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PROSPECTIVE OBSERVATIONAL STUDY OF CLINICAL PHARMACOLOGICAL PROFILE OF POLYVALENT ANTI-SNAKE VENOM IN SNAKE BITE PATIENTS TREATED IN A TERTIARY CARE CENTER

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ABSTRACT

Snake bite is a public health problem distributed mainly in the tropical and sub-tropical countries. India is one of the high prevalence countries. According to the World Health Organization reports India has the maximum number of envenomation and mortality due to snake bite. Result: Most of the patient with age group of 22 to 72 years. Among that 64.1% was male and 35.1 was female attended the serious condition of snake bite. explained about the patient received polyvalent anti-snake venom, total 75(96.9%) patient were rescued by giving ASV, one required hemodialysis and three of them were kept for observation (non-critically) Strengthening of public health systems that have reduce the number of deaths reduce to snakebite in state of Tamilnadu India.

Keywords: Snakebite, Anti-Snake Venom, Polyvalent Anti-Snake Venom, Adjuvant therapy, ASV.

INTRODUCTION

Snake bite is an acute medical emergency. It is one of the major causes of mortality encountered in tropical countries like India [1]. According to the World Health Organisation reports India has the maximum number of envenomation and mortality due to snake bite [2]. This information is an iceberg as majority of the snakebites occur in rural areas and are unreported. Krait, cobra and viper are the common poisonous snakes seen in South India [3].

Snakebite is an acute life threatening time limiting medical emergency. It is a preventable public

health hazard often faced by rural population in tropical and subtropical countries with heavy rainfall and humid climate [4,5]. The numbers of snakebite fatalities in India has long been controversial. There is a huge gap between the number of snakebite deaths reported from direct survey and official data. Only 7.23% snakebite deaths were officially reported [6,7]. Earlier hospital based reports estimated about 1,300 to 50,000 annual deaths from snakebites per year in India. The registrar General of India's Million Death Study 2001-2003 conducted to ascertain the cause of death based on interviews by

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medical personnel and social workers in over a million households in randomly selected locations around India. The Million Deaths Study reported 46,000 deaths by snakebite in India per year; non-fatal bites may be as high as 1.4 million per year [7-11]. This proportion represents about 45,900 annual snakebite deaths nationally or an annual age-standardized rate of 4.1/100,000, with higher rates in rural areas (5.4) and with the highest rate in the state of Andhra Pradesh (6.2). Annual snakebite deaths were greatest in the states of Uttar Pradesh (8,700), Andhra Pradesh (5,200), and Bihar (4,500). Other Indian states with high incidence of snakebites cases are Tamil Nadu, West Bengal, Maharashtra and Kerala [12,13]. Because a large proportion of global totals of snakebites arise from India, global snakebite totals might also be underestimated. [14].

Indian cobra and common Indian krait are the important species which cause neurotoxic snake bites. Study conducted by Dr. Veer Bahadur Singh in North West Rajasthan in 2012 had shown that there was a directly proportional relationship between morbidity rates and time interval of bite and treatment with anti-snake venom. Most patients required less than 40 vials of ASV and the duration of treatment averaged from 4 hours to 3 days [15]. Dr. Naganath Redewod et al., from Nagpur, Maharashtra stated in his study that early arrival, appropriate and adequate treatment with ASV will prevent development and progression of complications in snake bite patients [16]. Study conducted in Uttar Pradesh by Prakash Chandra pandey et al. concluded that initial bolus close of 10 vials of ASV led to successful management of neurotoxic snake bites. . Among adjuvant drugs 60% ranatidin and 58.9% chymoral forte was used.

MATERIAL AND METHOD

Cross sectional Prospective observational conducted to All Patients alleged to be bitten by snake and admitted in Coimbatore Medical College Hospital. Human ethical committee e's clearance obtained before stating the study. The period of study was 6 months between Nov 2017 to April 2018. Standard dose is followed in the management of neurotoxic snake bite, administration of a high initial bolus dose of 200 ml ASV and repeated doses of 100 ml ASV every 6 hours until signs of neurological recovery, given along with neostigmine and atropine and supported by A/C mode of ventilation resulted in an early recovery, a reduced total dose of ASV consumed, reduced the duration of mechanical ventilation, reduced the incidence of complications and thus was much more cost effective.

TREATMENT MANAGEMENT PLAN

Maintenance therapy:

- 2 vials of antivenom every 6 hours x 3 doses (given 6, 12, and 18 hours after initial control).
- May not be needed if close observation by physician expert is available.

Follow-up planning:

- Patient should return for worsening swelling not relieved by elevation, or abnormal bleeding (e.g. melena, gum bleeding, easy bruising).
- If fever, rash, or muscle/joint pains occur (i.e., suggesting serum sickness), patient should return.
- Patient should be given bleeding precautions (no contact sports, elective surgery, or dental work for 2 weeks).

Follow-up:

- Patients who did not require antivenom: as needed.
- Copperhead victims: as needed.
- Cottonmouth and rattlesnake victims: repeat labs (CBC, PT, fibrinogen) twice (2-3 days and 5-7 days after discharge), then as needed.

CRITICAL ACTIONS

- Avoid the following:
 - Cutting or suctioning wound.
 - Ice.
 - NSAIDs: avoid in rattlesnake/cottonmouth victims
 - Prophylactic antibiotics.
 - Prophylactic fasciotomy.
 - Routine use of blood products.
 - Electrical shock therapy.
 - Steroids, unless allergic phenomena observed.
 - Tourniquets.

RESULTS

Most of the patient with age group of 22 to 72 years. Among that 64.1% was male and 35.1 was female attended the serious condition of snake bite. Majority of cases were male and Maximum incidence of snake bite occurred in the age group of 5 to 10. Lower extremities were the site of bite in more than three fourth of the cases.

Table 2. explained about the drug used along with anti-snake venom among that Tab. chymoral forte and H2 blocker like ranitidine were frequently used, Treatment with polyvalent anti-snake venom:

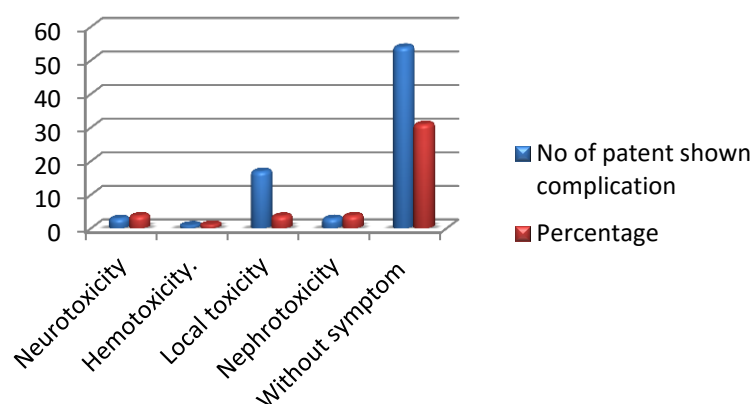
No of patient received anti-snake venom drug: 75

No of patient kept for observation: 03

No of patient undergone haemodialysis: 01

Table 3 explained about the patient received polyvalent anti-snake venom, total 75 patient were rescued by giving ASV, one required haemodialysis and three of them were kept for observation (non-critically). As per the complication concern with may symptom, neurotoxicity, hemotoxicity local and nephron toxicity was lower than the patient without complication which is 31%.

<div>Table 1. Social geography data</div> <div><div>Social geography data in Percentage</div><div><table><tr><td>Male</td><td>64%</td></tr><tr><td>Female</td><td>36%</td></tr></table></div></div>	Male	64%	Female	36%	<div>TABLE 3. Recipient of ASV</div> <div><div>Recipient of ASV</div><div><table><tr><td>ASV</td><td>75(96.2)</td></tr><tr><td>OBSERVATION</td><td>03(3.9)</td></tr><tr><td>HEAMODIALYSIS</td><td>01(1.3)</td></tr></table></div></div> <div>ASV: 75(96.2); Observation: 03(3.9); Heamodialsys: 01(1.3)</div>	ASV	75(96.2)	OBSERVATION	03(3.9)	HEAMODIALYSIS	01(1.3)																																															
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Table 4 . Type of complication**Table 4. Type of complication**

S.No	Complication	No of patent shown complication	Percentage
1	Neurotoxicity	3	3.8
2	Hemotoxicity.	1	1.2
3	Local toxicity	17	3.7
4	Nephrotoxicity	3	3.8
5	Without symptom	54	31

DISCUSSION

The present study was conducted after verifying, Type of symptom involved, warmth oedema, cellulites, gangrene of lower limb, No of patient received anti-snake venom. One individual shows anaphylaxis with anti-snake venom. Regular lab Investigation was done for the entire patient. HB %, WBC, RBC, Platelets, BUN, Urea, serum creatinine, LFT –TB, SGOT, SGPT, BT/CT, USG, Urine microscopy and ECG. The most of the patient comes with complication Neurotoxicity, Hemotoxicity. Local toxicity, vasculotoxic, Nephrotoxicity and more the 31% without any symptom. Treatment quality is highly varied, ranging from good quality in some areas, to very poor quality treatment in others. Cobra bite leads to early death hence reported less in hospital statistics as victim may not reach medical facility. The high fatality due to Krait bite is attributed to the non-availability of anti-snake venom (ASV), delayed and inappropriate administration of ASV, lack of standard protocol for management and inexperienced doctors and non-availability of ventilator or bag and valve [4]. In present study the potential fatality was low as treatment and emergency control was prompt, there has always been a crisis of ant-venom supply [4] and non –availability of effective ant-venom, poor potency, poor safety and the absence of published preclinical or well-designed clinical trial data for Indian ant-venoms are other concerns. Proper. it been proposed as a possible alternative therapy to antivenom is reduction of inflammation and pain so table no serratiopeptidase and some of the anti-inflammatory drug were uses because it

lessens the inflammation and pain caused by snake bites and other drug like H2 blocker, ceftriaxone, paracetamol and metronidazole were widely used in our clinical practices . In the state of Tamilnadu government much concern of death due to snakebite, and created holistic infrastructure to provide the ant venom and trauma facility to even primary health service level table 3 indicate the no of recipient received the ASV 96.2% and 3.9 % of patient kept for observation finally serviced. On one hand there is shortage of ASV but on the other hand scarce ASV is being wasted due to excessive dosage of ASV in the absence of a Standard Treatment Guideline [4]. Victims are not only misdiagnosed as - abdominal colic, and vomiting due to indigestion, appendicitis, stroke, head injury, ischemic heart disease, food poisoning, trismus, hysteria and Guillain-Barre' syndrome but also subjected to unnecessary investigations including MRI scans of the brain and lumbar puncture thus causing undue delay in ASV therapy. Delayed administration of ASV or waiting until victim develops systemic manifestations i.e., a 6 h wait results in systemic envenoming and high fatality (Bawaskar et al, 2008). In the current study we found the treatment and diagnosis was appropriately followed according to WHO guideline guidelines for the management of snakebites 2nd Edition, and standard treatment guidelines management of snake bite Quick Reference Guide July 2016 Ministry of Health & Family Welfare Government of India. Adjuvant therapy included in this study is table 2 Tab.Serratiopeptidase, Tab. Chymoral forte Inj.Neostigmine, Inj. Ampicillin,

Tab.Ranitidine Inj.Ceftriaxone, Cap. Cephalexin, Inj.Piptaz (Piperacillin (4000 mg) + Tazobactam (500 mg) Inj. Hydrocortisone, inj. Tramadol, Inj. Avil, Tab. Paracetamol, Inj.Thiamine, Tab. Atorvastatin, Inj. Frusemide, Inj. Metrogyl, Inj.Ondansetron and some of the required Hemodialysis. Among adjuvant drugs 60% ranatidin and 58.9% chymoral forte was used [15,16].

CONCLUSION

To reduce complications and deaths from snakebites, health systems need to be improved at various levels. Develop a policy by state government for snakebite, making it a notifiable disease, developing a

snakebite programme that includes standard treatment guidelines, training of health personnel and ensures an adequate supply, distribution and storage of good quality ant-venom. Strengthening of public health systems that have reduce the number of deaths reduce to snakebite in state of Tamilnadu India. This study is intended to analyse the time interval between the bite and treatment with ASV, average dose of ASV needed, adverse reactions encountered, complications due to snake bite, duration of treatment, abnormality in lab order parameters and clinical outcome of the snake bite patients admitted in our hospital.

REFERENCES

1. Prakash Chandra Pandey, Saruta Bajaj, Anubha Srivastava : A Clinico-Epidemiological Profile of Neuroparalytic Snake Bite: Using Low Dose ASV in a Tertiary Care Centre from North India: Journal of The Association of Physicians of India. 64, 2016.
2. Dr.NagnathRedewad, Dr.S.D.Bhaisare, Dr. Y.V. Bansod, Dr.Rohan Hire: Management and Outcome Study of Snake Bite Cases in Central India. Sch.J.App.Med.Sci., 2014;(ID):435-441
3. Dr.VeerBahadur Singh, Subhash Gaur, Deepak Kumar, BabulalMeena: Clinical Profile and Complications of Snake Bite Envenomation: Study from Tertiary Care Centre Bikaner: International Journal of Science and Research (IJSR), 4(6), 2015
4. Bawaskar HS, Bawaskar PH. Envenoming by the common krait (*Bungarus caeruleus*) and Asian cobra (*Naja naja*): clinical manifestations and their management in a rural setting. Wilderness Environ Med 2004;15:257-66.
5. Mohapatra B, Warrell DA, Suraweera W, Bhatia P, Dhingra N, et al. Snakebite mortality in India: a nationally representative mortality survey. PLoS Negl Trop Dis 2011;5:e1018.
6. Majumder D, Sinha A, Bhattacharya SK, Ram R, Dasgupta U, Ram A. Epidemiological profile of snake bite in South 24 Parganas district of West Bengal with focus on underreporting of snake bite deaths. Indian J Public Health 2014;58:17-21
7. Anil A, Singh S, Bhalla A, Sharma N, Agarwal R, Simpson ID. Role of neostigmine and polyvalent antivenom in Indian common krait (*Bungarus caeruleus*) bite. Journal of Infection and Public Health. 2010;3(2):83-7.
8. Anker RL, Anker KM, Straffon WG, Loiselle DS, Retarding the uptake of "mock venom" in humans: comparison of three first-aid treatments. Med J Aust. 1982, (5):212-4.
9. Antonypillai CN, Wass JA, Warrell DA, Rajaratnam HN. Hypopituitarism following envenoming by Russell's vipers (*Daboia siamensis* and *D. russelii*) resembling Sheehan's syndrome: first case report from Sri Lanka, a review of the literature and recommendations for endocrine management. QJM. 2011;104(2):97- 108.
10. Ariaratnam CA, Sjöström L, Raziak Z, Kularatne SA, Arachchi RW, Sheriff MH, et al. An open, randomized comparative trial of two antivenoms for the treatment of envenoming by Sri Lankan Russell's viper (*Daboia russelii*). Trans R Soc Trop Med Hyg. 2001;95(1):74-80.
11. Armentano RA, Bandt C, Schaer M, Pritchett J, Shih A. Thromboelastographic evaluation of hemostatic function in dogs treated for crotalid snake envenomation. J Vet Emerg Crit Care (San Antonio). 2014 Mar-Apr;24(2):144-53.
12. Bandyopadhyay SK, Bandyopadhyay R, Dutta A, Pal SK. Hypopituitarism following poisonous viperbite. J Indian Med Assoc. 2012 Feb; 110(2):120, 122.
13. Banerji RN, Sahni AL, Chacko KA. Neostigmine in the treatment of Elapidae bites. J Ass Physicins India 1972 July 20(7):503-9.
14. Bell DJ, Wijegunasinghe D, Samarakoon S, Palipana H, Gunasekera S, de Silva HA, et al. Neurophysiological findings in patients one year after snakebite induced neurotoxicity in Sri Lanka. Transactions of the Royal Society of Tropical Medicine and Hygiene 2010 May; 104(5): 351-6.
15. Belt PJ Malhotra A. Thorpe RS, Warrell DA, Wuster W. Russell's viper in Indonesia: snakebite and systematics. In: Thorpe RS, Wüster W, Malhotra A editions, Venomous snakes. Ecology, evolution and snakebite Oxford. , Clarendon Press, 1997 p. 219-34.
16. Bhat RN. Viperine snakebite poisoning in Jammu. J Indian Med Assoc. 1974 Dec 16; 63(12): 383-92.



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