INTERNATIONAL JOURNAL OF AGRICULTURE & BIOLOGY
1560–8530/2003/05–4–548–551
http://www.ijab.org

Clinical Manifestations of Poisonous Snake Bite and its Management in a Referral Hospital

M. MOHSIN RANA, YOSOUF HASSAN†, OBAID–UR–REHMAN‡ AND MOHAMMAD ALAM†
Mujahid Hospital, Faisalabad–Pakistan
†*Allied Hospital, Faisalabad–Pakistan*
‡*Rehman Hospital, Gojra, District Toba Tek Singh–Pakistan*
Corresponding author e–mail: ranamohsindr1@hotmail.com

ABSTRACT

Sudies were carried out to assess the incidence of different clinical manifestations of poisonous snake bite and its management in a tertiary referral hospital. All patients presenting with history of snake bite in casualty department of the hospital were assessed for clinical evidence of envenomation. Evidence of neurotoxicity, haemotoxicity, cardiotoxicity and local toxicity was specifically sought out with well defined parameters, individually and in combination, in all of these patients. Specific treatment with ASV was started and clinical outcome was recorded. The dose of ASV required in each case was noted. Out of 152 total presentations, 93 had definite evidence of envenomation. 72 patients had haemotoxicity, 21 had neurotoxicity, none had cardiotoxicity and 11 patients had additional evidence of local necrosis along with haemotoxicity. An average of 15 vials of ASV (minimum 4 & maximum 48) was needed to completely neutralize the evidence of envenomation.

Key Words: Snake bite; Neurotoxicity; Haemotoxicity; Cardiotoxicity; Local toxicity; Envenomation

INTRODUCTION

Snakes had been very common neighbours of humans in the recorded history. No other animal is surrounded by so many myths and mysteries like them. The fear arises from the deadly poison known as venom. The unblinking gaze of the snake contributes in the fear though this is their limitation, as they do not have any eyelids. Snake charmers' faith healers and quacks have been instrumental in spread of wrong information about the snakes. Due to this background people fear all snakes. This creature is found on both land and sea all over the world except the polar regions and parts of Australian continent. Majority of land snakes are not poisonous but are rather very useful in the agricultural ecosystem. All deep sea snakes are poisonous without exception. As all land snakes are excellent swimmers, envenomation may result from their bites in fresh water. The tropical and subtropical geographic areas, especially in the rural and agricultural background, have the maximum numbers of mortalities from poisonous snake bites (Qureshi & Sheri, 1975). Inadequate knowledge of first aid measures and the definitive therapy has led to so much un–necessary mortality (Wooldrige, 1993). Lack of facilities in rural areas also contribute to high mortality. Though there are very few snakes in the cities, teaching hospitals do get the referrals from the periphery. This topic was selected to highlight the facts about the poisonous snake bites and basic principles of its management.

MATERIALS AND METHODS

Cases reporting to Allied Hospital Casualty Department with history of snake bite were selected for evaluation of clinical evidence of envenomation. Only the cases with definite evidence of envenomation were enrolled for the study between a period from July 1997 to December 2001. Evidence of envenomation was decided on specific protocol given below and treatment was started on the given protocol. Complete neutralization of venom by clinical parameters was the end–point of treatment.

Assesment for evidence of envenomation. All the patients were assessed on four lines i.e. for evidence of haemotoxicity, neurotoxicity, cardiotoxicity and local toxicity. All assessment was done repeatedly for at least 24 hours, detailed one at presentation and simple ones at two hourly intervals, after a suspected bite before declaring a non–venomous snake bite.

Haemotoxicity. It manifests as spontaneous continued oozing of blood from site of bite or site of intravenous access, echymosis on surface especially on pressure points and bleeding from mucous membranes like conjuctival echymosis, epistaxis, haemoptysis, haematemesis and haematuria. If nothing so was visible at the time of first examination then "Twenty minute whole blood clotting test" was performed by drawing 5 ml of blood in disposable plastic syringe, left undisturbed for 20 minutes, and observed for evidence of clot formation. If clot doesn't form then envenomation has occurred. If frank evidence of haemotoxicity is evident then the evaluation was extended to assess for possible intracranial hemorrhage, intraperitoneal hemorrhage, gastrointestinal hemorrhage, excessive menstrual loss and intramuscular haemorrhage, which may present as compartment syndrome i.e. compressing some nerve or blood vessel. Effects of volume depletion and massive release of hemoglobin may lead to

acute renal shutdown. Measurement of hourly urine output and testing of urine for haemoglobin was started to make necessary adjustments in fluid and electrolyte management i.e. fluid overload and hyperkalemia. (Parikhs, 1985; Smith & Figgie, 1991)

Neurotoxicity. Clinically we assess neurotoxicity by testing for muscle power in cranial and limb muscles and for adequacy of ventilatory function. At the bedside, if patient can cough forcibly and the forceful blow is perceived at one meter, then ventilatory function is adequate.

Cardiotoxicity. It was assessed by routine parameters i.e. heart beat, blood pressure (BP), postural hypotension, dysrythmias and electrocardiogram (ECG) monitoring. Assessment is difficult as fear; panic, dehydration, intravascular volume loss and hypovolaemia due to hemorrhage from haemotoxicity, all will influence the cardiovascular system (CVS). These factors were kept in mind when analyzing the haemodynamic status. Cardiotoxicity will present as tachycardia, dysrythmias, hypotension and myocarditis with relevant changes in E.C.G. Cardiotoxicity alone is rare. It is usually in company with hemotoxicity and local necrosis (Abel *et al.*, 1973; Smith, 1990).

Local necrosis. It manifests by local swelling and pain worsened by oozing of blood from the site into subcutaneous and deeper tissues. Border of swelling and the proximal limit of pain with time were marked on the patient. Reassessment at 15–60 minutes was done to detect the extension of swelling and hence need to modify treatment. Assessment for compartment syndrome was done at every assessment in relevant area of the nerve and the vascular supply. All of this assessment was repeated in a simplified manner by asking the patient to lift both arms, then both legs and to blow at the examiners hand held at one meter distance and listening to cough (neurotoxicity), looking at skin, conjunctiva, mouth (haemotoxicity), looking for swelling at site of bite and for oozing of blood (local & haemotoxicity) and feeling the pulse rate, its rhythm and volume. If this examination shows some abnormality then a detailed examination was done.

Management. After documenting the evidence of envenomation, anti–snake venom (ASV) administration was started rapidly. Depending upon the clinical judgment of severity, one to four vials of anti–snake venom (10 ml each) diluted in isotonic saline to make 10 ml volume was given intravenously over 60 minutes while watching for signs and symptoms of anaphylaxis like skin rash, bronchospasm, urticaria, tachycardia and hypotension. At the end of one infusion, patient was re–assessed. If evidence of envenomation is still present, another dose of four vials was repeated again with same precautions for anaphylaxis. End point of treatment was considered to be the clinical neutralization of venom evident by arrest of further progression of muscular weakness, restoration of coagulability of blood, arrest of further progression of local swelling and stabilization of cardiovascular status.

The neurotoxicity is established at synaptic and post–synaptic level. The synaptic block is reversible by Neostigmine. Hence, every case of neurotoxicity was given intravenous (i.v.) Neostigmine 0.5–1.0 mg, while monitoring for bradycardia (reversible by atropine). If weakness improves then maintenance by using 2.5 mg Neostigmine i.v., repeated every 2–6 h, as needed, was given. Once ASV neutralizes venom then demand of Neostigmine will decrease and weakness will start recovering (Ansari & Sheikh, 2000). If the neurotoxicity is at post–synaptic level, then Neostigmine will be ineffective. Such patients were offered ventilatory support in ICU for 2–4 weeks until the synaptic receptors are regenerated.

Anaphylaxis. If anaphylaxis developed then the rate of administration of ASV was slowed down to half and antihistamine (Injection AVIL), Hydrocortisone 250 mg i.v. 4–hourly and Adrenaline infusion (l000 ml 0.9% NaCI and four injections of Adrenaline 1:1000) was started. Rate of Adrenaline infusion was adjusted to maintain B.P. and pulse rate near normal values. At the same time, other aspects of patients monitoring were kept in mind. Antitetanus Toxide (ATT), antibiotics if needed, surgical intervention for compartment syndrome after restoration of blood coagulability, monitoring urine output, fluid and electrolyte balance, managing pulmonary, gastrointestinal and intracranial haemorrhages and cardiovascular status, all were managed according to usual strategies.

RESULTS

During the study period of 54 months, 152 patients presented with history of snake bite. Only 93 had the evidence of envenomation at presentation or within 24 h period of observation which were enrolled for the study. Three patients died, two of intracranial hemorrhage and one of accidental disconnection of ventilatory support, all the others survived. Seventy two patients (77.4%) had evidence of clinical haemotoxicity. Of these, 11 patients (11.8%) had additional clinical evidence of local toxicity, which could not be clearly separated from the effect of associated oozing from the site of bite. Twenty one patients (22.6%) had clinical evidence of neurotoxicity. Clear–cut cardiotoxicity could not be assigned to any patient. An average of 15 vials of ASV were needed (maximum 48 and minimum 4). Out of 2l patients with neurotoxicity, 15 (77.4%) needed ventilatory support for an average period of 12 days (minimum 7 and maximum 26 days) after failing the trial of 'Neostigmine'. Other six patients (28%) responded to Neostigmine.

DISCUSSION

In this study, 152 patients presented with history of snake bite. Only 93 patients had definitive evidence of envenomation within an observation period of 24 h. Only about 20% of the snake species are reported to be poisonous

(Wooldridge, 1993). The figure in this study cannot be used to assess the percentage of poisonous snake bites because majority of the cases were referred due to the non availability of facilities, panic by the attendants or primary health worker or under the impression that one vial of ASV has not worked. Majority of nonpoisonous snake bites were not referred to the unit of the hospital.

Monsoon season in tropics increases the encounters resulting in higher incidence of snake bites. Venom is the natural secretion from the salivary glands. It is a mixture of special enzymes, which aids in killing of the prey and its digestion. This is the reason that even a newborn snake is venomous. Fangs are the specially designed teeth that carry the venom through either a central canal or a groove on the undersurface, from the glands to the victim's body. The amount of venom transferred in an individual bite is dependant on snake species and victim variables. Large snakes definitively have more venom especially after their hibernation. The longer the interval after the last meal the larger is the amount of venom available. Defensive snake bite is likely to transfer less venom than a hunting bite. Similarly, in the victims, a small body frame or a child needs larger dose of antivenom. The thickness of clothes worn by the victim and body part exposed or covered by it also determine the amount of venom transferred, even very thin clothing may offer a reasonable protection. Upto 30% of bites from even poisonous snakes may not result into any envenomation if the bitten area is covered.

Venom is classified into four groups according to its effect on the victim's body. Haemotoxic group causes disruption of normal coagulation process leading to active bleeding from almost everywhere in the body, both externally and internally. Extensive intra and extravascular haemolysis and its sequele follow in terms of acute renal shutdown and haemolytic jaundice. Neurotoxic group either leads to a synaptic block at neuromuscular junction by blocking acetylcholoine or causes a post receptor block. Paralysis of striated muscles is the clinical expression. Neostigmine reverse synaptic block. Acute myocarditis, dysrhythmias and vasodilatation are the clinical expression of cardiotoxicity. Local toxic group leads to severe local inflammation necrosis.

Once a patient presents to the doctor with a history of snake bite, actual or suspected, one and the only concern is whether envenomation (transfer of venom to victim) has occurred or not (Peterson & Meerdink, 1988; Rodney *et al.*, 2000; Khan & Naseem, 2002). Identification of fang marks and identity of snake are totally unimportant. (Russel, 1983; Methew & Gera, 2002). It is strongly suggested that general public shall be clearly educated not to attempt killing the snake only for the purpose of identification as it may lead to further casualties and the panic involved will speed up the spread of venom from site of bite and will also divert the attention from proper first–aid measures (Fraser, 1991; Forks, 1994; Laloo, 1997). Identification of snake also becomes unimportant in Pakistan because of availability of only polyvalent ASV for use in all patients. Even if univalent ASV was available, the same arguments hold that clinical manifestations are dictating the treatment. Individual patient may have more than one toxicity in any combination. (Chipaux *et al.*, 1991; Tu, 1991; Gold & Winger, 1994).

Anti–snake venom is prepared from horse serum. New preparations by genetic engineering technique are under process. Anti–snake venom is supplied in liquid form of 10 mL vial or as powder, which is reconstituted to make 10 mL volume. While using liquid preparation of anti–snake venom, one must be sure about the proper storage between 2–8^{o}C, otherwise potency of preparation will be questionable. In Pakistan, polyvalent anti–snake venom is derived from horse serum. This is to be given to every case, be it neuro, cardio, haemo or locally toxic. Upto 40 vials of anti–snake venom may be needed to neutralize the effect of venom in one patient. Even more may be justified especially when one is using the liquid preparation that might have lost some potency due to break in cold chain during transportation and storage. Anaphylaxis is not the indication to withhold or stop ASV (Hwng *et al.*, 1997). The venom has to be neutralized by anti–venom in adequate dose.

As antivenom is derived from horse serum, the anaphylaxis remains a potent threat during administration. Routine testing for the possible anaphylaxis by test dose offers no guarantee against it (Gold & Barish, 1992). Genetically engineered preparation will solve the problem of anaphylaxis. Even if anaphylaxis develops, there is no other alternative available. One has to give ASV under cover as discussed in materials and methods.

Another point worth mentioning in this study is the fact that there is no fixed dose of ASV. One has to give enough ASV to neutralize all the effects of venom with whatever dose is required (Wing *et al.*, 1996), average of 15 vials (maximum 48 and minimum 4). Delayed presentation is another very important concern. It is again strongly suggested that all the manifestations of envenomation do respond to ASV even after many days and this is especially true in cases of haemotoxicity. In this study, 19 patients who received some treatment at periphery and all these patients received only one vial of ASV and then were referred to Allied Hospital with the comments that patient is not responding. There is enough evidence that abnormal coagulability may be successful even after days of ASV use. In this study, all evidences of haemotoxicity were restored to normal by ASV use, in all cases. Even in the cases of two deaths, coagulability was restored to normal. Death occurred due to intracranial heamorrhage which occurred earlier.

The victim of neurotxic venom needs special mention. Here a word of caution is necessary that neurotoxicity may progress rapidly after an initial delay. Neurotoxicity is seen after cobra's bite in the subcontinent. The characteristic hood recognizes cobras. Folk wisdom also alerts to this fact through the saying, "Do not let the victim sleep, he may silently go blue and die" (Karlson & Persson, 1994). Six

patients with neurotoxicity responding to Neostigmine were tided over the period until ASV reversed neurotxic weakness. 15 patients needed ventilatory support. Here use of ASV is controversial. The dominant opinion holds in favor of not using ASV. Patient shall be tided over the period of muscular weakness by ventilatory support until new nerve endings regenerate. In this study, the average period was 12 days (minimum 7 and maximum 26 days). The 100% recovery speaks very clearly in favor of aggressive ventilatory support. The only death was accidental. One must be reminded of the fact that these patients are fully conscious and alert though paralyzed. Ambo–bag ventilation is very helpful in this situation at smaller facilities and during transportation. No patient shall be denied of this form of assistance until proper facilities are available.

After talking all the science, let us remind about the actual scenario of the snake bite that is the field. The following suggestions can be drawn:

1. One shall attempt to allay the anxiety by stressing upon the fact that around 80% of snakes are non–poisonous and even the bite from a poisonous snake may not lead necessarily to envenomation. Effective treatment is available and there is always a reasonable time available for the transportation of the victim to proper health care facility or the nearest military establishment as anti–snake venom is always part of the soldiers' kit during field exercises. ASV is available at all DHOs, ADHOs offices, DHQs, THQs and teaching hospitals, CMH and military establishment.

2. The bitten limb shall be splinted and immobilized. A loose tourniquet, which admits one finger, shall be applied on the limb proximal to the bite site. Limbs are the most common sites of bite while face and body are quite uncommon. Attempted suction of venom, incision and drainage of blood from bite site and cleaning, are all unnecessary, ineffective and potentially dangerous procedures. (Cruz & Alveraz, 1994; Sallehwa & Kumararatna, 1994; Sallehwa *et al*., 1994; Wing *et al*., 1996). If one can clearly identify the fang marks as two puncture marks just outside a rim of circular mark, one shall make sure that this patient must be transported to a proper healthcare facility.

3. A trained observer may decide to observe the patient while transportation arrangements are at standby notice, for a period of 24 h before declaring it as non venomous bite. If any evidence of envenomation appears, proper treatment steps shall be taken.

4. One may ask the attendants to ask patient to lift all four limbs, cough and blow at one hourly interval and report immediately for any inadequacy in muscle power or ventilatory power. This is very useful tip to public in deciding the urgency to seek medical help. Repeated examination is very important as the delayed absorption of venom is a documented fact and patient may simply drift into ventilatory failure silently.

CONCLUSIONS

1. 80% of snakes in our area are non poisonous, 2. Evidence of envenomation is the only indication of ASV administration, 3. All the evidence of envenomation must be neutralized by adequate dose of ASV, 4. Even delayed administration of ASV is effective in neutralization of the venom.

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(Received 11 August 2003; Accepted 13 September 2003)