

Anaphylactic Reactions After Administration of Anti Snake Venom for Envenomation: A Case Series**Mer RJ¹, Kakasaniya GG², Mehta DS³**¹Senior Resident, Department of Pharmacology, C. U. Shah Medical College, Surendranagar -363001, Gujarat, India²Senior Resident, Department of Pharmacology, GMERS Medical College, Morbi -363641, Gujarat, India³Professor & Head, Department of Pharmacology, Swaminarayan Institute of Medical Sciences and Reserach, Kalol, Gandhinagar -382725, Gujarat, India

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Abstract:**Introduction:** ASV and its rational use is the only definitive treatment to neutralize venom in circulation and in tissue fluid to save life in snake bite cases. Usually more than 20% cases develop either early (within few hours) or late (5 days or more) allergic reactions following ASV administration.**Objective:** To assess their causality according to WHO-UMC classification.**Methodology:** An interpretive observational primary study was conducted regarding anaphylactic reactions after administration of ASV after getting approval from institutional ethics committee. Available case records of anaphylactic reactions developed after administration of ASV were collected and analysed.**Results:** Total 4 cases of anaphylactic reactions were available. one patient developed itching, rashes over forearm and body area and another patient developed urticaria on both arms and axillary region after administration of ASV, third and fourth patient have developed urticaria, redness on forarms and abdominal area and also abdominal pain respectively. And in the first and third case rechallange of ASV was done so causality is certain while in second and fourth case rechallange was not so causality is probable.**Conclusion:** Patient and physician's awareness regarding adverse drug reactions(ADR) could possibly help in lowering incidence of such severe ADR.**Keywords:** Anti-snake venom(ASV), Envenoming, Anaphylactic Reactions.

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Introduction

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions (ADRs) Recently, its concerns have been widened to include herbals, traditional and complimentary medicines, blood products, biological, medical devices, and vaccines. The pharmacovigilance program of India was initiated with a goal to ensure that the benefits of use of medicine outweigh the risks and thus safeguard the health of the Indian population. It has an objective of monitoring the safety of the drugs and creation of ADR database for the Indian population.[1]

Snake bite is a common, neglected and frequently devastating environmental and occupational disease, especially in rural areas of tropical developing countries. It is a major public health problem in India with estimated annual snake bite incidence of about 2,50,000 out of which approximately 20% bites result in significant

envenoming which require anti-snake venom (ASV) administration. It is estimated that between 35,000 and 50,000 people die of snakebite in India each year.[2] Anti-venom is an immunoglobulin (Ig) usually pepsin refined F (ab)₂ fragments of IgG purified from the serum or the plasma of a horse or sheep that has been immunized with the venom of one or more species of snakes. In India, only polyvalent ASV is available. The anti-venins are produced against 4 most important venomous snakes of India Najanaja (Indian Cobra); Bungarus caeruleus (Indian common krait); Daboia russelii (Russell's viper); and Echiscarinatus (Saw-scaled viper). Each milliliter of polyvalent ASV produced in India neutralizes 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.[3,4]

Anti-snake venom (ASV) and its rational use is the only definitive treatment to neutralize venom in

circulation and in tissue fluid to save life in snake bite cases. Usually more than 20% cases develop either early (within few hours) or late (5 days or more) allergic reactions following ASV administration.[5] Considering the anaphylaxis after administration of ASV for envenomation thus the present study was planned to study safety profile of anti-snake venom, to collect case reports of anaphylactic reactions after anti snake venom administration for envenomation. and to assess their causality according to WHO-UMC classification.[6]

Material and Methods

Retrolective observational primary study was conducted at C.U. Shah Medical College and Hospital regarding allergic reactions after administration of ASV after getting approval from Institutional Ethics Committee [IEC(HR)/PUB-22/2023]. 4 case records of anaphylactic reactions were available after envenomation of ASV. 1st case, occurred on 01/11/2020, 2nd case occurred on 24/06/2021, 3rd and 4th cases occurred on 06/10/2021 and 08/10/2021 respectively. Data were collected and Interpretations were drawn out from that data and causality assessment was done according to WHO-UMC classification.

Case series

Case 1:

- A 35 years old male patient presented to emergency department of tertiary care teaching hospital with history of anaphylaxis reactions developed due to anti snake venom as patient was given anti snake venom at another hospital for snake bite. The vital signs of patient were normal. General and systemic examination was performed.
- To resolve this reactions patient was given Injection Avil (Pheniramine) and Injection Dexona (Dexamethasone) through IV Route, and patient reactions were resolved. As patient was having history of snake bite so, patient was administered IV snake venom anti serum (lyophilized) diluted in 500ml of DNS and rate of administration is 80ml/hr
- After 30mins of administration of IV snake venom anti serum (lyophilized) patient developed skin lesions with itching on face, forearms, arms, chest and abdomen area, skin lesions were multiple erythematous blanchable (figure 1). To resolve this reactions patient was given Injection Avil (Pheniramine) and Injection Dexona (Dexamethasone) through IV Route and patient reactions were resolved.
- So, through this we can suspect that after rechallenging with snake venom anti serum patient had developed reactions.
- Causality: Certain

Case 2:

- A 37 years old female patient presented to emergency department of tertiary care teaching hospital with history of snake bite around 6:00 am on 26/06/2021. On presentation patient's vital parameters were normal. A general and systemic examination was performed. Patient was given IV snake venom anti serum (lyophilized) diluted in 500ml of DNS and rate of administration is 80ml/hr.
- Soon after administration of snake venom anti serum (lyophilized) patient developed urticaria on both arms (figure 3), back and axillary region with Gabharaman. To resolve this reactions patient was given Injection Avil (Pheniramine) and Injection Dexona (Dexamethasone) through IV Route. After administration of Injection Avil and Injection Dexona patient reactions were subsided.
- Causality: Probable

Case 3:

- A 37 years old male patient presented to emergency department of tertiary care teaching hospital with history of snake bite around 4:00 am on 06/10/2021. Patient developed giddiness, drowsiness and heaviness of eyes after snake bite, so patient was given IV snake venom anti serum (lyophilized) diluted in 500ml of DNS and rate of administration is 80ml/hr.
- Soon after administration of snake venom anti serum (lyophilized) patient developed urticaria and redness on both forearms and abdominal area (figure 4). To resolve this reactions patient was given Injection Avil (Pheniramine) and Injection Hydrocort (100) (Hydrocortisone) through IV Route. After administration of Injection Avil (Pheniramine) and Injection Hydrocort (100) (Hydrocortisone) patient reactions were subsided.
- Patient was administered anti snake venom, and again patient developed similar reactions so we can suspect that after rechallenging of antisnake venom patient had developed reactions.
- Causality: Certain.

Case 4:

- A 15 years old female patient presented to emergency department of tertiary care teaching hospital with history of snake bite around 2:30 pm on 08/10/2021. Patient developed burning sensation overbite area, ptosis and uneasiness. So patient was given IV Snake antivenin diluted in 500ml of DNS and rate of administration is 80ml/hr.
- Soon after administration of Snake antivenin patient developed redness and urticaria over face and both forearms and she also

complained about abdominal pain. To resolve this reactions patient was given Injection Avil (Pheniramine) and Injection Dexona (Dexamethasone) through IV Route. After administration of Injection Avil (Pheniramine)

and Injection Dexona (Dexamethasone)patient reactions were subsided.

☐ Causality: Probable.

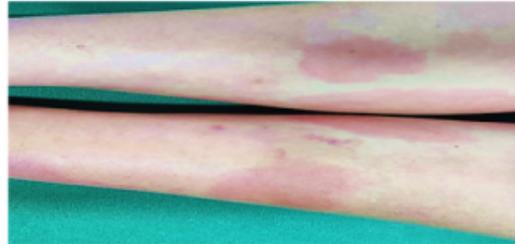


Figure 1:



Figure 2:



Figure 3:



Figure 4:

Discussion

WHO added snakebite envenoming to its priority list of neglected tropical diseases (NTDs) in June

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2017. A nationally representative study (Million Death study) noted--45,900 annual snakebite deaths nationally. In India, around 90% of snakebites are

caused by the 'big four' among the crawlers - common krait, Indian cobra, Russell's viper and saw scaled viper. Effective interventions involving education and antivenom provision would reduce snakebite deaths in India.[7]

Snake antivenoms are effective treatments to prevent or reverse most of the harmful effects of snakebite envenoming. They are included in the WHO Essential Medicines List and should be part of any primary health-care package where snake bites occur.[7]

ASV is the only available antidote for snake bite treatment. In India Polyvalent ASV is used. Monovalent ASV cannot be used as there are no specific means to identify the snake species.[8]

In the present case series, we reported anaphylactic reactions in patients due to polyvalent ASV, All the patients were treated with the recommended dose of lyophilized polyvalent snake venom antiserum refined equine serum. The 10 ml vial of polyvalent ASV contains Indian Cobra 0.60mg, Common Krait 0.45mg, Russell's viper 0.60mg, Saw Scaled Viper 0.45mg. which is comparable with the Prajapati H et al.[8]

Causality assessment was done by using WHO-UMC Causality Scale. The causality assessment shows that out of 4 cases 2(50%) were certain and 2(50%) were probable. This results are comparable with the Prajapati H et al.[8]

The most common reactions were urticaria, skin lesions, giddiness and drowsiness. Which were resolved by using antihistaminic and corticosteroids. Which were comparable with studies done by Premawardhena AP et al.[9], Gawarammana IB et al.[10] and de Silve et al.[11]

In present study, the severity of the reactions were mild to moderate and were early anaphylactic reaction occurred in the duration of the 10-180 minutes of starting ASV. Which are similar with the study done by Deshmukh VS et al.[12]

Conclusion

According to WHO-UMC Classification of causality, in first and third case rechallange of ASV was done so causality is certain while in second and fourth case rechallange was not done so causality is probable.

Patient and physician's awareness regarding adverse drug reactions (ADR) could possibly help in lowering incidence of such severe ADR.

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References

1. Adithan C. National Pharmacovigilance Programme. Indian J Pharmacol. 2005; 37:347.
2. Wardell DA. WHO/SEARO Guidelines for the Clinical Management of snake bite in Southeast Asia Region. Southeast Asian J Trop Med Public Health 1999;30(1):1-85.
3. Deoras PJ. Snake in India: National Book Trust India. New Delhi: National Book Trust, India; 1965. p. 33.
4. Tun Pe, Khin Aung Cho. Amount of venom injected by Russell's viper (*Viperarusselli*). Toxicon 1986;24(7):730-3.
5. 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):41-45.
6. The use of the WHO-UMC system for Standardised Case Causality Assessment [Internet]. [cited 2023 Aug 28]. Available from: <https://www.who.int/docs/default-source/medicines/pharmacovigilance/whocausality-assessment.pdf>.
7. Snakebite envenoming india [Internet]. World Health Organization; [cited 2023 Aug 29].
8. Prajapati H, Kansal D. Polyvalent Anti Snake Venom: Adverse drug reactions in children. International Journal of Comprehensive and Advanced Pharmacology [Internet]. 2017 Apr [cited 2023 Aug 29];02(02):66-7.
9. Premawardhena AP, de Silva CE, Fonseka MM, Gunatilake SB, de Silva HJ. Low dose subcutaneous adrenaline to prevent acute adverse reactions to antivenom serum in people bitten by snakes: randomised, placebo-controlled trial. BMJ. 1999; 318:1041e1043.
10. Gawarammana IB, Kularatne SA, Dissanayake WP, Kumarasiri RP, Senanayake N, Ariyasena H. Parallel infusion of hydrocortisone chlorpheniramine bolus injection to prevent acute adverse reactions to antivenom for snakebites.
11. de Silva HA, Pathmeswaran A, Jayamanne S, et al. Prevention of acute adverse reactions to snake antivenom after snakebite: multi-centre, randomized, controlled clinical trial. PLoS Med. 2011;8: e1000435.
12. Deshmukh VS, Motghare VM, Gajbhiye D, Sv B, Deshpande R, Pise H, Jaykare S. Study on Acute Adverse Drug Reactions of Antisnake Venom In A Rural Tertiary Care Hospital. Asian J Pharm Clin Res [Internet]. 2014 Nov. 1 [Cited 2023 Aug. 29];7(5):13-5.