

MANAGEMENT OF SNAKE ENVENOMATION

Dr. Shashi Kiran and Dr T.A. Senthilnathan, Department of Anaesthesia and Critical Care, Postgraduate Institute of Medical Sciences, Rohtak -124001. INDIA.

Address for correspondence: Dr. Shashi Kiran, 42/ 9J, Medical Enclave, Rohtak-124001. INDIA
e-mail: gupta3@vsnl.com

Introduction

Out of more than 3000 species of snake identifiable world wide, only one tenth of them are dangerous to human beings. There are three major families of venomous snakes:

- Elapidae (Land snakes like cobra, krait and coral snakes) - Snakes of this family have short & fixed fangs, which contain venom channels. Their tricolor bands (black red & yellow/ white) encircle the body and they lack laoreal shields (shield on the lateral aspect of head separating those shields bordering eyes from those bordering the nostril).
- Viperidae (Russell's viper, bamboo snakes) - These are further classified into pit vipers (crotalinae) and viperine vipers (Viperinae). Their fangs are long & movable. Their pupils are vertically elliptical. The ventral plates caudal to anus are in a single row. These snakes have a heat sensing pit as a small depression on the side of head for location of prey.
- Hydrophilidae (Sea snakes) - These snakes have a flattened tail.

Epidemiology

Although a major public health problem in many countries; the epidemiology of snakebite is still fragmentary, mainly due to lack of statistical data. This is compounded by the fact that the majority of victims come from rural areas, out of reach of the available medical facilities. It is estimated that snakebites may exceed 5 million per year, out of which approximately 100,000 develop severe sequelae. The incidence also shows a distinct seasonal pattern with a higher frequency in summers and during rains when the reptiles come out of their shelters. Epidemics of snake bite following floods owing to human & snake populations getting concentrated together have been noted in Pakistan, India & Bangladesh.

Snakebite is observed in all age groups, the majority (90%) affecting 11-50 year olds with males affected twice more often than females. Most bites occur between midnight and early morning and a large number of bites occur in fields, as most individuals are unable to spot the snake due to tall grass & crops. Fortunately every bite does not result in complete envenomation and more than half the victims escape without serious poisoning.

Table 1: Medically Important Snakes

S.NO	REGION	TYPES
I	North America:	Eastern Diamond Rattlesnake (<i>Crotalus adamanteus</i>) Western diamond rattlesnake (<i>C. atrox</i> , <i>C. viridis</i>) Bothrops atrox (fer-de-lance)
II	Central & South America:	Bothrops jararaca & tropical rattlesnake (<i>C. durissus</i> , <i>C. terrificus</i>)
III	Britain:	European adder (<i>Vipera berus</i>)
IV	Europe:	Long nosed viper (<i>V. ammodytes</i>)
V	Africa:	Night adder (<i>Causus</i> species) Puff adder (<i>Bitis arietan</i>) Mambas (four species of <i>Dendroaspis</i>)
VI	Africa & Asia:	Cobra (<i>Naja</i> species) Saw-scaled viper (<i>Echis carinatus</i>)
VII	Part of Asia:	Russell's viper (<i>V. russelli</i>) Malayan Pit viper (<i>Agkistrodon rhodstoma</i>) Sharp-nosed pit viper (<i>A. acutus</i>) Mamushi Pit viper (<i>A. halys</i>) Haliu viper (<i>Trimeresurus Flavoviridis</i>) Kraits (<i>Bungarus coeruleus</i> , <i>B. multicinctus</i>)
VIII	Pacific- Australian area:	Tiger snake (<i>Notechis scutatus</i>) Death adder (<i>Acanthophis antarcticus</i>) Taipan (<i>Oxyuranus scutellatus</i>) Papuan black snake (<i>Pseudechis Papuanus</i>) King brown (<i>Pseudechis australis</i>)

However, if sufficient venom is injected during the bite to cause serious poisoning, the mortality can be high.

PATHOPHYSIOLOGY

Snake venom is a very complex chemical poison, containing approximately 5-15 enzymes and 3-12 non-enzyme proteins & peptides besides carbohydrates and metals, which exerts toxic & lethal effects on skin, hematological, nervous, respiratory and cardiovascular systems (Table 2). Different species have differing proportions of above mixtures. The picture may be further complicated by the release of endogenous mediators such as histamine, bradykinin & adenosine. Therefore snake venoms cannot be classified purely as ‘neurotoxic’ or ‘cardiotoxic’, although they may have some predominantly specific action. The effects however may conveniently, though arbitrarily, be classified into vasculotoxic for vipers, neurotoxic for elapids & myotoxic for sea snakes.

Viper venom. This is primarily vasculotoxic. It causes rapidly developing swelling of the bitten part. Local necrosis is mainly ischaemic as thrombosis blocks the local blood vessels and causes dry gangrene. Systemic absorption is via lymphatics. Some vipers such as *Vipera berus* (European Viper) cause vomiting, abdominal pain, explosive diarrhoea and shock within a few minutes of bite, which resolves spontaneously within half an hour. Persistence of the shock may however be fatal. Several viper venoms result in intracranial haemorrhage due to direct endothelial damage by ‘haemorrhagin’ (a venom component), which however does not affect the coagulation. In contrast other viper venoms (*Crotalus*, *Bothrops*) affect coagulation and a very small amount of venom can cause complete fibrinogen consumption. It can also differentiate various species of vipers, which can help in instituting appropriate antivenom therapy.

Elapid venom. Local necrosis causes a picture like ‘wet gangrene’ with a characteristic putrid smell due to direct cytolytic action of venom. Systemic absorption occurs through venous channels. These result in primarily ‘neurotoxic features’ causing

selective neuromuscular blockade of the muscles of eyes, tongue, throat and chest leading to respiratory failure in severe poisoning.

Sea snake venom. The effects are both myotoxic and neurotoxic resulting in clinical and pathological changes typical of segmental myopathic lesions in the skeletal muscles. Muscle pains may be last for several months unless treated.

CLINICAL FEATURES OF SNAKEBITE

The clinical presentation of a snakebite victim varies with the size and species of snake, the number and location of bites, and the quantity of venom injected. As many 30% of Pit viper bites and 50% of elapid bites may result in no envenomation, sometimes referred to as “dry bites”. The venom channel is recessed above the tip of the fang and the venom injected may be reduced by poor penetration or glancing blows, causing venom to be lost over skin & clothing surface. The volume of the venom available to a particular snake may also be reduced by previous bites. The age and health of the victim are also important determinants in the clinical presentation. However, whether the snake is poisonous or non-poisonous and regardless of the venom injected, the commonest symptom following snakebite is ‘fright’ which may lead to a vasovagal episode (faint).

Usually the minority of victims who receive a venom dose large enough to cause systemic poisoning will already have signs of this by the time they seek medical help, and differentiation of viperine from elapid systemic poisoning is usually obvious from simple clinical evaluation. A persistent bloody ooze from the fang marks may suggest the presence of snake venom anticoagulant. In difficult cases the presence of pain out of proportion to the size of the wound suggests snake envenomation whereas mild pain is more normally caused nonvenomous snakes, arthropod bites (centipedes, spiders), bacterial fasciitis or myonecrosis.

Local manifestations

After envenomation local swelling starts within few minutes.

Table 2: Snake venom components and their effects

Component	Pit viper	Coral snake	Effect
Enzymes			
Proteinases	Heavy	Minimal	Tissue destruction, coagulation, anticoagulation
Hyaluronidase	Moderate	Moderate	Hydrolysis of connective tissue stroma
Cholinestrace	Minimal	Heavy	Catalyzes hydrolysis of acetylcholine
PhospholipaseA	Heavy		Haemolysis may potentiate neurotoxins
Phosphomesterase	Minimal	Heavy	Unknown
Phosphodisterase	Moderate	Moderate	Hypotension
Non-enzymes			
Neurotoxins	Minimal	Heavy	Flaccid paralysis
Cardiotoxins	Minimal	Heavy	Depolarizing

Fang marks may be difficult to see. Local pain with radiation and tenderness and a small reddish wheal are first to develop, followed by oedema, swelling and the appearance of bullae, all of which can progress quite rapidly and extensively. In most viper bites paraesthesia commences around the wound, and tingling and numbness over tongue, mouth & scalp can occur. The local bite may become necrosed & gangrenous. Russell's viper has been reported to cause Raynaud's phenomenon & gangrene in the limb other than the one bitten. Secondary infection including tetanus & gas gangrene can also result. Since the venoms are largely absorbed by the lymphatics, lymphangitis may appear early. Petichae or purpura may also be present due to the anticoagulant effect of some venom. These characteristic changes are useful clinically - for example if after a known Crotalid bite the victim demonstrates no local changes over next several hours of observation, he can be released from the hospital as significant envenomation is unlikely.

In contrast Elapid snakebites are associated with minimal local changes.

Systemic manifestations

Cobra and vipers produce symptoms within a few minutes to several hours after the bite. Sea snake bites almost always produce myotoxic features with 2 hours so that the bite can be reliably excluded if no symptoms are evident within this period. Although snakes are classified into predominantly neurotoxic, hemorrhagic and myotoxic types on the basis of their venoms, each species can result in any kind of manifestations.

- Viper bites - 75% cause envenomation, 35% mild, 15% severe. Pit viper venom can involve virtually every organ system. Nausea and vomiting are common and if present early suggest severe envenomation. Weakness, sweating, fever, chills, dizziness and syncope may occur. Some patients complain of a minty, rubbery or metallic taste in their mouths with increased salivation. Tingling or numbness in the tongue, scalp, face and digits are indications of moderate to severe envenomation as are fasciculations of the face, neck, back or the bitten extremity. Systemic anticoagulation can lead to gingival bleeding, epistaxis, hemoptysis, haematuria, haemetemesis and rectal bleeding or malena. Intra-abdominal or intracranial haemorrhages may occur. Visual disturbances may result from retinal haemorrhages. There may be tachycardia or bradycardia, often accompanied by hypotension. Delayed shock may occur due to excessive blood loss and hemolysis. Severe envenomation can result in pulmonary oedema as a result of destruction of the intimal lining of pulmonary blood vessels and pooling of pulmonary blood. The venom and associated hypotension along with haemoglobin, myoglobin and fibrin deposition in renal tubules can contribute to nephrotoxicity.

- **Elapid bites.** The venom of elapid bites is primarily neurotoxic. Neurotoxic features are a result of selective d-tubocurarine like neuromuscular blockade, which results in flaccid paralysis of muscles. Ptosis is the earliest manifestation of cranial nerve dysfunction followed closely by double vision. Paralysis usually then progresses to involve muscles of swallowing, but not strictly in that order.

Generally muscles innervated by cranial nerves are involved earlier. However pupils are reactive to light until terminal stages.

The muscles of the chest are involved relatively late with the diaphragm being most resistant. Respiratory paralysis is therefore often a terminal event. Even prior to respiratory failure, airway obstruction due to vomit or secretions can result in sudden death.

Reflex activity is generally not affected and deep tendon jerks are preserved until late. Symptoms that suggest severe envenomation include repeated vomiting, blurred vision, paraesthesiae around mouth and hyperacusis (increased sensitivity to sound), headache, dizziness, vertigo and signs of autonomic hyperactivity. Tachycardia, hypotension and ECG changes may occur. Tetanic contraction of heart following a large dose of cobra venom has also been documented.

- **Sea snakes.** Muscle pain is the most common presentation. Muscle necrosis may result in myoglobinuria and severe sea snake poisoning causes myoglobinuria and respiratory failure within a few hours. Coagulaopathy is not a feature of coral snake bites.

In severe systemic poisoning following either elapid or viper bites, the electrocardiogram may show T-wave inversion and ST segment deviation. In sea snake bites, an ECG is especially valuable in detecting hyperkalemia, which can result from damage to muscles. Tall, peaked T-waves in chest leads may appear within a few hours of bite and give early warning of impending death or acute renal failure.

Unusual presentations of snake envenomation

- A species *Naja nigricollis* (spitting cobra) can eject venom from a distance of 6-12 feet. The venom is aimed at victim's eyes resulting in conjunctivitis and corneal ulceration. It may result into anterior uveitis and hypopion. A dull headache may persist beyond 72 hours.
- Occasionally a recently killed snake or snakes with several heads can eject venom into those handling them.
- Rarely recurrence of snake envenomation manifestations may occur hours or even days after initial good response to the antivenom. This may be due to ongoing absorption of the venom.

MANAGEMENT OF SNAKEBITE

The management of snake envenomation is controversial. It can be divided into first aid and pre-hospital care, specific antivenom therapy and the supportive therapy.

First aid and prehospital care

Reassurance and immobilisation of the affected limb with prompt transfer to a hospital are of prime importance. The application of a "constriction band" to delay the absorption and venom spread has been advocated during transit to hospital for bites to the limb. A firm, but not tight, ligature may be applied just above the bite. The tension is correct if one finger can pass between the limb and the bandage. This will impede lymphatic drainage, but not arterial or deep venous flow. It should preferably not be released until the administration of anti-snake venom. If the limb becomes edematous the band should be advanced proximally. However, the band should not be left in place for too long due to the risk of venous thrombo-embolism and distal ischaemia. An increase in local envenomation has also been reported subsequent to release of the band. Venous or arterial tourniquets are contraindicated.

The site of bite should be wiped & covered with a handkerchief or dressing. Incision and mechanical suction of the bite (intended to open the puncture wound so that suction can be more effective) may be beneficial when performed by a health care worker within a few minutes of the bite in a victim who is more than 30 to 60 minutes from hospital. The incision should be parallel to the axis of the extremity and should be only approximately 6 mm long and 3mm deep and cross cuts or multiple cuts should be avoided.

Mechanical suction (“extractor” device found in Sawyer first aid kit) is preferable to mouth suction in order to avoid wound contamination with oral flora and to prevent possible envenomation of the rescuer through breaks in their oral mucosa. Suction should be maintained for about 30-60 minutes for maximal benefit, but due care should be taken as laceration of nerves, tendons & vessels has been reported following suction by untrained rescuers.

Application of cooling measures such as ice packs or cryotherapy, at the site of bite were initially advocated but have not been observed to be effective and this practice is not now recommended.

Anti tetanus toxoid should always be given following snakebite. There is controversy about use of drugs as part of first-aid care. It has been suggested that NSAIDS (Aspirin) may be beneficial to relieve local pain but it may precipitate bleeding especially if the venom is vasculotoxic. Paracetamol and / or codeine may be useful, however there are no clear-cut recommendations for the use of sedatives.

If the snake has been killed, it should be taken to hospital, otherwise it should be left alone, since attempts to find or kill it may result in further bites. The snake, even if judged to be dead, should be handled very carefully, since decapitated heads can bite for up to one hour!

Patient assessment

Evaluation should begin with the assessment of the airway, breathing and circulatory status. Oxygen should be administered to every envenomated patient and a large bore intravenous line

with normal saline or Ringer’s lactate established in the unbitten limb. Cardiac monitoring and pulse oximetry, if available, is indicated. Attempts should be made to determine whether a venomous snake has actually bitten the patient, and the severity of envenomation should be assessed. (Table 3)

During the initial evaluation, several locations on the bitten extremity (at the bite site and at least two sites more proximal) should be marked and the circumferences should be measured every 15 minutes until swelling is no longer progressing and every 1-4 hours thereafter. The extremity should be placed in a well-padded splint for at least 24 hours.

Laboratory Investigations

Although lab tests are of little value in the diagnosis of snake envenomation, nevertheless they are useful for monitoring the patient and deciding about specific interventions and prognosis. They should include a full blood count, electrolytes, glucose, creatinine, serum amylase, creatinine phosphokinase (CPK), prothombin time (PT), partial thromboplastin time (PTT), fibrinogen and fibrin degradation products (FDP’s). Commonly hyperkalaemia and hypoxaemia with respiratory acidosis may be seen, particularly with neuroparalysis. Urine examination can reveal haematuria, proteinuria, haemoglobinuria or myoglobinuria. Arterial blood gases and urine examination should be repeated at frequent intervals during the acute phase to assess progressive systemic toxicity.

Blood changes include anaemia, leucocytosis (raised white cell count) and thrombocytopenia (low platelet count). The peripheral blood film may show evidence of haemolysis especially in viperine bites. Clotting time and prothrombin time may be prolonged and a low fibrinogen may be present. Blood should be typed and crossmatched on the first blood drawn from the patient, as both direct venom and anti-venom effects can interfere with later cross matching. Some specialised centers can identify species of snake involved.

Non specific ECG changes such as bradycardia and atrio-ventricular block with ST,T segment changes may be seen.

Table 3: Assessment of severity of envenomation

No envenomation	Absence of local or systemic reactions, Fang marks +/-			
Mild envenomation	Fang marks (, moderate pain, minimal local oedema (0-15cms), erythema+, ecchymosis +/-, no systemic reactions			
Moderate envenomation	Fang marks+, severe pain, moderate local edema (15-30cms), erythema & ecchymosis +, systemic weakness, sweating, syncope, nausea, vomiting, anemia or thrombocytopenia			
Severe envenomation	Fang marks+, severe pain, severe local edema (>30cms), erythema & ecchymosis+, hypotension, parasthesia, coma, pulmonary edema, respiratory failure			
	Phosphomesteras	Minimal	Heavy	Unknown
	Phosphomesteras	Minimal	Heavy	Unknown

Recently EEG changes have also been reported in many patients of snake envenomation. They may manifest within hours of bite without any clinical features suggestive of encephalopathy.

Anti venom therapy

Anti snake venoms (ASV) are prepared by immunising horses with venom from poisonous snakes and extracting serum & purifying it. The WHO has designated the Liverpool School of Tropical Medicine as the international collaborating center for anti-venom production and testing. Anti-venoms may be species specific (monovalent) or effective against several species (polyvalent) (Table 4).

The correct use of antivenom is the most important component of the hospital care and not every bite, even with a poisonous snake, merits its use. Administration of anti-venom should be selective and based on severity of clinical symptoms. The main concern about the empirical use of antivenom is the risk of allergic reactions, its relative scarcity in some centers and the cost factor. Moreover in a study of Elapid envenomation, all victims with neuromuscular paralysis survived without receiving any anti-venom. Shamesh et al did a preliminary evaluation of the possibility of reducing the dose of anti-venom or totally avoiding it in some viper species. They concluded that about half of the bitten patients in their study did not show systemic symptoms and therefore did not require antivenom treatment. They further observed that anti-venom treatment based on systemic symptoms was effective and the dose required was also less than the fixed amount advocated for each patient, thereby reducing the incidence of serum sickness.

Administration of Antivenom

Antivenom should be given within 4-6 hours of the bite and the

dosage required varies with the degree of envenomation. Serum sensitivity should be tested by injecting 0.2 ml of antivenom subcutaneously. If a severe reaction occur within 15 minutes, anti-venom is contra-indicated. Adrenaline should be readily available in a syringe for moderate reactions that may occur despite negative tests for sensitivity. Initial dose should depend upon an estimate of amount of envenomation. (Table 5) However no upper limit has been described and up to 45 vials have been successfully used in a patient! In children and small adults (body weight <40 kgs) up to 50% higher dose of ASV should be administered to neutralise the relatively higher venom concentration.

ASV is administered intravenously either in an undiluted form at a rate of not more than 1ml per minute or diluted in 500ml of IV fluid & administered as rapidly as tolerated over 1-2 hours. Additional infusions containing 5-10 vials (50-100ml) should be repeated until progression of swelling in the bitten part ceases and systemic signs & symptoms disappear. However it is not advisable to infiltrate ASV at the local site. Delayed reactions may occur following anti-venom therapy and their frequency of occurrence is proportional to the amount of anti-venom administered. Therefore all patients receiving ASV should be observed for several days.

Role of Anticholinesterase Agents

Since Elapidae snakes result in primarily neurotoxic features as a result of selective d-tubocurarine like blockade, the post synaptic toxin of the venom leads to pathophysiological changes resembling those of myasthenia gravis; This prompted some of the workers to use anticholinesterase agents such as neostigmine in addition to a conventional antivenom therapeutic regimen with dramatic results. However the use of anticholinesterase drugs

Table 4: Types of anti-venoms

Name of Antivenom	Species
Polyvalent Wyeth Labs [Antivenin (cortilidae) polyvenom] United States	All North American pit vipers
King cobra antivenom	King cobra (<i>Ophiophagus hannah</i>)
Polyvalent <i>Naja naja</i> serum (common cobra) antislake venom CRI, Kausali, India	<i>Vipra russelli</i> (Russel's viper <i>Bunqarus ceruleus</i> (common krait) <i>Echis carinatus</i> (saw scaled viper)
Mono specific <i>Echis carinatus</i> antivenom, India	Indian species
Tiger snake antivenom, Australia	Sea snakebite & Afro-Asian elapids
Green pit viper antivenom	<i>Trimeresurus albolabris</i> , <i>Trimeresurus monticola</i>
Bothrops antivenoms, Brazil	
Monospecific antivenom from South African Institute for Medical Areas (SAIMR), Northern Nigeria	<i>Echis pyramidum leakeyi</i>
Poly specific German & French antivenoms	

Storage of ASV: Liquid -between +20 & +80C, Lyophilized - cool & dry place.

Envenomation	Dose
Mild	5 vials (50ml)
Moderate	5-10 vials (50-100ml)
Severe	10-20 vials (100-200ml) or more

alone without ASV has also been recommended. Neostigmine can be given as 50-100 (g/kg 4 hourly or as a continuous infusion. Edrophonium can also be used in dose of 10mg in adult or 0.25mg/kg in children over 2 minutes & if the response is positive then one can switch over to long acting preparations like neostigmine. However prospective studies are required to fully establish the efficacy of neostigmine with or without ASV. Glycopyrrolate 0.2 mg preceding neostigmine can be given, as unlike atropine it does not cross blood brain barrier

Supportive therapy

The patient should be moved to an appropriate are of the hospital - ICU will be required for severe envenomation. Fasciotomy should be undertaken in patients with compartment syndrome and debridement should be performed for necrotic tissue. Coagulopathies should be corrected with fresh frozen plasma and platelets. Blood transfusion should be given to replace blood loss from haemolysis & bleeding. Ventilatory support and haemodialysis may be necessary for pulmonary and renal complications due to severe envenomation. Corticosteroids are of no proven value and in fact may interfere with the action of ASV. However, corticosteroids may be used for hypersensitivity reactions to ASV. Prophylactic antibiotics are of no proven value. If infection occurs broad-spectrum cover such as ciprofloxacin and clindamycin should be used.

Intravenous immunoglobulin therapy has also been used for envenomation and it may improve coagulopathy but has no effect on neurotoxicity. Certain reports on the evaluation of intravenous immunoglobulin suggest that it may reduce the need for repeat antivenom therapy for envenomations associated with coagulopathy.

A compound (2-hydroxy 4-methoxy benzoic acid) isolated and purified from anatamul (*Hemidesmus indicus* R.Br.), an Indian herb, has also been observed to have potent anti inflammatory, antipyretic and antioxidant properties, especially against Russel's viper venom.

Analgesia should be given - opioids may be required.

Other envenomations

Scorpion venom poisoning.

There are more than 1,400 species of scorpions in the world but the number of medically important species is limited. The venom of the Bark scorpion (*C. exilicauda*) contains at least five distinct neurotoxins that stimulate depolarization of the neuro muscular junction & autonomic nervous system via release of acetylcholine, norepineprine & epinephrine. It may also have cardiotoxic effects.

Most stings are minor though serious envenomations can occur

in children. The sting is followed by the onset of intense local pain with hyperesthesia (increased skin sensitivity to touch) but local swelling and ecchymosis are absent. Systemic symptoms, when present, reflect sympathetic, parasympathetic and neuromuscular excitation. Tachypnoea, respiratory distress, wheezing, stridor, muscle fasciculations and spasm follow initial restlessness and anxiety. There may be convulsions, paralysis and involuntary voiding of stools/urine, priapism (persistent penile erection) and anxiety. Other systemic features may include hypertension, supraventricular tachycardia and hyperpyrexia.

The majority of stings can be treated with mild analgesics & cold compresses. In the event of severe envenomation, the patient should be resuscitated and appropriate symptomatic treatment should be instituted. A goat-derived anti-venom is available in Arizona. Most adults can be safely treated at home, but children should always be admitted and any child less than a year old or having neurological findings should be admitted to ICU.

Further reading

- Hawgood BJ, Hugh AR. Investigation and treatment of snakebite. *Toxicon* 1998;**36**:431-46.
- Theakston RDG, An Objective Approach to Antivenom Therapy and Assessment of First Aid Measures in Snakebite. *Annals of Tropical Medicine and Parasitology*. 1997;**91**:857-65.
- Iyaniwura TT: Snake venom constituents: biochemistry and toxicology (parts I & II). *Vet Hum Toxicol* 1991;**33**:468-80.
- Reid HA, Theakston RDG. The management of snake bite. *Bulletin of World Health Organisation*. 1986;**61**:885-95.
- Zamudio KR, Hardy DJ, Martins M, Greene HW. Fang tip spread, puncture distance and suction for snakebite, *Toxicon*. 2000;**38**:723-28.
- Sailor JG, Sagernan SD, Geller RJ, Eldridge JC, Fleming LL. Venomous snake bite: current concepts of treatment. *Orthopaedics* 1994;**17**:707-14.
- Reid HA. Diseases due to infection and Infestation. In: Sir Ronald Bodley Scott (ed.). *Price's Textbook of Practice of Medicine*. 12th edition: Oxford Medical Publications, London. 1978; 242-6.
- Norris RL. Envenomations. In: Rippe JM, Irwin RS, Alpert JS, Fink MP. (eds.) *Intensive Care Medicine*. 2nd edition. Little, Brown and Company, London. 1985;1266-78.
- Shemesh IY, Kristal C, Langerman L, Bourvin A. Preliminary evaluation of viper palaestinae snakebite treatment in accordance to the severity of the clinical syndrome. *Toxicon* 1998; **36**: 867-73.