethical. However, a trial of antivenom versus prazosin might well be of interest.

References


21. Lee JC, Spoonenburg DP. Role of alpha adrenerceptors in


