SNAKE ENVENOMATION

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Statistics are scanty regarding snake bite poisoning. In the world there are about 3,00,000 poisonous snake bites/year and 30,000-40,000 deaths mostly in South East Asia, Western hemisphere and Brazil(l). In India it is estimated that around 5000 people die of snake bites per year. In India 300 species of snakes exist and of these 80 species are reported to be poisonous.

Characteristics of Snakes(2)

In the Indian subcontinent four types of poisonous snakes are seen. They belong to five families or subfamilies cobras, kraits, mamba, coral snakes belong to *Elapidae,* Russell viper and saw scaled viper belong to *Viperidae,* the sea snakes to *Hydrophidae* and pit vipers to *Crotalidae.* The *Elapidae* have a head which is oblong with well developed head shields. The tail is long and tapering. The fangs are small and present in front of upper jaw. The cobra has a hood with a binocoellate mark. The kraits have either a steel blue body with a white cross bar or yellow body with black cross bands. The *Viperidae* have a triangular head with tiny head shields. Their fangs are big, erectile and sheathed, their eyes have vertical pupils.

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Venom

The venom is secreted by a pair of salivary glands. Two or occasionally more than one pair of teeth are modified to form sharp fangs with channels for venom. The orifice which discharges the venom is much above the tip of the sharp fang. The venom is discharged only if the orifice is in close contact with the wound. Even a slight clothing over the individual could prevent venom reaching the tissues.

The lethal dose for cobra, krait, russell viper and saw scaled viper are 120, 60, 150 and 80 mg toxin, respectively. The amount of venom injected per bite could be about 200, 22, 150 and 4.6 mg, respectively for the snakes mentioned above. The constituents of venom are incompletely understood and the exact role of the constituents are poorly studied(3). The venom contains toxic proteins and enzymes. The cobra venom contains neurotoxin, hemolysin, cardiotoxin, cholinesterase, nucleotidase and a potent inhibitor of cytochromoxidase. The viper venom contains hyaluronidase, hemolysin, hemorrhagins I and II, several proteolytic enzymes and phospholipase A.

The neurotoxins of cobra and alfa bungarotoxin in krait can exhibit a curare like effect on post junctional membrane of

motor end plate. The beta bungarotoxin has its effect on presynaptic motor nerve endings which leads to peripheral nerve paralysis and respiratory paralysis. The ceruleotoxin of Indian krait also acts on the post synaptic site without binding to the Ach receptor. The neurotoxins are small peptides with a molecular weight of 7000-8000. There are short neurotoxins consisting of 60-62 residues and long neurotoxins with 71-74 residues. About 60 different neurotoxins have been identified and sequenced. Their three dimensional structure suggests that neurotoxins have a central core and three loops. The toxicity is due to the aminoacid sequence 30-40 present in the second loop. It is interesting to note that the 20-30 sequence of the neurotoxins has a functional similarity with the 164-174 sequences of HIV glycoprotein 120 and the rabies virus glycoprotein and act through the nicotine acetylcholine receptors in the neuronal cells(4).

The cardiotoxin gives rise to irreversible depolarisatoin of cell membrane resulting in cardiac asystole, circulatory and respiratory collapse. The venom of vipers is usually toxic to the hemopoietic system. It may act either as an anticoagulant or procoagulant enzyme. It also gives rise to endolhelial damage with gaps allowing diapedesis at inter cellular junctions thus exacerbating the hemorrhagic tendency.

Clinical Features

Clinical features of both cobra and krait envenomation include burning pain, numbness, swelling and sloughing over the site of bite. Systemic features include drowsiness, ptosis, dysarthria, dysphagia, flaccid paralysis inability to clear frothy secretions and coma. Cardiac arrythmia and hypotension may also be seen. The neurotoxic and cytotoxic complications set in within few hours of the bite. The neurotoxic complications can be delayed upto 19 hours(5). In viper bites, locally there is a rapid swelling, edema, burning pain and oozing of blood. The severe clotting defect may be seen within an hour or so, which leads to internal and external hemorrhages. There may be hematuria, hematemesis, hemoptysis and intracranial hemorrhages. DIC like picture may be seen. Renal failure and shock may also be present.

In sea snake bites there is severe rhabdomyolysis, acute renal failure and shock.

Factors Determining Severity of Bite

Children are more seriously involved as the venom dose per body mass is more than adults. Children also have less proteins to bind circulating venom. They also have a smaller extracellular volume. These factors may lead to a rapid rise and thus greater plasma levels in children as compared to adults. Over the corpus, bites are more severe. If the snake venom glands are empty it indicates that venom has recently been discharged. If there are broken fangs they indicate a successful bite. Reportedly, some snakes have the ability to identify a small thermal target and can deliver a more accurate venom dosage. The large thermal size of an adult seems to confuse the snake resulting in unpredictable venom delivery.

Management

1. First Aid

The snake if possible should be caught and killed. Later the snake should be examined to find out whether it is poisonous or not. The venom glands and the fangs should be examined. More than 50% of the venom can be removed by first aid. The patient should be reassured. A crepe tourniquet

should be tied proximal to the wound and the joints should be immobilized on either sides of the wound with the help of a splint. The patient should be carried to the hospital as exercise will induce absorption of the venom. The tourniquet should only block the flow of lymphatics and veins and the arterial supply to the area should not be affected. The tourniquet should be loosened only after antivenin therapy has been started.

2. Local Management

The wound should be examined for fang marks. An incision of about 1 x 0.5 cm should be given at each fang mark site. Samples can be taken from the bite site for venom analysis by the Commonwealth serum laboratory venom detection kit(6). The wound be cleansed by local irrigation with normal saline after the arterial supply to the area should not be affected. The tourniquet should be loosened only after antivenin therapy has been started.

3. General Measures

Tetanus prophylaxis should be given. Antibiotic should be given to prevent infection. Analgesics and sedation may be indicated in some cases. IV fluids, fresh blood transfusion may be given to combat shock. Coagulation defects may be corrected by using fresh frozen plasma or fresh blood. If DIC is present heparin may be used. In neuroparalytic manifestations administration of neostigmin is indicated.

4. Antivenin Therapy

The decision to give antivenin therapy should be absolute. Antivenin is given intravenously after testing on the skin or conjunctival membrane for sensitivity. Manipulations involving the wound such as explorations and removal of the debris should be done under cover of antivenin as these procedures may release venom into the circulation from the depot in the wound. If the patient is sensitive, one could still give antivenin after premedication with adrenalin and antihistamines. Hydrocortisone may be given to prevent late complications of serum sickness.

Antivenin remains in circulation for 18-20 days. With antivenin therapy the mortality has definitely come down from 20% to 30%.

Monitoring of Antivenin Therapy: Enzyme linked immunoassay for specific venom antibody has been used to estimate the venom and antivenom levels(7,8). By using the ELISA technique it has been shown that the patients with old snake bites have venom specific antibodies 33 times more than the acute snake bites. The half life of antibodies is 2 to 3 years and persist for 1-7 years(9). The blood coagulation should also be monitored by simple grading of whole blood clotting method by Reid *et al.*(10). The coagulation defects correct within 12 hours of antivenin therapy, but may take 3 days and then repeated antivenin therapy may be required.

Antivenin preparations in India: We have polyvalent antivenom against cobra, krait, Russell viper and saw scaled viper prepared by Central Research Institute at Kasauli, Haffkine Institute at Bombay and Serum Institute of India at Pune. One ml of polyvalent antivenin can neutralize 0.6 mg of toxin of each of the species mentioned above. About 150-200 ml can be administered. Low doses may be used for mild and moderate cases of snake envenomation.

Snake Envenomation Studies in Children

Epidemiological studies on snake envenomation in children are few. In a

study from Papua New Guinea, children under 15 years constituted 26% of the total cases. The annual incidence rate and mortality rate was 81.8% and 4.3% in the rural and 3.0% and less than 1% in urban cities, respectively(ll). In a study from Australia, 71 children had snake bites over a period of 5 years (1971-75). Seventy three per cent were poisonous snake bites and 73% did not observe constitutional signs. Only 17% had signs of envenomation; 2 cases were treated with antivenin and 1 case died(12). In another study from Australia children constituted 30% of snake bite cases in a hospital over a period of 10 years(13). Indian studies on snake bite poisoning are few and are mainly hospital data. Lahori *et al.* has reported from Jammu on incidence of 1.6% of Hospital Pediatric admissions(14). Age distribution was 5-10 years; the youngest patient was 13 months old and 81.5% cases were from rural areas. The mortality in this series was 5%. In another series from Maharashtra in the years 1984-1988 Kumar *et al.* had seen 20 cases of snake bite poisoning and mortality was 3%(15).

Immunology of Snake Envenomation and Antivenin Therapy

Snake Venom Allergy: This is seen in patients who already had a previous exposure to snake bite/antivenin therapy(16). They react with general flushing, feeling of difficulty in breathing and tightness of chest and diffuse rash over the body.

Immunological Complications of Antivenin: The use of antivenin therapy is clouded. Many believe that with good supportive care alone, snake envenomation could be managed. The immediate and late reactions are so severe that in the West doubts have been raised about the role of antivenin therapy. In a study on 26 patients who received 507 doses of antivenin correlating with the clinical severity, immediate hypersensitivity was noticed in 23% of the cases and 50% developed late complications of serum sickness. The reactions were more to polyvalent antivenin and in older patients who were already exposed to equine protein(17).

Immunological. Detection of Snake Venom: ELISA kits have been used to detect the venom at the site of snake bite and also from blood and urine of the victim.

Humoral Response Following Snake Envenomation: People who handle snakes show an IgG response of human venom antibody about 9 days after a snake bite(18). The levels are highest around 12 days and drops after 19 days to a level higher than the basal level and then a secondary rise is seen. This response is protective in nature.

Active Immunization: Due to high mortality and morbidity, active immunization with a vaccine has been considered especially in people at high risk of snake bite, *i.e.,* those who are handling snakes in zoo, herpetarium, laboratory or snake catchers(19).

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