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Original Research Article

Use of anti-snake venom and clinical outcomes in snake envenomation: a prospective observational study

Shraddha M. Pore[1], Arvind V. Kumbhar[1], Ruchi D. Shah[1], Praveenkumar T. Patil[1]*, Sachin M. Patankar[2], Rohit N. Herekar[2], Sunita J. Ramanand[1]

[1]Department of Pharmacology, [2]Department of Medicine, Government Medical College, Miraj, Maharashtra, India

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***Correspondence to:**
Dr. Praveenkumar T. Patil, Email: drpraveentpatil@yahoo.in

ABSTRACT

Background: The only effective measure to prevent or reverse most of the manifestations of venomous snake-bite is timely administration of antisnake venom (ASV) with or without adjunctive treatment as necessary in each case. But recently several concerns have been raised with regard to use of polyvalent ASV. Hence the present study was conducted to assess use of ASV, early adverse reactions to ASV, adjunctive treatment and clinical outcomes in snake-bite patients, which would help to identify areas of problem and provide basis for planning strategies to increase rational use of drugs.

Methods: It was a prospective observational study approved by Institutional Ethics Committee. All indoor patients with systemic manifestations of snake envenomation were included in the study. All participants gave written informed consent. Data was obtained prospectively using a structured case record form. Descriptive statistics was used to express the results.

Results: Among 52 patients, snake-bite predominantly affected males (59.62%) than females (40.38%). The most common site of snake-bite was lower limb (65.38%). The main indication for ASV administration was vasculotoxic snake-bite (59.62%). Mean dose of ASV use was 18.21±15.51 vials. Mortality was seen in one patient. Majority of patients (28/52, 53.85%) received ASV in the range of 1-10 vials for the management of snake-bite.

Conclusions: The use and dose of ASV was appropriate in vasculotoxic snake-bite while few neurotoxic snake-bite patients needed higher than recommended dose.

Keywords: Adverse drug reactions, Anti snake venom, Prophylactic premedication, Snake bite, Systemic envenomation

INTRODUCTION

Snake-bite is an acute life- threatening, time limiting medical emergency and a major public health concern in India especially in rural areas. Direct estimates from a national mortality survey of 1.1 million homes by Mohapatra et al, show that there are about 45,900 annual snake-bite deaths nationally.[1]

The only effective measure to prevent or reverse most of the manifestations of venomous snake-bite is timely administration of antisnake venom (ASV) with or without adjunctive treatment as necessary in each case.[2] In India, polyvalent ASV produced by hyperimmunising horses against venoms of four common species of snake i.e. "Big Four" believed to be responsible for most deaths is widely used as precise identification of snake species is generally not possible. But recently several concerns have been raised with regard to use of polyvalent ASV. Given wide geographical and intraspecies variation in antigenicity of snake venoms and identification of other medically important snakes besides "Big Four" presently available ASV cannot be assumed to be uniformly effective especially in regions away from source of immunizing venoms.[3-10] Previous studies show that there is wide variation in management of snake-bite with respect to use of ASV, adjunctive treatment etc., although national snakebite management protocol and WHO guidelines for management of snakebite in South East

Asia are in place for quite long time.[11-17] Besides, limited availability and higher cost of ASV therapy are also well known.

With this background, we undertook the present study to assess use of ASV, early adverse reactions to ASV, adjunctive treatment and clinical outcomes in snakebite patients, since such data would help to identify areas of problem and provide basis for planning strategies to increase rational use of drugs.

METHODS

This prospective observational study was conducted at two tertiary care teaching hospitals affiliated to the same institute. The study was approved by institutional ethics committee. All participants gave written informed consent. All indoor patients irrespective of age and gender, showing systemic manifestations of snake envenomation were included in the study. Patients without systemic manifestations of snake envenomation, in whom adequate history could not be elicited due to problems such as language barrier and patients not willing to participate were excluded.

The protocol for management of patients with snakebites in these centers is as follows. All patients with suspected snakebite are admitted to ICU. They are monitored for at least 24 hours. ASV is administered to patients showing signs of systemic envenomation like clinically important coagulation abnormality or systemic effects such as ptosis or respiratory weakness. The initial and repeat doses are administered as clinically indicated. The ICU of these centers is equipped with ventilators and has facilities for haemodialysis.

The enrolled patients were observed from hospitalization to discharge or death. Information regarding demographics, type of snake-bite and its severity, details of ASV administration, pre medications, supportive treatment, occurrence of early adverse reactions to ASV and clinical outcomes etc. was obtained prospectively using a structured case record form.

Statistical analysis

Data was entered in Microsoft excel sheet. Descriptive statistics was used to express results about ASV use, early adverse reactions, premedication and clinical outcomes.

RESULTS

Data of 52 patients, satisfying inclusion and exclusion criteria, were available for analysis. Three patients received ASV without any apparent indication. These were excluded from analysis.

Mean age of the patient was 40.62±14.33 years. Snake-bite predominantly affected males (59.62%) than females (40.38%). The most common site of snake-bite was lower limb (65.38%). Mean length of hospital stay after snake bite was 4.73±3.41 days (Table 1).

The main indication for ASV was vasculotoxic snake-bite in 59.62% of cases followed by neurotoxic snake-bite in 38.46% of cases. Mean dose of ASV use was 18.21±15.51 vials. Mean time gap between snake-bite and first dose of ASV administration was 3.20±2.89 hours. Prophylactic medication, chlorpheniramine + hydrocortisone, was given in 26.92%. About 15.38% of patients experienced early reaction to ASV. Mortality was seen in one patient. Adjunctive treatment in the form of fresh frozen plasma, ventilatory support, debridement, dressing and oxygen supply was needed in (19/52, 36.53%) patients. 40.38% patients were given neostigmine + glycopyrrolate (Table 2).

From Figure 1, majority of patients (28/52, 53.85%) received ASV in the range of 1-10 vials for the management of snake-bite.

In the present study, none of the vasculotoxic snake-bite patients required >30 vials, whereas (5/20, 25%) neurotoxic snake-bite patients required >20 ASV vials for management (Figure 2 and 3).

DISCUSSION

Snake-bite and deaths due to snake envenomation has been identified as serious medical problem in rural India since pre-independence era.[3] In view of multiple issues raised with current ASV immunotherapy, region specific surveillance of ASV use and snake-bite management has assumed importance.[18] This prospective observational study of one year duration was aimed at assessing use of ASV, early adverse reactions to ASV, adjunctive treatment and clinical outcomes in two tertiary care government teaching hospitals.

Table 1: Demographic and other baseline characteristics of patients of snake bite (n=52).

Characteristics of patients		Value
Age (years)	Mean	40.62 (±14.33)
	Range	17-70
Gender	Male	31 (59.62%)
	Female	21 (40.38%)
Site of snake bite	Upper limb	15 (28.85%)
	Lower limb	34 (65.38%)
	Trunk	3 (5.77%)
Length of hospital stay (days)	Mean ± SD	4.73 (±3.41)
	Range	1-16

Demographic characteristics (Table 1) of study population shows, that snake-bite predominantly affects young males and lower limb was the most common site of bite. Vasculotoxic snake-bite was common than neurotoxic snake-bite and mean hospital stay was

4.73±3.41 days. Our findings are supported by several previous studies.[13,19,20] The mean time lag between bite and first dose of ASV was 3.20±2.89 hours, which was more or less similar to previous studies.[13,21]

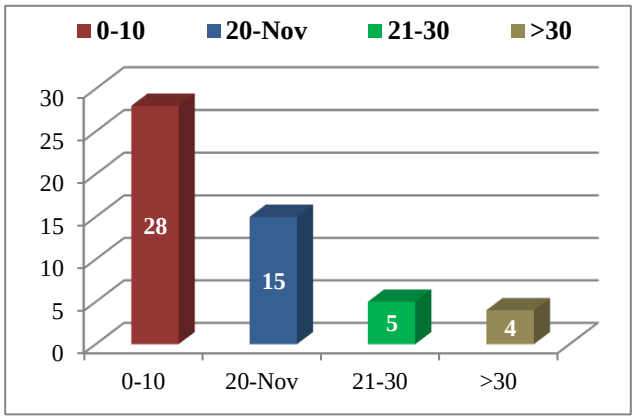

Figure 1: Frequency distribution of ASV vials used (n=52).

Mean dose of ASV in the present study was18.21±15.51 Vials. The frequency distribution (Figure 1) shows that majority of patients required ASV in the range of 1-10 vials.

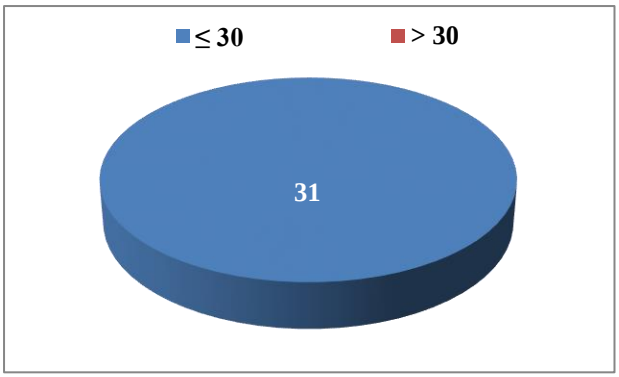

Figure 2: Number of vasculotoxic patients given recommended dose of ASV vials (n=31).

From Figure 2 and 3, all the vasculotoxic snake-bite patients (31) required ≤30 vials of ASV, while majority of neurotoxic snake-bite patients (15/20, 75%) required ≤20 vials. Based on the range of venom injected, the current Indian guidelines recommend maximum dose of 20 vials for neurotoxic and maximum dose of 30 vials for neurotoxic snake-bites.[2] But in the present study none of vasculotoxic snake-bite patient required >30 ASV vials, while about (5/20, 25%) neurotoxic snake-bite patients required >20 ASV vials. This finding may indicate low potency of ASV in some patients. Previous retrospective study conducted in these hospitals also documented high ASV use in about one-fourth of patients.[22] A hospital based prospective study by Saravu et al, showed an increase in dose of ASV with an increase in severity grade with corresponding delay in 'bite to needle time'.[13]

Some other studies have shown higher ASV dose for elapid bites or for viper bites.[20,23,24] In a recent study by Kakaria et al, reports timely institution of ventilatory support and fixed dose of 200ml of ASV along with anticholinesterase treatment to be sufficient even in severe elapid bites.[25]

Table 2: Indication, dose of ASV, premedication and clinical outcomes (n=52).

Characteristics		Value
Indications of ASV	Vasculotoxicity	31 (59.62%)
	Neurotoxicity	20 (38.46%)
	Neurotoxicity+ Vasculotoxicity	1(1.92%)
Dose of ASV (vials)	Mean±SD	18.21 (±15.51)
	Range	3-80
Time gap* (hours) between the snake bite and first dose of ASV administration	Mean±SD	3.2(±2.89)
	Range	0.5-17
Prophylactic premedication	Chlorpheniramine + Hydrocortisone	14 (26.92%)
	Only hydrocortisone	1(1.92%)
	Not given	37 (71.15%)
Reaction to ASV	Patients experiencing early reaction	8 (15.38%)
	Urticaria	3(5.77%)
	Anaphylaxis	2(3.85%)
	Giddiness	3(5.77%)
	Allergic reaction	2(3.85%)
Clinical outcome	Cured	35 (67.34%)
	Cellulitis	16 (30.77%)
	Death	1(1.92%)
Supportive treatment	Fresh frozen plasma	2(3.85%)
	Mechanical ventilation	4(7.69%)
	Dressing	11 (21.15%)
	Fasciotomy and debridement	1(1.92%)
	Oxygen by high flow mask	1(1.92%)
	Nil	33 (63.46%)
	Neostigmine+ Glycopyrolate	21 (40.38%)

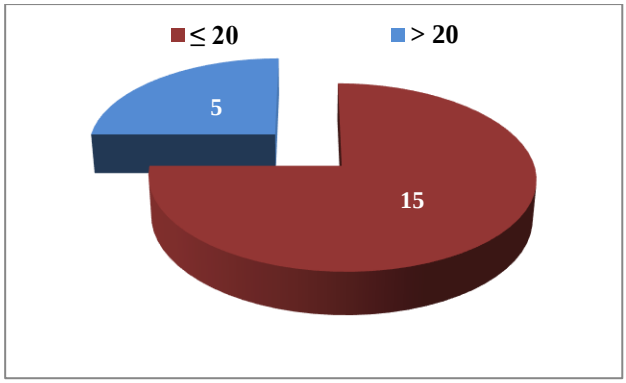

Figure 3: Number of neurotoxic patients given recommended dose of ASV vials (n=20).

About 15.38% of patients in the present study experienced early reaction to ASV (Table 2). All of these reactions were symptomatically treated and ASV therapy was completed successfully in all patients. This suggests that early reactions to ASV is not an important concern in ASV therapy, although occasionally serious ADRs to ASV or very high incidence of anaphylaxis have been reported with ASV therapy.[26,27]

Sensitivity testing or prophylactic premedication to prevent early hypersensitivity reactions to ASV is not recommended by National or International guidelines. But prophylactic premedication with hydrocortisone ± antihistaminic was used in 26.92% of patients in the present study. Mortality rate in the present study was 1.92%. Previous studies have reported variable mortality rates and increased mortality has been associated with severity of envenomation neurotoxic snake-bites and delayed ASV therapy.[13,19,20,22,28-31]

CONCLUSION

Thus in the present study, ASV dose and use was appropriate in the vasculotoxic snake-bites, while 25% of the neurotoxic snake-bite patients required more than 20 vials. Prophylactic medication to prevent early ADRs to ASV was used in about one-fourth of patients. These findings point towards need for development of appropriate hospital based protocol and training of physicians involved in management of snake-bite. Availability of region specific, highly potent antivenoms would also be highly desirable.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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