CHAPTER

113

Management of Snake Bite in India

Shibendu Ghosh, Prabuddha Mukhopadhyay

INTRODUCTION

India is a country known to the western population as a country of snake charmers and snake over centuries. Despite generation after generations some families in our country who play with snakes (snake charmers), we fail to protect the community from snake bite which requires at least education of the common people, how to protect themselves from snake bite as well as what to do after the bite has occurred.

The estimated death in India is 50,000/ yr, an underestimate because of lack of proper registration of snakebite. The real number of death in our country probably much higher. The persons or population at risk of snakebite in our country is around 50 million people which may occur any time in the life.

The infrastructure of the medical profession in India is mal-distributed in such a manner to protect this poor rural population against the snake bite. Scientifically and ethically we, the doctors can not treat the patients of snake bite properly. Moreover, ignorance of the people around the snake bite victims, the misbelieves about snake bite and ignorance of even the medical profession also play a large part to care this patients in a proper way. There are large number of conflicting protocols for dealing with first aid and treatment. In 2004,WHO established a snakebite Treatment Group, whose role was to develop recommendations to reduce mortality according to international norms. A primary recommendation was to establish a single protocol for both first-aid and treatment which contained evidence based procedures and was relevant to the Indian context. In July 2006, A National Snakebite Conference was convened, including Indian and International experts. Moreover publications issued by the WHO Regional Office for South-East Asia, written and edited by David A. Warrell in the year 2015 and enduring efforts of the scientist and doctors working in different regions of India is the back bone of this editorial. We have treated about 10000 cases of snake bite patients in Medical College Hospitals, Kolkata, Tarakeswer Rural Hospitals and Seba Nursing Home, Tarakeswar, Hooghly, West Bengal, SRI Hospitals, Betai, Nadia, West Bengal since 1987.

FIRST AID TREATMENT PROTOCOL

Much of the first aid currently carried out is ineffective and dangerous.

Recommended Method for India

Modified by our team in West Bengal.

The first aid being currently recommended is based around the mnemonic.

"CARRY NO R.I.G.H.T." It consists of the following:

CARRY = Do not allow victim to walk even for a short distance; just carry him in any form, specially when bite is at leg.

No - Tourniquate

No - Electrotherapy

No - Cutting

No - Pressure immobilization

Nitric oxide donor (Nitrogesic ointment/ Nitrate Spray)

R = Reassure the patient. 70% of all snakebites are from non-venomous species. Only 50% of bites by venomous species actually envenomate the patient.

I = Immobilize in the same way as a fractured limb. Use bandages or cloth to hold the splints, not to block the blood supply or apply pressure. Do not apply any compression in the form of tight ligatures, they don't work and can be dangerous!

G H = Get to Hospital Immediately. Traditional remedies have NO PROVEN benefit in treating snakebite.

T = Tell the Doctor of any systemic symptoms that manifest on the way of hospital.

Do not waste time for doing the first aid management.

This method will get the victim to the hospital quickly, without recourse to traditional medical approaches which can dangerously delay effective treatment, and will supply the doctor with the best possible information on arrival.

Traditional Methods to Be Discarded

TOURNIQUETS - TOURNIQUET USE IS CONTRAINDICATED IN INDIA

Risk of Ischemia and loss of the limb.

Increased Risk of Necrosis with 4/5 of the medically significant snakes of India.

Increased risk of massive neurotoxic blockade when tourniquet is released.

Risk of embolism if used in viper bites. Pro-coagulant enzymes will cause clotting in distal blood. In addition, the effect of the venom in causing vasodilatation presents

Table 1: Clinical Features of Snakebite

Feature	Cobra	Kraits	Russells Viper	Saw scaled Viper	Humped nose viper
Local Pain/ Tissue damage	Yes	No	Yes	Yes	Yes
Ptosis, Neurological sign	Yes	Yes	No*	No	No
Hemostatic abnormality	No	May Occour	Yes	Yes	Yes
Renal Complication	No	No	Yes	No	Yes
Response to neostigmine	Yes	±	No	No	No
Response to ASV	Yes	Yes	Yes	Yes	No

the danger of massive hypotension and neuroparalysis when the tourniquet is released.

They do not work! Venom was not slowed by the tourniquet in several experimental studies, as well as in field conditions. Often this is because they are tied on the lower limb or are incorrectly tied.

They give patients a false sense of security, which encourages them to delay their journey to hospital.

SNAKEBITE PREVENTION & OCCUPATIONAL RISK

The normal perception is that rural agricultural workers are most at risk but a large population residing in rural India and semi-urban places are also at risk of snake bite.

Preventative Measures

The areas, time of the day (night) and seasons of the year (monsoon), to be taken into account for preventative measure that usually the people of village adopt.

Diagnosis Phase

General assessment : Depending upon type of symptoms.

In addition some of the krait bite (Shochoureki) does not respond to ASV of Indian origin. In our study none of the Russell's Viper presented with neurotoxicity.

General signs and symptoms of Viperine envenomation

- Swelling and local pain.
- Tender enlargement of local lymph nodes as large molecular weight Viper venom molecules enter the system via the lymphatics.
- Bleeding from the different sites: 1.gingival sulci 2. Epistaxis 3. The skin and mucous membranes 4. sub-conjunctival hemorrhage 5. Acute abdominal tenderness which may suggest gastro-intestinal or retro peritoneal bleeding 6. The passing of reddish or dark-brown urine or declining or no urine output
- Vomiting.
- Hypotension resulting from hypovolaemia or direct vasodilatation.
- Low back pain, indicative of a early renal failure or retroperitoneal bleeding, although this must be carefully investigated as many rural workers involved in picking activities complain of back pain generally.
- Lateralizing neurological symptoms and asymmetrical pupils may be indicative of intra-cranial bleeding.
- Muscle pain indicating rhabdomyolysis.

General signs and symptoms of Elapid envenomation (Table 1)

- Swelling and local pain (Cobra), may be asymptomatic in case of krait patient often could not recognize the bite
- Local necrosis and/or blistering (Cobra).
- Descending paralysis, initially of muscles innervated by the cranial nerves, commencing with ptosis, diplopia, or ophthalmoplegia.
- Paralysis of jaw and tongue may lead to upper airway obstruction and aspiration of pooled secretions because of the patient's inability to swallow.
- Hypoxia due to inadequate ventilation can cause cyanosis, altered sensoriun and coma. This is a life threatening situation and needs urgent intervention.
- Paradoxical respiration, as a result of the intercostal muscles becoming paralyzed is a frequent sign. Stomach pain which may suggest sub mucosal hemorrhages in the stomach (Krait).
- Krait bites often present in the early morning with paralysis that can be mistaken for a stroke.

Late-onset envenoming

The patient should be kept under close observation for at feat 24 hours.

DIAGNOSIS PHASE: INVESTIGATIONS

20 Minute Whole Biood Clotting Test (20 WBCT)

Considered the most reliable test of coagulation and should be carried out at the bedside by treating physician. It can also be carried out in the most basic settings.

A few mililiter of fresh venous blood is placed in a new, clean and dry glass vessel and left at ambient temperature for 20 minutes. The vessel ideally should be a small glass test tube. The use of plastic bottles, tubes or syringes will give false, readings and should not be used.

The glass vessel should be left undisturbed for 20 minutes and then gently tilted, not shaken. If the blood is still liquid

then the patient has incoagulable blood. The must not be washed with detergent as this will inhibit the contact element of the clotting mechanism. The test should be carried out every. 30 minutes from admission for three hours and then hourly after that. If incoagulable blood is discovered, the 6 hourly cycle is then be adopted to test for the requirement for repeat doses of ASV.

MANAGEMENT OF SNAKE BITE IN GENERAL

Pain

Snakebite can often cause severe pain at the bite site; This can be treated with painkillers such as paracetamol.

Handling Tourniquets

Care must be taken when removing tight tourniquets which most of the time used. Sudden removal can lead to a massive surge of venom leading to neurological paralysis, hypotension due to vasodilatation etc.

- Before removal of the tourniquet, test for the presence of a pulse distal to the tourniquet. If the pulse is absent ensure a doctor is present before removal.
- Be prepared to handle the complications such as sudden respiratory distress or hypotension. If the tourniquet has occluded the distal pulse, then a blood pressure cuff can be applied to reduce the pressure slowly.

Anti Snake Venom (ASV)

After assessing patient whenever decision is taken for giving ASV, start ASV whatever dose is available in hand, do not wait for full dose to be available.

In India polyvalent ASV is only available, It is effective against all the four common species; Russells viper (Daboia russelii), Common Cobra (raja naja), Common Krait (Bungarus caeruleus) and Saw Scaled viper (Echis carinatus).

There are known species such as the Hump-nosed pitviper (Hypnale hypnale) where polyvalent ASV is known to be ineffective. In addition, there are regionally specific species such as Sochurek's Saw Scaled Viper (Echis carinatus sochureki) in Rajasthan, and Kalach in West Bengal where the effectiveness of polyvalent ASV may be questionable. These species should be detected first and special measures to be taken for these bites.

ASV Administration Criteria

ASV is a scarce, costly commodity and should only be administered when there are definite signs of envenomation. Unbound, free flowing venom, can only be neutralised when it is in the bloodstream or tissue fluid. In addition, Anti-Snake Venom carries risks of anaphylactic reactions and should not therefore be used unnecessarily.

Systemic envenoming

- Evidence of coagulopathy: Primarily detected by 20WBCT or visible spontaneous systemic bleeding.
- Evidence of neurotoxicity: ptosis, external ophthalmoplegia, muscle paralysis, inability to lift the head etc.
- Cardiovascular abnormalities: hypotension, shock, cardiac arrhythmia, abnormal ECG.
- Persistent and severe vomiting or abdominal pain.

Severe Current Local envenoming

- Severe current, local swelling involving more than half of the bitten limb (in the absence of a tourniquet). In the case of severe swelling after bites on the digits (toes and especially fingers) after a bite from a known necrotic species.
- Rapid extension of swelling (for example beyond thewaist or ankle within a few hours of bites on the hands or feet). Swelling a number of hours old is not grounds for giving ASV.
- Purely local swelling, even if accompanied by bite mark from an apparently venomous snake, is not grounds for administering ASV.

Prevention of ASV Reactions – Prophylactic Regimes

There is no statistical, trial evidence of sufficient statistical power to show that prophylactic regimes are effective in the prevention of ASV Reactions in India. Recent trial in Sri lanka using low dose adrenalin (0.25 ml) on good number of patient showed benefit but a proper study to be undertaken in India before making it a routine procedure as a prophylactic manner. Moreover, Indian population are at high risk for premature atherosclerosis and coronary artery disease. Any adverse effect before ASV may be detrimental as a social issue also. However putting the adrenalin via three way cannula or by puncturing the latex tube may be undertaken and to be injected in emergency. Prophylactic regime should be reserved for children and young adult if at all needed.

Two regimen are normally recommended

- 100mg of hydrocortisone and Hl antihistamine (10mg chlorpheniramine maleate IV) 5 minutes before ASV administration.

The conclusion in respect of prophylactic regimens to prevent anaphylactic reactions, is that there is no evidence from good quality randomized clinical trials to support their routine use. If they are used then the decision must rest on other grounds. But the regime have got an added advantage of decreasing the non-anaphylactic reaction such as febrile, allergic reaction, etc.

Adrenalin should not be used as premedication, when it will be required it should be given IV route without wasting time.

ASV Administration

Total required dose will be between 10 vials to 30 vials usually, as each vial neutralizes 6mg of Russells Viper venom. Not all victims will require 10 vials as some may be injected with less than 63mg. However, starting with 10 vials ensures that there is sufficient neutralizing power to neutralize the average amount of venom injected and

during the next 12 hours to neutralize any remaining free flowing venom, even in the large study from south India, the amount of ASV exceeded 50 vials in some patients. So decision of the treating physician is of utmost importance, because the guidelines may not be useful for all patients.

NO ASV TEST DOSE MUST BE ADMINISTERED

Test doses have been shown to have no predictive value in detecting anaphylactic or late serum reactions and should not be used. These reactions are not IgE mediated but Complement activated, They may also pre-sensitize the patient and thereby create greater risk.

ASV is recommended to be administered in the following initial dose:

Neurotoxic/ Anti Haemostatic 10 Vials

N.B. Children and pregnant women receive the same ASV dosage as adults. The ASV is targeted at neutralizing the venom. Snakes inject the same amount of venom into adults and children.

ASV can be administered in-two ways

- Infusion: liquid or reconstituted ASV in isotonic saline or glucose, may be started without any diluent fluid in volume overload patients.

All ASV to be administered over 1 hour at constant speed. Local administration of ASV, near the bite site, has been proven to be ineffective, painful and raises the intracompartmental pressure, particularly in the digits, it should not be used.

Snakebite in Pregnancy

Pregnant women are treated in exactly the same way as other victims. The same dosage of ASV is given. The victim should be referred to a gynecologist for assessment of any impact on the foetus.

ASV Reactions

Anaphylaxis can be rapid onset and can deteriorate into a life-threatening emergency very rapidly. Adrenaline should always be immediately available.

The patient should be monitored closely and at the first sign of any of the following:

Urticaria, itching, fever, chills, nausea, vomiting, diarrhea, abdominal cramps, tachycardia, hypotension, bronchospasm and angio-oedema

- ASV to be discontinued
- Children are given 0.01mg/kg body weight of adrenaline iv.
- In elderly noradrenalin and nitroglycerin infusion when hypotension is corrected can be given to avoid adrenalin induced arrhythmia which is common in elderly.

If after 10 to 15 minutes the patient's condition has not improved or is worsening,

- A second dose of 0.5 mg of adrenalin 1:1000 iv is given. This can be repeated for a third and final occasion but in the vast majority of reactions, 2 doses of adrenaline will be sufficient in children.
- If there is hypotension or hemodynamic instability, IV fluids should be given.

Once the patient has recovered, the ASV can be restarted slowly for 10-15 minutes, keeping the patient under close observation. Then the normal drip rate should be resumed.

Adrenalin should be given iv in case of anaphylactic reaction, because

1. Faster action
2. Predictable availability
3. Intra mascular haematoma in patient with coagulopathy can be avoided.

Late serum sickness reactions can be easily treated with an oral steroid such as prednisolone, adults 5mg 6 hourly, paediatric dose 0.7mg/kg/day. Oral antihistaminic provide additional symptomatic relief.

Neurotoxic envenomation

Neostigmine is an anticholinesterase that prolongs the life of acetylcholine and can therefore reverse respiratory failure and neurotoxic symptoms. It is particularly effective for post synaptic neurotoxins such as those of the Cobra.

In the case of neurotoxic envenomation where edrophonium is not available Neostigmine Test can be done. The neostigmine dose is 0.04 mg/kg IV and atropine/ glycopyrolate may be given by continuous infusion.

The patient should be closely observed for 1 hour to determine if the neostigmine is effective.

The following measures are useful objective methods to assess this:

a. Single breath count

b. Uncovered area of iris measured in mm

c. Inter incisor distance (Measured distance between the upper and lower incisors)

d. Length of time upward gaze can be maintained

e. FEV 1 or FVC (If available)

f. Water column measurement. (length of water column that can be held with blowing through tubes)

For example, if single breath count or inter incisor distance is selected the breath count or distance between the upper and lower incisors, and more objective water level measurement that much patient can blow are measured and recorded. Every 10 minutes the measurement is repeated. The average blood plasma time for neostigmine is 20 minutes, so by T+30 minutes any improvement should be visible by an improvement in the measure.

Recovery Phase

If an adequate dose of appropriate antivenom has been administered, the following responses may be seen:

1. Spontaneous systemic bleeding such as gum bleeding usually stops within 15-30 minutes.
2. Blood coagulability is usually restored in 6 hours. Principal test is 20WBCT.
3. Post synaptic neurotoxic envenoming such as the Cobra may begin to improve as early as 30 minutes after antivenom, but can take several hours.
4. Presynaptic neurotoxic envenoming such as the Krait usually takes a considerable time to improve reflecting the need for the body to generate new acetylcholine emitters.
5. Active haemolysis and rhabdomyolysis may cease within a few hours and the urine returns to its normal colour.
6. In patients who were in shock, blood pressure may increase after 30 minutes.

Repeat Doses: Anti Haemostatic

In case of anti haemostatic envenomation, the ASV strategy will be based around a six hour time period. When the initial blood test reveals a coagulation abnormality, the initial ASV amount will be given over 1 hour.

No additional ASV will be given until the next Clotting Test is carried out. This is due to the inability of the liver to replace clotting factors in under 6 hrs.

After 6 hours a further coagulation test should be performed and a further dose should be administered in the event of continued coagulation defect and in that case ASV to be given over 1 hr. CT tests and repeat doses of ASV should continue on a 6 hourly pattern until coagulation is restored or unless a species is identified as one against which polyvalent ASV is not effective.

The repeat dose should be 10 vials of ASV i.e. one full dose of the original amount. The most logical approach is to administer the same dose again, as was administered initially. Some Indian doctors however, argue that since the amount of unbound venom is declining, due to its continued binding to tissue, and due to the wish to conserve scarce supplies of ASV, there may be a case for administering a smaller second dose. In the absence of good trial evidence to determine the objective position, a range of vials in the second dose has been adopted.

Recurrent Envenomation

When coagulation has been restored no further ASV should be administered, unless a proven recurrence of a coagulation abnormality is established. If patient comes with features of coagulopathy ASV to be administered (10 Vials) There is no need to give prophylactic ASV to prevent recurrence (Srimannarayana et al, 2004). Recurrence has been a mainly U.S. phenomenon, due to the short half-life of Crofab ASV.

Indian ASVis a F(ab)2, product and has a half-life of over 90 hours and therefore is not required in a prophylactic dose to prevent re-envenomation. But if the patient comes even after few days reinstitute ASV therapy, because sometime absorption of snake venom depot under skin is erratic. If there is no improvement from the beginning of the whole blood clotting time, rather it goes on increasing then we are dealing with the snake bites which are not amenable to our usual polyvalent ASV.

ANTI HAEMOSTATIC MAXIMUM ASV DOSAGE GUIDANCE

Repeat Dose: Haematotoxic

The normal guidelines are to administer ASV every 6 hours until coagulation has been restored. However, what should the clinician do after say, 30 vials have been administered and the coagulation abnormality persists. A large study recently done from south India (Kerala) showed that upto 50 vials (500 ml) has been given for Haemotoxic poisoning.

- It has been established that envenomation by the Hump-nosed Pitviper (Hypnale hypnale) does not respond to normal ASV. This may be a cause as, in the case of Hypnale, coagulopathy can continue for up to 3 weeks.

Surgical Intervention

Whilst there is undoubtedly a place for a surgical debridement of necrotic tissue, the use of fasciotomy is highly questionable.

Fasciotomy is required if the intracompartmental pressure is sufficiently high to cause blood vessels to collapse and lead to ischemia. Now a days we are using multiple puncture technique using large bore needle.

What is important is that the intracompartmental pressure should be measured objectively using saline manometers or newer specialised equipment such as the Stryker Intracompartmental Pressure Monitoring Equipment.

RENAL FAILURE IN SNAKEBITE

The acute renal failure which occurs due to snake bite are multifactorial 1) Severe and persistent hypotension leading to acute tubular necrosis, 2) Hb and other cellular parts of RBC and others (myoglobin and rhabdomylysis 3) part of DIC 4) vasculitis 5) acute diffuse intersticial nephritis 6) extra capillary proliferative glomerulonephritis.

Most of the patients of acute tubular necrosis recovers by few weeks, with the help of occational need of haemodialysis, but who develops cortical necrosis requires reanal replacement therapy on along term basis. It is the hyperkalemia rather than elevated urea, creatinine requires dialysis. The hyperkalemia of snakebite AKI is a hypermetabolic hyperkalemia, which may kill the patient within few minutes and calcium gluconate and glucose insulin is mostly ineffective. Early urgent adequate treatment with ASV can reverse the whole process of deterioration of renal function which is far from our expectation in our country.

Renal failure is a common complication of Russells Viper and Hump-nosed Pitviper bites. The contributory factors

are intravascular haemolysis, DIC, direct nephrotoxicity and hypotension and rhabdomyolysis.

Renal damage can develop very early in cases of Russells Viper bite and even when the patient arrives at hospital soon after the bite, the damage may already have been done. Studies have shown that even when ASV is administered within 1-2 hours after the bite, it was incapable of preventing ARF.

NEUROLOGICAL MANIFESTATION IN SNAKEBITE

Neurological manifestation of snake bite pose an important problem for transportation from the site of bite to the hospital. A well designed study from PGI Chandigarh shows that just putting an airway tube and an AMBU bag decrease the morbidity to a great extent. Mechanical ventilation to be avoided as far as possible, as because most of the death in ventilated snake bite patient is due to Ventilator associated pneumonia. Early initiation and early weaning from ventilator is the strategy, noninvasive ventilator with a patent upper air way is better option.

Heparin and Botropase – No role

Referral Criteria

The primary consideration, in the case of neurotoxic bites, is respiratory failure. Capasity of neck lifting is good predictor of requirement of ventilator support. Refer such patient to the center equipped with invasive ventilation.

REFERENCES

1. Dr. Ian D Simpson. Management of Snakebite-The National,API WB branch, *update in Medicine* 2006; 88-93.
2. K Narvencar, Correlation Between Timing Of ASV Administration And Complication in Snake Bite, *JAPI* 2006; 54.
3. Gudilines For the Clinical Management Of Snake Bites In South- East Asia Region Written and edited by David A Warrell published by WHO, 2005.
4. J Srimannaryan, TK Dutta, A Sahai, S Badrinath. Rational Use of Anti-Snake Venom(ASV): Trial of Various Regimens in Hemotoxic snake Envenomation,*JAPI* 2004; 52:788- 792.
5. HS Bawaskar, Snake Venoms And Antivenoms: Critical Supply Issues. *JAPI* 2004; 52:11-13.
6. V paul, S pratibha, KA prahaald Jerry Earail, S Fracis, Francy Lewis, High-Dose Anti- Snake Venom Versus Low-Dose Anti Snake Venom in The treatment Of Poisonous Snake Bites- A Critical Study, *JAPI* 2004;52.