e-ISSN
2667-8675
Volume: 5 Issue: 1
May 2023

EJT
Eurasian Journal of Toxicology

www.dergipark.org.tr/ejtox

EPAT
Emergency Physicians Association of Turkey

EJT
Eurasian Journal of Toxicology

Dizinler

Scientific Indexing Services
http://www.sindexs.org/JournalList.aspx?ID=6204

Directory of Research Journals Indexing
http://olddrji.lbp.world/JournalProfile.aspx?jid=2667-8675

EuroPub
https://europub.co.uk/journals/8141

CiteFactor
https://www.citefactor.org/journal/index/28688#.YpdO92hByUk

Google Scholar
https://scholar.google.com/scholar?hl=tr&as_sdt=0%2C5&q=Eurasian+Journal+of+Toxicology&oq=

Asos Index
https://asosindex.com.tr/index.jsp?modul=journal-page&journal-id=393

Editorial

Dear Readers,

We present to you the first issue of our journal for 2023. In this issue, we have published 2 research articles, 4 case reports and 1 letter to editor that we think you will read with pleasure and interest. We hope that your scientific support will continue to increase in 2023. We would like to thank everyone who contributed to our journal for their support and contributions.

Best Regards.

Eurasian Journal of Toxicology Editorial Board

Contents

Original Article

Case Report

Letter to Editor

Original Article

Eurasian Journal of Toxicology

Evaluation of Plasma Total Thiol Levels in Patients with Carbon Monoxide Poisoning in the Emergency Department

Orhan DELİCE[1], Murat DAŞ[2], Gülhan KURTOĞLU ÇELİK[3], Havva ŞAHİN KAVAKLI[3], Salim NEŞELİOĞLU[4], Semra IŞIKOĞLU HATIL[5]

[1]Erzurum Regional Training and Research Hospital, Emergency Medicine Clinic, Erzurum, Türkiye
[2]Çanakkale Onsekiz Mart University, Faculty of Medicine, Department of Emergency Medicine, Çanakkale, Türkiye
[3]Ankara Yıldırım Beyazıt University, Ankara City Hospital, Emergency Medicine Clinic, Ankara, Türkiye
[4]Ankara Yıldırım Beyazıt University, Faculty of Medicine, Medical Biochemistry, Ankara, Türkiye
[5]Ankara Dışkapı Yıldırım Beyazıt Regional Training and Research Hospital, Medical Biochemistry, Ankara, Türkiye

Abstract

Objective: The study aimed to measure the levels of total thiol, an antioxidant parameter, in patients who presented to the emergency department (ED) with carbon monoxide (CO) poisoning under normobaric oxygen therapy (NBOT), evaluate the time-dependent changes in total thiol levels within the first 6 hours, and examine the course of antioxidants in CO poisoning.

Materials and Method: The study population consisted of 85 patients diagnosed with CO poisoning in the ED and 50 volunteers. Total thiol level was measured in the study group at the admission (T0), first (T1) and sixth hour (T6). Carboxyhemoglobin levels, cardiac markers, electrocardiography, and routinely requested tests were investigated in patients with poisoning. The total thiol level was measured in the volunteer group. Data analysis was performed with SPSS 16.0.

Results: There was a significant decrease in total thiol mean levels between T0 and T1 ($p < 0.01$), a significant increase between T1 and T6 ($p < 0.01$), and a significant increase between T0 and T6 ($p < 0.01$). No significant difference was found for T6 total thiol mean level between the patient and the control group ($p > 0.05$).

Conclusions: The significant decrease in the total thiol mean value from T0 to T1 may suggest that the oxidative stress continues within the first hour, and the initiation of the significant increase in the total thiol level within T1 may indicate that the oxidative stress decreased with treatment. Six hours of NBOT protocol is sufficient for acute CO poisoning in patients not requiring HBOT.

Keywords: Carbon monoxide poisoning, oxidative stress, antioxidant, total thiol level

Introduction

Carbon monoxide (CO) is a gas produced by the incomplete combustion of carbonaceous compounds, and its poisoning is associated with significant morbidity and mortality due to early and late complications[1,2]. The clinical presentation of CO poisoning differs according to the amount of CO in the environment, exposure duration, the health status of the victim, and the individual's metabolism factors[3]. As a result of poisoning, almost all systems are affected, especially vital structures such as the central nervous system, cardiovascular system, and respiratory system. Mortality is substantially associated with the involvement of those systems[4].

Oxidative stress has a major role in the pathophysiology of CO poisoning. Oxidative stress occurs with the binding of CO to hemoglobin and myoglobin and also free oxygen radicals that are increased by decreased function of oxidative enzymes such as cytochrome oxidase, guanylate cyclase, and nitric oxide synthase[5].

Antioxidants target to prevent the effects of increasing free oxygen radicals. Many antioxidants, such as enzymes, proteins, minerals, vitamins, glutathione, and thiol have been defined[6]. Thiols are a component of sulfhydryl groups attached to carbon atoms[7]. Thiols, which are endogenous molecules, help aerobic cells maintain in a reducing state despite the oxidizing environment. Thiols with exceptional antioxidant action provide a protective effect against cell damage induced by free radicals[8].

The primary aim of the study was to determine the dynamic changes of serum total thiol levels in patients admitted to the emergency department (ED) with CO poisoning receiving normobaric oxygen therapy (NBOT) at the time of admission (T0), the first (T1) and sixth hour (T6).

Material and Methods

This prospective case-control study was conducted in Ankara Atatürk Training and Research Hospital ED, after the approval of the ethics committee (2011/05/55). The informed written consent forms were received from each participant.

The patients with CO poisoning who presented to the ED within the first 6 hours after exposure to CO gas and received

Corresponding Author: Orhan DELİCE **e-mail:** orhandelice@gmail.com
Received: 26.01.2023 • **Revision**: 28.01.2023 • **Accepted:** 28.01.2023
Cite this article as: Delice O, Daş M, Kurtoğlu Çelik, Şahin Kavaklı H, Neşelioğlu S, Işıkoğlu Hatıl S. Evaluation of Plasma Total Thiol Levels in Patients with Carbon Monoxide Poisoning in the Emergency Department. Eurasian J Tox. 2023;5(1): 1-4

only NBOT between May 30, 2011, and November 15, 2011, were included in the study (n = 85). Blood carboxyhemoglobin (COHb) levels above 5% in non-smokers and 10% in smokers were accepted as CO poisoning. The control group participants (n = 50) were selected among the volunteer hospital personnel with similar characteristics in terms of age and gender distribution without any chronic diseases. Patients with a history of coronary artery disease, cerebrovascular disease, peripheral artery disease, and acute mesenteric ischemia were excluded. Patients younger than 18 years of age and those who refuse to participate were not included in the study.

Venous blood was collected from the antecubital regions of the patients at the admission (T0), the first (T1), and sixth hour (T6) after admission. Complete blood count, glucose, urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST) levels, sodium (Na), potassium (K), and calcium (Ca), creatinine kinase (CK), creatine kinase-MB (CK-MB), troponin I, and venous blood gases were studied routinely from the initial samples for each patient. The blood samples for total thiol measurement were kept at room temperature for 30 minutes and then centrifuged at 3500 rpm for 5 minutes. After centrifugation, the blood taken into Eppendorf tubes was stored at -80°C. All samples were dissolved simultaneously for the analysis.

Total serum thiol concentration or sulfhydryl group was measured by the method described by Elmman and modified by Hu. 5,5'-dithiobis (2 nitrobenzoic acid) (DTNB) interacting with thiol forms a highly colored anion with a maximum peak at 412 nm[9]. Total serum thiol values were obtained by adapting this method to the biochemistry analyzer (SIEMENS, ADVIA 2400, Japan) in the biochemistry laboratory of our hospital.

Data analysis was performed with SPSS 16.0 (IBM Corporation, Armonk, NY, USA). The Kolmogorov-Smirnov test was used for the normality analysis of data distribution. Descriptive statistics of the continuous and discrete numerical variables were expressed as mean ± standard deviation (± SD) and categorical variables were shown as number (n) and percentage (%). The student t-test was used to compare the study and control groups' selected parameters. The paired-sample t-test was used for the time-dependent changes in total thiol levels. Correlations analysis was performed for the relationship between the laboratory results A p value smaller than 0.05 was considered statistically significant.

Results

Of the 85 patients in the study group, 38 (44.7%) were male, and 47 (55.3%) were female. The mean overall age was 35.58 ± 14.57 (18-75). Twenty participants (40%) of those in the control group were male, and 30 were female (60%). The mean age of the control group was 34.3 ± 11.82 (18-60). The patient and the control group were similar in terms of age and gender distributions (p >0.05).

In the study group, the most common symptoms at admission were headache (81.2%) and nausea (72.9%). Chest pain (angina) was detected in 7 patients, and cardiac markers were found positive in 2 of those. Cardiac markers were also high in 2 patients who did not have any symptoms related to angina pectoris. The heart rate was above 120 beats/min in only 3 out of 9 patients with palpitations. Electrocardiographic pathologic changes suggesting cardiac ischemia were not detected in any of the patients. The distribution of the patient's symptoms was presented in Table 1.

Table 1: Symptoms of patients.

Symptom	%
Headache	81.2
Nausea	72.9
Dizziness	47.1
Vomiting	34.1
Syncope	18.8
Palpitation	10.6
Dyspnea	9.4
Angina	7.1
Speech disorder	3.5
Abdominal pain	2.4

The mean value of COHb (%) levels among the patient group was 23.198 ± 7.327. The patients were exposed to CO for an average of 174.88 ± 138.01 minutes. The most common exposure conditions were CO leaking from the stove (54.1%) and the water heater (42.4%). The demographic characteristics of the patients were summarized in Table 2.

Table 2: The demographic characteristics of the patients.

Characteristic	
Age (y), mean ± SD	35.58 ± 14.57
Gender	
Female (%)	47 (55.3)
Male (%)	38 (44.7)
Cause of poisoning (n)	
Stove	46
Water heater	36
Other	3
CO exposure duration (min), mean ± SD	174.88 ± 138.01
Admission method to the emergency department	
With an ambulance	61
By their own means	24
Vital signs	
Systolic blood pressure (mmHg)	121.50 ± 22.40
Diastolic blood pressure (mmHg)	77.17 ± 15.71
Pulse (beat/min)	87.67 ± 17.71
Respiratory rate (/min)	17.95 ± 3.80
Emergency department disposition (n)	
Discharge	79
Hospitalization	5
Transfer	0
Exitus	1

Table 3: Mean total thiol values of study and control groups

Parameter	Group	Time (hour)	Mean±SD
Thiol (µmol/l)	Patient	0th	423.16±86.94 (µmol/l)
		1st	370.90±67.47 (µmol/l)
		6th	474.56±48.52(µmol/l)
	Control	0th	482.94±92.18 (µmol/l)

The mean thiol value of the patients participating in the study was 423.16±86.94 µmol/l at T0, 370.90 ± 67.47 at T1, and 474.56 ± 48.52 at T6. The thiol value of the control group was measured as 482.94 ± 92.18 µmol/l (Table 3). When the means of total thiol levels at T0, T1, and T6 of the patients were compared, a statistically significant difference was determined. The mean thiol values of the patients at three different times and the thiol values of the control group were compared separately, and a statistically significant difference was observed between T0 thiol and the control group (p = 0.003). Also, the mean thiol value T1 and the control group differed (p = 0.001). However, there was no statistically significant difference between the thiol levels at T6 and the control group ($p > 0.05$).

There was a positive correlation between blood COHb levels and lactate levels of the patients in the study group (p <0.001). Correlations among other laboratory parameters are presented in Table 4.

Discussion

The study showed that the total thiol levels measured in patients followed up with the diagnosis of CO poisoning decreased in the first hour, and the levels measured at the 6th hour under NBOT increased up to the levels observed in the control group.

In CO poisoning, one of the primary damage mechanisms develops as a result of the deterioration of the balance against antioxidant activity due to an increase in oxidant production and insufficient antioxidant defense mechanism. With prolonged poisoning, tissue damage progresses, and mortality occurs[10]. Among the antioxidants, thiol groups have the highest concentration. The main sources of thiols are cysteine, homocysteine, methionine, and reduced glutathione (GSH) amino acids. The antioxidant capacity can be predicted by measuring the total thiol level in the plasma[11,12]. In 2009, Zhang J et al. measured the time-dependent changes in antioxidant levels and lipid peroxidation in order to understand the pathophysiology of neuronal damage in rats with CO poisoning. Malondialdehyde (MDA) level was also investigated for the detection of lipid peroxidation. They created CO poisoning by injecting CO into rats intraperitoneally. Considering the measurements made in the serum of rats on the 0th, 1st, 3rd, 7th, 14th, and 21st days from tissue samples taken from the cerebral cortex and hippocampus, the levels of MDA, as a lipid peroxidation marker, increased significantly. Another study found that antioxidant enzyme activities and glutathione increased on the 1st day but gradually decreased towards the 3rd, 7th, 14th, and 21st days[13]. In a study measuring mitochondrial oxidative stress as a result of hypoxia caused by CO poisoning in the brain of rats, catalase activity was investigated. The authors found that the activity of catalase, an antioxidant enzyme, decreased between 60 and 120 minutes under oxygen therapy but increased later[14]. Our study showed that thiol as an antioxidant increased gradually from the 0th to the 1st hour with NBOT in patients diagnosed with CO poisoning. The thiol values at T6 decreased and approached the thiol values of the control group, which consisted of almost healthy individuals.

In a randomized study performed on a series of 60 CO poisoning patients admitted to the hospital within 3 years in Spain in 2011, mitochondrial damage under NBOT was investigated by measuring mitochondrial complex IV activity. They divided the patients into two groups, the first group was composed of severe poisoning (n = 35) cases with a COHb level above 20%, and the second group was composed of moderate poisoning cases with a COHb level below 20% (n = 25). Two sessions of hyperbaric oxygen therapy (HBOT) were administered to 14 severe poisoning cases and 1 session to 21. Meanwhile, HBOT was performed in 14 of the moderate poisoning cases and NBOT in 11 of them. Mitochondria complex 4 activity was demonstrated to be significantly decreased in all severe and moderate poisoning cases compared to the control group. However, a more prominent decrease was detected in the group receiving HBOT. MDA level as the lipid

Table 4: Correlations of the laboratory parameters measured from patients.

	Ck-MB	Troponin	Lactate	COHb	Base Gap	WBC	Plt	Glucose
Ck-MB		$p < 0.01$ $r = 0.765$	$p < 0.01$ $r = 0.333$			$p < 0.01$ $r = 0.283$	$p = 0.012$ $r = 0.271$	$p = 0.036$ $r = 0.228$
Troponin			$p < 0.001$ $r = 0.425$		$p < 0.001$ $r = -0.424$		$p = 0.021$ $r = 0.249$	$p < 0.001$ $r = 0.401$
Lactate				$p < 0.001$ $r = 0.548$	$p < 0.001$ $r = -0.851$			$p < 0.01$ $r = 0.344$
COHb					$p = 0.004$ $r = -0.306$			$p < 0.01$ $r = 0.344$
Base Gap								$p < 0.01$ $r = -0.727$
WBC							$p < 0.01$ $r = 0.439$	

peroxidation activity indicator was high. As a result of HBOT and NBOT, the MDA level decreased significantly. There was a negative correlation between lipid peroxidation activity and mitochondria complex IV enzyme activity. While there was a correlation between COHb level and symptoms, no correlation was determined between mitochondria complex IV enzyme activity and symptom relief. Neurological sequelae developed in 5 patients, and although the decrease in mitochondrial complex IV enzyme activity was abnormal in those patients, normal levels were obtained with HBOT. Therefore, it was emphasized that mitochondria complex IV enzyme activity could be a valuable marker for treatment efficacy. It also raised the question of whether antioxidant therapy might be needed to reverse mitochondrial damage[14]. In our study, we found that thiol levels increased in patients with CO poisoning receiving NBOT. Since we referred patients who had HBOT indication to the relevant center where they could receive this treatment, their 1st, and 6th-hour total thiol values could not be measured. Thus, a comparison of thiol values between HBOT and NBOT could not be performed.

In the study by Taşkıran et al., the authors aimed to determine the changes in oxidative stress parameters in mitochondria by creating a CO poisoning model in rats[15]. Lipid peroxidation, cytochrome oxidase enzyme activity, and glutathione levels were measured from mitochondria in brain tissue (cortex, corpus striatum, and hippocampus). They found that cytochrome oxidase enzyme activity decreased in different parts of the brain in both groups, although at different rates. They reported that the glutathione level decreased in all rats with CO poisoning. In our study, we found that the thiol value decreased in patients with CO poisoning and increased after the start of NBOT. To reveal the role of oxidative stress in the pathophysiology of CO poisoning, Kavaklı et al. examined 88 patients in the emergency department and measured total oxidant status (TOS) and COHb levels[16]. Compared to TOS levels of the control group consisting of 35 healthy individuals, TOS levels of the patients diagnosed with CO poisoning were significantly higher. They reported that TOS, oxidative stress index (OSI), and COHb values measured after NBOT decreased significantly. In addition, TAS (total antioxidant status) levels measured after the treatment were compared with the TAS levels of the control group. They found no significant difference between the groups. Our study indicated that oxidative stress increased in CO poisoning, but after the oxygen treatment initiation, antioxidants increased while oxidative stress decreased.

The present study has several limitations. Firstly, the study was conducted in a single center on 85 patients. Secondly, we could not detect changes in total thiol values in patients receiving HBOT since our institution didn't have this modality.

Conclusion

In conclusion, thiol level increased significantly towards the 6th hour, although it decreased during the first hour (T0-T1). Increased oxidative stress and decreased antioxidants are the main changes in the pathophysiology of CO poisoning. The sixth-hour total thiol level of the patients with CO poisoning under NBOT reached the levels of healthy individuals which may suggest 6 hours of NBOT protocol is sufficient for acute CO poisoning in patients not requiring HBOT.

References

1. Maloney G. Carbon Monoxide Poisoning. In: Tintinalli JE. Stapczynski JS. Ma OJ,Cline DM, Cydulka RK, Meckler GD; Emergency Medicine. Mc Graw-Hill New York 2011; p.1410-1413.
2. Aslan S, Erol MK, Karcioglu O, Meral M, Cakir Z, Katirci Y. The investigation of ischemic myocardial damage in patients with carbon monoxide poisoning. Anadolu Kardiyol Derg. 2005; 5: 189-93
3. Raub JA. Health effects of exposure to ambient carbon monoxide. Global Change Science. 1999;1:331–351.
4. Satran D, Henry CR, Adkinson C, Nıcholson CI, Bracha Y, Henry TD. Cardiovascular Menifestations of moderate to severe carbon monoxide poisoning. J Am Coll Cardiol. 2005;45(9):1513-16.
5. Kao LW, Nanagas KA. Carbon monoxide poisoning. Emerg Med Clin North Am. 2004; 22: 985-1018
6. Brent J.A., Rumack H.H, Role of free radicals in toxic hepatic Injury 1.free radical biochemistry, Clinical Toxicolory,1991 ;31:139-171
7. Chung, K. et al. Generation of free radical by interaction of iron with thiols in human plasma and its possible significance. Thromb Res, v. 2005;116: 157-164
8. Pogockı D., Schöneıch C. Thiyl radicals abstract hydrogen atoms from carbohydrates: reactivity and selectivity. Free Radic Biol Med, 2001;.31: 98-107
9. Hu ML. Measurement of protein thiol groups and glutathione in plasma. Methods Enzymol 1994; 233: 380-385
10. Smith C, Marks Allan D, Lieberman M. Basic Medical Biochemistry. Second Edition. Philadelphia: Lippincott Williams & Wilkins; 2005;441-442
11. Yardim-Akaydin S, Ozkan Y, Ozkan E, Torun M, Simsek B. The role of plasma thiol compounds and antioxidant vitamins in patients with cardiovascular diseases. Clin Chim Acta. 2003; 338(1-2):99-105
12. Cao, G.; Alessıo, H. M.; Cutler, R. G. Oxygen-radicalabsorbance capacity assay for antioxidants. Free Rad BiolMed, v. 1993; **9**(14): 303-311
13. Zhang J, Piantadosi CA. Mitochondrial oxidative stress after carbon monoxide hypoxia in the rat brain. J Clin Invest. 1992 ;90(4):1193-1199.
14. Garrabou G. et al. Mitochondrial injury in human acute carbon monoxide poisoning: the effect of oxygen treatment. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2011;29(1):32-51.
15. Taskiran D, Nesil T, Alkan K. Mitochondrial oxidative stress in female and male rat brain after ex vivo carbon monoxide treatment. Hum Exp Toxicol. 2007 ;26(8):645-651.
16. Kavakli HS, Erel O, Delice O, Gormez G, Isikoglu S, Tanriverdi F. Oxidative stress increases in carbon monoxide poisoning patients. Hum Exp Toxicol. 2011; 30(2):160-164.

Original Article

Eurasian Journal of Toxicology

ECG Changes in Patients with Amitriptyline Intoxication; P, QT, QTC, T and PR Wave Dispersion: A Retrospective Study

Pınar Demir Gündoğmuş[1], İbrahim Gündoğmuş[2], Emrah Aksakal[3]

[1]Department of Cardiology, Kırıkkale Yüksek İhtisas Hospital, Kırıkkale, Turkey
[2]Department of Psychiatry, Kırıkkale Yüksek İhtisas Hospital, Kırıkkale, Turkey
[3]Department of Cardiology, Erzurum Education and Research Hospital, Erzurum, Turkey

Abstract

Objective: Amitriptyline intoxication is a life-threatening condition as it can cause cardiac arrhythmias. This study aims to examine the ECG changes in patients with amitriptyline intoxications who were admitted to the emergency department and to compare the P-wave, T-wave, QT, QTC, and PR dispersions with healthy controls.

Material and Methods: The sample of the current retrospective study consists of only 46 patients with amitriptyline intoxication and 65 healthy controls. The 12-channel ECG recordings of the participants were evaluated by two experienced cardiologists. P wave, T wave, QT, QTC, and PR distance, minimum, maximum, and dispersion values were measured. The obtained data were recorded on the data set and subjected to statistical analysis.

Results: There was no significant difference in sociodemographic variables between patients with amitriptyline intoxication and the control group. The main symptoms of the patients were as follows: 28.3% (n=13) lethargy, 32.6% (n=15) nausea-vomiting, 21.7% (n=10) unconsciousness, and 17.4% (n=8) other. According to the analysis of amitriptyline intoxication and ECG parameters of healthy controls, P-wave, T-wave, QT, QTC, and PR dispersion were higher in the intoxication group than in the healthy controls (p0.05). The patient group had a higher heart rate than the control group (p=0.026).

Conclusion: The current study found that P-wave, T-wave, QT, QTC, and PR dispersion were higher in the amitriptyline intoxication group than in the control group, which is thought to play a role in cardiac arrhythmias. Clinicians should be on alert for any ECG changes in these cases.

Keywords: Dispersion; ECG; Amitriptyline; Tricyclic antidepressant; arrhythmia.

Introduction

Intoxication is a pathological condition of the organism caused by the excessive consumption of a toxic substance due to its chemical structure. It is a dynamic process that manifests its effects intensely in a short time, can deteriorate rapidly, disrupt functions, and lead to life-threatening complications. It is a global health issue that causes morbidity and mortality[1]. Drugs are among the most common intoxicating agents due to their ease of access and prevalence[2]. Tricyclic antidepressants (TCA), paracetamol, and nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drug classes with toxic doses[3, 4]. Amitriptyline is the most commonly used drug in TCA intoxications[5]. Although its use has gradually declined, it is still widely used in clinical practice due to its high efficiency and low cost[6]. Therefore, this causes amitriptyline-related intoxications frequently in emergency departments[3, 7].

Cardiac side effects from drug intoxication play a significant role in morbidity and mortality. In drug-related intoxications that necessitate hospitalization, 15% of patients experience cardiovascular events that necessitate medical attention and may even result in death[8]. Besides vital symptoms, the most quickly obtained, easily accessible, and inexpensive test for detecting cardiac side effects is electrocardiography (ECG)[9]. Sodium channel blockage, slow calcium channel blockage, potassium channel blockage, and sodium-potassium ATPase blockage are the main mechanisms responsible for changes in ECG parameters[10]. Prolonged cardiac action potential and refractory period, as well as delayed atrioventricular node (AVN) conduction, can result in prolonged QRS, QTd, and PR times[11]. These effects are thought to be dose-independent, and QTd prolongation can be observed even at therapeutic doses. QTd prolongation is associated with mortality and arrhythmic events, and ECG is becoming more important in diagnosis and treatment management[9].

TCAs, commonly used in clinical practice, are known to increase the risk of sudden cardiac death due to adverse cardiac effects in intoxication cases. These drugs are thought to increase the risk of cardiac arrhythmia, which could lead to sudden cardiac death[12, 13]. As a result, ECGs are frequently used in cases of intoxication to assess the increased risk of arrhythmias. According to studies on ECG abnormalities, there may be pulse changes, arrhythmia, and transmission delays[14]. TCAs are known

Corresponding Author: İbrahim GÜNDOĞMUŞ **e-mail:** dribrahim06@gmail.com
Received: 25.01.2023 • **Revision**: 25.02.2023 • **Accepted:** 22.03.2023
Cite this article as: Demir Gündoğmuş P, Gündoğmuş İ, Aksakal E. ECG Changes in Patients with Amitriptyline Intoxication; P, QT, QTC, T and PR Wave Dispersion: A Retrospective Study. Eurasian J Tox. 2023;5(1): 5-10

to have cardiac effects via voltage-dependent Na+ and K+ channel blockage, as well as postsynaptic inhibition of central and peripheral α-adrenergic receptors. Arrhythmias, depolarization delay, conduction abnormality, and ectopic heartbeats can all result from voltage-dependent Na+ channel blockage[15]. In this context, ECG monitoring is important in amitriptyline intoxication, a TCA. Furthermore, there is inconsistency in the literature regarding arrhythmia and other cardiac side effects in amitriptyline intoxications[16-19]. Furthermore, as far as we know, there have been limited studies on the dispersion of ECG waves[12]. Examining the ECG parameters of amitriptyline intoxications will be useful in clarifying the management of this risky process.

In light of these data, and with the hypothesis that amitriptyline intoxication will result in lethal arrhythmia, the study aimed to reveal the ECG parameters of patients who were admitted to the emergency department with intoxication after taking only amitriptyline.

Materials & Methods

Participant

The clinical parameters and ECG findings of patients who were admitted to the Erzurum Region Training and Research Hospital emergency department between 6 February 2016 and 10 April 2020, due to excessive amitriptyline intake were analyzed retrospectively from the database and archive files in our study, which examined the relationship between amitriptyline intoxication and ECG findings. The control group consisted of 65 people who were admitted to the medical board for various reasons and did not differ in age or gender. The study included patients who were at least 18 years old. Patients with chronic diseases, those who use other medications or are suspected of using multiple medications, and patients whose biochemical parameters and electrolyte values are outside the normal reference range were excluded from the study due to the possibility of changes in ECG parameters. During the study period, 669 of 786 patients who presented to the emergency department with intoxication were excluded because they were taking medication other than amitriptyline, and 71 patients were taking other medications in addition to amitriptyline. Finally, the study included 46 amitriptyline intoxications and 65 healthy controls (Figure 1). Patients' sociodemographic information, their complaints when admitting to the emergency department, and the approximate dose of amitriptyline were all recorded. Before the study,

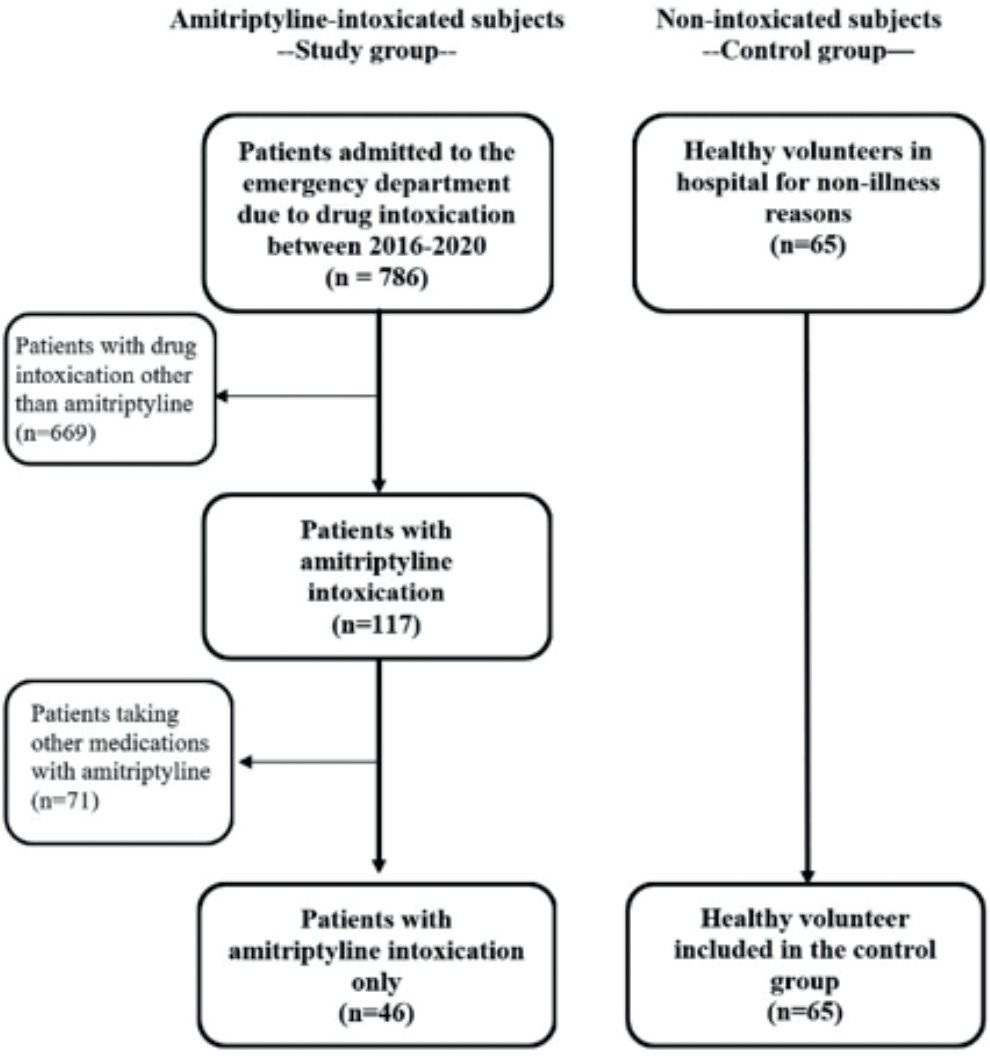

Figure 1: Flow chart of participants included in the study.

Table 1: Sociodemographic characteristics of the participants

Variable	Healthy Control Group (n=65)	Patient Group with Amitriptyline Overdose (n=46)	Statistic	d*f*	p
Age, years; mean±SD	25.06±7.10	25.47±3.50	t=0.363	60	0.718
Gender, n(%)			χ^2=0.530	1	0.467
Female	50 (76.9%)	38 (82.6%)			
Male	15 (23.1%)	8 (17.4%)			
Marital Status, n(%)			χ^2=1.447	2	0.485
Married	27 (41.5%)	24 (52.2%)			
Single	31 (47.7%)	19 (41.3%)			
Other	7 (10.8%)	3 (6.5%)			
Amitriptyline dose, mg; mean±SD (min-max)		465.76±189.61 (175-875)			
Main Symptoms and signs, n (%)					
Lethargy		13 (28.3%)			
Nausea-vomiting		15 (32.6%)			
Unconsciousness		10 (21.7%)			
Other		8 (17.4%)			

t: Student t test, χ^2:Chi-square test

consent was obtained from the Erzurum Region Training and Research Hospital Ethics Committee (Date: February 1, 2021, Decision no:2021/03-48).

Design

12-channel ECG recordings were obtained from healthy controls and patients while they were at rest at the time of admission to the emergency department (Cardiofax V; Nihon Kohden Corp., Tokyo, Japan). ECGs of all participants were transferred to a personal computer via scanner and analyzed using Adobe Photoshop software. In order to reduce the error rate, measurements were made by two experienced cardiologists using the electronic, digital measurement method. The P-wave, which expresses the atrial depolarization time, was measured in many different derivations and the difference between the longest and shortest time was defined as P-wave dispersion[20]. The QT interval was calculated as the time between the first QRS complex deflection and the end of the T-wave. QT intervals were measured in as many derivations as possible and corrected for heart rate using Bazett's formula (QTc=QT/√(R-R interval)[21]. The difference between the maximum and minimum QT intervals was defined as QT dispersion. The difference between the maximum and minimum QRS intervals was defined as QRS dispersion. The difference between the maximum and minimum PR intervals was defined as PR dispersion. The difference between the maximum and minimum T intervals was defined as T dispersion[22]. The obtained data were recorded on the data set and subjected to statistical analysis.

Statistical Analysis

SPSS 22.0 package program was used to perform statistical analyses on study data. Descriptive statistics were made with frequency and percentage for categorical variables and mean and standard deviation for continuous variables. Parametric assumptions were tested first in the comparison of continuous variables between the case and control groups, then the Student-T test was used, and the Chi-square test was used in the comparison of categorical variables. $p < 0.05$ values were considered statistically significant in all analyses.

Results

One hundred eleven participants in the study had a mean age of 25.30±5.27 years, with 79.3% being female. In terms of age (p=0.718), gender (p=0.467), and marital status (p=0.485), there was no statistically significant difference between the patients with amitriptyline intoxication and the control group (Table 1). The intoxication group received a mean dose of 465.76±189.61 (175-875) mg of amitriptyline. Furthermore, 28.3% (n=13) of those who were admitted to the emergency department with amitriptyline intoxication reported lethargy, 32.6% (n=15) nausea-vomiting, 21.7% (n=10) unconsciousness, and 17.4% (n=8) other symptoms (Table 1).

The ECG parameters of the participants are shown in Table 2. When the two groups were compared, the amitriptyline intoxication group (83.90±18.26) had a statistically higher heart rate than the control group

(91.58±16.83) (p=0.026). When the P-wave parameters of the study groups were compared, P_{max} (p0.001), P_{min} (p0.001), and P_{dis} (p=0.023) were statistically significantly higher in the amitriptyline intoxication group than in the control group. When the QT intervals were compared, it was observed that QT_{max} (p=0.012), QT_{dis} (p=0.002), and QTc_{dis} (p=0.002) were statistically significantly higher in the amitriptyline intoxication group than in the control group. When T-wave parameters were compared, T_{max} (p0.001), T_{min} (p0.001), and T_{dis} (p0.001) were found to be statistically significantly higher in the amitriptyline intoxication group than in the control group. When the QRS intervals were compared, it was found that QRS_{max} (p<0.001) and QRS_{min} (p<0.001) were statistically significantly higher in the amitriptyline intoxication group than in the control group. When the PR intervals were compared, it was observed that PR_{max} (p=0.008) and P_{dis} (p<0.001) were statistically significantly higher in the amitriptyline intoxication group than in the control group (Table 2).

Discussion

The most important result of the current study comparing amitriptyline intoxication with the case-control design and ECG parameters of healthy controls is that the intoxication group had higher P-wave, T-wave, QT, QTC, and PR dispersions than the healthy controls. We believe that the results of this study are significant because they can help in the development of treatment strategies for amitriptyline intoxications.

We evaluated the minimum, maximum, and dispersion (maximum-minimum difference) parameters of P-wave,

Table 2: Electrocardiography results of the groups.

Variable	Healthy Control Group (n=65)	Patient Group with Amitriptyline Overdose (n=46)	Statistic	d*f*	p
Heart rate, beat/m, mean±SD	83.90±18.26	91.58±16.83	t=-2.253	109	**0.026***
P wave, ms, mean±SD					
$P_{maximum}$	84.78±17.98	118.64±20.00	t=-9.156	109	**<0.001***
$P_{minimum}$	69.78±21.54	98.41±17.26	t=-7.761	109	**<0.001***
$P_{dispersion}$	15.00±14.71	20.23±9.07	t=-2.139	109	**0.023***
QT wave, ms, mean±SD					
$QT_{maximum}$	341.30±34.35	361.73±50.23	t=-2.545	108	**0.012***
$QT_{minimum}$	321.73±33.15	330.18±42.80	t=-1.121	109	0.265
$QT_{dispersion}$	19.56±23.66	31.55±15.35	t=-3.237	109	**0.002***
QTc wave, ms, mean±SD					
$QTc_{maximum}$	417.26±31.79	420.24±35.68	t=0.452	109	0.652
$QTc_{minimum}$	393.86±37.26	384.17±33.68	t=1.428	109	0.156
$QTc_{dispersion}$	23.40±27.32	36.07±15.54	t=-3.098	109	**0.002***
T wave, ms, mean±SD					
$T_{maximum}$	147.39±27.76	206.70±38.05	t=-9.494	108	**<0.001***
$T_{minimum}$	129.34±25.85	162.63±33.06	t=-5.944	107	**<0.001***
$T_{dispersion}$	18.04±17.59	44.07±16.49	t=-7.969	109	**<0.001***
QRS wave, ms, mean±SD					
$QRS_{maximum}$	74.78±12.95	103.03±17.23	t=-9.391	109	**<0.001***
$QRS_{minimum}$	53.91±17.31	85.52±17.20	t=-9.510	109	**<0.001***
$QRS_{dispersion}$	20.86±13.95	17.50±7.58	t=1.486	63	0.142
PR wave, ms, mean±SD					
$PR_{maximum}$	150.00±25.21	162.78±24.39	t=-2.682	109	**0.008***
$PR_{minimum}$	141.30±24.36	139.26±22.79	t=0.452	109	0.652
$PR_{dispersion}$	8.69±13.76	23.52±6.11	t=-7.691	109	**<0.001***

*:p<0.05, t: Student t test

T-wave, QRS-wave, QT, QTC, and PR distances in our study, which we believe may be predictors of cardiac arrhythmia in amitriptyline intoxication. We compared them to healthy controls because there is no clear information or data about the normal ranges of dispersion times in the literature[23]. As a result, we found that, with the exception of the QRS-wave, dispersions were higher in amitriptyline intoxications than in healthy controls. This result suggests that an overdose of amitriptyline causes dispersion in ECG parameters and may play a role in arrhythmia mechanisms. These results suggest that amitriptyline intoxication causes heterogeneity in cardiac electrical activity[24]. There are a few studies in the literature examining dispersion parameters in TCA excess intakes that have found that QT dispersion is higher in intoxication patients than in controls, which is consistent with our results[12]. The P-wave is a non-invasive ECG finding that indicates atrial depolarization. Atrial dysrhythmias, such as particularly atrial fibrillation, have been linked to increased P-wave dispersion[25]. QT dispersion is a ventricular repolarization time variability parameter that is thought to be an indicator of cardiac arrhythmia. In this context, our results provide important indicators for understanding lethal arrhythmias in amitriptyline intoxication.

It is also critical to monitor clinical signs in intoxication cases. However, in TCA intoxications, including amitriptyline, the clinical findings are variable and the symptoms are not specific, making diagnosis and follow-up difficult[12]. In general, symptoms such as changes in consciousness, agitation, confusion, drowsiness, nausea, and vomiting are observed in a dose-dependent manner[26]. The most common symptoms in our study, are consistent with the literature. These were lethargy, nausea-vomiting, and changes in consciousness. Because the central nervous system and cardiovascular system are more affected, it is critical to monitor the symptoms.

Another significant finding in our study is that, while multiple medication intakes play an important role in intoxication cases, they were excluded from the study to clearly see the effect of amitriptyline and to reduce confounding factors. When all of the results are considered together, we conclude that there may be a wide range of ECG findings in amitriptyline intoxications and that clinicians should be cautious about the development of almost any ECG finding in such intoxications. Furthermore, as far as we know, no other study in the literature examines ECGs, including dispersion, in amitriptyline intoxications as thoroughly as the current study.

The results of our study can be evaluated within some limitations. First of all, the retrospective design of the study and the limited sample size are important limitations. Furthermore, although only amitriptyline intoxication cases were included in our study, multiple medication uses, and drug doses were based on the declaration. On the other hand, the lack of follow-up of the clinical results of the patients is another important limitation. In addition, the inability to analyze the time elapsed between taking medication and applying to the hospital was another shortcoming for the study.

Conclusion

The current study found that amitriptyline intoxication increased P-wave, T-wave, QT, QTC, and PR dispersions more than controls. Because this difference may play a role in cardiac arrhythmias, clinicians should be careful about any type of ECG change in these severe intoxications. It would be beneficial to confirm the current study's findings with future animal trials and prospective studies.

Disclosure statement

Funding: This research received no specific grant and financial support from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest: The authors declare that there is no conflict of interest.

Ethics. Authorization was obtained from the local ethics committee (Date:01.02.2021, IRB: 2021/03-48), the study was conducted in accordance with the Helsinki Declaration Guidelines.

References

1. Mowry JB, Spyker DA, Brooks DE, McMillan N, Schauben JL. 2014 annual report of the american association of poison control centers' national poison data system (NPDS): 32nd annual report. *Clinical toxicology*. 2015;53(10):962-1147.
2. Yildiztepe E, Aksay NH, Demir Ö, et al. Analysis of the Year 2007 Data of Dokuz Eylül University Drug and Poison Information Center, Turkey/Dokuz Eylül Üniversitesi Ilaç ve Zehir Bilgi Merkezi 2007 Yili Verilerinin Analizi. *Türkiye Klinikleri Tip Bilimleri Dergisi*. 2010;30(5):1622.
3. Duran M, Uludag O, Yuzkat N. Analysis of adult intoxication cases treated in ICU: A sample from Adıyaman Region of Turkey. *Medical Science and Discovery*. 2016;3(2):71-75.
4. Campleman SL, Brent J, Pizon AF, et al. Drug-specific risk of severe QT prolongation following acute drug overdose. *Clinical Toxicology*. 2020;58(12):1326-1334.
5. Karaca O, Ertaşkın A. Epidemiology of self-poisoning with drug in the Central Anatolian Region in Turkey. *Cureus*. 2020;12(2)
6. McClure EW, Daniels RN. Classics in Chemical Neuroscience: Amitriptyline. *ACS chemical neuroscience*. 2021;12(3):354-362.
7. Ozenir M, Duru NS, Elevli M, Karakus A, Civilibal M. The Familial Factors and Demographic Characteristics of Children with Drug Poisoning. *Haseki Tıp Bulteni-Medical Bulletin Of Haseki*. 2013;51(4):157-161.
8. Manini AF, Nelson LS, Stimmel B, Vlahov D, Hoffman RS. Incidence of adverse cardiovascular events in adults following drug overdose. *Academic emergency medicine*. 2012;19(7):843-849.

9. Manini AF, Nair AP, Vedanthan R, Vlahov D, Hoffman RS. Validation of the prognostic utility of the electrocardiogram for acute drug overdose. *Journal of the American Heart Association*. 2017;6(2):e004320.

10. Lionte C, Bologa C, Sorodoc L. Toxic and drug-induced changes of the electrocardiogram. *Advances in Electrocardiograms: Clinical Applications 1st ed Rijeka, Croatia: InTech*. 2012:271-96.

11. Blaber MS, Khan JN, Brebner JA, McColm R. "Lipid rescue" for tricyclic antidepressant cardiotoxicity. *The Journal of emergency medicine*. 2012;43(3):465-467.

12. Yıldız C, Köylü R, Günaydın YK, Akıllı B, Yıldız G, Yıldırım ÖT. Evaluation of the Changes in T Peak-T End Interval and T Peak-T End/QT Ratio in Tricyclic Antidepressant Intoxication. *Eurasian Journal of Toxicology*. 2020;2(3):57-63.

13. Hennessy S, Bilker WB, Knauss JS, et al. Cardiac arrest and ventricular arrhythmia in patients taking antipsychotic drugs: cohort study using administrative data. *Bmj*. 2002;325(7372):1070.

14. Groleau G, Jotte R, Barish R. The electrocardiographic manifestations of cyclic antidepressant therapy and overdose: a review. *The Journal of emergency medicine*. 1990;8(5):597-605.

15. Avci A, Uzucek M, BugraYapici S, et al. The New Markers of Ventricular Dispersion in Patients with Acute Poisoning with TCAs: Tp-e Interval and Tp-e/QTc Ratio. *Signa Vitae*. 2020;1(4)

16. Güloğlu C, Orak M, Üstündağ M, Altuncı YA. Analysis of amitriptyline overdose in emergency medicine. *Emergency Medicine Journal*. 2011;28(4):296-299.

17. Buckley NA, Chevalier S, Leditschke IA, O'Connell DL, Leitch J, Pond SM. The limited utility of electrocardiography variables used to predict arrhythmia in psychotropic drug overdose. *Critical Care*. 2003;7(5):1-7.

18. Olgun H, Yldrm ZK, Karacan M, Ceviz N. Clinical, electrocardiographic, and laboratory findings in children with amitriptyline intoxication. *Pediatric emergency care*. 2009;25(3):170-173.

19. Caksen H, Akbayram S, Odabaş D, et al. Acute amitriptyline intoxication: an analysis of 44 children. *Human & experimental toxicology*. 2006;25(3):107-110.

20. Dilaveris PE, Gialafos JE. P-wave dispersion: A novel predictor of paroxysmal atrial fibrillation. *Annals of Noninvasive Electrocardiology*. 2001;6(2):159-165.

21. Bazett H. An Analysis of the Time-Relations of. *Heart*. 1920;7:353.

22. Tse G, Yan BP. Novel arrhythmic risk markers incorporating QRS dispersion: QRSd×(T peak− T end)/QRS and QRSd×(T peak− T end)/(QT× QRS). *Annals of Noninvasive Electrocardiology: the Official Journal of the International Society for Holter and Noninvasive Electrocardiology, Inc*. 2017;22(6)

23. Irdem A, Akpinar M, Celebi E, Aygun F, Dursun H. P-wave changes associated with Chiari network in the right atrium. *Pediatric Cardiology*. 2020;41(8):1773-1776.

24. Okutucu S, Aytemir K, Oto A. P-wave dispersion: what we know till now? *JRSM cardiovascular disease*. 2016;5:2048004016639443.

25. Alegría-Barrero E, Alegría-Barrero A, Gómez JJG, Juan-Aracil GR. Chiari's network and paroxysmal atrial fibrillation. *Revista Española de Cardiología (English Edition)*. 2011;8(64):727-728.

26. Mills KC. Tricyclic antidepressants. In Tintinalli JE, Kellen G, Stapczynski JS, editors. Emergency Medicine A Comprehensive Study Guide. 6th ed. New York: McGraw-Hill; 2004. pp. 1025-33.

Case Report

Eurasian Journal of Toxicology

Rapid Death from Aluminum Phosphide Poisoning

Mustafa ALPASLAN[1]

[1]Nevsehir State Hospital, Department of Emergency Medicine, Nevsehir, Türkiye

Abstract

Aluminum phosphide is a chemical used as an insecticide and pesticide to improve the storage conditions of agricultural products. Combined with the humidity in the air or after being taken orally as a tablet, it reacts with the acidic environment of the stomach and turns into phosphine gas and can cause poisoning. Suicidal use is also common. When poisoning develops, deep metabolic acidosis, hypotensive shock, acute respiratory failure, multi-organ failure, cardiac arrest and death may occur. Resistant hypotension and deep metabolic acidosis are the most important indicators of poor prognosis. In this case, an 18 year old male patient was brought to the emergency room after taking 3 tablets of aluminum phosphide. The patient was unconscious and had hypotensive shock. Despite gastric lavage, massive fluid replacement, positive inotropes, sodium bicarbonate, intravenous N acetyl cysteine loading, and hemodialysis, the patient died 6 hours after admission to the emergency department.

Keywords: aluminum phosphide, phosphine gas, pesticide poisoning

Introduction

Phosphine gas is an extremely poisonous gas. It is mostly used to improve the storage conditions of agricultural products such as animal feed, leaf tobacco, and grain, and to repel or kill pests such as rodents and insects[1]. Aluminum phosphite is a chemical used as an insecticide and pesticide, and after being taken orally as a tablet, it reacts with the acidic environment of the stomach and turns into phosphine gas. When poisoning develops, deep metabolic acidosis, hypotensive shock, acute respiratory failure, multi organ failure, cardiac arrest and death may occur[2]. There is no specific antidote and most cases result in death[3].

Case Report

An 18 year old male patient was brought to the emergency department of our hospital by ambulance after taking medication for suicide. He was unconscious and his Glasgow Coma Score (GCS) was evaluated as 11. According to the anamnesis taken from the relatives it was learned that he took three aluminum phosphide tablets. The patient's pupillary response was +/+ isochoric, unconscious, respiration was mildly tachypneic and superficial. Blood pressure was 75/55 mmHg, pulse was 120, fingertip oxygen saturation was 94, fingertip blood glucose was 121, and body temperature was 36.2ºC. Gastric lavage was performed, taking into account the recommendations of the National Poison Information Center. Activated charcoal was not given. Brain tomography imaging was performed on the patient and it was observed to be normal. When laboratory tests are evaluated; WBC: 14.3, AST: 13 U/L, ALT: 8 U/L, Creatinine: 1.5 mg/dl , INR: 1.22, Na:134 mmol/L, K: 3.3 mmol/L, pH : 7.19, HCO3: 12 mmol/L, lactate: 8.49 mmol/L. In accordance with the recommendations of the National Poison Counseling Center, the patient was loaded with 150 mg/kg N-Acetyl Cysteine treatment within 1 hour and admitted to the intensive care unit. Blood gas results after 2 hours; pH: 6.95, HCO3: 7.9 mmol/l and lactate: 11.83 mmol/l. While the creatinine value of the patient increased to 2.28 mg/dl, hypoglycemia developed in the patient. The patient did not have any urine output, and his blood pressure decreased to 50/20 mmHg. The patient was intubated, positive inotropic, sodium bicarbonate treatment was given. Hemodialysis was

Corresponding Author: Mustafa ALPASLAN **e-mail:** mustafalpaslan@gmail.com
Received: 11.01.2023 • **Accepted:** 30.01.2023
Cite this article as: Alpaslan M. Rapid Death from Aluminum Phosphide Poisoning. Eurasian J Tox. 2023;5(1): 11-13

started in the patient who did not respond to the treatment. The patient developed cardiac arrest and resulted in death.

Discussion

Although phosphine gas is extremely deadly, it causes poisoning when aluminum phosphite is taken orally, combined with hydrochloric acid in the stomach or moisture in the air, and enters the body through inhalation[4]. Biological warfare weapon is also used as a terrorist agent due to its poisoning by inhalation[6-7]. In mostly agricultural countries, organophosphate poisoning is the first and aluminum phosphite poisoning is the second[9]. Under normal conditions, the odor that emerges after the reaction of aluminum phosphide, an odorless colorless chemical, resembles the smell of rotten fish or garlic[7].

Phosphine gas disrupts oxidative phosphorylation in all organs and tissues systemically by stopping the cytochrome c oxidase enzyme from working in the body. Free oxygen radicals are formed by inhibiting the peroxidase, superoxide dismutase and catalase enzymes. Thus, the membrane structure of the cells is disrupted and protein denaturation develops[5]. According to studies, the toxic dose range could not be clearly determined, and intakes of more than 0.15-0.50 grams were found to be fatal[9]. The first symptoms of patients with suspected poisoning may be respiratory distress, hypotension, nausea, vomiting, dizziness, drowsiness, fainting, seizures, and coma. In the future, deterioration in kidney and liver functions may be observed. If poisoning is suspected, early admission and prompt treatment can improve the prognosis. As for suicidal purchases, the risk of mortality increases due to the late application. Deep metabolic acidosis and resistant hypotension are the two main indicators of poor prognosis[7]. With the deterioration of cell membrane function seen in the mechanism of poisoning, too much fluid is lost to the extravascular space, which causes deep hypotension[6-7].

In this case, there was suspicion of ingestion of approximately 3 tablets (9 grams). The patient had drowsiness and impaired consciousness at the first admission. The patient had sweating, tachypnea, and hypotension. While the creatinine value was 1.5 mg/dl at the time of application, it increased to 2.28 mg/dl at the second hour. There was no deterioration in liver function tests. According to the blood gas results analyzed at the time of the patient's arrival, there was profound metabolic acidosis. High dose, delayed admission, and clinical and laboratory findings included all poor prognostic factors. It ultimately resulted in death 6 hours after admission.

While intervening in all cases with aluminum phosphide poisoning or suspected aluminum phosphide poisoning, health personnel should take care of themselves in the first place and care should be taken to use protective equipment such as gloves, masks and glasses. All clothes of the patient should be taken off and purification should be ensured by washing with plenty of water, including the eyes[4]. The first goal in treatment should be to replace the fluid that escapes into the extracellular space with intravenous hydration[7]. The use of positive inotropes will not be effective without fluid administration and should be given after massive fluid loading therapy. In addition to the fact that using inotropes in the early period does not provide much benefit, it has been observed that cardiac arrhythmia may develop by increasing oxygen consumption in myocardial cells[9].

It is predicted that free oxygen radicals secondary to the enzyme inhibition mechanism created by aluminum phosphide poisoning in the body play a major role. Intravenous N-acetyl cysteine (NAC), calcium gluconate, magnesium sulfate, trimetazidine, and pralidoxime treatments are the most commonly used treatments[2-5-8]. Hemodialysis is not recommended as a routine treatment.

In the literature, resistant hypotension and metabolic acidosis have mostly been observed in aluminum phosphide poisonings that developed unintentionally or with the intention of committing suicide, resulting in death[2-5-6-10]. However, there have also been cases who were treated in the early period and discharged despite hypotensive shock[1-2-3].

Aluminum phosphide poisoning has started to become one of the most common cases due to misuse, inhalation transmission and especially suicidal purchases. There have been cases with good prognosis with early diagnosis and treatment. Resistant hypotension and profound metabolic acidosis are the two worst prognostic markers. In these cases, patient detoxification and massive fluid replacement are extremely important. Especially those who are engaged in agriculture should be informed that this chemical is extremely deadly. The sale of aluminum phosphide tablets must be strictly controlled and restricted.

References

1. Tolunay O., Çelik T., Yücel G., Özdemir U., Atmış A., Sucu A. et al. A Rare but Deadly Poisoning: Aluminum Phosphide Poisoning. J Pediatr Emerg Intensive Care Med, 2017;4:27-9.
2. Ekinci F., Dinçer R., Horoz Ö.Ö., Kendir Ö.T., Petmezci E., Tolunay İ et al. Aluminum phosphide poisoning: two pediatric cases and two separate clinical outcomes. J Pediatr Emerg Intensive Care Med. 2017;4:72-6.
3. Hakimoğlu S., Dikey İ., Sarı A., Kekeç L., Tuzcu K., Karcıoğlu, M. Successful management of aluminum phosphide poisoning resulting in cardiac arrest. Turk J Anaesth Reanim. 2015;43:288-290.
4. Gurjar M, Baronia AK, Azim A, Sharma K. Managing aluminum phosphide poisonings. J Emerg Trauma Shock. 2011;4:378-84.
5. Yalçın D. , Candan B. F. , Mutlu M. , Yelken B. A Rare Case of Aluminum Phosphite Inhalation Intoxication. Eskisehir Med J. 2022; 3(2): 234-238.

6. Belen V. K. , Yoldaş A. , Karakuş A. Aluminum phosphide poisoning. Eurasian Journal of Toxicology. 2022; 4(1):27-28.
7. Etemadi-Aleagha A, Akhgari M, Iravani FS. Aluminum phosphide poisoning related deaths in Tehran, Iran, 2006 to 2013. Medicine. 2015;94(38):e1637.
8. Chaudry D, Rai AS. N-acetyl cysteine in aluminum phosphide poisoning: Myth or hope. Indian J Crit Care Med. 2014;18:646-7.
9. Bogle R.G., Theron, P., Brooks P., Dargan P.I., Redhead J. Aluminum phosphide poisoning. Emerg Med J. 2006;23:3.
10. Terece C., Soğukpınar V. O., Özdemir N., Polat S. Infant Death Due to Aluminum Phosphide Intoxication, An Uncontrolled Insecticide Used: Case Report. Eurasian J Tox. 2019; 1(1): 33-36.

Case Report
Eurasian Journal of Toxicology

Reversible Splenial Corpus Callosum Lesion and Carbamazepine

Sinan ELİAÇIK[1], Gülsüm CİL[2]

[1]Hitit University, School Of Medicine, Department of Neurology, Çorum, Türkiye
[2]Bafra State Hospital, Department of Neurology, Samsun, Türkiye

Abstract

Background: Reversible splenial lesion syndrome (RESLES) at corpus callosum (CC) has been defined in many clinical conditions. Although the etiopathogenesis of transient focal lesions in the CC splenium has not been clarified, many theories remain on the agenda, especially in epilepsy patients.

Case presentation: A 38-year-old male patient with idiopathic generalized epilepsy was admitted to the emergency department with complaints of frequent seizures. It was reported by his relatives that he had stopped carbamazepine treatment for the last three days. After his last epileptic attack, he had been headache, nausea, vomiting, decreased visual acuity, and prolonged confusion. The patient with diffusion restriction at the level of splenium CC in magnetic resonance imaging (MRI), whose seizure frequency increased, was evaluated by a neurology doctor. In his electroencephalography, spike waves were observed in both hemispheres, which were frequently generalized. The same lesion was not observed in the diffusion and MRI taken eight days later in the patient who had no seizures in the follow-up.

Conclusion: Studies have shown that CC damage results in the disruption of cortical functions, with disconnection of the cerebral hemispheres and disturbances in consciousness. The clinical spectrum includes a fairly wide symptomatology. RESLES of the CC is an infrequent finding on MRI. Some of these lesions are associated with epileptic seizures, the sudden withdrawal of the antiepileptic drug, or usage. RESLES, which we reviewed with etiology and clinical findings, still remains a mystery. It will be clarified with wide-ranging studies.

Keywords: Reversible Splenial Corpus Callosum Lesion, epilepsy, carbamazepine.

Introduction

Reversible splenial lesion syndrome (RESLES) at corpus callosum (CC) has been defined in many clinical conditions for example malignancies, infections, metabolic disturbances, etc. Many neurological disorders are associated with lesions affecting the splenium of the corpus callosum (SCC). The spectrum of symptoms is broad and clinical presentations may be indistinguishable. Although the etiopathogenesis of transient focal lesions in the corpus callosum splenium has not been clarified, many theories remain on the agenda, especially in epilepsy patients[1,2].

Case presentation

A 38-year-old male patient with idiopathic generalized epilepsy was admitted to the emergency department with complaints of frequent seizures. After the last seizure, he had headaches, nausea, vomiting, and decreased visual acuity, as well as confusion prolonged. In the history of the patient with generalized epilepsy; It was learned that he had generalized tonic-clonic seizures since the age of eight and that he was under antiepileptic treatment, but he did not comply the treatment. Our patient had been using carbamazepine 1200mg/day since 2019. It was reported by his relatives that he had stopped carbamazepine treatment for the last three days. In his neurological examination, there was a prolonged postictal confusion state. Vital signs were within normal limits. No abnormal findings were detected in the biochemistry and hemogram tests, and the patient's infection parameters were evaluated as normal. Diffusion magnetic resonance imaging (MRI) was performed in the emergency department. The patient with diffusion restriction at the SCC level (Figure 1) was seen by the neurologist

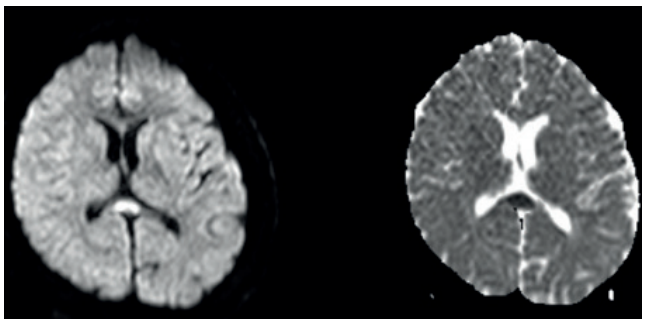

Figure 1:

Corresponding Author: Sinan ELİAÇIK **e-mail:** sinaneliacik@gmail.com
Received: 20.01.2023 • **Accepted:** 27.03.2023
Cite this article as: Eliacik S, Cil G. Reversible Splenial Corpus Callosum Lesion and Carbamazepine. Eurasian J Tox. 2023;5(1): 14-16

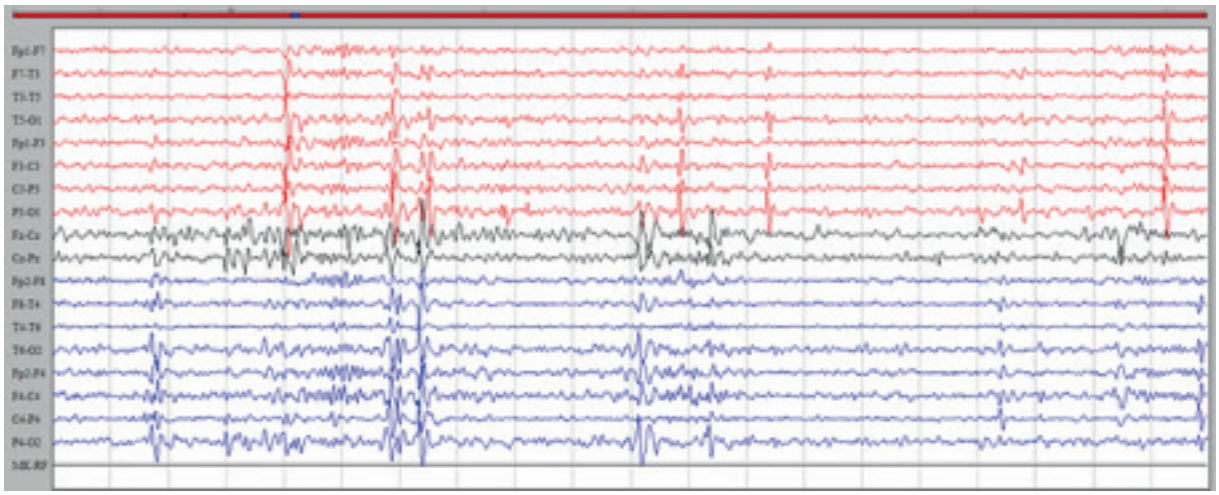

Figure 2:

with a preliminary diagnosis of ischemic stroke. In his electroencephalography, spike waves were observed in both hemispheres, which were frequently generalized (Figure 2). Antiepileptic treatment with levetiracetam 1000 mg/day was started. The seizure of the patient, who was followed up in the neurology service, did not recur and his neurological examination was evaluated as normal two days later. The same lesion was not observed in the diffusion and brain MRI taken eight days later in the patient who had no seizures in the follow-up (Figure 3). In this case, CC transient lesions will be reviewed together with the literature.

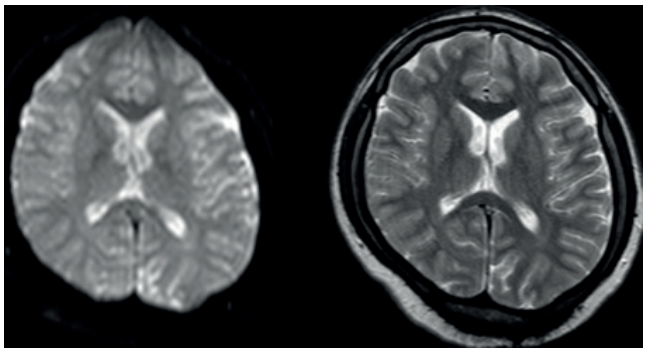

Figure 3:

Discussion

The CC plays a vital role in brain function. Studies have shown that its damage results in the disruption of cortical functions, with disconnection of the cerebral hemispheres and disturbances in consciousness[3]. There have been various terms used to describe splenial lesions; mild encephalitis with a reversible lesion in the splenium (MERS), RESLES, and cytotoxic lesions of the corpus callosum (CLOCCs). MERS is an acute cliniconeuroradiological syndrome characterized by mild encephalopathy or encephalitis presenting as a reversible solitary mass in the central portion of the SCC[4]. However, encephalitis/encephalopathy is not always mild. The spectrum of RESLES includes MERS. CLOCCs are various entities associated with a variety of causes with restricted diffusion, and some of these lesions are irreversible. The splenial lesion of MERS and RESLES contains two different patterns according to the lesion location: Type 1, an isolated lesion located in the center of the splenium of CC, mostly round or oval, with some of the lesion extended along the splenium; type 2, a lesion centered in the splenium and extended into other brain areas[4-7]. Our case of RESLES was all isolated symmetrical lesions in SCC without any extracallosal lesions. Most of the previous descriptions of RESLES have been in the case report format; thus, the incidence of RESLES remains unknown[8].

RESLES of the CC is an infrequent finding on MRI. Some of these lesions are associated with epileptic seizures, the sudden withdrawal of the antiepileptic drug (AED), or usage. While different hypotheses have been generated, its pathophysiology is still not well understood. The possible mechanisms for the restricted diffusion of the SCC include intramyelinic edema, reversible demyelination, damage to the blood-brain barrier, arginine vasopressin release, and inflammatory cell-induced cytotoxic edema[8-10]. Antiepileptic drug toxicity and associated changes in salt homeostasis and transhemispheric seizure propagation are other suspected mechanisms[11,12]. Treatment with antiepileptic drugs like carbamazepine and the rapid concentration changes of drugs can influence fluid balance systems through arginine vasopressin release. These drugs can also increase the number of pro-inflammatory and pro-convulsive cytokines. Öztoprak et al. proposed a possible mechanism of onset in RESLES for patients experiencing seizures. The authors suggest that the discharge of the corpus callosum disseminated in seizures caused a decrease in free water dispersion in the CC. Further studies are needed to investigate this mechanism[8,13]. A lesion of the SCC in patients with epilepsy might be induced by a rapid and relatively long-lasting reduction of antiepileptic drugs and is not associated with toxic drug effects or high seizure frequency[10].

Clinical symptoms included headaches, amnesia, confused consciousness without seizure, nausea, vomiting, and diarrhea, fever, dizziness, visual disturbances, and sensorimotor hemiparesis, dysmetria, dysarthria. The heterogeneity in the clinical manifestations makes RESLES hard to predict before MRI. We present an epileptic patient who was found to have an isolated, reversible lesion in the SCC associated with the sudden withdrawal of carbamazepine. Reversible SCC lesions were also reported in non-epileptic patients using other AEDs[14,15]. In the literature, transient corpus callosum splenium lesions caused by the reduction of levetiracetam, in addition to carbamazepine, have been presented. On the other hand, temporary corpus splenium lesion caused by decreasing antiepileptic doses in epilepsy patients under mono or polytherapy has been reported in many case reports[11,16].

In the case series in which 23 patients with diffusion restriction in the CC were examined, a reversible lesion had observed in 10 patients, and an oval or round lesion with a central location in the CC was detected, similar to our case. In this case series, a symmetrical boomerang-shaped lesion was observed in marchiafava bigami syndrome, while eccentric, irregular lesions had observed in SCC in stroke patients[17].

RESLES has a benign prognosis and is usually associated with complete recovery without any obvious neurological sequelae shortly after the acute course, as in our patient.

Conclusion

RESLES, which we briefly reviewed with their extensive etiology and clinical findings, still remains a mystery. These lesions will be more understandable with new case series and long-term follow-up.

References

1. Tetsuka S. Reversible lesion in the splenium of the corpus callosum. *Brain Behav.* 2019 9;e01440. 10.1002/brb3.1440 .
2. Jing C, Sun L, Wang Z, et al. Reversible splenial lesion syndrome due to oxcarbazepine withdrawal: case report and literature review. J Int Med Res. 2018; 46: 1277-1281.
3. Blaauw J, Meiners LC. The splenium of the corpus callosum: Embryology, anatomy, function, and imaging with pathophysiological hypothesis. Neuroradiology 2020;62:563–585.
4. Notebaert A, Willems J, Coucke L, et al. Expanding the spectrum of MERS type 2 lesions, a particular form of encephalitis. Pediatr Neurol. 2013; 48: 135-138.
5. Zhang S, Ma Y, Feng J. Clinicoradiological spectrum of reversible splenial lesion syndrome (RESLES) in adults: a retrospective study of a rare entity. Medicine (Baltimore) 2015;94: e512.
6. Yuan J, Yang S, Wang S, et al. Mild encephalitis/encephalopathy with reversible splenial lesion (MERS) in adults-a case report and literature review. BMC Neurol. 2017; 17: 103.
7. Dong K, Zhang Q, Ding J, et al. Mild encephalopathy with a reversible splenial lesion mimicking transient ischemic attack: a case report. Medicine (Baltimore) 2016; 95: e5258.
8. Lu PI, Hodes JF, Zheng X, et al. Reversible Splenial Lesion Syndrome with Some Novel Causes and Clinical Manifestations. Intern. Med. 2020;59, 2471–2480.
9. Tada H, Takanashi J, Barkovich AJ, et al. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. Neurology 2004;63(10): 1854-1858. PMID: 15557501. DOI: 10.1212/01.wnl.0000144274.12174.cb
10. Gurtler S, Ebner A, Tuxhorn I, et al. Transient lesion in the splenium of the corpus callosum and antiepileptic drug withdrawal. Neurology 2005;65:1032–1036
11. Prilipko O, Delavelle J, Lazeyras F, et al. Reversible cytotoxic edema in the splenium of the corpus callosum related to antiepileptic treatment: report of two cases and literature review. Epilepsia 2005;46: 1633-1636.
12. Doherty MJ, Jayadev S, Watson NF, et al. Clinical implications of splenium magnetic resonance imaging signal changes. Arch Neurol 2005;62: 433-437.
13. Öztoprak İ, Engin A, Gümüs C, et al. Transient splenial lesions of the corpus callosum in different stages of evolution. Clin Radiol 2007;62: 907-913.
14. Da Rocha AJ, Reis F, Gama HP, et al. Focal transient lesion in the splenium of the corpus callosum in three non-epileptic patients. Neuroradiology 2006;48(10): 731-735.
15. Kim JH, Choi JY, Koh SB, et al. Reversible splenial abnormality in hypoglycemic encephalopathy. Neuroradiology 2007;49(3): 217-222.
16. Sawagashira R, Narita H, Hashimoto N, et al. Transient lesions of the splenium of the corpus callosum following rapid withdrawal of levetiracetam. Epileptic Disord 2017;19: 379-382.
17. Förster A, Apfaltrer P, Al-Zghloul M, et al. Diffusion Restricted Lesions in the Splenium of the Corpus Callosum. In vivo 2022: 36: 1354-1359.

Case Report

Eurasian Journal of Toxicology

Unusual Excessive Swelling of the Tongue after Calcium Acetate Ingestion: A Case Report

Aleyna DAL[1], Bahadır TAŞLIDERE[2]

[1]Faculty of Medicine, Bezmialem Vakif University, Istanbul/ Turkey
[2]Department of Emergency Medicine, Faculty of Medicine, Bezmialem Vakif University, Istanbul/ Turkey

Abstract

Common side effects of calcium acetate include increased blood calcium levels, nausea-vomiting, diarrhea, and fatigue, while side effects of unknown incidence include "swelling". We present the case of an allergic reaction limited to tongue swelling alone, not showing other anaphylactic symptoms. Our case was a female patient who applied to the emergency department with the complaint of isolated tongue swelling three hours after using calcium acetate for treatment. It should be kept in mind that calcium acetate, a food additive, may cause this in patients with the complaint of isolated tongue swelling, but the cause of which cannot be determined.

Keywords: Calcium Acetate, Allergic Reactions, Swelling of Tongue, Drug Interaction

Introduction

Calcium acetate is used to treat hyperphosphatemia in patients with chronic renal failure. Because in these patients, the serum phosphorus level rises as a result of decreased glomerular filtration rate. High serum phosphorus is associated with increased morbidity and mortality[1]. Along with its needed effects, calcium acetate may cause some unwanted effects. Common side effects of calcium acetate include increased blood calcium levels, nausea-vomiting, diarrhea, and fatigue, while side effects of unknown incidence include "swelling"[2].

In spite of the fact that the known very rare side effects of the oral form of calcium acetate include swelling of the mouth, face, lips, tongue, or throat, the number of reported cases is few. We present the case of an allergic reaction limited to tongue swelling alone, not showing other anaphylactic symptoms.

Case Report

A 68-year-old obese Turkish female patient with a medical history of chronic kidney disease, diabetes mellitus, and hypertension controlled with irbesartan-hydrochlorothiazide, furosemide, and calcium channel blockers was admitted to the emergency department with complaints of excessive tongue swelling and fatigue (Figure 1, 2). During the initial examination, the patient had difficulty speaking, could only use two-word phrases, and could only breathe through the nose. Her tongue had filled the entire oral cavity. Her relatives described how these symptoms started to increase about 2 hours before she came to the Emergency Department (ED). No other part of her face or body had any swelling. There was no history of an associated rash. She had no abdominal pain, allergies, or history of angioedema. In the first evaluation, it was learned that the patient had just started oral calcium acetate tablet therapy. The calcium acetate tablet was the only medication she took orally in the three hours before the presentation. The patient's vital signs are as follows: blood pressure 176/74 mmHg, heart rate 74 beats per minute, respiratory rate 23 beats per minute, body temperature 36.2 °C, oxygen saturation 98% (at room temperature and at room air). In the physical examination, rhonchi were heard in all lung areas due to forced inspiration. The oropharyngeal examination could not be performed due to excessive swelling of the

Corresponding Author: Bahadır TAŞLIDERE **e-mail:** drbahadir@yahoo.com
Received: 18.01.2023 • **Revision:** 28.03.2023 • **Accepted:** 29.03.2023
Cite this article as: Dal A, Taşlıdere B. Unusual Excessive Swelling of the Tongue after Calcium Acetate Ingestion: A Case Report. Eurasian J Tox. 2023;5(1): 17-19

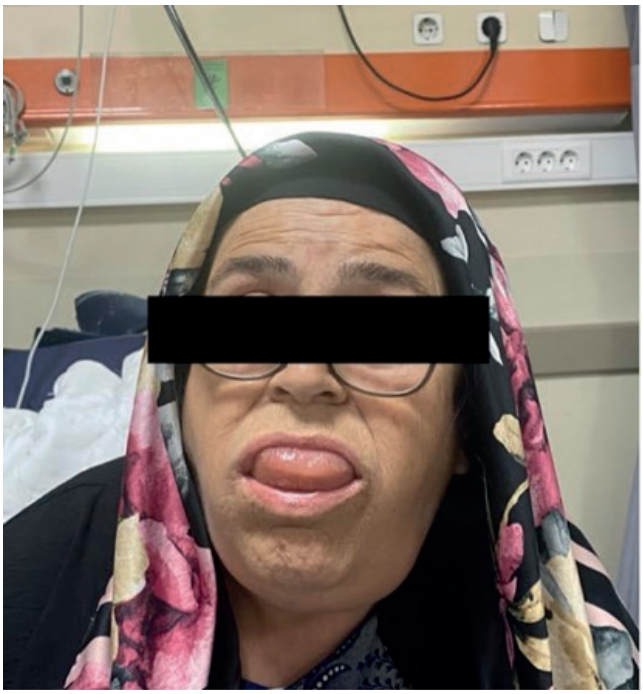

Figure 1: Tongue swelling front view

Figure 2: Tongue swelling side view

tongue, and uvula edema could not be evaluated. Besides, she had difficulty tolerating his oral secretions. There was no itching, redness, urticaria, or angioedema on the skin or mucosa, which were other signs of anaphylaxis. In the blood results taken at the first application by the patient, the sodium value was 118 mmol/L. The patient immediately received methylprednisolone (80 mg), pheniramine (45.5 mg), pantoprazole (40 mg), and normal saline (1000 ml). Epinephrine (intramuscular 0.5 mg) was administered intramuscularly to relieve the patient's complaint. After the second dose of adrenaline (intramuscular 0.5 mg) was given, the swelling in her tongue began to subside, and she was able to speak 2 hours later. Necessary warnings were given to the patient about the drugs she used, and she was discharged.

Discussion

Our case was a female patient who applied to the emergency department with the complaint of isolated tongue swelling three hours after using calcium acetate for treatment. A common cause of angioedema is allergies. This condition usually occurs as a result of the body's response to medications. People with angioedema may have swelling in parts of the body (face, eyelids, ears, mouth, tongue, hands, feet, or genitals). A small number of studies have reported cases of drug-induced language disorders[3], but a comprehensive overview of drugs associated with tongue disorders as an adverse effect is not available. In total, 121 (7.4%) of the 1645 drugs have been associated with tongue disorders as adverse drug reactions[4]. The most common drug-induced tongue disorders are glossitis, tongue edema, tongue discoloration, and burning tongue[4]. Tongue edema was reported in 22 drugs (1.3% of 1645 drugs).

Our patient did not have any of the systemic symptoms, hypotension, or dermatological symptoms seen during the anaphylactic reaction5,6. The differential diagnosis was, of course, angioedema. We performed literature searches using conventional medical databases. In the literature, only one patient who had swelling of the tongue after the use of calcium acetate was reported7. Calcium acetate is a phosphate binder used in the treatment of hyperphosphatemia. Besides, it has another common usage area. It is used as an acidity regulator (additive number E263) or buffering agent, nutritional supplement, flavor enhancer, and preservative in foods8. It should be kept in mind that calcium acetate, a food additive, may cause this in patients with the complaint of isolated tongue swelling, but the cause of which cannot be determined. It is impossible to form a general opinion with only one reported case. This case can be a starting point for future research.

Conclusion

The use of calcium acetate for therapeutic purposes may be more common than thought because calcium acetate is also used as a food additive. Clinicians should be familiar with its side effects to properly assess the potential for serious adverse events..

References

1. Wang Y, Xie G, Huang Y, Zhang H, Yang B, Mao Z. Calcium acetate or calcium carbonate for hyperphosphatemia of hemodialysis patients: a meta-analysis. PLoS One. 2015; 10(3): e0121376.
2. Drugs.com. Calcium acetate Side Effects from Drugs.com; (*Updated:* 11 Jan 2023). Available from: https://www.drugs.com/sfx/calcium-acetate-side-effects.html
3. Alharbi FA, Alharthi AA, Alsaadi FN. Perindopril-induced angioedema of the lips and tongue: a case report. Journal of Medical Case Reports. 2018; 12(1): 1-4.
4. Aziz Y, Rademacher WMH, Hielema A, Wishaw SBP, van Diermen DE, de Lange J, Rozema FR. Oral adverse effects: drug-induced tongue disorders. Oral diseases 2021; 27(6), 1528-1541.
5. Reed LK, Meng J, Joshi GP. Tongue swelling in the recovery room: a case report and discussion of postoperative angioedema. Journal of clinical anesthesia. 2006; 18(3), 226–229.
6. Coskun B, Saral Y, Ozturk P, Karincaoglu Y, Cobanoglu B. Calcium acetate-induced linear fixed drug eruption. Dermatology (Basel, Switzerland). 2005; 210(3), 244–245.
7. Rossi A, Osborn L. A Case Report of Angioedema and Anaphylactic Shock Induced by Ingestion of Polyethylene Glycol. Clinical practice and cases in emergency medicine. 2020; 4(2), 189–192.
8. Food additives. What're the Uses of Calcium Acetate (E263) in Food and Hyperphosphatemia Treatment?; (*Updated:*14 Jan 2023). Available from: https://foodadditives.net/acidity-regulator/calcium-acetate/

Case Report
Eurasian Journal of Toxicology

Seven Siblings Admitted to Emergency with Datura Poisoning: Cases from Northern Syria

Murat TEPE[1], Bahadır KARACA[2], Burak ÇELİK[3], Buğra YILDIRIM[4]

[1]Kilis Prof Dr Alaeddin Yavaşça State Hospital, Department of Emergency Medicine, Kilis, Türkiye
[2]University of Health Sciences, Istanbul Sancaktepe City Hospital, Department of Emergency Medicine, Istanbul, Türkiye
[3]Kırşehir Training and Research Hospital, Department of Emergency Medicine, Kırşehir, Türkiye
[4]Kilis Prof Dr Alaeddin Yavaşça State Hospital, Department of Pediatrics, Kilis, Türkiye

Abstract

Datura Stramonium (DS) is a wild and herbaceous plant that grows widely. It contains atropin, hyoscyamine and scopolamine. DS can cause severe poisoning with severe anticholinergic syndrome. Poisoning occurs as a result of its unconscious consumption for healing purposes, abuse due to its hallucinogenic efffects or accidental comsumption of the plant. The purpose of this study is to discuss the approach to DS poisoning and the treatment modalites of anticholinergic syndrome by presenting the cases of seven siblings who were admitted to hospital with vast variety of anticholinergic symptoms caused by DS poisoning.

Keywords: Datura stramonium, poisoning, anticholinergic effects

Introduction

Datura Stramonium (DS) is a wild and herbaceous plant that grows widely and is popularly called by many different names such as devil apple, pipe flower, jimson grass, abu lily, gin grass, tatula, tatala or pork patina[1]. DS can cause poisoning with severe anticholinergic syndrome and it contains atropine, hyoscyamine, and scopolamine[2]. Anticholinergic symptoms; mydriasis, dry-red skin, hallucinations, agitation, hyperthermia, urinary retention, decreased bowel motility, convulsion, delirium, confusion, speech disorder, hypertension, nausea, abdominal pain, erythema, ataxia, fasciculations, and muscular rigidity[3]. In this article, we aimed to present the clinical information of seven siblings who were admitted to the hospital with different symptoms after eating DS, and two of them were followed up in the pediatric intensive care unit and discharged with recovery.

Case Reports

Seven siblings aged one to eight years applied to the emergency department of our hospital with various complaints such as skin symptoms, nausea-vomiting and changes in consciousness about one hour after they ate the plant they found in the garden. It was understood that the plant brought to the hospital by their families was DS (Figure 1).

A 7-year-old female patient had complaints of nausea-vomiting, skin rash, and altered consciousness. On physical examination, she was conscious, and her orientation and cooperation were impaired. Pupillary mydriatic, mucous membranes were dry, and diffuse redness was present on her body, which faded with pressure and was not raised from the skin. Other system examinations were evaluated as normal. Fever: 38 C, heart rate 118/min, oxygen saturation: 98%, respiratory rate: 22/min. Hemogram and biochemistry results evaluated in the emergency department were within normal reference ranges. The patient, who was evaluated as anticholinergic poisoning due to DS consumption, was admitted to the pediatric intensive care unit.

During his intensive care hospitalization, he had a delirium picture including visual hallucinations, meaningless speech, unconscious movements, and spatial and temporal disorientation. Oxygen support, intravenous hydration, and

Corresponding Author: Murat TEPE **e-mail:** dr_tepe@hotmail.com
Received: 19.12.2022 • **Accepted:** 31.03.2023
Cite this article as: Tepe M, Karaca B, Çelik B, Yıldırım B. Seven Siblings Admitted to Emergency with Datura Poisoning: Cases from Northern Syria. Eurasian J Tox. 2023;5(1): 20-92

Table 1: Age, gender, physical examination and treatment status of the cases.

Case Number	Age	Gender	Skin lesion	Neurological sign	Mydriasis	GIS findings	Tachycardia	Hospitalization	Treatment and follow up
1	One	Female	+	-	+	+	-	-	IV hydration and ER follow up
2	Three	Female	+	-	+	+	-	-	IV hydration and ER follow up
3	Five	Female	+	-	+	+	-	-	IV hydration and ER follow up
4	Six	Female	+	-	+	+	-	-	IV hydration and ER follow up
5	Seven	Male	+	+	+	+	+	+	IV Diazepam and hydration and ward follow up
6	Seven	Female	+	+	+	+	+	+	IV Diazepam and hydration and ward follow up
7	Eight	Female	+	-	+	+	-	-	IV hydration and ER follow up

diazepam treatment for his agitations were given, and his symptoms regressed after approximately 24 hours. After 48 hours of follow-up in the pediatric intensive care unit, the patient was discharged with full recovery.

A 7-year-old male patient had complaints of nausea-vomiting, skin rash and altered consciousness. On physical examination, she was conscious, and her orientation and cooperation were impaired. Pupillary mydriatic, mucous membranes were dry, and diffuse redness was present on her body, which faded with pressure and was not raised from the skin. Other system examinations were evaluated as normal. Fever: 37.5 C, heart rate 110/min, oxygen saturation: 97%, respiratory rate: 21/min. Hemogram and biochemistry examination results in the emergency room were within normal reference ranges. The patient, who was evaluated as anticholinergic poisoning due to DS consumption, was admitted to the pediatric intensive care unit.

During his intensive care hospitalization, he had a delirium picture including visual hallucinations, meaningless speech, unconscious movements, and spatial and temporal disorientation. Oxygen supplementation, intravenous hydration, and diazepam treatment for his agitations were given, and his symptoms resolved after approximately 30 hours. After 48 hours of follow-up in the pediatric intensive care unit, the patient was discharged with full recovery.

Abdominal pain and skin findings were prominent in the complaints of the other 5 siblings aged 1 to 8 years. On physical examination, there were diffuse skin rashes that were not raised from the skin, which faded with pressure, and mydriasis. There were no changes in consciousness. Vital signs were within normal ranges. On physical examination, there were no pathological findings other than skin rash and mydriasis. The patients who underwent intravenous fluid therapy and follow-up in the emergency department did not have any additional complaints after 12 hours of observation and were discharged with recommendations.

Discussion

The anticholinergic symptoms observed in DS poisoning depend on the atropine, scopolamine and hyosyamine contained in the plant[4]. The first and most specific manifestations of anticholinergic poisoning due to DS toxicity; dryness of the skin and mucous membranes, diffuse skin redness, mydriasis and sinus tachycardia. In more severe cases, it can lead to multiple organ failures and neurological symptoms such as delirium and coma[5]. All of our cases had diffuse skin rashes and findings of mydriasis. Except for two patients who were followed up in the intensive care unit, there were no neurological symptoms.

Poisoning due to Datura Stramonium is mostly caused by the wrong and unconscious consumption of herbal medicine in the cases in our country. It is used orally by people with acne, eczema, and hemorrhoids complaints, and locally by making an ointment by people with muscle and joint pain complaints1. DS poisoning seen in western countries is generally caused by abuse in the form of consumption as cigarettes due to its euphoric and hallucinogenic effects in young adults[6]. All of our cases are pediatric patients and there is accidental consumption.

The main treatment in DS poisoning consists of supportive treatment and care. Gastric lavage can be applied in cases admitted in the first hour after ingestion. Activated charcoal is recommended. Benzodiazepines can be given to patients with agitation. Physostigmine, a cholinesterase inhibitor, can be given in resistant cases[7]. Physostigmine easily crosses the blood-brain barrier and reaches peak activity 5 minutes after administration. It can

be given intravenously in doses of 0.5-2 mg, without faster than 1 mg/min. Serious side effects such as hypotension, bradycardia, convulsions and asystole are known[8]. None of our patients had resistant delirium or agitation that would require physostigmine. Most of the cases followed up due to DS poisoning are discharged in less than 48 hours[9]. While 2 of our patients that we followed up in the intensive care unit were discharged within 48 hours, the other 5 patients were discharged after 12 hours of follow-up in the emergency room.

Conclusion

In conclusion, wild plant poisoning should be considered in all patients presenting to the emergency department with anticholinergic findings and complaints of unknown origin, and patients should be evaluated and questioned in this respect.

References

1. Kurt, D. D., Korulmaz, A., Alakaya, M., & Arslanköylü, A. E. Deliryuma yol açan nadir bir intoksikasyon: Datura stramonium. *Mersin Üniversitesi Sağlık Bilimleri Dergisi*, *15*(1), 128-132.
2. Trancă SD, Szabo R, Cociş M. Acute poisoning due to ingestion of Datura stramonium -- a case report. Rom J Anaesth Intensive Care 2017;24:65-8.
3. Bıçakcıoğlu M, Gedik E, Şayan H, et al. Hayatı Tehdit Eden Datura Otu Zehirlenmesi. Türkiye Klinikleri J Med Sci 2014; 34:417-9.
4. Celbek G, Güneş H, Güngör A, et al. [Anticholinergic syndrome after trial of Datura stramonium: A case report]. Konuralp Tıp Dergisi 2010; 2:35-7.
5. Shebani, A., Hnish, M., Elmelliti, H., Abdeen, M. M., & Ganaw, A. (2021). Acute poisoning With Datura stramonium plant seeds in Qatar. *Cureus*, *13*(12).
6. Spina, S. P., & Taddei, A. (2007). Teenagers with Jimson weed (Datura stramonium) poisoning. *Canadian Journal of Emergency Medicine*, *9*(6), 467-469.
7. Wax PM, Young AC. Anticholinergics. In: Tintinalli JE, Stapczynski JS, Ma OJ, Cline DM, Cydulka RK, Meckler GD, editors. Tintinalli's emergency medicine: a comprehensive study guide. 7th ed. New York: McGraw-Hill; 2011:1305-8
8. Chung, W. M., Chian, Y. Y., & Azmir, A. (2018). Datura fruit poisoning. *Med J Malaysia*, *73*(6), 453-454.
9. Disel, N. R., Yilmaz, M., Kekec, Z., & Karanlik, M. (2015). Poisoned after dinner: dolma with Datura stramonium. *Turkish journal of Emergency medicine*, *15*(1), 51-55.

Letter to Editor

Eurasian Journal of Toxicology

Aluminum Phosphide Poisoning

Ali KARAKUŞ[1]

[1]Hatay Mustafa Kemal University, Faculty of Medicine, Emergency Department, Hatay, Türkiye

Dear Editor,

Aluminum phosphide, is a fumigant with high insecticide power in all life stages of insects, which is harmful in stored products. It is in the form of tablets or granules and is highly lethal and has no antidote. It inhibits the enyzme of cytochrome oxidase. Complications may develop as a result of inhaling phosphine gas or oral intake. Respiratory, circulatory, gastrointestinal tract and nervous system, kidney and liver may be affected. Shock, Acute Respiratory Distress Syndrome (ARDS), aspiration pnomony, anemia, metabolic acidosis, electrolytic disorder, coma, hipoxy, hemorrhage, pericardide are poor prognosis criterion. Leukopenia indicates severe toxicity. The lethal dose is 0.15-0.5 g and death is in evitable even when buying 3-5 tablets. Arrhythmia is responsible for death in the first 24 hours. The mortality rate varies between 37-100%. Treatment consists entirely of supportive treatment (liquid, dopamine, oxygen, mechanical ventilation, gastric washing, activated charcoal, bicarbonate, hemodialysis)[1-3].

We aimed to present the case that developed systemic complications in follow-up, but we discharged with healing as a result of appropriate follow-up and treatment. A 16 year old female patient was rushed to the emergency room two hours ago for drinking more than she knew the amount of the drug containing aluminum phosphide for suicidal purposes. When the patient arrived, his general condition was moderate, conscious, pale sweaty appearance and tachypnea, breathıng: 26/min, TA:60/40mmHg, Pulse:135/min, fever:37 degree systemic examination showed no abnormalities. Initial blood values, electrocardiography (ECG) and chest x-ray were normal. The patient was followed up in the emergency department. 1000 ml serum physiological started. In order to reduce the formation of phosphine gas (with alkalism), oral bicarbonate was started. TA:100/70mmHg in the 2nd hour of follow-up and chest pain developed. The first Troponin I value was: 0.02 (0-0.06 ng/ml). In echocardiography (ECHO) ejection fraction was determined 57%. In the blood gas, PH was 7.32 and there was metabolic acidosis. Her acidosis level improved in the 6th hour of the followup. The control Troponin value was 0.21. Asetil salisilik acid started at 100 mg. At the 12th hour white blood cell (4-11 k/ml) decreased from 12000 to 4000. However no abnormality was detected in other

Corresponding Author: Ali KARAKUŞ **e-mail:** drkarakus@yahoo.com
Received: 27.12.2022 • **Revision:** 24.03.2023 • **Accepted:** 27.03.2023
Cite this article as: Karakuş A. Aluminum Phosphide Poisoning. Eurasian J Tox. 2023;5(1): 23-25

hemogram values. At the 20th hour, her chest pain gone and her troponin values increased up to 1.45. No ECG change detected. Her acidose improved and lokopenia not seen. The patient's control, liver and kidney function tests and ECHO were normal. No abnormality was detected in the followups, polyclinic controls and laboratory values on the third day of the hospitalization. The patient was discharged from the hospital with suggestions.

Aluminum phosphide is an extremely mortal toxic substance. During the follow up sun wanted complications can develop. Merely satisfactory results can be achieved with valid, timely and appropriate supportive treatments.

References

1. Gurjar M, Baronia AK, Azim A, Sharma K. Managing aluminum phosphide poisonings. Journal of emergencies, trauma and shock. 2011;4(3):378.
2. Bogle R, Theron P, Brooks P, Dargan P, Redhead J. Aluminium phosphide poisoning. Emergency Medicine Journal. 2006;23(1):3-7.
3. Mehrpour O, Jafarzadeh M, Abdollahi M. A systematic review of aluminium phosphide poisoning. Arhiv za higijenu rada i toksikologiju. 2012;63(1):61.