

Original article

Antisnake venom use: A retrospective analysis in a tertiary care centre

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Abstract:

Context: Treatment with antisnake venom (ASV) is life saving yet dangerous. ASV usage remains a very risky business. The incidence of early adverse reaction varies between 5-80%

Aims: The objectives were to evaluate the pattern of use of ASV in a tertiary care hospital and to study the immediate adverse effects following ASV use.

Settings and Design: The study setting was the Medical Record Library of the institution. This was a retrospective study.

Material and Methods: A retrospective analysis of medical records of snake bite cases admitted to the institution from January 1 2006-June 30 2006 was done. Data collection was done on a structured proforma. Descriptive analysis was used to express the result. Data was analyzed using Microsoft Excel worksheet 2007 and SPSS 16.

Results: A total of 88 case sheets were analyzed. 83(94%) of them received polyvalent ASV making a mean usage of 12.19 vials (Confidence Interval=10.19,

14.19). The incidence of adverse drug reaction to ASV was 23% (early anaphylaxis) which was slightly more in males', 26% as compared to that in females 16%. All were managed symptomatically and the ASV infusion was restarted after the patient became stable.

Conclusions: Snake bite is a medical emergency with the only proven specific antidote being ASV. Careful usage of antivenom with special concerns on the cost, dose and side effects calls for rational and appropriate use of antivenin and suggest that it should not be a routine adjunct in the management of envenomation.

Key words: antisnake venom, utility, tertiary care centre, allergic reactions

Introduction:

Envenomation by the snakes is a challenging medical emergency. Antisnake venom (ASV) is a specific, antidote to snake venom. Even though Indians were the the pioneers in the preparation of ASV there is no satisfactory data available regarding total amount of ASV required to

reverse the clinical effects of venom in a particular case.¹

Background: About five million snake bite cases occur worldwide every year with a mortality of 100,000 deaths of which half of the victims are in the India.² There are about 216 species of snakes identifiable in India of which 52 are poisonous.³ Snake venoms are not single toxins but a cocktail of many enzymes, polynucleotide toxins, non-toxic proteins, carbohydrates, metals, lipids, free amino acids, nucleotides and biogenic amines.⁴ Venoms are classified into hemotoxic, neurotoxic, cardiotoxic, myotoxic and those that cause local toxicity. The SEAR guidelines⁵ states that ASV should not be used without evidence of systemic envenomation or severe local swelling.

Rationale

ASV treatment is life saving yet dangerous. In India only polyvalent serum is available which is used as an antidote to venoms of all the snakes. There is considerable irrationality in the usage of ASV probably due to fear, lack of experience and improper training. Sometimes it is administered in non indicated cases and avoided in indicated case due to fear of anaphylaxis. ASV usage not only neutralizes the venom and avoids the toxic progression of it but also increases the patient comfort .It is the cost and the allergic manifestation of ASV that has become consideration. ASV usage remains a very risky business the incidence of early adverse reaction varies between 5-80% .⁶ This study was initiated to study the pattern of use antisnake venom in Medical

College Hospital .The objectives were to evaluate the pattern of use of ASV in a tertiary care hospital and to study the immediate adverse effects following ASV use.

Subjects and Methods

The study setting was the Medical Record Library of the institution. This was a descriptive study. Approval was obtained from the research committee and institutional ethics committee. A retrospective analysis of medical records of snake bite cases admitted to the institution traced using the International Classification of Disease code-10 (T-63) from January 1 to June 30, 2006 was done. All cases with documented diagnosis of snake bite were included. Data collection was done on a structured proforma approved by the Ethics committee. It contained demographic details, location of the bite, type of snake, details of use of antisnake venom, any anaphylaxis to ASV and management with other supportive measures. All statistical testing was 2 sided with significance level of 5%. Descriptive analysis was used to express the result. Data was analyzed using Microsoft Excel worksheet 2007 and SPSS 16.

Results:

A total of 88 case records were analyzed. Majority of the patients were in the age group of 31-45 years with a mean age of 37.7 years. The male: female ratio was 2.4:1. Hemotoxic envenomation was seen in 76% of which 63% had severe bleeding manifestations. Renal failure occurred in

34% of which 60% underwent dialysis. Neurotoxicity was seen in 17% and all developed ptosis. Local reaction alone was seen in only 6 patients. The mortality rate was 1%. There was only a single death which was attributed to severe hemotoxic envenomation. 94% patients received ASV. All the patients received tetanus toxoid also. Antibiotic coverage was given in 93% and other supportive measures like atropine and neostigmine, blood transfusion, and dialysis was also given.

83(94%) received polyvalent ASV. A total of 1012 vials of ASV were used in 83 patients making a mean usage of 12.19 vials (Confidence Interval=10.19, 14.19). Minimum dose of ASV used was 2 and maximum dose was 35 vials. 10 vials were the most frequently administered dose (in 42.68%).

The preparation used was lyophilized powder which was reconstituted and given as intravenous infusion in 5% dextrose/NS. None received test dose and in none ASV was given locally.

The incidence of adverse drug reaction to ASV was 23%. Among the males the incidence was slightly more 26% as compared to that in females 16%. The mean age was 31 years.

All the 19 patients who developed the adverse effect developed early anaphylaxis. Majority (63.16%) developed Type II-pyrogenic reactions with itching, chills and rigor. There were a few cases (6) of Type I reaction with urticaria and rash and 1 patient developed bronchospasm. All the

allergic reactions were managed with pheniramine maleate and methylprednisolone after stopping the ASV infusion. After 15-30 minutes the infusion was restarted at a rate in which the patient tolerated. None of the patients got premedication with adrenaline or pheniramine and methylprednisolone. Late serum sickness could not be identified as there was no further follow up.

Antibiotics were used commonly as combination therapy, commonest being that of ampicillin and cloxacillin; cloxacillin was the single most commonly used antibiotic. The other main classes of antibiotics used were cephalosporins, metronidazole and mupirocin.

Neurotoxic bites were managed with atropine and neostigmine. Hemotoxic bites were given whole blood, fresh frozen plasma and platelet concentrates.

Discussion:

Snake bite is a medical emergency with the only proven specific antidote being ASV. Polyvalent antsnake venom in India is a valuable antidote to snake venom action. While the absolute cost of antivenin is high, this may be less than the cost of management without antivenin. ASV usage remains a cautious and brave step with the incidence of early adverse reaction varying between 5-80%.⁶

The incidence of snake bite and anaphylactic reactions were both common in males and this might be due to the fact

that males travel more at night rather than females. This study focused on the pattern of antsnake venom usage and the adverse reactions linked to it. 94% patients received polyvalent ASV. Even if monovalent ASV would have been available we could use it only if we could specifically identify the species of the snake which is seldom possible because of the wide variety of snakes found in India. The fact that clinical manifestations dictate the treatment with the possibility of any patient developing more than one toxicity also justifies the usage of polyvalent ASV.⁷

In this study six patients had local envenomation and 82 patients had systemic envenomation. Of the six patients with local toxicity one had severe local swelling and received antivenom. The SEAR guidelines⁵ says that ASV should not be used without evidence of systemic envenomation or severe local swelling. The systemic envenomation should be evident from 20 minute Whole Blood Clotting Time (WBCT), signs of spontaneous visual recognition of neurological impairment as ptosis and severe local swelling evident from swelling rapidly crossing a joint/involving half the bitten limb in the absence of tourniquet. Purely local swelling is not a ground for administering ASV. This shows that antsnake venom was given only in indicated cases in our institution.

Wing et al⁸ states that one has to give enough ASV to neutralize all the effects of venom with whatever dose required, average of 15(maximum 48 and minimum 4).

In India polyvalent ASV is available which contain antibody against cobra, Russell's viper, common krait and saw scaled viper. It is found that the fatal dose of cobra venom is 120 mg, krait 60 mg, Russell's viper 150 mg and Echis 80 mg of venom. About 0.6 mg of cobra venom, 0.6 mg of Russell's viper, Krait 0.45 mg and 0.45 mg of Echis can be neutralized by 1 ml of polyvalent ASV and hence the ASV required empirically is 200, 250, 134 and 10.22 ml. for cobra, Russell viper, krait and saw scaled viper respectively.⁹ This justifies the dose of ASV used in our institution.

There are 2 methods of administration of ASV.¹⁰ One is to administer antivenom as intravenous (IV) push injection which is economical; saving the use of intravenous fluid, IV sets and cannulae. This method has the advantage that the dispenser giving the antivenom must remain with the patient during the time when some early reactions may develop. Another method is to give it as an IV infusion of the reconstituted freeze dried or neat liquid antivenom. The intravenous fluid should be normal saline in the case of cobra, krait and saw scaled viper and dextrose/dextrose normal saline in case of Russell's viper. ASV should be administered over 1 hour or as rapidly as tolerated over 1-2 hours⁵. In this study all the patients received reconstituted ASV as intravenous infusion as rapidly as tolerated by the patient.

Published research reveals that ASV test doses have been abandoned. They have no predictive value in anaphylaxis or late serum reactions and may pre-sensitize the patient to the problem.¹¹ In this study also

none of the patients who received ASV had prior testing for hypersensitivity.

Out of the 83 patients who received ASV, 19 developed anaphylaxis of which type II pyrogenic reactions accounted for the majority. The incidence of type I reaction was much less compared to that of type II reactions. Since the study was done retrospectively the data regarding the development of delayed anaphylaxis could not be determined.

ASV available for use has escaped the mandatory stringent clinical trials. ASV reactions are more linked to the manufacturer of ASV than the nature of venom. Various studies have reported the incidence of adverse reactions between 5-80%.^{6,12,13} Scott et al¹⁴ found that no allergic reactions to antivenin crotalidae polyvalent (ACP) while Cannon et al¹⁵ found reactions in 5.4% of their patients William et al¹² reported that adverse reactions to ASV were significantly lower with adrenaline premedication.

The incidence of adverse reactions in this study was comparable to that obtained in other studies. None of the patients received premedication with adrenaline.^{12, 16} This can be justified by the fact that adrenaline is a life saving drug for the treatment anaphylaxis and need not be given to all the patients in the fear that anaphylaxis may occur. Genetically engineered preparation will solve this problem of anaphylaxis. Anaphylaxis is not an indication to withhold

or stop ASV. Even if anaphylaxis develops, there is no other alternative variable. One has to give ASV under cover.¹⁰

All the patients received tetanus toxoid irrespective of their immunization status and though the usage of antibiotics is controversial^{17, 18, 19} in the Indian set up antibiotic usage is essential so as to prevent secondary infections

The main limitations of our study were the retrospective nature of data collection which would underestimated the incidence of acute hypersensitivity reactions. The occurrence of serum sickness could not be determined as follow up data was unavailable. No standard grading scale was used to assess envenomation, making to difficult to compare outcomes Species of snake and victims first hand description identifying the snake was seldom documented.

Conclusion

Antisnake venom which is a life saving weapon is the only proven antidote but it's a double edged sword because of the allergic reactions associated with it. 94% patients studied received ASV of which 23% developed allergic reactions. There was no fixed dose as the individualized doses were titrated according to patients symptoms. Careful usage of ASV with special concerns on the cost, dose and side effects are essential in the routine management of snake envenomation.

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