

Invited Article



Scorpion Sting :Update

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Abstract

Scorpion envenomation is an important public health hazard in tropical and sub-tropical regions. Envenomation by scorpions can result in a wide range of clinical effects, including, cardiotoxicity, neurotoxicity and respiratory dysfunction. Out of 1500 scorpion species known to exist, about 30 are of medical importance. Although a variety of different scorpion species exist, majority of them produce similar cardiovascular effects. Scientists and clinicians have studied patho-physiology of scorpion envenomation by critical observations of clinical, neurotransmitters studies, radioisotope studies, echocardiography and haemodynamic patterns. Regimen including scorpion antivenom, vasodilators, intensive care management have been tried to alleviate the systemic effects of envenoming. In spite of advances in patho-physiology and therapy the mortality remains high in rural areas due to lack of access to medical facilities, moreover the medical attendee from developing tropical countries may not be aware of the advances in the treatment of scorpion sting. 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 used.

"To him who devotes his life to science, nothing can give more happiness than increasing the number of discoveries, but his cup of joy full when the results of his studies immediately find practical application"

Louis Pasteur

Introduction

Scorpion envenomation is an occupational hazards for farmers, farm labors, villagers, migrating population and hunters. Except for *Hemiscorpius Lepturus*, all venomous scorpion species, belong to the large family *Buthidae*.¹ The most notorious ones are found in the genera *Buthus* (Mediterranean Spain to the Middle East), *Parabuthus* (western and southern Africa), *Hottentotta* (South Africa to south east Asia), *Tityus* (central America, south America and the Caribbean), *Leiurus* (northern Africa and middle East), *Androctonus* (northern Africa to southeast Asia), *Centruroides* (southern united states, Mexico, central America and Caribbean) and *Mesobuthus* (through out the Asia) (Figure 1).

Scorpions are generally found in dry, hot environments, although some species also occur in forest and wet savannas. All species are nocturnal, hiding during the day under stones, wood or tree barks. The risk of scorpion sting is higher in rural



Fig. 1 : An Indian Red scorpion *Mesobuthus Tamulus*

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areas, but some species are found close contact with man, and live around or inside human dwelling.²

Epidemiology

The annual number of scorpion stings cases exceeds 1.23 million, of which over 32250 may be fatal.¹ During 60s and 70s, cases fatality rate of up to 30% were reported from Kokan region.^{3,4} Since the advent of vasodilators prazosin,⁵ captopril,⁶ Nifedipine,⁷ sodium nitroprusside, hydrazine, scorpion antivenom^{5,7,8} and intensive care management the fatality is dropped to <2-4%.⁹

Real incidence, morbidity and deaths are scarce, because most of victims don't seek medical treatment or public health structure and prefer to consult traditional healers moreover scorpion sting

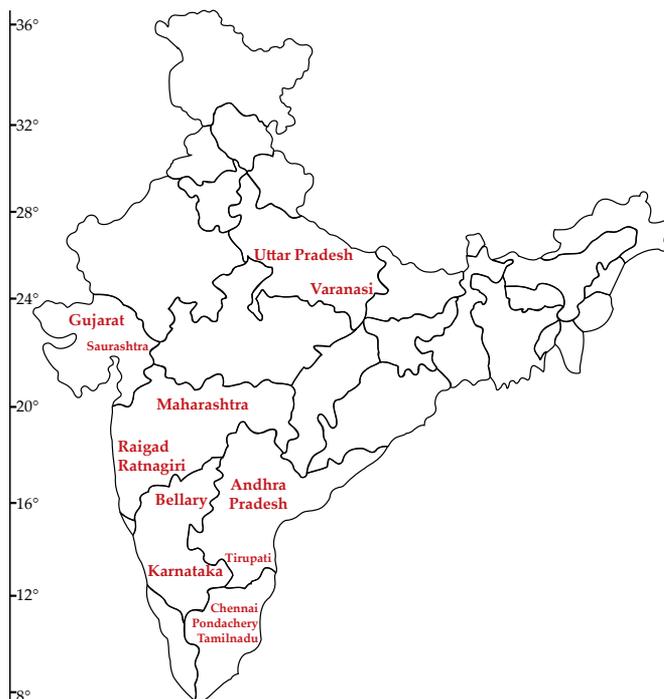


Fig. 2 : Endemic regions of venomous scorpion sting in India



Fig. 3 : Black scorpion *Palmaneus Gravimanus*

is not included in a list of notifiable diseases, the actual burden of scorpion stings is likely to be underestimated. Seven regions where scorpion stings poses significant public health concern are north –Sahara Africa, south Africa, near and Middle East, south India, Mexico and south Latin America.¹ In north America, medically important species includes *Androctonus Australis*, *S. Mauretanicus*, *Buthus Occitanus* and *Leiurus quibquestriatus*. Tunisia is amongst the countries which are most affects, with almost 40,000 sting cases reported each year.¹⁰

The venomous species, in the middle East, are *Androctonus Crassicauda*, *Mesobuthus Tamulus*, *Mesobuthus Eupeus*, *Parabuthus Liosoma*, *B. Occiptanus* and *L. Quinquetriatus*. In Khuzestan, South-west Iran, scorpion stings are amongst the leading causes of death. Although a variety of species are found in the region, 90% of fatalities are attributed to *Hemiscorpion lepturus*.¹¹ This species, also known as thin –tailed scorpion, possesses a venom which is highly cytotoxic.¹² Saudi Arabia, venomous species are a. *Crassicauda* and *L. Quinquetriatus* are incremented in most sting, irrespective of lethal venomous species the insignificant fatality is due to medical excellent facilities and supportive care. In Israel serious scorpion sting amongst the children and life –threatening envenoming is rare in healthy adults.¹³

In Asia epidemiological data on scorpion stings is scarce. India is the most affected, with a reported incidence of 0.6%.¹ A retrospective analysis of the calls received by the national poison information center (NPIC) between April 1999 and March 2002 showed that, out of 995 calls, 6 involved scorpion sting.¹⁴ During hot months March to June and September to October daily cases of sever scorpion sting are received at endemic areas western Maharashtra, Karnataka, Andhra Pradesh, Saurashtra and Tamil Nadu (Figure 2). 11-15 severe scorpion sting due to *Mesobuthus Tamulus* species of scorpion per month reported from kokan region.^{4,5,15,16,17} Higher incidence of scorpion sting occurred during hot months attributed to increase in agriculture activities.^{3,15,16,17}

Scorpion, Venom Biochemistry and Pharmacology

Scorpions are eight legged arthropods in the class Arachnid, they are viviparous and cannibalistic. Scorpion have been able to survive in heat, drought, freezing conditions for weeks, desert condition and starvation for months and total immersion of water for days. This remarkable power of adoption makes their survival



Fig. 4 : Priapism , sweating and salivation

independent of ecological condition and gives the species an unbroken continuity in adverse climatic conditions. During the day time scorpions take shelter under bark of trees, dry firewood or cow dung, in the piles of bricks, paddy husk, beddings, loose tiles of hut, in the shoes left empty over night, pockets of trousers and shirt, carving, crevices of windows and doors. The venomous scorpion tend to have weak –looking pincers, thin bodies but thick tail (Figure 1).¹⁸ Terminal bulbous of the segmented tail contains pair of venom secreting gland telson with sharp semi curve stinger. The venom vesicle surrounded by striated muscular layer facilitating and regulating venom ejections. This ability explains the variation of intensity of symptoms and existence of “dry” sting without envenoming.¹ *Palmaneus Gravimanus* (big black) scorpion (Figure 3) from scorpionidae species causes severe pain with mild swelling, sweating, local fasciculation, spasm of underneath muscle at the sting site and transient cardiac involvement.^{15,19}

Scorpion Venom

The lethality of scorpion venom varies with species. Scorpionidae evokes severe excruciating pain which radiates along with corresponding dermatomes, while sting by buthidae species can result a life threatening systemic effects.^{15,16,18} Venom is deposited in skin deep to subcutaneous tissue, almost complete absorption of the venom from sting site would occur in 7-8 hours. 70% of maximum concentration of venom in the blood reached within 15 minutes and time needed to reach maximum venom blood concentration is 101± 8 minutes in experimental animals, half life of intravenously injected venom is between 4 to 7 minutes and takes 4.2 to 13.4 hours for elimination from blood.²⁰ Scorpions venom is a cocktail of several low molecular weight basic proteins, neurotoxins, nucleotides, aminoacids, oligopeptides, cardipotoxins, nephrotoxin, hemolytic toxins, phosphodiesterase, phospholipase A, hyaluronidase. Acetylcholineesterase, glycosaminoglycans, histamine, serotonin. 5-hydroxyptamine and proteins that inhibit protease, angiotnsinase and succinate –dehydrogenase, ribonuclease, 5- nucleotidase. Multiple toxins may be present in the venom of a single species of scorpion capable to produce a potent synergic effects in victim.^{21,22} Neurotoxins of scorpion venom content is highly lethal than neurotoxin of snake venom. The LD50 of some scorpion neurotoxins have been analyzed to be 10 fold more potent than cyanide.²³ The yellow scorpion *Leiurus Quinquetriatus* (LQ) and *Mesobuthus Tamulus* have been reported among the most lethal scorpion species.²² The main molecular targets of scorpion neurotoxins are the voltage gated sodium channels and potassium channels including calcium



Fig. 5 : Ropy salivation

activated potassium channels, explained scorpion neurotoxins act mainly on excitable cells of nerves and muscles.^{21,22} Iberiotoxin and tamulotoxin content of scorpion *Mesobuthus Tamulus* venom are the only selective inhibitor of potassium channel and blocking effects of scorpion toxins on the potassium channel the action potential across excitable cell membrane becomes prolonged. Sodium and potassium channel toxins of scorpion venom mediate synergistic effects responsible for intense and persistent depolarization of autonomic nerves with massive release of autonomic neuromuscular neurotransmitter evokes an “autonomic storm”.^{24,25} The stimulation of nitergic nerves supplying penile smooth muscle may be explain the priapism observed in severe scorpion envenoming (Figure 4).^{15,22}

Asian black scorpion belonging to scorpionidae family flourished in South –East-Asia. High concentration of nor-adrenaline and acetyl choline contents of scorpion venom account for localising the algesic effect of acetyl choline. Role for nor-adrenaline could also explain the prolonged local burning pain at the site of sting.²² *Buthus Tamulus* induced vasosensory response involved alpha- adrenoceptors for blood pressure and vagal efferent for heart rate changes.²⁶ In experimental study sustained catecholamine decrease was recorded despite re-envenomation. Prolonged or repeated sympathetic stimulation is blunted because of exhaustion of the catecholamine store.²⁷ Injection of *Buthus Tamulus* venom in rat elicited an initial transient hypotensive effects (cholinergic) and secondary prolonged hypertensive effects (adrenergic) effect. The hypertensive effects is dose dependent.²⁸ *Hemiscorpion Lepturus* venom evokes severe inflammatory response syndrome (SIRS). Pro-inflammatory cytokines linked to the severely scorpion envenomed patients are TNF –alpha, IL-1 and IL-6, recently gelatinolytic, caseinolytic and hyaluronidase and metalloproteinase cause injury to the skin, blood cells, cardiovascular and central nervous system.²⁹

Scorpion toxins have proved to be extremely versatile tools in ion channel research.^{21,22,25} Phaiodotoxin content of Mexican scorpion increases the window current resulting in action potential prolongation. While reduction in widow current is reported to be responsible for ventricular arrhythmias in Brugada syndrome. In severe scorpion sting victim continuous prolonged stimulation of sodium neuronal channels by *Mesobuthus Tamulus* venom result Paralysis of cardiac neuronal sodium channel manifest Brugada syndrome. Perhaps drug derived from scorpion toxin could increase the sodium current, and treat the Brugada syndrome.³⁰

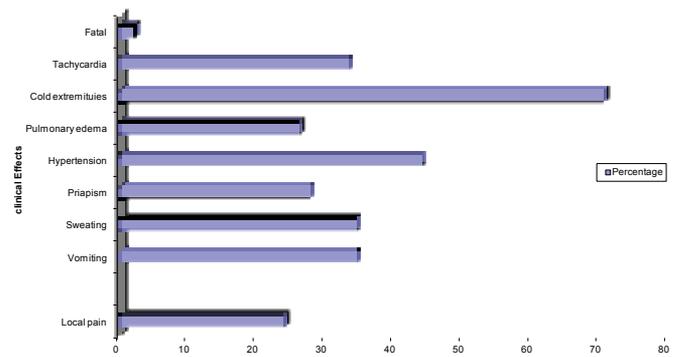


Fig. 6 : Clinical signs and symptoms

Clinical Manifestations

Clinical effects of the envenomation depends upon the species of scorpion and lethality and dose of venom injected at the time of sting. Severe effects is seen in first victim than envenomed by same scorpion to subsequent victim. Severity of envenoming is related to age, size of scorpion and the season of the sting and time lapsed between sting and hospitalization.^{27,31} Severity of scorpion sting occur in children with 3.9-10% fatality irrespective of intensive care management from Israel, Turkey and India.^{9,32,33,34} Clinically “autonomic storm” evoked due to venomous envenoming is characterized by transient parasympathetic (vomiting, profuse sweating, ropy salivation (Figure 5), bradycardia, ventricular pre mature contraction, priapism in male, hypotension) and prolonged sympathetic (cold extremities, hypertension, tachycardia, pulmonary edema and shock) stimulation (Figure 6).^{7,15,16,20,35}

On basis of clinical manifestations at the time of arrival to hospital and according to severity they are graded in 4 grades.⁸

Grade 1: severe excruciating local pain at the sting site radiating along with corresponding dermatomes, mild local oedema with seating at the sting site, without systemic involvement.

Grade 2: signs and symptoms of autonomic storm characterized by acetyl choline excess or parasympathetic stimulation and sympathetic stimulation

Grade 3: cold extremities, tachycardia, hypotension or hypertension with pulmonary edema (Respiratory rate > 24 per minute, basal rales or crackles in lungs).

Grade 4: tachycardia, hypotension with or without pulmonary edema with warm extremities (warm shock).

Sixteen scientists involved in the management of scorpion sting from endemic areas of scorpion sting were invited from Algeria, Argentina, Bolivia, Egypt, India, Israel, Mexico, Morocco, Saudi Arabia, Tunisia and Turkey. They attended the meeting (ADELF congress) at Rabat- morocco held on 6 and 7th may 2009 and consensus was reached to include three classes as follows.³⁶

Class I : Local manifestations

Class II : Systemic involvement

Class III : Cardiogenic failure, hypotension, ventricular arrhythmia, bradycardia, cardiovascular collapse, Respiratory failure- cyanosis, dyspnoea, pulmonary edema, Neurological failure

Glasgow score < 6 (in absence of sedation), paralysis.

Local Manifestations



Fig. 7 : Tight tourniquet may result in gangrene

Soon after sting patient experience severe excruciating radiating pain from sting site usually toes and fingers. Inconsolable, incessant crying in a child which is of sudden onset is diagnostic sign of scorpion sting. Due to pain there is transient bradycardia, rise in blood pressure, mild sweating but extremities are warm.¹⁵ Sudden tap at and around the site of sting induces severe pain and withdrawal is diagnostic sign of sting called "TAP sign". Severe pain without systemic involvement suggestive of benign or dry sting by venomous species.^{1,15} Edema and inflammation at the sting site blunt the sodium channel blocker action of lidocaine. Infiltration of Single dose 1.5-2 ml of lidocaine without adrenaline around the sting site, oral acetaminophen or NSAID, cold therapy at the sting site and oral diazepam make the victim more comfortable. Pain conduction is blunted and it is tolerable or mild due to vasoconstriction caused by liberated circulating catecholamine due to envenoming by venomous species. Reappearance of severe pain accompanied by improved peripheral circulation by vasodilation suggest recovery.³⁷ Local incision, tight tourniquet, application of potassium permanganate, herbal remedies lead to local tissue damage, infection and gangrene (Figure 7).

Systemic Manifestations

Vomiting : Transient projectile vomiting is due to autonomic storm often seen in a patient envenomed by *Mesobuthus Tamulus* (India), *Androctonus Crassicauda* and *Leiurus Quinquestriatus* (Saudi Arabia), *Tityus Serrulatus* (Brazil), *Centruoides* (Mexico), *Leiurus Quinquestriatus* (Israel). Vomiting is due to serotonic content of venom.³⁸

Profuse sweating : sweat literally flows all over body clinically it is called "skin diarrhea". Sweating persist for 3-17 hours.³⁹

Salivation : Thick ropy salivation (Figure 5) due to stimulation of bronchial mucus glands, which is difficult to expectorate occurs soon after sting and it persists for 2-4 hours. Excessive salivation and bronchial secretion are indirect contributing factors for respiratory failure.^{39,40}

Priapism : Priapism seen in almost all victims of pediatric age group and 20% adults patients envenomed by scorpions of Buthidae family except *Hemiscorpion*. Priapism is diagnostic of venomous envenoming but its absence or disappearance did not correlate the outcome. It persists for 5-16 hours.^{15,32,38,40}

Vomiting, sweating, salivation, priapism a diagnostic cardiac premonitory signs and symptoms of scorpion sting suggestive of free circulating venom in the blood, can be accessible to

antivenin therapy.^{8,15}

Cold extremities – Cold extremities are due to severe vasoconstriction a vascular response to liberated circulating catecholamine. Cold extremities persisted for 12-26 hours. Skin over palm and dorsum look like a washer man hand. Cold extremities are accompanied with severe cardiovascular manifestations. Recovery is accompanied with improvement in skin temperature. And at rural setting it is an ideal clinical monitor for lay person or relatives of victim.

Mydriasis : Dilated poorly or non reacting pupils often seen in early phase of autonomic storm associated with raised blood pressure. Pupillary effects are due to alpha receptor stimulation of dilator pupillary muscles by excessive circulating catecholamine.^{15,24,27}

Cardiovascular system mostly affected by venomous sting. Clinical manifestations depends upon the duration of envenoming. Hypertension, cardiac arrhythmias, tachy-bradycardia, pulmonary edema, hypotension and shock are not the different syndromes but of one process of ongoing autonomic storm.¹⁶

Hypertension : 45-70% victims reported within 30 minutes to 8 hours of sting have raised blood pressure ranging from 140/90 to 200-230/130-160 mm hg. with Bradycardia (heart rate 42- 58 per minute).^{23,41} Main complaints are headache, chest discomfort, suffocation and per oral parasthesia. Clinical examination shows para-sternal systolic lift, apical bulge, proto-diastolic gallop and transient grade 2/6 apical systolic murmur of mitral regurgitation due to papillary muscle dysfunction^{7,16} children look agitated confused and have propped up eyes, oculogyric phenomenon, puffy face, decreased level of consciousness and convulsions; manifestations encephalopathy with blood pressure measurements between 95 and 99 percentile for age and sex of child.^{9,16,23,34,40} If untreated the hypertensive effect is long lasting and result in development of myocardial failure and pulmonary edema.^{23,37,42,43,44,45} Hyper-renemia and sympathetic stimulation results in rapid and significant increase level of epinephrine, norepinephrine, endothelin, atrial natriuretic peptide due to sting by Buthidae species. Accumulation of angiotensin II accelerate the myocardial injury and oxygen demand.^{45,47,48,49} Alpha receptors stimulation plays an important part in the pathogenesis of hypertension and pulmonary edema due to scorpion sting.⁵⁰

Tachycardia : 15-20% cases reported after 6-7 hours of sting develop supraventricular tachycardia (heart rate 110-240 per minute). At times Sudden onset of tachycardia occurs in a recovering hospitalized patient.¹⁷ Tachycardia with cold extremities is due to effect of raised level of circulating catecholamines by toxin on beta adrenergic receptors.^{7,47} However mark tachycardia occur after 10-12 hours of hospitalization with hypertension accompanied with warm extremities with or without pulmonary edema suggestive of warm shock.⁵¹ Impaired left ventricular filling, reduction in cardiac out put due to mark tachycardia particularly in children result in delirium and convulsion due to anoxia to the brain.¹⁷

Hypotension : Short lasting initial hypotension is due to hypovolemia as a result of vomiting, sweating, salivation and cardiac arrhythmias.²⁶ Delayed long lasting hypotension attributed to reduction in systemic vascular resistance a hypokinetic phase accompanied by raised heart rate, hypotension with shock reflecting an alter left ventricular contractility.^{51,52} In a hospitalized patient on 2 or 3rd day of admission asymptomatic hypotension with bradycardia but good volume pulse with warm extremities accompanied with prolonged QTc interval is due



Fig. 8 : Tented T waves

to depletion of catecholamines from nerve terminals because of autonomic storm. Venom inhibits kinase II enzyme and lead to accumulation of bradykinin a neuromuscular agent incriminated for development of pulmonary edema and hypotension.⁵²

Pulmonary edema : 888 scorpion sting cases studied during 19 years at primary health centers over western coast of Maharashtra of these 167 (19%) had pulmonary edema.⁵³ Irrespective of differ species similar reports of pulmonary edema recorded from Israel, Turkey, Brazil and Saudi Arabia.^{7,33,54,55} Out of 428 children of scorpion sting studied over 13 years, 294 (68.7%) had pulmonary edema with respiratory rate 30 per minute, agitation, sweating with high plasma protein concentration reported from Tunisia.⁴³ Pulmonary edema develop within 30 minutes with severe hypertension and may develop after 36 hours of sting with hypotension and tachycardia. Clinically characterized by acute onset of dyspnoea (Respiratory rate >24 per minute), tachycardia, summation gallop, systolic murmur, cold extremities, sudden onset of intractable cough, bilateral moist rales and low volume fast thready pulse. During the month September and October cases may manifest sudden onset of massive pulmonary edema with central cyanosis, intractable cough with continuous expectoration of blood stained froth from mouth and nostril.

Neurological manifestations- *Centruroides Exilicada* the bark scorpion, seen in Arizona, new Mexico, western Texas, southeast California and Nevada, venom is highly neurotoxin. *Mesobuthus Tamulus* may cause focal neurological presentation include hemi paresis, hemorrhagic or thrombotic stroke. DIC is main contributory factors for neurological manifestations.⁵⁶ Bahloul M et al from Tunisia reported 78% cases had neurological complications due to *Androctonus Australus* envenomation. Patient presented with coma, convulsions, hyperthermia, miosis and mydriasis, brain edema had poor outcome. Majority of victims neurological complications are secondary due to brain anoxia caused by pulmonary edema and cardiovascular failure.⁵⁷

Acute Pancreatitis : In Trinidad incidence of acute pancreatitis due to *Tityus Serrulatus* envenoming is 80%.⁵⁸ Envenomation by *Leiurus Quienquestriatus* in Israel children causes abdominal pain, vomiting, agitation and discomfort with raised plasma immunoreactive cationic trypsin.⁵⁹ Pancreatitis due to scorpion

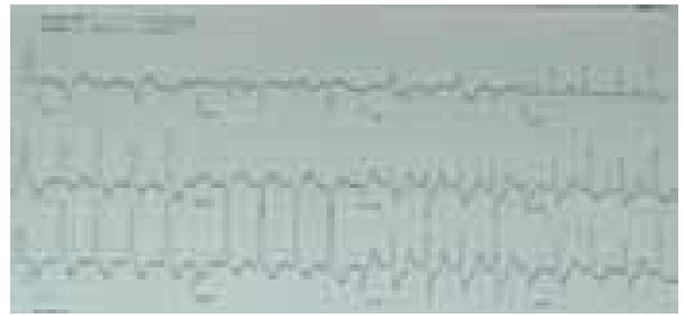


Fig. 9 : Non sustained ventricular tachycardia in scorpion sting victim

sting is rare in India.⁶⁰

Death within 30 minute of sting can occur due to lethal ventricular arrhythmia. High fatality due to scorpion sting in India attributed to delay in reporting to hospital due to poor transport, reporting to *tantrik*, medical officer is not aware of western line of treatment or he had never treated severe scorpion sting before. Excessive administration of fluids, atropine increase the severity of pulmonary edema. Steroids increase the necrotizing effects of circulating catecholamines and oxygen demand of myocardium. Digitalis enhances already increased myocardial contraction and oxygen requirement. Antihistamines and venom both act synergically by inhibiting Ca⁺ dependent potassium activating channels lead to QTc prolongation may cause sudden death. Actual transport of severe scorpion sting cases to nearest big hospital delays the treatment and add to their deaths.^{3,6,15,17,18,32,33,34,37,41,61,62}

Haemodynamics: Karnad DR from India studied haemodynamic pattern in 8 scorpion sting cases of *Mesobuthus Tamulus* sting. He recorded severe vasoconstriction and hypertension in mild envenoming, while predominant left ventricular dysfunction with normal systemic vascular resistance causing pulmonary edema or severe hypotension is related to the fluid balance. Warm shock with or without pulmonary edema is the result of biventricular dysfunction and irreversible vasodilatation.⁵¹ Abroug F et al from Tunisia reported the cardiac dysfunction and pulmonary edema is due to reduction in left ventricular compliance and increased impedance to left ventricular emptying.^{52,63} Increased systemic pressure without rise in systemic vascular resistance attributed to rise in cardiac output a inotropic phase, were vasodilators are preferred. Inotropic phase is an early phase of envenomation characterized by hypertension and enhanced ventricular contractility.^{5,23} Hypokinetic phase the hallmarks of which, hypotension and shock, reflect the altered left ventricular contractility dobutamine is preferred.^{63,64} Ignition of myriads of circulating mediators responsible for potent cardio-respiratory consequence of severe envenoming.⁶⁵ Electron microscopes study of fatal scorpion sting victim showed contraction band necrosis with ruptured and hyper contraction sarcomers as a result of excessive catecholamine similar to pheochromocytoma.⁶⁶

Echocardiographic changes - Echo shows poor global myocardial contractility 12-15 hours of sting, with low ejection fraction, decreased left ventricular performance, trivial mitral regurgitation, abnormal diastolic filling for five days to four weeks. Diminished or hypokinetic left ventricular global movement with decrease systolic function seen in scintigraphic study. At times systolic and diastolic frames shows no change in diameter, flat septum with no systolic thickening.^{67,68} There is good correlation between clinical improvement and return

of the left ventricular wall motion toward normal due to *Mesobuthus Tamulus* sting.⁶⁹ Serial echocardiography is useful

to follow changes in left ventricular function and possibility of development of cardiomyopathy.^{70,71} Similar findings are reported from Brazil, Israel and Saudi Arabia.^{72,73}

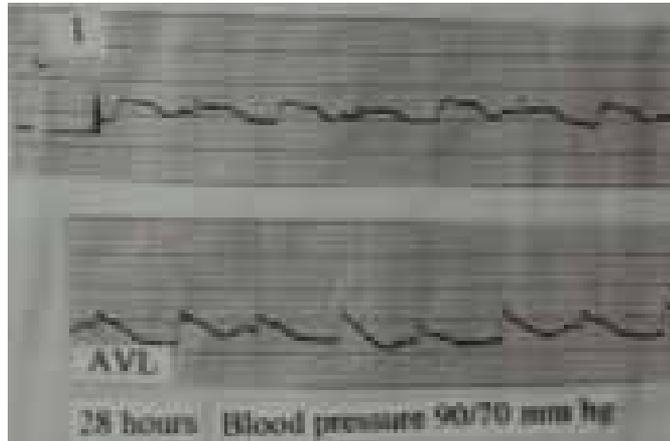


Fig. 10 : PQRST alternan

Electrocardiogram : ECG is the most important and diagnostic and easily available tool at rural setting. No victim with systemic involvement shows normal ECG. RST segment and T waves are most frequently affected. Arrowhead tented T wave look like Ashoka tree indicates acute injury, while tent shaped look like Christmas's tree indicated recovery (Figure 8). Early myocardial infarction like pattern, atrial arrhythmias, non-sustained ventricular tachycardia (Figure 9) and varies conduction defect due to injury to the conducting system. PQRST or T waves alternans suggest serious myocardial injury (Figure 10). Prolonged QTc and conduction defect restore to normal within one week, T wave inversion persist for few weeks. Low voltage, wide QRS complex, tachycardia, hemiblock and mark ST segment depression carries bad prognosis. At times despite of good clinical status of victim ECG s showed mark



Fig. 11 : Unilateral, bilateral, diffuse pulmonary edema



Fig. 12 : Pulmonary edema and recovery with oral prazosin



Fig. 13 : Chaotic atrial and ventricular arrhythmias regressed by scorpion antivenom and oral prazosin

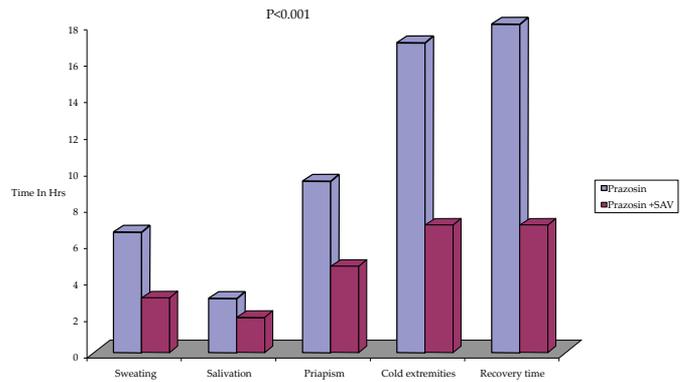


Fig. 15 : Recovery -prazosin plus scorpion antivenom Vs prazosin

Table 1 : Result of efficacy of prazosin versus prazosin + antivenom

Clinical sign	Prazosin	Prazosin + antivenom	P
Sweating, mean (SD) hours	6.6(2.60)	3(1.1)	0.001
Salivation,mean (SD) hours	3(1.9)	1.9(0.9)	0.008
Priapism mean (SD) hours	9.4(1.5)	4.7(1.5)	0.001
Cold mean (SD) extremities	17.3(6.6)	8.5(5.3)	0.001
Number with hypotension	19(54.3)	12(34.50)	0.001

Bawaksar HS and Bawaskar PH- BMJ 2010;341:c7136 doi /10;1136/bmj.c7136

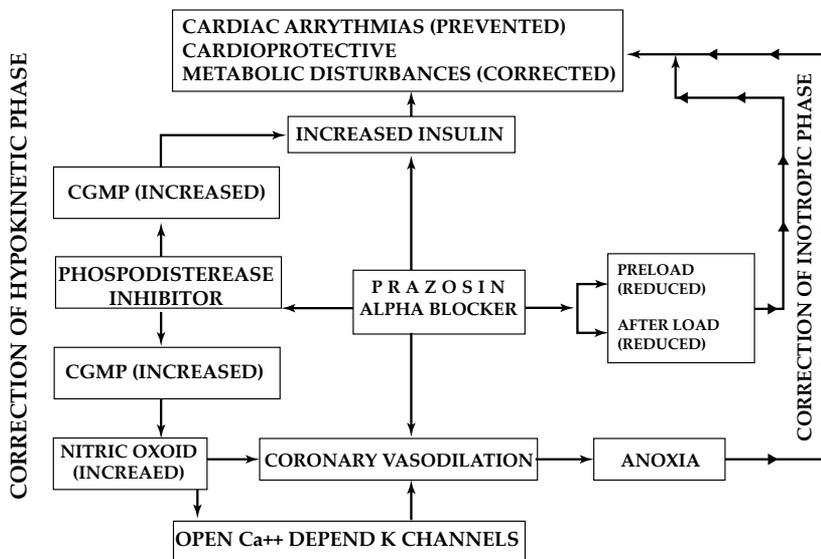


Fig. 14 : Effects of prazosin

abnormality.^{34,37,41,72,74}

Chest X-ray

Cardiogenic pulmonary edema characterized by unilateral distribution or batwing appearance of lung edema due to left ventricular failure and simultaneous localized increase in pulmonary vascular permeability induced by venom. While the patchy and peripheral distribution of lung edema with air bronchograms are radiological features of pulmonary edema due to increased vascular permeability (Figures 11, 12).^{15,54,75}

Laboratory investigations : Rise in leukocyte count in range 11400-41400 per/cu/mm within hour of sting.^{54,76} Rise in cardiac enzyme, cytokines, platelet activating factors, renin, angiotensin II, serum potassium, urine and serum catecholamine, hyperglycemia, serum amylase and reduction in insulin level occur.^{23,76,74, 76,77,78,79}

Management

During later half of last century irrespective of various regimens including decongestive agents, lytic cocktail, propranolol, insulin glucose drip, the fatality due to scorpion sting varies from 20 to 29%.^{3,4} Since the advent of scorpion antivenom, vasodilators and intensive care facilities the fatality is almost negligible due to severe envenoming.^{8,9,14,42,55,68}

Fluid loss due to vomiting, sweating and salivation may complicate the clinical course. Every effort should be made to correct the fluid balance.

Scorpion antivenom (SAV) : Without skin test, SAV must be administered as early as possible and through venous route. *Mesobuthus Tamulus* envenoming causes transient parasympathetic and prolonged sympathetic stimulation. Signs and symptoms suggestive of parasympathetic stimulation indicate circulating unbound venom and can be neutralized by antivenom. Thus by neutralizing circulating venom SAV subsequently prevents the sympathetic overstimulation and its consequences. In Mexico, since the advent of excellent wide use of potent SAV the fatality dramatically reduced during the last decade.

SAV is specific treatment of scorpion sting's therapy has been a matter of debate and controversy during the last five years. But recent randomized controlled trials have overcome the controversy regarding beneficial effects of early administration of SAV. Boyer V et al found that intravenous administration of antivenom resolved the neurological manifestations within four hours. SAV reduced the requirement for concomitant sedation with midazolam and decreased the levels of circulating unbound venom.⁸⁰ SAV is available almost in all tropical and subtropical countries with encouraging reports. Recently Razi Institute from Iran a polyvalent scorpion antivenom inhibits the gelatinase enzyme activity of *Hemiscorpion lepturus* and improves the prognosis.²⁹

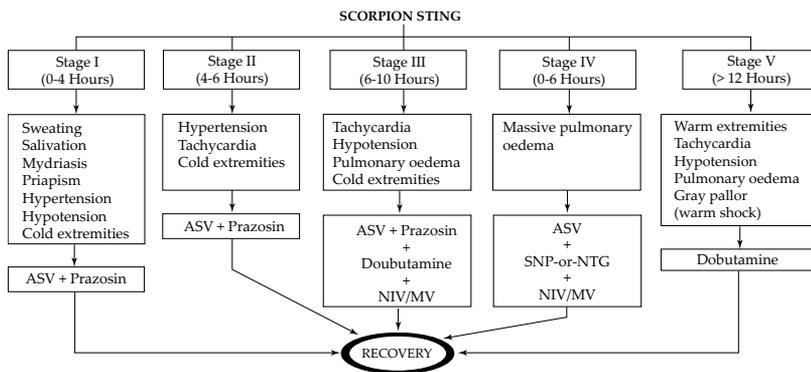


Fig. 16 : Management of scorpion sting

ASV: Antiscorpion venom; SNP: Sodium nitroprusside; NTG: Nitroglycerine; NIV: non-invasive ventilator; MV: Mechanical ventilator

Since 2002, nonspecific F(ab)2 SAV has been available for clinical use from Haffkine Biopharma Mumbai. *Mesobuthus Tamulus* is common in western maharashtra, saurashtra, kerala, Andhra pradesh, Tamil Naidu and Karnataka states of India where morbidity and mortality due to stinging have been reported.^{3,4,5,6,14,56,69,71,79}

Prazosin is widely used for management of *Mesobuthus Tamulus* sting (Figure 14).^{5,17,37,55,45,77} Bawaskar and Bawaskar did a prospective, randomized trial of scorpion antivenom plus prazosin versus prazosin alone in the treatment of severe *Mesobuthus Tamulus* sting at a general hospital Mahad, authors randomized 70 cases (antivenin plus prazosin 35) and (prazosin alone 35) (Figure 14) (Table 1).

Patients in the antivenom plus prazosin group required significantly ($p < 0.001$) fewer doses of prazosin than the prazosin group. Concluded that addition of scorpion antivenom to prazosin enhances recovery time and shortens hospital stay of patients with grade 2 *Mesobuthus Tamulus* envenomation. The maximum volume of venom injected in one sting by Indian red scorpion is 1.5 mg, and each ml of antivenom is capable of neutralizing 1.2 to 1.5 mg venom hence we used 30 ml of antivenom, however more may be required for severe sting. No participant had a mild or severe reaction to antivenom. High circulating catecholamine induced by venom prevent a reaction to antivenom and act as a prophylaxis against anaphylaxis.^{8,81,82}

Vasodilators hydralazine, isosorbide dinitrate, nifedipine have been advocated for the treatment of scorpion sting, these agents cause reflex tachycardia and increases myocardial oxygen demand. Massive life threatening pulmonary edema were time is great enemy necessitate rapid unloading and vasodilatation by sodium nitroprusside drip.^{5,6}

Prazosin

Alpha receptors stimulation plays an important role in the pathogenesis of scorpion sting.^{22,50} Prazosin is a phosphodiesterase inhibitor, it reduces preload and left ventricular impedance without raising heart rate.⁸³ Prazosin is a simple scientific pharmacological and physiological antidote to scorpion venom actions, it is easily available at rural setting.^{8,26} In an experimental study support that scorpion sting involvement of peripheral alpha-1 adrenergic receptors for pressure response this is the reason why prazosin an alpha-1 blocker has been successfully used to reverse the toxicity.²⁶ 619 victims of severe envenoming by *Mesobuthus Tamulus* admitted at Mahad 180 Km on Bombay-Goa high way. 341 (50.5%) had raised blood pressure, 167 (27%) presented in pulmonary edema, 111 (18%) had tachycardia

with hypotension all these cases recovered with oral prazosin 250-500 microgram every 3 hourly interval.⁵³ Out of 293 children of age 1-16 years administered oral prazosin of these 23 (7.8%) reported 12 hours of sting was brought in moribund, comatose and had multi-organ failure died.¹⁷ Prazosin is widely used and its beneficial effects in scorpion sting cases have been reported from endemic regions of India,⁷⁷ Saudi Arabia.⁵⁵ Turkey⁸⁴ Impressive reduction in case fatality from *Mesobuthus Tamulus* sting 26% in 1961 and 6% in 1980 and currently <1% this shows that it is possible when dedicated care is available at a specific center. In an endemic regions of venomous scorpion sting, the prazosin is a darling amongst the drug kept ready at out patient department tray, even two tablets are carried in purse by consultants of this areas.⁷⁶

Angiotensin converting enzyme inhibitor captopril improves the diuretic induced pulmonary edema and cardiogenic shock due to scorpion sting.⁶ Victims who presented in hypokinetic phase due to both ventricular dysfunction, clinically characterized by hypotension, shock, tachycardia, delirium with or without pulmonary edema and warm extremities, these cases improves with dobutamine infusion 5-20 microgram /kg/min.^{51,64,76} 7 out of 11 children had myocardial dysfunction and decompensated shock in addition to dobutamine responded to nitroglycerine (NTG) drip 0.5 to 5 microgram /kg/min by improving heart dysfunction and reduction in pulmonary congestion. Venodilator action of NTG reduces the preload of the heart and it improves the intrapulmonary shunting and also relaxes the epicardial coronary arteries and its collaterals.⁸⁵ Amiodarone a neuromodulator improves the survival by reduction of serum nor-epinephrine level in four children with scorpion sting, had severe left ventricular dysfunction with raised troponin and serum nor-epinephrine.⁸⁶

Pulmonary edema cases improves with dobutamine, mechanical or non-invasive ventilation or by helmet-derived non-invasive pressure support ventilation.^{52,54,64,87}

Prevention

False ceiling under loose tiles of roof and bamboo cot with scrupulous use of mosquito net protect from scorpion sting. In endemic areas of venomous sting clothing, beddings, shoes, package should be vigorously shaken out and checked for scorpion without blindly putting hands. Sandal did not prevent sting. Pesticides like organophosphates, pyrethrins and chlorinated hydrocarbons are known to kill scorpions. One should not sit touching to mud walls. At times of opening the school the tables and rooms (roof, walls and floor) should be thoroughly cleaned and washed.

Conclusion

Early hospitalization and administration of accurate dose of scorpion antivenom, prazosin and closely monitoring the victim in intensive care unit will save many lamented life (Figure 15). Periodic training for peripheral doctors regarding management of scorpion sting should be arranged. Scorpion sting should be included as notifiable disease. Scorpion sting should be included in a regular medical teaching at least in tropical and subtropical countries.

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