

OUTCOME OF PATIENT WITH NEUROPARALYTIC SNAKE BITE TREATED WITH LOW DOSE (50 ML) V/S HIGH DOSE (100 ML) ASVD. P. Singh¹, Hemant Mahur², Lalit Kumar Raiger³, Kripa Shanker Jhirwal⁴**HOW TO CITE THIS ARTICLE:**

D. P. Singh, Hemant Mahur, Lalit Kumar Raiger, Kripa Shanker Jhirwal. "Outcome of Patient with Neuroparalytic Snake Bite Treated with Low Dose (50 ML) v/s High Dose (100 ML) ASV". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 36, August 18; Page: 9379-9384, DOI: 10.14260/jemds/2014/3209

ABSTRACT: It was always been a matter of great-controversy regarding the dosage protocol of anti-snake venom (ASV) in the management of snake envenomation. The only definitive treatment of poisonous snake bite is ASV administration. **MATERIAL AND METHODS:** This study was carried out for a period of two years. All patients of neuroparalytic snake bite who presented to the emergency department were included in this prospectively study. **RESULTS:** Fifty eight patients of neurotoxic snake bite became eligible for the study over a period of 2 yrs. By using chi-square test, the outcomes in low and high bolus dose group were statistically non-significant ($P>0.05$). Statistical analysis showed no significant difference in both groups. From this study it can be firmly concluded that low dose ASV is as effective as high dose in treatment of neurotoxic snake bite.

KEYWORDS: ASV: Anti snake venom.

INTRODUCTION: It was always been a matter of great-controversy regarding the dosage protocol of anti-snake venom (ASV) in the management of snake envenomation. The only definitive treatment of poisonous snake bite is ASV administration. In INDIA, ASV is prepared by hyper immunizing equines against the four common Indian snakes like Cobra, common Krait, Russel viper and saw scaled viper. Physicians when confronted with neurotoxic snake bites are most of the time is dilemma, with the following queries in mind:

1. What should be the initial bolus dose of ASV?
2. Whether repeated doses of ASV are to be administered? (as being routinely given in viper bites based on the coagulation parameters)
3. Whether anticholinesterase should be administered to all cases, if yes then in what doses and for how long?

Currently the initial bolus dose in case of Cobra and Krait bite is 100ml of ASV i.e. 10 vials.⁽¹⁾

More antivenom should be given if severe signs of envenoming persist after 1-2 hrs.^[1] The neurotoxins of elapid are rapidly absorbed into the blood stream compared with viperidae venom as the latter is absorbed via lymphatics.^[1] Hence, repeated doses of ASV are required in viperidae snake bites but not in elapid bites. Several studies have reported successfully treating neurotoxic envenoming without the use of ASV.⁽²⁾

Anticholinesterases have a variable but potentially harmful effect in patients with neurotoxic envenoming especially when postsynaptic neurotoxin is involved.^(1, 2, 12)

So many trials have addressed the minimum effective dose of ASV in viper bite.⁽³⁾ As per our best knowledge, there are no trials addressing the question of optimal dose of ASV in neurotoxic (elapid) bite. Very few clinical trials have been performed till date to establish the appropriate initial dose and in most cases antivenom is used empirically based on the individual experiences and observations of the physicians.

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Further, optimization of therapy may lead to reduced dose requirements of ASV in the therapy of neurotoxic snake bite. Keeping this in mind trial was conducted using two protocols (high dose versus low dose of ASV in neuroparalytic snake bite).

MATERIAL AND METHODS: The study was carried over a period of 2 yrs in RNT Medical College and Associate Group of Hospital, Udaipur. All patients of neuroparalytic snake bite who presented to the emergency department were included in this prospective study. The snake bite was confirmed either by a reliable history or fang mark.

Inclusion criteria used was presence of signs of envenomation either systemic or local. Patients who did not show any signs of envenomation and patients who had received anti snake venom prior to admission to this institution were excluded from the study. Neurological envenomation was said to be present if patient had any of the following findings suggestive of neurotoxic snake bite: ptosis, diplopia, dysphagia, dysphonia, muscle paralysis/weakness, respiratory distress and confusion. Using the above inclusion criteria 58 patients became eligible for the study.

A detailed clinical history regarding bite i.e., time since bite, site of bite, symptoms of envenomation and complications was taken at the time of presentation. Thorough clinical examination was carried out. The time taken by the patients to arrive at the hospital from the time of bite i.e. time between the bite and administration of ASV on arrival at hospital was noted.

Laboratory investigation performed at admission included: SpO₂ (oxygen saturation), electrocardiogram, chest radiograph, serum biochemistry, haemogram and coagulation parameters. All patients were transferred to MICU from casualty and medical ward. Special investigation such as ultra sonography and CT scan were carried out as and when required.

A total of 26 patients required ventilator assistance through their course of stay at hospital and were gradually weaned off as they recovered.

Meticulous attention was paid to asepsis, nutrition, humidification of inhaled air, regular endotracheal toileting and continuous monitoring of hemodynamic and respiratory mechanics variables. Weaning was accomplished once adequate respiratory effort reappeared. A short T-piece trial was given and patients were extubated if they had normal bulbar reflexes and did not show any worsening during the period of T-piece trial.

Eligible patients were randomly allocated to either high (100ml) or low (50ml) ASV bolus dose group. In high bolus 100 ml of ASV was given intravenously after test dose dilution in 200ml of normal saline (glass bottle) over a period of one hour and in low bolus dose group 50 ml was given in the same way over one hour.

In both groups anticholinestrase in the form of injection Neostigmine, was given in doses of 0.5 mg half hourly for four doses and then at increasing interval of 2-12 hourly for next 48-96 hours according to clinical response. Atropine was combined in doses of 0.6 mg IV for every two doses of Neostigmine to neutralize muscarinic side effect of Neostigmine. The outcome between low and high bolus dose group were compared using chi-square test.

The end point of study was complete recovery of respiratory paralysis, neurological improvement or death. Other data regarding age, sex, site of bite, time delay, type of snake, antibiotics and other supportive measures were collected.

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RESULTS: Fifty eight patient of neurotoxic snake bite became eligible for the study over a period of 2 yrs, baseline characteristics of the groups are presented in Table 1.

Sl. No.	Variable	High bolus dose	Low bolus dose	Significance
1.	No. of patients	20	38	NS P > 0.05
2.	Age < 30 yrs > 30 yrs	13 7	17 21	NS P > 0.05
3.	Sex M F	10 10	22 16	NS P > 0.05
4.	N-B time < 12 hrs > 12 hrs	19 1	31 1	NS P > 1.05
5.	Pt. requiring ventilatory support	5	19	NS P > 0.05
6.	Pt. not requiring ventilatory support	15	19	NS P > 1.05

Table 1: Baseline characteristics

The youngest patient was of 14yrs of age while oldest was of 60yrs. Out of 50 patient, 20 were included in high bolus dose group and 38 were in low bolus dose group. Ventilator was used in 24 patient (5 were in high bolus dose group and in 19 low bolus dose group).

Thirty two patients were male (55%) while twenty six were female (45%). Out of 58 patients, 50 cases were presented within 12 hours of snake bite and 8 after 12 hours. Twelve patient's snakes were identified, of which 10 were Krait- and 2 were cobra. An attempt was made to compare the outcome between the high and low bolus dose group. The findings are summarized as follows (Table 2).

Sl. No.	Variable	High bolus dose	Low bolus dose	Significance
1.	Mortality	1	1	-
2.	Duration of ventilatory support requirement in hours Mean (SD) range	N=5 40.26±29.9 (4-96 hrs)	N=19 25.63±18.9 (5-60 hrs)	NS P > 0.05
3.	Duration of hospital stay in days	5.6±1.75 (3-8)	4.3±1.66 (2-8)	NS P > 0.05
4.	Duration of anticholinesterase requirement in days	3.47±1.27	3.1±1.758	NS P > 0.05

Table 2

The mean duration of ventilator requirement was 40.26 hrs and 25.63 hrs, hospital stay 4.6 days and 4.3 days and anticholinesterase requirement 3.47 days and 3.1 days respectively in high and low bolus dose group. By using chi-square test, the outcomes in low and high bolus dose group were statistically non-significant (P>0.05). There were two mortality in our study one from each study group.

As evident in table-2, that low dose of ASV is effective as high dose of ASV in relation to mortality as well as requirement of ventilatory support, duration of hospital stay and no anaphylaxis

with ASV. Statistical analysis showed no significant difference in both groups. From this study it can be firmly concluded that low dose ASV is as effective as high dose in treatment of neurotoxic snake bite.

DISCUSSION: Neuroparalysis leading to type 2 respiratory failure is the most important cause of mortality in victim bitten by venomous snake of elapidae family.^[3,6,7] Cobra and Krait venom mainly affect the musculature of eyes, tongue, throat and chest leading to respiratory failure.^[8] The characteristics neuromuscular paralysis, the respiratory paralysis and cardiotoxicity are now known to be due to peripheral action of the toxin.^[9]

Typically, neuromuscular symptoms develop early, but after Krait bite, there may be delay of more than 10 hours.^[2] Extraocular muscles are most sensitive to neuromuscular blockage and in some patients, the only feature of envenomation is ptosis and ophthalmoplagia.⁽²⁾

The only effective treatment of poisonous snake bite is ASV administration. Until now high dose of ASV were recommended in neuroparalytic snake bite. However there are few reported studies in literature wherein neuroparalytic snake bite was treated by mechanical ventilation and supportive measures alone, with excellent result.^[4,5,11]

On extensive review of literature we could not find any such study comparing low doses of ASV with high dose in management of neuroparalytic snake bite. Through this study an attempt was made to compare the outcome of low dose of ASV with high dose.

As evident from Table 2 it is encouraging to note that low dose ASV is as effective as high dose in reducing mortality and other parameters like ventilatory requirement, duration of hospital stay and anticholinestrage requirement. On statistical analysis there was no significant difference in the outcome of both the groups ($P < 0.05$).

Two patients, one from each group who died, had sustained irreversible hypo-ischemic cerebral injury because of delay in reaching the hospital (More than 12 hours). Delayed arrival in hospital is in important factor contributing to a fatal outcome in such victim.^[7]

Immediate endotracheal intubation is necessary for airways protection and prevention of aspiration in patients with bulbar involvement.^[10] Mechanical ventilation generally is easy and without complications in such patients, as they are not diseased and have normal pulmonary mechanics.

In this study, the median duration of ventilation was 40.26 hrs in high dose and 25.63 hrs in low dose group. The difference was statistically insignificant. The duration of mechanical ventilation in snake bite victims is usually short since neuroparalysis reverse quickly with prompt administration of ASV.^[10]

In fact, our aim was to wean patients as quickly as possible because of the fear of increased risk of ventilation associated pneumonia with prolonged ventilation. Three patients had developed this complication, as they required mechanical ventilation for prolonged period. Two patients developed cardiac arrest which were revived by cardiopulmonary resuscitation and had complete recovery.

From present study, this can be concluded that low dosage of ASV (50 ml) is as effective as high dosage (100 ml) in management of neuroparalytic snake bite. In developing country like ours where there is scarcity of ASV as were as there is economically constraints because of high cost of ASV, low dosage of ASV can be used with excellent results.

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It can be confirmed by further studies using larger sample size and subsequently practicing will greatly reduce the requirement of ASV in treatment of neuroparalytic snake bite.

Previous Study: Low dose of snake antivenom is as effective as high dose in patients with severe neurotoxic snake envenoming R Agarwal, A N Aggarwal, D Gupta, D Behera, S K Jindal *Emerg Med J* 2005;22:397–399. doi: 10.1136/emj.2004.020727.

REFERENCES:

1. Warrell DA. Injuries, poisoning and allergic reactions caused by animals. In: Oxford Textbook of Medicine. Weatherall DJ, Ledingham JGG, Warrell DA (eds): Oxford University Press, Oxford, 1984; 6. 35-6.47
2. Warrell DA, Looareesuwan S, White NJ, Theakston RD, Warrell MJ, Kosakarn W, et al. Severe neurotoxic envenoming by the Malayan krait *Bungarus candidus* (Linnaeus): response to antivenom and anticholinesterase. *BMJ*. 1983; 286: 678–680.
3. Tariang DD, Philip PJ, Alexander G, Macaden S, Jeyaseelan L, Peter JV, et al. Randomized controlled trial on the effective dose of anti-snake venom in cases of snake bite with systemic envenomation. *J Assoc Phys India*. 1999; 47(4): 369–371
4. Bomb B S, Roy S, Kumawat D C. Do we need anti-snake venom for management of elapid ophitoxemia? *J Assoc Physicians India* 1996. 44:31–33.
5. Pochanugool C, Limthongkul S, Sitprija V, Benyajati C. Management of cobra bite by artificial respiration and supportive therapy. *J Med Assoc Thai*. 1994; 77: 161–164
6. Warrell DA. Animal toxins. In: Manson's Tropical Diseases. Cook G (ed): W.B. Saunders, London 1996; 468-515.
7. Looareesuwan S, Viravan C, Warrell DA. Factors contributing to fatal snake bite in the rural tropics: analysis of 46 cases in Thailand. *Transactions of Royal Society of Tropical Medicine and Hygiene* 1988; 82: 930-934.
8. Mitra S. Snake bite in India and its management. *J Indian Med Assoc* 1987; 85: 129-131.
9. Chatterjee SC: Management of snake bite cases. *J Indian Med Assoc* 1965; 45: 654-659.
10. Vijayendra HS, Puri GD, Bharadwaj N: Management of snake bites in north India. *Indian J Anaesthesia* 1998; 42: 65-67
11. Mehta SS, Kelkar PN, Parikh NN. Respiratory failure after snake bite poisoning successfully treated with prolonged artificial ventilation, *Indian J Anaesth* 1968; 16: 273-275.
12. Benedee RN. Neostigmine in management of snake bite. *J Indian Med Assoc* 1982; 78:61-63.
13. Agrawal PN, Aggarwal AN, Gupta D, Behera D, Prabhakar S, Jindal SK. Management of respiratory failure in severe neuroparalytic snake envenomation. *Neurol India* [serial online] 2001 [cited 2005 Aug 4]; 49: 25-8.
14. Reid H. A.. Cobra-bites. *Br Med J* 1964; 2: 540-545.

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