

To Compare the Efficacy, Safety and Cost-Effectiveness of Two Different Antisnake Venom Formulations (Antisnake Venom Powder and Antisnake Venom Liquid) at DHQ Hospital Badin

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Abstract:-

Objectives: To identify which Antisnake venom formulation is more effective, safe and cost effective on patients with snake bite.

Method: The retrospective study was conducted at the Indus Hospital Badin, Pakistan, and comprised data of patients, with snake bite from 1st January to 31st December 2020 and patients were treated as per institutional protocol. Data was collected from Health management and information system (HMIS) software and analyzed using Statistical Package of social sciences (SPSS) 21.

Results: Out of 159 patients, 124 patients were treated with Antisnake venom (Liquid) and 35 patients were with Antisnake venom (Powder). Total 441 vials of Antisnake venom (Powder) administered on 35 patients (12.6 vials per patient) and cost per patient estimated as 16,632 Pakistani rupees, furthermore hospital stay of patients with Antisnake venom (Powder) was 6-12 days and in the case of Antisnake venom (Liquid), total 512 vials used on 124 patients (4.12 vials per patient) and cost per patient estimated as 2,318.592 Pakistani rupees much less than patients treated with Antisnake venom (Powder).

Conclusion: Antisnake venom (Liquid) is more effective, safe and cost-effective than Antisnake venom (Powder).

Keywords:- Antisnake Venom, Snake Bite, Safe, Cost-Effective, Pakistan.

I. INTRODUCTION

Snake bite is a threat to public health in many parts of the world, especially in the rural tropics where snakes are most abundant¹ Snake bite affects millions of people around the world. According to study, death ratio of snake bite patients is 1,25,000 globally and in India about 35,000 to 50,000 reportedly die of snake bite and unreported cases even more.⁹ There is need of improvement in therapeutic approaches to reduce mortality and morbidity associated with this neglected

tropical disease². There are more than 3000 species of snakes in the world, and of them, some 600 are venomous and over 200 are considered medically important. It is estimated that nearly 5.4 million people are bitten each year with up to 2.7 million envenomation, causing mortality in 81,000 to 138,000 cases. Morbidity is also enormous and around 400,000 amputations and other permanent disabilities occur annually. The most fearful complications of venomous snakebite are muscle paralysis that may arrest breathing, bleeding disorders that can lead to life threatening bleeding irreversible kidney injury and tissue damage that can cause permanent disability and limb amputation.¹

In South Asia nearly 70% mortality occurs in India, Pakistan, Bangladesh, Nepal and Srilanka.^{2,3}

In Pakistan, snake bite cases mostly reported from the Punjab and the Indus delta in Sindh. These areas represent the hub of agricultural activity.¹

Many Indian Medicinal plants are used in the management of snake bite cases especially in the rural areas, however only few species have been studied scientifically and still less has their active components isolated both structurally and functionally.⁸ Ibrahim Sani and co in 2020 published that *Parkia biglobosa* stem bark, *Calotropis procera* root and *Sterculia setigera* stem bark have Antisnake venom properties¹².

According to one guidelines flavonoids, polyphenons, saponins, tannins and terpenoids also contain Antisnake venom properties they bind with toxic proteins of snakes and make them inactive¹³.

Despite of plants and phytochemicals, Antisnake venom medications are commonly used throughout the world with aim of more effective, cost effective and less toxic medication utilized for patients.

II. ANTIVENOM

The only available treatment against snake bite is the usage of Antisnake venom. The first Antisnake venom was developed by Alberte Calmette against the Indian Cobra (*NajaNaja*). Antisnake venom made by immunizing mammals such as horse, goat, rabbit with particular snake venom and the specific Immunoglobins are isolated from the blood³.

According to one study, there is no any universally accepted standards or guidelines for the proper dose and frequency of Antisnake venom.⁴

But according to Biological Production Division National Institute of Health Islamabad, Pakistan the dose of Antisnake Venom serum is 10-30 ml and severe cases it may go up to 200 ml. One third of initial dose can be administered locally around the wound and remaining two third of dose intravenously. The second dose can be repeated two hours after the first dose or even earlier depending on the condition of the patient and severity of symptoms.⁵

The subject animal will undergo an immune response to the venom, producing antibodies against the venom's active molecule which can then be harvested from the animal's blood and used to treat envenomation. Antivenom is classified into types, Monovalent antivenom when they are effective against a given species venom. Polyvalent when they are effective against a range of species.⁴

Antisnake venom serum is sterile preparation containing purified and concentrated immunoglobulins obtained from the serum of healthy horse immunized against the venom of the following four common poisonous snakes:

1. Cobra *NajaNaja*
2. Krait *Bungarus Caeruleus*
3. Russel's Viper *Vipera russeli*
4. Saw scaled Viper *Echis Carinatus*.⁵

In our study we compared the efficacy, safety and cost-effectiveness of two available formulations of Antisnake venom serum at DHQ Badin which will reduce hospital stay of patients and improve quality of life.

III. METHODS

➤ *Study setting, design and period*

This retrospective study was conducted at district headquarter Hospital (DHQ) Badin from January to March 2020, after receiving ethical approval from the Institutional Review Board (IRB Committee) of Indus Hospital Karachi.

Data was collected from HMIS and put in Excel sheet then it was analyzed using SPSS.

➤ *Inclusion and exclusion criteria*

All those patients who diagnosed with snake bite regardless of age and gender and whom Antisnake venom administered was included in our study. However, those patients other than snake bite whom Antisnake venom not administered were excluded from the study.

➤ *Statistical treatment*

The data was collected, coded, cleaned, and analyzed on the IBM SPSS version 26. Mean with STD was evaluated for continuous variables while frequency with percentage was calculated for categorical data. Association among variables was observed by the Chi-square test. A P-value of ≤ 0.05 was considered significant.

IV. RESULTS

The data was collected retrospectively from patients' medical records and recruited 159 patients in this study. The number of patients who received the NIH liquid anti-venom was 124 while those who got Powder anti-venom was 35. There were 108(67.9%) were male and 51(32.1%) were female. The mean age of the patients was 32.5 ± 12.9 years while the median was 30 with an IQR of 19 years. It was observed that before the treatment with the anti-venom there were 27 patients who had jelly-clotted blood and on the other hand in 97 patients the blood was not clotted at all. After the initiation of treatment, patients who received liquid NIH antivenom resulted in clotting of the blood of all patients, on the contrary, there were 5(14.2%) patients out of 35 in the powder antivenom group in whom blood did not clot. NIH liquid antivenom showed 100% efficacy because in these patients' blood was clotted in all samples while powder antivenom showed an efficacy of 85.7% as blood was clotted in 30 out of 35 patients and in 5 patients blood remain jelly clotted **Table 1**.

Table:1 Pre and post antivenom Blood clotting status n (%)

Pre antivenom Blood clotting status		After antivenom Blood clotting status		Total 159
		Clotted	Jelly Clotted	
NIH	Jelly Clotted	27(100)	0	27
	Not Clotted	97(100)	0	97
	Total	124(100)	0	124
Powder	Clotted	2(100)	0	2
	Jelly Clotted	14(87.5)	2(12.5)	16
	Not Clotted	14(82.4)	3(17.6)	17
	Total	30(85.7)	5(14.3)	35

There was a statistically significant difference between pre and post-antivenom clotting profiles ($p < .0001$) which again established the effectiveness of the treatment **Table 2**.

Table:2 Pre and post-antivenom differences in clotting factors profile

	Pre Antivenom	Post Antivenom	P-value
APTT	100.6 ± 77.7	30 ± 11.7	< 0.001
PT	54.1 ± 69	16.1 ± 15.2	< 0.001
INR	2.1 ± 1.9	1.1 ± 0.2	< 0.001

We also compared the difference in clotting profile in the two anti-venoms and didn't observe any statistically significant difference between the two treatments but clinically detected NIH was much better to correct the blood clotting profile as compared to powder antivenom because the mean PT, APTT, INR was more corrected in the patients who were treated with NIH than those who were treated with powder { (43.1 ± 75.4 vs 19.8 ± 43.3) (76.5 ± 78.4 vs 49.9 ± 65.4) and (0.97 ± 2 vs 0.82 ± 1.4) } **Table 3**.

Table:3 Comparison of two Antivenom in terms of cost-effectiveness and improvement in blood clotting profile

Variables	NIH	Powder	P- value
Difference in Cost	6808.5 ± 4338.8	23043 ± 19924.7	<0.001
Difference in PT	43.1 ± 75.4	19.8 ± 43.3	0.662
Difference in APTT	76.5 ± 78.4	49.9 ± 65.4	0.377
Difference in INR	0.97 ± 2	0.82 ± 1.4	0.295

The cost-effectiveness of the two treatments was also calculated and it emerged that NIH is very cost-effective when compared with the powder anti-venom. The mean cost of NIH liquid antivenom was PKR 6808.5 ± 4338.8 which is much less than the mean cost of powder anti-venom PKR 23043 ± 19924.7 ($p < 0.0001$)

We also counted the number of vials of both antivenom used in patients and then calculated the total cost. we noticed that a total of 512 of the NIH vials were used in 124 patients which cost about PKR 790016. on the other hand, 441 vials of this powder anti-venom were used in only 35 patients and the cost was PKR 582120.

Out of 35 patients treated with Antisnake venom powder, 32 patients were diagnosed as snake bite and 3 patients were diagnosed as snake bite with other complications like Hypertension, Diabetes mellitus and Chronic Kidney

disease. 33 patients treated in Hospital while 2 patients referred to other tertiary care hospital. 3 patients developed fever and itching after administration of Antisnake venom powder while 32 patients showed no any significant Antisnake venom powder related reaction.

Out of 124 patients treated with Antisnake venom NIH, 109 patients were diagnosed only as snake bite while 15 patients were diagnosed as snake bite with other complications like Hypertension (3), Tuberculosis (2), Epilepsy (2), Asthma (2) followed by one one patient of Peptic ulcer, Diabetes, Acute Kidney injury, Human immunodeficiency virus and Arthritis. 120 patients were treated here in Hospital and 4 patients referred to other tertiary care hospital for further management. Only one patient developed itching after administration of Antisnake venom NIH managed by antihistamine medication while 123 patients were out of any Antisnake venom NIH related problems.

V. DISCUSSION

As per our knowledge current study is first done here at DHQ Badin, every year lots of patients are treated with both formulations of Antisnake venom but this type of comparison never done before.

According to our study Antisnake venom (Liquid) is more effective than Antisnake venom (Powder) because it quickly normalized patient's Activated prothrombin time and Prothrombin time with 1 to 2 doses only. As indicated only 1 to 2 doses required hence hospital stay of patients reduced just 1 to 3 days (The chances of Hospital acquired infections reduced) but in case of Antisnake venom (powder) 4 to 5 doses used per patient and hospital stay of patients ranged from 5 to 10 days even further, so chances of other infections increased.

Furthermore, as we calculated cost, per patient cost of Antisnake venom (Powder) was 12,724.8 and per patient cost related to Antisnake venom (Liquid) was 2,318.592 much less than Antisnake venom (Powder).

⁶According to one study, Antisnake venom causes severe adverse reactions like anaphylaxis, this study was conducted in Bangladesh between 1999 and 2001, out of 35 patients, 20 patients developed anaphylactic reaction, which then managed with injection Adrenaline.⁶

However, no any significant Antisnake venom related problem we observed with both formulations, only itching like symptom appear on 1 to 2 patients this may due to proper administration via intravenous infusion of both Antisnake venom formulations.

⁷Administration of Antisnake venom via intravenous infusions is the best way to titrate the dose and reduce total dose and adverse effects.⁷

¹⁰Although Antisnake venoms has been used for many years but selection of suitable Antisnake venom with low cost was a problem which has been tried to solve in this article.¹⁰

¹¹Huma and co worked on similar topic in 2013. They compared both Antisnake venom of NIH and powder in Mithi and Umerkot, but they focused mainly on cost and adverse reactions caused from both Antisnake venom¹¹, we further evaluate their studies by addition of more variables like hospital stay of patients and and outcome on patients either treated in hospital or referred in other hospital etc.

VI. CONCLUSION

Our study revealed that utilization of Antisnake venom (Liquid) is safe, effective and cost-effective for patients as well as any organization.

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