

Efficacy of scorpion antivenom plus prazosin compared with prazosin alone for scorpion sting in children: A cross sectional study

R. Nagarjun, Pooja G. Manoli* and A. Ashoka

Department of Pediatrics, Jagadguru Jayadeva Murugarajendra Medical College (JJMMC), MCC B Block, Kuvempu Nagar, Davanagere-577004, Karnataka, India

Received: 27th January 2024; Accepted: 15th May 2024; Published: 01st July 2024

Abstract: *Background:* Scorpion sting can pose as a life threatening acute medical emergency, which, if not attended to on an emergency basis can result in mortality. Scorpion venoms are a composed of a complex mixture of proteins. There has been documentary evidence that scorpion antivenom and prazosin, an alpha blocker are very effective in reducing the mortality rate following scorpion bite. *Aim:* To compare the time required for complete resolution of the autonomic manifestations associated with prazosin alone and prazosin with antiscorpion venom in children with scorpion sting envenomation. *Methods:* This was a cohort study including 44 children less than 18 years of age, presenting to the paediatric emergency or outpatient department with scorpion sting within 10 hours of sting from the 2 hospitals attached to J.J.M Medical College, Bapuji Child Health Institute and C.G Hospital from November 2019 to November 2021. *Results:* The mean age was 10.35 ± 3.76 in the prazosin + antivenom group and in the prazosin group was 11.58 ± 3.87 years. Males were commonly affected. In the present study, overall, 14 cases (16.67%) presented within 4 hours of bite and 30 (83.3%) cases after 4 hours of bite. The clinical features seen in the prazosin alone group and prazosin + anti venom group was cold extremities, excessive sweating, CNS effects and cardiac involvement. 58.33% had evidence of grade 3 envenomation. The days of hospitalization was 5.39 days +2.72 days in the group prazosin + antivenom and in the group prazosin alone it was 9.27 ± 4.57 days. Higher doses of prazosin were used in those who received prazosin alone, mean was $8.50 \text{ SD } \pm 1.89$ and in group prazosin + antivenom, the mean was $6.00 \text{ SD } \pm 2.11$. Higher post medication cardiac dysfunction was seen in prazosin + antivenom, i.e 27.27% and the group prazosin alone it was 9.09%. *Conclusion:* As compared to prazosin alone the combination of prazosin with antivenom is very effective by reducing the time to alleviate the autonomic over activity.

Keywords: Prazosin, Prazosin + Antivenom, Scorpion, Envenomation.

Introduction

Scorpion sting can pose as a life threatening acute medical emergency, which, if not attended to on an emergency basis can result in mortality [1-2]. It is remarkable to note that, although, there are more than 86 species of scorpions that are known to mankind, only two are poisonous, i.e. *Mesobuthus tamulus* (Indian red scorpion) and *Heterometrus swammerdami* (Indian black scorpion) [3]. Children have a small built as compared to adults; hence, they are more likely to have a rapid deterioration and increased severity of symptoms because of their greater body surface area. Scorpion venoms are composed of a complex mixture of proteins [4]. The short chain peptides that consists of approximately 22 to 47

amino acids, interferes with the action of the of potassium ion channels and the long-chain peptides that consists of approximately 59 to 76 amino acid residues exerts its action by modifying the channel gating properties of the sodium channels [5-6]. Additional venoms that are present in the scorpion venom, have an action on the calcium and chloride ion channels, hyaluronidases, lysozymes and phospholipases [7].

Most of the complex toxins that are seen in the scorpion venom have an action on the ionic channels that play an imperative role in maintaining the resting membrane potential of cells that are excitable like cells of the muscular and the nervous system [6]. They

produce persistent depolarization of autonomic nerves with release of neurotransmitters from the adrenal medulla and parasympathetic and sympathetic nerve endings (the “autonomic storm”). These neurotransmitters are largely responsible for the toxic cardiovascular manifestations [6]. The toxin may also directly affect myocardial contractility and excitability. Central nervous system effects include irritability, muscle rigidity, altered consciousness and convulsions [8]. Prazosin is an anti-sympathetic agent that acts by blocking the alpha one postsynaptic region, thereby, abolishing the effects of the increased levels of catecholamines that occur following scorpion bite. Through this, it helps in reducing the progression of severe systemic disease [9].

There has been documentary evidence that scorpion antivenom and prazosin, an alpha blocker are very effective in reducing the mortality rate following scorpion bite [10]. Therefore, the aim of our study was to compare the time required for complete resolution of the autonomic manifestations associated with prazosin alone and prazosin with antiscorpion venom in children with scorpion sting envenomation.

Material and Methods

This was a cohort study including 44 children less than 18 years of age, presenting to the paediatric emergency or outpatient department with scorpion sting within 10 hours of sting from the 2 hospitals attached to J.J.M Medical College, Bapuji Child Health Institute and C.G Hospital from November 2019 to November 2021.

Exclusion Criteria:

1. Patient presenting with unknown bites.
2. Children aged >18 years of age.
3. Patients not willing to be included in the study.
4. Children with organic systemic infections especially CNS abnormalities.

Clinical Composite Scoring system (CCS) was used for assessment of severity of symptoms. The maximum CCS that could be attained is 25 and the minimum is zero. Patients with CCS 5-25 were included in the study, those with CCS of <5 at the time of admission were excluded.

SAV administration protocol: A single 30 mL dose of monovalent Mtamulus antivenom was added to 100 mL of normal saline, infused intravenously over 30 min, irrespective of the patient’s age, as per the protocol followed by Bawaskar and Bawaskar [8]. During the intravenous infusion, the patient was closely observed for anaphylactic reactions. Maximum of 4 doses were administered depending on the response.

Prazosin administration protocol: Tablet prazosin was given at a dose of 30 µg/kg/dose. The same dose was repeated at intervals of 3 hours until the extremities were warm. Children with complications were discharged only after they were stable and off the drugs for 24 h. Children who were administered SAV were observed for a period of 24 h post-SAV administration. Children with both AScV and Prazosin labeled group A and only Prazosin were labeled as group B.

Results

Based on age group: In the group prazosin+antivenom group, the mean age was 10.35±3.76 and in the prazosin alone group the mean was 11.58 years ± 3.87 years. (p=0.78)

Based on gender: Out of 44 patients, there were 36 males (81.8%) and 8 females (18.18%). In the prazosin + antivenom group there were 18 males (81.81%) and 4 females (18.18%). In the prazosin alone group, there were 17 males (77.27%) and 5 females (22.72%). (p=0.17)

Time of presentation after bite: In the present study, overall, 14 cases (16.67%) presented within 4 hours of bite and 30 (83.3%) cases after 4 hours of bite. In the prazosin + antivenom group we had 6 cases (27.27%) presented within 4 hours of bite and 16 (72.72%) cases after 4 hours of bite. In the prazosin alone group 6 cases (27.27%) presented within 4 hours of bite and 30 (72.72%) cases after 4 hours of bite. Between the two groups statistical analysis was done, the p value was 1, statistically not significant hence the two groups are comparable (Table 1).

Table-1: Time of presentation after bite

Time of presentation after bite	Group Prazosin + Antivenom	Prazosin Alone	Total	Group Prazosin + Antivenom	Prazosin Alone	Total	Mean/ SD
Less than 4 hours	4	5	9	9.09%	11.36%	20.45%	4/4.68
More than 4 hours	18	17	35	40.91%	38.64%	79.55%	18/5.34
P value – 0.08							

Table-2: Clinical features

Clinical Features	Cold Extremities	Excessive Sweating	CNS Effects	Cardiac Involvement
Prazosin Alone	20	18	11	1
Prazosin + Antivenom	21	15	13	2
Total	41	33	24	3
Prazosin Alone	90.91%	81.82%	50%	4.55%
Prazosin + Antivenom	95.45%	68.18%	59.09%	9.09%
Total	93.18%	75%	54.55%	6.82%
P value	0.33	0.33	0.58	0.33

Clinical features: The clinical features seen in the prazosin alone group and prazosin + anti venom group was cold extremities, excessive sweating, CNS effects and cardiac involvement. Between the two groups statistical analysis was done, the p value was more than 0.05, statistically not significant hence the two groups are comparable in terms of clinical features (Table 2).

Grade of envenomation: Between the two groups statistical analysis was done, the p value was 0.85, statistically not significant hence the two groups are comparable in terms of grade of envenomation. 58.33% had evidence of grade 3 envenomation. The grade of envenomation had a positive correlation to the onset of the disease.

Days of hospitalization: The days of hospitalization was 5.39 days + 2.72 days in the group prazosin + antivenom and in the group prazosin alone it was 9.27+ 4.57 days the p value the difference was statistically significant. (p= 0.0489)

Doses of prazosin: We noted that the higher doses of prazosin were used in those who received prazosin alone mean was 8.50 SD ± 1.89 and in group prazosin + antivenom the mean

was 6.00SD ±2.11. The p value the difference was statistically significant. (p=0.01) (Table 3).

Table-3: Doses of prazosin

Doses of Prazosin	Group Prazosin + Antivenom	Prazosin Alone
Mean	6.00	8.50
SD	2.11	1.89
P value	0.0148	Significant

Post medication cardiac dysfunction: Post medication cardiac dysfunction was seen in 18.18% of which in the group prazosin + antivenom it was 27.27% and the group prazosin alone it was 9.09% the p value the difference was statistically significant. (p= 0.042) (Table 4).

Days of hospitalization: The days of hospitalization was 5.39 days + 2.72 days in the group prazosin + antivenom and in prazosin alone it was 9.27 days+ 4.57 days the p value the difference was statistically significant. (p= 0.0489) (Table 5).

Post Medication Cardiac Dysfunction	Prazosin + Antivenom	Prazosin Alone	Total	Prazosin + Antivenom	Prazosin Alone	Total	P value
Yes	6	2	8	27.27%	9.09%	18 (18%)	0.042
No	16	20	36	72.73%	90 (91%)	81 (82%)	

Days of hospitalization	Mean duration	Less than 5 days	5 to 7 days	More than 7 days	Less than 5 days	5 to 7 days	More than 7 days
Antivenom + Prazosin	5.39 SD±2.72	9	5	1	60.00%	33.33%	6.67%
Prazosin	9.27 SD±4.57	4	3	8	26.67%	20.00%	53.3%
Total	7.25 SD +2	13	8	9	43.33%	26.67%	30.00%
P Value	0. 0489						

Discussion

The high incidence of severe and frequently fatal clinical symptoms, particularly in children, make scorpion sting envenomation a significant and grave global public health concern [11]. Scorpions inject their victims on the skin before injecting their poison subcutaneously using a stinger at the end of their multisegmented tail. The primary route by which venom is transported to the systemic circulation is through the lymphatics [12].

Natu et al noted that the males had a higher involvement which is in concurrence with our study [13]. Heart failure and cardiogenic pulmonary edema are the main causes of death from envenomation, with severity being correlated with hemodynamic and cardio-respiratory changes. On the other hand, its pathophysiology is still not well understood. Urgent care and intensive care are necessary for a few hours to several days due to the potentially fatal consequences of myocarditis and pulmonary edema [14]. The juxtaglomerular apparatus is affected by the venom of the scorpion, which causes these symptoms. The clinical features noted in our study were cold extremities, excessive sweating, CNS effects and cardiac involvement.

Himmatrao Saluba Bawaskar et al noted that the adverse effects when prazosin plus scorpion antivenom group compared with the prazosin alone groups were sweating (1.1) v 6.6 (2.6);

salivation 1.9 (0.9) v 3 (1.9); priapism 4.7 (1.5) v 9.4 (1.5). In the present study, it was observed that prazosin + antivenom group showed adverse effects such as pulmonary embolism was seen in 3 cases (20.00%), tachycardia in 4 cases (26.67%), bradycardia was seen in 2 cases (13.33%), hypertension was seen in 4 cases (26.67%), hypotension was seen in 1 case (6.67%) and sweating in 12 cases (80.00%). In the group prazosin, the adverse effects pulmonary embolism was seen in 4 cases (26.67%), tachycardia was seen in 2 cases (13.33%), bradycardia was seen in 3 cases (20.00%), hypertension was seen in 5 cases (33.33%), hypotension was seen in 2 cases (13.33%), sweating was seen in 13 cases (86.67%) and priapism was seen in 1 case (6.67%) [10].

Natu, et al noted that patients from the antivenom plus prazosin group recovered earlier (mean 8 hours) than those in the prazosin group (17.7 hours) [13]. However, the present study shows faster recovery in prazosin +antivenom group (7 hours) as compared to prazosin group. In the present study, lower doses of prazosin were used in the prazosin+antivenom which is comparable to the study by Bawaskar et al [12]. We noted that the prazosin+antivenom group had significantly lesser mortality than the antivenom group.

Post medication cardiac dysfunction was seen in 27.27% in the group prazosin + antivenom

and the group prazosin alone it was 9.09%. A study by Kumar PA et al. confirmed that administration of scorpion antivenom and prazosin within 4 hours of sting can reduce the cardiovascular morbidity and mortality. Lower rates of mortality was seen in the prazosin + antivenom group [15].

Conclusion

Our observation supports the data that prazosin + antivenom is an effective drug in serious cases of

scorpion envenomation with significant sympathetic symptoms. Prazosin + antivenom is fast acting, easily available, relatively cheap, free from any anaphylaxis, and highly effective. However, prazosin alone group shows high post medication cardiac dysfunction. As compared to prazosin alone the combination of prazosin with antivenom is very effective by reducing the time to alleviate the autonomic over activity.

Financial Support and sponsorship: Nil

Conflicts of interest: There are no conflicts of interest.

References

1. Isbister GK, Bawaskar HS. Scorpion envenomation. *New England J of Medicine*. 2014; 371(5):457-463.
2. Firoozfar F, Saghafipour A, Jesri N. Scorpions and their human mortality report in Iran: a review article. *Iranian J of Public Health*. 2019; 48(12):2140.
3. Dehghani R, Rabbani D, Hoseindoost GR, Mashayekhi M. Deadly scorpion habitats of Iran. *Indian J Fund Appl Life Sci*. 2014;4:480-484.
4. Zeh DW. Beyond the Sting: The Biology of Scorpions. Gary A. Polis, Ed. Stanford University Press, Stanford, CA, 1990. xxvi, 587 pp., illus. \$85. *Science*. 1990; 249(4973):1176-1177.
5. Billen B, Bosmans F, Tytgat J. Animal peptides targeting voltage-activated sodium channels. *Current Pharmaceutical Design*. 2008; 14(24):2492-2502.
6. Shen H, Li Z, Jiang Y, Pan X, Wu J, Cristofori-Armstrong B, Smith JJ, Chin YK, Lei J, Zhou Q, King GF. Structural basis for the modulation of voltage-gated sodium channels by animal toxins. *Science*. 2018; 362(6412).
7. Hmed B, Serria HT, Mounir ZK. Scorpion peptides: potential use for new drug development. *J Toxicol*. 2013; 2013:958797.
8. Bawaskar HS, Bawaskar PH. Scorpion sting. *J Assoc Physicians India*. 1998; 46(4):388-92.
9. Tiwari L, Kumar M, Srivastava M. Scorpion sting: Myriad presentation in PICU. *J of Pediatric Critical Care*. 2019; 6(3):40.
10. Bawaskar HS, Bawaskar PH. Efficacy and safety of scorpion antivenom plus prazosin compared with prazosin alone for venomous scorpion (*Mesobuthus tamulus*) sting: randomised open label clinical trial. *BMJ*. 2011; 342.
11. Gupta V. Prazosin: a pharmacological antidote for scorpion envenomation. *J Trop Pediatr*. 2006; 52:150-151.
12. Ranu Alpay N, Satar S, Sebe A, Demir M, Topal M. Unusual presentations of scorpion envenomation. *Hum Exp Toxicol*. 2008; 27:81-85.
13. Natu VS, Kamerkar SB, Geeta K, et al. Efficacy of anti-scorpion venom serum over prazosin in the management of severe scorpion envenomation. *J Postgrad Med*. 2010; 56:275-280.
14. Adhisivam B. Of prazosin and purses. *Lancet*. 2006; 368(9550):1870.
15. Kumar PA, Krishnamurthy S, Srinivasaraghavan R, Mahadevan S, Harichandrakumar KT. Predictors of myocardial dysfunction in children with Indian red scorpion (*Mesobuthus tamulus*) sting envenomation. *Indian Pediatrics*. 2015; 52(4):297-301.

Cite this article as: Nagarjun R, Manoli PG and Ashoka A. Efficacy of scorpion antivenom plus prazosin compared with prazosin alone for scorpion sting in children: A cross sectional study. *Al Ameen J Med Sci* 2024; 17(3): 257-261.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial (CC BY-NC 4.0) License, which allows others to remix, adapt and build upon this work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

*All correspondences to: Dr. Pooja G. Manoli, Assistant Professor, Department of Pediatrics, Jagadguru Jayadeva Murugarajendra Medical College (JJMMC), MCC B Block, Kuvempu Nagar, Davanagere-577004, Karnataka, India. E-mail: pjmnanoli@gmail.com