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Adverse Reaction Profile Following Ant-snake Venom Administration in Snakebite in a Tertiary Care Hospital: A Retrospective Cross-sectional Study

Girish Narayan[1], Sharath Krishnaswami[2], Shakuntala Kandikuppa Murty[4]

Author's Affiliation:
[1]Associate Professor, [3]Professor & HOD, Department of Emergency Medicine, St. John's Medical College, Koramangala, Bengaluru, Karnataka 560034, India. [2]Senior resident, Department of Anaesthesiology, Sakra World Hospital, Marathahalli, Bengaluru, Karnataka 560103, India.

Corresponding Author:
Girish Narayan, Associate Professor, Department of Emergency Medicine, St. John's Medical College, Koramangala, Bengaluru, Karnataka 560034, India.

E-mail: girishn.md@gmail.com

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Abstract

Introduction: Anti-snake venom therapy for snakebite envenomation is as associated with adverse drug reactions. The spectrum of reactions that are seen are wide and inconsistent. Given the annual incidence of snakebites at 2.7 million, and the frequent administration of anti-snake venom, an awareness of types of these reactions is required. *Aims:* To describe the adverse reactions seen during anti-snake venom therapy and treatment options used. *Settings and design:* Retrospective cross-sectional design in a Tertiary care Hospital. *Methods:* For a period of two years from January 1st, 2010 to December 31st, 2011 all cases diagnosed to have ani-snake venom reactions were identified retrospectively. Following identification, case record review was undertaken to collect data regarding the demographics, envenomation, characteristics of the reaction and treatment employed. *Statistical analysis used*: Descriptive statistics for demographic features of age and sex were obtained. Age was analyzed as a continuous variable and further categorization was done. Proportions of type of envenomation, ADRs and post-reaction medication were also calculated. *Results:* Forty-one cases were identified to be included in the study population. The mean age was 33 ± 13.3 years. Urticaria, chills, dyspnea/bronchospasm, tachycardia, bradycardia and hypotension were seen in 48.8%, 19.5%, 17.1%, 39%, 19.5% and 51.2% of the population respectively. 34.2% of reactions were treated with a combination of pheniramine, hydrocortisone and epinephrine. *Conclusions:* The results suggest that there is wide range of possible adverse reactions when anti-snake venom is given. Hypotension is a frequent life-threatening event and should be watched for. Though therapy is similar in other studies there are no clear guidelines for the same. Premedication needs to be evaluated further.

Keywords: Adverse drug reactions; Anti-snake venom; Snakebite; envenomation.

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Introduction

Snakebite envenomation is a typical medical emergency encountered in India. Worldwide the World Health Organization estimates an incidence of 2.7 million per year with a mortality rate ranging from 81,000 to 1,38,000 particularly affecting low- and middle-income countries (LMICs).[1] Annually in India, approximately 2,50,000 bites occur, and 46,000 deaths are attributed to this cause.[2,3] The treatment

of envenomation is dependent on judicious use of ant-snake venom (ASV). Equine sourced ASV that neutralizes the venom of the "Big-four" venomous species of snakes usually responsible for cases in the country. They are Bungarus caeruleus (Indian common krait), Daboi russelli (Russell's viper), Echis carinatus (Saw-scaled viper) and Najanaja (Indian cobra).[3] Adverse drug reactions (ADRs) to equine proteins are well known to occur during ASV administration. These ADRs extend from mild (urticaria, nausea and vomiting) to the severe (hypotension and bronchospasm). Proportions of ADR are vary from 43 to 81%. Reports indicate that 15–40% of ADRs may be severe and life-threatening.[4]

Detecting ADR's during ASV administration can be challenging in the emergency department. Considering the full-range of potential scenarios of reactions, we undertook this study to describe the various ADRs seen during ASV therapy in a tertiary care emergency department.

Materials and Methods

A retrospective cross-sectional study was undertaken in the Department of Emergency Medicine at a tertiary care hospital in a major urban city. A total of 41 patients identified to have ADR's when receiving ASV were included as the study population. Data were collected from case sheets. The study period was from January 1st, 2010 to December 31st, 2011. The ED case register was used to identify ASV ADR cases. Subsequently case records were reviewed to confirm the occurrence of urticaria, chills, tachycardia, bradycardia, dyspnea/bronchospasm or hypotension during intravenous ASV delivery and that the treating doctor had diagnosed these features as ADR. These patients were considered as cases for the study population. Demographic data regarding age and sex were extracted from the case sheets. Clinical information regarding the type of envenomation, characteristics of ADR and post-reaction therapy was also collected.

The Institutional Ethics Review board approved the study before data collection for the study commenced.

Statistical analysis

Descriptive statistics for the demographic features of age and sex were obtained. Age was analyaed as a continuous variable mean and spread were estimated. Subsequently age was further categorized into three groups <20 years, 21–40 years and >41 years. Proportions of type of envenomation, ADRs and post-reaction medication were also calculated. Stata version 14.2 was used for statistical analysis.

Results

A total of 41 ASV ADR cases were identified in the study period. The mean age of the study population was 33 ± 13.3 years, with the youngest and oldest at 14 and 65 years respectively. 23 (56.1%) of the study population was between the ages of 21 and 40 (Table 1).

Table 1: Distribution of age and sex among ant-snake venom ADR cases

Variable	Frequency	Percentage
Age		
<20 years	7	17.1
21–40 years	23	56.1
>40 years	11	26.8
Sex		
Male	28	68.3
Female	13	31.1
Total	41	100

Table 2: Distribution of envenomation among ant-snake venom ADR cases

Envenomation	Frequency	Percentage
Neurotoxic	10	24.4
Hematotoxic	21	51.2
Local	4	9.8
Mixed	6	14.6
Total	41	100

The predominant sex was male at 28 (68.3%) with females at 13 (31.3%). ASV was initiated most often for hematotoxic envenomation, seen in 51.2% (21) of cases in which ADR developed (Table 2). Neurotoxic, local and mixed envenomation was seen in 10, 4 and 6 patients of the study population, respectively.

The clinical features of the ADRs seen were variable (Table 3). Mild features of urticaria and chills were observed in 48.8% and 19.5% of the patients, respectively. 21 (51.2%) patients of those diagnoses as ASV ADRs presented with hypotension. However, tachycardia was seen only in 16 patients; conversely, bradycardia was seen in 8 patients. Majority 97.4% of patients had more than one feature of a reaction present in them. The therapeutic strategies to deal with the ADRs were as varied as the presentation (Table 4). In 6 of the study population, ASV was completely discontinued. Twelve patients received only one drug to treat the ADR. They received either Pheniramine, Hydrocortisone or Epinephrine. 14 (34.2%) of the cases identify with ASV ADRs were given Pheniramine, Hydrocortisone and Epinephrine. 21.9% of the sample received any two of the three above-mentioned drugs. In the study population, there was one recorded death, and four patients were ventilated for respiratory failure.

Table 3: Characteristics of ant-snake venom ADRs

Characteristics	Present *n* (%)	Absent *n* (%)	Total
Urticaria	20 (48.8)	21 (51.2)	41 (100)
Chills	8 (19.5)	33 (80.5)	
Dyspnea/Bronchospasm	7 (17.1)	34 (82.9)	
Tachycardia	16 (39)	25 (61)	
Bradycardia	8 (19.5)	33 (80.5)	
Hypotension	21 (51.2)	20 (48.8)	

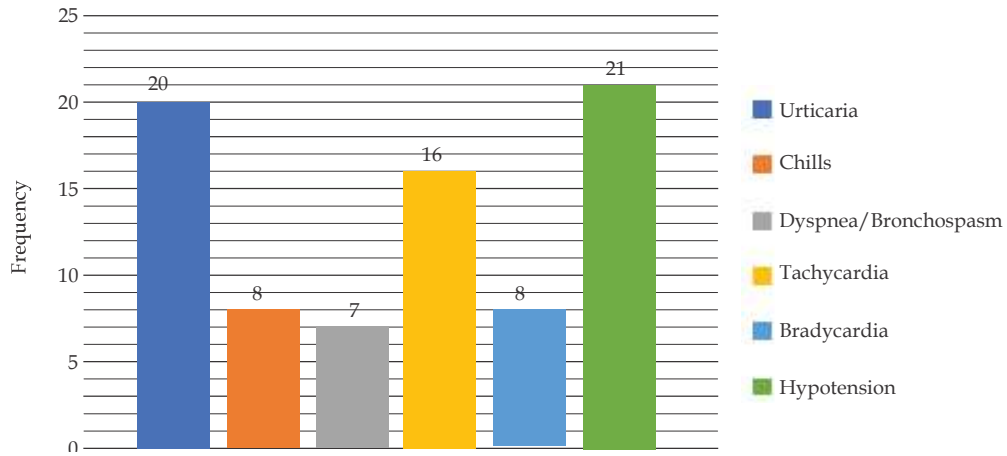

Fig. 1: Frequencies of various ADRs seen in the study population.

Table 4: Therapeutic interventions in ant-snake venom ADRs

Interventions	Frequency	Percentage
Stopping ASV	6	14.6
Pheniramine	4	9.8
Hydrocortisone	5	12.2
Epinephrine	3	7.3
Pheniramine + Hydrocortisone + Epinephrine	14	34.2
Pheniramine + Hydrocortisone	8	19.5
Hydrocortisone+ Epinephrine	1	2.4
Total	41	100

Discussion

Our study highlights the range of possible presentations when ASV reactions do occur. Though urticaria and chills were quite common in our population, similar studies in Maharashtra suggests these features occur less often at around 1–5%.[3,5] An ADR profile from Papua New Guinea suggests that hypotension occurrence was only one in twenty-five patients studies compared to our results it was much lower.[6] Comparable snakebite envenomation ADR profiles from within the country also suggest that hypotension is less frequent at 12.5%, contrasting to our numbers.[3,5,7] One possible explanation for this is that the dosage of ASV given may have been different in both these study groups. Research also indicates that the treatment strategies of ADRs vary with the severity of the reaction. Clinicians use a combination of steroids and antihistamines usually, with epinephrine being reserved for severe reaction and when hypotension is present. Some studies advocate the use of premedication with steroids, antihistamines or epinephrine; however, this evidence is not based on controlled trials and dosage of premedication is not uniform or standardized.[4,8]

Our study has several limitations. The first being that that 41 patients may not be representative of all ADR cases. Selection bias in the study sample was possible as inaccurate recording in the emergency register, as well as patients who did not agree on admission and were discharged before developing ADRs, would have led to non-recruitment causing selection bias. As details regarding ADRs and therapy provided were recorded for case records, the possibility of information bias when recording clinical data has to be considered. As patients who did not develop ADRs were not included in the study, no inference can be made regarding the risk of ADRs when patients were given ASV.

Conclusion

In view of the wide spectrum of ADRs seen when ASV is given, it would be prudent for clinicians to aware of these effects. Treatment options have to be standardized, and recommendations should be developed to prevent inaccurate treatment. ASV administration should be as per guidelines to prevent indiscriminate use and possible occurrence of ADRs. The one area of research which is warranted is regarding the use of premedication when giving ASV. Further evaluation of drugs and appropriate dosages needs to be evaluated before drawing a conclusion on their benefits.

References

1. Williams DJ, Faiz MA, Abela-Ridder B, et al. Strategy for a globally coordinated response to a priority neglected tropical disease: Snakebite envenoming. PLOS Neglected Tropical Diseases 2019;13(2):e0007059.
2. Gutiérrez JM, Calvete JJ, Habib AG, Harrison RA, Williams DJ, Warrell DA. Snakebite envenoming [published correction appears in Nat Rev Dis Primers. 2017 Oct 05;3:17079]. Nat Rev Dis Primers. 2017;3:17063.
3. Deshpande RP, Motghare VM, Padwal SL, et al. Adverse drug reaction profile of anti-snake venom in a rural tertiary care teaching hospital. J Young Pharm 2013;5(2):41–5.
4. De Silva HA, Pathmeswaran A, Ranasinha CD, et al. Low-dose adrenaline, promethazine, and hydrocortisone in the prevention of acute adverse reactions to antivenom following snakebite: A randomised, double-blind, placebo-controlled trial. PLoS Med 2011;8(5):e1000435.
5. Pore SM, Ramanand SJ, Patil PT, et al. A retrospective study of use of polyvalent anti-snake venom and risk factors for mortality from snake bite in a tertiary care setting. Indian J Pharmacol 2015;47(3):270–74.
6. Williams DJ, Jensen SD, Nimorakiotakis B, et al. Antivenom use, premedication and early adverse reactions in the management of snake bites in rural Papua New Guinea. Toxicon 2007;49(6):780–92.
7. Ryan NM, Kearney RT, Brown SG, et al. Incidence of serum sickness after the administration of Australian snake antivenom (ASP-22). Clin Toxicol (Phila) 2016;54(1):27–33.
8. Premawardhena AP, de Silva CE, Fonseka MM, et al. Low dose subcutaneous adrenaline to prevent acute adverse reactions to antivenom serum in people bitten by snakes: randomised, placebo-controlled trial. BMJ 1999;318(7190):1041–3.