ORIGINAL ARTICLE

Comparative analysis of high-dose anti-snake venom VS low dose anti-snake venom on morbidity and mortality following poisonous snake bites

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Abstract

Background: Snake bite is an important preventable health hazard. Patients with snake envenomation present to the emergency department with significant morbidity and mortality and emergency healthcare professionals are faced with the challenge of deciding an optimal anti-snake venom (ASV) dose.

Objective: To compare the effect of administration of two different dosage regiments of ASV (high versus low) on the morbidity and mortality among patients following snake envenomation.

Material and Methods: This prospective, cohort was conducted upon a sample of 114 snake bite patients (chosen via non-probability – consecutive sampling), of all genders and aged 18 to 60 years, presenting to the study setting from January 2016 to December 2020. The patients were randomly designated into two groups-A (High Dose ASV Regimen - Intermittent bolus dosage of 100 ml of ASV as a loading dose followed by 50 ml every 6-hours till whole blood coagulation time (CT) became normal) and B (low dose ASV Regimen - 30 ml of ASV as a loading dose followed by 30ml continuous infusion every 6-hours till coagulation time became normal). The data pertaining to treatment was recorded onto a structured questionnaire and analyzed using SPSS version 21 and Excel 2016.

Results: Among the 114-patients enrolled in to the study, 72.81% were males, while the remaining 27.19% were females. The mean age of sample stood at 31-years (SD±11). In patients with mild, moderate and severe envenomation, the dosage requirements needed to obtain a normal CT were 137.5 ml, 343.8 ml and 433.3 ml in Group A – High Dose Regimen (HDR) and 128.6 ml, 221.3 ml and 213.7 ml for Group B – Low Dose Regimen (LDR). In the low-dose group there were 5-deaths giving a mortality rate of 8.78%, 9-(15.79%) required dialysis and 3(5.26%) required ventilatory support. In the high-dose group there were seven deaths giving a mortality rate of 12.28%, 13(22.8%) required dialysis and 3(5.26%) required ventilator support. The average hospital stay for the low-dose group was 8.42 days while that of the high-dose group was 9.02 days.

Conclusion: After careful consideration, it can be concluded that the low dose regimen yield a better patient outcome in terms of anti-snake venom volume used, morbidity and mortality entailed and the hospital stay.

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Introduction:

Of the 2,000 species of snake known, about 400 species are venomous and these may be responsible for at least 50,000 snake bites reported annually.[1] Many of those bitten by snakes fail to survive, leading to a high fatality count especially in parts of the world where snakes are numerous and access to the anti-venins is not readily available; 4 million in Asia; 1 million in Africa; 300,000 in central and South America and 100,000 in other continents.[2]

Table 1:

Age group (years)	Male	Female	Total
Up to 25	10	04	14
26 to 35	34	13	47
36 to 45	26	09	35
46 to 55	11	04	15
56 and above	02	01	03
	83	31	114

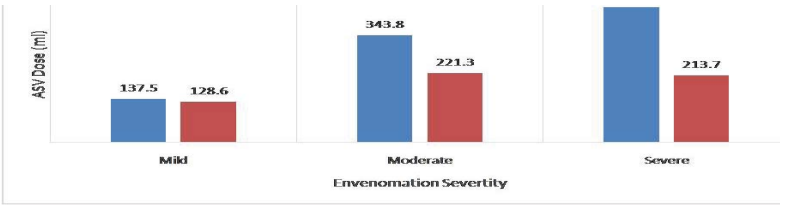

Table 2:

Variable		HDR	LDR
Mortality		12.28%	8.78%
Morbidity	Need for Ventilator Support	5.26%	5.26%
	Need for dialysis	22.8%	15.79%
Average Hospital Stay (days)		9.02	8.42

In Asian countries, fatalities by snake bites have been reported increasingly every year presumable due to the increased deforestation and migrations of these poisonous animals towards human populations.[3] In Pakistan, 40,000 snake bites are reported annually, which result in up to 8,200 fatalities. In Nepal, more than 20,000 cases of envenoming occur each year, with 1,000 recorded deaths. In Sri Lanka, around 33,000 envenomed snake bite victims are reported annually from government hospitals. A postal survey conducted in 21 of the 65 administrative districts of Bangladesh estimated an annual incidence of 4.3 per 100,000 population and a case fatality of 20%. However, existing epidemiological data remain fragmented and the true impact of snake bites is very likely to be underestimated.[4]

Snake bite is an important occupational injury affecting farmers, plantation workers, herders, and fishermen. Open-style habitation and the practice of sleeping on the floor also expose people to bites from nocturnal snakes. Several epidemiological studies have outlined characteristics of snake bite victims in the region. Bites are more frequent in young men, and generally occur on lower limbs. The incidence of snake bites is higher during the rainy season and during periods of intense agricultural activity.[5] The common poisonous snakes found in Southern Sindh are Cobra (Naja Naja); Indian Krait (Vipera Russeli Russeli); Russel's Viper (Vruss Elisamensis) commonly called Dabois; Saw scaled viper also called Lundibala or Jalabi in Sindh fork lore.[6]

Health workers in First Level Care Facilities (FLCF), are usually poorly trained to manage snake bite envenoming, which is a complex emergency. A recent survey conducted in Pakistan showed that many doctors were unable to recognize systemic signs of envenoming.[7] Another study in northwest India revealed that most snake bite victims presenting at healthcare centers received inadequate doses of anti-snake venom (ASV).[8]

Improving the knowledge of care-givers at all levels of the health system is a challenge of paramount importance and great urgency in South Asia and crucial in the effective management of snake bites. However, since no unanimous effective dose is agreed upon and research is scare in this area, deciding upon an effective dose is challenging even for the most experienced emergency healthcare professionals. The fact that ASV is expensive and often scarce, research is needed to decide upon a judicious dosage regimen.

Material and Methods:

This prospective, cohort study was conducted upon a sample of 114 snake bite patients (chosen via non-probability – consecutive sampling), of all genders and aged 18 to 60 years, presenting to the study setting from January 2016 to December 2020. The patients were randomly designated into two groups-A (High Dose ASV Regimen - Intermittent bolus dosage of 100 ml of ASV as

a loading dose followed by 50 ml every 6-hours till whole blood coagulation time (CT) became normal) and B (low dose ASV Regimen - 30ml of ASV as a loading dose followed by 30ml continuous infusion every 6-hours till coagulation time became normal).

Patients were excluded from the study if they presented more than 24 hours after the bite or if they gave history of any bleeding diathesis or any other previous neurological abnormality. Patients who had manifested allergy to the anti-snake venom were also excluded from the study. The patients in the either of the groups were first administered a sensitivity test (2 vials of ASV diluted in 100ml of dextrose or saline over 2 hours).

All patients were given I.M. tetanus toxoid and IV hydrocortisone 100 mg. Whenever required, blood transfusion was given to the hemotoxic cases. Snakes were identified either by direct examination of the snakes when brought by the patients or on the basis of the signs, symptoms, and results of the investigations. The end point of the study was normalization of hematological or neurological parameters or death. The data pertaining to treatment was recorded on to a structured questionnaire and analyzed using SPSS version 21 and Excel.

Results:

Among the 114-patients enrolled into the study, 72.81% were males, while the remaining 27.19% were females. The mean age of sample stood at 31-years (SD±11).

In patients with mild, moderate and severe envenomation, the dosage requirements needed to obtain a normal CT were 137.5ml, 343.8ml and 433.3ml in group A – High Dose Regimen (HDR) and 128.6ml, 221.3ml and 213.7ml for group B–Low Dose Regimen (LDR).

In the low-dose group there were 5-deaths giving a mortality rate of, 9-required dialysis and three required ventilator support. In the high-dose group there were 7-deaths, 13 required dialysis and 3-required ventilator support. The average hospital stay for the low-dose group was 8.42 days while that of the high-dose group was 9.02 days.

Discussion:

Though the use of anti-snake venom (ASV) has been in existence for many years, there is no universally accepted standard regarding the optimum dose of anti-snake venom, its frequency of administration and duration of therapy. SR Vijeth et al., have found in their trial that the mean effective dose of anti-snake venom required in a snake bite case with envenomation is about 180ml (18 vials). Tariang et al have reported that the mean dose anti-snake venom required to manage a case with envenomation effectively is 4.7 vials.[9,10]

In a study by Paul V et al., authors found no additional advantage of giving fixed 12 vials (120ml) of anti-snake venom over 6-vials (60ml) of ASV.[16] However all the cases included in that study were those who arrived within 24-hours of bite, whereas most cases in our setup report well after that.[11]

The average dose of anti-snake venom required in low dose regimen in our study was significantly lower than that required in HDR. The lower requirement in low dose regimen was probably due to the delivery of anti-snake venom by continuous infusion and thus more accurate titration of dose, as opposed to delivery by multiple bolus doses in HDR. Continuous intravenous infusion may be the best method to exactly titrate the dose of anti-snake venom, and at the same time it does not necessarily cause slower correction of clotting time, as evidenced in this study.[12]

Repeated high doses of anti-snake venom to restore the clotting time to normal within the shortest time, do not seem to be necessary to reduce the ultimate morbidity and mortality. A smaller dose sufficient to bring down the clotting time and make the

clotting time graph take a downward trend seems to be sufficient to manage the case effectively and safely. The body's detoxifying system will bring down the clotting time eventually though it may take a slightly longer time. This delay does not seem to affect the morbidity and mortality as shown by the results of this trial.[13]

In this trial, the mortality rate and the percentage of cases requiring dialysis is more in the HDR. One of the possible explanations is that the anti-snake venom made from equine protein may be causing subclinical toxic effects in a patient who has already multi-organ involvement, and this may tilt the balance adversely against the patient.[14]

The economic significance of the result of this study is considerable for the developing countries in Asia and elsewhere where the major cross-section of patients afflicted falls within the lower income group. The difference in the dosage of anti-snake venom between the HDR and LDR is 6-vials. We feel that there is scope for further trials using a still smaller dose of anti-snake venom. [15]

Conclusion:

After careful consideration, it can be concluded that the low dose regimen yield a better patient outcome in terms of anti-snake venom volume used, morbidity and mortality entailed and the hospital stay.

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Role and contribution of authors:

Afreen Fazal, collected the data, references and did the initial writeup.

Shua Nasir, collected the data, references and wrote the discussion part of the article.

Lal Shehbaz, collected the data, references and helped in introduction writing.

Huma Mumtaz, collected the data, referencs and helped in tabulation of data and also helped in result writing.

Syed Jehanzeb Asim, critically review the article and made useful changes.

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