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Research

Severe Scorpion Envenomations in Pediatric Intensive Care Unit

Çocuk Yoğun Bakım Ünitesinde Akrep Sokması Olguları

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ABSTRACT

Objective: This study aimed to determine the general characteristics and warning signs for the more severe (grade 3) clinical course in severe scorpion envenomations in the pediatric intensive care unit (PICU).

Methods: This retrospective, cross-sectional study was conducted in 12 beds tertiary care PICU in Antalya Training and Research Hospital. Patients admitted to the PICU between 2017-2021 due to severe scorpion envenomation were admitted to the study.

Results: It was found that there were 2,208 admissions to the intensive care unit during the study period (4 years), and 73 (3.3%) of these cases (35 female and 38 male) were followed up for severe scorpion envenomation. The median age was 52 (26-89) months. Yellow scorpions were described by parents or eyewitnesses in 65 patients (89%) and black scorpions in 8 (11%). Peripheral sympathetic activity (cold extremities, diaphoresis) signs (n=55, 75.3%), hypertension (n=35, 47.9%), and tachycardia (n=21, 28%) were the most common findings. The most common echocardiographic findings were mild-to-moderate mitral regurgitation and systolic dysfunction in 31 (42.5%) and 19 (25.9%) cases, respectively. Sixty-two (89%) patients had grade 2 envenomations findings and 12 (11%) had grade 3. High pro-BNP, hyperglycemia, and hyperamylasemia were observed more frequently in grade 3 than in grade 2 patients on admission. All patients received anti-venom therapy and 7 (9.5%) of them required a second dose of anti-venom therapy due to the unregressed clinical course. Twenty-seven patients (37%) required inotropics, s and the most commonly used inotropics were milrinone in 17 (23.3%) patients and dobutamine in 12 (16.4%) patients. The median PICU length of stay was 4 (3-5) days and the median hospital stay was 5 (4-6) days. All patients survived to discharge.

Conclusion: Hyperamilasemia, hyperglycemia, and elevated pro-BNP levels on admission may be warning signs of more severe (grade 3) patients. Mild-to-moderate mitral regurgitation may be more commonly observed echocardiography findings than systolic dysfunction in severe cases (grade 2 and 3).

Keywords: Scorpion stings, intensive care units, pediatric, hyperamylasemia

ÖZ

Amaç: Bu çalışmanın amacı çocuk yoğun bakım ünitesinde (ÇYBÜ) takip edilen ağır akrep ısırığı olgularının genel özelliklerini ve daha ağır (grade 3) seyirli olgular açısından uyarıcı bulguları ortaya koyabilmektir.

Gereç ve Yöntem: Bu retrospektif, kesitsel çalışma Antalya Eğitim ve Araştırma Hastanesi'nde 12 yataklı üçüncü basamak ÇYBÜ'de yürütülmüştür. ÇYBÜ'ye 2017-2021 yılları arasında ağır akrep sokması nedeniyle yatırılan olgular çalışmaya dahil edildi.

Bulgular: Çalışma periyodunda (4 yıl) çocuk yoğun bakım ünitesine 2.208 olgunun yatırıldığı ve bu olguların 73 (%3,3) tanesinin (35 kız ve 38 erkek) akrep sokması olguları olduğu tespit edildi. Ortanca yaş 52 (26-89) aydı. Ebeveynler tarafından yapılan tanımlamaya göre 65 (%89) olguda sarı akreplerin, 8 (%11) olguda ise siyah akreplerin sorumlu olduğu görüldü. Periferik sempatik aktivite bulguları (soğuk ekstremiteler ve terleme) 55 (%75,3) olguda, hipertansiyon 35 (%47,9) olguda ve taşikardi 21 (%28) olguda mevcuttu. En sık gözlenen ekokardiyografi bulguları 31 olguda (%42,5) hafif-orta mitral kapak regürjitasyonu ve 19 (%25,9) olguda görülen sistolik disfonksiyondu. Altmış beş (%89) olguda grade 2 akrep sokması bulguları varken 12 olguda (%11) grade 3 bulgular mevcuttu. Başvuru sırasında pro-BNP yüksekliği, hiperamilasemi ve hiperglisemi grade 3 olgularda grade 2 olgulara göre daha sık gözlendi. Tüm olgular anti-venom tedavisi alırken 7 (%9,5) olguda klinik gidişin gerilememesi

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nedeniyle ikinci doz tedavi gerekli oldu. Yirmi yedi (%37) olguda inotrop gereksinimi olurken bu olguların 17'sinde (%23,3) milrinon, 12'sinde (%16,4) ise dobutamin kullanıldı. Ortanca çocuk yoğun bakım süresi 4 (3-5) gün, ortanca hastane yatış süresi ise 5 (4-6) gün olarak tespit edildi. Olgular arasında mortalite gözlenmedi.

Sonuç: Başvuru sırasında gözlenen hiperamilazemi, hiperglisemi ve yüksek pro-BNP düzeyleri daha ağır (grade 3) seyirli olabilecek hastalar açısından uyarıcı bulgular olabilir. Hafif-orta düzeydeki mitral regürjitasyonun ağır olgularda (grade 2 ve 3) sistolik disfonksiyona göre daha sık gözlenebilen bir ekokardiyografi bulgusu olduğu görülmektedir.

Anahtar Kelimeler: Akrep sokmaları, yoğun bakım ünitesi, pediatrik, hiperamilazemi

INTRODUCTION

Scorpions, the oldest arthropod species living on Earth, have been a major problem throughout human history. Nearly 3,000 species of scorpions have been described worldwide, and they live everywhere in the world except Antarctica. In Turkey, 27 species of scorpion have been described in four families (Buthidae, Iuridae, Scorpionidae and Euscorpiidae) (1). The most medically important scorpion species in Turkey are Androctonus, Leiurus and Mesobuthus species from the family Buthidae (2). Although the most cases of scorpion envenomation in Turkey occur below the 39th parallel (central and southern Aegean region, the Mediterranean region, and central, west, and southwestern region of Anatolia), the risk of scorpion envenomation exists in all regions of Turkey (3). The main causes of death in scorpion envenomation are hemodynamic disturbances and pulmonary edema. This study reveals the general characteristics of scorpion envenomation in children and determination of variables that may lead to early recognition of the most severe (grade 3) patients.

METHODS

This retrospective cross-sectional study was conducted in a 12-bed tertiary care pediatric intensive care unit (PICU) of Antalya Training and research Hospital that admits approximately 500 medical and surgical patients annually and is located on the southwestern coast of Turkey. The severity of the patients was determined according to the staging system used by Khattabi et al. (4). Only local manifestations are grade 1, non-life-threatening systemic manifestations (hypertension, nausea, convulsions, lethargy, tachycardia, etc.) are grade 2 (severe), and life-threatening systemic manifestations (hypotension, ventricular arrhythmia, bradycardia, collapse, respiratory failure, neurological failure) are defined as grade 3 (more severe). According to our scorpion stings protocol, only patients with systemic symptoms (grade 2 and 3) were admitted to the PICU.

Equine antivenom (Androctonus crassicauda) was used for anti-venom therapy. Before the anti-venom infusion, a skin test was performed routinely. Five milliliters (one ampoule) of anti-venom was diluted with 50 milliliters of normal saline and infused over 30 min in all patients.

Patient records (between 2017 and 2021) were retrospectively reviewed after University of Health Sciences Turkey, Antalya Training and Research Hospital Ethics Committee approval was obtained (decision no: 1/28, date: 04.03.2021). Patient demographics, signs and symptoms on admission, echocardiography findings, laboratory results, specific treatments (anti-venom, doxazosin), intensive care treatments (inotropic and vasoactive medications, sedatives, respiratory support), intensive care, and length of hospital stay were recorded. Patients, whom scorpion could not be observed and were treated with suspicion based on clinical findings were excluded from the study.

Systolic dysfunction was defined by an ejection fraction of less than 55% (40-55% mild, 30-40% moderate, and <30% severe). Hyperglycemia was defined as blood glucose level >140 mg/dL (5), elevated creatine kinase (CK) defined as CK level >200 U/L (laboratory upper limit), elevated troponin T defined as troponin level >14 ng/L (6), elevated myoglobin level defined as myoglobin level >72 ng/mL (laboratory upper limit), elevated pro-BNP defined as pro-BNP level >300 ng/L (7), hyperamylasemia defined as amylase level >110 U/L (8), hyperlipasemia defined as lipase level >160 U/L (9), and leukocytes (white blood cells) >10x10^3/mm^3 (laboratory upper limit) was defined as leukocytosis.

Statistical Analysis

Categorical variables were expressed as n (%) and continuous variables were expressed as median (interquartile range: 25p-75p). The chi-square test or Fisher's Exact test was used to compare categorical variables between the two groups. Mann-Whitney U test was used for the comparison of continuous variables between the two groups. Statistical calculations were performed with the Statistical Package for Social Sciences (SPSS) for Windows version 23 and MedCalc for Windows version 14.8.1.

RESULTS

It was found that there were 2,208 admissions to the PICU during the study period (4 years), and 73 (3.3%) of these cases (35 female and 38 male) were followed up due to severe scorpion envenomation. Fifty-one (69.8%) of the patients were admitted to the PICU between June and

September. Yellow scorpions were described by parents or eyewitnesses in 65 patients (89%) and black scorpions in 8 (11%). The demographic features of the patients are presented in Table 1.

Peripheral sympathetic activity signs (cold extremities, diaphoresis) were the most common findings on admission (n=55, 75.3%). Other common findings were shortness of breath in 22 (30.1%) patients, hypertension in 35 (47.9%) patients, nausea in 27 (37%) patients, bradycardia in 2 (2.7%) patients, tachycardia in 21 (2.8%) patients, hypotension in 7 (9.6%) patients, priapism in 3 (4.1%) patients, and pulmonary edema in 5 (6.8%) patients.

Abnormal laboratory findings in the patients were as follows. Hyperglycemia in 19 (26.8%), leukocytosis in 47 (66.2%) patients, hyperamylasemia in 25 (42.4%) patients, elevated troponin T in 41 (59.4%) patients, elevated myoglobin in 31 (68.9%) patients, elevated pro-BNP in 17 (23.3%) patients, and elevated CK was detected in 49 (71%) patients (Table 2). Lipase elevation was not observed in the patient.

The median ejection fraction of the patients on echocardiography was 63% (52-66). The most common abnormal echocardiographic finding was mild-to-moderate mitral regurgitation, which was noted in 31 (42.5%) patients. Other abnormal echocardiographic findings were mild systolic dysfunction in 17 (23.2%), moderate systolic dysfunction in 2 (2.7%) patients, and mild tricuspid regurgitation in 13 (17.8%) patients.

All patients received anti-venom therapy and 7 (9.5%) of them required a second dose of anti-venom because of the unregressed clinical course. The most commonly used treatment agent was doxazosin in 49 (67.1%) patients. Furosemide was used in 23 (31.5%) patients. Twenty-seven (37%) patients required inotropic and/or vasoactive support. The following inotropic and vasoactive agents were used in the patients: milrinone in 17 (23.3%) patients, dobutamine in 12 (16.4%) patients, epinephrine in 9 (12.3%) patients, dopamine in 4 (5.5%) patients, and norepinephrine in 5 (6.8%) patients. Dexmetatomidine was used in 21 (28.8%) patients for its sedative, analgesic, and sympatholytic properties. Seventeen patients (22.2%) required invasive positive pressure ventilation and five patients (5.6%) required invasive mechanical ventilation.

Cardiac arrest and cardiopulmonary resuscitation were required in two (2.7%) patients. The median PICU length of stay was 4 (3-5) days and the median hospital stay was 5 (4-6) days. All patients were discharged without morbidity or mortality, except for one patient who developed neuromotor disability because of cardiac arrest.

DISCUSSION

Scorpion envenomation is an important health problem in children, especially those under 5 years of age. This is because most of the reported deaths occur under the age of 5 years (10). It is recommended that patients with scorpion envenomation who present with systemic symptoms should be followed up in the PICU (11). In this study, we show the general characteristics and frequency of children with severe scorpion envenomations in our PICU. The main findings of this study are relevant to laboratory and echocardiographic results. Hyperglycemia, hyperamylasemia, and elevated pro-BNP occur more frequently in grade 3 cases than grade 2 cases. Echocardiographic findings show that mild-to-moderate mitral regurgitation is more common than systolic dysfunction. Although there was no death in our cases, pulmonary edema, which led to cardiac arrest in one case, was seen as the potentially most fatal complication.

It has been reported that the pancreas is frequently but transiently affected in systemic scorpion envenomations (12). Animal studies show that scorpion venom increases biliary and duodenal motility, causing increased pancreatic amylase production (13,14). Although there were no

Table 1. Demographic features of patients (n=73)

Age (months)		52 (26-89)
Age groups	0-24 months	15 (20.5%)
	24-84 months	39 (53.4%)
	84-144 months	11 (15.1%)
	>144 months	8 (11%)
Gender	Female	35 (47.9%)
	Male	38 (52.1%)
Sting site	Head and neck	1 (1.4%)
	Trunk	4 (5.5%)
	Upper extremity	32 (43.8)
	Lower extremity	36 (49.3%)
Stings count	1	63 (86.3%)
	2	10 (13.7%)
Time between sting and PICU admission (hours)		4 (3-6)
Severity	Grade 2	62 (84.9%)
	Grade 3	11 (15.1%)
PRISM score		5 (4-8)
Length of PICU stay (days)		4 (3-5)
Length of hospital stay (days)		5 (4-6)

PICU: Pediatric intensive care unit, PRISM: Pediatric risk of mortality
Severity of scorpion sting was defined by Khattabi et al. (4)

Table 2. Differences between grade 2 and grade 3 scorpion envenomation patients

		Grade 2 (n=62)	Grade 3 (n=11)	p-value
Age (months) median (25-75p)		52 (26-91)	46 (22-57)	0.23
Gender (female/male)		30/32	5/6	0.8
Scorpion	Yellow n (%)	54 (87.1%)	11 (100%)	0.2
	Black n (%)	8 (12.9%)	0	
Admission after sting (hours) median (25-75p)		4 (3-6)	5 (3-12)	0.25
PRISM* score Median (25-75p)		5 (4-7)	12 (8-12)	**<0.001**
Perpiheral sympathetic activity signs n (%)		46 (74.2)	9 (81.8%)	0.58
Hypertension n (%)		28 (45.2%)	7 (63.6%)	0.33
Hypotension n (%)		0 (0%)	7 (63.6%)	**<0.001**
Nause n (%)		18 (29%)	9 (81.8%)	**0.001**
Bradycardia n (%)		0 (0%)	2 (18.2%)	**0.02**
Tachycardia n (%)		16 (25.8%)	5 (45.5%)	0.18
Ejection fraction (%) median (25-75p)		65 (60-69)	48 (40-52)	**<0.001**
Systolic dysfunction n (%)		8 (12.9%)	11 (100%)	**<0.001**
Mitral insufficiency n (%)		20 (32.3%)	11 (100%)	**<0.001**
Tricuspid valve regurgitation n(%)		4 (6.5%)	9 (81.8%)	**<0.001**
pro-BNP (ng/L) median (25-75p)		85 (63-205)	1153 (965-16120)	**<0.001**
Elevated pro-BNP		8 (12.9%)	9 (81.8%)	**<0.001**
Troponin T (ng/L) median (25-75p)		15 (3-177)	515 (512-607)	**<0.001**
Elevated troponin T		30 (51.7%)	11(100%)	**0.002**
Myoglobine (ng/mL) median (25-75p)		87 (30-191)	454 (171-463)	**0.001**
Elevated myoglobine		22 (61.1%)	11 (100%)	**0.04**
Creatinin kinase (U/L) median (25-75p)		248 (163-412)	264 (208-356)	0.78
Elevated creatinin kinase		38 (65.5%)	11 (100%)	**0.02**
Blood glucose (mg/dL) median (25-75p)		116 (102-132)	207 (144-230)	**<0.001**
Hyperglycemia		10 (16.7%)	9 (81.8%)	**<0.001**
White blood cells ($10^3/mm^3$) median (25-75p)		11.3 (7.6-14.4)	20.9 (17.7-26.9)	**<0.001**
Leucocytosis		36 (60%)	11 (100%)	**0.01**
Amilase (U/L) median (25-75p)		77 (59-148)	153 (113-179)	0.09
Hyperamilasemia		16 (33.3%)	9 (81.8%)	**0.003**
Lactate (mmol/L) median (25-75p)		2.2 (1.2-3.1)	4.4 (4.3-4.6)	**<0.001**
Lipase (U/L) median (25-75p)		14 (10-27)	20 (8-23)	0.6
Inotropic support n (%)		16 (25.8%)	11 (100%)	**<0.001**
Non-invasive respiratory support n (%)		6 (9.7%)	11 (100%)	**<0.001**
Invasive mechanical ventilation n (%)		0 (0%)	5 (45.5%)	**<0.001**
Length of Intensive care stay (days) median (25-75p)		4 (3-5)	5 (4-38)	**0.03**
Length of hospital stay (days) median (25-75p)		5 (4-6)	7 (4-38)	**0.03**
Morbidity n (%)		0 (0%)	1 (9%)	0.15

PRISM: Pediatric risk of mortality

statistically significant differences between grade 2 and grade 3 patients in terms of amylase blood levels, there were significant differences in the frequency of hyperamylasemia between the groups. It seems that hyperamylasemia is more common in patients with grade 3 than in patients with grade 2. Although hyperamylasemia is a common manifestation of scorpion sting, we think that pancreatitis is rare because there was no lipase elevation in our patients.

Hyperglycemia is a well-known phenomenon in patients with scorpion envenomation. It is caused by increased catecholamine secretion and other hormonal mechanisms during scorpion envenomation. It has been reported that hyperglycemia during scorpion envenomation is an indicator of disease severity (15). In our study, hyperglycemia was observed in 26.8% of all cases. However, it was observed with a frequency of 81.9% in grade 3 patients and was significantly different from grade 2.

Myocardial injury during scorpion envenomation is a known entity and it is thought that the underlying mechanism may be direct or indirect (severe hypertension) myocardial damage associated with elevated catecholamines or direct myocardial toxicity of scorpion toxins (16,17). Cardiac troponins are the most sensitive biomarkers of myocardial damage. In the early phase (first six hours) of myocardial injury, the most sensitive biomarker is myoglobin (18). However, myoglobin is found not only in the heart but also in greater amounts in striated muscle. In cases such as scorpion bites, where striated muscle may be affected, elevated myoglobin levels may be observed independently of cardiac injury. In a study conducted in southeastern Turkey, it has been reported that severe cases of scorpion envenomation had higher CK levels than mild and moderate cases (11). In our study, grade 3 patients had higher myoglobin, troponin, lactate, and pro-BNP levels than grade 2 patients.

Echocardiographic examination of scorpion bites can determine the degree of heart failure and other dysfunctions (19). In a prospective echocardiographic study conducted in India, it has been reported that heart failure associated with scorpion envenomation can be diagnosed with a frequency of approximately 70% (20). In another study conducted in Israel, the incidence of heart failure was reported to be about 10%. In a study conducted in the Egean region in Turkey (Mesobuthus gibbosus), heart failure and associated pulmonary edema occurred with a frequency of 8.7% (21). In our study, echocardiographic heart failure (low ejection fraction) was found with a frequency of 26%. However, the patients included in our study were those with systemic symptoms, so they do not represent all emergency admissions. Although systolic dysfunction is frequently mentioned in the echocardiographic findings in all studies, our study shows that mitral valve dysfunction (mild to moderate regurgitation) may be seen more frequently.

Antitoxin infusions, inotropic and vasodilator treatments are the main methods of treatment in children with severe scorpion envenomation. In severe cases, the administration of scorpion antitoxin as early as possible increases efficacy (22,23) Bawaskar and Bawaskar (24,25) reported that prazosin is a promising agent to reduce mortality in children with severe scorpion envenomation. The mortality-reducing effect of prazosin was clarified by controlled studies (historical controls) in the following years (26). Doxazosin is an alpha-adrenoreceptor blocker like prazosin but has a longer elimination half-life than prazosin (22 versus 3 h). It has been reported that doxazosin may have the same success rate as prazosin when prazosin is unavailable (27). We used doxazosin instead of prazosin because prazosin was not available at our hospital.

Milrinone is a medicine that has inotropic, lusitropic, and vasodilatory effects. It has the advantage over dobutamine that it does not show tolerance or attenuation of its effects and has a better systemic vasodilatory effect (28). These effects make milrinone a promising agent for treating scorpion envenomation (29). There is no comparative randomized controlled trial of milrinone and dobutamine in scorpion envenomation.

Pulmonary edema is the most dangerous manifestation of scorpion envenomations. There are two different mechanisms responsible for developing pulmonary edema after scorpion envenomation. One of them is the increased permeability of the alveolocapillary membrane due to the direct damage caused by the scorpion venom (30). The other type of pulmonary edema is the cardiogenic type, which is associated with biventricular failure because of venom toxicity (31). In this study, pulmonary edema occurred in only five patients and one of them suffered cardiac arrest due to acute severe hypoxemia.

Single-center data and a retrospective study design are the main limitations of this study. The causative scorpion species could not be clearly defined because the parents' descriptions did not provide sufficient data to clearly identify the scorpion species. Only patients with severe scorpion envenomation were included in this study, so the results cannot be generalized to all cases of scorpion bites.

CONCLUSION

Scorpion envenomation is an important public health issue. Hyperamilasemia, hyperglycemia, and elevated pro-BNP

levels on admission may be warning signs of more severe patients. Mild-to-moderate mitral regurgitation may be more common than systolic dysfunction in severe cases.

ETHICS

Ethics Committee Approval: This study was reviewed and approved by University of Health Sciences Turkey, Antalya Training and Research Hospital Ethics Committee (decision no: 1/28, date: 04.03.2021).

Informed Consent: Informed consent could not be obtained because of the retrospective study design.

Authorship Contributions

Surgical and Medical Practices: H.S.K., G.Ö., A.K., Y.B., E.A.O., Concept: H.S.K., E.A.O., Design: H.S.K., G.Ö., A.K., Y.B., E.A.O., Data Collection or Processing: H.S.K., Analysis or Interpretation: H.S.K., G.Ö., A.K., Y.B., E.A.O., Literature Search: H.S.K., Writing: H.S.K.

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