EXPERIENCE WITH VIPERINE ENVENOMATION

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ABSTRACT

Two hundred and twenty one cases of viperine envenomation, who presented to hospital without specific treatment, seen over an twenty five years period, have been presented. Mild, moderate and severe envenomation was encountered in 33 per cent, 47 per cent and 20 per cent respectively. Bites on feet and ankles were seen in 85.5 per cent of cases. The average time interval between bite and hospitalisation was 4.8 hours, range being 15 minutes to 7 days. Local swelling was observed in 97.7 per cent, hematuria in 62 per cent, mucosal haemorrhages in 24.8 per cent and haematemesis in 19 per cent of patients. Average Antisnake Venom (ASV) required in mild, moderate and severe envenomation was 50 ml, 147.5 ml and 324 ml respectively. Major complications observed were renal failure in 10, intracompartmental syndrome in 3, intracerebral bleed and septicaemia in 2 each. One patient each developed finger gangrene, osteomyelitis, perirenal haematoma, sinus bradycardia and uncontrolled bleeding. Blood transfusion was required in 32 patients. Reactions to ASV were seen in 12 patients and overall there were 5 deaths.

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KEYWORDS: Antisnake venom; Viperine envenomation.

Introduction

In India, snake envenomation accounts for 15,000-20,000 deaths per year [1-4]. Russel's viper and saw scaled viper (*Echis carinatus*) are two widely prevalent vipers in India and over two thirds of viperine bites and deaths in Jammu, Rajasthan and adjoining areas are due to saw scaled vipers [2]. This small stumpy snake measuring 25-75 cms, camouflages well with the surroundings, strikes with lightening speed and accounts for maximum bites and deaths all over the world [1-4]. Viper venom, a high molecular weight mixture of enzymes and toxins, travels by lymphatics and has a vasculotoxic effect. Systemic manifestations of both Russel's viper and saw scaled viper are similar [1-5]. Snakebite is an occupational hazard for Armed Forces personnel. Despite managing a large number of snakebite cases each year, there is no uniformity in its management. We describe here our experience in management of 221 cases of viperine envenomation in peripheral hospitals equipped with basic investigative facilities. The main emphasis of this study is on the clinical approach and antisnake venom protocol.

Material and Methods

Over twenty five years period from 1971-1995, 221 patients were identified to have developed viperine envenomation. Basis of diagnosis was either identification of snake brought by the patients, description of the snake if seen and/or classical vasculotoxic envenomation. All patients were thoroughly examined at admission and throughout the hospital stay for local and systemic signs of envenomation. Investigative profile included bleeding time

(BT), clotting time (CT), platelet count, prothrombin time, peripheral smear, urine examination, liver function tests, renal function tests and ECG. BT and CT were repeated 6 hourly till they normalised and for subsequent 48 hours. Fibrinogen and its degradation products, CSF and X-ray chest etc. were done whenever required/feasible. Effect of tourniquet was studied by recording CT before and 1/2 hour after its release. Bites were classified as mild, moderate and severe as per following criteria [5].

Mild : Only fang marks with local swelling and normal CT.

Moderate : Mild + prolongation of CT or evidence of bleeding.

Severe : Systemic bleeding tendencies, DIC, renal failure or severe hypotension.

Polyvalent antisnake venom (ASV) (Haffkine Institute Biolab, Mumbai) was given slowly in an intravenous infusion diluted in three times of its volume in isotonic saline or 5 per cent glucose, over 1 1/2-2 hours. In mild envenomation 50 ml, in moderate 100 ml and in severe 150-200 ml. of ASV was administered on admission. ASV administration was preceded by an intradermal test dose of 0.1 ml on volar aspect of forearm. ASV was repeated in a dose of 50-100 ml 6 hourly till CT remained prolonged. In initial cases, we gave steroids and antihistaminics along with ASV. However, we abandoned steroids as a routine after initial 44 cases. Supportive therapy included crystalloids or colloids and blood if haemoglobin dropped below 5 gm/dl. The facility to differentiate DIC from primary pathological fibrinolysis (PPF) was not available in peripheral centres. Heparin was not given to any patient. Patients who developed serum sickness were treated with short course of steroids and antihistaminics.

Results

There were 199 males and 22 females with mean age 27.1 years (range 11 to 70 years). Thirty nine patients (17.6%) brought the snake, which was identified as saw scaled viper in 37 and Russel's viper in 2 cases. One hundred and ninety seven patients had 2 fang marks and 18 had 1 fang mark, while in 6 cases no fang marks could be identified. One hundred and eighty nine cases

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(85.5%) had bites on the feet or ankles, 10 (4.5%) on the lower one third of leg and the remaining 22 (9.9%) had bites on the forearm or fingers. The time gap between the bite and reporting to the hospital averaged 4.8 hours (range 15 minutes to 7 days). Local swelling or discoloration appeared in 20 minutes (range 15 - 30 minutes). In 5 cases no local swelling could be appreciated (two and three of these turned out to be of moderate and severe envenomation respectively).

Seventy three cases (33%) had mild envenomation, 104 (47%) had moderate and 44 (19.9%) had severe envenomation. The average dose of ASV administered in mild, moderate and severe cases were 50, 147.5 and 324 ml respectively (maximum 800 ml). CT profile following the release of tourniquet is shown in Table 1. The salient clinical features in these 221 patients have been summarised in Table 2.

TABLE 1
CT before and 30 minutes after release of tourniquet (n=22)

Number	Clotting time in minutes		Difference (minutes)
	Before Release of tourniquets	30 mins after release	
1	7	16	9
2	15	20	5
3	16	21	5
4	17	22	5
5	6	45	39
6	10	16	6
7	5	25	20
8	18	18	0
9	12	16	4
10	45	45	0
11	30	30	0
12	13	17	4
13	30	30	0
14	45	45	0
15	17	17	0
16	8	45	37
17	6	25	19
18	15	22	7
19	16	20	4
20	17	22	5
21	10	17	7
22	8	16	8

Total 184 (mean = 8.36)

Complications and Outcome

Ten patients (4.52%) developed acute renal failure, five of whom required dialysis support and two died. Three patients developed intracompartmental syndrome. Their presentation was with calf pain and impending gangrene of the lower limb. Fasciotomy brought the crisis under control. Two patients developed intra cerebral bleed, one presented with hemiplegia and eventually made good recovery while the other patient died due to uncontrolled convulsions. One patient each developed perirenal hematoma, uncontrolled bleeding resulting in death (reported to hospital 48 hours after bite), gangrene of finger requiring amputation, osteomyelitis of distal phalanx of ring finger probably due to cuts received during first aid and sinus bradycardia with a heart rate of 42 per minute which responded only to ASV. There were 5 deaths

TABLE 2
Clinical manifestations (n=221)

Symptoms	No of cases	Percentage of cases
Fang marks	215	97.28
Local swelling/discoloration	216	97.73
Bleeding from local site	48	21.7
Haematoma/mucosal haemorrhages	55	24.88
Local blisters/gangrene	26	11.76
Lymphadenitis	19	8.59
Epistaxis	10	4.52
Haematemesis/Melena	42	19
Renal shut down	10	4.52
Severe anaemia, < 5 gm/dl	32	14.47
Haematuria (gross/microscopic)	50/87	22.6/39.36

(2.36%).

Discussion

Unlike cobra and krait, vipers have long and hinged fangs. Saw scale viper (*Echis carinatus*) venom has numerous enzymes and toxins. *Haemoragin* opens the capillary endothelial pores by damaging the intercellular junctions and allows the fluid to exude out. Local swelling is attributable to proteases, phospholipases, and membrane damaging polypeptide toxins and endogenous autocoids released by venom. *Ecarin* an important constituent of venom aids in conversion of prothrombin to thrombin and hence starts the cascade of coagulation. In brief all patients develop DIC which may be self limiting [6-8]. Experimental studies show that venom keeps getting absorbed from the site of bite for upto 3 weeks though significant absorption is over in initial 2-3 days [9].

Beneficial effect of tourniquets and incision in these patients has been debated and due to high incidence of infections, use of incisions is not recommended. Osteomyelitis is one of the dangerous infections due to deep cuts [2]. Tourniquets however do appear to have a beneficial effect as they slow the venom absorption.[10] Sudden prolongation of CT following release of tourniquets has been reported by one of the co-authors while studying the effect of incision and tourniquet in viperine bites [11]. Warrell et al reported high incidence of gum bleeding (57%), lymphadenitis (50%) and low incidence of hematuria (28%) though other Indian data and ours suggest otherwise [2,5]. Intracerebral, thalamic or pituitary bleed though not common, have been well recorded [2,12,13]. Though literature is emphatic, we did not find correlation of severity or duration of envenomation with local swelling, rather some of the patients of moderate/severe envenomation had minimal/ no local

swelling. Bhat also had similar observation [2]. These variations are probably due to the snake species differences and the venom constituents.

Besides DIC some patients have primary pathological fibrinolysis (PPF). Viper venom proteases digest fibrinogen or there is primary increase in plasminogen activators thus rendering fibrinogen non-clottable; this is different from secondary fibrinolysis, where platelet count also goes down. Peripheral smear is usually normal in PPF unlike DIC where evidence of microangiopathic haemolytic anaemia is present. Based on the state of incoagulable blood, normal peripheral smear, normal BT and platelet count we suspected PPF in 4 patients. However confirmation requires Euglobin clot lysis and Protamine sulphate test, facilities, for which were not available with us in peripheral centres. This, entity probably is under diagnosed [14]. Preliminary reports suggest that heparin is harmful while epsilon amino caproic acid is beneficial in this setting [15]. Of the 17 patients seen in a tertiary centre, 9 had moderate and 6 had severe envenomation. Twelve of these had evidence of frank DIC. However all our patients of DIC and suspected PPF responded well to ASV alone.

Renal failure is a well recognised complication of viperine envenomation. Chugh et al have reported ARF in 8.69 per cent of their patients [17,18], the low incidence in our study is explainable since most of the cases were seen early at primary hospital. Hypotension, intravascular hemolysis, DIC, myoglobinuria, microangiopathic haemolytic anaemia and sepsis are some of the factors responsible for acute tubular necrosis, which remains the commonest cause of ARF in these patients [18,19]. The direct tubulotoxicity of viper venom has not been convincingly proved [17-19].

Literature recommends ASV institution only if signs of severe envenomation appear i.e. on appearance of severe bleeding tendencies, hypotension or swelling in more than half the limb. This also emphasises that outcome of these patients is largely dependent on the time gap between the bite and institution of specific therapy [1-4]. Since the degree of local swelling at presentation and thereafter did not correlate with the degree of envenomation, we could not find any marker/predictor as to who will develop moderate/severe envenomation. Our initial 28 patients served as controls (18 retrospective and 10 prospective). Despite local swelling and fang marks ASV was not instituted as CT was normal and swelling was minimal though mean time gap between bite and hospitalisation was 7.1 hours. Though 5 (17.8%) of these did make uneventful recovery, 15 (53.5%) developed

moderate and 8 (28.5%) developed severe envenomation. Based on this observation, we have been treating all, even mild cases of envenomation with ASV.

The available data suggests that snake venom keeps getting absorbed from bite site for a period upto 3 weeks [9]. We came across over a dozen cases whose CT had normalised following the initial therapy and had remained normal for subsequent 24-48 hours; but after a day or two CT again got prolonged necessitating ASV therapy, emphasising the requirement of close monitoring of these patients for a minimum period of one week. Fourteen patients reported more than 48 hours following the bite including a lady who presented 7 days after the bite with hemiplegia and systemic bleeding tendencies. All these patients except 2 who succumbed to renal failure responded well to ASV with no residual damage. We strongly recommend institution of ASV in presence of bleeding tendencies even if patient comes days after the bite.

Twelve (5.42%) cases developed reaction to ASV and were managed with antihistaminics/adrenaline and/or steroids. The incidence is low compared to the 21 per cent reported by Warell et al [4]; this is probably explainable by different antigenic components of ASV and rapidity of administration. We gave ASV in drip form over 1 1/2-2 hours while some workers have given it in bolus form. We do not recommend bolus injections of ASV unless the condition of the patient is hopeless. Four patients (1.8%) developed serum sickness 8-10 days after the ASV, all of these responded to short course of steroids.

Based on our study following conclusions can be drawn:

(i) Viperine envenomation requires early and repeated institution of ASV besides supportive therapy. We feel ASV should be given early without waiting for severe envenomation to develop.

(ii) Local swelling was not observed to correlate with severity or duration of envenomation.

(iii) ASV should not be denied if a patient reports with prolonged CT even days after the bite.

(iv) Slow infusion of ASV rather than bolus is recommended. Adverse reactions of ASV are not alarming and are easily manageable.

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