Management of Scorpion Envenomation: Need For A Standard Treatment Protocol Using Drugs and Antivenom

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Scorpion venoms are a complex mixture of proteins. The short chain peptides (22 to 47 amino acids) interfere with the function of potassium ion channels while long-chain peptides (59 to 76 amino acid residues) modify the channel gating properties of the sodium channel. Other venoms identified include those that act on the calcium and chloride ion channels, hyaluronidases, lysozymes and phospholipases. Many of the toxins act on ion channels that play an important role in maintaining resting membrane potential of excitable cells like neurons and myocytes. They produce persistent depolarization maintaining resting membrane potential of excitable cells like neurons and myocytes. They produce persistent depolarization and excitability. Central nervous system effects include irritability, muscle rigidity, altered consciousness and convulsions.

Scorpion envenomation following sting of the Indian red scorpion, Mesobuthus tumulus is a common emergency in several parts of rural India. This and all other venomous scorpions of clinical importance belong to the Buthidae family of scorpions, which are widely distributed in warmer parts of the old and new worlds. Majority of deaths following scorpion envenomation in most parts of the world occur due to cardiovascular dysfunction. Neurological complications are more common than cardiovascular manifestations after sting by scorpions of the Centruroides species found in North America, but also occur in a few cases stung by other species of scorpions, especially children. Hemodynamic and observational studies show that mild envenomation results in severe vasoconstriction resulting in hypertension. More severe cases have left ventricular dysfunction, with increased pulmonary wedge pressure and pulmonary oedema. Systolic as well as diastolic ventricular dysfunction has been demonstrated by echocardiography and radionuclide studies. In patients who are dehydrated due to sweating, vomiting or diuretic therapy, pulmonary edema may be absent but low cardiac output with hypotension may predominate. In well hydrated patients, blood pressure and cardiac output may be normal but pulmonary edema is prominent. The most severely affected patients present with low cardiac output, elevated pulmonary artery wedge pressures, pulmonary edema and severe cardiogenic shock.

While severe cases require intensive care, ICU facilities are commonly lacking in rural areas where scorpion stings are common. Fortunately, work of observant and enterprising physicians like Dr Bawaskar from Mahad, Maharashtra, have helped develop regimen involving use of vasodilators like the alpha-blocking drug prazosin, which can be easily used in primary care facilities. While afterload reduction will help reverse several of the cardiovascular derangements in mild (hypertensive) or moderate envenomation (pulmonary edema), it does little to improve cardiac contractility which is a major abnormality in patients with cardiogenic shock. Inotropic agents are required at this stage and the study by Patil et al in this issue of the journal shows how dobutamine is successful when used in these patients. Besides afterload and myocardial contractility, the need for attention to preload has been highlighted by our studies. Unless the patient is adequately hydrated, use of afterload reducing drugs or diuretics can cause precipitous hypotension. Inotropic drugs too may not achieve the desired hemodynamic effects in dehydrated hypovolemic patients.

The regimen commonly followed in our ICU involves proper restoration of fluid volume as the first step. Intravenous fluids are necessary in most patients. After fluid resuscitation, patients with a systolic arterial pressure > 90 mmHg receive oral prazosin or captopril for afterload reduction. Some patients who have improvement in pulmonary edema but a drop in blood pressure require further fluid infusion. Patients with severe envenomation and cardiogenic shock should not be treated with vasodilators; inotropic agents like dobutamine, or vasopressors like dopamine must be infused immediately and vasodilators introduced only after the shock is reversed. Few patients who have respiratory fatigue and exhaustion require mechanical ventilation. A recent report from Turkey describes the successful use of noninvasive ventilation in these patients; this could be tried in conscious patients who are not vomiting. While there is considerable data from uncontrolled studies showing that a protocol like this could reduce mortality, this has also been confirmed by two controlled studies using historical controls.

Despite drug therapy, mortality following scorpion envenomation remains high. Factors associated with increased mortality include age < 5 years, weight < 25 kg, long interval between envenomation and hospitalization, altered consciousness (GCS ≤ 8/15), azotemia, acidosis and leucocytosis (> 25000 cells/mm³).

Administration of scorpion antivenom to patients presenting with cardiovascular manifestations of envenomation has not been conclusively shown to be of benefit. While uncontrolled studies have shown promise, a large randomized controlled study in Tunisia failed to show any benefit of serotherapy. On the other hand, antivenom against the predominantly neurotoxic North American Centruroides species has been found to be useful in preventing morbidity and mortality. Experimental studies on...
pharmacokinetics of the venom show that the relatively small peptides are rapidly distributed in the blood and tissues, unlike polyvalent antibodies in antivenom. A recently concluded study showed that intravenous rather than intramuscular administration, and use of larger doses of commercially available antivenom against the Indian red scorpion may be of benefit (Natu VS, personal communication).

More recently, proteomic analysis using sophisticated chromatographic techniques and mass spectroscopy has been performed on venom of many species of scorpions including Tityus, Androctonus spp, and the Asian black scorpion (Heterometrus longimanus). This has spurred research to identify epitopes that could be targets for antibodies in antivenom. The efficacy of equine antivenom containing polyclonal antibodies has been disappointing. Use of smaller antibody fragments like the Fab or F(ab′)2 may hold the key to find specific antibodies that neutralize the toxins from scorpion venom. With faster redistribution in vascular and extravascular compartments, these smaller molecules may potentially be able to neutralize toxins at sites that were hitherto inaccessible. An effective equine F(ab′)2 antibody against Centruroides spp is already commercially available (Acramynin®) in Mexico. Research on development of a similar antibody against the cardiotoxic venom of Androctonus aurialis hector has already reached an advanced stage. Even smaller fragments of antibodies include single chain antibody fragments (ScFv) and nanobodies. Development of antivenom made from these novel antibody fragments which can be safely administered intravenously and devoid of risk of anaphylaxis or allergy may considerably reduce morbidity and mortality from scorpion envenomation in the near future. More importantly, prophylactic use of these antivenoms in patients stung by venomous scorpions could even prevent development of toxic manifestations. Ability to detect scorpion venom in serum or urine of envenomated victims could further aid in identifying patients who require serotherapy.

Research along these lines at premier Indian centers for immunology and vaccine research directed towards developing safe and effective antivenom preparations is the need of the hour. This would decrease the need for drug therapy and intensive care which are often inaccessible in rural areas.

References