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ARAŞTIRMA / RESEARCH

Comparison of two types of polyvalent snake antivenom used in treatment

Tedavide kullanılan iki tip polivalan yılan antivenomunun karşılaştırılması

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Abstract

Purpose: In this study; we aimed to compare the effectiveness of the two types of polyvalent snake antivenom and to determine the possible local and systemic reactions in patients who admitted to the emergency department with snake bite.

Materials and Methods: We performed this retrospective study on 30 patients who complained of snakebite. We grouped the patients according to the antivenom type (PoliseraTM or Polivalan TM) which they received. Demographic characteristics of the patients, vital signs, local tissue findings, and laboratory parameters were recorded in the standard data form. The following data were also recorded; the number of vials of snake antivenom used in each group, additional doses of venom were administered, and whether any local or systemic reaction to antivenom has developed or not.

Results: Thirty patients were included in the study. 16 patients were administered PoliseraTM (Group 1) snake antivenom and 14 patients were administered Polivalan TM (Group 2) snake antivenom. Patients in Group 1 were given an average of 9.1±7.3 vials, while patients in Group 2 were given an average of 11.6±12.7 vials. More allergic reactions-urticaria, fever, and cellulite were observed in the group receiving PolivalanTM antivenom.

Conclusion: Different methodologies arising from the production of antivenom, pyrogen contamination, and differences in packaging can cause different effects and side effects even in products with the same dose and antivenom content.

Keywords:. Antivenom, emergency, envenomation, snakebite

Öz

Amaç: Bu çalışmada; acil servise yılan ısırması ile başvuran hastalarda kullanılan iki tip polivalan yılan antivenomun etkinliğinin karşılaştırılması ve olası lokal ve sistemik yan etkilerin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışmaya yılan ısırması şikayeti olan 30 hasta dahil edildi. Hastalar aldıkları antivenom tipine (PoliseraTM veya PolivalanTM) göre gruplandırıldı. Hastaların demografik özelliklerinin yanı sıra, vital bulguları, lokal doku bulguları ve laboratuvar parametreleri standart veri formuna kaydedildi. Her grupta kaç vial yılan anti serumu kullanıldığı, kaç kez ek doz venom ihtiyacı olduğu; antivenoma karşı herhangi bir reaksiyon gelişip gelişmediği kaydedildi.

Bulgular: Çalışmaya 30 hasta dahil edildi. 16 hastaya Polisera TM (Grup 1) yılan antivenomu, 14 hastaya PolivalanTM (Grup 2) yılan antivenomu verildi. Grup 1'deki hastalara ortalama 9.1±7.3 vial antivenom verilirken, Grup 2'deki hastalara ortalama 11.6±12.7 vial verildi. PolivalanTM antivenom alan grupta daha fazla alerjik reaksiyon-ürtiker, ateş ve selülitgözlendi.

Sonuç: Pirojen kontaminasyonu, üretimden kaynaklanan farklı metodolojiler ve ambalaj farklılıkları aynı doz ve içeriğe sahip antivenom ürünlerinde bile farklı etkilere ve yan etkilere neden olabilir.

Anahtar kelimeler: Acil, antivenom, yılan ısırması, zehirlenme

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INTRODUCTION

Mortality and morbidity due to snakebites are most commonly seen in South Asia, South East Asia, and Sub-Saharan Africa. According to the data of the World Health Organization (WHO), more than 5 million snakebites occur every year worldwide and 50% of them are dry bites. There are at least 1.8-2.7 million poisonings related to snakebites, and deaths between 81.410 and 137.880 are reported per year [1, 2]. In Turkey, snakebites are more common in warm regions such as the Mediterranean region, Southeast, and Eastern Anatolia regions [3]. An average of 40 snake species lives in our country. Of these, 28 are non-poisonous and 13 are poisonous [4]. The Viperidae (viper) family is the most common group in our country among the poisonous species. The most common subtypes are *V. pontica, V. raddei, V. ammodytes, V. xanthina, V. lebetina, V. barani, V. wagneri, V. ursinii,* and *V. monspessulanus* [1].

Snake venom is one of the most complex venoms found in nature. The level of toxicity depends on several factors, such as the type of the venom injected, its amount, location of the bite, and the patient's susceptibility to intoxication [5]. It may exhibit cytotoxic, myotoxic, hemorrhagic, and neurotoxic effects, causing severe clinical consequences [6]. Careful and close monitoring of patients, supportive treatment, and antivenom treatment can significantly reduce morbidity and mortality [7]. Snake antivenom (Polisera™, Vetal Serum, Adıyaman) started to be produced for the first time in our country in 2014 to be used in the treatment of snake bites [8]. Then, Polivalan™ snake antivenom (5ml), which was distributed by the Public Health Directorate, started to be produced in 2019. Both antivenoms contain globulins against *V. ammodytes, V. xanthina, V. Lebetina* species, which are commonly seen in our country [9]. In this study, we aimed to determine the clinical features of patients who presented to emergency department with snakebites, to compare the effectiveness of the two types of polyvalent snake antivenom and to determine the possible local and systemic reactions.

MATERIALS AND METHODS

Patients over 18 years of age who presented to the tertiary hospital emergency department due to snakebite, between April, 01st 2019 and March, 31st 2020 were included in the study. Patients with known hematological disorders, patients using anticoagulants - antithrombotic treatment, patients who were previously allergic to snake antivenom, patients who were administered snake antivenom at another hospital and referred to our hospital, patients who had a dry bite and did not require antivenom treatment, and patients whose file information was not fully accessible were excluded from the study. As a result, thirty patients, whose file data were available, were included in the study.The study was planned as a retrospective observational case series.

For this study, ethics approval was obtained from Adana Governorship, Provincial Health Directorate, Adana City Education and Research Hospital, Clinical Research Ethics Committee with the decision no: 55/817 dated 22.04.2020.

Procedure

As of August 14, 2019, our hospital pharmacy has an only new type of Polivalan™ snake antivenom. Before this date, the Polisera™ snake antivenom was in use for the patients who presented for snakebite, while the Polivalan™ snake antivenom was applied to patients who presented after this date. The contents of both antivenoms are the same; every 10 milliliters of antivenoms have at least 500 LD_{50} *Macrovipera lebetina*, 500 LD_{50} *Montivipera xanthina* and 1000 LD_{50} *Vipera ammodytes* horse-derived antitoxic globulins F(ab')2 that neutralize snake venoms [9]. The patients were classified into two different groups according to the type of antivenom used (Polisera™ snake antivenom, Polivalan™ snake antivenom). Sixteen patients were administered PoliseraTM (Group 1) snake antivenom and 14 patients were administered Polivalan TM (Group 2) snake antivenom.

In addition to the demographic characteristics of the patients, vital signs, local tissue findings, and laboratory parameters were recorded in the standard data form. Clinical staging was performed according to traditional snake bite severity grading scale (Table 1) [10]. The following data were also recorded; the number of vials of snake antivenom used in each group, additional doses of venom were administered, and whether any local or systemic reaction to antivenom has developed or not. Systemic findings (petechiae, bleeding, dyspnea, myocardial ischemia, kidney failure), coagulopathy (thrombocytopenia, prolongation in PTZ and aPTT), rhabdomyolysis (creatine kinase elevation, pain in the extremity), improvement or progression in tissue edema,

duration of stay in the emergency room were also recorded. A platelet count below <150.000/mm^3 was accepted as thrombocytopenia. Laboratory tests were repeated every 4-6 hours according to the patient's clinical findings.

Patients were monitored in the emergency critical care unit, and vital signs were followed. An appropriate fluid replacement was given, and urine outflows were monitored. All patients underwent wound care and, if necessary, tetanus prophylaxis. The limb with the bite was immobilized at the time of admission to the emergency department. The bitten area was marked for monitoring the edema and evaluating the treatment response. Antivenom was given by diluting in serum saline according to the clinical stage. An additional dose of antivenom was given in the event of edema exceeding the region of the marking or tissue tension in the limb or in case of coagulopathy.

Table 1. Traditional snake bite severity grading scale[10]

Severity (Grade)	Manifestations	Amount of Antivenom Recommended
0 (No envenomation)	Local or systemic signs or symptoms absent	-
1 (Minimal)	Local swelling, absence of systemic signs, normal laboratory findings	2-4 vial
2 (Moderate)	Swelling extending past bite site (6–12 in), ≥1 systemic sign or symptom, abnormal laboratory findings	5-9 vial
3 (Severe)	Marked (>12 in) swelling, tissue loss, multiple or severe systemic symptoms, immediate systemic signs, rapid progression of symptoms	10-15 vial
4 (Very severe)	Rapid development of local reaction, ecchymoses, necrosis, blebs, blisters, swelling severe enough to obstruct venous or arterial flow, swelling may involve ipsilateral trunk	>15 vial

Statistical analysis

SPSS 21 package program (SPSS Inc, Chicago, Illinois, USA) was used for the statistical evaluation of the data obtained in the study. Continuous data were summarized as mean, standard deviation, while categorical data were summarized in numbers and percentages. Categorical data were compared with the Chi-square test. The Kolmogorov-Smirnov test was used to compare the means of the parameters examined, and the Student's t-test was used in the evaluation performed with the histogram in the two groups comparisons when the variables were normally distributed, and the Mann Whitney U test was used for the abnormally distributed variables.

RESULTS

Thirty patients, whose file data were available, were included in the study. Six (20%) of the patients were female, and 24 (80%) were male. The mean age was 41±13 (min-max= 20-66). Sixteen patients presented before August 14, 2019, were administered Polisera™ (Group 1) snake antivenom, and 14 patients presented after that date were administered Polivalan™ snake antivenom (Group 2). The demographic characteristics, vital signs, and location of the bite of the patients were compared according to the treatments they received in Table 2. The clinical stages of the patients were classified according to their worst conditions during their follow-up. In Group 1; 25% (n = 4) of patients were Grade 1, 62.5% (n = 10) were Grade 2 and 12.5% (n = 2) were Grade 3. In Group 2; 35.7% (n = 5) of patients were Grade 1, 35.7% (n = 5) were Grade 2 and 28.6% (n = 4) were Grade 3. Two of Grade 3 patients in Group 1 were Grade 2 at the time of presentation and progressed to Grade 3 during follow-up. There was no statistically significant difference between the treatment patients received and their clinical stages. (P = 0.313)

Antivenom treatment dose was decided according to the clinical stage. Patients in Group 1 were given an average of 9.1±7.3 vials, while patients in Group 2 were given an average of 11.6±12.7 vials. There was no statistically significant difference between the number of antivenoms used in the treatment groups (p = 0.517). The need for additional doses of

antivenom was decided according to the clinical findings, tissue edema, and laboratory abnormalities (coagulopathy). The mean frequency of the antivenom administration of Group 1 was 2.9±1.4, whereas that of Group 2 was 3.6±3.2 times (P = 0.461).

A comparison of local and systemic complications developed during the follow-up of the patients between the groups is shown in Table 2. Cellulite was observed in 85.7% (n = 12) of the cases in Group 2, and the difference was statistically significant compared to Group 1 (p=0.038). Fever was observed in 30% (n= 9) of all cases and thrombocytopenia in 33.3% (n=10). Rhabdomyolysis was observed in 23.3% (n = 7) cases with pain, tenderness in the area of the bite, and elevated creatine kinase.

Comparison of the complications developed due to antivenom treatment among patients was made in Table 2. In Group 2, allergic reactions and / or urticarial plaques were seen in 64.3% (n = 9) patients (p <0.001). Hypotension was observed in 28.6% (n = 4) patients after antivenom infusion (p=0.102).

Table 2. Patient demographics and admission details

	Group 1 (n=16)	**Group 2 (n=14)**	**p**
Gender (n)			
Female	3	3	0.855
Male	13	11	
Age (year) mean±SD	41.4±13.5	40.6±12.9	0.859
Mean arterial pressure (mmHg) mean±SD	89.6±11.7	91.3±12.6	0.700
Heart beat (beat/min) mean±SD	74.2±14.2	80.1±12.7	0.250
Bite location (n)			
Hand	5	3	0.730
Feet	5	6	
Finger	5	3	
Toe	1	2	
Severity (Grade) (n)			
Grade 0	0	0	0.313
Grade 1	4	5	
Grade 2	10	5	
Grade 3	2	4	
Grade 4	0	0	
Antivenom vials (mean±SD)	9.1±7.3	11.6±12.7	0.517
Antivenom application frequency (mean±SD)	2.9±1.4	3.6±3.2	0.461
Local and systemic complications (n)			
Cellulite	8	12	0.038
Lymphedema	7	6	0.961
Thrombocytopenia	3	7	0.070
Fever	2	7	0.025
Rhabdomyolysis	3	4	0.526
Myocardial ischemia	0	1	0.277
Dyspnea	0	1	0.277
Complications against antivenomas (n)			
Allergic reaction-Urticaria	0	9	<0.001
Hypotension	1	4	0.102
Anaphylaxis	0	2	0.118
Ventricular Tachycardia	0	1	0.277
Length of hospital stay (/hour) (mean±SD)	28.6±20.4	47.6±33.8	0.069

Group 1: Patients using Polisera antivenom Group 2: Patients using Polivalan antivenom

Clinical deterioration was detected in 5 patients receiving Polivalan™ antivenom during their hospitalization. The clinical-stage progressed from Grade 2 to Grade 3 in 4 patients and Grade 1 to Grade 2 in 1 patient.

Case samples

Case 1

A 28-year-old male patient. The patient needed 25 vials of antivenom. Platelet level decreased to 75.000/mm^3, creatine kinase level increased to 381 IU/L, there was progress in edema. Intravenous mannitol was administered to regress lymphedema. The patient needed an additional dose of antivenom. Hyperemia was seen in the whole body after the 2nd dose of antivenom. Antihistamine and steroids were administered. On the 4th day of hospitalization, the patient was discharged with the recommendation of leg immobilization.

Case 2

A 50-year-old male patient. Local tissue edema progressed in the follow-up, and a total of 10 vials of antivenom were applied. Mannitol was given. After the 2nd dose antivenom, dyspnea developed. No skin finding and hypotension occurred. The patient with bronchospasm was given oxygen, nebular salbutamol, and intravenous steroids. On the 2nd day of hospitalization, the patient was discharged with the recommendation of arm immobilization.

Case 3

A 39-year-old male patient. (Figure 1) A total of 16 vials of antivenom were applied to the patient. Platelet level decreased to 86.000/mm^3 creatine kinase: increased to 910 IU/L, there was progress in edema. Cardiac markers were detected high at the time of admission (CK-MB: 13 μg / L, High Sensitive Troponin I: 514 ng/L).

The patient had sinus tachycardia on the electrocardiogram (ECG). Ejection fraction was 55% in echocardiography; there was no global or segmental wall motion abnormality. The patient needed an additional dose of antivenom. Anaphylactoid reaction developed after the 2nd dose of antivenom, and the patient had hypotension and urticaria. Adrenaline, antihistamine, and steroids were administered. Post-treatment body temperature was 38.5 ° C. Cold application, and paracetamol infusion were applied. On the 5th day of hospitalization, the patient was discharged with the recommendation of leg immobilization.

Case 4

A 45-year-old female patient. A total of 19 vials of antivenom were applied to the patient, who was determined as Grade 2. Platelet level decreased to 118.000/mm^3; there was progress in edema. The patient needed an additional dose of antivenom. The patient developed fever and cellulite. When taking antivenom infusion for the 4th time, the patient developed pulsed ventricular tachycardia. Antivenom infusion was stopped. The heart rhythm improved spontaneously. On the 6th day of hospitalization, the patient was discharged with the recommendation of arm immobilization.

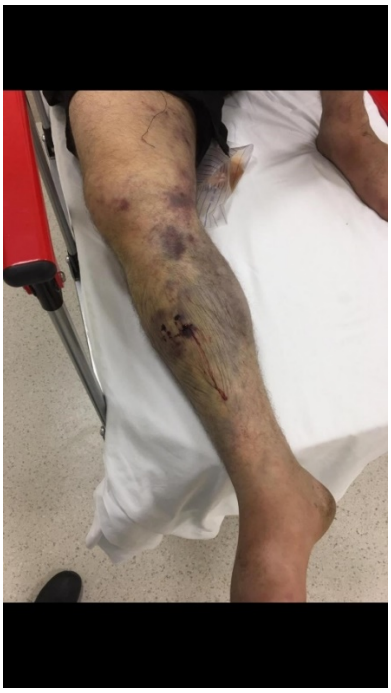

Figure 1. (Case 3) A 39-year-old male patient. Grade 3 envenomation with snakebite patient local tissue finding. Definite teeth traces at the bite site; the two holes which are two centimeters apart from each other where swelling, pain, haemorrhagic and color change occur.

Case 5

A 57-year-old male patient. The patient needed six vials of antivenom. Platelet level decreased to 148.000/mm^3 Creatine kinase: increased to 674 IU/L. The patient developed fever and cellulite. The

patient needed an additional dose of antivenom. Anaphylactoid reaction developed after the 3rd dose of antivenom, and the patient had hypotension and urticaria. Adrenaline, antihistamine, and steroids were administered. On the 2nd day of hospitalization, the patient was discharged with the recommendation of leg immobilization.

Laboratory parameters, according to the given treatments, are compared in Table 3. In Group 2 patients, the mean WBC count after 24 hours was 18.2 ± 7.4 (p = 0.038), and the mean CRP level was 63.2 ± 39 (p = 0.013); the mean values were statistically significantly higher.

Table 3. Laboratory parameters of the patients

	On Admission			6th hour			24th hour		
	Group 1	Group 2	p	Group 1	Group 2	p	Group 1	Group 2	p
WBC (10^3µL)	10.7±3.5	12.1±5.6	0.398	10.7±2.8	19.2±17.4	0.066	12±2.6	18.2±7.4	0.038
Hemoglobin (g/dl)	14.2±1.7	14.9±1.5	0.248	13.6±1.5	14.1±1.3	0.294	13±1.4	13.1±1.3	0.864
Platelet (10^3µL)	201.9±58	217.9±52.7	0.440	202.4±58	196.5±57.6	0.783	194.2±42.7	168±66	0.335
PTZ (sn)	12.2±1	12.4±1.5	0.594	12.7±0.6	12.9±1	0.383	12.1±0.9	12.7±1.3	0.263
aPTT (sn)	22.7±2.4	22.4±2.1	0.758	22.3±2.5	22.3±1.9	0.975	21.6±1.4	22.4±2.3	0.416
INR	1±0.1	1±0.1	0.689	1±0.05	1.1±0.08	0.538	1±0.08	1±0.12	0.365
Glucose (mg/dl)	119.9±31	118.9±26.7	0.930	143.4±72	144.6±42.5	0.959	111.8±20.1	128.9±32.8	0.263
Urea (mg/dl)	32.7±7.7	33.4±6.1	0.796	28.4±7.2	28.6±7.2	0.924	27.5±10.2	28±6.6	0.901
Creatinine (mg/dl)	0.8±0.1	0.8±0.2	0.571	0.6±0.2	0.7±0.2	0.064	0.6±0.1	0.7±0.1	0.706
AST (IU/L)	28.4±8.6	29.3±9.4	0.798	23.9±6.5	28.6±15.2	0.272	21.2±6.2	23.4±10	0.636
ALT (IU/L)	25.6±14.4	24.5±18.2	0.852	19.9±12	27.8±20.2	0.192	16.8±12.4	22.1±13	0.425
Amylase (IU/L)	63.5±19	65.4±21	0.801	52.9±15	54.1±20.4	0.854	56.2±9.4	41.2±15.8	0.059
Sodium (mmol/L)	138.3±2.1	139.8±1.5	0.030	137.7±2	138.7±2.4	0.217	138.5±2.1	139.1±1.9	0.563
Potassium (mmol/L)	4.4±0.4	4.3±0.4	0.562	4.3±0.4	4±0.4	0.021	4.2±0.3	4±0.4	0.261
CK (IU/L)	166.5±88	265.6±219.5	0.107	118.1±67.3	192.9±171.9	0.119	130.2±93.8	180.3±170	0.605
CK-MB (µg/L)	2.7±2.3	3.7±4.8	0.450	2.1±1.7	2.5±3.1	0.632	1.4±0.3	2.9±3.7	0.320
Troponin I (ng/L)	5.7±5.5	16.6±47.4	0.368	4.9±5.8	41.1±136.1	0.296	5±2.8	24.2±61.1	0.458
CRP	6.4±7.2	3.3±3.5	0.165	8.1±10.6	16.9±15.5	0.078	14.1±24.7	63.2±39	0.013

Group 1: Patients using Polisera antivenom; Group 2: Patients using Polivalan antivenom; **CK:** Creatinine kinase; **CK-MB:** Creatinine kinase- Myocardial band; a**PTT:** Activated partial thromboplastin time; **CRP:** C-Reaktive Protein; A**LT:** Alanine transferase **PTZ:** *Protrombin Time;* **AST:** Aspartate transferase; **WBC:** White blood cell; *Value other than reference values

The length of hospital stay for Group 1 patients was 28.6 ± 20.4 hours, while for Group 2 patients, it was 47.6 ± 33.8 hours. There was no statistically significant difference between the two groups (p = 0.069). Despite developing complications, no death due to snakebite or antivenom treatment was observed.

DISCUSSION

In our study, a significantly higher rate of allergic reactions-urticaria, fever, and cellulite was observed in the group receiving Polivalan™ antivenom. The number of antivenoms used and the length of hospital stay was higher in the group receiving Polivalan™ antivenom. Besides, severe life-threatening side effects such as anaphylaxis, arrhythmia (ventricular tachycardia), hypotension due to antivenom use were seen in patients receiving a new type of Polivalan™ antivenom.

Antivenoms are antibody preparations derived from the plasma of the animals such as horses or sheep by injecting venoms of poisonous animals into these animals. Antivenoms contain the entire Ig G molecule or Fab fragments, or F(ab')2 fragments to which only the antigen binds [11]. In many centers around the world, it is possible to produce snake toxins required for antivenom production with recombinant technology. However, while creating venom pools, antivenom producers still obtain the poison required for antivenom by the mechanical stimulation method of poison glands called 'milking.' Significant toxicological and antigenic differences have been reported, even in the same snake populations, due to the geographic regions in which

they are located. There zfore the antibody efficacy of venom pools obtained by the milking method can vary. Another important stage in the production phase is the stabilization process of antivenoms, known as the freeze-drying technique. In this process, because of the structural changes that the toxins are subjected to due to the stress, the effectiveness of the two venoms with the same toxicity profile may differ [12]. In addition, as a result of the batch-to-batch variation out from the factory, there may be differences between the antivenom success and effectiveness even in antivenoms produced at different times in the same production facility. Also, the recommended dosage warnings that the manufacturers encode on the packs are often obtained with the LD_{50} and ED_{50} in the laboratory mice and are mostly clinically unreliable [6]. All these factors in the production stage may be support the reason why two polyvalent antivenoms with the same contents we use in our study have different antivenom efficacy and side effect profile.

Antivenom treatment is indicated in the case of systemic or regional envenomation. Systemic envenomation findings include spontaneous systemic bleeding, coagulopathy (INR > 1.2 or > 4-5 seconds above PT control or thrombocytopenia), neurotoxicity findings, cardiovascular anomaly (hypotension, shock, arrhythmia, etc.), acute kidney injury (increased urea creatinine, oliguria/anuria) and hemoglobinuria, rhabdomyolysis. Regional signs of envenomation are local swelling, which includes more than half of the extremity within 48 hours after the bite, swelling after the finger bite, swelling that exceeds the wrist and ankle within hours, expansion in the lymph node that drains the bitten limb [6]. The snake antivenom was applied according to the presence of the findings of the envenomation and clinical stage in our study. The ideal dose and clinical-stage for antivenom dosage and treatment in the literature are still controversial. Roberts and Otten suggested not using antivenom for Grade 0 and 1, using 4 to 10 vials for Grade 2, and 10 to 40 vials for Grade 3 [13], while Scharman et al. staged the patients as Grade 0, 1, 2, 3, 4 and suggested using 0-4, 5-9, 10-15, 15 and over vials, respectively [10]. We think that the type of antivenom used is also effective in these numbers. New protocols where a low dose of antivenom application is effective coming to the fore today. However, even in these protocols, up to 17% allergy can be observed [14, 15]. Although the difference between the mean number of antivenom used in our study, the frequency of additional dose antivenom administration, and the length of hospital stay was not statistically significant, it was mathematically higher in the group that received Polivalan™ antivenom.

The early reaction may occur within hours, while late reaction can occur five days after due to the use of snake antivenoms. This fact may increase mortality and morbidity [13]. Early anaphylactic reactions due to the use of antivenom can be observed on a wide scale from urticaria to life-threatening anaphylactic shock. Most of these reactions occur due to complement activation by IgG aggregates / residual Fc fragments or by stimulation of mast cells/basophils by antivenom proteins. Pyrogenic (endotoxin) reactions are associated with pyrogen contamination during the production of antivenom. It occurs 1-2 hours post-infusion. Fever, vasodilation, hypotension can be observed. Hypotension and shock often occur as a result of systematical leakage from plasma in the bitten limb, vasodilation, or cardiac damage. Due to the possibility of all kinds of arrhythmia, myocardial damage, and hyperkalemia, ECG should be requested for patients. Late (serum disease-type) reactions occur on average in 7 days. Fever, vomiting, diarrhea, myalgia, lymphadenopathy, proteinuria, recurrent urticaria, and rarely encephalopathy can be observed [6]. A higher rate of complications and side effects were observed statistically after the Polivalan™ antivenom in our study. More allergic reactions-urticaria, fever, and cellulite were observed in the group receiving Polivalan™ antivenom. Also, severe life-threatening side effects such as anaphylaxis, arrhythmia (ventricular tachycardia), hypotension were seen in patients receiving a new type of Polivalan™ antivenom. It is possible that the fever and infection table, that is, pyrogenic (endotoxin) reactions, which we see more frequently in the patients we applied Polivalan™, are caused by contamination of the antivenom during production or distribution. Another cause of fever may be a common wound infection and cellulite in patients.

After Polivalan™ antivenom, tissue edema regressed more limitedly and progress in clinical stages of patients and deterioration in laboratory parameters were observed more frequently. Existing tissue edema caused wound infection and a higher rate of cellulite (WBC, CRP count correlates with this condition). Increased tissue edema caused more additional doses of antivenoms and longer length of hospital stay. Anaphylaxis was seen in 2 patients, ventricular tachycardia was seen in 1 patient,

shortness of breath was seen in 1 patient, and hypotension was seen in 4 patients of 14 patients who received Polivalan™ in our study. This number may not be statistically significant due to the recent use of antivenom and the study being conducted in a limited number of cases. However, it is clinically significant due to potentially fatal side effects.

As a conclusion, antivenoms are an important part of treatment because of their potential to reverse pathophysiological processes in snakebites. However, important side effects related to the use of antivenom may be seen. Different methodologies arising from the production of antivenom, pyrogen contamination, and differences in packaging can cause different effects and side effects even in products with the same dose and antivenom content. Prospective studies to be conducted with a larger case series with antivenoms used in our country will help to determine this effect and side effect profile better.

Yazar Katkıları: Çalışma konsepti/Tasarımı: MG, SS; Veri toplama: MG, ÖY, SA, Çİ, CİE; Veri analizi ve yorumlama: MG, SS, ÖY, Çİ, CİE; Yazı taslağı: MG, SS, ÖY, Çİ, CİE; İçeriğin eleştirel incelenmesi: MG, SS, ÖY, SA; Son onay ve sorumluluk: MG, SS, ÖY, Çİ, CİE; Teknik ve malzeme desteği: MG, SA, Çİ, CİE; Süpervizyon: MG, SS, ÖY, Çİ, CİE; Fon sağlama (mevcut ise): yok.
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