Polyvalent Anti Snake Venom: Adverse drug reactions in children

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Abstract

Snakebite is one of the important causes of mortality in our country. Anti-snake venom (ASV) is administered in the management of snake bite. In India polyvalent ASV is used. There is risk of anaphylactic reaction. It should be used cautiously with regard to its dose and adverse reactions. We are reporting few cases of adverse drug reaction due to ASV particularly in children.

Keywords: Anaphylactic Shock, Adverse drug reactions, Polyvalent ASV

Introduction

Snake bite is a major public health problem in India. It is a very common health hazard, especially in rural areas of Himachal Pradesh. It is estimated that in India, the annual snake bite incidence is about 250,000 and out of which approximately 20% bites result in significant envenoming which requires ASV administration.(1) It is estimated that between 35,000-50,000 people die of snake bite in India each year.(2) ASV is composed of antibodies derived from immunized animals; hence, the use of heterologous proteins for human treatment involves the possibility of adverse reactions due to the activation of the immune system. The ASV is highly effective, but likely to cause severe adverse reactions. Adverse effects may range from mild symptoms like shivering, nausea and fever to serious problems such as bronchospasm and anaphylactic shock, even when the most refined ASV is administered.(3) In the present case series we are presenting some cases of adverse reactions in children due to polyvalent ASV administration including fatal cases reported in our tertiary care hospital.

Case Histories

Case 1: 7 year old female child reported to emergency with complaint of snake bite. General and systemic examination was performed. Patient was hospitalized and treated symptomatically. Five vials of ASV diluted in 100ml of normal saline were administered at the rate of 10-15 drops per minute. After 10 minute of starting of infusion, she experienced anaphylactic shock with pulmonary bleeding. The decision was made to stop the infusion immediately. Symptomatic treatment for the event was administered. But the patient did not recover from the event. This was the serious adverse event leading to death of patient.

Case 2: 5 year old male child reported in emergency with complaint of snake bite. Patient was hospitalized and treated symptomatically. Patient was administered polyvalent ASV. Five vials of ASV diluted in 100ml of normal saline were administered at the rate of 10-15 drops per minute. After 5 minute of starting infusion he experienced anaphylactic shock .The infusion was stopped immediately. Symptomatic treatment for the event was administered, but the patient did not recover from the events. After some hours he developed acute renal failure and metabolic acidosis. Patient died due to cardiac arrhythmias after anaphylactic shock.

Case 3: 17 year old male child reported in emergency with complaint of snake bite. Patient was administered polyvalent ASV. The dose of ASV was 5 vials diluted in 100ml of normal saline and administered at the rate of 10-15 drops per minute. After 10 minutes of infusion, he experienced anaphylactic shock with hypotension. Symptomatic treatment for the event was administered but the patient did not recover from the events. This was the serious adverse event leading to death of patient.

Case 4: 4 year old male child reported in emergency with complaint of snake bite. Patient was hospitalized and treated symptomatically. Patient was administered polyvalent ASV. The dose of ASV was 5 vials diluted in 100ml of normal saline and administered at the rate of 10-15 drops per minute. He experienced severe shivering and delirium after 10 minute of infusion. The infusion was stopped immediately. Symptomatic treatment for the event was administered. The patient recovered from the event.

Case 5: 17 year old male child patient was hospitalized due to snake bite. Polyvalent ASV was administered to the patient. Dose of ASV given to the patient was 5 vials diluted in 100ml of normal saline and administered at the rate of 10-15 drops per minute. After 1 hr of starting of infusion he experienced shivering, palpitation. The decision was made to stop infusion immediately. Symptomatic treatment for the event was given to the patient. The patient recovered from the event.

Case 6: 3 year old female child was hospitalized due to snake bite. Polyvalent ASV was administered to the

patient. Dose of ASV was 5 vials diluted in 100ml of normal saline and administered at the rate of 10-15 drops per minute. After 10 minute of infusion she experienced anaphylactic shock, dizziness, and vomiting. The decision was made to stop infusion. Symptomatic treatment for the event was given to the patient. The patient recovered from the event.

Case 7: 14 year old male child patient reported to emergency department with complain of snake bite. The patient got hospitalized. General and systematic examination was performed. Polyvalent ASV was administered to the patient. Dose regimen was 5 vials diluted in 100ml of normal saline and administered at the rate of 10-15 drops per minute. After 10 minute of starting of infusion, she experienced anaphylactic shock with vomiting and hypotension. The decision was made to stop the infusion. Symptomatic treatment for the event was given to the patient. The patient recovered from the event.

Discussion

Snake bite is a major health hazard that leads to high mortality .It is a medical emergency. 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. In the present case series we reported adverse reaction in children due to polyvalent ASV. All the patients were treated with the recommended dose of lyophilized polyvalent enzyme refined equine immunoglobulin ASV according to WHO/SEARO guidelines for the clinical management of snakebites. The 10 ml vial of polyvalent ASV contains Indian Cobra (naja naja) 0.60mg, Common Krait (bungarus caeruleus) 0.45mg, Russell's viper (Vipera russelii) 0.60mg, Saw Scaled Viper (Echis carinatus) 0.45mg. We observed that the adverse reaction occurred only in pediatric patients in our tertiary care hospital. The age of the patients in present case series ranged from 3 to 17 years, Mean age ± SD was 9.57± 6.21. The causality assessment was done by using WHO-UMC Causality Scale. The causality assessment shows that out of 7 cases, 3(42.8%) were possible and 4 (57.14%) were probable. The duration from starting of polyvalent ASV infusion to the onset of the adverse reaction varied from 5 minute to 60 minutes. This is similar to previous study done by H A de Silva.[4] Therefore patients receiving polyvalent ASV should be closely observed for 1-2 hrs to monitor the adverse reactions. The most common presentation of reactions in these cases was shivering, dizziness, and delirium. Patients suffered from moderate to severe reactions like hypotension and anaphylactic shock leading to death of 3 patients. The ASV reactions were treated with adrenaline, anti-histaminics and steroids. There was a trend of using prophylactic anti-histaminic and corticosteroids. Attempts to prevent early reactions which included pretreatment with epinephrine, anti-histaminic, corticosteroids and reduction in speed and concentration of intravenous ASV administration have not been effective in adequately designed clinical trials.[5-6] We observed seven cases of adverse reaction, out of which 3 (42.8%) were fatal and 4 (57.1%) lead to prolonged hospitalization. Previous study has also shown a higher risk of adverse reactions to ASV and even increased mortality among children with snake envenomation compared to adults similar to our study.[7]

Conclusion

In conclusion, the record keeping of snake bite cases and adverse drug reactions following polyvalent ASV administration are far from satisfactory in the tertiary care hospitals. There is a need of adequate documentation of each and every adverse reaction that occurs due to ASV in terms of onset, duration, severity and outcome. This study provides insight into occurrence and severity of adverse reactions due to polyvalent ASV.

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References

1. Warell DA, ed. WHO/SEARO Guidelines for the Clinical Management of Snake Bite in South East Asia Region. SE Asian J Trop Med Pub Health 1999;30:1-85.
2. Warrell DA, ed. WHO/SEARO Guidelines for the Clinical Management of Snake Bite in South East Asia Region New Delhi; 2010:1-67.
3. Dart RC, Mcnally J. Efficacy, safety, and use of snake antis in the United States. Ann Emerg Med. 2001;37(2):181-88.
4. H A de Silva, Nicole M Ryan, H J de Silva. Adverse reactions to snake anti, and their prevention and treatment BJCP.2015:7.
5. Fan HW, Marcopito LF, Cardoso JL, França, OS, Malaque MS, Ferrari, and RA et al. Sequential randomized and double blind trial of promethazine prophylaxis against early anaphylactic reactions to anti for both rops snakebites. BMJ 1999; 318:1451-52.
6. Dassanayake AS, Karunanayake P, Kasturiratne KT, et al. Safety of subcutaneous adrenaline as prophylaxis against acute adverse reactions to anti- serum in snakebite. Ceylon Med J 2000;47:48-49.
7. Usman M Sani, Nma M Jiya, Paul K Ibitoye, Mohamad M Ahmad. Presentation and outcome of snake bite among children in Sokoto, North-Western Nigeria. Sahel Med J 2013;16(4):148-53.