A DISSERTATION ON

"A CLINICAL STUDY ON THE EFFECTIVENESS OF EARLY PRAZOSIN THERAPY IN CHILDREN WITH SCORPION STING"

THE TAMIL NADU DR. MGR. MEDICAL UNIVERSITY, CHENNAI–600032, TAMILNADU.

In partial fulfillment of the regulations

For the award of the degree of

M.D. DEGREE BRANCH-VII

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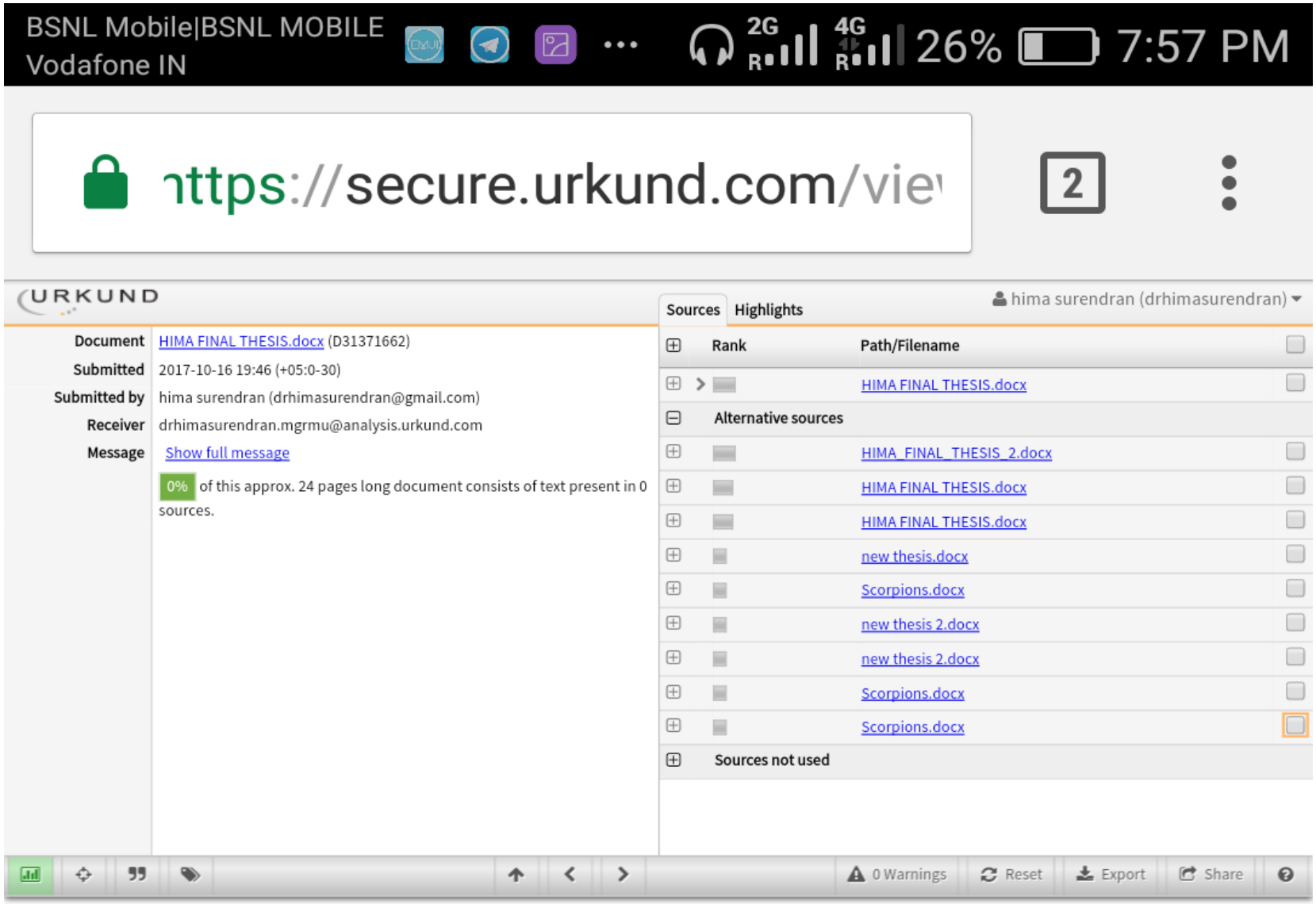
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Dr. HIMA SURENDRAN I Year, Post Graduate Student of MD (Paediatrics), GMKMC, Salem-30.	"A clinical study on the effectiveness of early prazosin therapy in children with scorpion sting"	Dr. D. Sampath Kumar, MD., DCH., Associate Professor of Paediatrics, GMKMC, Salem.	Approved

The Ethical Committee examined the studies in detail and is pleased to accord Ethical Committee approval for the above Post Graduate student of this College to carry out the studies with the following conditions.

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To
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ABSTRACT

Scorpion sting is a frequent event in tropical and sub-tropical countries. Nearly 1,000 species of scorpion are known worldwide, which belongs to six families. Around 86 species of this family are found in India. These are found abundantly in Western Maharashtra, parts of Karnataka, Andhra Pradesh, Saurashtra, Pondicherry and Tamil Nadu. Mesobuthus tamulus or Indian red scorpion is the most lethal of all scorpion species. Indian red scorpion, is venomous and its envenomation is fatal if not treated in time.[2]

Scorpion sting in children is a life threatening emergency. Most of the children with severe envenomation die due to the toxin, whereas it is a relatively less serious condition in adults. Reliable statistics are not readily available for this common rural accident. Numerous envenomations are unreported and true incidence is not known. Case fatality rates of 3-22% were reported among children hospitalized for scorpion stings in India.[1] Most of the deaths due to scorpion sting are attributed to cardiopulmonary complication such as myocarditis and acute pulmonary edema.[7]

Outcome of scorpion sting depends upon the dose of the venom, the age of the child, the season of the sting and the time lapse between the sting and hospitalization. The time gap between the scorpion sting and

presentation to the hospital is one of the significant risk factors which determine better outcomes and mortality. Children who present after 6 hours of the sting have a significantly higher mortality rate. [5]

Prazosin, a postsynaptic alpha –1 blocker, counteracts the effects of excessive catecholamines and arrests the development of severe systemic features. It is used at the dose of 30µg/kg/dose. It has been found to be an effective drug for scorpion sting envenomation and it has reduced the mortality rate to 1% as compared to a 30% mortality rate in the pre-Prazosin era.[5]

Most of the Scorpion sting cases admitted in tertiary care center are being referred in a state of peripheral circulatory failure due to lack of knowledge regarding the clinical course and the outcome, as there are not many relevant clinical studies on risk factors predicting outcome of scorpion sting envenomation in this particular geographical area, we would like to conduct this study to know the risk factors that predict the outcome of scorpion sting envenomation in children upto 12 years.

KEYWORDS: scorpion sting early administration prazosin

AIMS AND OBJECTIVES

- To study the effectiveness of early prazosin therapy in children with scorpion sting.

- The determine whether time gap between sting and hospital admission as one of the significant risk factors which determine outcome and mortality.

MATERIALS AND METHODS

CASE SELECTION: 100 Cases of suspected and clinically proven scorpion sting at Govt Mohan Kumaramangalam Medical College, Salem during January 2016 to December 2016.

Type of the study:

Prospective observational hospital based time bound study

OBSERVATION

In children with scorpion sting early administration of prazosin help in reduction of complication.

CONCLUSION

The early administration of prazosin is effective in reducing the morbidity and mortality of scorpion sting.

INTRODUCTION

Scorpions are homogeneous group of arthropods comprising about 1500 species. Only 30 species belongs to the family Buthidae, are very dangerous to humans. These are active at night during the summer season, but often live in houses or near inhabited areas.[1]

Scorpions are eight legged belongs to arthropods in the class Arachnid and they are viviparous.[1] The lifestyle makes their survival independent of ecological condition. Scorpions are predatory arachnids of the order Scorpiones. Eight legged scorpions are easily identified by pair of grasping pedipalps and the narrow segmented tail, ending with a venomous stinger. Scorpion size range from 9 mm to 23 cm. *Typhlochactasmitchelli* being one among the smallest and *Heterometrusswammerdami* being one among largest.[1]

Though scorpion stings are painful but usually do not cause any harm to human.Most dangerous species are found in South America, Africa, and western Asia and may need emergency medical care.

86 different types of species of scorpions are present in our country. *Mesobuthus tumulus* (Indian red scorpion) and *Heterometrus swammerdami* are of medical importance.([1,27])

Mesobuthus tamulus the Indian red scorpion is one of the most dangerous scorpion species in the world. ([1,2,11,12])These are found abundantly in southern parts of our country, in western Maharashtra, northern Karnataka, Andhra Pradesh, and Tamilnadu. Children are at high risk to develop severe scorpion envenomation manifestations like cardiac, respiratory and neurological complications when compared to the adults.

Complications following the scorpion sting can be multisystemic,can affect mainly cardiovascular system. The Cardiovascular manifestations are particularly prominent following stings by Indian red scorpion.[3] Cardiovascular toxic effects and acute pulmonary oedema are the most important life- threatening complications of scorpion envenomation. (1). Cardiogenic shock, acute myocarditis and pulmonary oedema are responsible for majority of the death due to scorpion sting. Cardiac involvement generally occurs as left ventricular systolic dysfunction.

Prazosin, a competitive post-synaptic alpha1adrenoreceptor antagonist is the first line of management for scorpion sting, since stimulation of alpha receptor plays an important role in the progression of clinical features

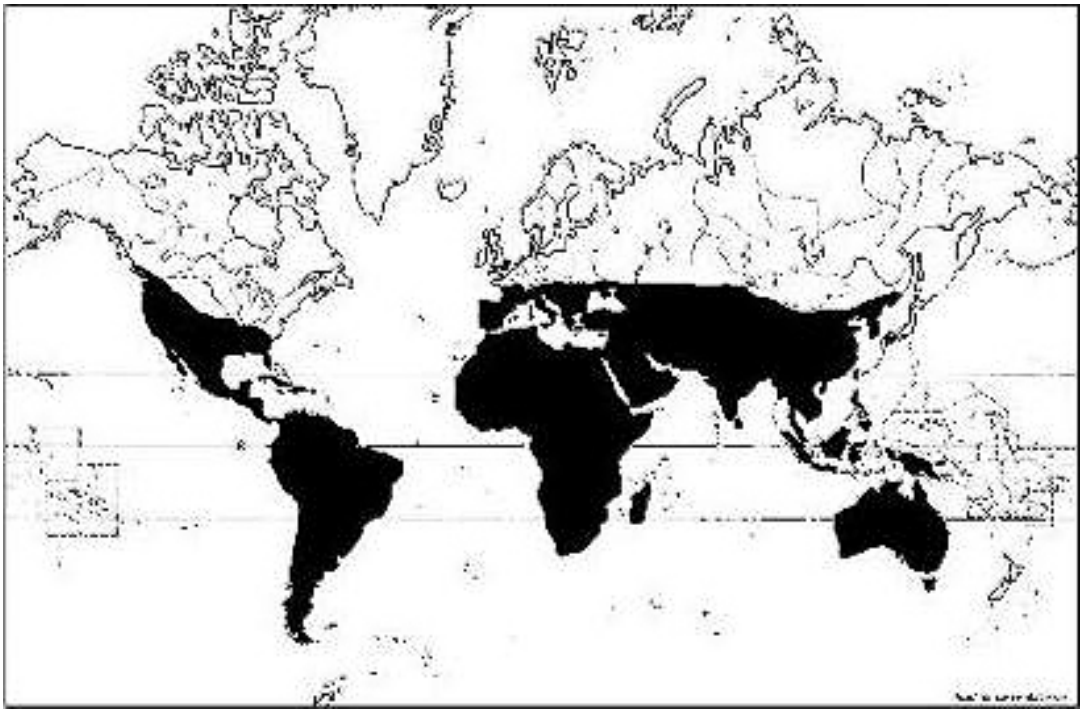
Prazosin suppresses the sympathetic outflow and activates the potassium channels which are inhibited by venom. Prazosin cause reduction of the preload, afterload and blood pressure without an increase in the heart rate.

Both the metabolic and hormonal effects of alpha receptor stimulation are reversed by the drug. Hence prazosin is considered as a cellular and pharmacologic antidote to the scorpion venom and is cardioprotective.

The mortality was less in cases which were treated with Prazosin. This could be due to the protective effect of Prazosin on the cardiovascular and the respiratory systems.

BURDEN OF THE DISEASE

Scorpion sting envenomation is an acute life threatening medical emergency.[1] It is a common event in the tropical, subtropical and the temperate zones of the world. It causes significant health burden in some rural areas of South India.[11,12]



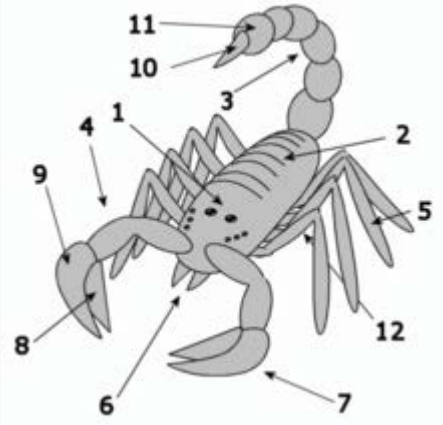
Scorpion venom is a poison with selective activity in mammals and vertebrates.[16] Depending on the type of scorpion, its venom leads to different complications. As the toxin has a complex structure consisting of neurotoxic proteins, salts, acidic proteins, and organic components, it may cause hematological, neurological, and cardiovascular symptoms.[17,18]

Scorpion stings are primarily accidental. Scorpion does not usually cause venom injection into the human body. When scorpion stings it controls ejaculation of venom. Hence stings may be sting can be total, partial or non-venomous.

THE SCORPION STING

- THE SCORPION : MORPHOLOGY
- THE SCORPION VENOM –BIOCHEMISTRYAND EFFECTS
- CLINICAL FEATURES
- COMPLICATIONS
- INVESTIGATIONS
- MANAGEMENT

MORPHOLOGY OF SCORPION



Scorpion anatomy:
1 = Cephalothorax or *Prosoma*;
2 = Abdomen or *Mesosoma*;
3 = Tail or *Metasoma*;
4 = Claws or *Pedipalps*
5 = Legs;
6 = Mouth parts or *Chelicerae*;
7 = pincers or Chelae;
8 = Moveable claw or *Tarsus*;
9 = Fixed claw or *Manus*;
10 = Stinger or *Aculeus*;
11 = *Telson* (follows anus in previous joint).

The body of a scorpion has two parts :

- The head (cephalothorax)
- The abdomen (opisthosoma)

  Opisthosoma is subdivided into

  - Mesosoma, broad anterior preabdomen
  - Metasoma, narrow tail-like posterior postabdomen.

Cephalothorax(head)

The cephalothorax or *prosoma* consists of the

- Eyes
- Mouth
- Pedipalps (the pedipalps of scorpions have claws or pincers)
- Four pairs of walking legs.

  The exoskeleton is very thick and durable, which protects from predators. Scorpions have two eyes on the top of the cephalothorax.

  The pedipalp is a segmented, clawed like appendage used for immobilization of prey, defense and sensory purposes.

Mesosoma

The mesosoma is the broad part of the abdomen (opisthosoma). It comprises of the anterior seven segments (somites) of the opisthosoma, each covered by a sclerotosed plate dorsally.

Metasoma

The metasoma is commonly known as the scorpion's "tail". It consists of five segments, of which the fifth segment of metasoma contain the telson. The scorpion's telson is also called the stinger. The stinger contains the vesicle which has a pair of venom glands.

THE SCORPION VENOM

The Indian red scorpion's (*Mesobuthus tamulus'*) venom is a potent sodium channel activator. The venom can cause stimulation of the autonomic nervous system, leading to massive release of endogenous catecholamines([11,12)].

The venom at first cause a transient cholinergic phase, followed by sustained hyperactivity of adrenergic system.

Factors determining the clinical manifestation:([9)]

The species of scorpion

The dose of venom injected

The season of sting

Fig 1 Indian red scorpion (Mesobuthus tamulus)

COMPOSITION OF SCORPION VENOM

The venom apparatus of scorpion consists of vesicle having a pair of joined glands in the telson, the last segment of the post abdomen. The vesicle is surrounded by striated muscular layer regulating ejection of venom([12,13,14)].

Scorpion venom is a complex mixture of toxins and enzymes which act on ion channels of excitable cells.

The venom of the single scorpion have multiple toxins which interact with each other, thereby altering the response of the ion channels involved causing complex and rapidly progressive symptoms([12)].

The sodium channel are most important targets for the toxin binding. Toxins belong to two main types toxins-α and toxins-β([13].

Toxins-α are otherwise called potential-dependent because α toxins have receptor affinity proportional to polarization of membrane. Alpha toxins act only when the channel is opened and hence inactivate the closing potential of the sodium channel. It can cause strong depolarization of the membrane, followed by fall in the excitability. At higher doses, it cause prolongation of the action potential of excitable cells and can lead to paralysis and cardiac arrhythmia.([14]

B Toxins, obtained from the venom of American scorpions, also act on the sodium channel but on another site which gets activated at a lower action potential and is independent of membrane potential. The stimulation by β Toxins can result in myoclonic or spastic muscular response.([14]

SCORPION VENOM BIOLOGY

Scorpion venom is a water-soluble, antigenic, heterogenous mixture, as demonstrated on electrophoresis studies.([12] This heterogeneity accounts for the variable patient reactions to the scorpion sting. However, the closer the phylogenetic relationship between the scorpions, the more similar the immunological properties. Furthermore,

the various constituents of the venom may act directly or indirectly and individually or synergistically to manifest their effect([13]). In addition, differences in the amino acid sequence of each toxin account for their differences in the function and immunology. Thus, any modifications of the amino acid sequence result in modification of the function and immunology of the toxin.

The scorpion venom consists of different polypeptides and enzymes. Venom consists of:([13])

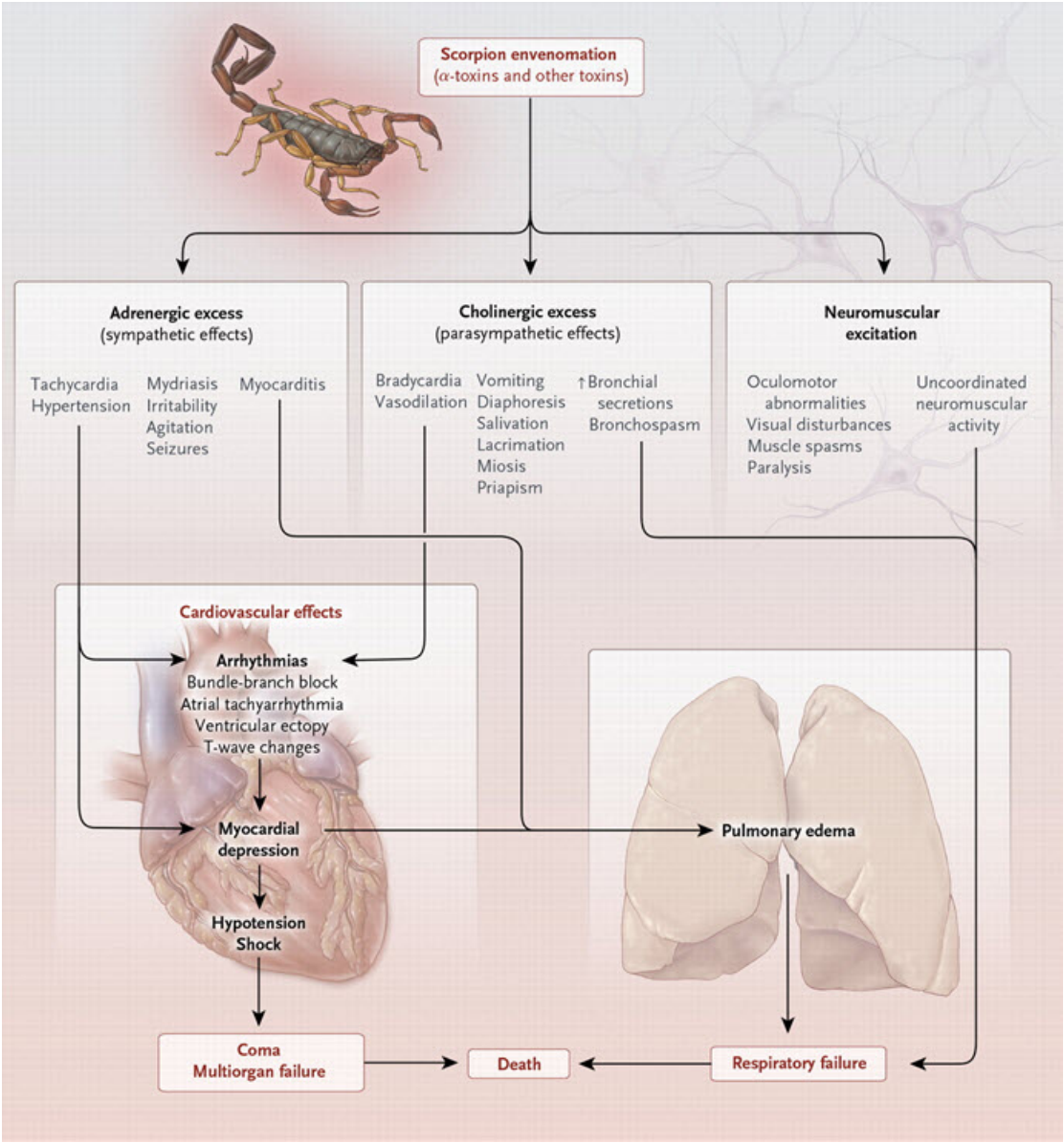
(1) neurotoxin, which acts on the respiratory, vasomotor centers, nerve terminals and end plates of muscles.

(2) hemolysins, agglutinins, lecithin, cardiotoxins, nephrotoxins, hyaluronidases, phosphodiesterases, phopholipases, glycosaminoglycans, histamine, tryptophan and cytokines.

Neurotoxins are the most important agent that block the sodium channels (beta-toxins). ([13])There is massive release of endogenous catecholamines into the circulation of victim due to delayed activation of sodium neuronal channels by the venom. The major molecular targets of the neurotoxins are the voltage gated sodium channels and potassium channels including calcium activated potassium channels. The only selective inhibitors of potassium channel are Iberiotoxin and tamulotoxin content of the scorpion *Mesobuthus tamulus*.([11]) Both sodium and

potassium channel blocking toxins of scorpion venom cause addictive effects which leads persistent depolarization of autonomic nerves .This is termed as “autonomic storm” response. ([6)]

The stimulation of nitrergic nerves supplying penile smooth muscles may explain the cause of priapism observed in scorpion envenomation in some male children ([4)](the nerves run in independent pathway to supply smooth muscle of penis for vasodilation)



Scorpion Venom Biochemistry

The lethality of scorpion venom varies from species to species. Venom is injected in skin deep to subcutaneous tissue. The absorption of the venom from sting site would occur in around 7-8hours. 70% of maximum concentration of venom in the blood is reached within 15 minutes.([11])

Scorpions venom is a cocktail of many low molecular weight basic proteins, neurotoxins, nucleotides, aminoacids, oligopeptides, cardiotoxins, nephrotoxin, hemolytic toxins.

High concentration of noradrenaline and acetyl choline in the scorpion venom is responsible for localising the algesic effect of acetyl choline. Role for noradrenaline explain the prolonged local burning sensation at the site of sting. *Buthus Tamulus* induced vasosensory response involved alpha-adrenoreceptors for blood pressure and vagal efferent for heart rate changes. Prolonged or repeated sympathetic stimulation is blunted because of exhaustion of the catecholamine store. Injection of *Buthus Tamulus* venom in rat elicited an initial transient hypotensive effects (cholinergic) and secondary prolonged hypertensive effect. The hypertensive effects is dose dependent.

Pro-inflammatory cytokines linked to the severely scorpion envenomed patients are TNF–alpha, IL-1 and IL6,hyaluronidase and metalloproteinase cause injury to the skin, blood cells, cardiovascular and central nervous system([12)]

Effect of Venom on Ion Channels, Alpha Receptors and Myocardium

Scorpion venoms are species-specific complex mixture of short neurotoxic protein. The venom contains free aminoacids, serotonin, hyaluronidase and enzymes that act on trypsinogen.([3)

Voltage dependant ion channels are altered by the venom. The side chains of scorpion venom are positively charged. This is important to bind to specific membrane channels. Alpha (of *Buthus*sp.) and beta (of *Centruoides*sp.) toxins act on sodium channel. Scyllatoxin, charybdotoxin of *Leiurus*species and *Tityus*toxin act primarly on potassium channels. The toxin acts by opening sodium channel at presynaptic nerve terminals and inhibiting calcium dependant potassium channels. Autonomic storm is thus initiated.([6)

Alpha receptors stimulation by the toxin plays a major role, leading to features like hypertension, tachycardia, myocardial dysfunction, pulmonary edema and cool extremities. Raised angiotensin I levels facilitate the sympathetic outflow through conversion to angiotensin II. Excess catecholamines cause accumulation of endothelins and vasoconstriction.([12)

The unopposed effects of alpha receptors stimulation lead to suppression of insulin secretion, hyperglycemia, hyperkalemia, free fatty acids and free radicals accumulation injurious to myocardium. Cardiac sarcolemmal defects, depletion of glycogen content of heart, liver and skeletal muscles were produced by Indian red scorpion venom([3)]

Effect of Venom on Hemopoietic System, Brain and Lungs

Changes in blood coagulation profile can occur in scorpion envenomation.The presence of acute disseminated intravascular coagulation (DIC) after scorpion venom injection have been reported. Direct effect of toxins on neurons could contribute to seizures and encephalopathy. Hemiplegia has been attributed to fibrin deposition resulting from DIC. The sudden rise in blood pressure due to sympathetic stimulation, rupture of perforating arteries, intracerebral hemorrhage and cerebral infarction due to DIC can also occur in scorpion sting.([11)]

Effect of Venom on Skin, Kidney, Liver and Pancreas

Local inflammation is unusual in Indian red scorpion envenomation. But yellow scorpion (*Buthuscosmobuthus*and *Hemiscorpus*) seen in Iran produce varied skin reaction, namely, erythema, edema, lymphangitis and severe necrosis. Polypeptide variations of different venoms could account for this phenomenon.

Scorpion Venom and Systemic Inflammatory Response

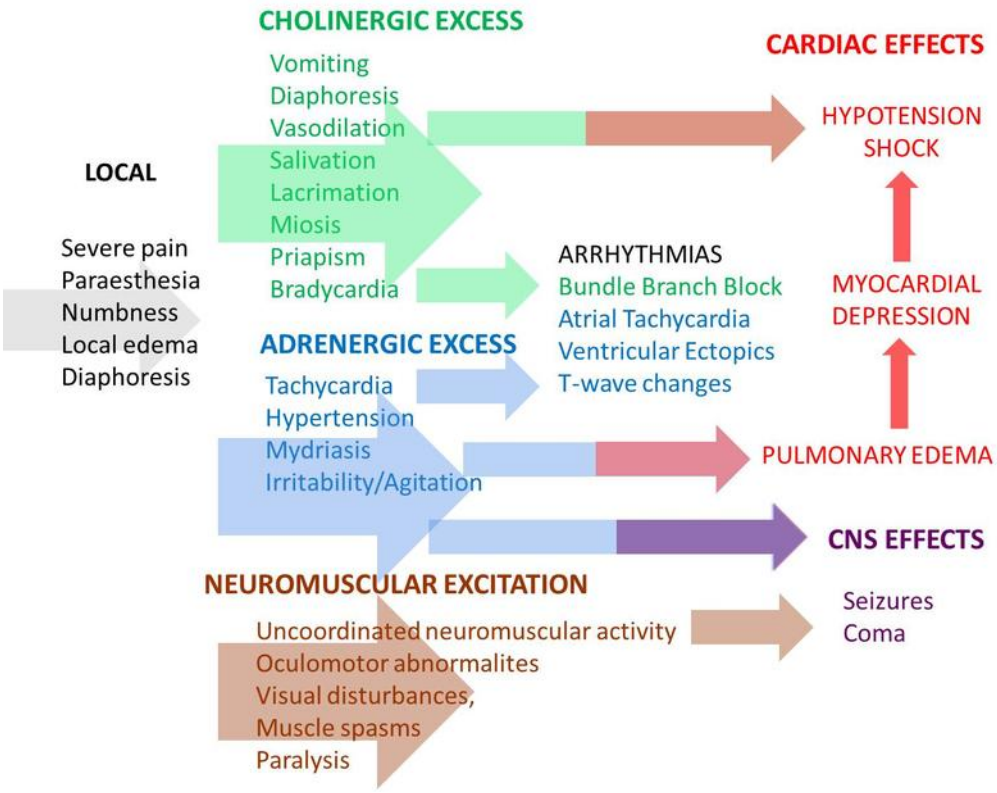
Systemic inflammatory response like syndrome is triggered during envenomation caused by scorpion species *Tityusserrulatus*. Increased levels of Interleukin-6, IL-1a and IFN- gamma were seen in all patients. Increased serum levels of IL-6, IL-1 Beta, nitric oxide and alpha1-antitrypsin declined after initial rise in children who survived. Endothelial nitric oxide (e NOS) is constitutively expressed by endothelium but inducible nitric oxide (i NOS) is expressed in response to stimuli such as proinflammatory cytokines.

CLINICAL FEATURES

Clinical effects of the envenomation depend upon the species of scorpion and lethality and dose of venom injected at the time of sting. Severity of envenomation is related to age, size of scorpion and the season of the sting and time lapsed between sting and hospitalization.

Severity of scorpion sting occur in children with 3.9-10% fatality irrespective of intensive care management.

Clinically “autonomic storm” evoked due to venomous envenoming is characterized by transient parasympathetic (vomiting, profuse sweating, excessive salivation, bradycardia, ventricular premature contraction, priapism in male, hypotension) and prolonged sympathetic stimulation(cold extremities, hypertension, tachycardia, pulmonary edema and shock)



Pain

The first symptom of scorpion envenoming is localized pain. Pain is present in majority(around 90 %) of cases of envenomation and may be associated with edema and erythema (in 20% of cases), more rarely small blister.

Whenever local pain was severe, there was often no further progression of symptoms. Older children report paresthesia near the sting site. Some children complain pain at Sting site during recovery. Serotonin found in scorpion venom is thought to contribute to pain associated with scorpion.

Autonomic Storm

Overstimulation of the sympathetic system increases blood levels of catecholamines, resulting in a characteristic “adrenergic (autonomic) storm”. ([11)

The features of autonomic storm

- Cardiovascular features

  - Tachycardia
  - peripheral vasoconstriction
  - hypertension
  - diaphoresis

- Metabolic features

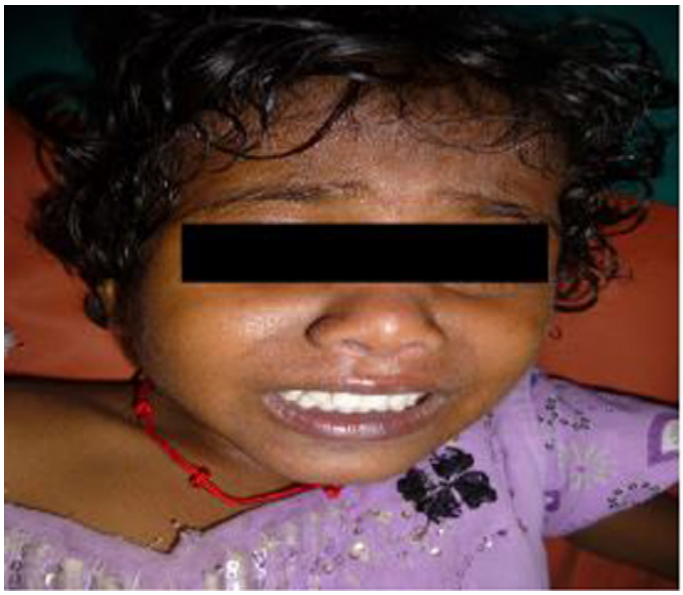
  - hyperthermia
  - hyperglycemia

- Respiratory features

  - bronchial dilation
  - tachypnea

- neuromuscular features

- tremor and agitation
- convulsions



In contrast, a cholinergic (or muscarinic) syndrome can occur involving the parasympathetic nervous system. This combines a hypersecretion syndrome (salivation, sweating, vomiting, urinary incontinence, bronchial hypersecretion, and diarrhea), abdominal pain, miosis, bronchospasm, bradycardia with hypotension and, in the male, priapism. This syndrome seems to be rarer, delayed, or masked by the adrenergic storm.

Vomiting, salivation, sweating, priapism and bradycardia are early diagnostic signs. Sweating and salivation persist for 6-13 hours. Increased

oral secretions and bronchorrhea in the early cholinergic phase can worsen respiratory compromise.

Tachycardia seen within 4 hours persist for 24-72 hours. Tachycardia, hypertension, myocardial dysfunction, pulmonary edema and shock is spectrum of autonomic storm. Vomiting and palmoplantar sweating precede development of myocardial injury. Marked tachycardia, S3 gallop and ice-cold extremities are seen.([12)

Hypertension lasts for 4-8 hours in many due to outpouring of catecholamines from adrenal stimulation; due to direct stimulation of sympathetic centers in medulla. Hypertensive stress on myocardium, direct myocyte toxicity and catecholamines induced injury contribute to rhythm disturbances and LV failure.

Hypotension and bradycardia can be encountered within 1-2 hours of sting due to cholinergic stimulation; hypotension and tachycardia later (4-48 h) indicate severe LV dysfunction. During recovery stage (48-72 h) hypotension can be seen; but the extremities are warm with good volume pulse.

CARDIOVASCULAR MANIFESTATION

Cardiovascular manifestations are particularly prominent following stings by Indian red scorpion.[3] Cardiovascular toxic effects and acute pulmonary oedema are the most important life- threatening complications of scorpion envenomation. (1). Cardiogenic shock and pulmonary oedema are responsible for majority of the death due to scorpion sting. Cardiac involvement generally occurs as left ventricular systolic dysfunction. The impairment of ventricular function contributes to the development of acute pulmonary oedema. The rapid increase of cardiac muscle enzyme and sudden deterioration of cardiac function after scorpion sting are seen which leads to development of acute myocarditis. The damage is basically triggered by the venom resulting in adrenergic expression or the direct effect of the toxin on myocardial fibrils. Immediately following the scorpion sting, autonomic storm is established which is responsible for hypertension, tachycardia, pulmonary oedema, and shock.(2). Scorpion bites infrequently have serious clinical sequelae, including myocardial infarction, acute pulmonary edema, cardiogenic shock and even death.

PATHOPHYSIOLOGY

The pathophysiology of cardiac dysfunction secondary to the scorpion sting is not yet very clear.

- Myocardial ischemia caused by coronary spasm: Release of the vasoactive, inflammatory and thrombogenic peptides and amine containing inflammatory mediators like histamine, serotonin, bradykinin, leukotrienes, thromboxane which act on the coronary vasculature and induce coronary artery vasospasm,facilitate platelet aggregation as well as thrombosis.[4]
- Direct cardiotoxic effect of the venom causing toxic myocarditis by reduction of Na-K-ATPase and adrenergic myocarditis by releasing adrenaline and noradrenaline from neurons, ganglia and adrenals, thereby increasing myocardial oxygen demand by direct inotropic and chronotropic effect on already compromised myocardial blood supply.[5]
- Anaphylactic reaction: Release of allergenic proteins causes anaphylactic shock leading to hypotension with vasodilation and decreased of intravascular volume with reduced myocardial perfusion.
- Scorpion venom inhibits angiotensin converting enzyme (ACE), resulting in accumulation of bradykinin, which is implicated in the development of pulmonary edema.[6

- The direct effect of scorpion venom on the cardiac fibrils and the adrenergic expression triggered by the venom are mostly responsible for cardiac dysfunction. In some of the studies, effects made by the cytokines released after scorpion sting, such as neuropeptide Y and TNF-alpha also contribute for cardiac complication. All these mechanisms, separately or simultaneously, are thought to contribute to cardiac function (3).
- Catecholamine mediated cardiac dysfunction is considered multifactorial. The massive release of catecholamine results in increased heart rate, coronary spasm, and vasoconstriction occurring in the microcirculation, thus causing myocardial hypoperfusion and hypoxemia(3). At the similar time, increase in the intracellular concentration of catecholamines contribute to the direct toxic effect on myocardial cells and cardiac dysfunction.
- The stimulation of alpha receptors leads to the development of tachycardia, myocardial dysfunction, acute pulmonary oedema, and circulatory disorder. If the catecholamines get depleted in the later stage after sting, hypotension, systolic function disorders, and pulmonary disorders will be observed (3).

There have been reports in the literature to support that the majority of the scorpion sting presenting with cardiovascular system symptoms have temporarily left ventricle dysfunction and cardiac function have returned

to normal after the medical treatment (5). In these patients, temporary ischemia of cardiac muscle develops secondary to the spasm of microvessels and decreased perfusion of the myocardium which develops as a result of the adrenergic discharge (3). Most cases recover clinically in a short time after scorpion sting.

Agitation is an important clinical parameter used for determining the severity of the scorpion sting. In a study which evaluated the patients who developed acute pulmonary oedema following scorpion sting, a significant relationship was found between agitation and development of pulmonary oedema (7).

The laboratory values of cardiac markers like CK, CK-MB, LDH, and troponin values are used as indicators of cardiac damade. In cases of scorpion sting with clinical cardiac manifestation, troponin-I may initially be at normal levels. During the due course of observation of these patients, troponin-I reaches its maximum level at 24 - 36 hours.In majority of cases, the clinical cardiac symptoms of increased cardiac enzymes and pathological ECG and ECHO findings have been reported to rapidly recover within 5 days to normal levels within a week of effective treatment.

The scorpion venom cause the stimulation of the peripheral sympathetic nerve endings along with the release of catecholamines from

the adrenal medulla .The catecholamine release from medullary center can occur either due to direct stimulation as well as through parasympathetic stimulation).[6], [11] The scorpion venom act as a powerful arrhythmogenic agent. Pulmonary edema and cardiac damage are due to several factors.[2], [4],[5],[6] *Fluid loss* due to vomiting, salivation and perspiration complicate the clinical course and hemodynamic abnormalities in many children.

Pulmonary edema may develop within 30 minutes to three hours after a sting due to myocardial dysfunction. Tachypnea or intractable cough at admission could mean pulmonary edema in evolution. Close monitoring is needed to detect and treat pulmonary edema. Children appear pale (‘ashen pallor of skin’) with clammy skin and have tachycardia with elevated blood pressure, retractions, nasal flaring and grunting. Pink frothy sputum described in adults is not always present in children. Death within 30 minutes in some is due to ventricular arrythmias. Non-cardiac pulmonary edema due to ARDS is commonly reported from Brazil (*Tityusserrulatus*scorpion)

Central nervous system manifestations are rarely seen. Encephalopathy, convulsions within 1-2 hours of sting, acute rise in arterial blood pressure with rupture of unprotected perforating arteries, cerebral hemorrhage,

stroke and central respiratory failure have been reported. The acute rise in BP needs rapid correction to prevent cerebrovascular accident.

INVESTIGATIONS

- **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.

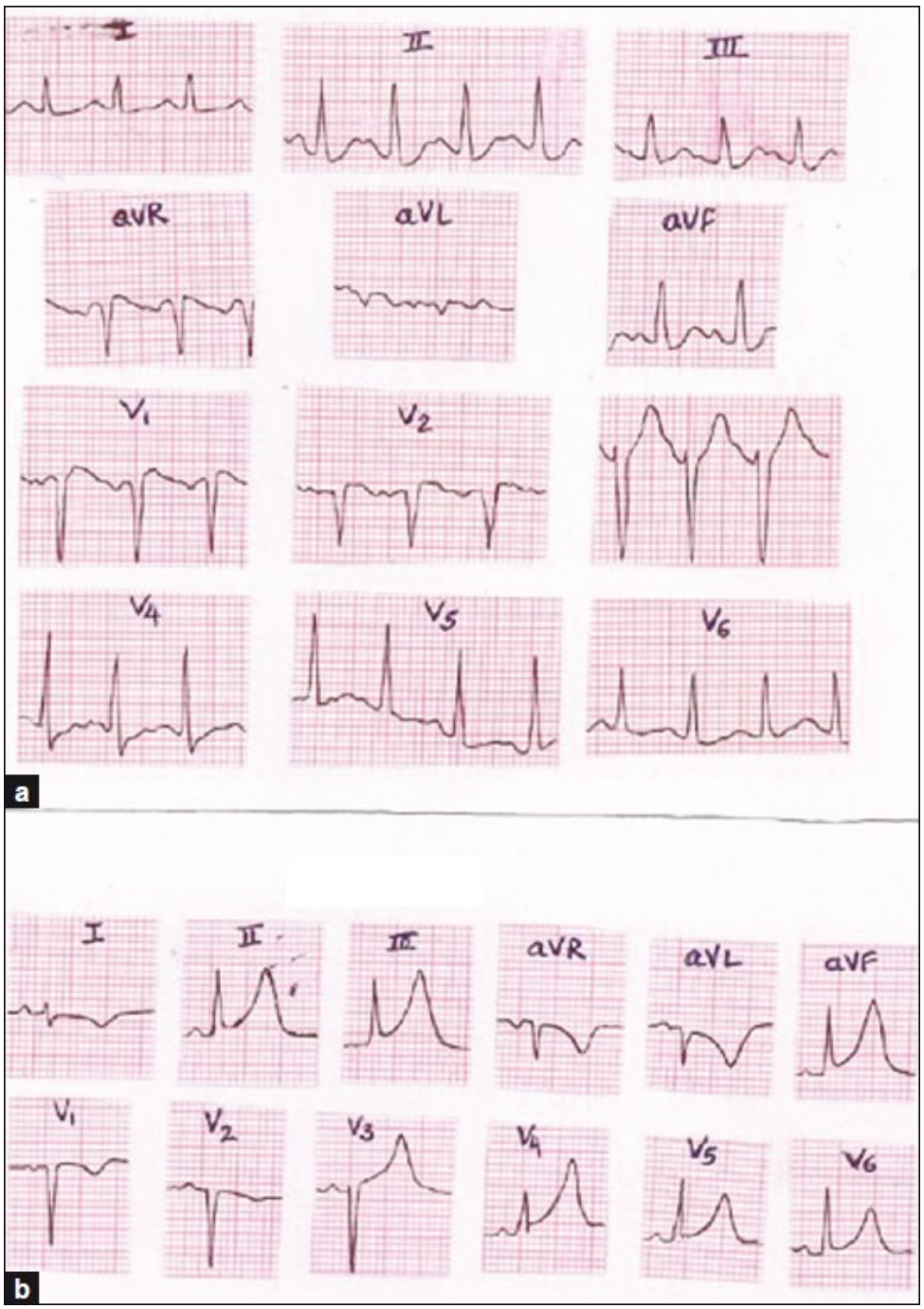
Electrocardiographic findings(11)

- Peaked T waves in V2-6
- ST segment elevation in leads I, aVL
- increased QR interval(ventricular activation time)
- Left ventricular hypertrophy by voltage criteria.

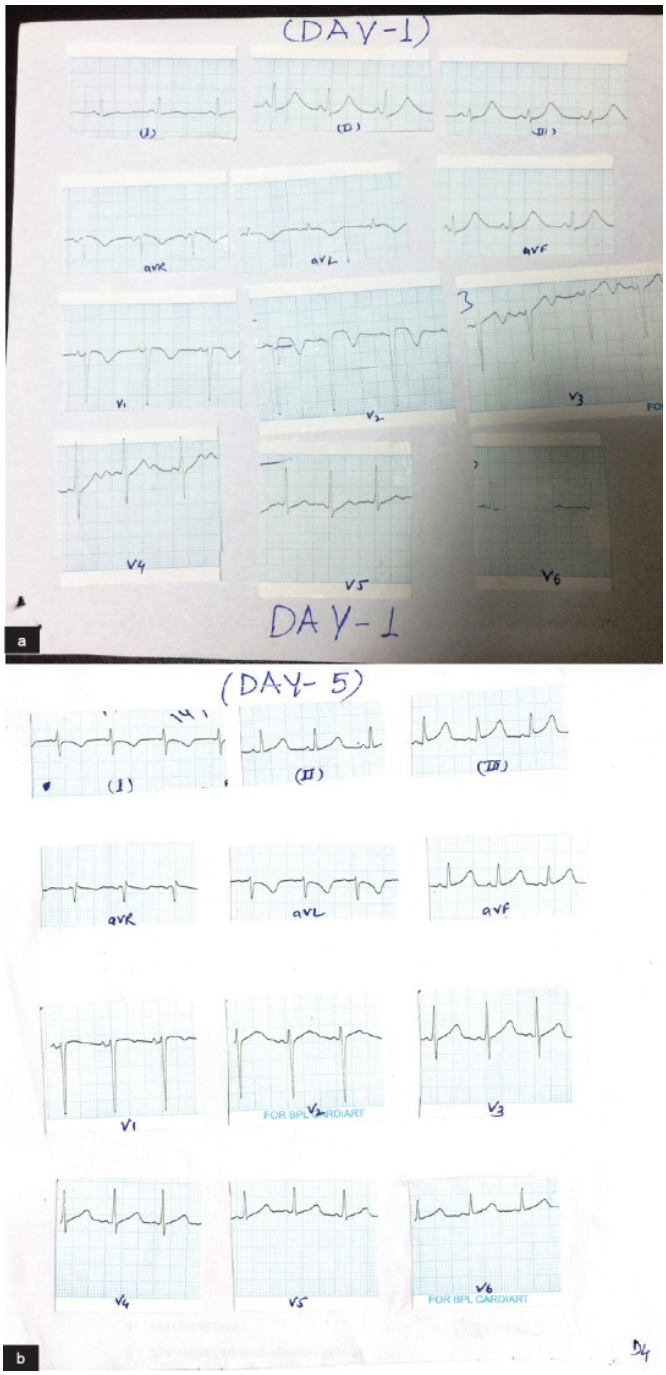
Note: poor prognostic features include low voltage complexes throughout the record and left anterior hemiblock.

A routine serial ECG must be included for the early detection of cardiac manifestation and if required cardiac markers and echocardiogram for early diagnosis of acute cardiac complication.

Arrow head tented T wave look like Ashoka tree indicates acute injury, while tent shaped look like Christmas's tree indicated recovery. Early myocardial infarction like pattern, atrial arrhythmias, nonsustained ventricular tachycardia and varies conduction defect due to injury to the conducting system. 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 ECGs show marked abnormality.



a) Electrocardiogram showing sinus tachycardia with secondary "ST-T" changes. (b) ECG on the next day showing normal sinus rhythm with "T"wave inversions in leads I, aVL, and ST segment elevation with concavity.

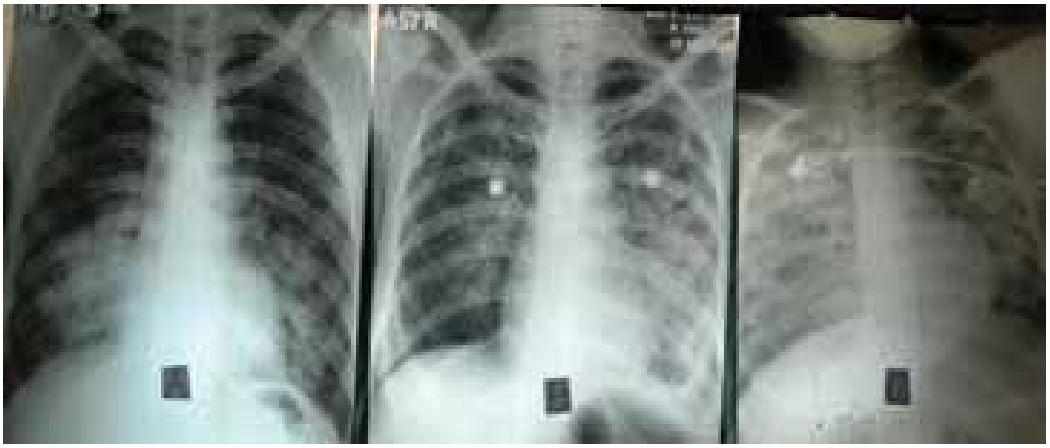


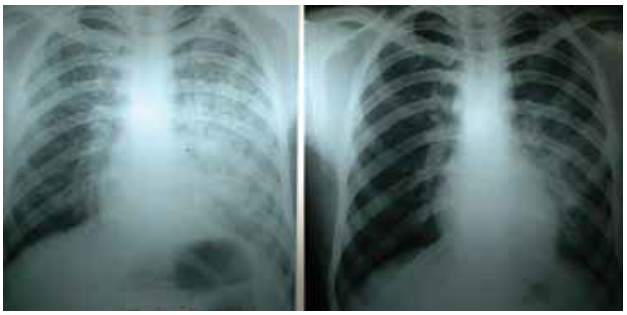
A)ECG of the patient on the day of admission showing secondary ST- T changes and tachycardia (B) ECG of the patient on day 5th showing T wave inversion in lead I and aVL

- **Chest X-ray**

Acute pulmonary edema can be either cardiogenic or non cardiogenic in orgin.(6)

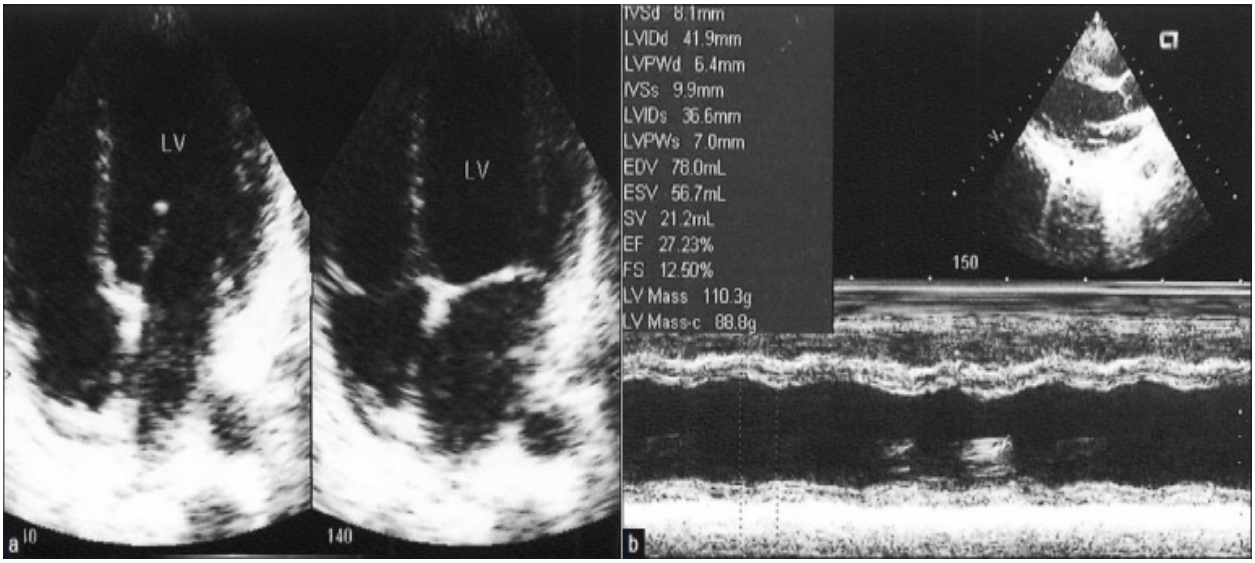
- The cardiogenic pulmonary oedema characterized by unilateral distribution or batwing appearance of lung edema is due to left ventricular failure and simultaneous localize increase in pulmonary vascular permeability induced by venom.
- The non cardiogenic pulmonary oedema characterised by patchy and peripheral distribution of lung edema with air bronchograms due to increased vascular permeability alone.





Echocardiography

Echocardiography findings include the left ventricular systolic dysfunction. Occasionally left ventricular dilatation with regional wall motion abnormalities may be seen.(7)



Echocardiogram (apical four-chamber view) demonstrating hypokinesia of interventricular septum, (b) Echocardiogram (parasternal long axis view M mode) demonstrating hypokinesia of interventricular septum and inferior posterior wall with LVEF 28%.

Laboratory investigations :

Increase in leukocyte count can occur within hour of sting. 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 may occur.

MANAGEMENT

Prazosin, a competitive post-synaptic alpha1adrenoreceptorantagonist is the first line of management for scorpion sting, since stimulation of alpha receptor plays an important role in the progression of clinical features.(1)

MECHANISM OF ACTION

Prazosin suppresses the sympathetic outflow and activates the potassium channels which are inhibited by venom. Prazosin cause reduction of the preload, afterload and blood pressure without an increase in the heart rate. Prazosin counteract the vasoconstriction caused by endothelins by the accumulation of cyclic GMP (cGMP).(8)This is done by inhibiting phosphodiesterase enzyme leading to decreased formation of inositol triphosphate.cGMP, is the second messenger of nitric oxide in vascular endothelium (eNOS) and myocardium,can prevent further myocardial injury. Both the metabolic and hormonal effects of alpha receptor stimulation are reversed by the drug. Hence prazosin is

considered as a cellular and pharmacologic antidote to the scorpion venom and is cardioprotective.(8)

Prazosin reverses both the inotropic and hypokinetic phases and reverses the metabolic effects which are caused by depressed insulin secretion .So the early administration of Prazosin reduces the mortality which is associated with encephalopathy, due to neutralization of the adverse effect of catecholamine released into brain

DRUG DOSAGE

Prazosin is available as scored 1 mg tablet. Sustained release tablets are not recommended in scorpion sting. The dose recommended is 30 microgram/kg/dose. The drug is given immediately in all children with evidence of autonomic storm. It should not be given prophylatically in children with pain as the only symptom. In children with vomiting, drug can be given through a nasogastric tube. After administering prazosin, caretaker is advised not to lift the child inorderto prevent the effects of ‘First dose phenomenon’ of prazosin. Oral feeds must be encouraged. If necessary, intravenous maintenance fluids can be given to correct dehydration due to excessive sweating and vomiting.

MONITORING AFTER DRUG INTAKE

Prazosin can be given irrespective of blood pressure unless hypovolemia is ruled out. Vitals like Blood pressure, pulse rate and respiration need to be monitored every 30 minutes for 3 hours, every hour for next 6 hours and later every 4 hours till the improvement of the child. Prazosin need to be repeated in the same dose at the end of 3 hours after assessing the clinical response and later every 6 hours till extremities are warm, dry. Not more than four doses are required in majority of cases of scorpion sting.(8)

Pain and Fluid Management

Pain relief is important since it alleviates anxiety and reduce stress on the myocardium. When pain is severe, NSAIDS can provide prolonged relief. Local ice packs, xylocaine (local anesthetic), dehydroemetine (counter irritant) and streptomycin (neuromuscular blockade) have been reported to be helpful. Benzodiazepines (Diazepam) is useful to quieten a restless child after scorpion sting. Benzodiazepines act via opening of chloride ion channel through GABA action, thereby diazepam antagonises the ability of the toxin to stimulate specific ion channel.(9)

Oral fluids must be encouraged whenever possible due to the loss of fluid due to profuse sweating and vomiting. Parenteral fluids are required in children with tachypnea and altered sensorium,. Fluid requirement has to be balanced properly. In children with pulmonary edema, CVP monitoring is nesessary.

Treatment of Pulmonary Edema

Pulmonary edema in scorpion sting is usually secondary to myocardial dysfunction. Treatment of myocardial dysfunction is primarily supportive inspite of diagnostic and therapeutic advancement in medicine.(11)

In children with pulmonary edema with or without hypertension, main target is to relieve afterload without compromising the preload.Adequate cardiac output is maintained to prevent fluid overload in scorpion sting. Hence dobutamine infusion at the rate of 5-15 mg/kg/min with vasodilatation through sodium nitroprussideat 0.3-5 mg/kg/min or nitroglycerine at 5 mg/min is preferred. Prazosin need to be administered an hour before termination of sodium nitroprusside drip. If SNP is unavailable, isosorbidedinitrate 10 mg every 10 minutes sublingually as an alternative drug. Morphine, a standard drug for pulmonary edema, must be avoided in scorpion sting, since narcotics can worsen dysrhythmias.(11)

ADVANCED SUPPORTIVE MANAGEMENT

Close attention to airway management is necessary. Intubation and mechanical ventilation are sometimes needed due to effects of venom. Pulmonary edema is the most important cause of mortality in children and should be treated with propped up position, nasal oxygen, intravenous loop diuretics and prazosin. Inotropic support with dopamine and dobutamine 5–15 mg/kg/minute is advised for 36– 48 hours in warm hypotensive shock patients.

Cardiac arrhythmias are often self-limiting. Tachyarrhythmias are managed by intravenous metoprolol or esmolol and bradyarrhythmias can be treated with atropine. Hypertension and pulmonary edema respond to nifedipine, nitroprusside, hydralazine, or prazosin.(1) Defibrination syndrome is managed conservatively or with heparin, fresh blood transfusion or fibrinogen infusions.

SPECIFIC TREATMENT BY ANTIVENOM

Scorpion antivenom as the specific treatment has been a matter of controversy during last 5 years; many of the previous studies shown that SAV does not alleviate hemodynamic changes or cardiogenic pulmonary edema, or prevent death and the outcome was the same for victims treated with antivenom and without antivenom.(15) But some recent randomized controlled trials have overcome the controversy regarding beneficial effects of early administration of SAV. Commercially prepared antivenins are available in several countries for some of the most

dangerous species. SAV is expensive and polyvalent antivenin, can be effective for scorpion sting cases for use anywhere in the world. The dosage is 5–25 mL of antivenom diluted in two to three volumes of isotonic saline is given intravenously over an hour. If there is no significant improvement, further doses of antivenom can be given.The total dose of antivenom required is 30–100 mL in severe scorpion envenomation(15)

Scorpion antivenom is effective when the victim is brought at an early stage of scorpion sting ,in a stage of acetylcholine excess. The cholinergic phase is indicative of free circulating scorpion venom, which can be neutralized by SAV. Intravenous administration of antivenom can rapidly reverses the systemic toxic features but not the local symptoms. Test dose is not required as there are high circulating catecholamines and anaphylaxis is rare. Addition of SAV to prazosin enhances recovery and shortens the hospitalisation in children with grade 2–4 *Mesobuthus tamulus* envenomation in our country.(11)

Scorpion venom reach the the ion channels very rapidly. Hence venom to be neutralized with antivenom, it has to be administered within 30 minutes of sting. Antivenom against the toxins of Indian scorpions is not available in the market for clinical use. The antivenom is not useful in those children who reach the hospital late, already with cardiac manifestation(15). It is not proved whether antivenom is useful in preventing the cardiovascular manifestations. The prazosin neutralize the effects of overstimulated autonomic nervous system whereas antivenom neutralize toxin already bound to receptors on sodium channel.

Unhelpful Treatment

- *Lytic Cocktail*

Lytic cocktail is a combination of Pethidine, Promethazine and Chlorpromazine. The alpha blocking effect of chlorpromazine might be beneficial in scorpion sting. Pethidine may convert sublethal dose of scorpion venom into lethal one and may interfere with protective respiratory reflexes.

- *Morphine*:

  Morphine is age old drug for treatment of acute pulmonary oedema. Morphine is not used for treating pulmonary oedema in scorpion sting since it worsens dysrhythmia.

- *Steroids*

  Steroids might enhance the necrotizing effects of excessive catecholamines on myocardium.(9)

- *Atropine*

  Complete abolition of parasympathetic effects may permit the domination of the overstimulated sympathetic system. Atropine potentiates tachycardia, sustains hypertension and further aggravates myocardial injury.

- *Nifidepine*

  Reflex tachycardia and negative inotropic effect caused by nifidipine warrants its use in scorpion sting eventhough it got antihypertensive and vasodilatory action.

- *ACE Inhibitors*

  The use of ACE inhibitors like Captoprilcan aggrevatehyperkalemia. It can also inhibit breakdown of bradykinin, which is involved in pulmonary edemadue to scorpion sting.

The effectiveness of prazosin therapy in scorpion sting was scientifically established in our country during the mideighties. The clinical experience of Bawaskar and Bawaskar is confirmed by the experimental study done by Gueron.In the preprazosin era from 1961-1983, 25-30% mortality due to pulmonary edema was reported in scorpion victims from Western India. After the emergence of prazosin (1984 onwards) the mortality is reduced drastically to less than 1%.Case fatality rate in children due to scorpion sting has also declined after prazosin was introduced as the first line of management.

Prevention

- False ceiling under loose tiles of roof and bamboo cot are the often places of stay for scorpion which should be cleaned regularly and maintained.
- In endemic areas of venomous sting clothing, beddings, shoes, package should be vigorously shaken out and checked for scorpion.
- Pesticides like organophosphates, pyrethrins and chlorinated hydrocarbons are known to kill scorpions.
- During opening the school the tables and rooms including roof, walls and floor should be thoroughly cleaned and washed.

THE REVIEW OF LITERATURE

1. A prospective study was conducted by Bawaskar & Bawaskar to evaluate the clinical features of severe scorpion sting in children and the management at a rural setting. 12 patients with severe scorpion sting referred from primary health center were presented in this study. Eight children had complication of pulmonary edema and hypotension; two had pulmonary edema and hypertension, one each presented with hypertension and tachycardia. Oral administration of prazosin, dobutamine intravenous infusion and sodium nitroprusside infusion (SNP) were given for symptomatic management. Despite use of SNP and dobutamine infusion two children of massive pulmonary edema. Anti scorpion venom was given which does not prevent the cardiovascular manifestations of severe scorpion sting. But early administration of oral prazosin therapy was useful in preventing the severity of scorpion envenomation.[1]
2. A study done by by Pol. R et al for evaluation of the clinical presentation, outcome and the efficacy of early Prazosin therapy in scorpion sting envenomation at a tertiary care hospital in Bagalkot, India.[2]

   A total of 240 children were studied prospectively. The data included demographics, the time of presentation to the hospital, the

clinical features, and the premedication which was given before arrival of the patients at the hospital, clinical response to the oral Prazosin and the outcome in the hospital was analysed. Among 240 children, 18 (7.5%) children expired may be due to the usage of premedication with antihistaminics and steroids in these children.

A postsynaptic alpha –1 blocker, Oral Prazosin is an effective drug for scorpion sting envenomation. It was concluded that Scorpion sting envenomation is an acute life threatening emergency and an early presentation to the hospital and an early intervention with Prazosin can improve the recovery in the scorpion sting.

3. In the study done by Biswal. N et al, Children aged below 13 years with history of scorpion sting were studied. Clinical features, complications, drug therapy and outcome of the cases was studied from year 1992-97 retrospectively and during 1997-2000 prospectively. Cases presented within 4 hours of sting were given Prazosin (30 µ/Kg/dose)single dose and were observed. Those who presented after 4 hours & above without features of envenomation received symptomatic treatment. Cases with signs of scorpion sting envenomation were given oral Prazosin(30 µ/Kg/dose) every 6 hourly until they recover.

4. Children with complications like acute pulmonary edema (APE) were treated with dobutamine and sodium nitroprusside drip. Complicated cases were monitored in PICU as per the treatment protocol, and was observed that there was significant reduction in overall mortality(P<0.0155) [4]
5. A prospective study done by Prasad R et al to identify and to correlate various factors affecting the outcome of children with scorpion sting envenomation treated with prazosin.The study showed that all children with scorpion sting had perspiration and cold periphery. Except two, who had sting over the trunk, rest of the children had sting over extremities. Shock was present in 48(53.3%), whereas myocarditis, encephalopathy, pulmonary edema and priapism were present in 38(42.2%), 32(35.5%), 34(37.8%), and 28(31.1%) children, respectively.[4] Among total cases eight (8.9%) children had died. The mean value of blood pressure, electrolytes like sodium and potassium among survivors and non-survivors were not significant. Mortality was obviously high in children presented after 6 hour of

   sting. The children with complications like metabolic acidosis, tachypnea, myocarditis, acute pulmonary oedema, encephalopathy and priapism had significantly higher mortality.[3]

6. In retrospective study conducted by Bahloul M et al to study epidemiological and clinical manifestations after severe scorpion envenomation to define the factors for the poor prognosis in children. The medical records of 685 children aged less than 16 years admitted for scorpion sting were assessed. There were 558 children (81.5%) in the grade III group (with cardiogenic shock and pulmonary edema or severe neurological manifestation like coma and/or convulsion. 127 children(18.5%) in the grade II group (with systemic manifestations). A statistically significant association was found between the development of SIRS and heart failure. Temperature of 39°C and higher was associated with the presence of pulmonary edema, with a sensitivity of 20.6%, a specificity of 94.4%, and a positive predictive value of 91.7%. Blood sugar levels above 15mmol/L were significantly associated with a heart failure. Glasgow coma score ≤8/15, pulmonary edema, and cardiogenic shock were associated with poor prognosis. The presence of SIRS, temperature 39°C and higher, and blood sugar levels above 15mmol/L were associated with heart failure.
7. Al-Hemairi et al conducted an observational descriptive study to evaluate the epidemiological and clinical features of scorpion envenomation in children. A total of 41 children 11 yrs of age or younger, who got admitted at the emergency department at Rabigh

General Hospital due to documented scorpion stings from February 2007 to July 2011 were analysed. The mean age of scorpion sting was 5.4years ranging from 9 months to 11year. Male patients were 22 (53.6%). The peak frequency of scorpion stings was observed in the month of June .Majority of the stings were on exposed parts of the limbs mainly lower limbs in 30 patients (73%). Local signs like redness, swelling and pain were the most common clinical manifestations and observed in 61% of patients. Most common systemic manifestations were restlessness and irritability (31.7%) followed by vomiting in 26.8% children and cold extremities in 19.5% children. All the patients received scorpion antivenom according to guidelines of Ministry of Health Saudia Arabia. One child died while others were discharged within three days of admission. It was concluded that though majority of scorpion stings in children have a good prognosis, severe complications and death may occur. I

8. n a study by Sagarad et al., high cardiac troponin levels in scorpion sting cases were shown to be a useful indicator in prediction of myocarditis as well as in planning for early treatment (8).
9. In a study by Sundararaman et al., it was found that scorpion sting was a risk factor in the long-term for development of idiopathic dilated cardiomyopathy (6).

CLINICAL STUDY

- **AIMS AND OBJECTIVES**
- **MATERIALS AND METHODOLOGY**
- **OBSERVATION AND RESULTS**
- **DISCUSSION**
- **CONCLUSION**

AIMS AND OBJECTIVES OF THE STUDY

- To study the effectiveness of early prazosin therapy in children with scorpion sting.
- To determine whether time gap between sting and hospital admission as one of the significant risk factors which determine outcome and mortality.

MATERIALS AND METHODS

TOPIC

A CLINICAL STUDY ON THE EFFECTIVENESS OF EARLY PRAZOSIN THERAPY IN CHILDREN WITH SCORPION STING

CASE SELECTION: 100 Cases of suspected and clinically proven scorpion sting

TYPE OF STUDY:

Prospective observational hospital based time bound study.

INCLUSION CRITERIA:

Children in the age group 2-12 years admitted to GMKMCH, Salem with

1. History of scorpion sting

2. Clinically suspected cases of scorpion sting

EXCLUSION CRITERIA:

- Other animal/insect bites
- The children whose parents are unwilling for the study

STUDY METHADOLOGY

All cases which satisfy the inclusion criteria will be taken into study. Duration of the study will be from January 2016 to December 2016.

After admission to the hospital, informed consent will be taken from the parents.

Careful history and detailed clinical examination will be done at the time of admission.

Scorpion sting patients are selected and examined clinically for local manifestation like pain and swelling, diaphoresis, salivation, cold extremity, features of autonomic storm. The children were examined for development of complications like myocarditis, acute pulmonary oedema, shock, ARDS, encephalopathy.

- Local manifestation:
  - Pain
  - swelling

- Cholinergic symptoms :
    - vomiting
    - salivation
    - sweating
    - priapism
- Adrenergic symptoms :
    - palpitation
    - breathlessness

COMPLICATIONS OF SCORPION STING

- Myocarditis
    - Tachycardia
    - muffled heart sound
    - gallop rhythm
    - systolic murmer
- Acute pulmonary oedema
    - Tachypnea
    - Pink frothy sputum
    - Bilateral crepitation

Regular monitoring will be done for next 24 hours or till the patient shows clinical improvement as is necessary in each case and entered in the proforma. Each child is managed according to clinical manifestation. Asymptomatic children will be kept under observation for 24 hours with repeated monitoring of vital signs. Symptomatic children will be managed according to their clinical status on the basis of the treatment protocol. Cases with autonomic storm will be given Prazosin 30µg/kg/dose, next dose will be repeated after 3 hours followed by every 6 th hourly till recovery, maximum 4 doses will be given.

RESULTS

The present study was conducted at the department of Paediatrics,Govt. Mohan Kumaramangalam Medical College hospital, Salem from JAN 2016TO DEC 2016.

This study was conducted on 100 clinically suspected or proven cases of scorpion sting between age group 2 years to 14 years of age.

Statistical methods:

Complication was considered as primary outcome variable. Time from sting to admission and first dose of prazosin are considered as primary explanatory variables. Age and gender other explanatory variables.

Descriptive analysis: Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion

for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots.

The association between explanatory variables and complication was assessed by cross tabulation and comparison of percentages. Chi square test was used to test statistical significance. Data was presented in stacked bar chart.

P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.(1)

RESULTS:

A total of 100 children including data analysis

Table1: Descriptive analysis of Age in study population (N=100)

Age	Frequency	Percentages
2 to 4 years	22	22.00%
5 to 8 years	51	51.00%
9-12 years	27	27.00%

Figure : Pie chart of Age distribution in study population (N=100)

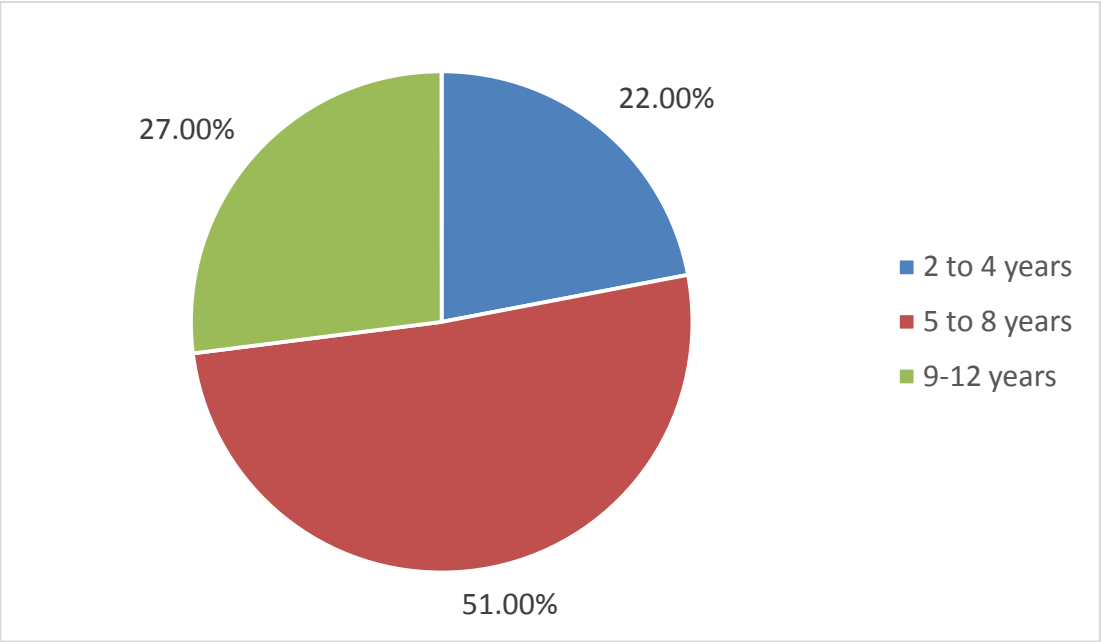


Table2: Descriptive analysis of Gender in study population (N=100)

Gender	Frequency	Percentage
Male	58	58.00%
Female	42	42.00%

Figure: Pie chart of Gender distribution in study population (N=100)

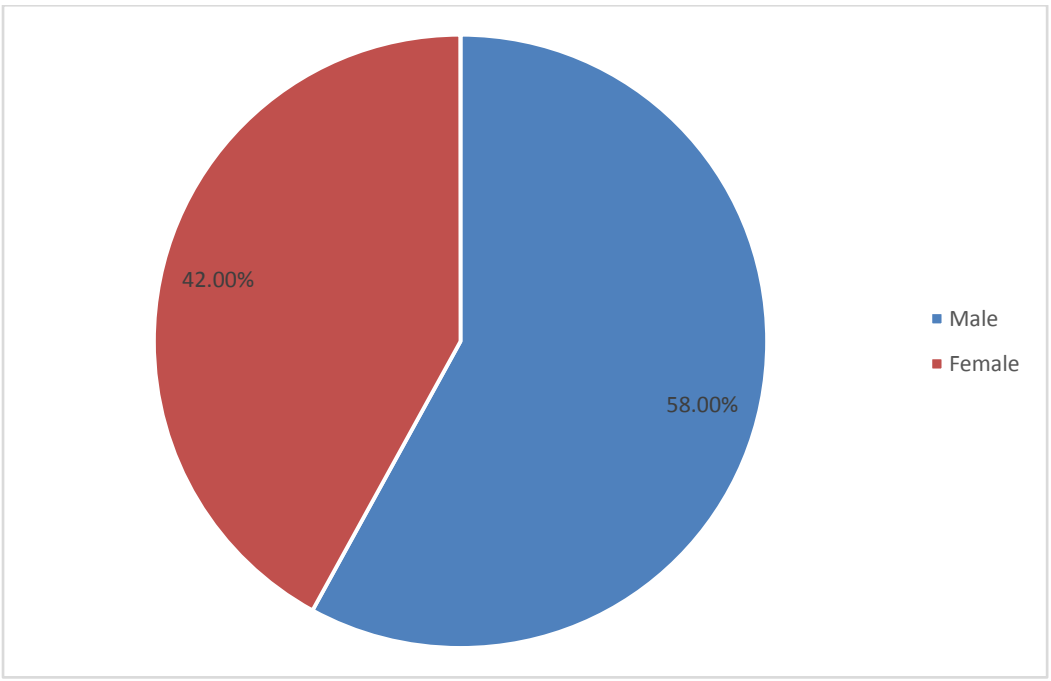


Table 3: Descriptive analysis of time from sting to admission in study population (N=100)

Time From Sting to Admission	Frequency	Percentage
<2 hours	33	33.00%
3 to 6 hours	48	48.00%
7 to 12 hours	17	17.00%
>12 hours	2	2.00%

Figure: Pie chart of time from sting to admission distribution in study population (N=100)

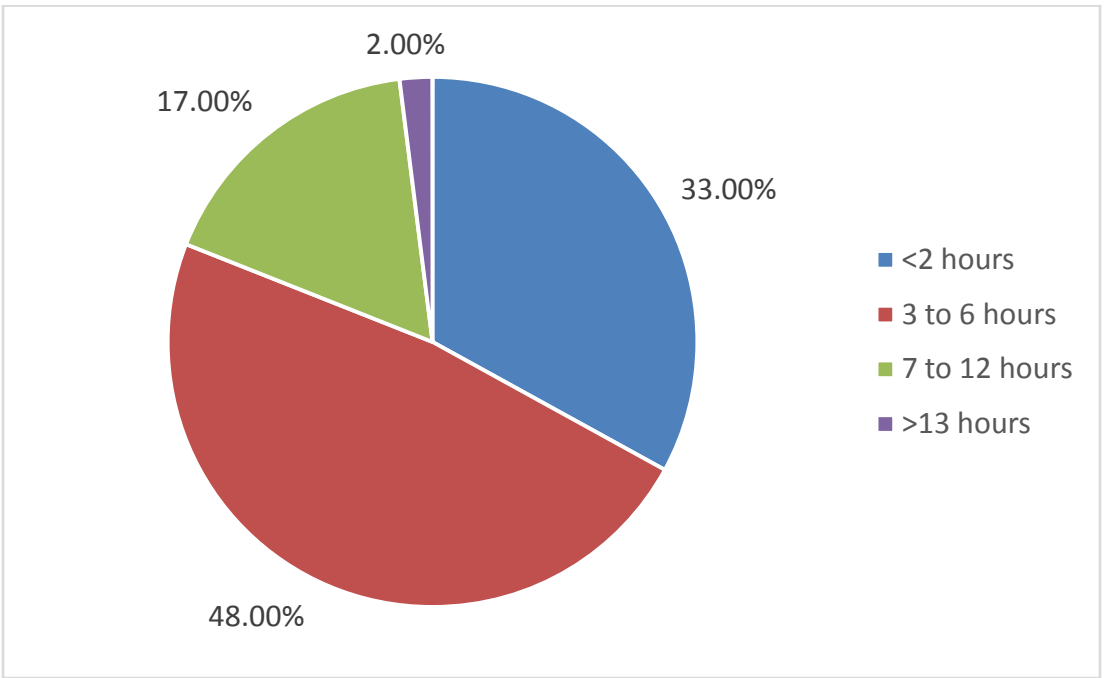


Table 4: Descriptive analysis of administration of the first Dose of Prazosin in study population (N=100)

First Dose of Prazosin administration	Frequency	Percentage
<2 hours	24	24.00%
3 to 6 hours	56	56.00%
7 to 12 hours	18	18.00%
>12 hours	2	2.00%

Figure : Pie chart of first dose of Prazosin administration distribution in study population (N=100)

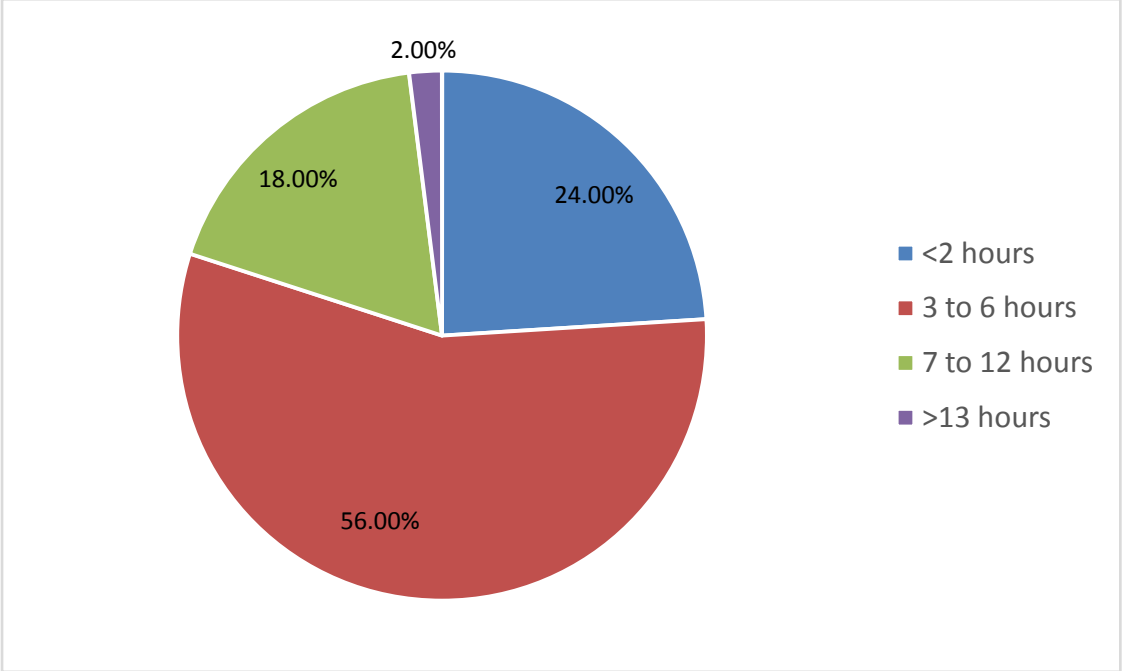


Table 5: Descriptive analysis of distribution of Local symptoms in study population (N=100)

Local	Frequency	Percent
Pain	66	66.00%
Swelling	6	6.00%
Nil	34	34.00%

Figure: Pie chart of Local symptom distribution in study population (N=100)

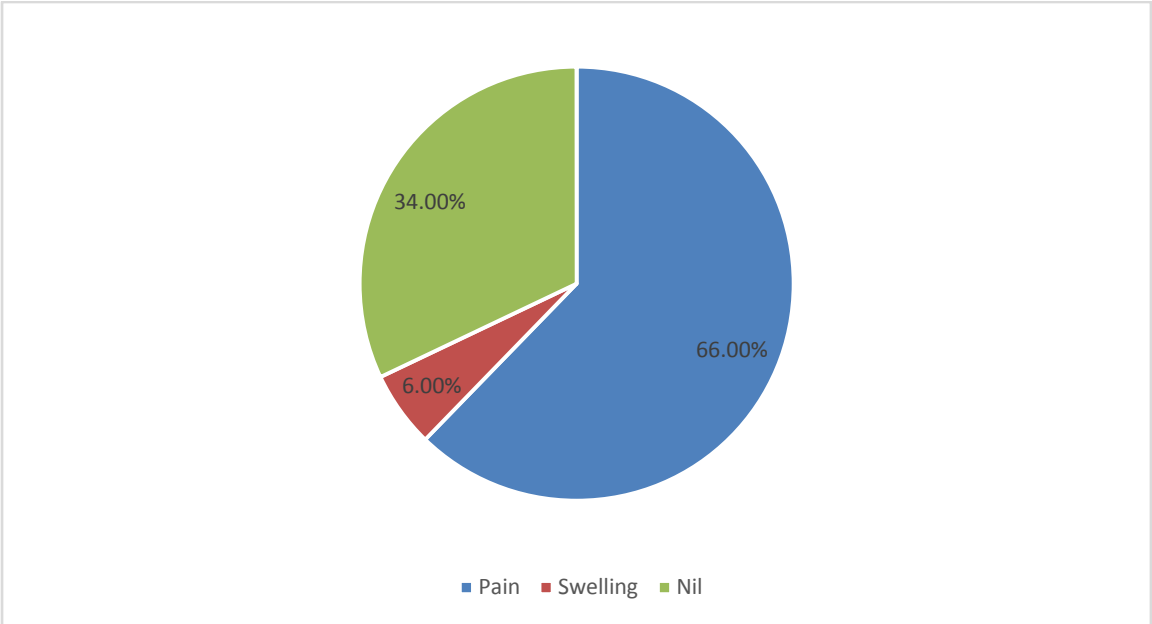


Table 6: Descriptive analysis of distribution of Autonomic symptoms in study population (N=100)

Autonomic	Frequency	Percent
Sweating	73	73.00%
Salivation	34	34.00%
Vomiting	42	42.00%
Tachycardia	45	45.00%
Priapism	20	20.00%

Figure : Pie chart of Autonomic symptom distribution in study population (N=100)

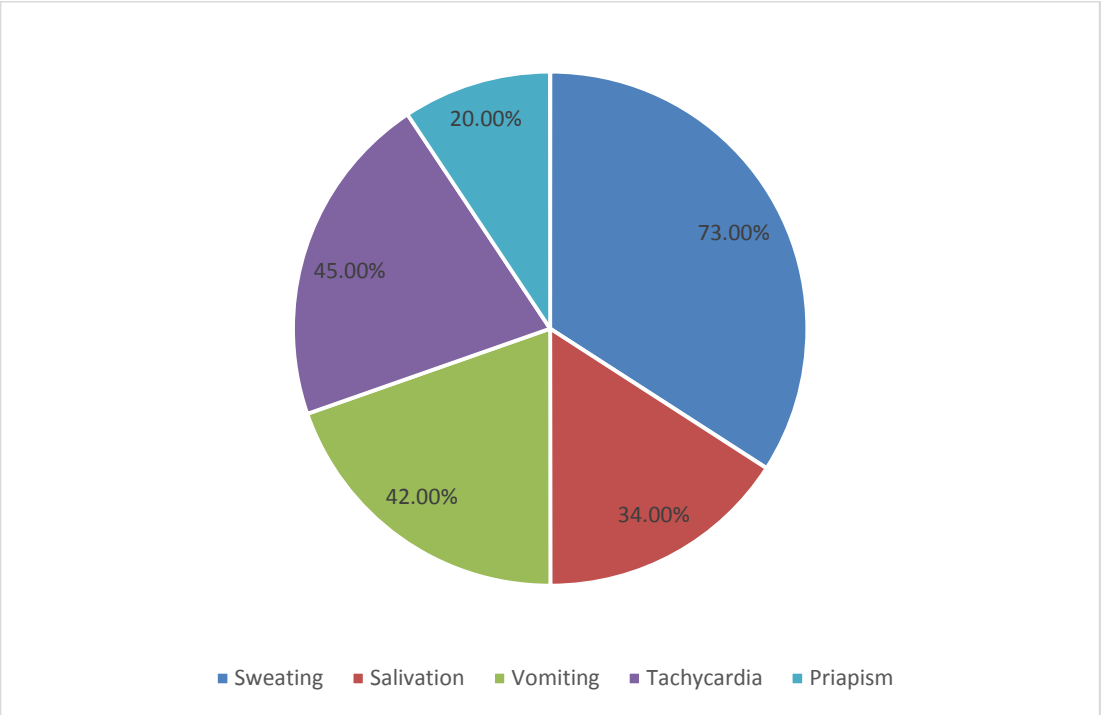


Table 7: Descriptive analysis of distribution of Complication in study population (N=100)

Complication	Frequency	Percent
Nil	62	62.00%
Myocarditis	16	16.00%
Acute pulmonary oedema	15	15.00%
Cardiogenic shock	22	22.00%
Neurological	2	2.00%

Figure : Bar chart of complication distribution in study population (N=100)

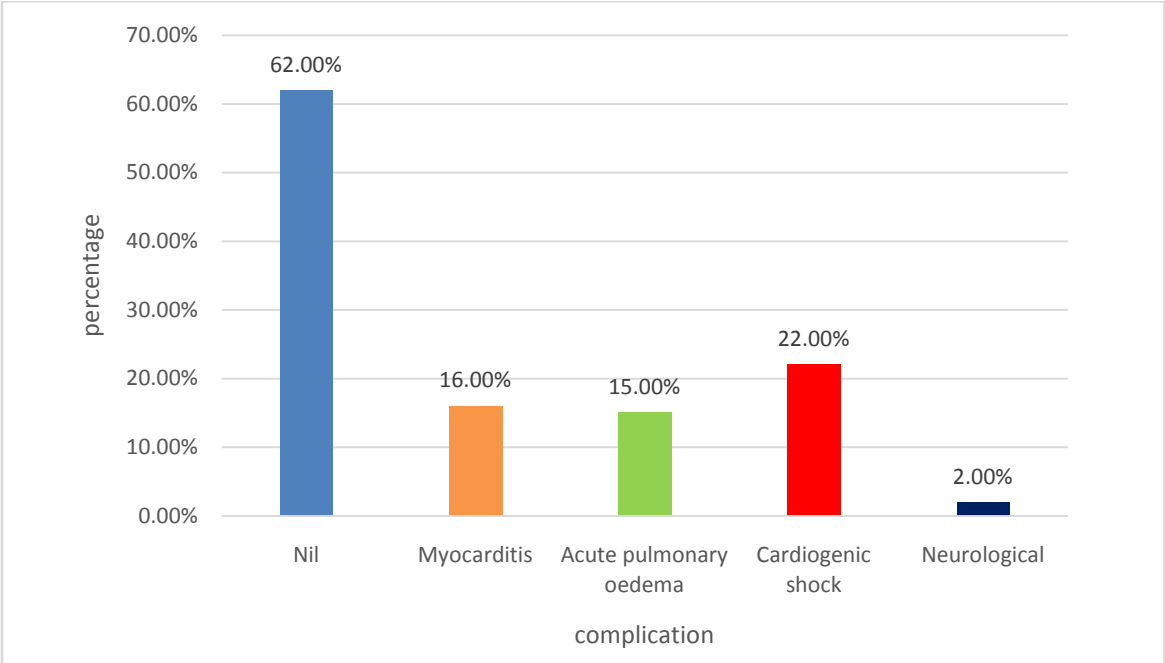


Table8: Association of Myocarditis with demographic of study population (N=100)

Demographic	Myocarditis		Chi square	P-value
	Present	Absent		
Age				
2 to 4 years (N=22)	2 (9.090%)	20 (90.90%)	2.957	0.228
5 to 8 years(N=51)	7 (13.72%)	44 (86.27%)		
9-12 years(N=27)	7 (25.92%)	20 (74.07%)		
Gender				
Male (N=58)	9 (15.51%)	49 (84.48%)	0.024	0.877
Female(N=42)	7 (16.66%)	35 (83.33%)		

Table 9: Association of Myocarditis with time from sting to admission of study population (N=100)

Time from sting to Admission	Myocarditis	
	Present	Absent
<2 hours(N=33)	1 (3.030%)	32 (96.96%)
3 to 6 hours (N=48)	4 (8.333%)	44 (91.66%)
7 to 12 hours (N=17)	9 (52.94%)	8 (47.05%)
>13 hours(N=2)	2 (100%)	0 (0%)

*No statistical test was applied considering “0” subjects in one of the cells

Table 10: Association of Myocarditis with first Dose of Prazosin administration of study population (N=100)

First Dose of Prazosin	MYOCARTITIS	
	Present	**Absent**
<2 hours (N=24)	0 (0%)	24 (100%)
3 to 6 hours (N=56)	5 (8.928%)	51 (91.07%)
7 to 12 hours(N=18)	9 (50%)	9 (50%)
>13 hours(N=2)	2 (100%)	0 (0%)

*No statistical test was applied considering "0" subjects in one of the cells

Table 11: Association of ACUTE PULMONARY OEDEMA with demographic of study population (N=100)

Demographic	ACUTE PULMONARY OEDEMA		Chi square	P-value
	Present	**Absent**		
Age				
2 to 4 years (N=22)	3 (13.63%)	19 (86.36%)	0.633	0.729
5 to 8 years(N=51)	9 (17.64%)	42 (82.35%)		
9-12 years(N=27)	3 (11.11%)	24 (88.88%)		
Gender				
Male (N=58)	10 (17.24%)	48 (82.75%)	0.544	0.461
Female(N=42)	5 (11.90%)	37 (88.09%)		

Table 12: Association of Acute Pulmonary Oedema with time from sting to admission of study population (N=100)

Time from sting to Admission	Acute Pulmonary Oedema	
	Present	**Absent**
<2 hours(N=33)	0 (0%)	33 (100%)
3 to 6 hours (N=48)	3 (6.25%)	45 (93.75%)
7 to 12 hours (N=17)	11 (64.70%)	6 (35.29%)
>13 hours(N=2)	1 (50%)	1 (50%)

No statistical test was applied considering “0” subjects in one of the cells

Table 13: Association of acute pulmonary oedema with first dose of prazosin of study population (N=100)

First Dose of Prazosin administration	Acute Pulmonary Oedema	
	Present	**Absent**
<2 hours (N=24)	0 (0%)	24 (100%)
3 to 6 hours (N=56)	2 (3.571%)	54 (96.42%)
7 to 12 hours(N=18)	12 (66.66%)	6 (33.33%)
>13 hours(N=2)	1 (50%)	1 (50%)

No statistical test was applied considering “0” subjects in one of the cells

Table 14: Association of cardiogenic shock with demographic of study population (N=100)

Demographic	Cardiogenic shock		Chi square	P-value
	Present	Absent		
Age				
2 to 4 years (N=22)	6 (27.27%)	16 (72.72%)	0.553	0.759
5 to 8 years(N=51)	11 (21.56%)	40 (78.43%)		
9 to12 years(N=27)	5 (18.51%)	22 (81.48%)		
Gender				
Male (N=58)	17 (29.31%)	41 (70.68%)	4.301	0.038
Female(N=42)	5 (11.90%)	37 (88.09%)		

Table 15: Association of CARDIOGENIC SHOCK with TIME FROM STING TO ADMISSION of study population (N=100)

TIME FROM STING TO ADMISSION	CARDIOGENIC SHOCK		Chi square	P-value
	Present	Absent		
<2 hours(N=33)	7 (21.21%)	26 (78.78%)	9.671a	0.022
3 to 6 hours (N=48)	6 (12.5%)	42 (87.5%)		
7 to 12 hours (N=17)	8 (47.05%)	9 (52.94%)		
>13 hours(N=2)	1 (50%)	1 (50%)		

Table 16: Association of cardiogenic shock with first dose prazosin of study population (N=100)

Dose Prazosin	Cardiogenic shock		Chi square	P-value
	Present	Absent		
<2 hours (N=24)	2 (8.333%)	22 (91.66%)	8.991a	0.029
3 to 6 hours (N=56)	11 (19.64%)	45 (80.35%)		
7 to 12 hours(N=18)	8 (44.44%)	10 (55.55%)		
>13 hours(N=2)	1 (50%)	1 (50%)		

Table 17: Association of Neurological with demographic of study population (N=0)

Demographic	Neurological	
	Present	Absent
Age		
2 to 4 years (N=22)	0 (0%)	22 (100%)
5 to 8 years(N=51)	0 (0%)	51 (100%)
9-12 years(N=27)	2 (7.407%)	25 (92.59%)
Gender		
Male (N=58)	0 (0%)	58 (100%)
Female(N=42)	2 (4.761%)	40 (95.23%)

*No statistical test was applied considering “0” subjects in one of the cells

Table 18: Association of Neurological with time from sting to admission of study population (N=100)

Time from Sting toAdmission	Neurological	
	Present	**Absent**
<2 hours(N=33)	0 (0%)	33 (100%)
3 to 6 hours (N=48)	0 (0%)	48 (100%)
7 to 12 hours (N=17)	1 (5.882%)	16 (94.11%)
>13 hours(N=2)	1 (50%)	1 (50%)

*No statistical test was applied considering “0” subjects in one of the cells

Table 19: Association of Neurological with first Dose Prazosin of study population (N=100)

First Dose of Prazosin	Neurological	
	Present	**Absent**
<2 hours (N=24)	0 (0%)	24 (100%)
3 to 6 hours (N=56)	0 (0%)	56 (100%)
7 to 12 hours(N=18)	1 (5.555%)	17 (94.44%)
>13 hours(N=2)	1 (50%)	1 (50%)

*No statistical test was applied considering “0” subjects in one of the cells

DISCUSSION

Scorpion sting envenomation is an acute life threatening medical emergency.

The study was to evaluate the effectiveness of early prazosin therapy in scorpion sting and to determine the whether the time duration between sting and first dose of prazosin as a significant factor to determine the final outcome.

- In the study 100 cases of suspected and clinically proven scorpion sting are selected. Majority (51%) of the children belong to the age group of 5 to 8 years. Among all,58% were male children.
- In the study, majority of the children (48%) got admitted in our hospital between 3 to 6 hours of scorpion sting, whereas 33 % reach the hospital before 2 hours of sting,17 % by 7 to 12 hours and 2 percent of cases got admitted after 12 hours.
- In the study first dose of prazosin was administered in cases with the features of autonomic storm.24 % cases were administered prazosin within 2 hours of hospitalisation,56 % between 3 to 6 hours,18 % by 7 to 12 hours and 2 % after 12 hours.
- Local symptoms were present in 72 %of cases of which 66 children had local pain.6 percent of cases had swelling at the sting site.

- The study population was analysed for the features of autonomic storm. Majority of the children had sweating, which account for 73 percent.

  Salivation was found in 34 % of cases, vomiting in 42 %, tachycardia in 45 %.Among the male children 20 % presented with priapism.

- In the study 38 % of children with scorpion sting suffered from complication. Majority (22%) had cardiogenic shock as complication.

- 27.2 percent of children with complication presented as cardiogenic shock belong to the age group of 2 to 4 years.Cardiogenic shock was present in half of the cases presented after 12 hours, nearly half(47%)of those who got admitted between 7 to 12 hours of sting. The children who got admitted early had fewer incidence of cardiogenic shock in 6 children admitted by 3 to 6 hours and 7 cases admitted before 2hours of sting. The difference in time of sting from admission of two groups was statistically significant which is evident from p value of 0.022 indicating early admitted children had a better outcome as in previous studies.

- The cardiogenic shock was observed in 2 children who had been administered the first dose of prasozin before 2 hours of hospitalisation. Cardiogenic shock in 19.6 % of children who came

by 3 to 6 hours. The incidence was high in those who received the first dose of prazosin lately, as 44.4 % of children who received the first dose between 7 to 12 hours, and 50 % cases after 12 hours.The p value came out to be 0.029 which again implied the fact that there is statistically significant difference between the two groups in terms of early prazosin administration.

- 16 percent of children with complication presented as myocarditis, which is observed in the same frequency in the age group of 5 to 8 years and 9 to 12 years. Myocarditis was present in all the cases presented after 12 hours, more than half(52.9%)of those who got admitted between 7 to 12 hours of sting. The children who got admitted early had fewer incidence of myocarditis, in 8.3 % admitted by 3 to 6 hours and 3% of cases admitted before 2hours of sting.
- The myocarditis was not observed in any of the children who had been administered the first dose of prasozin before 2 hours of hospitalisation. Myocarditis was present in 8.9 % of children who came by 3 to 6 hours. The incidence of myocarditis was high in those who received the first dose of prazosin lately. This was clearly evident in the study as 50 % of children who received the first dose between 7 to 12 hours, all the cases after 12 hours had myocarditis. The p value of acute myocarditis with age and sex of

study population was 0.228 and 0.877 which is not statistically significant, which indicates age and sex are not determinants in scorpion sting.

- 15 % had acute pulmonary oedema, which is observed in the higher frequency in the age group of 5 to 8 years(17.6%). The children who got admitted early had fewer incidence of acute pulmonary oedema, in 6.2% who got admitted by 3 to 6 hours and none of the cases admitted before 2hours of sting.
- The acute pulmonary oedema was present in half of the cases presented after 12 hours, more than half (64.7%) of those who got admitted between 7 to 12 hours of sting. The acute pulmonary oedema was not observed in any of the children who had been administered the first dose of prazosin before 2 hours of hospitalisation. The acute pulmonary oedema was present in 3.5 % of children who came by 3 to 6 hours. The incidence of high in those who received the first dose of prazosin lately, which was evident in the study as 66.6% of children who received the first dose between 7 to 12 hours, half of the cases after 12 hours had pulmonary oedema.
- Neurological manifestation is seen as rare complication of scorpion sting. Only 2 cases presented with neurological features, both cases present after 12 hours.

- One case among 100 chilren,5 year old male child presented at 10 hours after scorpion sting without referral with features of shock, myocarditis and pulmonary oedema expired inspite of shock correction,prazosin therapy,
- intubation, ventilatory and ionotrope support.

CONCLUSION

Scorpion sting is a life threatening medical emergency especially in the rural areas of our country. The effectiveness of early administration of prazosin in reducing complications from scorpion sting was evident in our study as well as other studies. It was clearly found in the study that those children admitted earlier had a better outcome as in other studies. It was well proved in the study that prazosin is not only helpful in reducing autonomic symptoms but also cardioprotective which help in reducing complications like cardiogenic shock, myocarditis and acute pulmonary oedema.

The causes for higher mortality in a case of scorpion sting may be due to:

- late presentation to the hospital
- late administration of prazosin
- Associated multiple systemic involvement.

The mortality was less in cases which were treated with Prazosin. This could be due to the protective effect of Prazosin on the cardiovascular and the respiratory systems.

Oral Prazosin is fast acting, easily available, cheap, free from

any anaphylaxis and highly effective. Early intervention with oral. Prazosin and the appropriate use of dobutamine can hasten the recovery in the scorpion sting victim. Most of the cases with acute pulmonary oedema, encephalopathy and myocarditis, who came after 6 hours of the sting, had higher mortality and morbidity

The study highlights the early administration of prazosin in case of scorpion sting. Prazosin is fast acting, easily available, cheap, free from any anaphylaxis and highly effective and can be administrated safely in a primary health center before early referral, thereby preventing further complication and mortality in children with scorpion sting. Timely referral of the cases with scorpion sting and early therapy with Prazosin can be life saving.

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PATIENT CONSENT FORM

STUDY DETAIL: **CLINICAL STUDY ON THE EFFECTIVENESS OF EARLY PRAZOSIN THERAPY IN CHILDREN WITH SCORPION STING**

STUDY CENTER: GOVT.MOHANKUMARAMANGALAM MEDICAL

COLLEGE, SALEM

Patients Name :

Patients Age :

Identification Number:

Patient may check ( ) these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all myquestions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation

to it, even if I withdraw from the study I agreeto this access. However, I understand that my identity will not be

revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

Patients Name and Address: Place

Signature of investigator :

Study investigator’s Name :

Place

Date

PROFORMA

- Name : case no:
- Age :
- Sex :
- Address:
- Phone no:
- IP NO:
- Date of admission:

PRESENTING COMPLAINTS

- Local manifestation:
  - pain
  - swelling
- Cholineric symptoms :
  - vomiting
  - salivation
  - sweating
  - priapism
- Adrenergic symptoms :
  - palpitation
  - breathlessness

COMPLICATIONS

- Myocarditis
    - Tachycardia
    - muffled heart sound
    - gallop rhythm
    - systolic murmer
- Acute pulmonary oedema
    - tachypnea
    - pink frothy sputum
    - bilateral crepitation
- Time of scorpion sting :
- Time of hospital admission :
- Details of treatment given in the peripheral hospital (from the reference letter)
- Time of administration of prazosin therapy:
- Time lapse between sting and 1 dose prazosin administration :
- Complication of the sting (if any) :

TIME OF DRUG	< 1 HR	2 HR	3 HR	4 HR	5 HR	6 HR	7 HR
MYOCARDITS							
A/C PULMONARY OEDEMA							
CARDIOGENIC SHOCK							
SEIZURE							
STROKE							

TIME OF DRUG	8 HR	9 HR	10 HR	11 HR	12 HR	>12 HR
MYOCARDITIS						
A/C PULMONARY OEDEMA						
CARDIOGENIC SHOCK						
SEIZURE						
STROKE						

MASTER CHART

SL NO	NAME	AGE	SEX	TIME FROM STING TO ADMISSION	1 st DOSE PRAZOSIN	LOCAL						COMPLICATION
		2-5 YEARS=1 5-8YEARS=2 8-12 YEARS=3	MALE=1 FEMALE=2	<2 HR = 1 2-6 HR = 2 6-12 HR = 3 >12 HR = 4	<2 HR = 1 2-6 HR = 2 6-12 HR = 3 >12 HR = 4	PAIN = 1 SWELLING = 2 NIL=3	SWEATING PRESENT =1 ABSENT =2	SALIVATION PRESENT =1 ABSENT =2	VOMITING PRESENT =1 ABSENT =2	TACHYCARDIA PRESENT =1 ABSENT =2	PRIAPISM PRESENT =1 ABSENT =2	NIL = 1 MYOCARTITIS = 2 ACUTE PULMONARY OEDEMA = 3 CARDIOGENIC SHOCK =4 NEUROLOGICAL = 5
1	PUGAL	2	1	1	2	1	1	1	1	2	2	4
2	RAMESH	1	1	2	2	1	1	2	2	2	1	2
3	SHARMILA	2	2	2	2	1	1	1	1	1	2	1
4	MANIKANDAN	3	1	2	2	1	1	2	1	2	2	1
5	SINDHU	1	2	1	1	1	1	1	2	1	2	1
6	SENTHIL	2	1	3	3	3	2	2	1	2	2	2,3,4
7	SAKHTI	2	1	2	2	1	1	1	2	2	1	1
8	ANU	3	2	2	2	1	1	2	1	1	2	1
9	DEENA	2	1	1	1	1	2	2	1	2	1	4
10	TAMIL	1	2	1	2	1	2	1	2	1	2	1
11	SRINIVAS	2	1	2	2	3	1	2	2	2	2	4
12	KUPPAYE	3	1	1	1	1	1	1	1	1	2	1
13	GOMATHI	2	2	2	2	1	1	2	2	1	2	1
14	KUPPAYE	1	1	1	1	1	1	1	2	2	1	1
15	VINODINI	2	2	3	3	3	2	2	1	1	2	2,3,4
16	SANDIYA	2	2	1	1	1	2	1	2	1	2	1
17	MOHANA	3	2	2	2	1	1	2	2	1	2	1
18	BAKIYAM	1	1	2	2	1	1	2	2	2	1	3
19	MANIKANDAM	2	2	2	3	1	1	1	2	2	2	3
20	SURYA	3	1	2	2	1	2	2	2	1	2	1
21	SRINIVAS	1	1	3	3	1	1	1	1	2	2	1

22	AJITHA	3	2	4	4	1	2	2	2	1	2	2,4,5
23	NAVEEN	2	1	2	2	1	1	1	2	1	2	1
24	RAJI	2	2	1	1	1	1	2	2	2	2	1
25	ANITHA	2	2	1	1	1	1	2	2	2	2	1
26	NAVEEN	1	1	1	2	3	1	2	1	1	1	4
27	PRABHU	3	1	2	2	3	2	1	2	2	2	4
28	THANGARAJ	2	1	1	1	1	1	1	2	1	2	1
29	SUGANYA	1	2	1	2	3	1	2	2	2	1	1
30	VINODINI	2	2	2	2	1	1	2	1	1	2	1
31	KAVITHA	3	2	3	3	3	1	2	2	1	2	2,3,5
32	SEKAR	2	1	2	2	1	2	2	2	1	1	1
33	SIVA	2	1	2	2	3	1	1	1	1	2	2
34	BALA	2	1	2	2	1,2	1	2	2	2	2	1
35	VASUKI	1	1	3	3	1	1	2	1	11	2	2
36	RAMANI	2	2	1	1	1	1	2	2	2	2	1
37	FATHIMA	3	2	2	2	1	1	1	1	2	2	2
38	PAPPATHI	3	2	1	1	3	1	2	2	1	2	1
39	GOMATHI	2	2	1	1	1	1	2	2	2	2	1
40	PRIYAN	2	1	2	2	3	2	1	2	2	2	4
41	RAJA	3	1	3	3	1	1	2	1	2	1	2
42	SURESH	2	1	2	2	1	1	2	2	1	2	1
43	GOPI	1	1	2	2	3	2	2	2	2	1	1
44	RAJ	2	1	2	2	1	2	1	1	2	2	1
45	SUGANYA	2	2	1	1	3	1	2	2	2	2	1
46	LOGESH	3	1	3	3	1	2	2	2	1	2	1
47	AMRITHA	3	2	2	2	3	1	2	1	1	2	1
48	RAJ	2	1	1	2	1	1	2	1	2	2	4
49	SEKAR	1	1	3	3	3	1	1	2	2	1	4
50	ASOK	2	1	2	2	1	1	2	1	1	2	1
51	VINU	2	2	2	2	1	1	2	2	2	1	1
52	GOMATHI	3	2	2	2	1	1	2	1	2	2	1
53	RAJ	3	1	3	3	1	1	2	2	2	2	2,3
54	SENTHIL	2	1	2	2	3	1	1	2	1	2	1

55	SURYA	2	1	1	2	1,2	1	2	1	2	1	2
56	GANGA	1	2	1	1	1	1	2	2	1	2	1
57	BALKIS	3	2	1	1	1	1	2	2	2	2	1
58	FATHIMA	2	2	2	2	1	1	1	1	1	2	1
59	KISHORE	2	1	3	3	1,2	2	2	1	1	2	2,3
60	ANITHA	3	2	2	2	1	1	2	2	2	2	1
61	AJAY	1	1	1	1	1	1	1	2	2	2	4
62	ARUNA	2	2	1	1	3	1	2	1	1	2	1
63	ASOK	2	1	2	2	3	1	2	2	2	1	1
64	AMRITHA	2	2	2	2	3	1	1	1	2	2	2
65	ARUL	3	1	2	2	1	1	2	2	2	2	1
66	SAKHTI	1	1	3	3	3	2	2	1	1	2	3,4
67	MOHAN	1	1	2	2	3	1	2	1	2	2	1
68	AKILA	2	2	2	2	3	1	1	2	1	2	1
69	ARUNA	3	2	3	3	3	1	2	2	2	2	2,4
70	KISHORE	2	1	2	2	3	2	2	1	1	2	4
71	MEENA	2	2	4	4	3	1	1	2	2	2	2,3
72	MOHAN	3	1	1	1	3	2	2	1	2	2	1
73	PRADEEP	1	1	1	2	3	1	2	2	1	1	1
74	KARUNA	2	2	2	2	1	1	1	1	1	2	1
75	KEERTHI	2	2	2	2	1	2	2	1	2	2	1
76	KAMALA	1	2	3	3	1,2	1	2	2	1	2	3,4
77	KISHORE	3	1	2	2	1	2	1	1	1	1	1
78	RAJA	3	1	2	2	3	1	2	2	2	2	1
79	MOHAN	2	1	2	2	1	1	2	1	2	2	3
80	KUMAR	2	1	3	3	1	2	1	2	2	2	3,4
81	KUMARI	3	2	2	2	1	2	2	1	2	2	4
82	GANESH	2	1	1	1	1,2	1	2	2	1	2	1
83	PRIYA	2	2	1	1	3	1	1	1	2	2	1
84	DINA	3	1	1	1	3	1	2	2	1	2	1
85	MANOJ	1	1	2	2	1	1	2	1	2	1	1
86	MATHEW	2	1	1	1	3	2	2	2	2	2	1
87	KISHORE	3	1	2	2	1	1	1	2	2	2	4

88	KARTHIK	2	1	3	3	1	1	2	1	2	2	3
89	KAMALA	3	2	1	1	3	1	1	2	2	2	1
90	KEERTHIRAJ	2	1	1	1	1	1	2	2	2	2	1
91	AKILA	2	2	1	1	1	1	2	1	2	2	1
92	AMRITHA	2	2	2	2	1	2	1	2	1	2	1
93	AMMINI	1	2	2	2	3	1	2	2	1	2	1
94	ASOK	3	1	3	3	1,2	2	1	1	1	2	2,3
95	ARUN	1	1	2	2	3	1	2	2	1	2	1
96	MANOJ	2	1	1	2	1	2	2	2	2	1	4
97	MEKHA	1	2	2	2	3	1	1	1	1	2	1
98	RAJ	2	1	3	3	1	2	2	1	1	2	3,4
99	ARUN	1	1	1	2	1	1	2	2	2	1	4
100	RAMESH	2	1	2	2	1	2	1	1	1	1	1