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ARAŞTIRMA / RESEARCH

Prospective analysis of cardiovascular drug intoxication

Kardiyovasküler ilaç zehirlenmelerinin ileriye dönük analizi

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Abstract

Purpose: The aim of this study is to provide data about diagnosis, treatment, and results of the patients poisoned by drugs affecting the cardiovascular system.

Materials and Methods: Patients aged 18 and over who applied to the emergency department with drug poisoning affecting cardiovasculer system were included in the study. The demographic data, drugs and doses, emergency treatment and the time of development of shock or bradycardia, treatment, antidotes and invasive procedures were recorded.

Results: In our study twenty-five patients, 8 (32 %) male and 17 (68 %) female, were included. At the admission, 56 % (n=14) had hypotension, 8 % (n=2) had bradycardia, at the second hour 76 % (n=19) had hypotension, 16 % (n=4) had bradycardia. Within 6 hours after admission, 80 % (n=20) patients had hypotension, 28 % (n=7) patients had bradycardia at least once. Fifty-two percent (n=13) of the patients calcium, 36 % (n=9) glukagon, 32 % (n=8) lipid, 12 % (n=3) atropine, 20 % (n=5) positive inotropes were given.

Conclusion: Lipid therapy produces positive results in patients who did not improve with calcium, glucagon and fluid therapy. Patients who received calcium channel blockers experienced more cardiogenic shock and bradycardia was more common in patients receiving beta-blockers.

Keywords:. Cardiovascular drug poisoning, beta-blocker, poisoning, calcium channel blocker.

Öz

Amaç: Bu çalışmanın amacı, kardiyovasküler sisteme etkili ilaçlarla olan zehirlenme hastalarını inceleyerek literatüre tanı, tedavi ve sonuçlarla ilgili veri kazandırmaktır.

Gereç ve Yöntem: Çalışmaya hastanemiz acil servisine kardiyovasküler sisteme etkili ilaç zehirlenmesiyle başvuran 18 yaş ve üzeri hastalar alındı. Olguların demografik verileri, aldıkları ilaçlar ve dozları, acil tedavisi ve yatışı sırasında şok veya bradikardi gibi hayati bulguların gelişme zamanı, zehirlenmenin tedavisi, antidotlar ve yapılan invaziv girişimler kaydedildi.

Bulgular: Çalışmaya 8 (% 32,0)'i erkek, 17 (% 68,0)'si kadın olmak üzere 25 hasta dahil edildi. Olguların başvurusunda % 56,0 (n:14)'sında hipotansiyon, % 8,0 (n:2)'inde bradikardi saptanırken, 2. saat vitallerinde % 76,0 (n:19)'sında hipotansiyon, % 16,0 (n:4)'sında bradikardi olduğu belirlendi. Başvurudan sonraki 6 saat içerisinde % 80 (n:20) hastada hipotansiyon, % 28 (n:7) hastada bradikardi en az bir kere görüldü. Hastaların; % 52,0 (n: 13)'sine kalsiyum, % 36,0 (n: 9)'sına glukagon, % 32,0 (n: 8)'sine lipit, % 12,0 (n: 3)'sine atropin, % 20,0 (n: 5)'sine pozitif inotrop kullanıldı.

Sonuç: Kalsiyum, glukagon ve sıvı tedavisi ile sonuç alınamayan hastalarda lipit tedavisinin olumlu sonuçlar yarattığı görülmüştür. Kalsiyum kanal blokeri alan hastalarda beta-bloker alan hastalara oranla daha çok kardiyojenik şok, beta-bloker alanlarda ise daha çok bradikardi görülmüştür.

Anahtar kelimeler: Kardiyovasküler ilaç zehirlenmeleri, beta-bloker, zehirlenme, kalsiyum kanal blokeri.

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INTRODUCTION

Poisoning has been one of the major issues that has threatened human health since ancient times[1]. The overall ratio of poisoned patients is reported as 0.5%–5.0% of all patients in emergency rooms[2]. The same ratio is reported as 0.07%–0.7% in emerging countries[3].

According to 2008 data of the Turkish National Poison Council, the most frequent factors of acute poisoning are drugs (analgesics, antidepressants, antihistamines, antihypertensives, antiepileptics, etc.), pesticides, domestic chemicals, poisonous gases (carbon monoxide), and poisonous animal bites.[4] According to these data, paracetamol (6.78%) is the most common drug on the list of the top 50 drugs that cause the most poisoning, and no cardiovascular drugs are included on this list (beta-blockers, calcium channel blockers, and antiarrhythmics)[4]. Although cardiovascular drug poisoning is not common, it poses a high-level risk of mortality[5].

Cardiovascular drugs are more potent than other drugs, and shock, bradycardia, and organ failure as a result of perfusion disorders can cause death. Lipid emulsion therapy (LET) is a current treatment for patients with beta-blockers and calcium channel blocker poisoning. Studies on cardiovascular drug poisoning are very limited in Turkey. Current treatment algorithms are based on insufficient evidence.[6] This study was aimed at providing data for treatment algorithms and guidelines to be created, and the treatments applied to the patients and the efficacy of the treatments are discussed.

MATERIALS AND METHODS

Study population

This study was planned as a prospective observational study. This study was approved by the local ethics committee (Cukurova University, Faculty of Medicine; 06 July 2018, meeting number 79, decision number 42) and followed the recommendations of the ethical principles published in the Declaration of Helsinki developed by the World Medical Association (WMA). The clinical information for informed consent was explained in detail to all patients who were included in the study after obtaining written consent. In the mean of the parameters examined in this study, the medium effect size (effect size = 0.80) was assumed to be a difference, the alpha significance level was calculated as 0.05 95% power, and the sample was calculated as a total of 25 patients. The study group comprised 25 patients who presented to the Cukurova University Emergency Medicine Clinic with cardiovascular drug poisoning. A patient with calcium channel blocker poisoning was not included in the study because she was brought to the emergency room with cardiac arrest and did not respond to resuscitation. Another patient was excluded from the study because she had previously used drugs that had cardiovascular effects. Two patients who did not meet the inclusion criteria were excluded from the study. A total of 25 patients were included in the study, which was conducted at the Emergency Department (ED) of Cukurova University's Faculty of Medicine from 2017–2020. Twenty-five consecutive patients over 18 years of age who arrived at the ED with suicidal or accidental cardiovascular drug poisoning were included in the study after their written consent. Patients who had used cardiovascular drugs in their medical history, had had poisoning with drugs that do not have an effect on the cardiovascular system, patients with medical conditions (such as sepsis, bleeding, and acute coronary syndrome) other than drug intoxication that may cause hypotension and/or arrhythmia at the time of admission to the emergency department, patients who came to the emergency department with cardiopulmonary arrest and did not respond to resuscitation, patients younger than 18 years of age, and patients who did not consent to participate in the study were considered as exclusion criteria.

The subjects were asked in detail about their demographic data, anamnesis, the drugs they used, and comorbidities. They were questioned about whether there had been previous suicide attempts or any psychiatric disorders. In order to make the correct diagnosis as early as possible, all cases were evaluated for toxidromes when they came to the ED. All the antidotes and symptomatic treatments were initiated immediately for patients with symptoms of poisoning.

Laboratory analysis

The complete blood count (CBC) and biochemical parameters of the patients were measured from blood taken from the vein in the antecubital region at first admission: white blood cell count (WBC), hemoglobin, hematocrit, platelet, blood urea nitrogen (BUN), creatinine, sodium, potassium, alanine

aminotransferase (ALT), aspartate aminotransferase (AST), lactate, creatine kinase-MB (CK-MB), high-sensitive troponin I (hsT-I), prothrombin time (PTT), INR, activated partial thromboplastin time (aPTT), venous blood gases, and drug levels (that can be analyzed in the forensic medicine laboratory in the blood) were measured. An automatic measuring device, a Sysmex XN 10 automated meter (Automated Hematology Analyzer XN series, Sysmex Corporation, 1-5-1 Wakinnohama-Kaigandori Chuo-ku, Kobe 651-0073, Japan), was used to perform the CBC measurements. Biochemical parameters were performed using the automatic measuring device Beucher Coulter AU5800 (Beckman Coulter GmbH Europark Fichtenhain B 13 47807 Krefeld, Germany). Blood gas measurement was performed using a Radiometer ABL 800 flex device. Drug blood level measurements were done using the Shimadzu 8040 Liquid Chromatography Tandem Mass Spectrometer LC/MS/MS System device in the forensic medicine laboratory.

Follow-up and evaluation of patients

Patients who came to the ED with acute cardiovascular drug poisoning were included in the study. The agents to which the patients were exposed were grouped according to their pharmacological features. All patients with cardiovascular drug poisoning who came to the ED were transferred to the emergency critical unit. The patients were taken into a safety circle. Attempts were made to stabilize the vital signs of the patients by ensuring respiratory, circulatory, and airway safety. The presence of shock or symptomatic bradycardia, the treatment of intoxication, the antidotes used, the invasive procedures, and the extracorporeal methods performed were recorded in detail.

Statistical analysis

The SPSS 23.0 package program was used for the statistical analysis of the data. Categorical measurements were summarized in terms of numbers and percentages. The mean, deviation, and minimum-maximum were used for continuous measurements. While the chi-square test was used to analyze the categorical expressions, the adjusted Bonferroni test was used to analyze the differences between the groups. The Kruskal-Wallis test was employed to analyze the differences between the parameters that did not show a normal distribution. The statistical significance level was taken as 0.05 for all tests.

RESULTS

Twenty-five patients admitted to the ED with cardiovascular drug poisoning were included in this study. Eight of the patients were male (32%), and 17 were female (68%). Other demographic data are shown in Table 1. 4% (n = 1) of the patients were accidentally poisoned, while the other 96% (n = 24) were due to suicide attempts. A psychiatric disorder was found in 44% (n = 11) of the patients. Moreover, 32% (n = 8) of the patients had attempted suicide before. Drug addiction was found in 12% (n = 3) of the patients with symptoms of smoking, opiate addiction, and alcohol addiction (Table 1). 64% (n = 16) of the patients' symptoms were due to beta-blockers, 28% (n = 7) to calcium channel blockers, 4% (n = 1) to anti-arrhythmics, and 4% (n = 1) to alpha-agonists (Table 1). The patients had been poisoned by propranolol, amlodipine, metoprolol, nebivolol, and verapamil in 36% (n = 9), 16% (n = 4), 12% (n = 3), 12% (n = 3), and 8% (n = 2), respectively. The remaining four patients had alpha methyldopa, diltiazem, carvedilol, and propafenone (Table 1).

56% (n = 14) of the patients had hypotension, and 8% (n = 2) had bradycardia in their vital signs at hospital admission. However, it was determined that 60% (n = 15) of the patients had hypotension, and 28% (n = 7) of them had bradycardia in their sixth hour when vitals were checked at the hospital. No statistically significant difference was found in the hourly tracking of vital symptoms of the 25 patients with cardiovascular drug poisoning in the ED (Table 2).

Fluid resuscitation was applied to all 25 patients during the treatment period. The patients were hospitalized in the emergency service critical care unit for an average of 2.0 ± 3.39 days (Table 3).

In the emergency department, calcium, glucagon, lipid, atropine, and positive inotropes were given to 52% (n = 13), 36% (n = 9), 28% (n = 7), 12% (n = 3), and 20% (n = 5) of the patients, respectively. Although intubation was needed for 4% (n = 1) of the patients and a pacemaker for 4% (n = 1), hemodialysis, hemofiltration, plasmapheresis, and intraaortic balloon pump treatment were not used (Table 3).

Table 1. Patients poisoned by drugs that are effective on the cardiovascular system Examination of their introductory features, poisoning patterns, the groups of drugs they take, how many different drugs they are poisoned with. (n: 25)

Measurement		**Avg±sd**	**Min-Max**
Age		35.52±14.73	18-66
BMI		25.59±5.39	19.5-43.3
Measurement		**Frequency (n)**	**Percentage (%)**
Sex	Male	8	32.0
	Female	17	68.0
Profession	Employed	7	28.0
	Unemployed	18	72.0
Education Status	N/A	3	12.0
	Primary School	8	32.0
	Middle School	5	20.0
	High School	6	24.0
	University	3	12.0
Admission Type	Ambulance	7	28.0
	By their own means	3	12.0
	Transfer	15	60.0
Drug-substance addiction	Opiad addicted	1	4.0
	Smoking	1	4.0
	Smoking,alcohol	1	4.0
	No	22	88.0
Psychiatric illness	Yes	11	44.0
	No	14	56.0
Suicide attempt before	Yes	8	32.0
	No	17	68.0
Poisoning cause	Accidentally	1	4.0
	Suicide	24	96.0
Drug groups	Beta-blockers	16	64.0
	Calcium channel blockers	7	28.0
	Anti-arrhythmics	1	4.0
	Alpha-agonists	1	4.0
Drugs	Alpha methyldopa	1	4.0
	Amlodipine	4	16.0
	Diltiazem	1	4.0
	Carvedilol	1	4.0
	Metoprolol	3	12.0
	Nebivolol	3	12.0
	Propafenone	1	4.0
	Propranolol	9	36.0
	Verapamil	2	8.0
	Single drugs	11	44.0
	Two drugs	4	16.0
	More than two drugs	10	40.0
Total		25	100.0

Table 2. Vital symptoms of the patients as of 1st, 2nd, 4th, 6th hours after hospital arrival (n: 25).

		Beta-Blockers (n:16)	Calcium channel blockers (n:7)	Anti-arrhythmics (n:1)	Alpha-agonists (n:1)	p*
		n(%)	n(%)	n(%)	n(%)	
Blood pressure (initial)	Low	8 (50.0)	5 (71.4)	1 (100.0)	0 (0.0)	0.346
	Normal	8 (50.0)	1 (14.3)	0 (0.0)	1 (100.0)	
	High	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	
Pulse (initial)	Low	1 (6.3)	1 (14.3)	0 (0.0)	0 (0.0)	0.376
	Normal	14 (87.5)	3 (42.9)	1 (100.0)	1 (100.0)	
	Tachycardia	1 (6.3)	3 (42.9)	0 (0.0)	0 (0.0)	
Blood pressure (1 hour)	Low	11 (68.8)	6 (85.7)	1 (100.0)	1 (100.0)	0.693
	Normal	5 (31.3)	1 (14.3)	0 (0.0)	0 (0.0)	
Pulse (1 hour)	Low	2 (12.5)	1 (14.3)	0 (0.0)	0 (0.0)	0.801
	Normal	14 (87.5)	5 (71.4)	1 (100.0)	1 (100.0)	
	Tachycardia	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	
Blood pressure 2 hour	Low	14 (87.5)	3 (42.9)	1 (100.0)	1 (100.0)	0.111
	Normal	2 (12.5)	4 (57.1)	0 (0.0)	0 (0.0)	
Pulse 2 hour	Low	4 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.444
	Normal	12 (75.0)	7 (100.0)	1 (100.0)	1 (100.0)	
Blood pressure 4 hour	Low	12 (75.0)	6 (85.7)	1 (100.0)	1 (100.0)	0.827
	Normal	4 (25.0)	1 (14.3)	0 (0.0)	0 (0.0)	
Pulse 4 hour	Low	6 (37.5)	0 (0.0)	0 (0.0)	0 (0.0)	0.485
	Normal	9 (56.3)	7 (100.0)	1 (100.0)	1 (100.0)	
	Tachycardia	1 (6.3)	0 (0.0)	0 (0.0)	0 (0.0)	
Blood pressure 6 hour	Low	9 (56.3)	5 (71.4)	1 (100.0)	0 (0.0)	0.450
	Normal	7 (43.8)	2 (28.6)	0 (0.0)	1 (100.0)	
Pulse 6 hour	Low	5 (31.3)	1 (14.3)	0 (0.0)	1 (100.0)	0.415
	Normal	11 (68.8)	5 (71.4)	1 (100.0)	0 (0.0)	
	Tachycardia	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	

* $p<0.05$

In terms of the drug levels studied, they were positive in 64% (n = 16) of the patients, 24% (n = 6) could not be studied due to the lack of a kit for a particular drug, and 12% (n = 3) were found to be negative (Table 3). Three patients with negative blood drug levels were poisoned with propranolol, and two had bradycardia. It was statistically reasonable that the patients poisoned by calcium channel blockers had received significantly higher positive inotrope treatments than the other treatments (Table 3).

The creatinine levels of the patients who were poisoned with calcium channel blockers were higher than the patients in the other group, and the difference between them was statistically significant (Table 4).

Table 3. The analysis of treatment methods for cardiovascular drug poisoning (n: 25)

		Beta-Blockers (n:16)	Calcium channel blockers (n:7)	Anti-arrhythmics (n:1)	Alpha-agonists (n:1)	p*
		n(%)	n(%)	n (%)	n(%)	
Amount of fluid given		1687.5±928.7 (500-4000)	2071.42±886.4 (500-3000)	500.0±0.0 (500-500)	1000.0±0.0 (1000-1000)	0.354
Calcium given	Yes	8 (50.0)	5 (71.4)	0 (0.0)	0 (0.0)	0.355
	No	8 (50.0)	2 (28.6)	1 (100.0)	1 (100.0)	
Glucagon given	Yes	5 (31.3)	4 (57.1)	0 (0.0)	0 (0.0)	0.451
	No	11 (68.8)	3 (42.9)	1 (100.0)	1 (100.0)	
Lipid given	Yes	4 (25.0)	4 (57.2)	0 (0.0)	0 (0.0)	0.569
	No	12 (75.0)	3 (42.9)	1 (100.0)	1 (100.0)	
Atropine given	Yes	2 (12.5)	0 (14.3)	0 (0.0)	0 (0.0)	0.958
	No	14 (87.5)	6 (85.7)	1 (100.0)	1 (100.0)	
Positive inotrope given	Yes	1 (6.3)	4 (57.1)	0 (0.0)	0 (0.0)	0.038*
	No	15 (93.8)	3 (42.9)	1 (100.0)	1 (100.0)	
Intubation used	Yes	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0.444
	No	16 (100.0)	6 (85.7)	1 (100.0)	1 (100.0)	
Intraaortic balloon pump	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.000
	No	16 (100.0)	7 (100.0)	1 (100.0)	1 (100.0)	
Pacemaker used	Yes	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0.444
	No	16 (100.0)	6 (85.7)	1 (100.0)	1 (100.0)	
Measurement of blood drug level	Negative	3 (18.8)	0 (0.0)	0 (0.0)	0 (0.0)	0.087
	Positive	9 (56.3)	7 (100.0)	0 (0.0)	0 (0.0)	
	Lack of kit	4 (25.0)	0 (0.0)	1 (100.0)	1 (100.0)	
Day of hospitalization		1.19±1.22 (0-3)	4.29±5.79 (0-17)	1.00±0.0 (1-1)	0.00±0.0 (0.0)	0.213

* p<0.05

Table 4. The analysis of laboratory results for cardiovascular drug poisoning (n: 25)

		Beta-Blockers (n:16)	Calcium channel blockers (n:7)	Anti-arrhythmics (n:1)	Alpha-agonists (n:1)	p*
		n(%)	n(%)	n(%)	n(%)	
Creatinine	< 1 normal	16 (100.0)	4 (57.1)	1 (100.0)	1 (100.0)	0.033*
	> 1 high	0 (0.0)	3 (42.9)	0 (0.0)	0 (0.0)	

* p<0.05
All patients were discharged after treatment.

DISCUSSION

Cardiovascular drug poisoning is rare. However, these poisonings can be very fatal[5,7]. Cardiotoxic drugs decrease the contractility and electrical activity of the myocardium when taken in high doses. These patients were admitted to the hospital with bradycardia, hypotension, arrhythmias, gastrointestinal symptoms, and neurological symptoms[8]. It is highly significant to have information about these kinds of symptoms in order to understand the severity of the poisoning[9]. Due to the ease of access to cardiovascular drugs, they are deliberately used by patients to overdose[10].

The quality of the current evidence available for the management of cardiotoxic drug poisoning is low[6]. In our study, the mean age of the patients included in the study was 35.52 years. The female/male ratio was 2:1. Although a few studies have a majority of male subjects, most of the studies have shown that, in general, patients with poisoning were female[9,11]. While the presence of psychological illness was observed in 44% (n = 11) of the patients, it was observed that 32% (n = 8) of the patients had

attempted suicide before. Nearly half of the poisoned patients had a psychological disorder, and a high rate of patients who came with a suicide attempt were found to have a history of attempted suicide before.

In the literature, the application of orogastric lavage and active charcoal is recommended within the first hour after poisoning; this occurs in cases of normal drugs. In most patients who take a beta-blocker overdose, symptoms start within two hours, and it takes six hours for all the symptoms to present[12]. In our study, the number of patients with hypotension or bradycardia was higher at the sixth hour compared with the initial vitals of the patients. Lately, gastric lavage has also been recommended for poisoning caused by modified extended-release tablets[13]. It was determined that the patients in our study had arrived at any hospital between four and 14 hours after taking the drugs, an average of 9.48 hours. The reason for this difference was that most of the patients were transferred to us from other hospitals.

During the study, hypotension symptoms were observed at least once in 20 patients when their blood pressure was checked at arrival, in the first hour, second hour, fourth hour, and sixth hour, while it was observed that bradycardia had occurred at least once in nine of the patients. The hypotension was originally the result of the sodium, calcium channel blockade, and vasodilator effects of beta-blockers. Moreover, dehydration due to excessive nausea and vomiting may also contribute to hypotension. Bradycardia and the reversal of hypotension are the primary targets in the treatment of beta-blockers and calcium channel blocker toxicity. For this purpose, hydration, antidote therapy, atropine, and vasopressors are frequently used during the treatment[14]. On the other hand, calcium, glucagon, lipid therapies, and high-dose insulin euglycemia treatments are also used to reduce and reverse the effects of the drugs. Due to the risk of hypoglycemia and application monitoring difficulties in high-dose insulin therapy, lipid therapy is the priority treatment method. There are four different theories regarding the effectiveness of lipid emulsion therapy in poisoning. One of these theories is that long-chain fatty acids activate voltage-dependent calcium channels in cardiac myocytes. The amount of calcium in the cytosol increases. This theory may be the reason why lipid emulsion therapy was effective in our patients[15].

According to the results of our study, beta-blockers and calcium channel blockers can cause both hypotension and bradycardia. While the prevalence of bradycardia and hypotension symptoms in beta-blocker poisoning is very similar, it was determined that in calcium channel blocker poisoning, hypotension is more common than in bradycardia. According to studies, lipid emulsion therapy is recommended in hemodynamically unstable patients who do not respond to conventional treatments[16]. Other studies have stated that patients poisoned with cardiac drugs other than propranolol may benefit from dialysis treatment[17]. In our study, it was observed that the shock in patients up to the early antidote and lipid therapy might return to normal without any extracorporeal treatments and intra-aortic balloon pump therapy. However, it has been reported that these two methods of treatment may be vitally important when applied to patients who do not respond to medical treatment[8]. A pacemaker should be inserted in the early period in patients with bradycardia, despite drug treatments[18,19].

When all the other treatment methods applied to the our patients were examined, it was determined that it had been appropriate to use hydration for all patients, calcium for 52%, glucagon for 36%, lipid for 28% whose symptoms did not get better, or whose general condition was poor with these treatments, atropine for 12% with symptomatic bradycardia, positive inotropes for 20% who were non-responsive to fluid resuscitation, and a pacemaker in the 4% who had symptomatic bradycardia and complete A-V block, despite the inotropes and all the other treatments.

Although acute renal failure occurred in three cases of calcium channel blocker poisoning, it did not occur in beta-blocker poisoning in patients with hypotension. We believe thatthat acute renal failure occurred because of perfusion impairment up to persistent hypotension caused by calcium channel blockers. In our study, the drug levels of 19 out of 25 patients were examined, including propranolol, metoprolol, diltiazem, verapamil, and amlodipine. On the other hand, examinations for other drugs, such as carvedilol, nebivolol, alfa methyldopa, and propafenone, were not possible due to the lack of specific kits. It was observed that clinical symptoms are relevant to the blood drug level of calcium channel blockers, except in beta-blocker poisonings. However, to clarify this relationship, more patients should be examined.

There are some limitations to our study. The first is that it was a single-center study. The second limitation is the small number of patients. This is due

to the low incidence of poisoning with cardiotoxic drugs. It would be more appropriate to include more patients with longer-term cohort studies. Another limitation was the inability to measure drug levels in some of the patients included in the study. The reason for this is that there were no study kits in the laboratory where the analyses were conducted.

In conclusion, lipid therapy produced positive results in patients who did not improve with calcium, glucagon, or fluid therapy. Patients who received calcium channel blockers experienced more cardiogenic shock, and bradycardia was more common in patients receiving beta-blockers. We believe that the cut-off values we obtained can contribute to the literature and to future large-scale, multi-centered prospective studies.

Yazar Katkıları: Çalışma konsepti/Tasarımı: MOT, OT, TK; Veri toplama: ÖT, TK, MOT, YT; Veri analizi ve yorumlama: AS, AA, AAA, MOT; Yazı taslağı: MOT, YT, HSS; İçeriğin eleştirel incelenmesi: MOT, AA, NRD, HES, BŞANÖM; Son onay ve sorumluluk: MOT, AS, AAA, NRD, YT, ÖT, TK, BŞA, HES, AA; Teknik ve malzeme desteği: -; Süpervizyon: AAA, NRD, AA, AS; Fon sağlama (mevcut ise): yok.
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