Scorpion Envenoming – A Step Ahead

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Mesobuthus Tamulus, an Indian red scorpion, is a lethal species which flourishes all over India. A case fatality rate of 30% has been reported from the coastal regions of Maharashtra on account of acute refractory massive pulmonary edema consequent upon scorpion sting [1]. Medical scientists maintained a grim silence towards century-old life-threatening scorpion envenomation which afflicted farmers, laborers and villagers in large numbers. Subsequently, close clinical observations confirmed that vomiting, sweating, cold extremities and priapism in males are ominous signs which precede the development of life-threatening cardiac manifestations of scorpion envenomation [2]. In an attempt to reduce the severity and fatality of scorpion sting, various regimens – including lytic cocktail, insulin-glucose drip, beta-blockers, digoxin, diuretics, rotating tourniquets to extremities, and nifedipine – were tried with little success.

Scorpion venom is a cocktail of many toxins; majority of them are small peptide toxins which target the ion channels. Most lethal toxins that have the greatest medical consequence are the scorpion alpha toxins which consist of 61 to 76 polypeptides that bind to voltage-gated sodium channels on the human victim. Alpha toxin inhibits the inactivation of the neuronal sodium channels resulting in a prolonged depolarization and neuronal excitation. Other toxins in the scorpion venom act on potassium and calcium channels with negligible effects on humans [3]. Delayed closure of the neuronal sodium channels result in pouring of endogenous catecholamines (epinephrine and nonepinephrine) and other vasoactive peptide hormones such as neuro-peptide-Y and endothelin-1 [3]. Their simultaneous stimulation results in an 'autonomic storm' characterized by parasympathetic effects like vomiting, profuse sweating, salivation, priapism in males, bradycardia, hypotension, premature ventricular ectopics, and coronary sinus rhythm disturbances. Excessive respiratory secretions may cause early respiratory failure; these effects are often short lasting and less severe, usually seen soon after the sting. These effects can be decreased if scorpion antivenom (SAV) is administered within four hours of the sting [4]. High morbidity and fatality due to scorpion envenomation is associated with features of severe vasoconstriction, hypertension, tachycardia, cool extremities, increased myocardial impedance, myocardial injury, pulmonary edema, lethal sustained arrhythmias, and cardiogenic shock, due to long lasting sympathetic excitation [4,5]. Alpha receptor stimulation plays a important role in the pathogenesis of pulmonary edema due to scorpion sting, in addition to catecholamine-induced myocarditis (coagulation myocytolysis and contraction bands) [6] and myocardial ischemia due to coronary vasoconstriction and possibility of direct effect of venom on the heart [7].

Extensive clinical and hemodynamic studies of severe scorpion envenomation have confirmed that fatality is mostly due to refractory pulmonary edema [5]. In the year 1983, pulmonary edema was successfully treated with sodium nitroprusside drip at primary health centers (Eureka moment) [8]. However, since the advent of oral Prazosin – a post-synaptic alpha-1 receptor blocker – the fatality reduced substantially [9]. Prazosin reduces preload and left ventricular impedance without causing tachycardia (intact presynaptic receptors). Cardio-vascular effects of oral prazosin hemodynamically mimic the intravenous sodium nitroprusside (*sonide*) drip. Hence, prazosin is often called oral *sonide*. Its phospodiesterase inhibitory action results in cellular accumulation of cyclic GMP – an endothelin inhibitor, and insulin release from beta cells of pancreas rectifying the metabolic effects caused by excessive alpha receptor stimulation and circulating catecholamines. Cyclic GMP blunts the myocardial response to liberated circulating catecholamines. Prazosin is called physiological and pharmacological antidote to scorpion venom action [10]. Prazosin antagonizes the after-effects of venom-liberated catecholamines, and has no action on the venom *per se*. The venom deposited at the sting site acts like a depot, and gradually releases into the circulation. With oral prazosin, victims take 12 to 48 hours to recover, and during this period close monitoring in an intensive care unit is needed. Irrespective of oral prazosin, about 10% pediatric cases develop marked tachycardia, hypotension, pulmonary

edema and shock with warm extremities, which necessitates intravenous dobutamine, nitroglycerine and ventilator support for 24-96 hours [9,11]. However, since 2004, mono-specific SAV has been made available for clinical use. Recently, two successive scientific trials have confirmed that the simultaneous use of prazosin and SAV hastens the recovery, and further reduces the fatality to less than 1% in adults [12] and children [13]. It is important to note that antivenom will not be effective once severe envenomation develops, and the parasympathetic effects of venom are over [14].

Steroids enhance the necrotizing effects of circulating catecholamines which further damages the myocardium and worsens the clinical manifestations [9]. Antihistamines, by inhibiting the potassium channels, prolong the QT interval which may result in sudden unexpected death of a recovering patient, and therefore should be avoided [9]. Calcium channel blockers can further depress the myocardium and precipitate pulmonary edema, and also should be avoided [10]. Diuretics enhance the development of pulmonary edema and shock, and must be avoided in severe scorpion envenomation [15].

In this issue of *Indian Pediatrics*, Anand Kumar, *et al*. [16] confirmed that administration of scorpion antivenom and prazosin within 4 hours of sting can reduce the cardiovascular morbidity and mortality [16]. The authors have meticulously analyzed the clinical data, and identified the risk factors of myocardial dysfunction due to *Mesobuthus Tamulus* envenoming. Their study warned the treating doctors regarding early referral and early administration of SAV plus prazosin, and strict avoidance of steroids, antihistamines and diuretics. This paper further confirms that simultaneous use of prazosin and scorpion anti-venom is the mainstay of treatment of scorpion envenomation.

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