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Original Research Article

A comparative study in the outcome between the two fixed doses of polyvalent anti snake venom, 10 vials versus 20 vials, with mechanical ventilation in children with severe neurotoxic snake envenomation

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ABSTRACT

Background: Every year about 50,000, people die of snake bites in India. Anti-snake venom and mechanical ventilation is mainstay of treatment in cases with severe neurotoxic envenomation. ASV is costly and scarce resource. There is lack of universal consensus towards the optimal dose of ASV in management protocol for children with severe neurotoxic snake envenomation. Objective was to compare the difference in outcome between two fixed doses of ASV, 10vials versus 20 vials, in children with severe neurotoxic snake envenomation
Methods: This comparative observational study was carried out for a period of 3 years in Department of Pediatrics of SVS Medical College, Mahabubnagar, Telangana, India. Children with history of snake bite and clinical evidence of neuroparalysis were included. In addition to the mechanical ventilation and other supportive measures, every alternate patient was administered with 10vials (low dose) and 20 vials (high dose) of ASV over 1 hour. Outcome was compared between the two groups.
Results: Of the 62 patients, 32 were in each group. The median time to extubation was 41 hours and 39.5 hours and mean duration of the hospital stay was 4.6 days and 4.5 days among the low dose and high dose groups, respectively. There were three deaths, one from low dose group and two from high dose group.
Conclusions: There was no significant difference in outcome between the 10 vials vs 20 vials of ASV in addition to mechanical ventilation in treatment of children with severe neurotoxic snake envenomation. So, 10 vials of ASV can be utilized to reduce the cost of treatment.

Keywords: Anti-snake venom, Mechanical ventilation, Neuroparalysis, Snake bite

INTRODUCTION

Snake bite is an acute life threatening medical emergency. India has the highest number of deaths due to snake bites in the world. The estimated death in India is 50,000/yr, an underestimate because of lack of proper registration of snakebite.[1-3] There are about 52 species are known to be poisonous out of total 216 species of snakes that are identifiable in India. The venomous snakes found in India belong to three families Elapidae, Viperidae and hydrophidae (Sea Snakes). The most common Indian elapids are *Naja naja* (Indian Cobra) and *Bungarus caeruleus* (Indian Krait), *Daboia russalie* (Russells' Viper) and *Echis carinatus* (Saw scaled viper).[3-5] The bites of common cobra, king cobra and krait cause predominantly neurotoxicity. Soon after the bite, the patient complains of a sinking feeling, drowsiness, blurring of vision, diplopia, dysphagia and dyspnoea. There will be paralysis of palate, tongue, pharynx and respiratory muscles. There will be a flaccid paralysis of the limbs, associated with hypotonia and a diminution in the tendon reflexes. Coma and death can happen due to respiratory failure or shock in 6-48 hrs.[6]

The management of neurotoxic snake envenomation includes administration of anti-snake venom (ASV) and ventilatory support. The ASV is targeted at neutralizing the venom. The amount of venom neutralized by 1 ml of ASV is approximately 0.6 mg and 0.45 mg for cobra and krait respectively. Though the use of ASV has been in existence for many years, there is no universally accepted standard regarding the optimum dose of ASV, its frequency of administration and duration of therapy in children with severe neurotoxic snake envenomation requiring mechanical ventilation.[7,8] In India, different treatment centers use different doses of ASV ranging from 10 vials to 30 vials. Different clinical trials have found different mean effective dose of ASV (varying from 47 ml to about 180 ml) required in cases with envenomation. [9,10]

This study was conducted to compare the effects of two fixed dose regimes; 10 vials ASV versus 20 vials ASV, on the outcomes of children with severe neurotoxic snake envenomation. This is particularly important because ASV is a scarce and costly commodity.

Written consent was obtained from the patients attendants for this research. Ethical clearance was obtained from institutional ethical committee after evaluating a pilot study where 10 vial of ASV was found to be safe and effective.

METHODS

This prospective observational study was conducted at Department of Pediatrics, SVS Medical College, Telangana, South India, for a period of 3 years from April 2017 to March 2020.

Inclusion criteria

Children brought with history of snake bite and features of neuroparalysis were included in this study.

Exclusion criteria

- Children with previous neurological disease and patient with neuroparalysis without history or clinical evidence of snake bite.
- Children with snake bite without evidence of neuroparalysis.
- Children who had manifested allergy to the ASV requiring complete stoppage of administration of full dose of ASV.

Snake envenomation was diagnosed based on the history of snakebite and neurotoxic manifestations (drooping of eyelids, drooling of saliva, difficulty to swallow, and / or difficulty to hold neck), presence of fang marks, presence of local manifestations such as swelling, cellulitis, and blister formation, or if the dead snake was brought in for identification.

Detailed history was obtained from guardian, which included history of bite, site of bite, type of snake, and time of bite. Treatment received prior to hospitalization was also obtained. Thorough clinical examination was performed including site of bite, local reaction at the bite site and systemic features, and viral signs and features of neuroparalysis such as drooping of eyelids, drooling of saliva, difficulty to swallow, and difficulty to hold neck (Brocken neck sign). Investigations reports were documented including arterial blood gases, serum biochemistry, complete blood count, and coagulation profile.

All patients were managed with polyvalent anti-snake venom (Haffkine Institute, Mumbai, India), mechanical ventilation and other supportive measures according to the departmental protocol for management of patients with neurotoxic snake envenomation. Every alternate patient was categorized into low dose group and high dose group. Low dose group received 10 vials and high dose group received 20 vials of anti-snake venom (ASV). Anti-snake venom was administered over 1 hour in all patients and no repeat doses were given. None of the patients were administered with Neostigmine or other cholinesterase inhibitors.

The primary outcome measures were the duration of mechanical ventilation (time in hours from the onset of intubation to extubation) and the duration of Pediatric intensive care unit stay. Mortality and other complications during the pediatric intensive unit stay were also recorded.

Comparison between low dose group and high dose group is done using chi- Square test. $p < 0.05$ is considered significant.

RESULTS

During the 3 year study period, 62 patients of severe neurotoxic snake envenomation were included, 32 in the high dose (20 vials) and 32 in the low dose group (10 vials) (Table 1). Snake bite was confirmed by report of the guardians, clinical evidence of progressive descending neuroparalysis, and recognition of snakes by guardians. Nine dead snakes were brought for identification: 6 kraits and 3 cobras. Venom specific enzyme immunoassay for identification of exact species of snake was not done due to non-availability of the test in our institute.

At admission, all patients had signs of neuroparalysis (drooping of eyelids, drooling of saliva, difficulty to swallow, and / or difficulty to hold neck), and evidence of hypercapnic respiratory failure (PaO_2 <60 mmHg and $PaCO_2$ >45 mmHg). Low dose group received 10 vials and high dose group received 20 vials of polyvalent anti-snake venom. No repeat doses were given in either group.

Five patients in the low dose group and six in the high dose group showed hypersensitivity reactions to polyvalent anti-snake venom, and were treated with promethazine and hydrocortisone. None of the patient developed anaphylaxis.

The median time to extubation in the low dose and high dose SAV groups was 41 and 39.5 hours respectively, p value >0.05 and was not statistically significant. The mean duration of the hospital stay was 4.6 days and 4.5 days among low dose and high dose group, respectively. p value of >0.05, which was statistically not significant. Seven patients, 3 from low dose group and 4 from high dose group had ventilator associated pneumonia.

There were three deaths, one from low dose group and two from high dose group. p value >0.05. There was no statistically significant difference between the two groups with regard to the mortality rate. All these three patients were brought late to the hospital; they had probably sustained irreversible neurological damage before reaching the hospital. All other patients improved and were discharged.

Table 1: Baseline characteristics and outcome of patients of severe neurotoxic snake envenomation with low dose and high dose anti-snake venom.

	Low dose group	High dose group
Number of patients	32	32
Male/Female	18/14	20/12
Mean (SD) age, years	10.4 (4.5)	12.2 (4.7)
Delay in presentation after bite, hours	6.4 (5.6)	6.2 (4.5)
Median extubation time (range, hours)	41 (18 to 138)	39.5 (14 to 168)
Mean (SD) Hospital stay (days)	4.6 (2.0)	4.5 (3.0)
Mortality	1	2

DISCUSSION

Bite of cobra and krait causes neurotoxic envenomation. The blockade of neurotransmission occurs due bind of toxin post-synaptically in cobra bite and both pre-synaptic and post-synaptically in krait bite. The neurotoxic snake envenomation results in progressive, descending neuroparalysis and presents with dropping of eyelids (ptosis), drooling of saliva, dysphagia, dysphonia, and difficulty to hold neck. This progresses into respiratory failure, which is the cause of mortality.[11]

Polyvalent anti-snake venom (ASV) is the specific antidote for snake bite envenomation. ASV neutralizes the circulating venom. Early administration of ASV prior to the bind of neurotoxins to the target receptors may prevent neuroparalysis.[2,5,6]

Although ASV has been used for many years, there is no universal consensus on the optimal dose of administration. ASV is a costly drug with limited availability at peripheral hospitals in India. Presynaptic blockade suggested being irreversible; these patients when on ventilator, administration of high dose of ASV late in the course may not have much benefit.

In our study, we evaluated whether there is a significant difference in the outcome with administration of 20 vial of ASV over 10 vials in patients with severe neurotoxic envenomation. We found no significant difference in the outcome between the two groups. Our study was in conformity with the study by V Paul et al PC Pandey et al and Srikant R. Gadwalkar.[7,11,12] In their study, V Paul et al. have confirmed that a smaller fixed dose of ASV is sufficient to manage snake bite cases with evenomation effectively yet economically. Study by PC Pandey and SR Gadwalkar et al found that low dose ASV administration and ventilatory support can provide sufficient cure if patients reach on time to the hospital.[11,12]

BR Daswani et al found that lower doses of ASV are as effective as the conventional high dose without being associated with higher mortality or morbidity.[13] This was in conformity with our results. Study by Paul V et al reported that high doses of ASV, apart from being non-superior and more costly, may at times turn out to be more harmful.[7] RR Das et al reported that, by using the low dose schedule, the savings can vary from 500 to 2000 rupees (10-40 US$) per patient (excluding that for hospital stay and other therapies).[14] Therefore, the use of 10 vials of ASV has economic significance. Lower dose has lower cost, which translate into huge savings to the patient and the community.

There are certain limitations in our study. Firstly, we only studied patients with severe neurotoxic envenomation requiring mechanical ventilation. Hence, the results of our study may not suggest that it should be applied to all snake bites. Secondly, the majority of the bite in our area was by krait as identified by guardians/ bystanders or brought the killed snake. We had not conducted venom specific enzyme immunoassay for exact identification species of the snake due to non-availability of the test in our institute.

CONCLUSION

In conclusion, within the limitations of the present study, there is no significance difference in the outcome with administration of 10 vials vs. 20 vials polyvalent anti-snake venom with mechanical ventilation in patients with severe neurotoxic snake envenomation.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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