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Pharmacy Newsletter

Management of Scorpion Envenomation

Scorpion stings are a major public health problem in many underdeveloped tropical countries. For every person killed by a poisonous snake, 10 are killed by a poisonous scorpion. Out of 1500 scorpion species, 50 are dangerous to humans. Almost all of these lethal scorpions, except the *Hemiscorpius* species, belong to the scorpion family called the Buthidae. The lethal members of the Buthidae family include the genera of *Buthus, Parabuthus, Mesobuthus, Tityus, Leiurus, Androctonus,* and *Centruroides*. These lethal scorpions are found generally in the given distribution:

HIGHLIGHTS

Buthus - Mediterranean area
Parabuthus - Western and Southern Africa
Mesobuthus - Asia
Tityus - Central and South America, Caribbean
Leiurus - Northern Africa and Middle East
Androctonus - Northern Africa to Southeast Asia
Centruroides - Southwest USA, Mexico, Central America

MESOBUTHUS TAMULUS

Scorpion stings cause a wide range of conditions, from severe local skin reactions to neurologic, respiratory, and cardiovascular collapse. Potency of venom varies with the species, with some producing only a mild flu and others producing death within an hour. Venom deposited via intravenous route can cause symptoms only 4-7 minutes after the injection, with a peak tissue concentration in 30 minutes (progress to a maximum severity within 5 hours) and an overall toxin elimination half-life of 4.2-13.4 hours through the urine. The symptoms generally persist for 10-72 hours.

Mortality/Morbidity:

Most deaths occur during the first 24 hours after the sting and are secondary to respiratory or cardiovascular failure. Children and elderly persons are at the greatest risk for morbidity and mortality.

Signs and Symptoms:

The signs of the envenomation are determined by the scorpion species, venom composition, and the victim's physiological reaction to the venom. Signs and symptoms do not have an apparent sequence. Thus, predicting the evolution of signs over time is difficult. Furthermore, a false recovery followed by a total relapse is common.

A person who has been stung by a scorpion usually has four signs, with the most common being mydriasis, nystagmus, hypersalivation, dysphagia, and restlessness. The mode of death is usually via respiratory failure secondary to anaphylaxis, bronchoconstriction, bronchorrhea, pharyngeal secretions, and/or diaphragmatic paralysis, even though venom-induced multiorgan failure plays a large role. Children present with the same symptoms and signs as adults,

Lab Studies

- Electrolyte evaluation is warranted in patients with venom-induced salivation, vomiting, and diarrhoea.
- Coagulation parameters should be measured for venom-induced defibrination because, at high concentrations, the venom is an anticoagulant.
- Glucose levels should be measured to evaluate for hyperglycaemia from liver and pancreas dysfunction.
- Creatine kinase and urinalysis help evaluate for venom-induced excessive motor rhabdomyolysis.
- Patients may have increased LFTs levels from venom-induced liver cell destruction.

Local treatment:

1. A negative-pressure extraction device (i.e., the extractor) may be useful, although the benefit is unproven. Apply it to the sting site after incision. Oral extraction is contraindicated.
2. Use ice bags to reduce pain and to slow the absorption of venom via vasoconstriction. This is most effective during the first 2 hours following the sting.
3. Immobilize the affected part in a functional position below the level of the heart to delay venom absorption.
4. Calm the patient to lower the heart rate and blood pressure, thus limiting the spread of the venom.
5. For medical delay secondary to remoteness, consider applying a lymphatic-venous compression wrap 1 inch proximal to the sting site to reduce superficial venous and lymphatic flow of the venom but not to stop the arterial flow. Only remove this wrap when the provider is ready to administer systemic support. The drawback of this wrap is that it may intensify the local effects of the venom.
6. Apply a topical or local anaesthetic agent to the wound to decrease paresthesia; this tends to be more effective than opiates.
7. Administer local wound care and topical antibiotic to the wound.

Drug Therapy:

1. Administer tetanus prophylaxis
2. Administer systemic antibiotics if signs of secondary infection occur
3. For hyperdynamic cardiovascular changes, administration of a combination of *beta-blockers with sympathetic alpha-blockers* is most effective in reversing this venom-induced effect. Avoid using beta-blockers alone because this leads to an unopposed alpha-adrenergic effect. Also, *nitrates* can be used for hypertension and myocardial ischemia. For hypodynamic cardiac changes, a titrated monitored fluid infusion with afterload reduction helps reduce mortality. A *diuretic* may be used for pulmonary edema in the absence of hypovolemia, but an *afterload reducer*, such as prazosin, nifedipine, nitroprusside, hydralazine, or angiotensin-converting enzyme inhibitors, is better. *Inotropic medications*, such as digitalis, have little effect, while dopamine aggravates the myocardial damage through catecholaminelike actions. Dobutamine seems to be a better choice for the inotropic effect. Finally, a pressor such as norepinephrine can be used as a last resort to correct hypotension refractory to fluid therapy.
4. Administer *atropine* to counter venom-induced parasympathomimetic effects.
5. Administer *barbiturates* and/or a benzodiazepine continuous infusion for severe excessive motor activity.
6. Administer *Benzodiazepines* to counteract excessive motor activity and nervous system excitation.
7. The use of *steroids* to decrease shock and edema is of unproven benefit.

   Note: *Scorpion Antivenom* is not available in Pakistan

Activity:

Rest and immobilisation of sting site is recommended to prevent rapid absorption of the venom into the circulation.

Inpatient Care:

Inpatient care is dictated by the severity of the envenomation and consists of stabilising the patient, providing supportive therapies, and preventing complications.

Outpatient Care:

Patients displaying local nonascending reactions to the venom may be discharged after six hours of observation, with close follow-up. If the patient was treated with a pressure bandage, the symptoms may be delayed and inpatient observation is warranted. Inform the patient about the possibility of persistent pain or paresthesia at the sting site.

Managing Toxic Methanol poisoning

Methanol is a highly toxic alcohol found in a variety of commercial products from paint stripper to industrial solvents to xerographic copier solution etc. Post ingestion, it is rapidly absorbed from the gastrointestinal tract and distributed in body water. The natural progression of the poisoning leads to accumulation of toxic metabolites, including formic acid and formaldehyde. It is these metabolites that have the ability to induce metabolic acidosis, nausea/vomiting, seizures, stupor, coma, calcium oxaluria, acute tubular necrosis, blindness and death. The amount of methanol ingested to toxic proportions varies among individuals. A dose of more than 30 ml methanol is considered potentially lethal.

Obtaining blood levels of methanol after a toxic ingestion may be difficult, since it metabolises to respective metabolites in the blood. It is for this reason that both methanol concentration and acid base balance as determined by the serum electrolyte (anion gap) and /or arterial blood gas analysis should be frequently monitored. Methanol concentrations in excess of 50 mg/dL are thought to be an absolute indication for the treatment with an antidote

The treatment plan is based on three 'specific' modalities: suppression of metabolism by alcohol dehydrogenase to toxic products, dialysis to enhance removal of methanol and its toxic product, and alkalinization to counteract metabolic acidosis.

So, a general treatment principle would consist of:

1. Emptying the stomach (if indicated)
2. Correction of the acidosis
3. Ethanol or Fomepizole administration to inhibit formation of toxic metabolites
4. Rapid reduction of body burden of both methanol and formate by haemodialysis
5. Intensive supportive care for multiple organ/system failure

Suggested dosing regimen for Ethanol includes:

	Oral	Intravenous
Loading dose	1 mL/kg of 95% ethanol, diluted	10 mL/kg of 10% ethanol in 5% dextrose over 30-60 minutes
Maintenance dose	0.1-0.2ml/kg/hour of 95% ethanol, diluted	1-2 mL/kg of 10% ethanol in 5% dextrose over 30 minutes

Note: In an emergency, an equivalent amount of any alcoholic drink may be administered orally**.**

Blood ethanol concentrations needs to be monitored hourly to maintain a concentration of >100 mg/Dl

Fomepizole, an FDA approved antidote, is quite expensive and probably not found in Pakistan. Dose for Fomepizole is 15 mg/kg IV followed by 10 mg/kg IV every 12 hours. After withdrawing appropriate dose from the vial, Fomepizole should be diluted to at least 100 mL using 0.9% Sodium Chloride or 5% Dextrose injection.

For methanol poisoning, folic acid 1mg/kg (50-70 mg) IV every 4 hours for the first 24 hours for a total of 6 doses is also added to the therapy plan to replenish folate dependent systems which are responsible for the oxidation of formic acid to CO in humans. Strong clinical data for this addition however is scarce. Source: http://www.pulsepakistan.com/

Facts About Therapeutic Drug Monitoring

Therapeutic Drug Monitoring (TDM) is defined as the use of drug concentrations to optimise drug therapy for individual patient. The idea that intensity and duration of pharmacological response is dependent on serum concentration was first reported by Marshalland, then tested for the screening of antimalarials during World War II. Since 1960s extensive research was directed in developing specific and sensitive analytical methods for serum drug concentration measurements.

Currently, drug concentration assays most widely available in hospital laboratory are for: antiepileptics (Carbamazepine, Ethosuximide, Phenobarbital, Phenytoin and Valproic acid), cardiac drugs (Digoxin, Procainamide and Quinidine), antibiotics (Aminoglycosides and Vancomycin), Theophylline, Cyclosporine and Lithium.
As a general rule, the serum drug concentrations are affected by following factors:

- Patient's renal or hepatic function
- Protein binding capacity (Albumin level)
- Electrolytes (particularly K^{+} and Mg^{+2})
- Sample timing with respect to dose (loading as well as maintenance) and route
- Drug-Drug Interaction
- Drug-Food interaction

Adverse Drug Reaction Update

Warfarin and Alopecia

Alopecia due to warfarin-therapy has occurred; incidence range from 5 percent to reports as high as 78%. Alopecia is reported to occur after both acute and chronic use .The response is directly related to the highest warfarin dose given and not to the duration of treatment. Hair is shed diffusely two or three months after an adequate dose of the drug. Marked hair loss is rare and hair growth resumes once warfarin is discontinued (Alopecia may recur upon warfarin re-challenge). Two case reports in which ubidecarenone (30 milligrams daily) reversed warfarin-induced alopecia despite continuation of warfarin therapy are available (Micromedix

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