Antivenom use in bite and sting cases presenting to a public hospital

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ABSTRACT

BACKGROUND: To evaluate the distribution of bite and sting cases presenting to a district public hospital and the use of antivenom in scorpion sting and snake bite cases.

METHODS: The demographic characteristics of patients with bites/stings reporting to a public hospital in 2014, the agent involved, the season of reporting, severity of clinical findings during presentation, and use of antivenom in scorpion sting and snake bite cases were evaluated retrospectively. χ^2 test was used for statistical analysis.

RESULTS: Bite and sting cases comprised 0.5% of all the patients reporting to the hospital's emergency department, with scorpion sting cases comprising almost half (54.2%) of these hospital presentations, followed by Hymenoptera (bee and wasp) sting (30.8%) and snake bite (5.5%) cases. Unnecessary antihistamine administration was found to be significantly high in asymptomatic patients (p=0.00006). Furthermore, antivenom use was found to be significantly high in patients with scorpion sting and snake bite despite the absence of systemic or local indications (p<0.0001, γ^2 =80.595).

CONCLUSION: The study results showed that antivenom was used in scorpion sting and snake bite cases even when it was not indicated. Therefore, primary practitioners should be provided training for management of envenomation cases and should be made aware of the updated guidelines and references to raise their knowledge levels.

Keywords: Antivenom; scorpion; snake; sting,bite.

INTRODUCTION

Background

Poisonous animal bites and stings are one of the causes for patients visiting the emergency departments. Animals such as scorpions, snakes, bees/wasps, and centipedes are some of the agents involved in bite and sting cases, and such cases are particularly common in spring and summer. The prevalence and causes of these cases exhibit regional variation, and mortality may be observed, particularly in association with snake bites and scorpion stings.^[1]

The proportion of bites and stings among all poisoning cases

is 2.1% according to the American Association of Poison Control Centers' National Poison Data System Report for 2015, 1.8% according to a National Poisons Information Center report for 2008, and 2.4% according to the Dokuz Eylul University (DEU) Faculty of Medicine Drug and Poison Information Center report for 2007.^[2-4] Bites and stings generally occur in the extremities.^[5] The severity of poisoning and clinical symptoms vary across all bites and stings, depending on the site of the bite or sting, the agent, the amount of venom and its potency, the presence of any underlying cardiovascular disease such as diabetes, and age.^[6]

The commonly encountered bites and stings include scorpion and Hymenoptera (bee and wasp) stings and snake bites. In

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addition to pain, erythema, and swelling that are generally observed locally around the bite or sting area, clinical findings such as nausea, vomiting, hypotension, hypertension, tachycardia, seizure, anaphylaxis, and bleeding disorders may be seen, depending on the characteristics of the venom. Severe systemic findings and even mortality may be observed in pediatric patients, particularly in scorpion envenomation cases. ^[7,8] The neurotoxins present in the snake venom can cause direct tissue injury, damage to cellular components, and nerve signaling disorders. ^[1,9]

The general approach in all bite and sting cases involves symptomatic support therapy in addition to local wound site care, analgesic therapy, and tetanus prophylaxis. Antivenom must be administered in accordance with appropriate systemic and local indications in scorpion sting and snake bite cases. Although antivenoms represent the basic step of treatment in life-threatening envenomation cases, particularly scorpion sting and snake bite cases, they also cause severe side-effects. Mild clinical findings such as nausea, vomiting, fever, and urticaria or severe findings such as anaphylaxis, hypotension, cyanosis, and loss of consciousness may occur in association with antivenom use.^[10]

Few studies have investigated the epidemiological characteristics of bite and sting cases in Turkey. There are no recorded data concerning non-indicated antivenom administration in snake bite and scorpion sting vases. We investigated the prevalence of bite and sting cases, the information concerning presentations of which to emergency departments in Turkey is limited, among envenomation cases presenting to a public hospital. Furthermore, we investigated the prevalence of inappropriate antivenom use in scorpion sting and snake bite cases.

Importance

The number of studies investigating the epidemiological characteristics of bite and sting cases is very limited. In particular, there is no previous research concerning the prevalence of non-indicated, unnecessary antivenom use in snake bite and scorpion sting cases in Turkey.

Goals of This Investigation

The purpose of this study was to determine the epidemiological characteristics of bite and sting cases. Little is known about the prevalence of emergency department presentations of bite and sting cases in Turkey, their general characteristics, and the level of unnecessary antivenom use.

MATERIALS AND METHODS

Approval for this cross-sectional, descriptive research was granted by the DEU Non-Interventional Research Ethical Committee. This study was performed at the Dr. Faruk Ilker Bergama Public Hospital Emergency Department in the province of Izmir in the Aegean region of Turkey, the

emergency department of which receives approximately 70,000 cases per year. All bite and sting cases presenting to the emergency department in 2014 were identified by scanning International Classification of Diseases ICD-10 codes on the hospital's electronic medical record system. Patient files were extracted from the archives. Bite and sting cases were evaluated in terms of the agent involved; the patient's age and sex; the month, season, and location of bite/sting; time elapsed since the bite/sting; presence of local and systemic clinical findings; treatment administered (antihistamine therapy and antivenom use in snake bites and scorpion stings); and length of hospital stay. Clinical findings were evaluated as mild, moderate, or severe based on the severity of envenomation scores (European Association of Poison Centers and Clinical Toxicologists/International Programme on Chemical Safety).[11] Antivenom use was also assessed depending on the presence of systemic and local indications in patients with snake bites or scorpion stings (Table 1).[12,13]

Statistical Analysis

All the data collected were recorded onto a prepared patient record form and then entered onto Statistical Package for the Social Sciences 15.0 (SPSS Inc., Chicago, IL, USA) software. Patients aged under 18 years were classified as children and those over 18 years as adults. χ^2 and Fisher's exact tests were used for the statistical analysis of the numerical data. P<0.05 was regarded as significant.

RESULTS

Bite and sting cases comprised 0.5% (n=273) of all the patients presenting to the hospital's emergency department in 2014. The female/male ratio in all bite and sting cases was 0.9; mean ages were 38.8 ± 1.4 years in males and 40.5 ± 1.5 in females. The child age group comprised 9.5% (n=26) of these presentations.

The majority (n=140, 51.3%) of presentations to the emergency department occurred between 13:00 and 17:59 pm. In addition, 74.7% of the cases presented to the emergency department within I h of the sting or bite, with all the cases presenting within 6 h. In terms of season, 65.2% (n=178) of the patients presented in the summer, 19.4% (n=53) in the spring, and 15.4% (n=42) in the fall.

Scorpion stings comprised more than half of the presentations in both children and adults (54.5%, n=149). Bee stings were the second most common cause of the presentations to the emergency department (30.8%, n=84). The rates of presentation to the emergency department due to snake and spider bites were 5.5% (n=15) and 1.1% (n=3), respectively (Table 2). Additionally, among all the cases, those presenting to the emergency department due to bites/stings in the upper extremity were 70.3%, in the lower extremity were 20.2%, in the head were 20.2%, and in the trunk were 2.2%.

Table 1.	Indications for antivenom administration depending on the presence of local and clinical findings in scorpion sting and snake bite cases
	Antivenom indications

Local Systemic Scorpion CVS symptoms: heart failure, cardiogenic shock, pulmonary edema, Rapid extension of swelling involving envenomation tachycardia, arrhythmia, dyspnea, hypertension, hypotension, electrocarmore than half of the bitten limb diographic abnormalities, and priapism. Hypersecretory syndrome: salivation, sweating, bronchorrhea, nausea, vomiting, diarrhea, and urination. GIS symptoms: abdominal distension and abdominal cramps NMS symptoms: dysfunction of either skeletal or cranial muscles: confusion, agitation, fasciculation, dystonia, vision disorders, ptosis, and aberrant eye movements dysfunction of both skeletal and cranial muscles: convulsions, paralysis, and Glasgow score ≤6 (in absence of sedation). Snake Hemostatic abnormalities: Spontaneous systemic bleeding (clinical), Local swelling involving more than half envenomation coagulopathy (20WBCT or other laboratory tests such as prothrombin of the bitten limb (in the absence of a time), or thrombocytopenia tourniquet) within 48 h of the bite NMS symptoms: Ptosis, external ophthalmoplegia, paralysis etc. and gen-Swelling after bites on the digits (toes eralized rhabdomyolysis (muscle aches and pains, hyperkalemia) and especially fingers). Rapid extension of swelling (for example, beyond CVS symptoms: Hypotension, shock, cardiac arrhythmia (clinical), and the wrist or ankle within a few hours abnormal ECG of bite on the hands or feet) Acute kidney injury (renal failure): Oliguria/anuria (clinical), rising blood creatinine/ urea (laboratory). Hemoglobinuria, myoglobinuria dark Development of an enlarged tender brown urine (clinical), or other evidence of intravascular hemolysis lymph node draining the bitten limb CVS: Cardiovascular system; GIS: Gastrointestinal system; NMS: Neuromuscular system.

Pain was present in the bite or sting area in 52.8% (n=159) of the cases; nausea was present in 7.7% (n=21), hypotension in 6.2% (n=17), hypertension in 4.0% (n=11), tachycardia in 3.7% (n=10), and vomiting in 1.5% (n=4) cases. When all bite and sting agents were evaluated separately, pain was found to

Table 2. Distribution of bite and sting agents in children and adults

Agents		ildren -17 y)		lults 18 y)	All age groups		
	n	%	n	%	n	%	
Scorpion	13	50.0	136	55.0	149	54.5	
Snake	2	7.7	13	5.3	15	5.5	
Spider	0	0	3	1.2	3	1.1	
Bee	7	26.9	77	31.2	84	30.8	
Centipede	2	7.7	16	6.5	18	6.6	
Unknown	2	7.7	2	0.8	4	1.5	
Total	otal 26 100.0		247	100.0	273 100		

be present in the wound area in 80.0% of snake bite, 66.7% of snake and centipede bite, 65.5% of Hymenoptera (bee and wasp) sting, and 51.0% of scorpion sting cases; furthermore, pain was the most common finding (Table 3). When clinical findings were assessed according to the envenomation severity scores, mild clinical findings were observed in 57.5% (n=157) and moderate clinical findings in 1.8% (n=5) of the cases, whereas 40.7% (n=111) cases were asymptomatic.

Treatment of Bites and Stings

Local wound care and tetanus prophylaxis were applied to all the bite and sting cases (100%, n=273), and antihistamines were administered to 97.1% (n=265) cases. Furthermore, antihistamines were administered to 92.8% (n=103) of asymptomatic patients. Notably, unnecessary antihistamine administration in asymptomatic cases was significantly high (p<0.0001).

Antivenom was used in 28.2% (n=42) of scorpion sting cases and in 60% (n=9) of snake bite cases. The rate of antivenom administration in the presence of local and/or systemic indications in scorpion sting cases was 100.0% (n=11); however,

Table 3. Distribution of clinical findings by agents														
Findings	Sco	rpion	Sį	oider	Sr	nake	E	Bee	Cen	tipede	Un	known	To	otal
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Pain in the bite area	76	51.0	2	66.7	12	80.0	55	65.5	12	66.7	2	50.0	159	58.2
Nausea	11	7.4	0	0.0	0	0.0	9	10.7	- 1	5.6	0	0.0	21	7.7
Hypotension	10	6.7	0	0.0	1	6.7	4	4.8	2	11.1	0	0.0	17	6.2
Hypertension	6	4.0	0	0.0	- 1	6.7	2	2.4	0	0.0	0	0.0	11	4.0
Tachycardia	4	2.7	0	0.0	2	13.4	2	2.4	2	11.1	0	0.0	10	3.7
Vomiting	2	1.3	0	0.0	0	0.0	-1	1.2	ı	5.6	0	0.0	4	1.5

	Scorpion sting					Snak	e bite		Total			
Systemic and/or local indications	Antivenom administered		Antivenom not administered		Antivenom administered		Antivenom not administered		Antivenom administered		Antivenom not administered	
	n	%	n	%	n	%	n	%	n	%	n	%
Yes	11	100.0	0	0.0	3	100.0	0	0.0	14	100.0	0	0.0
No	31	22.5	107	77.5	6	50.0	6	50.0	37	24.7	113	25.3

Agent				Lengt	th of hospi	tal stay (ho	urs)			
	0	–6	7.	-12	13	3–24	24	–48	To	otal
	n	%	n	%	n	%	n	%	n	%
Scorpion	128	85.9	18	12.1	1	0.7	2	1.3	149	100.0
Snake	7	46.7	8	53.3	0	0.0	0	0.0	15	100.0
Spider	3	100.0	0	0.0	0	0.0	0	0.0	3	100.0
Bee	84	100.0	0	0.0	0	0.0	0	0.0	84	100.0
Centipede	16	88.9	2	11.1	0	0.0	0	0.0	18	100.0
Unknown	4	100.0	0	0.0	0	0.0	0	0.0	4	100.0
Total	242	88.6	28	10.3	ı	0.4	2	0.7	273	100.0

antivenom was also used in 22.5% (n=31) of scorpion sting cases with no systemic and/or local indication. The rate of antivenom use in snake bite cases in the presence of the indications was 100.0% (n=3); this rate was 50% (n=6) in the absence of the indications. Antivenom use in the absence of local and/or systemic indications was significantly high (p<0.0001, χ^2 =80.595) (Table 4).

The length of hospital stay was 6 h in 88.6% (n=242), 12 h in 10.3% (n=28), 24 h in 0.4% (n=1), and 48 h in 0.7% of all bite and sting cases (Table 5). Of all the patients, 85% were dis-

charged as fully healed, while 15% were referred to a higher-level health facility for advanced treatment; we were unable to follow-up these referred patients. However, in the remaining 85% patients who were followed-up, no severe clinical findings based on the envenomation severity scores were observed. No patient died due to bites or stings in our hospital during the study period.

DISCUSSION

In addition to evaluating the epidemiological and clinical char-

acteristics of bite and sting cases presenting to a district public hospital providing primary health services, this study also investigated the use of antivenom in terms of its indication in scorpion sting and snake bite cases.

Bite and sting cases comprised 0.5% of all the envenomation cases presenting to the emergency department. The proportion of bite and sting cases among the emergency presentations as per the epidemiological data in different studies is approximately 0.7%.[14,15] Although our results are compatible with the data from the literature, the true incidence cannot be calculated exactly. This is because a significant part of bite and sting cases, which are more commonly encountered in rural areas, are treated at home using traditional methods only and such patients do not visit a hospital.[9] In our study, we determined that scorpion sting cases comprised a large part of emergency presentations due to stings. Scorpion sting cases were followed by Hymenoptera (wasp and bee) sting cases. One study involving a retrospective analysis of bite and sting cases over a 17-year period at the Dokuz Eylul University Poison Information Center reported that scorpion sting cases represent approximately one in three such cases, followed by snake bite, centipede sting, spider bite, and Hymenoptera (bee and wasp) sting cases;[16] the proportion of snake bite cases was found to be low. In the majority of research performed to date, scorpion stings have been found to comprise a large proportion of envenomations, with Hymenoptera (bee and wasp) stings comprising another commonly encountered envenomation. However, one epidemiological study on all bite and sting cases presenting to all emergency departments in the USA in 2001-2004 reported that insect bites and stings were the most common causes for these cases at 39.0%, followed by bee and wasp stings at 17.0% and spider bites at 13.5%. In contrast to our results, the same study reported levels of 0.8% and 1% for scorpion stings and snake bites, respectively.[15] Factors such as regional climatic features, vegetation cover, and the socioeconomic and cultural variations in the presenting population may underlie the variations in the abovementioned levels among these studies.

As also reported in previous studies, bite and sting cases largely occurred in the summer, when the weather is considerably warmer; when people spend more time outside; and when snakes, scorpions, and other bite and sting agents are active. ^[15,17] The fact that bites and stings frequently occurred in the upper extremities is another finding compatible with those of the previous studies. ^[18]

The most common clinical finding in bite and sting cases, when agents were analyzed separately and together, was pain in the bite/sting area. Toxin-related pain, erythema, and swelling are the most common local findings in scorpion and bee/wasp sting and snake bite cases.^[7,19] Because our study was a retrospective analysis, no data regarding the development of erythema and swelling were available in the patient

records; however, the common observation of pain was compatible with that in the literature.

The most common clinical findings following pain in our patients with scorpion stings included nausea, hypotension, and hypertension. There are two species of poisonous scorpion in Turkey: Mesobuthus gibbosus and Androctonus crassicauda.[20] Digestive enzymes and neurotoxins present in scorpion venom are responsible for the clinical findings present in scorpion sting cases. In addition to local findings, severe systemic clinical findings such as hypertension, hypotension, tachycardia, sweating, muscle weakness, double vision, nystagmus, convulsion, and coma may be seen. Moderate toxic findings such as hypotension and tachycardia were observed in our study. This also suggests that although species screening is not possible, M. gibbosus species scorpions, which are widely found in the Aegean region and give rise to moderate toxic findings, are responsible for majority of scorpion envenomations.[20]

Similarly, systemic findings in snake bite cases included hypotension, hypertension, and tachycardia. Approximately 50.0% of snake bites are dry bites, resulting in no clinical findings. The venom of viper-type snakes in Turkey contains large numbers of proteolyic enzymes, anticoagulants, cardiotoxins, hemotoxins, and neurotoxins and can cause direct tissue damage, cellular blood component compromise, and signal transmission disorders. The number of snake bites in Turkey is low, and the great majority of findings are thought to develop in association with dry bites or bites from non-venomous snakes, even though species screening has not been possible. Page 1241

The most severe systemic finding associated with Hymenoptera stings is anaphylaxis, a potentially fatal allergic reaction. The prevalence of bee/wasp sting-related anaphylaxis varies between 1.2% and 3.5%.[19] Although moderate systemic findings such as hypotension and tachycardia were recorded in association with Hymenoptera stings in our study, no serious anaphylactic reaction was observed.

For the treatment of patients with bites and stings, the patient must first be stabilized and wound care and tetanus prophylaxis must be administered. All cases in our study were recorded as receiving wound site care and tetanus prophylaxis. However, antihistamines and corticosteroids were administered to almost all the patients with no clinical findings. Systemic antihistamine and corticosteroid administration has been reported to be effective in the presence of extensive local reaction or urticaria in the bite/sting area. [25] Additionally, this combination has been reported to exhibit no acute efficacy in anaphylaxis that may result due to both venom and antivenom. [9,19,26,27] Clinical studies have also shown that antihistamine and steroid therapy is not effective in preventing anaphylaxis that may develop particularly before antivenom use. [28,29] We determined that antihistamine therapy was used

unnecessarily in our studied cases. Therefore, physicians in emergency departments need to be made aware of antivenom use only where indicated through professional training seminars.

Various clinical classification systems have been established to guide treatment and facilitate follow-up in scorpion sting and snake bite cases. If antivenom is administered in the light of these indications, unnecessary antivenom use and complications arising from antivenom use can be avoided. In our study, we found that significantly high levels of antivenom were used in conditions where no relevant clinical findings were observed, in both scorpion sting and snake bite cases. Antivenom, or passive immunotherapy, is obtained through enzymatic purification of IgG antibodies separated from plasma components of animals that are hyperimmunized against snake or scorpion venoms, and there are indications for its use in selected patients with systemic clinical findings, depending on the species involved.[12] This is because antivenoms, frequently obtained using sera from different animal species such as horses, may cause allergic reactions when they are administered to humans. The most serious and life-threatening of these allergic reactions is early anaphylactic reaction proceeding with hypotension, bronchospasm, and angioedema developing within approximately 10-180 min of antivenom administration. Pyrogenic reaction developing within I-2 h of antivenom administration and proceeding with fever, shivering, and hypotension is another more moderate reaction, but one that can prolong the length of hospital stay if not treated. In addition, delayed-type hypersensitivity reactions may also be observed I-I2 days after antivenom administration.[9] There is no scientific evidence for antihistamine and steroid administration for prophylactic purposes to prevent antivenom use-related complications. Therefore, antivenom use when not indicated may lead to a risk of severe, life-threatening complications. There is a lack of sufficient information concerning inappropriate antivenom use in the literature. One study conducted on emergency physicians in Japan regarding knowledge levels concerning indications for antivenom use and snake bite management reported physicians' knowledge levels to be inadequate.[30]

The reasons for antivenom use when not indicated in this study may include the emergency department where the study was performed being a primary emergency department attached to a public hospital; the great majority of physicians working in the emergency department being general practitioners; and the inability to perform advanced procedures such as local nerve blockage for severe pain, particularly in scorpion sting cases. General practitioners serving in emergency departments, therefore, need to be provided professional training seminars accompanied by updated guidelines to raise awareness regarding appropriate management of such cases. Additionally, the number of emergency medicine physicians who have completed specializations in emergency medicine, who monitor the contemporary guidelines, and

who are capable of managing all forms of invasive and non-invasive procedures that may be required in the emergency department needs to be increased.

All bite and sting cases presenting to the Dr. Faruk Ilker Bergama Public Hospital resolved completely. Mortality and morbidity in bite and sting cases vary across regions. Mortality rates in Asia and Africa vary between 4 and 162 people in 100,000, whereas only 6000 deaths occur annually in India and Bangladesh.[31,32] Because bites and stings are more common in regions with warm tropical climates, mortality and morbidity levels are also higher in such regions. Difficulties in accessing emergency health services in rural areas and interruptions to services also increase these rates. The absence of mortality in our study may be attributed to the great majority of envenomations being mild or moderate. Although we were unable to access the results of cases transferred to advanced centers, we doubt that any bite or sting-related mortality occurred in these patients, with no severe clinical findings observed during referral.

Conclusion

The great majority of bite and sting cases can be treated with local wound care, analgesics, and tetanus prophylaxis without causing significant systemic effects, and genuine antivenom use indications are present in only a very few cases. In this study, we determined that antivenom was used when not indicated in scorpion sting and snake bite cases. General practitioners working in primary institutions, therefore, need to be provided training in managing such cases in the light of contemporary guidelines and references to raise their knowledge levels. Non-indicated antivenom use causes various complications in patients and also imposes medical and economic losses on the health system by creating difficulties in obtaining antivenom when it is genuinely indicated.

Limitations

Out study is retrospective, cross-sectional, single center, and time-limited and, therefore, does not entirely represent the entire population. Because the study was performed by scanning records, only the limited amount of data recorded in those records could be analyzed. Patients could not be evaluated in terms of antivenom use-related delayed reactions after discharge or referral.

Conflict of interest: None declared.

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ORİJİNAL ÇALIŞMA - ÖZET

Bir devlet hastanesine başvuran ısırma ve sokma olgularında antivenom kullanımı

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AMAÇ: Bir ilçe devlet hastanesine başvuran ısırma ve sokma olgularının dağılımı ve akrep sokmalarında ve yılan ısırmalarında antivenom kullanımının değerlendirilmesi.

GEREÇ VE YÖNTEM: Devlet hastanesine 2014 yılı içerisinde bildirilen ısırma-sokma olgularının demografik özellikleri, ısırma sokma etkeni, mevsim, başvuru sırasında klinik bulguların ciddiyeti, akrep sokmalarında ve yılan ısırmalarında antivenom kullanımı geriye yönelik olarak değerlendirildi. İstatistiksel analizde ki-kare testi kullanıldı.

BULGULAR: Tüm olgular arasında, ısırma ve sokmaların oranı %0.5 idi. Akrep sokma olguları, hastane başvuruların yarısından fazlasını (%54.2) oluştururken, akrep sokmaların, arı sokmaları (%30.8) ve yılan ısırmaları (%5.5) izliyordu. Semptomsuz hastalarda, gereksiz antihistaminik uygulaması istatistiksel olarak anlamlı oranda yüksekti (p=0.00006). Akrep sokmalarında ve yılan ısırmalarında, sistemik ya da lokal endikasyon olmamasına rağmen antivenom kullanımı anlamlı oranda yüksekti (p<0.0001, χ ²=80.595).

TARTIŞMA: Çalışmamızda, akrep sokmalarında ve yılan ısırmalarında, endikasyon olmadığı durumlarda da antivenom kullanıldığını saptadık. Bu nedenle, ısırma sokma olgularının yönetiminde, birinci basamakta çalışan pratisyen hekimlere güncel kılavuzlar ve kaynaklar eşliğinde bilgilendirme amaçlı eğitimler verilmelidir.

Anahtar sözcükler: Akrep; antivenom; ısırma-sokma; yılan.

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