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Editorial

Değerli Okuyucular,

Dergimizin 2022 yılı ikinci sayısı sizinle paylaşıyor olmaktan dolayı mutluyuz. Dergimiz bu sayıdan sonra tamamen İngilizce olarak yayınlanacaktır.

Dergiyi bilimsel açıdan en ileri seviyeye çıkarmak için Dergimize destek ve katkılarınızın artarak devam edeceğinizi ümit ediyoruz.

Dergimize katkısı olan editörler, yazarlar, hakemler başta olmak üzere derginin hazırlanıp sizlerin okumasına hazır hale getirilmesinde desteği olan bütün herkese ve ATUDER (Acil Tıp Uzmanları Derneği) Yönetim Kurulu ile Başkanımız Prof. Dr. Başar Cander'e destek ve katkıları nedeniyle teşekkür ederiz.

Saygılarımızla.

Eurasian Journal of Toxicology Editörler Kurulu

Dear Readers,

We are happy to share the second issue of our Journal for 2022 with you. Our journal will be published entirely in English after this issue.

We hope that your support and contributions to our Journal will continue to increase in order to bring the journal to the most advanced level scientifically.

We would like to thank everyone who contributed to our journal, especially the editors, authors, referees, and everyone who supported the preparation of the journal and making it ready for you to read. Also we would like to thank to The Board of Directors of The Emergency Medicine Physicians Association of Turkey (EPAT) and President of EPAT, Dear Başar Cander for their support and contributions.

Regards.

Eurasian Journal of Toxicology Editorial Board

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The Relationship between Blood Lactate Levels and Clinical Outcomes in Patients Taking Drugs for Suicide: A Retrospective and Descriptive Study

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Abstract

Introduction: Acute poisoning that causes significant morbidity and mortality worldwide is a preventable public health problem. In the evaluation of critically ill patients in emergencies, lactate is a useful biomarker. This study aims to investigate whether the mortality, morbidity, and intensive care hospitalization of patients presenting to the emergency department with drug intake for suicide can be determined by the blood lactate levels measured on admission.

Material-Method: Patients over the age of 18 who presented to the emergency department between 1 January 2019 and 1 January 2020 due to acute poisoning were included in this single-center retrospective study. The relationship between the blood lactate levels measured on admission and the clinical outcome of the patient was examined. The student t-test was used to compare groups with normally distributed data, while the chi-square test was used for non-normally distributed or ordinal data. $p<0.05$ was considered statistically significant.

Findings: The data of 223 patients were analyzed. The median age was 28, and the female ratio was 68.6%. The most commonly ingested drugs were analgesics with 35%, other drugs with 33.6%, antidepressants with 24.7%, and other psychotropics with 22.4%. 192 of the patients were discharged following the treatment, 31 patients were admitted to the service or intensive care unit, and 3 patients died within the first 24 hours after the intensive care unit admission. When the factors related to hospitalization were examined, male gender, high mean age, high lactate level, and analgesic and other psychotropic drug intake were found to be related to hospitalization. On the other hand, old age (48.00, ±16.70), high lactate levels (6.77, ±6.52), and low bicarbonate levels (17.40, ±3.05) were associated with mortality.

Conclusion: Blood lactate measured on admission is an important biomarker to predict both mortality and morbidity in patients presenting to the emergency department due to the use of drugs for suicidal purposes.

Keywords: emergency department, lactate level, mortality, suicidal drug intake.

Özet

Giriş: Dünya çapında önemli morbidite ve mortaliteye neden olan akut zehirlenme, önlenebilir bir halk sağlığı sorunudur. Acil durumlarda kritik hastaların değerlendirilmesinde laktat yararlı bir biyobelirteçtir. Bu çalışmada intihar amaçlı ilaç alımı ile acil servise başvuran hastaların mortalite, morbidite ve yoğun bakım yatışlarının başvuru sırasında ölçülen kan laktat düzeyleri ile belirlenip belirlenemeyeceğini araştırmak amaçlanmıştır.

Gereç-Yöntem: Bu tek merkezli retrospektif çalışmaya 1 Ocak 2019 ile 1 Ocak 2020 tarihleri arasında akut zehirlenme nedeniyle acil servise başvuran 18 yaş üstü hastalar dahil edildi. Başvuru sırasında ölçülen kan laktat düzeyleri ile hastanın klinik sonucu arasındaki ilişki incelendi. Normal dağılan verilere sahip grupları karşılaştırmak için öğrenci t testi, normal dağılmayan veya sıralı veriler için ki-kare testi kullanıldı. $p<0,05$ istatistiksel olarak anlamlı kabul edildi.

Bulgular: 223 hastanın verileri analiz edildi. Ortanca yaş 28, kadın oranı %68,6 idi. En sık alınan ilaçlar %35 ile analjezikler, %33,6 ile diğer ilaçlar, %24,7 ile antidepresanlar ve %22,4 ile diğer psikotroplardır. Hastaların 192'si tedavi sonrası taburcu edildi, 31 hasta servise veya yoğun bakıma alındı ve 3 hasta yoğun bakıma yatıştan sonraki ilk 24 saat içinde öldü. Hastaneye yatış ile ilgili faktörler incelendiğinde erkek cinsiyet, yaş ortalamasının yüksek olması, laktat düzeyinin yüksek olması, analjezik ve diğer psikotrop ilaç alımının yatışla ilişkili olduğu saptandı. Öte yandan yaşlılık (48.00, ±16.70), yüksek laktat seviyeleri (6.77, ±6.52) ve düşük bikarbonat seviyeleri (17.40, ±3.05) mortalite ile ilişkilendirildi.

Sonuç: Acil servise intihar amaçlı ilaç kullanımı nedeniyle başvuran hastalarda, başvuru sırasında ölçülen kan laktatı hem mortalite hem de morbiditeyi öngörmede önemli bir biyobelirteçtir.

Anahtar kelimeler: acil servis, laktat düzeyi, mortalite, intihar amaçlı ilaç alımı

Introduction

Acute poisoning is a preventable public health problem that causes significant morbidity and mortality worldwide[1]. Acute poisonings can be either intentional (suicide attempt) or unintentional (accidental). Intentional poisoning is usually encountered in adults. Acute poisoning is estimated to be responsible for more than one million diseases worldwide annually and continues to increase each year[1-3]. In Turkey, the types of poisoning cases differ due to geographical diversity, socio-economic status, and differences in cultural practices. While drugs are the most common causes of poisoning, carbon monoxide, alcohol, food, fungi, organophosphate, and corrosive substances are the other common causes of poisoning[4,5]. The mortality rate due to poisoning is 1% in developed countries, whereas this rate is between

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3-5% in developing countries[4]. Patients who attempt suicide generally have higher mortality[6]. Therefore, effective and prompt medical intervention is vital to prevent morbidity and mortality in acute poisoning.

In the emergency department, lactate is a useful biomarker in the evaluation of critically ill patients[7]. Hyperlactatemia is seen in hypoxic conditions such as circulatory failure and severe anemia as well as in conditions that are not hypoxic but cause oxygen use problems such as malignancies, liver or kidney failure, and serious infections[8]. The most common causes of lactic acidosis are sepsis, shock, severe heart failure, and severe trauma[9]. The value considered abnormal in hyperlactatemia is 2 mmol/L and above. Mortality is higher in patients with lactate levels between 2 and 4 mmol/l compared to patients with lower lactate levels[10]. Hyperlactatemia >4 mmol/l is significantly associated with in-hospital mortality[11].

To our knowledge, there are no studies evaluating the relationship between blood lactate levels and clinical outcomes in patients who ingest drugs for suicide. This study aimed to investigate whether the mortality, morbidity, and intensive care hospitalization of patients presenting to the emergency department with drug intake for suicide can be determined by the blood lactate levels measured on admission.

Material and Methods

In this single-center retrospective study, patients presenting to the emergency department of a 700-bed tertiary training and research hospital to which an average of 200,000 patients present annually between January 1, 2019 and January 1, 2020 were included. The study was approved by the Bozyaka Training and Research Hospital Ethics Committee (Ethics committee decision number: 2022/90).

Patients over 18 years who presented to the emergency department due to acute poisoning were included. Patients who were under 18, were pregnant, had trauma, experienced circulatory failure, had severe anemia, suffered from malignancies, had a previous history of liver or kidney failure, had serious infections, used alcohol and recreational drugs, used rat poison, organophosphate, and caustic substance, and whose laboratory data could not be obtained were excluded from the study. According to the ICD 10 system, coding T36-T50 (poisoning by drugs, drugs and biological substances), T51-T65 (toxic effects of major non-medicinal substances according to the source), and X60-X84 (intentional self-harm) were used. For this purpose, age, gender, drug or drugs that cause poisoning, the amount taken by the patient, complete blood count (leukocyte, hemoglobin, platelet and biochemical values; urea, creatinine, alanine aminotransferase, and aspartate aminotransferase)) and blood gas analysis (pH, lactate) parameters on admission to the emergency department and clinical outcome (discharge, ward and intensive care admission) were reached using the hospital information management system database. Additionally, the patient's history, physical examination findings, and vital signs during admission were obtained from patient records.

Blood gas analysis was measured on the autoanalyzer (XN-1000, Sysmex Corp. Kobe, JAPAN) after venous blood gas collection.

Statistical Analysis

Statistical analysis was performed with the IBM SPSS Statistics Version 26. Quantitative data were expressed as mean±standard deviation, while qualitative data as frequency and percentage. Normality analysis was performed for continuous variables. The student t-test was used to compare two groups with normally distributed data, whereas the chi-square test was used for non-normally distributed or ordinal data. $p<0.05$ was considered statistically significant.

Results

A total of 223 patients who met the criteria were included in the study covering the period between 1 January 2019 and 1 January 2020 (Figure 1). The median age of the patients was 28 (min-max: 18-67), and the female ratio was 68.6% (153/223). Considering taken drugs, the frequency of analgesics was 78 (35%), other drugs 75 (33.6%), antidepressants 55 (24.7%), and other psychotropics 50 (22.4%) (Table 1). The mean systolic blood pressure of the patients on admission was 124.94 (±15.10) mmHg, diastolic blood pressure was 73.48 (±10.37) mmHg, and the pulse rate was 90.39/min (±19.82). In the blood gas measured on admission, the mean pH was 7.38 (±0.52), HCO_3 23.12 (±2.46), and lactate 2.24 (±1.46) (Table 1). 192 of the patients were discharged after follow-up and treatment in the emergency department, 31 patients were admitted to the service or intensive care unit, and 3 patients died within the first 24 hours after hospitalization in the intensive care unit (Table 1).

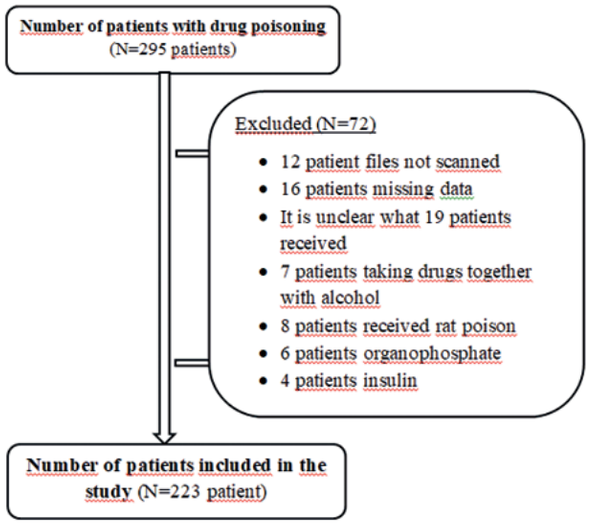

Figure 1: Study flow diagram

Table 1: Characteristics of study subjects

Characteristics	Number (%), mean, median, SD±
Age, y, median (range)	28(18-67)
Female sex	153/223(68.6%)
Comorbidity	
Hypertension	7/223 (3.1%)
Diabetes Mellitus	3/223 (1.3%)
OCD*	3/223 (1.3%)
Depression	3/223 (1.3%)
Asthma /COPD*	5/223 (2.2%)
Bipolar	3/223 (1.3%)
Others	14/223(6.5%)
Drugs	
Antidepressants	55/223 (24.7%)
Other psychotropics	50/223 (22.4%)
Analgesics	78/223(35%)
Antibiotics	41/223(18.4%)
Antiepileptic	14/223(6.3%)
Antihypertensive	11/223(4.9%)
Others	75/223(33.6%)
Clinics	
Discharge	192/223(86.1%)
Service + intensive care hospitalization	31/223(13.9%)
Mortality	3/223 (1.3%)
Vitals	
Systolic BP*	124.94(±15.10)
Diastolic BP*	73.48(±10.37)
Pulse rate	90.39(±19.82)
RR*	18.37(±5.12)
Saturation,%	97.39(±5,.67)
GCS*	15.00(3-15)
Laboratory	7.38(±0.52)
pH	23.12(±2.46)
HCO3*	2.24(±1.46)
Lactate	

*OCD: Obsessive Compulsive Disease, COPD: Chronic Obstructive Pulmonary Disease, BP: Blood Pressure, RR: Respiratory Rate, GCS: Glaskow Coma Score, HCO_3: Bicarbonate

Table 2: Demographic and laboratory findings related to hospitalization

	Hospitalization		
	No (n=192)	Yes (n=31)	
	N,%, mean, ±SD	N,%, mean, ±SD	P value
Gender			
Female	137 (89.5%)	16 (10.5%)	**0.028**
Male	55 (78.6%)	15 (21.4%)	
Age, mean	30.24 (±10.78)	35.65 (±11.69)	**0.011**
Systolic BP*	124.77 (±15.21)	125.94 (±14.59)	0.690
Diastolic BP*	73.64 (±10.24)	72.55 (±11.31)	0.589
Pulse rate	89.50 (±18.13)	95.94 (±18.13)	0.222
Respiratory rate	18.42 (±5.42)	18.10 (±2.68)	0.748
Saturation	97.34 (±6.07)	97.68 (±1.74)	0.758
GCS*	14.97 (±0.36)	13.81 (±2.85)	**0.030**
pH	7.38 (±0.048)	7.38 (±0.078)	0.853
HCO_3	23.22 (±2.43)	22.52 (±2.59)	0.142
Lactate	2.15 (±1.41)	2.80 (±1.70)	**0.021**
The number of drugs			
1	128 (66.7%)	16 (51.6%)	0.104
>=2	64 (33.3%)	15 (48.4%)	
Antidepressant	45 (23.4%)	10 (32.3%)	0.290
Other psychotropics	38 (19.8%)	12 (38.7%)	**0.019**
Analgesics	72 (37.5%)	6 (19.4%)	**0.049**
Antiepileptic	11 (5.7%)	3 (9.7%)	0.420
Antihypertensive	9 (4.7%)	2 (6.5%)	0.653
Antibiotic	35 (18.2%)	6 (19.4)	0.881
Others	63 (32.8%)	12 (38.7%)	0.519

*BP: Blood Pressure, GCS: Glaskow Coma Score

When the factors related to hospitalization were examined, there was a statistical difference in favor of male patients (p=0.028) in terms of hospitalization. While 21.4% of male patients were hospitalized, only 10.5% of female patients were hospitalized. We observed that the mean age of hospitalized patients was statistically significant compared to non-hospitalized patients, 35.65 (±11.69) and 30.24 (±10.78) (p=0.011), respectively. Patient vitals other than low glaskow coma score (GCS) on admission were not significant in terms of hospitalization (Table 2). In addition, we found that the lactate level at the time of admission was statistically correlated with hospitalization (p=0.021). When the intensive care or ward hospitalizations of the patients were examined according to the drug group, other psychotropic drugs intake and analgesic drugs intake were associated with hospitalization (p=0.019 and p=0.049, respectively) (Table 2).

In our study, only three patients died. All 3 patients died within 24 hours after they were admitted to the intensive care unit from the emergency room. 2 of these three patients who developed mortality had comorbid disease, one patient had DM and the other had COPD. When we examine the factors associated with mortality, we observed that the mean age of these three patients was 48 years, the mean HCO3 on admission was 17.4 (±3.05), and the initial blood lactate level was 6.77 (±6.52). These three factors were statistically significant in terms of mortality (p= 0.007, <0.001, and <0.001, respectively). We could not observe any relationship between all other factors and mortality (Table 3)

Discussion

In this study, we found that the blood lactate level measured on admission is useful in identifying critically ill patients presenting to the emergency with drug intake for suicide. We also showed that blood lactate levels are an independent variable of mortality in those patients. In addition, we found that age and HCO_3 values were associated with mortality. In our results, gender, age, low GCS, and blood lactate levels were statistically significant between hospitalized and non-hospitalized patients. These results contribute to identifying critically ill patients so that earlier action can be taken for the patient.

Table 3: Examination of demographic and laboratory findings related to mortality

	Mortality		
	No (n=220)	Yes (n=3)	
	N,%, mean, ± SD	N,%, mean, ±SD	P value
Gender Female Male	 151 (68.6%) 69 (31.4%)	 n/a n/a	0.942
Age, mean	30.76 (±10.82)	48.00 (±16.70)	**0.007**
Systolic BP*	124.92 (±15.19)	125.67 (±5.13)	0.932
Diastolic BP*	73.48 (±10.37)	73.67 (±13.01)	0.976
Pulse rate	90.46 (±19.93)	85.67 (±8.37)	0.678
RR	18.41(±5.14)	15.33 (±3.06)	0.320
Saturation	97.39 (±5.70)	97.00 (±3.61)	0.906
GCS*	14.87 (±0.86)	10.33 (±6.43)	0.346
pH	7.38 (±0.05)	7.23 (±0.07)	0.062
HCO_3*	23.20 (±2.36)	17.40 (±3.05)	**<0.001**
Lactate	2.18 (±1.23)	6.77 (±6.52)	**<0.001**
The number of drugs 1 >=2	 142 (64.5%) 78 (35.5%)	 n/a n/a	0.939
Antidepressant	45 (23.4%)	10 (32.3%)	0.726
Other psychotropics	38 (19.8%)	12 (38.7%)	0.649
Analgesics	72 (37.5%)	6 (19.4%)	0.202
Antiepileptic	11 (5.7%)	3 (9.7%)	0.652
Antihypertensive	9 (4.7%)	2 (6.5%)	0.692
Antibiotic	35 (18.2%)	6 (19.4)	0.502
Others	63 (32.8%)	12 (38.7%)	0.991

*BP: Blood Pressure, RR: Respiratory Rate, GCS: Glaskow Coma Score, HCO_3: Bicarbonate

Lactate is the end product of the glycolytic breakdown of glucose during anaerobic respiration. It is produced by the tissues in the body in cases of insufficient oxygen supply to the tissues, increased oxygen demand, and inadequate oxygen use[9]. Hyperlactatemia is associated with increased morbidity and mortality[12]. In a systematic review, Kruse et al. reported that blood lactate level is useful for risk assessment in patients admitted to the hospital acutely and is valuable in estimating in-hospital mortality, especially with serial lactate sampling[12]. In a retrospective study of 6098 patients conducted to define unexpected death within 24 hours of hospital admission, Blum et al. showed that lactate is the strongest independent parameter predicting death within 24 hours of admission[13]. In our study, similar to the literature, we found that blood lactate levels were significantly higher in both hospitalized patients and patients who died [2.18 (1.23) vs. 6.77(6.52), p<0.001].

The blood lactate concentration reflects the balance between lactate production and excretion in tissues. In healthy and resting humans, the blood lactate concentration is normally 0.5-1.8 mmol/L[13]. Blum et al. reported that mortality is predicted in patients with blood lactate higher than 2 mmol/L, and the death rate increases as the level increases[13]. Bou Chebl et al found that the mortality rate was 7.1 times higher when lactate levels were >2 mmol/L in critically ill patients, and 29.4 times higher if lactate levels were >4 mmol/L[14]. Schollin-Borg et al. considered the normal lactate level <2.44 mmol/L and found that the 30-day mortality was 3.54 times higher for lactate 2.44-5.0 mmol/L and 4.45 for lactate >5.0 mmol/L[15]. In a retrospective study, Pedersen et al. divided lactate levels into three groups; low lactate (0-1.9 mmol/L), medium lactate (2-3.9 mmol/L), and high lactate (≥4 mmol/L), and reported that 7-day mortality was 2.9% in low-lactate patients, 7.8% in moderate lactate patients, and 23.9% in high lactate patients[10]. In our study, the lactate values of hospitalized and non-hospitalized patients were 2.80 and 2.15, respectively. Additionally, the lactate values of patients with and without mortality were 6.77 and 2.18, respectively.

In a retrospective cohort study of 5360 adult patients whose lactate was measured within 4 hours after admission to the emergency department, Petersen et al. revealed that age is a very important prognostic factor for mortality[10]. In a prospective observational cohort study conducted on 747 patients, Data et al. reported that mortality increases significantly among age groups[7]. In their retrospective study on 450 patients, Bou Chebl et al. emphasized that higher lactate levels are associated with higher hospital mortality and longer emergency room and hospital stays. They also emphasized that mortality increases with age and that there is an important relationship between the increase in lactate values and mortality in patients under 65 [14]. Similarly, in our study, we showed that age was significantly higher in predicting mortality both in hospitalized patients and in patients who died.

In their study of 211 patients in whom a Medical Emergency Team call was received, Schollin-Borg et al. found significant differences in age, lactate, and oxygen saturation between survivors and non-survivors, but did not find any significant relationship between systolic blood pressure, respiratory rate, and heart rate. Accordingly, they stated that the first blood lactate measurement is useful in the evaluation of the severity of the disease and a better indicator of mortality compared to traditional vital signs[15]. In their study on 348 critically ill patients, Jansen et al. showed that serum lactate level has a better prognostic value than vital signs such as blood pressure[16]. Similar to the aforementioned studies, in our study, we could not find a significant difference between traditional vital signs between hospitalized and non-hospitalized patients, and between those with and without mortality.

In a prospective observational cohort study conducted on 747 patients, Data et al. reported that there is a statis-

tically significant difference in bicarbonate levels in terms of 30-day mortality, and low bicarbonate levels significantly increase mortality[7]. In our study, we showed that there was a statistically significant difference between survived patients and patients who died.

Limitations

The study had several limitations. First, the data were collected retrospectively. Second, it is a single-center study. Third, the study population was relatively small. Fourth, it can be stated that only blood lactate levels were evaluated on admission and serial serum lactate levels could not be measured. In addition, the relationship between the presence of comorbid disease and lactate elevation has not been evaluated.

Conclusion

Blood lactate level is an important determinant of mortality in the emergency department. In patients presenting to the emergency department with drug ingestion for suicide, both mortality and intensive care hospitalization decisions can be made with the blood lactate levels measured during admission. Further multicenter research to be conducted with more patients is needed.

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Original Article

Eurasian Journal of Toxicology

Retrospective Evaluation of Clinical and Epidemiological Characteristics of Scorpion Sting Cases Presenting to the Emergency Department in Izmir

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Abstract

Objectives: The aim of this study is to evaluate the epidemiological and clinical features of scorpion sting cases admitted to the emergency department of a tertiary hospital in the Izmir province.

Materials and Methods: This is a retrospective cross-sectional study. Patients who applied to the emergency department because of scorpion sting between 2000-2022 years were included in the study. Demographic and clinical data and laboratory test results of the patients were searched through the hospital's electronic database. Student t test was used to compare the difference between two independent groups. P<0.05 was considered statistically significant.

Results: A total of 101 patients were included in the study. It was observed that the scorpion sting in the extremity was associated with the elevation of white blood cell count, neutrophil count, and creatine kinase level (p=0.0030, p=009, and p=0.001, respectively). Additionally, the elevation of white blood cell count, neutrophil count and potassium level were found to be significant for the development of critical illness (p<0.001, p<0.001, p=0.009, respectively).

Conclusion: Although severe poisoning findings are seen in scorpion sting cases in Izmir province, the mortality risk is low. White blood cell count, neutrophil count, and potassium level can be used as a warning tool for serious disease.

Keywords: Scorpion sting, poisoning, toxicology, epidemiology

Özet

Amaç: Bu çalışmanın amacı İzmir bölgesinde 3. Basamak bir hastanenin acil servisine başvuran akrep sokması vakalarının epidemiyolojik ve klinik özelliklerinin değerlendirilmesidir.

Gereç ve Yöntem: Bu çalışma, retrospektif kesitsel bir çalışmadır. Çalışmada 2000-2022 yılları arasında acil servise akrep sokması nedeniyle başvuran hastalar dahil edildi. Hastalara ait demografik ve klinik veriler ile laboratuvar test sonuçları hastanenin elektronik veri tabanında tarandı. Bağımsız iki grup arasındaki farkın karşılaştırılmasında student t test kullanıldı. P<0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışmaya toplam 101 hasta dahil edildi. Akrep sokmasının ekstremitede olmasının beyaz küre sayısı, nötrofil sayısı ve kreatin kinaz seviyesindeki yükseklikle ilişkili olduğu görüldü (sırasıyla p=0.0030, p=009 ve p=0.001). Ayrıca beyaz küre sayısı, nötrofil sayısı ve potasyum düzeyi kritik hastalık gelişimi için anlamlı bulundu (sırasıyla p<0.001, p<0.001, p=0.009).

Sonuç: İzmir bölgesinde akrep sokması vakalarında ciddi zehirlenme bulguları görülsede mortalite riski düşüktür. Beyaz küre sayısı, nötrofil sayısı ve potasyum düzeyi ciddi hastalık için uyarıcı olarak kullanılabilir.

Keywords: Akrep sokması, zehirlenme, toksikoloji, epidemiyoloji

Introduction

Although scorpion bites are more common in tropical and semi-tropical regions, they can be seen all over the world. It is known that about 50 of 1753 scorpion species in the world are poisonous and 20-25 are mortal[1,2]. There are approximately 1,200,000 scorpion stings cases in the world annually and approximately 3000 deaths occur due to scorpion stings[3]. Mortal scorpion species in Turkey are generally seen in the Southeast Anatolia region. The most common scorpion species in the Aegean region is Mesobuthus gibbosus (Anatolian yellow scorpion), which is a non-lethal poisonous scorpion species[4].

Although the most common findings in scorpion stings are local pain, swelling and redness, serious systemic findings that can result in death can also be seen. Poisonous scorpion species often contain venom, which is a mixture of cardiac toxins, nephrogenic toxins, neurogenic toxins, and hemolytic toxins. Deaths are mostly associated with heart failure and pulmonary congestion[5]. Since the effects of different scorpion species in different regions vary, it would be a beneficial approach for the hospitals in the region to

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develop their own treatment and follow-up protocols against scorpion sting cases.

According to the epidemiological studies conducted to date, the Aegean region is the geographical region with the lowest incidence of scorpion bites[6]. Therefore, studies in this region are very limited. This study was carried out to examine the clinical features and treatment approaches of scorpion sting cases admitted to the emergency department of a tertiaryvhospital in the Izmir province.

Material and Methods

Study Design and Setting

This study is a cross-sectional study conducted retrospectively. The study was carried out with patients presented to the emergency department of a tertiary hospital in Izmir between 2000 – 2022 years. Ethics committee approval with an application number of 2022-GOKAE-0246 was obtained before starting the study.

Patient Selection

Patients admitted to the emergency department due to scorpion sting between 2000-2022 were included in the study. Pregnant women, patients who used alcohol or drugs within 24 hours before applying to the emergency department, and patients who had simultaneous multitrauma were excluded from the study.

Data Collection Tools

The age, gender, scorpion sting site, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, white blood cell (WBC) count, neutrophyl count, lymphoside count, platelet (PLT) count, international normalized ratio (INR), Activated Partial Thromboplastin Clotting Time (APTT), creatinin, creatin kinase (CK) and potassium (K) levels, development of serious disease and treatment administered in the emergency room of the patients who met the inclusion criteria were searched through the hospital's electronic database and recorded in the case report form. Severe disease was defined as presence at least one of hypotension, tachycardia, hypoxia, altered mental status, organ failure, need for intensive care or need for intubation.

Statistical Analysis

We used IBM SPSS statistics version 26 for Windows to analyse the data obtained from the study. The skewness-kurtosis value, the shapiro wilkins test and the kolmogov smirnov test were used to determine whether the data were normally distributed. Numerical data were given as mean and standard deviation. Categorical data were given as numbers (n) and percentages (%). When comparing the mean of two independent groups, the student-t test was used because the data fit the normal distribution. Categorical parameters were analyzed using the chi-square and Fischer exact test. $P<0.05$ was considered statistically significant.

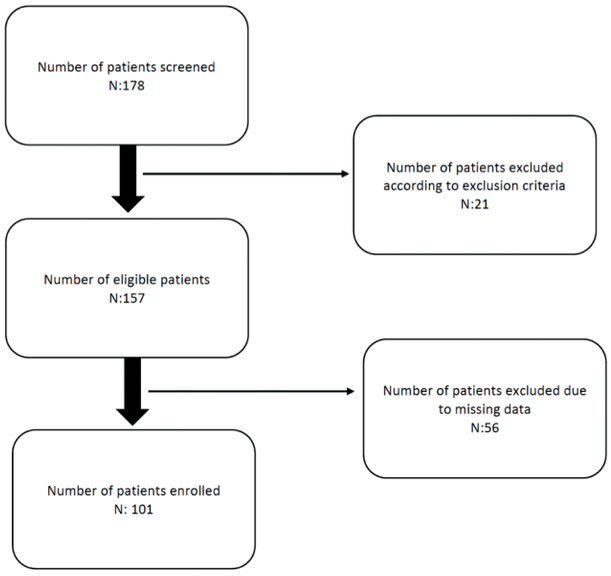

Figure 1: Work Flow Chart

Results

In the present study, 178 patients were screened, and after the patients excluded due to exclusion criteria and missing data, a total of 101 patients were analyzed. The work flow chart was presented in Figure 1. The mean age of the patients was 44 ± 18 years and 57 (56.4%) were female and 44 (43.6%) were male. In 27 (26.7%) of the patients, the scorpion sting site was on any extremity, while in 74 (73.3%) patients the scorpion sting site was in a body region other than the extremity. A total of 7 (6.9%) patients required scorpion antivenom treatment and mortality was not observed in any patient. Other descriptive characteristics of the patients were presented in Table 1.

When the vital signs and laboratory values of the patients were examined, the mean systolic blood pressure (SBP) of the patients was 132 ± 25, the mean diastolic pressure (DBP) was 71 ± 12, the mean pulse rate was 76 ± 16, the mean WBC count was 9.5 ± 3, mean neutrophyl count was 2.70±1.78, the mean PLT count was 243000 ± 71000, the mean INR value

Table 1: Descriptive characteristics of the patients

		Mean (%)
Sting Site	Non-extremity	27 (26.7%)
	Extremity	74 (73.3%)
Tetanus vaccine	No	76 (75.2%)
	Yes	25 (24.8%)
Antivenom	No	94 (93.1%)
	Yes	7 (6.9%)
Analgesia	No	68 (67.3%)
	Yes	33 (32.7%)
Antibiotheraphy	No	96 (95%)
	Yes	5(5%)
Steroid	No	58 (57.4%)
	Yes	43 (42.6%)

Table 2: Comparison of clinical features and laboratory test results of patients according to scorpion sting site

	Non-extremity N:27	Extremity N:74	Total	p
SBP (mmHg)	137 ± 26	131 ± 26	133±26	0.375
DBP (mmHg)	72 ± 12	71 ± 13	71±12	0.790
Pulse rate (/min)	75 ±9	77 ±17	76±15	0.644
WBC	9.18 ± 3.22	11.07 ± 4.00	10±4.91	0.030
Neutrophyl	5.67 ± 2.94	7.90 ± 3.95	7.30±3.83	0.009
Lymphoside	2.74 ± 1.40	2.69 ± 1.91	2.70±1.78	0.910
PLT	229000 ± 63000	254000 ± 72000	247,000 ± 70,000	0.116
INR	1.04 ± 0.10	2.45 ± 11.73	2.07±10.04	0.535
APTT	29 ± 17	25 ± 4	26.44±9.33	0.077
Creatinin	0.82 ± 0.22	0.83 + 0.18	0.83±0.19	0.830
CK	59 ± 13	152 ± 143	127±130	0.001
Potassium	4.23 ± 0.41	4.30 ± 0.45	4.31±0.48	0.485

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White blood cell, PLT: Platelet, INR: International normalization ratio, CK: Creatin kinase.

was 2.1 ± 10, CK was 115 ± 132 and mean K value was 4.3 ± 0.5. When the patients were divided into two groups according to the bite site, it was seen that the WBC count, neutrophyl count and CK value of the patients with scorpion sting on any extremity was significantly higher than the patients had a scorpion bite on the trunk, head or neck. There was no significant difference between the groups in terms of other laboratory results and vital signs. The mean of all vital signs and laboratory values of the patients and their comparisons between the groups are presented in Table 2.

When compared according to the presence of critical illness, high levels of WBC, neutrophyl and potassium were found to be associated with severe illness. Other laboratory parameters and vital signs were not significant in terms of serious disease. The distribution of the mean values of the laboratory tests and vital signs of the patients according to the severity of the disease was given in Table 3.

Considering the distribution of the cases according to the months, it was observed that the highest number of emergency visits due to scorpion sting was in August. In the seasonal distribution of cases, summer was the season with the highest number of applications to the emergency department with scorpion sting. The distribution of cases by months was shown in figure 2.

Discussion

In this study, scorpion sting cases in Izmir province were examined. There was no death due to scorpion sting in the region, but it was determined that serious disease could develop which can be predicted by an increase in WBC, neutrophils, lymphocytes and potassium.

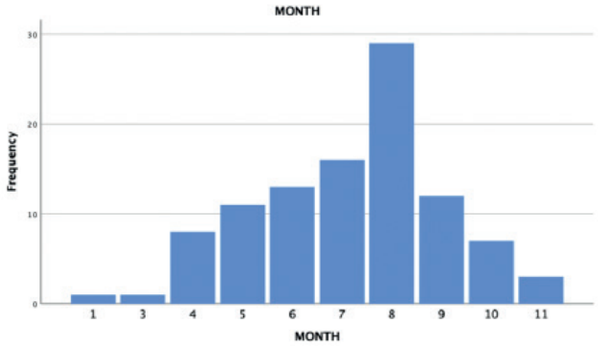

Figure 2: The distribution of cases by months

Deaths due to scorpion stings in Turkey are mostly seen in the Southeastern Anatolia region, where some of the most dangerous scorpion species live. As far as is known, Mesobuthus gibbosus, a scorpion species seen in Izmir, is poisonous but not mortal[4]. In a study conducted by Ozan et al., 24,261 scorpion sting cases were examined across Turkey and it was seen that none of the cases were mortal[7]. Rich et al. in a pediatric study evaluating scorpion stings in the Aegean region, reported no deaths[8]. In this study, no case resulted in mortality, consistent with the literature.

While scorpion stings are mostly seen in the lower and upper extremities, the head and neck are the body parts where the scorpion bite is least seen[9,10]. Bosniak et al. divided the scorpion sting areas into four as lower extremity, upper extremity, trunk and head-neck and reported that the scorpion sting site had no effect on the severity of the disease[11]. In this study, scorpion sting site was examined in two groups as extremity and non-extremity, and it was seen that the extremity was the body part most affected by scorpion sting. The reason for the high CK level in scorpion sting cases

Table 3: Comparison of clinical features and laboratory test results of patients according disease severity

	Non-critical (n:85)	Critical (n:16)	Total	p
SBP (mmHg)	132±25	135±35	133±26	0.715
DBP (mmHg)	71±11	75±18	71±12	0.289
Pulse (/min)	76±15	82±18	76±15	0.125
WBC	9.38±2.85	16.87±2.16	10±4.91	<0.001
Neutrophyl	6.08±2.7	13.8±1.9	7.30±3.83	<0.001
Lymphoside	2.54±1.14	3.56±3.61	2.70±1.78	0.038
PLT	244,000±71,000	263,000±66,000	247,000±70,000	0.328
INR	2.26±10.9	1.10±0.13	2.07±10.04	0.672
APTT	26.70±10	24.80±4.20	26.44±9.33	0.453
Creatinin	0.80±0.18	0.91±0.19	0.83±0.19	0.065
CK	123±140	148±31	127±130	0.484
Potassium	4.26±0.47	4.60±0.47	4.31±0.48	0.009

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White blood cell, PLT: Platelet, INR: International normalization ratio, CK: Creatin kinase,

in which the extremity is affected may be the presence of more muscle tissue in the extremities. Therefore, in cases of scorpion sting in which the extremities are affected, it should be evaluated in terms of CK elevation, which may cause nephropathy if not treated appropriately. In addition, it is thought that WBC and neutrophil levels were increased due to local or systemic inflammation developed in the scorpion sting cases.

Celik et al., in a study conducted in pediatric patients, have shown that the increase in the leukocyte, neutrophil, PLT and glucose levels of the patients was associated with the severity of the disease[12]. In this study, we observed that WBC, neutrophil, leukocyte and K elevations were associated with the development of serious disease. This was thought to be due to the systemic inflammatory response and rhabdomyolysis in severe disease.

With the effect of increasing air temperature, both scorpions are more active and people go to rural and natural areas more. Therefore, scorpion sting cases are more common in summer[6]. In this study, it was seen that the most cases of scorpion stings are seen in August, and when evaluated seasonally, the most cases are seen in the summer season.

This study has some limitations. Retrospective nature is the main limitation of this study. Due to the large number of missing data, detailed treatment information of the patients could not be accessed, and the long-term effects of scorpion poisoning could not be evaluated.

Conclusion

This study suggests that scorpion sting cases in Izmir province may show signs of severe poisoning, but are not mortal. WBC, neutrophil, lymphocyte and K can be used predictively for the development of severe disease.

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Review

Eurasian Journal of Toxicology

Carbon Monoxide Poisoning

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Abstract

Carbon monoxide (CO) is an odorless, colorless and tasteless poisonous gas with a molecular weight similar to air in low concentrations. For this reason, CO, which is also defined as the "silent killer", is one of the most common causes of fatal poisoning. Mortality depends on the duration of exposure to CO and its concentrations. Carbon monoxide poisoning, is still among the leading poisonings in the world. Whether it is for suicidal purposes or as a result of accident, it is a preventable, important cause of morbidity and mortality. In this review, it is aimed to review the pathophysiology, causes, diagnosis, treatment, prognosis and complications of CO poisoning. It has been tried to explain what needs to be done in diagnosis and treatment, and current treatment approaches.

Keywords: Carbon monoxide, poisoning, emergency

Özet

Karbon monoksit (CO), düşük konsantrasyonlarda havaya benzer moleküler ağırlığa sahip kokusuz, renksiz ve tatsız zehirli bir gazdır. Bu nedenle "sessiz katil" olarak da tanımlanan CO, en sık ölümcül zehirlenme sebeplerindendir. Ölüm oranı, CO'ya maruz kalma sürelerine ve konsantrasyonlarına bağlıdır. Karbon monoksit intoksikasyonu halen dünyada ön sıralarda yer alan zehirlenmeler arasında yer almaktadır. Gerek suisidal amaçlı, gerekse kaza sonucu olsun, önlenebilir, önemli bir morbidite ve mortalite sebebidir. Bu derlemede CO zehirlenmesinin patofizyolojisi, nedenleri, tanısı, tedavisi, prognozu ve komplikasyonlarının gözden geçirilmesi amaçlanmıştır. Tanı ve tedavide yapılması gerekenler, güncel tedavi yaklaşımları anlatılmaya çalışılmıştır.

Anahtar Kelimeler: Karbon monoksit, zehirlenme, acil

Introduction

Carbon monoxide (CO) is formed when hydrocarbon-based fuels and materials are not completely burned. The poisonous gas is formed when an oxygen and a carbon atom bond. It is known as the silent killer because it is colorless, tasteless and odorless. It is formed by the combustion of fuels such as natural gas, coal, wood used in heating, tobacco smoke, the burning of energy sources used in factories and motor vehicles. In addition, volcanic eruptions, forest fires and the emission of gases also cause the formation of CO[1].

It is one of the most abundant air pollutants, so every individual is exposed to CO by breathing on a daily basis. However, small amounts of CO are produced endogenously, mainly through the catalysis of heme and heme-containing proteins, and processes such as lipid peroxidation and photooxidation. Therefore, very low amounts of endogenous CO are found in each individual, but their levels can vary with physiological as well as pathological conditions[2]. Indoor CO concentrations in the air are below 30 ppm, about twice the amount in open air[3].

Although the World Health Organization (WHO) and national health and safety agencies have clear guidelines on tolerance limits for CO exposure, this poisoning is the main cause of non-fire-related accidental poisoning deaths in most countries[4].

Carbon monoxide; It is 10-15% bound to proteins such as myoglobin and cytochrome oxidase, but less than 1% is soluble in plasma. This causes tissue hypoxia. As a result, all systems are affected, especially respiratory, peripheral, central nervous system and cardiovascular system. Clinical findings vary according to the systems involved[5].

The clinical diagnosis of CO poisoning is difficult due to nonspecific symptoms[5]. It has symptoms such as fatigue, headache, dizziness, nausea. The causes of CO poisoning are attributed to other diseases and are misdiagnosed[6].

The management of CO poisoning primarily consists of symptomatic treatment and oxygen therapy. Hyperbaric oxygen (HBO) therapy is usually available for more severe cases in a pressurized chamber. Although HBO therapy reduces carboxyhemoglobin (COHb) half-life[7], its advantages are still questioned due to the lack of

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conclusive evidence that it improves survival and reduces morbidity[8,9].

Pathogenesis

From the lungs, CO passes into the blood through the alveoli. Reversible binding occurs at the same iron atom on the heme site where oxygen binds; the product of this binding is COHb. The affinity of CO for hemoglobin is 230-270 times greater than that of oxygen[10]. Carbon monoxide can cause toxicity even at low concentrations. In the case of poisoning, the oxygen-hemoglobin dissociation curve shifts to the left and the release of oxygen to the tissues is prevented[11]. Oxygen uptake by the tissues is impaired and the oxygen capacity that can be carried in the blood decreases. This condition is called "chemical anemia" or "anemia-like effect"[12]. Ten percent of the absorbed CO is bound to myoglobin and cytochrome c oxidase, while less than 1% dissolves in plasma[13]. Exposure duration, respiratory functions, oxygen concentrations, partial CO in the environment and ventilation of the environment are important in the course of the clinical picture in CO poisoning[14]. The basis of the pathophysiology of poisoning is that CO forms a bond with cytochrome c oxidase, myoglobin, and nitric oxide synthetase apart from hemoglobin and causes direct cellular damage[15]. Carbon monoxide binds with high affinity to cardiac myoglobin and has approximately 40 times greater affinity for myoglobin than oxygen. Carboxymyoglobin causes a shift to the left[11]. In other words, it is carbon monoxide that binds to the mitochondrial cytochrome system and impairs oxidative phosphorylation. This change causes a decrease in oxygen carrying capacity, impaired oxygen release at the tissue level, and cellular hypoxia. Carbon monoxide poisoning can cause signs ranging from contractile dysfunction, heart rate changes, mild and temporary cardiac damage to necrosis. This causes a further deterioration in oxygen use in the heart and muscle tissue. Cardiac contractility and output decrease the oxygen required for aerobic metabolism as a result of the higher affinity of CO binding to cardiac myoglobin. This may be responsible for cardiac dysfunction and arrhythmia[7]. Oxygen transport to peripheral tissues is further reduced. Carbon monoxide disrupts the mitochondrial respiratory chain at the level of cytochrome c oxidase, decreases the glutathione level and is directly toxic to mitochondria[10]. While cytochrome c oxidase has a low affinity for CO, it has a higher affinity for oxygen and binds to CO in severe hypoxia[16]. As a result of CO poisoning, skeletal muscle may be damaged and acute tubular necrosis, cellular ischemic necrosis and rhabdomyolysis may develop[17]. Carbon monoxide increases transcapillary leakage, lipid peroxidation and free radical formation in plasma, and increases leukocyte sequestration at the endothelial surface[18]. The brain is also very sensitive to the toxic effects of CO. The main mechanism in CO-related brain injury is hypoxia due to COHb formation. Ischemic and anoxic brain injuries are caused by a decrease in oxygen transport and mitochondrial oxidative phosphorylation. Causes cognitive deficits in survivors[19]. To ischemic brain damage; it can cause depolarization, oxidative stress, inflammation, acidosis, ionic imbalance and apoptosis. Decreased oxidative phosphorylation and ATP (adenosine triphosphate) synthesis due to inactivation of Ca ATP'ase increases brain damage[20]. Mitochondrial membrane depolarization, neurotransmitter release and cell death occur due to the activation of lipases and proteases in the cell as a result of the decrease in ATP[20]. Cellular dysfunction and increased apoptosis activate glutamate N-methyl D-aspartate receptors[11]. The increase in NO release occurs when CO binds to hemoproteins in platelets and enters into competitive competition with nitric oxide (NO). It produces peroxynitrite, which worsens tissue hypoxia and further impairs mitochondrial function[7,12]. Activated platelets can stimulate neutrophil degranulation and myeloperoxidase (MPO) release. Myeloperoxidase; it increases the inflammatory effects as a result of further degranulation, adhesion and neutrophil activation. The formation of free oxygen radicals is thought to be caused by proteases released from neutrophils by oxidizing xanthine dehydrogenase to xanthine oxidase in endothelial cells[21]. Neurological and cardiac injuries from CO poisoning contribute to the inflammatory cascade.

Clinic

In CO poisoning, patients may present with non-specific complaints. The diversity of clinical complaints is one of the most challenging aspects of making the diagnosis. Patients with CO poisoning may present with different clinical pictures ranging from headache and flu-like complaints to hemodynamic deterioration and profound mental status changes. A high level of suspicion is important for the disease. A detailed history is very important in diagnosing CO poisoning. CO poisoning should be considered in patients brought from a motor vehicle working in closed garages (mostly in non-accidental poisonings) or from burning buildings. There may be a gas leak that the patients working in the workplace with a dangerous gas environment are not aware of, or a leaky natural gas pipe may be present in those who are poisoned at home. In these cases, clues should be sought in the patient's history, such as headaches that resolve after leaving the workplace or home, and behavioral changes.

During CO heme catabolism, it does not endogenously produce more than 1% COHb. Certain disease states, such as hemolytic anemia or severe sepsis, can lead to 3-4% COHb levels as a result of hemoglobin breakdown[22]. Carboxyhemoglobin levels above 10% in smokers and over 2% in non-smokers are considered abnormal and can lead to clinical findings[28]. The first symptom that starts when COHb levels reach 10% is headache. Usually the clinical picture is

Table 1: Carboxyhemoglobin (COHb) saturation (%) levels and symptoms

CO-Hb (%)	Clinical symptoms
< 1	normal range (due to endogenous production)
< 10	smoker's blood (no symptoms)
10–20	fatigue, headache, tinnitus
20–30	fatigue, nausea, vomiting, headache,
30–40	severe headache, nausea, vomiting, dizziness
40–50	syncope, confusion, increased respiration and heart rate
50-60	coma, convulsions, depressed breathing
60–70	coma, convulsions, cardiopulmonary depression, often fatal
70 <	respiratory failure, death

not correlated with COHb levels[10].

Clinical symptoms and signs; it was found to depend on the duration of exposure to CO, its concentration, number of minute ventilations, metabolic rate, and hemoglobin concentration[24]. CO poisoning affects many systems, primarily the heart, kidney, skeletal muscle, peripheral and central nervous system. In CO poisoning, signs and symptoms may appear quickly, or they may appear days or weeks later. Hearing disorders and chest pain can be seen in the late period[10]. Since the oxygen consumption of the brain and heart is high, cardiovascular and neuropsychiatric symptoms occur in the early period[25].

It has been reported that CO poisoning, findings vary according to COHb levels, and this relationship is shown in Table 1.[26]:

In CO poisoning, delayed neurologic syndrome (DNS) may develop 7-240 days later. Personality changes, dementia, memory loss, behavioral disorders, learning difficulties, parkinsonism, attention and concentration disorders, apraxia, psychosis, paralysis, chorea, incontinence or peripheral neuropathy may be observed in these patients[13]. Delayed neurologic syndrome is more common in patients with more pronounced initial symptoms, and 75% of patients recover without additional specific treatments[5]. The systems and clinical findings seen in patients with CO poisoning are shown in Table 2[25].

An increase in cardiac output is seen to compensate for the cardiotoxic effect caused by myoglobin to which CO binds with its high affinity. The main manifestations of cardiac involvement are dysrhythmia and ischemia. Aspiration, heart failure, and hypoxia secondary to pulmonary edema and depression of the central nervous system are other common manifestations[24]. Carbon monoxide intoxication causes ventricular fibrillation as well as lowers the malignant ventricular arrhythmia threshold and may lead to early death[27]. Carbon monoxide poisoning can cause atrial and ventricular fibrillation, premature atrial and ventricular contractions, ST-T wave changes[34], supraventricular tachycardia, QT prolongation[29]. In CO poisoning, drugs that cause QT prolongation should be avoided; because there are studies showing a correlation between prolongation of the QT interval and CO levels[29].

Table 2: The symptoms and clinical findings seen in patients with CO poisoning.

SYSTEM	CLINICAL FINDINGS
Cardiovascular System	ECG changes, tachycardia, bradycardia, cardiomegaly, angina pectoris, premature ventricular contraction, myocardial infarction, A-V Block, atrial fibrillation, ventricular fibrillation, shock
Central and Peripheral Nervous System	Agitation, cerebral edema, behavioral disorders, cognitive impairment, ataxia, muscle rigidity, parkinsonism, peripheral neuropathy, psychosis, memory disorders, personality changes, fecal and urinary incontinence, coma, convulsions,
Genitourinary System	Acute renal failure, glucosuria, proteinuria, hematuria, myoglobinuria, menstrual disorders, stillbirth, abortion, decreased sperm count and testicular size,
Gastrointestinal (GI) System	Hepatomegaly, gastrointestinal bleeding, gastric ulcer,
Hematological System	Pernicious anemia, erythrocytosis, leukocytosis, thrombotic thrombocytopenic purpura
Endocrine System	Acute hyperthyroidism, hyperglycemia, decreased T3 level
Dermatological	Gangrene, bullae, alopecia erythema, blisters, ulcer
Musculoskeletal System	Valkman's Contracture, muscle necrosis, osteomyelitis
Otological Ophthalmological Cochlear and vestibular system disorders	Retinopathy, blindness, retinal hemorrhage, papilledema, optic atrophy

Although the coronary arteries are normal in patients with CO poisoning, left and right ventricular dysfunction may occur. Patients suspected of being exposed to CO poisoning, electrocardiogram (ECG) changes, cardiac marker elevation, existing symptoms, or known left ventricular dysfunction should be evaluated, including echocardiogram, myocardial perfusion scintigraphy, and coronary angiogram[28].

More specific symptoms of chronic CO exposure include dizziness, chronic fatigue, abdominal pain, paresthesias, polycythemia, diarrhea, and recurrent infections[30].

Diagnosis

The most important criterion in diagnosis is the patient's history. As the symptoms are not specific in 30% of the patients, they can be overlooked[13]. Failure to recognize CO poisoning can lead to cardiovascular morbidity, delayed neuropsychiatric sequelae, and mortality due to continued exposure to a hazardous environment. Therefore, with a high degree of suspicion, careful history and timely treatment, significant improvement is achieved in the treatment of patients with CO poisoning. In these patients, the COHb level is not important in the evaluation of the clinical course. In fact, there are studies stating that laboratory results may not be helpful in diagnosing CO poisoning[31]. However, there

are also studies stating that intoxication should be considered as severe in patients with high lactate levels and low pH[32].

Diagnosis of acute CO poisoning usually depends on 3 factors:

1. History of possible exposure to a CO source,
2. Presence of symptoms consistent with CO poisoning,
3. COHb levels greater than 5% in nonsmokers or more than 10% in smokers[34].

Other considerations in fire situations are other toxic gases (such as cyanide and phosgene) and the lack of oxygen from oxygen consumption during combustion. Since cyanide is detoxified by binding to methemoglobin (MetHb), attention should be paid to the concentration of MetHb in the patient's blood when assessing toxicity. Therefore, COHb, cyanide and MetHb should be measured in cases where fire is suspected[35].

In cases of automobile exhaust gas inhalation, inhalation of nitrogen oxide leads to the production of MetHb, which needs to be considered in addition to COHb. Although methemoglobinemia is not common, high MetHb concentrations have been reported in some cases[36].

Tachycardia, hyperthermia and tachypnea, hypertension or hypotension may be present. Strawberry color on the skin, which is a classic finding, is rare. Pallor is more common. Bright red retinal veins (which is a sensitive early finding), retinal hemorrhage in the form of flame burn, homonymous hemianopsia, papilledema can be seen in the eye. Pulmonary edema can be seen as noncardiogenic. Metabolic acidosis may occur secondary to lactic acidosis due to ischemia. Myocardial involvement may also occur frequently as a result of CO exposure. Even 5-10% increases in COHb levels can trigger post-exercise angina in people with a history of coronary disease. However, even in young and healthy individuals, high levels of COHb can depress the myocardium. Sinus tachycardia is the most common ECG finding. Myocardial ischemia, infarction and arrhythmias can be seen secondary to hypoxia. , Electrocardiogram changes can be seen in patients with cardiovascular disease, even if the COHb level is low[37].

Electrocardiogram, troponin, creatine kinase (CK), and creatine kinase-MB (CK-MB) levels should be measured to avoid missing silent ischemia. Myoglobin and lactate dehydrogenase are increased in cardiac injury and rhabdomyolysis. Moderate leukocytosis may occur with CO exposure. Since thrombotic thrombocytopenic purpura and disseminated intravascular coagulation may develop, investigations and total blood count should be performed. In severe poisonings, hyperglycemia, lactic acidosis, and hypokalemia may occur. Therefore, glucose and electrolyte should be checked. Since acute renal failure may develop secondary to myoglobin, renal function should be evaluated[30]. There may be an increase in liver function tests in favor of fulminant hepatitis. Since glucosuria and proteinuria may also be present in chronic poisoning, urinalysis should be performed.

Imaging methods

Lung X-ray imaging should be performed in patients considered for HBO therapy. Although rare, ground-glass appearance, peribronchial cuff findings, intraalveolar edema or perihilar fullness findings can be seen on imaging, and these are indicators for poor prognosis.

Brain tomography (CT): it is not helpful in diagnosis. It can be used in differential diagnosis[13]. Basal ganglia are prone to toxic metabolic abnormalities and systemic disease processes. The most characteristic finding is the presence of focal hypodense lesions in the basal ganglia[38]. Involvement in the cerebellum and brain stem is less common[39]. Diffuse hypoxic encephalopathy, focal cortical damage, diffuse brain atrophy, and white matter demyelination may be seen[40].

Magnetic resonance imaging: it is far superior to CT. Pathological changes in the brain are spongy necrosis of the cerebral cortex, necrosis of the globus pallidus, demyelination of the cerebral white matter, and necrosis of the hippocampus[39].

Treatment

Early diagnosis and treatment have a very important role in the prognosis in suspected CO poisoning. In principle, the diagnosis of CO poisoning is based on clinical symptoms and suspected or confirmed exposure[34].

If possible, treatment should begin in the area of intoxication. The patient should be immediately removed from the polluted area of the poisoning and moved to an environment with fresh air. The patient should be started to breathe 100% O2 quickly with a reservoir mask and supportive treatment should be given[41]. In order to provide 100% O2 to the patient, O2 should be inhaled at 15 L/min with a non-re-breather mask or an O2 mask with a reservoir. It has been reported that the half-life of CO is 320 minutes with fresh air breathing, 74 minutes with 100% O2 respiration, and 20-23 minutes with hyperbaric oxygen (HBO) treatment at 2.5-3 absolute atmosphere[41,42].

Oxygen therapy until clinical symptoms regress or if there is no cardiopulmonary complication, until the COHb level falls below 5%; if there is a cardiopulmonary complication, it should be given until the COHb level falls below 2%. This period is usually around 4-6 hours. It has been reported that HBO therapy reduces mortality when administered in the first 6 hours. Hyperbaric oxygen therapy is more successful than normobaric oxygen therapy in the prevention of late-occurring neuropsychiatric symptoms[30].

Hyperbaric oxygen indications: the decision to treat the patient with HBO is controversial; however, treatment

is most often indicated at the scene or in hospital if unconsciousness, new neurological deficits or changes in mental status, end-organ ischemia (ECG changes), pH less than 7.1, or the patient is pregnant (especially if COHb is greater than 20%)[43]. Hyperbaric oxygen therapy is indicated if the COHb value is greater than 25%, which supports the clinical status in non-pregnant women. Hyperbaric oxygen therapy is not recommended if cardiopulmonary resuscitation is needed, if hemodynamically unstable, or if the patient has emphysema or chronic bronchitis[13,44].

Hyperbaric oxygen; it is the delivery of 100% oxygen under an absolute pressure of 2-3 atmospheres for 60 to 90 minutes. In severe cases of CO poisoning, it is administered twice daily to help repair reperfusion injury. In moderately severe cases with milder neurological deficits and symptoms, one session of treatment is sufficient. The timing of HBO is important and is most beneficial when done within the first 6 hours after exposure[45].

The severity of the poisoning; it depends on the exposure time, the CO concentration in the environment and the basic health status of the exposed person. While useful for diagnosis when detected, the first measured COHb is not a reliable way to measure severity or predict long-term outcomes[46]. The presence of neurological and cardiac symptoms indicative of tissue hypoxia, such as loss of consciousness and chest pain, is important in assessing the severity of exposure.

Ischemic injury may present with neurologic manifestations, but detection of cardiac ischemia requires ECG changes and cardiac enzyme monitoring (troponin I, CK, and CK-MB). Myocardial injury is very common, especially in those with unconsciousness or underlying vascular disease or both[47].

In supportive care; for those who are unconscious, the airway should be protected and intubation should be performed if necessary.

Serial ECG and cardiac enzyme monitoring should be performed in patients with unconsciousness, a history of cardiovascular disease, chest pain, or ECG changes.

In CO poisonings caused by smoke inhalation as a result of being in the fire, CO and cyanide poisoning should be considered and hydroxycobalamin, which is the cyanide antidote, should be applied. There is no pharmacological antidote for CO poisoning[12,42].

Prognosis

Survivors of acute CO poisoning show nearly double the long-term mortality compared with a standard population. This is more pronounced in those who are deliberately exposed than in those who are accidentally exposed[48]. Major causes of death include alcoholism, motor vehicle accidents, other accidents, and intentional self-harm, suggesting underlying neurological or psychiatric complications[23]. The quality of life of survivors is severely affected. In a study evaluating patients 51 days after poisoning, lower cognitive performance, more depression, and more post-traumatic stress disorder were found[49].

Conclusion

The prognosis of patients with CO poisoning depends on the severity of the poisoning and the clinical situation at the time of presentation. The clinical picture of CO poisoning is non-specific, although cardiac and neurological symptoms are most common. Therefore, besides cardiac and neurological diagnoses, CO poisoning should not be ignored. Treatment should be done accordingly. Treatment should be based on the diagnosis. If the symptoms are mild or moderate and there are no neurological findings, they can be discharged 4-6 hours after treatment[50]. Patients with severe intoxication should be followed up for delayed neurocognitive deficits after treatment and discharge.

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Olgu Sunumu
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Yoğun Bakımda Nadir Bir Olgu; Fampridin toksisitesi; Olgu Sunumu

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Abstract

Fampridine, (4 AP, 4-Aminopyridine, dalfampridine) is a drug that acts by blocking potassium channels and is effective in nerve damage. It is used in the treatment of diseases such as multiple sclerosis (MS), spinal cord injuries, Lambert-Eaton syndrome and myasthenia gravis. There are very few cases of fampridine toxicity in the literature. There is no antidote treatment for toxic intakes of this drug, which has very serious side effects, but symptomatic treatment should be started early.Here, a case followed in the intensive care unit with fampridine toxicity is presented.

Keywords: Fampridine, Multiple sclerosis, Intoxication

Özet

Fampridine, (4-AP, 4-Aminopiridin dalfampridine), potasyum kanallarını bloke ederek etki eden ve sinir hasarında etkili olan bir ilaçtır. Multipl skleroz (MS), omurilik yaralanmaları, Lambert-Eaton sendromu ve miyastenia gravis gibi hastalıkların tedavisinde kullanılmaktadır. Literatürde fampiridin toksisitesine yönelik oldukça az sayıda olgu bulunmaktadır. Oldukça ciddi yan etkileri olan bu ilacın toksik alımlarında antidot tedavi bulunmamaktadır fakat semptomatik tedaviye erken başlanmalıdır. Burada fampridin toksisitesi ile yoğun bakımda takip edilen bir olgu sunulmuştur.

Anahtar Kelimeler: Fampridine, Multipl skleroz, İntoksikasyon

Giriş

Multipl skleroz (MS), merkezi sinir sistemi beyaz cevherini tutan, ilerleyici, otoimmün nörolojik bir hastalıktır[1]. Genç erişkinlerde sık görülen bu hastalık klinik basit yakınmalardan, ciddi nörolojik bulgulara kadar pek çok şekilde karşımıza çıkabilir. Tedavisi kesin değildir. Halen pek çok yeni ilaç denenmektedir[2]. Fampiridin (4-aminopyridine, dalfampridine), voltaj kapılı potasyum kanallarını seçici olarak bloke ederek, nöromüsküler iletimi kolaylaştırarak etki gösteren bir ilaçtır ve MS, Myastenia Gravis, Eaton-Lambert Sendromu ve nörolojik bozuklukların tedavisi için kullanılmaktadır[3,4].

Toksik dozlarda fampiridin alımı, voltaja duyarlı K^+ iyon kanallarını bloke ederek sinapslarda ve nöromüsküler kavşaklarda asetilkolin seviyelerini arttırır. Bunun sonucu olarak, hiperaktivite, baş dönmesi, deliryum, koreoatetoz ve nöbet gibi ciddi klinik tablolar görülebilir. Burada özkıyım amaçlı yüksek doz fampiridin alan bir hasta ve yoğun bakım takip ve tedavi süreci sunulmuştur.

Olgu Sunumu

Otuz dört yaşında kadın hasta evde baygın bulunması üzere acil serviste değerlendirildi. Yakınlarından alınan anamnezde yaklaşık sekiz yıldır MS, beş yıldır hipertansiyon ve diyabetes mellitus tanısı olduğu öğrenildi. Oral antidiyabetik, oral hipertansiyon ilacı ve MS tedavisi için fampiridin (günde 2 kez 10 mg tablet) ve ocrelizumab (6 ayda 1) kullandığı belirtildi. Son zamanlarda depresif bulguları olduğu fakat tedavi almadığı öğrenildi. Evde kullandığı fampiridin tablet kutusundan yaklaşık 35 adet eksik olduğu söylendi.

Fizik muayenede; bilinç açık, GKS 14 idi. Solunum takipneik ve oksijen saturasyonu %79, arteriyel kan basıncı 154/76 mm/Hg, kalp atım hızı 96 atım/dk, ateşi normotermik olarak saptandı. Hastaya intoksikasyon ön tanısı ile gastrik lavaj yapılarak aktif kömür tedavisi verildi. Yoğun bakıma takip ve tedavi amaçlı yatırıldı. Hastanın maksimum dozun (0,6 mg/kg) yaklaşık 6 katı gibi yüksek bir miktarda fampiridin aldığı düşünüldü. Geçmişte sol fasiyal paralizi öyküsü olması nedeniyle sol üst göz kapağın-

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da sekel düşüklük mevcuttu. Alt ekstremite kas gücü 2/5 olarak saptandı, üst ekstremite kas gücü normal idi, ancak üst ekstremitede kasılmaları mevcuttu. Hastanın Babinski refleksi bilateral pozitif idi. Patolojik başka refleksi olmayan hastanın takiplerinde bu kasılmalara bilinç değişikliği eşlik etmeye başladı. Oksijen saturasyonu düşen ve bilinci bozulan hasta entübe edildi. Mekanik ventilatöre bağlandı. Kasılmaları devam eden hastaya beyin bilgisayarlı tomografi (BBT) çekildi. BBT normal olarak raporlandı. Nöbet aktivitesi olmayan hastada mevcut kasılmalar fampiridin yüksek dozuna bağlandı. Hastaya midazolam infüzyonu başlandı. Hastanın laboratuvar sonuçlarında; kan glukozu: 260 mg/dl, CPK: 408 U/L, CK-MB: 58 U/L, myoglobin 428ng/ml olarak saptandı. Sodyum: 136mEq/L, Potasyum: 4,36mEq/L, Klor: 106 mEq/L, Bikarbonat: 14 mEq/L, Kreatinin: 0,9 mg/dL idi. Arter kan gazında Ph: 7,31, pCO_2: 29, pO_2: 37, SpO_2: %67, Anyon açığı: 11, Laktat: 3,3 mg/dl olarak saptandı. Etanol, asetominofen düzeyleri ve diğer laboratuvar test sonuçları normal idi. EKG sinüs ritminde, kalp hızı 96 atım/ dk idi.

Acil serviste aranan zehir danışma tarafından, aritmi, kalp yetmezliği ve kardiyak arrest gelişme riski açisından takip edilmesi için yoğun bakım takibi önerildi. Hasta kardiyolojiye konsulte edildi ve hastaya EKG takibi yapıldı. İlacın antidotu olmaması neden ile hastaya yoğun bakımda semptomlarına yönelik tedavi uygulandı. Kardiyoloji tarafından hastaya 6 saatte 1 olacak şekilde troponin takibi önerildi. Takiplerinde troponin değerinde iki kat artış olan hastaya, ilacın potansiyel yan etkileride göz önüne alınarak üçlü antikoagülan tedavi başlandı. Hastaya nefroloji tarafından fampiridinin dağılım hacmi yüksek olması nedeniyle diyaliz düşünülmedi. Yatışının yaklaşık yetmişinci saatinde genel durumu düzelen hastada oksijenlenme düzeldi ve ekstübe edildi. Hastanın sedasyon amacıyla 3 gün boyunca aldığı midazolam infüzyonu kesildikten sonra kasılmaları olmadığı görüldü. Takiplerinde troponin değerleri normale dönen, EKG de aritmi saptanmayan hasta yatışının dördüncü günü nöroloji servisine devredildi. Servise gitmeden önce psikiyatri ile görüşülerek sertralin 50 mg günde bir defa olacak şekilde başlandı ve sonrasında poliklinik kontrolü önerildi.

Tartışma

Multipl skleroz, patolojisinde çevresel veya genetik etkenlerin yer aldığı, miyelin hasarının başrolde olduğu kronik bir santral sinir sistemi hastalığıdır. Etiyolojisi tam olarak aydınlatılmamıştır ancak otoimmun sebepler sorumlu tutulmaktadır[1]. Hastalar genellikle asemptomatik dönemden, akut alevlenmelerin yaşandığı atak dönemlerine dalgalı bir klinik seyir gösterirler. Parezi, paralizi gibi motor bulgular, optik nörit, çift görme gibi görsel bulgular, depresyon, uykusuzluk gibi duygu durum bozuklukları görülebilir. Bazen bu bulguların varlığı ile tanı konulur. Genellikle genç yaşta ve kadınlarda erkeklere göre daha sık görülen bu hastalıkta bulguların nonspesifik olması nedeni ile tanı konulması zor bir hastalıktır. Özellikle iş gücü kaybı gibi sosyoekonomik sonuçları da olan oldukça ciddi bir sağlık sorunudur. Bizim hastamızda olduğu gibi depresif semptomlar, özkıyım girişimi gibi ciddi sonuçlara sebep olabilir. Tanıda; atak sırasında yapılan fizik muayene, kan tetkikleri, nörokognitif testler, beyin omurilik sıvısı (BOS) incelemesi (lgG ve oligoklonal bant görülmesi), MS plaklarının saptanması için manyetik rezonans görüntüleme yöntemi, uyarılmış potansiyel testleri kullanılabilir. Tedavide, hastalık modifiye edici ajanlar (İnterferon, Dimetil Fumarat), intravenöz ajanlar (Alemtuzumab, Natalizumab ve Mitoksantron), monoklonal antikorlar ve otolog hematopoetik kök hücre nakli kullanılır[5-7].

Fampiridin, voltaj kapılı potasyum kanallarını seçici olarak bloke ederek, nöromüsküler iletimi kolaylaştırarak etki gösteren bir ilaçtır. MS'de yürüme güçlüğü olan yetişkin hastalarda yürümeyi iyileştirmek için endikedir. Hayvanlar üzerinde yapılan çalışmalarda fampridin aşırı dozu ile salivasyon, titreme, terleme, konvülsiyonlar ve kardiyak arrest gibi ciddi yan etkiler görülmüştür. Fakat insanlar üzerine etkisini gösteren sınırlı sayıda olgu bulunmaktadır. Nörolojik yan etkileri yanında ciddi kardiyak etkiler (aritmi, kalp yetmezliği ve kardiyak arrest) görülmektedir[4,8]. Olgumuzda hafif nörolojik bulgular ve troponin yüksekliği gibi kardiyak bulgular olmasına rağmen ek problem yaşanmamıştır.

Literatürde fampiridin aşırı doz alımı ile ilgili az sayıda olgu sunumu bulunmaktadır. 100 mg fampiridin alımı sonrası nöbet aktivitesi görülen ve antiepileptik tedavi verilen hasta taburcu edilmiş ve yan etki olarak kısa süreli hafıza kaybı görülmüştür[9]. Özkıyım amaçlı yüksek dozda fampiridin alımı olan olgularda, klinik olarak koreiform hareketler ve nöbet görülmüş ve hastalardan biri entübe edilmiş ve sonrasında iki olguda antiepileptik tedavi ile taburcu edilmiştir[10,11]. Aynı zamanda ülkemizde fampiridinin yüksek doz alımı ile ilgili literatürde makaleye rastlanmamıştır.

Sonuç olarak; doz aşımında oldukça ciddi yan etkileri olabilen fampiridinin toksik alımlarında antidot tedavi bulunmamaktadır. Hastamızda olduğu gibi hava yolunun güvenliğinin öncelikle sağlanması için entübasyonun geciktirilmemesi, yoğun bakımda takip ve tedavinin erken başlanması, mortalite ve morbiditeyi azaltması açısından oldukça önemlidir.

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Case Report
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Quetiapine Induced Myocarditis

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Abstract

This article reports myocarditis related to overdose of quetiapine. An 18-year-old female patient who used 25 mg of quetiapine for anxiety disorder attempted suicide with twenty quetiapine pills. The patient developed palpitations, shortness of breath, pleuritic chest pain, and confusion in the emergency room. ST-elevation and right bundle branch block were detected on D1-aVL lead in the patient's ECG. The cardiac markers were significantly elevated. The patient was hospitalized and treated in the internal medicine intensive care unit. Drug-induced myocarditis was resolved by two weeks of treatment. This case report presents a case of myocarditis induced by quetiapine overdose.

Keywords: Quetiapine, myocarditis, drug-induced myocarditis

Özet

Bu makale, ketiapin doz aşımına bağlı miyokarditi bildirmektedir. Anksiyete bozukluğu nedeniyle 25 mg ketiapin kullanan 18 yaşında kadın hasta, 20 adet ketiapin hapı ile intihar girişiminde bulundu. Acil serviste hastada çarpıntı, nefes darlığı, plöretik göğüs ağrısı ve konfüzyon gelişti. Hastanın EKG'sinde D1-aVL derivasyonlarında ST elevasyonu ve sağ dal bloğu saptandı. Kardiyak belirteçler önemli ölçüde yükseldi. Hasta dahiliye yoğun bakım ünitesinde tedavi altına alındı. İlaca bağlı miyokardit, iki haftalık tedaviyle düzeldi. Bu vaka raporu, ketiapin doz aşımının neden olduğu bir miyokardit vakasını sunmaktadır.

Anahtar Kelimeler: Ketiapin, myokardit, ilaca bağlı myokardit

Introduction

Drug-induced cardiotoxicity is one of the most severe adverse reactions associated with the use of antidepressants and antipsychotic drugs[1]. Although rare, several drugs can cause potentially fatal side effects in psychiatry clinics, including myocarditis. Myocarditis is an inflammatory disease of the myocardium [2,3].

Although the most common cause is viral infections, seldomly drugs can cause myocarditis. Myocarditis due to quetiapine, an atypical antipsychotic drug used in the treatment of schizophrenia, bipolar disorder, and major depressive disorder, is extremely rare [4,5].

Case report:

An 18-year-old female patient who took 25 mg of quetiapine a day because of her anxiety disorder was brought to the emergency room after using 20 quetiapine tablets for suicide. In her anamnesis, it was learned that she had taken the tablets one hour before she was brought to the hospital. She was admitted to the internal medicine intensive care unit after developing palpitations (evaluated as sinus tachycardia) while observing the emergency room.

ST-elevation and right bundle branch block were detected in the DI-aVL leads in the patient's first ECG. The patient's initial troponin value was below 0.01 pg/ml (reference value: 0-60 pg/ml), and CK-MB was 3,62 ng/ml (reference value: 0-5 ng/ml) in the emergency room. When the measurement was repeated 3 hours later, troponin was measured as 7168 pg/ml and CK-MB was measured as 32,47 ng/ml. The patient, who was being treated in the intensive care unit, had dyspnea, pleuritic chest pain, and confusion in the 6th-hour examination. Acute myocardial infarction, aortic aneurysm, coronary spasm, cardiomyopathy, pulmonary embolism and myocarditis were considered as the differential diagnosis of the patient. It was seen the level of cardiac markers was elevated in the blood samples collected from the patient in the intensive care unit. Results of the blood sample tests were measured as Troponin I: 10416 pg/ml, CK-MB: 19.5 ng/ml. WBC count was 7880 µl (reference value: 4500-11000/µl).

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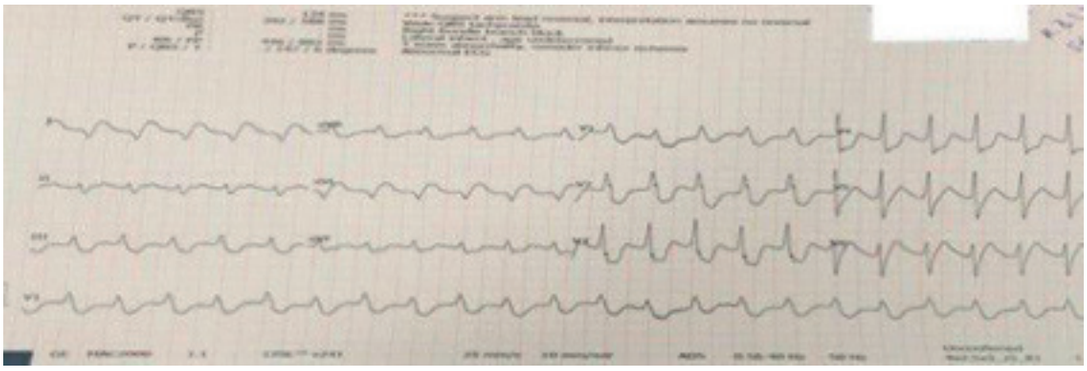

Figure 1: Electrocardiogram showing ST elevation in DI - aVL leads.

There were no signs of eosinophilia in the blood count of the patient (eosinophil count was 100/µl; reference value:0-700/µl). The eosinophil count was normal in the blood counts performed daily during hospitalization. In addition, CRP levels were within the normal range. Pulmonary embolism diagnosis was ruled out because of the D-dimer value was normal (0,22 mg/L; reference value:<0,55 mg/L).

Invasive coronary angiography was performed because the cardiac markers of the patient were rose, S-T segment elevation in D1-AVL leads and right bundle branch block were also found to be high in the first ECG (Figure 1).

There was a deterioration in left ventricular function on her echocardiography (ECHO). Left ventricular ejection fraction (LVEF) was found to be reduced by 40% (typically 50-70 percent). Apart from this, no finding suggesting myocardial infarction, such as reduced wall motion, was found on ECHO. Coronary arteries were normal in coronary angiography.

In addition, Psychiatric consultation was requested for the patient. Quetiapine was discontinued after the psychiatric evaluation. The patient was given ramipril 2,5 mg, fraxiparine 5700 IU/0,6 ml once a day, and ibuprofen 600 mg three times a day during treatment. On the second day of hospitalization in the intensive care unit, troponin decreased to 5420 pg/ml and CK-MB to 9,49ng/ml. The complaints of shortness of breath and chest pain were vanished, though palpitations occurred occasionally. The treatment of the patient was completed in the intensive care unit for ten days. During this time, the patient's symptoms improved. After the resorption of the edema in the lung base on the chest X-ray and the ECG findings improved, the patient was taken to the internal medicine service. The patient, whose treatment continued in the service for ten days, was discharged with full recovery at the end of this period.

Discussion

Quetiapine is a dibenzothiazepine derivative second generation antipsychotic agent. Clozapine, a structurally similar dibenzodiazepine derivative second-generation antipsychotic, is similar to quetiapine in terms of its mechanism of action and side effects, including cardiac adverse event [6,7]. It has been found that approximately 1-3% of patients treated with clozapine developed myocarditis [8,9]. In comparison, cases of quetiapine-induced myocarditis are much rarer.

The patient's symptoms and signs indicated a cardiac disorder. In the ECG, the increase in the blood levels of cardiac markers accompanied by the elevation of the ST segment in the D1-aVL leads indicated that the heart muscle is damaged. The absence of myocardial infarction findings in coronary angiography and the decrease in ejection fraction in ECHO revealed that there is another pathology that impairs the pump function of the heart other than ischemic damage. No narrowing or occlusion of the coronary arteries was found on angiography. Thus, the diagnosis of the patient was confirmed as myocarditis.

The patient did not have flu-like symptoms or symptoms suggestive of viral diarrhea during the two weeks prior to admission to the Hospital. Therefore, the possibility of viral myocarditis was ruled out.

Getting a score of 7 in the evaluation of the case according to the Naranjo scale, which is used to determine whether any pathological findings occurred on the patients due to an adverse reaction is, indicating a strongly possible adverse drug reaction[10]. As a result, myocarditis due to quetiapine overdose was diagnosed.

In the literature, there are three cases of myocarditis associated with the use of quetiapine to date. In one of these cases, quetiapine was used alone, in the other cases combined with lithium or methylphenidate [4,5,7]. We present the second case of myocarditis related to quetiapine treatment alone.

Although the underlying mechanism has not been fully elucidated, it is thought that drug-induced myocarditis may occur by one of two different mechanisms:The first one is the direct toxic effect of the drug on the cardiac muscle; the other one is hypersensitivity. Hypersensitivity seems to be the primary underlying mechanism in cases of olanzapine and clozapine-associated myocarditis [11-13]. Nonetheless, it seems difficult to make the same definition for quetiapine-induced myocarditis cases. Eosinophilia and morbilliform rash were

present in the case where quetiapine was used in combination with Lithium. However, there was no other finding suggestive of hypersensitivity such as eosinophilia in the other two case reports and our case. Since it is known that lithium can cause morbilliform eruptions, considering the presence of morbilliform rash in the first case, it can be thought that the hypersensitivity reaction was caused by lithium[14,15]. In the light of this knowledge, it is more likely that the direct toxic effect of quetiapine on the heart muscle played a role in the development of myocarditis. However, examination with biopsy or other methods is necessary to reveal this possibility. It should be noted that the limitation of this study is that myocardial biopsy and cardiac MRI could not be performed because the patient did not accept them. However, the findings described above depict that the case was an idiosyncratic reaction or a direct toxic effect due to quetiapine.

Drug-induced myocarditis is a rare but potentially fatal adverse effect. Psychiatrists should be alert that when symptoms suggestive of cardiac pathologies such as palpitations, fatigue, chest pain, and shortness of breath develop in patients using second-generation antipsychotic drugs such as quetiapine, drug-induced myocarditis may be an underlying factor, among other reasons.

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Case Report

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Neutropenia Induced by Medications Used in Psychiatric Treatment: A Case Report

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Abstract

Changes in blood parameters may occur during the use of psychiatric drugs. In such cases, the general condition of the patient and the blood parameters are closely monitored and the treatment is discontinued or the medication is changed. The purpose of this case report was to be alert to the possibility of side effects such as neutropenia due to antipsychotic drugs and to draw attention to the management of these patients.

Keywords: Antipsychotic medications, antiepileptic drugs, neutropenia

Özet

Psikiyatrik ilaçların kullanımı sırasında kan parametrelerinde değişiklikler meydana gelebilir. Bu gibi durumlarda hastanın genel durumu ve kan parametreleri yakından takip edilerek tedavi kesilir veya ilaç değiştirilir. Bu vaka raporunun amacı, antipsikotik ilaçlara bağlı nötropeni gibi yan etki olasılığına karşı uyanık olmak ve bu hastaların yönetimine dikkat çekmekti.

Anahtar Kelimeler: Antipsikotik ilaç, antiepileptik ilaç, nötropeni

Introduction

Neutropenia is defined as an absolute neutrophil count below 15000/mm^3. Absolute Neutrophil Count measures the percentage of neutrophils in your white blood count. If the neutrophil count is below 1,000-1,500/mm^3, it is classified as mild, below 500-1000/mm^3 as moderate, below 500/mm^3 as severe, and below 200/mm^3 as very severe[1]. Agranulocytosis is an acute condition involving severe and dangerous neutropenia. In Western countries, the death rate of drug-induced agranulocytosis is 5-10% [2]. In the case of agranulocytosis, due to many drugs, destruction occurs against neutrophil precursors[3].

Hematological side effects in patients using psychiatric drugs can lead to significant problems. In the literature, it has been stated that neutropenia may occur due to antipsychotics (0.13% due to chlorpromazine) and antiepileptics (0.4% due to valproic acid). Therefore caution should be exercised[2].

Case

A 57-year-old female patient presented to the emergency department with complaints of painful urination and fever that had recently started. The patient had no other diseases besides bipolar disorder and diabetes mellitus. She had been followed for 30 years for bipolar disorder but did not use regular medication. The patient had been hospitalized and treated at a psychiatric hospital 1.5 months ago due to a manic episode. The patient started using chlorpromazine 100 mg/day, clonazepam 2 mg/day, valproic acid 500 mg/day, and lithium 300 mg/day about 15 days ago.

In her examination, she was conscious, oriented-cooperative, her effect was compatible with her temperament, and she had no delusions or hallucinations. Other systemic examinations were normal. Body temperature was 37.3, respiratory rate was 18/minute, heart rate was 90/beat, and blood pressure was 120/60 mmHg. In the examinations of the patient, it was found that WBC: 2.840 /mm^3, neutrophil abso-

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lute count: 500 /mm^3, lymphocyte total count 1100 /mm^3, hemoglobin 11.5 g/dl, hematocrit 33.5%, platelet 213000/mm^3. The patient's blood lithium level was 0.276 mmol/L, and Valproic acid was 42.75 mg/dl. Renal function tests, liver function tests, and blood-electrolyte levels were normal in routine biochemistry tests. No disease thought to cause neutropenia was found in the patient's history.

Internal medicine, infectious diseases and psychiatry consultations were made. Imaging and peripheral smear were also normal. No disease related to general medical conditions was found. It was thought that the neutropenia picture was caused by the drugs used by the patient. Therefore, the psychiatric treatments used by the patient were stopped. The patient was admitted to the psychiatry service to clarify the question of which of the drugs causes neutropenia.

Discussion

It is known that hematological conditions such as leukopenia, neutropenia, agranulocytosis, thrombocytopenia, anemia, leukocytosis, thrombocytosis, eosinophilia, and platelet function changes occur to drugs used in psychiatric treatments. Leukopenia is the name for cases where the white blood cell values fall below 3000/mm^3. In neutropenia, the neutrophil count falls below 1500/mm^3. Agranulocytosis means that there are no granular type leukocytes (neutrophil, basophil, eosinophil) in the circulation[3]. Antipsychotic drugs can cause neutropenia. For example, cases of thrombocytopenia, anemia, and neutropenia have been reported approximately two weeks after using clonazepam[4]. There have been some studies evaluating the effect of valproic acid on leukocyte subtypes. It has been reported that 0.4% of patients treated with this drug develop leukopenia[5]. Similarly, in a study by Bartels et al., valproic acid reduced the absolute neutrophil count[6]. Rahman et al. investigated the incidence of hematological side effects in patients using quetiapine, valproic acid and both together between 2004 and 2007. According to the results of this research; It was observed that neutropenia developed in 6% of patients using quetiapine, 26% of patients using valproic acid, and 44% of patients using both[7]. Likewise, lithium may also change laboratory parameters in the early stages of treatment[8]. These side effects usually disappear with dose reduction or discontinuation of treatment[9]. The treatment of our case was also stopped. The patient was followed up for close psychotic status and hematological examinations. Symptomatic treatment was planned because of dysuria and fever. He was admitted to the psychiatry department. The blood parameters of the patient, whose antipsychotic and antiepileptic treatment were discontinued during the follow-ups, improved rapidly. In such cases, the drugs used by the patient should be discontinued and regular hemogram follow-up should be performed to control the development of neutropenia.

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