

A prospective observational study of drug usage in the management of snake bite patients and their outcome in a tertiary care teaching hospital

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ABSTRACT

Background: The objectives of the study were to assess the pattern of management of snakebite especially with respect to use of anti-snake venom and other supportive treatment given and to assess the effect of anti-snake venom on different types of snakebite and to assess their outcome.

Methods: A prospective observational study was conducted over a period of 6 months, after getting approval from Institutional Ethics committee. Total of 144 snake bite patients were analysed for six months duration for use of anti-snake venom and other supportive treatment in their management and were assessed for their outcome like recovery, morbidity and mortality.

Results: Out of 144 snake bite patients analysed, 71.5% had poisonous type and 28.4% had non-poisonous type of snake bite. Among the total number of snakebites, 47.2% were unknown type and among the known type 25% were viper, 13.2% cobra, 7.6% krait, 6.3% sea snake and 0.7% green snake. Anti-snake venom (ASV) was given to 62 patients depending on severity, of which, 22 patients developed reaction to ASV. Patient with reaction to ASV were treated with corticosteroid and antihistamine injection. Morbidity was seen in 29.1% of patients who developed either cellulitis or gangrene of bitten area, which was more commonly seen among viper bite patients (54.7%).

Conclusions: Snakebite is one of the commonest tropical diseases leading to envenomation and poisoning especially in rural areas of tropical countries which has to be treated as early as possible to prevent complications. Majority of the cases in our study were of viper bite and most of them have recovered after treatment.

Keywords: Anti-snake venom, Morbidity, Viper

INTRODUCTION

Snakebite is one of the commonest occupational hazards that is seen in South Asian region, which may be because of the population density, widespread agricultural activities, numerous venomous snake species and lack of functional snake bite control programmes. According to WHO estimation, 35,000-50,000 people are dying per year due to snake bite in India.¹

In the year 2009, snakebite was included in the list of neglected tropical disease by WHO. There were 61,507

snake bites with 1,124 mortality in 2006; 76,948 bites and 1359 deaths in 2007 according to the data provided by the government of India.²

Since most of the snakebite patients approach traditional healers for treatment and are not registered in hospital, accurate statistics of morbidity and mortality is not available which could be higher than the recorded number of cases.²

Out of 3,000 species of snake that is known, 300 types of venomous snakes are found in India. Some of the major

families of poisonous snakes found in India are Elapid, which includes common cobra (*Naja naja*), king cobra and Common krait (*Bungarus caeruleus*, Banded krait, Sind krait), viperidae- (*Russell's viper*), *Echis carinatus* (saw scaled or carpet viper), and pit viper and hydrophidae (sea snakes).³

Types of snake venoms include:

1. Neurotoxic venoms: affects the neuromuscular junction.
2. Haemotoxic venoms: affects cardiovascular system and blood
3. Cytotoxic venoms: targets specific cellular sites.⁴

Viper bite causes haemotoxicity, cobra bite produces neurotoxicity and krait bite causes combination of both.⁵

Identification of type of snake species is one of the important aspects in the management of snakebite patients which will help the treating clinician to plan for an appropriate treatment accordingly, anticipate complications that can occur due to different species and improve the outcome in a snakebite patient.¹

Snake venom is a complex mixture of proteins, peptides, non-protein toxins, carbohydrates, lipids, amines and other molecules. Composition of different snake varies according to the geographical locations, based on diet, age, season and environment. Elapid and viperid venoms constitutes for 25-70% and 80-90% of enzymes respectively. Some non-enzymatic polypeptide toxins and non-toxic proteins are also present.⁶

Enzymes like phospholipase A2, hyaluronidase, α neurotoxins are the major cause for toxic effects of snake venom, phospholipase A2 damages platelets, red blood cells, leukocytes, skeletal muscle, vascular endothelium, peripheral neuron and myoneural junction. Venom spreads through tissues due to hyaluronidase and the proteolytic enzymes leading to local edema, blistering and necrosis.⁷

The neurotoxic venoms disrupt the neuromuscular junction by acting at the molecular level and thereby it limits the muscular activity. Hemotoxic venom leads to destruction of various systems in the body, but its main effect is on circulatory system leading to haemolysis.² The elapid venom contains acetylcholinesterase, which can cause tetanic paralysis by acting at the neuromuscular junction.²

In humans, snakes usually inject venom subcutaneously or intramuscularly and the average dry weight of venom injected at a strike is approximately 60mg (*N.naja*), 13 mg (*E.carinatus*) and 63 mg (*D. russelii*) respectively.² Patients with venomous snake bite present with signs and symptoms ranging from fang marks with or without local pain and swelling to life threatening coagulopathy, renal failure and shock.⁸

Antivenomous serum is the only effective therapy available for the treatment of snake bite and envenomation.⁹ The time elapsed after the bite is of vital importance, because with the passage of time more venom gets bound to the tissues and thus becomes less manageable with ASV.²

Anti-venom which is an immunoglobulin (IgG) is got by purifying the serum or the plasma of a horse or sheep that is being immunized with the venom of one or more species of snakes. Only polyvalent ASV is available in India. The anti-venom that is produced in India are mainly against the "big four" venomous snakes that are found in India. The ASV vial that is manufactured in India can neutralize 0.6 mg dried Indian cobra venom, 0.45 mg dried common krait venom, 0.6 mg of dried Russell's viper venom and 0.45 mg of dried saw-scaled viper venom in per ml.¹⁰

Polyvalent antivenomous serum is not effective in all poisonous snakebites, interspecies variation in venom composition can occur. Hypersensitivity reactions are also associated with antivenomous serum.¹¹

Side effects of anti-venom include:

- Anaphylactic reactions, like difficulty in breathing, reddening of skin, swelling of eyes and face, fever.
- Pyrogen reaction which may be due to the action of high concentrations of non-immunoglobulin proteins.
- late serum sickness with inflammation of joints, enlargement of lymph glands.¹²

A lack of simple airway management equipment such as resuscitation bags and laryngoscopes lead to the difficulty in treating many patients and increases mortality in neurotoxic venom poisoning.¹³

Prophylactic use of antibiotics has no benefits after snakebite, except when the wound is incised or tampered with instruments that are unsterile, antibiotic treatment is required to prevent the development of bacterial infection.⁸ Fatality due to snake bite may be due to large variation in species, shortage in anti-snake venom (ASV), poor compliance with treatment protocols, lack of public education and clear policy to deal with the problem.²

Snake bite is one of the most neglected health issues in rural communities causing morbidity and mortality. It is a common occupational hazard mainly in farmers, plantation workers, herders and labourers leading to significant morbidity and mortality that remains largely unreported. Hence this study is being done in tertiary care teaching hospital to study the drug usage in snake bite patients and their outcomes.

METHODS

The materials for the present study were collected from patients admitted with history of snake bite under

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It was prospective observational study.

Study was conducted for a period of 6 months from the month of January 2016 to June 2016. 144 patients admitted in Medicine ward with history of snakebite were enrolled in the study.

Collection of data

- Written consent was taken before starting the study.
- Data regarding patient age, time of snake bite, time of admission, symptoms of snake bite and signs of venomous snake bite were collected.
- Data regarding use of antsnake venom and other supportive treatment and their outcome were collected.
- Data regarding effect of antsnake venom on different snake bites were collected.
- Patient was followed till discharge from the hospital.

All the patients who were admitted with history of snakebite to the hospital were assessed for type and symptoms of snake bite. Bleeding and clotting time were done and other required lab investigations were carried out. Administration of ASV depended on the severity of snakebite, lab investigation and also the treating physician.

Inclusion criteria

- All patients admitted with the history of snake bite (poisonous and non-poisonous) for treatment to Medicine ward.

Exclusion criteria

- All patient or relatives who didn't give consent for the study.
- Patient discharged against medical advice were excluded from the study.
- Patient who were already started on antsnake venom in other hospital were excluded from the study.

Statistical analysis

All collected information was entered in excel sheet and analysed using Statistical Package for Social Sciences version 20 software, 2015. Descriptive statistics and other suitable statistical methods were used for analysing data.

RESULTS

Total of 144 patients were analysed of which 71.5% were poisonous and 28.5% were non-poisonous type of snakebite (Figure 1). Different types of snakebite were differentiated by the fang mark, type of snake, symptoms of snakebite in relation to neurotoxicity, haemotoxicity or cytotoxicity. On analysing for different types of

snakebites, 47.2% of cases were of unknown type of snakebite, where the type of snake was not identified, 52.8% of cases were of known type of snakebite, where patient had either identified the type of snake or had brought the snake to the hospital. Out of 52.8% of known bites, maximum number of cases was of viper bite (25%) and minimum was of green snake bite (0.7%) (Figure 2).

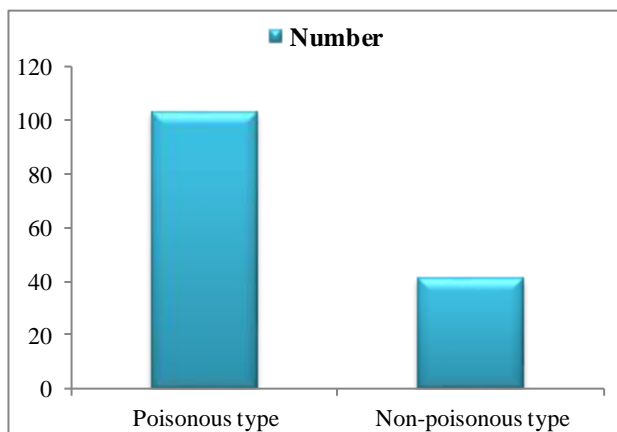


Figure 1: Different types of snakebite.

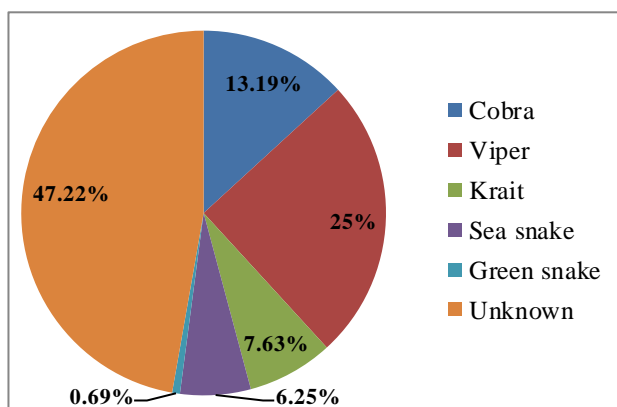


Figure 2: Types of snake in percentage.

Maximum number of snakebite cases were seen among males (86%), between the age group of 25-40 years (Table 1) i.e. the active age group of population and due to their dwelling lifestyle.¹

Commonest site of snakebite that was seen in our study was lower limb (68.8%). First aid treatment was received by 50.7% of cases. Patient received first aid treatment which was in the form of tying tourniquet, sucking blood from the site of bite or using herbal medicine by approaching the traditional healer in their locality (Table 1).

Antsnake venom (ASV) was used in 43% of cases depending on patient condition and physicians decision. Among 62 cases in whom the ASV was used, 24 patients recovered and 38 cases went into morbidity (morbidity due to cellulitis or gangrene of the affected limb). All the 4 cases with poisonous type of bite in whom the ASV was

not used went into morbidity, total of 42 patients went into morbidity (Table 2), and there was no mortality cases recorded due to snake bite during our study period.

Table 1: Demographic and other basal characteristics of patients with snakebite.

Gender	Number (%)
Male	86 (59.7)
Female	58 (40.3)
Age (years)	Number (%)
10-25	19(13.2)
25-40	64 (44.4)
40-55	40 (27.8)
>55	21 (14.6)
Site of snake bite	Number (%)
Upper limb	44 (30.6)
Lower limb	99 (68.8)
Head & neck	1 (0.7)
First aid treatment	Number (%)
Yes	73 (50.7)
No	71 (49.3)
ASV	Number (%)
Yes	62 (43)
No	82 (56.9)
No. of Vials used	Number
Minimum	1
Maximum	29
Mean	9.77
Reaction to ASV	Number (%)
	22 (35.5)

Reaction to ASV was seen in 22 (35.5%) cases in our study, hypersensitivity reaction to ASV was in the form of chills and rigors or rashes for which they were treated with

Table 2: Different types of snake bite and their outcome.

Type of snake	No. (%)	ASV used	Outcome		Morbidity without use of ASV
			Recovery	Morbidity	
Cobra	19 (13.2)	15 (78.9)	3(20)	12 (80)	0
Viper	36 (25)	32 (88.9)	10 (31.3)	22 (68.7)	1
Krait	11 (7.6)	3 (27.2)	2 (66.7)	1 (33.3)	1
Unknown	68 (47.2)	12 (17.6)	9 (75)	3 (25)	2
Total	134	62	24	38	4

Table 3: Treatment given in snakebite patients.

Treatment given	Number (%)
Tetanus toxoid	122(84.7)
Antibiotics	81 (56.3)
Serratiopeptidase	49 (34)

In order to prevent complications that can develop due to envenomation, antsnake venom has to be administered as early as possible in snakebite.¹⁴ The severity of a venomous bite is more dangerous than the antivenom if it

inj.hydrocortisone and inj.chlorpheniramine, there were no complications following reaction to ASV.

Out of 144 cases, Tetanus toxoid was given to 122 (84.7%) cases of snakebite. Antibiotics were prescribed in 81 (56.3%) cases, inj. cefotaxime, inj. ceftriaxone, inj. metronidazole, inj. amikacin were some of the antibiotics that were used to treat infection following snakebite. About 49 (34%) cases were also treated with serratiopeptidase to decrease the swelling in patients with cellulitis following snakebite (Table 3).

Time gap in the treatment of snakebite cases affects the outcome. In our study out of 14 cases who reported to the hospital within 30min of snakebite, most of them recovered except for 2, went into morbidity. As it is seen in Table 4, as the time gap increased, number of cases with morbidity also increased i.e. from 14.3% of morbidity in less than 30 min to 46.2% of morbidity in more than 5 hrs. Increased time gap may be due to poor access to the hospital, since it is a rural area, time elapsed in travelling to hospital, the first aid treatment that the population follow in case of snakebite or due to lack of knowledge about snakebite (Table 4).

DISCUSSION

Snake bite remains one of the emergencies and antivenom is the one of the specific treatment for snake bite envenomation, but the ASV that are available at present cover only a very limited number of medically significant species. ASV is less effective in snakebite caused by other species, besides "big four".¹¹

remains untreated, while active management of venomous snakebites through proper guidelines should be practiced without fear.¹⁵ Most of the cases that we came across during our study were of poisonous type 71.5%, which is almost similar to the result that was seen in the study done by Punde DP which showed 67.5% cases of poisonous type of snakebite.¹⁶

Laboratory investigations like bleeding time and clotting time were done and also patient was assessed clinically for the type of snake bite prior to the administration of ASV.

The 20 min whole blood clotting test is one of the simple, rapid and reliable test of coagulopathy.¹⁷ ASV sensitivity test is done prior to its administration.⁷

Table 4: Time gap between snakebite and treatment and outcome.

Time gap	Number of cases	Number of morbidity (%)	Number of recovery (%)
<30 min	14	2 (14.3)	12 (85.7)
½ hr -2 hrs	89	23(25.8)	66 (74.2)
2-5 hrs	28	11(39.3)	17 (60.7)
>5 hrs	13	6 (46.2)	7 (53.8)

In our study lower limb was the commonest site involved (68.8%) in snakebite, since most of the patients were agriculturists working in agricultural field which is in contrast to the study done by Punam AG et al, where they found commonest site involved was upper limb 52.09%.¹⁸

According to WHO, the recommended dose of antivenom is the amount that is required to neutralize the venom that is injected into patient by snake per bite, for example: Russell's viper injects about 60mg of venom in the first bite. As each vial of polyvalent ASV neutralizes 6mg of Russell's viper venom, the initial dose should be 8 to 10 vials to ensure that the majority of the victims are covered by the initial dose. Usually bleeding stops within 15 to 30 min, but it takes about 6 hrs to normalize coagulation. About 30 min is required to improve the neurotoxicity, but 24 to 48hrs is required for full recovery.⁷

In our study out of 144 patients ASV was used in 62 (43%) patients, maximum ASV was used in viper bite cases (88.9%). Reaction to antivenom is one of the challenges in treating snakebite cases. In our study reaction to ASV was seen in 22 (35.5%) cases, who recovered on treatment without any complication. A study done by Vinod D et al also found reaction to ASV in 31 (62%) patients which is higher when compared to our study.¹⁰

Acute reaction to antivenom may be due to type I (IgE-mediated) hypersensitivity, but reaction to ASV is also seen in patients who are not previously exposed to equine proteins.¹² The effect of immunoglobulin aggregates or immunoglobulin fragments, including Fc, which are even found in highly refined antivenoms, type I hypersensitivity, complement activation may be the reason for early reaction.¹⁹

According to the WHO Guidelines for the Production, Control and Regulation of Snake Antivenom Immunoglobulins published in 2010, adverse reactions are classified as: 1) early reactions (i.e. pyrogenic reactions and anaphylactic reactions), or 2) late reactions (i.e. serum sickness). Both IgE and non IgE mediated reactions together are considered to be "anaphylactic reaction", thus the word "anaphylactoid reaction" is eliminated.²⁰

Antivenom can be given as slow iv infusion rather than bolus injection to prevent rate of reaction.¹⁹

The factors like manufacturing practices, physicochemical characteristics of products, and intrinsic characteristics of heterologous immunoglobulins determine the safety profile of antivenoms.²⁰

Antibiotics are not recommended in the treatment of snakebite cases, but in our study antibiotics were used in almost all of the cases. Since patient used to come to hospital after first aid treatment because of which there was delay in time when the patient reached the hospital which can lead to infection at the bite site, antibiotics was prescribed to prevent the infection. First aid treatment was given in 50.7% of cases in our study. A study done by Chauhan S et al showed that 70 (49.3%) cases received first aid treatment prior to admission which is higher when compared to our study.²¹ Soft tissue infections are a major complication of snakebite with local envenomation. Extensive tissue destruction caused by the proteolytic property of snake venom leads to bacterial infection of the wound by snake's indigenous oral flora.²²

Since most of the population in rural area follow the traditional healer's treatment, lot of time is lost which may be fatal to patient, because time is very important since time lag leads to spread of venom in tissue leading to morbidity and mortality. The recommended first aid measure is to reassure the patient with snakebite, immobilize the bitten limb with splint or sling, and has to be transported to the nearby hospital for appropriate treatment. Walking is contraindicated since it can lead to muscular contraction which increases the absorption of venom.¹

Viperbite is one of the commonest poisonous snake bite seen in South Asian countries. Among the different species of viper, Russell's viper is the one which is commonly seen in paddy fields.²² Since this study was done in rural area of Karnataka where the major occupation of the population is agriculture, viper bite was commonly seen and maximum number of morbidity was seen with viper bite cases (84.3%).

The concept of big four poisonous snake is followed in India, though there are many other species of poisonous snakes which are unrecognised. There are no studies in support of these snakes, hence ASV which is one of the mainstay of treatment is not manufactured against these unrecognised snakes leading to ineffectiveness of ASV and fatality.

However effort is being made by the toxinological researchers to improve the safety, efficacy, affordability towards antivenoms. Access to new proteomics, gene sequencing and bioinformatics technology is adapted by the researchers to improve the management of snakebite cases.²³

Poor access to treatment, inappropriate first aid treatment, and vital time lost in transport and lack of education may be the leading cause of morbidity. Since snakebite leads to morbidity and mortality, it has socio-economic impact on poor population of rural area in terms of cost of treatment and the long-term effects on the health and ability of survivors to work. This can be reduced by improving the accessibility and affordability towards antivenom treatment.²⁴

CONCLUSION

Snakebite is a neglected tropical disease in rural area. Development of region specific, highly potent antivenom, & prospective evaluation of its safety & efficacy is needed. Attempt should be made to prepare venomous toxoid to immunize farmers and the population at risk against venomous snake toxins. The risk is increased by lack of information about simple measures of prevention, occupational hazard risks and inappropriate first-aid measures, hence educating the population at risk especially population in rural areas is of utmost importance. Improving the knowledge of both care-givers and rural community is crucial.

A national policy should be formulated and implemented to ensure prompt availability and effective use of ASV in rural areas of the country. Development of appropriate local guidelines & training of healthcare workers involved in the treatment of snake bite is equally important.

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