

The Effect of Neutrophil/Lymphocyte Ratio and Mean Platelet Volume on the use of Antivenom in Snake Bites and Scorpion Stings

Yılan ve Akrep Sokmalarında Nötrofil/Lenfosit Oranı ve Ortalama Trombosit Hacminin Antivenom Kullanımına Etkisi



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ABSTRACT

Objective: We evaluated the distribution, use of antivenom, treatments applied during the follow-ups, and effects on the use of NLR and MPV antivenom in cases of snake bites and scorpion stings followed in the paediatric intensive care unit (PICU) and the effects of these cases on the length of stay in the intensive care unit and hospital.

Materials and Methods: Demographic characteristics of the patients followed in the PICU and the severity of their clinical findings at admission, antivenom use after snake and scorpion bites were retrospectively examined from the clinical course in the hospital automation system and archived file records.

Results: Of 38 patients who were followed up in the PICU for snake and scorpion bites, half were followed up for snake bites and half for scorpion bites. Antivenom treatment was applied according to the clinical stage. There was a positive correlation between antivenom-administered patients and NLR ($p<0,05$). When snake bites and scorpion stings were examined separately, there was a positive correlation between antivenom application and NLR in snake bites ($p<0,05$), but no correlation was found in scorpion stings ($p>0,05$).

Conclusion: Consequently, antivenom therapy is the main treatment for snake bites and scorpion stings. We think that the NLR value will be significant in deciding to apply antivenom to patients, especially in snake bites. In addition, those with high NLR values need to be closely observed in terms of compartment development.

ÖZET

Amaç: Çocuk yoğun bakım ünitesinde (ÇYBÜ) yılan ve akrep sokmasıyla takip edilen hastalarda NLR VE MPV değerlerinin antivenom kullanımına etkisini ve bu değerlerin yoğun bakım ünitesi ve hastanede kalış sürelerine etkisini değerlendirmek amaçlandı.

Gereç ve Yöntem: Yoğun bakım ünitesinde izlenen hastaların demografik özellikleri ve başvuru anındaki klinik bulgularının şiddeti, yılan ve akrep sokması sonrası antivenom kullanımı, hastane otomasyon sistemindeki klinik seyir ve arşivlenen dosya kayıtlarından retrospektif olarak incelendi.

Bulgular: ÇYBÜ'de yılan ve akrep sokması nedeniyle izlenen 38 hastanın yarısı yılan, yarısı akrep sokması nedeniyle takibe alındı. Klinik evreye göre antivenom tedavisi uygulandı. Antivenom uygulanan hastalar ile NLR arasında pozitif korelasyon saptandı ($p<0,05$). Yılan sokması ve akrep sokması ayrı ayrı incelendiğinde antivenom uygulaması ile NLR arasında yılan sokmasında pozitif korelasyon bulunurken ($p<0,05$), akrep sokmasında ise herhangi bir korelasyon bulunmadı ($p>0,05$).

Sonuç: Sonuç olarak yılan sokması ve akrep sokmalarında ana tedavi antivenom tedavisidir. Özellikle yılan sokmalarında hastalara panzehir uygulama kararı vermede NLR değerinin önemli olacağını düşünüyoruz. Ayrıca NLR değeri yüksek olanların kompartman gelişimi açısından yakından izlenmesi gerekir.

Keywords:

Paediatric intensive care
Snake and scorpion bite
Neutrophil/lymphocyte ratio
Antivenom administration

Anahtar Kelimeler:

Çocuk yoğun bakım
Yılan ve akrep ısırığı
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INTRODUCTION

Snake bites and scorpion stings cause serious health problems in tropical regions. Snake bites and scorpion stings are very important causes of mortality and morbidity that require urgent intervention (1). More than 50,000 cases of snake bites and scorpion stings are reported annually in developing countries, and more than 2,600 deaths are reported annually due to these poisonings. Snake bites and scorpion stings generally cause serious deaths in tropical regions (2,3).

Snake bites and scorpion stings in Turkey are mostly seen in hot regions, especially in the southern regions. The

composition of snake venom causes biochemical and toxicological consequences that determine a wide variety of clinical manifestations. Some of the toxins in snake venom cause local tissue damage and may lead to permanent sequels, while others cause neurotoxic manifestations such as respiratory paralysis, systemic effects such as hemorrhage, acute kidney injury, cardiotoxicity including rhabdomyolysis, autonomic hyperactivity, or thrombosis. These toxins show the properties of platelet aggregation, thrombin-like activity, procoagulant metalloproteases, and factor V and X activators, which are involved in the activation of the coagulation pathway. Venoms found

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in Viperidae snakes cause systemic symptoms such as bleeding, coagulation disorders and hypovolemic shock. Scorpion venom is a mixture of many toxins and enzymes. The most important event that reveals systemic findings is that toxins affect excitable cells, especially sodium channels. Because of these effects of toxins on cells, sympathetic or parasympathetic system activation occurs due to the increase in catecholamines and the increase in inflammation products contributes to the emergence of this clinic. In addition, as a result of increased levels of catecholamines, inflammation products and vasoactive substances, severe clinical consequences such as pulmonary edema, heart failure and autonomic storm occur (4,5).

There are debates about antivenom applications in animal bites and stings. This is especially important in patients in the risk group such as children and the elderly. There are limited studies on animal bites and stings in children, and it has been reported that antivenom applications reduce mortality in children (6).

The neutrophil/lymphocyte ratio (NLR) is calculated using neutrophil and lymphocyte values in the hemogram and is an indicator whose popularity is increasing these days. NLR is generally accepted as an indicator and prognostic marker of subclinical inflammation. NLR increases in inflammatory diseases, but there is no defined cut-off value or upper NLR limit for paediatric patients in the literature (7,8). Forget et al. reported a normal value for NLR in healthy adults between 0.78 and 3.53 (9).

Mean platelet volume (MPV) is an important marker in determining platelet functions and prognostic features of some diseases. In addition, MPV is an indicator of platelet aggregation, thromboxane A2, thromboglobulin release and platelet activation. It has been shown in clinical practice that hemogram parameters such as NLR and MPV can be used as markers of systemic inflammation in a wide variety of diseases. MPV is directly in the hemogram. NLR can be obtained by dividing the number of neutrophils by the number of lymphocytes (10-12).

We evaluated the distribution, use of antivenom,

complications developed during the follow-ups, the treatments applied during the follow-ups and effects on the use of NLR and MPV antivenom in cases of snake bites and scorpion sting followed in the paediatric intensive care unit (PICU) and the effects of these cases on the length of stay in the intensive care unit and hospital. In addition, we aimed to contribute to the literature by comparing the results of the obtained data with standard applications.

MATERIALS AND METHODS

Demographic characteristics of the patients followed in the PICU between 01/01/2018-24/08/2022, the severity of their clinical findings at admission, antivenom use after snake and scorpion bites and complications before and after antivenom were retrospectively examined from the clinical course in the hospital automation system and archived file records. Only snake bites and scorpion stings were included in the study, while excluding other animal bites. European viper antiserum (10ml/vial) and scorpion serum (5ml/1vial) provided by the Ministry of Health were used as snake and scorpion serums and were administered intravenously.

The SPSS program and Excel programs were used for the statistics of the study. Categorical variables were summarized as numbers and percentages. Continuous variables are summarized as the mean and standard deviation. Spearman rank correlation coefficient was used to evaluate the obtained data. Statistical significance level was set as $p < 0.05$ in all tests.

Approval no 188 dated 30/09/2022 for the study was obtained from the ethics committee of Diyarbakır Gazi Yaşargil Training and Research Hospital.

RESULTS

Of the 3006 patients followed in the PICU, 38 were hospitalized for snake bites and scorpion stings. Half of the patients were followed up for snake bites and the other half for scorpion stings. 57.9% of the patients were male. The mean age was 109.18 ± 64.53 months. July, August, and September were the months with the most frequent admissions, with eight patients each. The least application was in November with one patient. 71.1% of

Table 1: Demographic data of patients.

	Snake n=19	Scorpion n=19
Age (months) n (%)	129.47 ± 61.94	88.89 ± 61.28
Gender (n) Male/Female	12/7	10/9
The direct application to the hospital n (%)	5 (26.3%)	8 (42.1%)
Country n (%)	16 (84.2)	11 (57.9%)
Town center n (%)	3 (%15.8)	8 (%42.1)
Time to hospital arrival after bite (hour) Mean ± St.dev.	1.66 ± 1.16	1.11 ± 0.46
Glasgow Coma Scale Mean ± St.dev.	14.68 ± 0.95	14.11 ± 1.88
Prism score Mean ± St.dev.	10.0 ± 2.94	10.74 ± 4.18
Intensive care stay (hour) Mean ± St.dev.	41.37± 36.53	24.63 ± 21.48
The length of the hospital stay (hour) . Mean ± St.dev.	110.16± 95.07	47.47 ± 28.22
The presence of local extremity findings n (%)	14(73.7%)	7 (36.8%)
The presence of systemic manifestations n (%)	7 (36.8%)	9 (47.4%)
Compartment syndrome n (%)	2 (10.5%)	-

the patients applied from the rural areas and 28% from the city centre. While 34.2% of the patients applied directly to the hospital, the remaining 65.8% were transferred from other hospitals. The mean time to hospital admission after the bite was 1.38±0.91 hours. The mean Glasgow Coma Scale of the patients was 14.39±1.49, and the mean Prism III score was 10.37 ±3.58. The mean length of stay in the intensive care unit was 33.71±20.75 hours and the mean hospital stay was 78.82±56.11 hours (Table 1).

Of the 19 patients with snake bites, three had local edema, three had one joint edema, and eight had edema that went beyond one joint. Edema was not detected in five patients. Orthopaedic consultation was requested in 7 (37%) patients with snake bites and compartment syndrome developed in two patients. Fasciotomy was performed in patients who developed compartment syndrome. Edema

was not detected in 12 patients with scorpion stings. Local edema was observed in six patients who developed edema, and edema in one joint was observed in one patient. There was no patient with edema that went beyond the joint in scorpion stings. Limb elevation was performed in 11 patients with snake bites and one patient with scorpion sting. None of the patients with scorpion stings required orthopaedic consultation and none developed compartment syndrome. (Table 2).

Antivenom was administered to 11 patients with snake bites and 15 patients with scorpion stings. The centers where the applied antivenom were made and their amounts are given in Table 3. The mean time of first antivenom administration after exposure was 2.15±1.34 hours. Re-dose of antivenom was needed in 7 (63.6%) patients in snake bites and in 2 patients in scorpion stings. Repeat

Table 2: Local and systemic findings and antivenom administration in patients.

		No antivenom administered				Antivenom administered	
		Snake	Scorpion	Snake	Scorpion	Snake	Scorpion
Local findings	Yes	14(74%)	7(37%)	3(16%)	-	11(58%)	7(37%)
	No	5(26%)	12(63%)	5(26%)	4(21%)	-	8 (42%)
Systemic findings	Yes	7(37%)	9(47%)	-	-	7(37%)	9(47%)
	No	12(63%)	10(53%)	8(42%)	4(21%)	4(21%)	6(32%)
Edema	No edema			5(26%)	4(21%)	-	8(42%)
	Localized			2(11%)	-	1(5%)	6(32%)
	In a joint			1(5%)	-	2(11%)	1(5%)
	Exceeded the joint			-	-	8(42%)	-

Table 3: The centers where antivenom is given and the amount of antivenom administered in the centers.

Where the antivenom were administered	Snake bite				Scorpion bite	
	The amount of antivenom (doses)					The amount of antivenom (doses)
	1 dose	2 doses	4 doses	5 doses	Doses	
First centre. n	3	0	0	0	9 doses	
Our hospital. n	0	3	1	4	6 doses	

Table 4: Correlation analyzes between variables.

	Mean	Std. Deviation	NLO	MPV	Length of stay in the PICU (hours)	Length of hospital stay (hours)	Antivenom administered
NLR	7.41	8.98					
MPV	9.33	1.37	.240				
Length of stay in the PICU (hours)	33.00	30.75	.45**	0.006*			
Length of hospital stay (hours)	78.82	76.11	.67**	0.27*	.82**		
Antivenom administered	0.68	0.47	.41**	0.06*	.51**	.49**	
Repeat doses of antivenom	0.35	0.49	0.37*	0.17*	.63**	.59**	c

*: Correlation is significant at the 0.05 level (2-tailed).

** : Correlation is significant at the 0.01 level (2-tailed).

c: Cannot be computed because at least one of the variables is constant.

doses were administered an average of 6.22 ± 2.05 hours after the first dose. Only in snake bites, four patients received a second dose of antivenom 4 hours after the first dose. Local findings were detected in 21 patients and systemic findings were detected in 16 patients. The most common local finding was edema; and the most common systemic finding was tachycardia. All patients were vaccinated against tetanus.

Antivenom treatment was applied according to the clinical stage. A total of 26 patients were treated with antivenom. Antisera provided by the Ministry of Health as snake and scorpion serum were administered intravenously. The allergic reactions were observed in 2 patients and fever in 1 patient due to antiserum. Other than these, no reaction was observed.

The mean NLR was 7.41 ± 8.8 and the mean MPV was 9.32 ± 1.37 at the time of the first admission. There was a positive correlation between antivenom-administered patients and NLR ($p < 0.05$). When snake bites and scorpion stings were examined separately, there was a positive correlation between antivenom application and NLR in snake bites ($p < 0.05$), but no correlation was found in scorpion stings ($p > 0.05$). No correlation was found between MPV values and antivenom use ($p > 0.05$). In addition, no significant correlation was found between antivenom repeat doses and NLR. There was a positive correlation between NLR and ICU follow-up and hospital stay. We found that as the NLR level increased, the length of the hospital stay was prolonged ($r: 0.45/0.67$ and $p < 0.05$, respectively) (Table 4). The mean NLR and MPV of two patients who developed compartment syndrome due to snake bites were significantly higher (14.67 ± 9.34 and 9.15 ± 1.20 , respectively). In patients who developed compartment syndrome, the first antivenom application time was observed as 1 hour after the bite. A repeat dose of antivenom was administered to a patient who developed compartment syndrome at the 4th hour, and repeat doses were administered to the second patient at 4th hours and 10th hours. No mortality was detected in our patients.

DISCUSSION

In our study, there were 38 cases, half of which were snake bites, and the other half were scorpion stings. Most of our patients were boys and adolescents who applied during the summer. The most common finding observed in our cases was local edema and the most common systemic finding was tachycardia. Our data overlap with studies reported with scorpion bites and snake stings. Snake toxin contains enzymes and proteins. These enzymes and proteins cause severe inflammatory responses and ultimately tissue damage. In snake bites, symptoms such as local swelling, edema and hematoma may include vomiting, circulatory collapse, convulsions, coma, disseminated intravascular coagulopathy, compartment syndrome, acute kidney failure, intracranial haemorrhage, and death (13,14). Edema developed in 74% of our patients and compartment syndrome developed in two of our patients followed up with snake bites, and fasciotomy was performed.

Antivenom therapy is the main treatment for snake bites and scorpion stings (15). In the study of Neslihan Zengin et al. in 23 patients with scorpion stings, antivenom was

applied to 14 (60.8%) patients in Turkey. In a study conducted with snake bites in 61 patients, antivenom was administered to 44 (72.1%) patients (16). In our study, antivenom was administered to 11 patients with snake bites and 15 patients with scorpion stings, and these rates are similar to those in previous studies.

MPV and NLR were measured in the laboratory as part of complete blood counts. Studies have suggested that increased MPV and NLR are associated with inflammation (12). Elbey et al. showed that high NLR levels are associated with prolonged hospitalization and different clinical course in adult patients with snake bites (17). Conversely, in a study conducted by Aktar et al. with paediatric patients, they could not find a relationship between MPV, NLR, and the severity of snake bites (18). In our study, there was a statistically significant positive correlation between NLR during the patients' admission to the intensive care unit and antivenom use, length of hospital stays, length of stay in the intensive care unit, and re-administration of antivenom ($p < 0.05$). In fact, the mean NLR and MPV of two patients who developed compartment syndrome in snake bites were much higher than the mean values at the time of first admission. However, this relationship was not observed in scorpion stings ($p > 0.05$). In addition, in scorpion stings, no statistically significant positive correlation was observed between MPV and antivenom use, length of hospital stay, length of stay in intensive care unit, and readministration of antivenom ($p > 0.05$) (Table 4). There are no studies on the relationship between scorpion stings and MPV and NLR. It was thought that this situation might be because the toxins in snake venom cause local tissue damage and show the properties of platelet aggregation, thrombin-like activity, procoagulant metalloproteases and factor V and X activators, which are involved in the activation of the coagulation pathway and show their effect by affecting the inflammatory processes more. None of our patients died due to snake bites or scorpion stings.

Consequently, antivenom therapy is the main treatment for snake bites and scorpion stings. There is a need for clearer data regarding the follow-up of these patients and their decisions regarding the use of antivenom. Recently, there have been studies on the severity of the disease and the length of the hospital stay with NLR in paediatric patients with snake poisoning (12,18). We think that the NLR value will be significant in deciding to apply antivenom to patients, especially in snake bites. In addition, those with high NLR values need to be closely observed in terms of compartment development. Studies with larger patient groups are needed to elucidate the severity of the disease in snake bites and scorpion stings.

Conflict of Interest: No conflict of interest was declared by the authors.

Ethics: This study was approved by the Diyarbakır Gazi Yaşargil Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (Date: 30/09/2022, Number: 188).

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