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Değerli meslektaşlarımız;

Bilimsel dergiler, akademik faaliyetlerin temel düsturu olan bilgiyi üretmek, üretilmiş bilginin yayılmasını sağlamak ve bilgiyi bilimin hizmetine sunmak amaçlarının vazgeçilmez aracılarıdır. Bu yüzden, teknoloji alanındaki tüm gelişmelere ve insanlar arasındaki iletişim ve bilgi aktarımındaki devrim niteliğinde başkalaşmaya rağmen hala akademik dünyanın vazgeçilmez temel taşlarından biri olmaya devam etmektedirler. Bizler de Acil Tıp Uzmanları Derneği'nin (ATUDER) çatısı altında, yepyeni bir misyon ve vizyon ile yayın hayatına kazandırdığımız Eurasion Journal of Toxicology Dergisi'nin ilk sayısı ile başta acil tıp camiası olmak üzere tüm tıp camiasının huzurlarında olmaktan büyük onur duyuyoruz...

Tıbbın diğer alanlarına göre çok daha genç fakat doğası itibari ile bir o kadar da dinamik olan acil tıp alanı ülkemizdeki çeyrek yüzyıllık deneyiminde alana özgü bilimsel dergi ihtiyacını erken dönmede fark etmiş ve bu anlamda önemli yol kat edilmiştir. Dünya genelinde bakıldığında, acil tıp dergilerin temel ilgi alanlarını toksikoloji, travma bakımı ve resüsitasyon gibi acil tıbbın temel konularının oluşturduğu gözlemlenmektedir. Bunlar içinde de toksikoloji daha fazla öne çıkmaktadır. Zira, acil hekimleri, akademik acil tıp hizmetlerinin hızlı yükselişinin de etkisiyle, toksikolojinin konusu olan zehirlenmiş hastalar için, yalnızca ilk karşılaştıkları hekim değil aynı zamanda taburculuğa kadar tüm tıbbi bakımlarını üstlenen hekimler haline gelmiştir. Bu büyük bilgi birikimi ve tecrübe bizlere, elinizdeki eserin omurgasını oluşturan özgüveni bahşetmiş bulunmaktadır.

İlk sayımızı ilgi ve beğenilerinize sunarken, öncelikle bu derginin fikir babası, her konudaki yol göstericiliği, yol açıcılığı ve yol arkadaşlığı ile en büyük destekleyicisi olan ATUDER Başkanı Prof.Dr. Başar CANDER hocamıza, bu fikir aklımıza düştüğü günden beri gecelerini gündüzlerine katarak tüm zorlukları kolaylaştıran yakın çalışma arkadaşlarımıza yürekten teşekkürü bir borç biliriz. İlk sayının planlanan tarihten daha önce çıkabilmesine imkân sağlayan, klinik pratiklerini, deneyimlerini ve birikimlerini güncel gelişmeler ve kılavuzların ışığında, kanıta dayalı tıp prensipleri içerisinde bizlerle paylaşan siz değerli meslektaşlarımızın yoğun ilgisine özel olarak minnettarız.

Bilgiyi üretme, paylaşma ve çoğaltma yolunda önemli bir başvuru kaynağı olarak literatürdeki yerini almasını, bilimin ışığına katkıda bulunmasını umut ettiğimiz dergimizin sizinle var olacağının altını çizmek isteriz... Hepinizin, hepimizin yolunu aydınlatması umut ve temennisiyle...

> Tüm editöriyal kurul adına baş editörler; Prof. Dr. Zeynep ÇAKIR Prof. Dr. Yunsur ÇEVİK

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Eurasian Journal of Toxicology

Carbon Monoxide Poisoning

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Abstract

Carbon monoxide (CO) poisoning is the most common cause of mortality due to inhalation toxicity. CO can affect multiple systems in the body and manifest a wide range of symptoms; thus, the diagnosis of CO poisoning can easily be overlooked. In reality, the cases of CO poisoning is much higher than reported, which makes it crucial to take first-step protective measures. The most sensitive tissues to CO poisoning are vital organs (brain, heart) with a high oxygen demand. Neuropsychiatric syndrome which may develop in the chronic period (three to 240 days) should also be considered. If diagnosed, the treatment of CO poisoning should be symptomatic and aimed at removing carboxyhemoglobin (COHb) from the blood, coupled with provision of effective basic life and advanced cardiac life support. The best way to remove COHb is to deliver 100% oxygen. Hyperbaric oxygen (HBO) therapy reduces COHb much faster; therefore, patients with the indications of HBO therapy should be started on this treatment without delay.

Keywords: carbon monoxide, poisoning, hyperbaric oxygen, carboxyhemoglobin

Özet

Karbonmonoksit (CO) zehirlenmesi; İnhalasyon zehirlenmelerine bağlı ölümlerin en sık sebebidir. CO, Birçok sistemi etkileyerek çok çeşitli semptomlar gösterebilir ve CO zehirlenmesi tanısı atlanabilir. Toplumda karbonmonoksit zehirlenmesi olguları, kayıtlarda bildirildiğinden daha fazladır. CO zehirlenmesi ile mücadele etmede ilk adım koruyucu tedbirler olmalıdır. CO zehirlenmesine en duyarlı dokular oksijen ihtiyacı yüksek olan hayati organlardır (beyin, kalp). Akut dönemde görülebilen nörolojik, kardiyak durumlar haricinde kronik dönemde (3-240 gün) gelişebilecek nöropsikayatrik sendrom unutulmamalıdır. Teşhis edilmesi halinde tedavi semptomatik ve kandan karboksihemoglobini (COHb) uzaklaştırmaya yönelik olmalıdır. Aynı zamanda etkili bir temel yaşam desteği ve ileri kardiyak yaşam desteği sunulmalıdır. COHb'yi uzaklaştırmanın en iyi yolu %100 oksijen verilmesidir. Hiperbarik oksijen (HBO) tedavisi COHb'yi çok daha hızlı düşürür. HBO tedavi endikasyonu olan hastalara HBO tedavisi gecikmeden başlanmalıdır.

Anahtar kelimeler: karbon monoksit, zehirlenme, hiperbarik oksijen, karboksihemoglobin

Introduction

By definition, poisoning is the destruction or injury of cells by inhalation, ingestion, injection or absorption of a toxic substance. Carbon monoxide (CO) is an odorless, tasteless, colorless, non-irritating gas produced by the combustion of fuels. CO exposure differs according to societies, climatic conditions, and development levels of countries. In countries with cold climate conditions, especially during the winter months, CO poisoning is associated with the use of heating equipment (e.g., stove, water heater, and boiler), while in developed countries, it is mostly reported to be caused by household and industrial accidents, exhaust gases, and suicide attempts. Some professional groups, such as firefighters, police, and industrial workers are also at higher risk of poisoning¹⁻⁴.

More than 50,000 people are admitted to the emergency department every year in the US due to CO poisoning⁵. However, in Turkey, there are insufficient studies on the incidence of CO poisoning. In one study conducted in 2010, the number of referrals to the emergency department due to CO poisoning was reported as 10,154⁶. It is clear that due to insufficient records and the insidious nature of CO poisoning, its actual incidence is much higher. Toxicity-associated death is most commonly caused by CO poisoning, and the research into the mortality rates of this emergency reveals that it varies according to country and climate conditions⁷⁻¹⁰. Since CO is odorless and colorless, it is difficult to diagnose; thus, the actual mortality rate is higher than registered^{11,12}.

Pathophysiology of CO poisoning

CO affects the tissues in different ways:

CO binds to hemoglobin (Hb) with an affinity of 200-300 times higher than oxygen and forms the carboxyhemoglobin (COHb) molecule. COHb causes hypoxia and asphyxia in the tissue by preventing the transport of oxygen in the blood and its release into the tissues.

- CO destroys mitochondrial function by binding to cytochrome-c oxidase, and thus causing oxidative phosphorylation and leading to lactate formation and acidosis.
- CO also binds to myoglobin with 20-50 times higher affinity than oxygen, causing myocardial damage through tissue hypoxia and leading to rhabdomyolysis.
- COHb causes leukocyte-dependent inflammatory changes and lipid peroxidation in the brain. In addition, it results in demyelination edema in the white matter and reperfusion injury¹³⁻¹⁵.

Diagnosis and clinical features

The first and most important step in the diagnosis of this emergency is to suspect that the patient may have CO poisoning and obtain a targeted history. The diagnosis of CO poisoning is based on a high COHb level measured by an arterial or blood gas sample together with a compatible history and physical examination findings¹³. The normal blood COHb level is below 3%, but it can reach 10-15% in smokers. Symptoms often start at a COHb of 10% and 30%, and death can be seen at 30% or higher. However, the COHb level el alone is not reliable in determining the clinical features of the patients^{16,17}. Not only the blood concentration of COHb, but also the exposure time determines the severity of poisoning. It has been shown that exposure to CO at a low dose but over a long time may lead to more severe and longer-term toxicity than acute high-dose exposure^{18,19}.

The best way to determine COHb is to measure it in arterial or venous blood gas. A non-invasive CO-oximeter can also be used for this purpose; however, there are different opinions concerning the measurement of the COHb level with this method due to its sensitivity being lower compared to invasive blood gas analysis. However, CO-oximeter measurement is often undertaken as the first step due to its non-invasive nature, reproducibility, and low cost; nevertheless, it should not be used alone for diagnosis^{15,20}.

Other methods employed in the diagnosis of CO poisoning include blood gas analysis, biochemistry tests (blood urea nitrogen, creatinine, etc.), cardiac biomarkers showing myocardial damage (troponin, myoglobin, etc.), urinalysis (myoglobinuria, hematuria, proteinuria, etc.), electrocardiography (ECG), computed tomography (e.g., brain edema), and magnetic resonance imaging (MRI) (demyelinating damage, brain edema, etc.)^{12,21}.

Clinical Presentation

The tissues with high metabolic needs (brain, heart) are at high risk. Classical symptoms include non-specific complaints, such as headache, dizziness, nausea, vomiting, dyspnea, and/or chest pain. Headache is the most common complaint at 91%^{22,23}. None of the symptoms are pathognomonic. Redness can also be seen in the cheeks; however, this alone has no sensitivity for diagnosis. Neurological sequelae, acute renal failure, myocardial damage, syncope, and rhabdomyolysis are associated with the severity of CO poisoning²³⁻²⁶. In addition, the mortality rate of patients followed up after exposure to CO poisoning has been found to be three times higher than the normal population. Another important clinical condition is delayed neuropsychiatric syndrome, which is characterized by cognitive changes, personality changes and movement disorders that may develop in the later period (within three to 240 days). This syndrome, usually occurring within 20 days of poisoning, may be temporary or permanent²⁷⁻³⁰.

Patients can be safely discharged after treatment, even in the presence of simple symptoms, such as headache, nausea, and vomiting. However, if symptoms suggestive of brain and myocardial damage; e.g., syncope, loss of consciousness, or chest pain are observed, hospitalization is required for a longer follow-up and treatment¹⁴.

Management

The main aim of treatment is to provide oxygen for the vital organs as soon as possible and remove COHb from the blood. Effective basic life support and advanced cardiac life support are also crucial. Furthermore, the treatment of CO poisoning is based on a symptomatic battle against the inflicted injuries (such as seizure and cardiac arrhythmia) and the conditions that may develop in the future (e.g., myoglobinuria, rhabdomyolysis, compartment syndrome, and neuropsychiatric syndrome). If necessary, the physical activities of the patients should be restricted for one to three weeks, body oxygen requirement should be reduced, and the patients should be called for a follow-up after discharge, bearing in mind that neurological and cardiac damage can later develop^{13,31,32}.

In CO poisoning, antidote treatment aims to remove COHb from the blood by providing oxygen. Under normal atmospheric pressure, the life of COHb is four to six hours in ambient air, decreasing to 40-80 minutes through the provision of 100% normobaric oxygen. Using hyperbaric oxygen (HBO) therapy, the half-life of COHb is reduced to 15 to 30 minutes^{33,34}.

Hyperbaric oxygen (HBO)

This is used as primary or adjunctive therapy for various medical conditions. In this therapy, the patient breathes 100% oxygen intermittently at 1 to 3 ATA in a pressure chamber with single or multiple occupancy. HBO therapy is most commonly used to treat decompression sickness and gas embolism in cases of CO poisoning and tissue hypoxia. Other uses of this therapy include anaerobic infections (gas gangrene, diabetic foot), compartment syndrome, acute traumatic ischemia (crash injury), refractory osteomyelitis, radiation-related bone and soft tissue necrosis, and thermal burns³⁵⁻³⁹.

HBO increases the production of free oxygen radicals (superoxide, hydroxyl radical, peroxides, aldehyde hypochlorite, and hypochlorite) and shows bactericidal activity against anaerobic bacteria without defense systems to these radicals. HBO therapy shortens the half-life of COHb that occurs in CO poisoning. Breathing 100% oxygen under normal atmospheric pressure increases the amount of dissolved oxygen in the blood up to five times. At higher pressures, HBO can increase the amount of dissolved oxygen in the plasma up to 20 times, which is sufficient for the supply of oxygen to the cells, regardless of hemoglobin at rest^{40,41}.

HBO indications in CO poisoning are;

- Coma,
- Loss of consciousness in any period after CO poisoning,
 COHb level being >30-40% (>15% for pregnant patients
- and those with a history of cardiac disease,
- Severe metabolic acidosis,
- ECG changes suggestive of myocardial damage and increased cardiac enzymes,
- Symptoms not regressing within four to six hours of normobaric 100% oxygen application^{13,20}.

Untreated pneumothorax is an absolute contraindication to HBO therapy. Relative contraindications include obstructive pulmonary disease, asymptomatic pulmonary bleb, or bullous lung on chest X-ray, upper respiratory or sinus infections, recent ear or thoracic surgery, uncontrolled fever, and claustrophobia (8,40). In studies with a limited range, adverse events that may occur as a result of HBO therapy have been reported as hypertension, seizure, ear and sinus barotrauma, claustrophobia, oxygen toxicity, dizziness, and pneumothorax⁴².

Follow-up and discharge

Clinical improvement in patients presenting with CO poisoning is more significant than the COHb level. Patients that have an indication of HBO therapy should be referred to an HBO center. Normobaric 100% oxygen should be started immediately in patients with no organ damage and 10-30% of COHb levels, and they should be monitored for at least four to six hours. The patients can be discharged when their COHb level falls below 10% and complaints (headache, nausea, dizziness) begin to disappear. However, HBO therapy should be initiated (or the patients should be referred to an HBO center) if the clinical status does not improve within four to six hours of normobaric 100% oxygen treatment. It should also be kept in mind that there may be neurologic and cardiac damage in the late period^{19,43}.

Discussion

The prediction and prevention of exposure to CO are less costly and more effective in the battle against CO poisoning. CO poisoning occurs more frequently especially in the winter months due to the burning of CO sources for heating purposes. Daily weather conditions and waft can also affect exposure^{4,6,44}. In this regard, citizens should be informed about meteorological conditions and the correct use of fuels. In the literature, it was also reported that CO exposure was higher in certain occupational groups⁴⁵. Therefore, in these occupational groups, the use of protective equipment, detectors that can measure the CO level, and appropriate ventilation systems should be made obligatory.

CO is insidious and its diagnosis can be overlooked unless the doctor suspects a poisoning case. An appropriate diagnosis is possible through a combination of appropriate clinical manifestation and high blood COHb levels. The best method for determining the COHb level is to measure it in arterial or venous blood gas. Despite the conflicting opinions about the use of a non-invasive CO-oximeter on the fingertip, it still presents as a feasible method due to its non-invasive nature, reproducibility, ease of clinical use, and low cost^{13,20,21}. However, further studies are needed concerning this issue.

Patients presenting with acute renal failure or myocardial and neurological damage have high rates of mortality and morbidity^{21,29}. These patients should be hospitalized immediately and the HBO therapy should be started. After a longterm monitoring, these patients can be safely discharged if their COHb is reduced to the normal level; however, it is crucial to follow up these patients after discharge.

Although HBO therapy is the most widely accepted method of treatment in CO poisoning, there are publications suggesting that it does not reduce long-term neurological sequelae and mortality⁴⁶. Furthermore, the longer time between CO exposure and HBO therapy, and loss of consciousness or coma at the time of hospital admission have been found to significantly increase the incidence of delayed neuropsychiatric syndrome⁴⁷. Despite the lack of a conclusive consensus on the indications for HBO therapy, it should be started without any delay in appropriate cases^{4,22}. In addition, normobaric 100% oxygen should be administered until HBO therapy is started considering that both treatments accelerate the removal of CO from the blood^{23,48}.

In a study conducted with 12 patients presenting with severe CO poisoning, a low Glasgow coma score, and a high COHb level (38-79%), the authors applied therapeutic red cell-exchange therapy and discharged 11 patients after rapid clinical improvement⁴⁹. In another study, 17 patients treated with the same method for CO poisoning were all discharged with full recovery⁵⁰. In both studies, it was emphasized that therapeutic red cell-exchange therapy may be an effective treatment for reducing morbidity and mortality in CO poisoning. However, both studies were undertaken with a small number of patients; thus, further studies with larger case series are needed.

Conclusion

CO poisoning is the most common cause of death due to toxicity. It should be kept in mind that CO can affect all body systems, and primarily the vital organs. In addition to coma and cardiac damage observed in the acute period, other events, such as delayed neuropsychiatric syndrome can also develop. Exposure to CO is higher in winter and in certain occupational areas, which require protective measures to be taken. To date, HBO therapy has been reported to be the most widely accepted treatment in the literature. Therefore, in patients with relevant indications, HBO therapy should be started immediately.

The author declares no conflict of interest.

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Original Article

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The Effects of Magnesium Levels on Prognosis in Organophosphate Poisoning

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Abstract

Objectives: To investigate the predictive value of magnesium, neutrophil/lymphocyte ratios (NLR) in determining the severity of morbidity and mortality in patients with organophosphate poisoning (OP) admitted to the emergency department.

Materials ad Methods: This study was conducted retrospectively by scanning the medical recordings of patients aged over 18 years who were admitted to our emergency department with OP between 2010 and 2015. The demographic characteristics, medical history, laboratory findings, and Glasgow Coma Scale (GCS) scores of the patients were recorded.

Results: The data of 153 patients, 91 males and 62 females, were evaluated. There was no significant correlation between the changes in magnesium, hemoglobin, hematocrit, leukocytosis, platelets, potassium, calcium, glucose, alanine aminotransferase (ALT), troponin, and mortality in patients with OP (p>0.05). There was a significant relationship between the increase in lactate dehydrogenase (LDH) (p=0.004), low lymphocyte count (p=0.003), decreased cholinesterase (p=0.001), higher (NLR) (p=0.002), GCS (p<0.001), mechanical ventilator (MV) requirement (p<0.001), age (P=0.009), vasopressor treatment (p<0.001), and mortality.

Conclusion: No significant relationship determined between magnesium levels and prognosis. Low lymphocyte count, decreased cholinesterase, increased LDH and NLR in patients with OP were significantly correlated with mortality. Increased NLR ratio, one of the parameters in routine hemograms, may give information to physicians about the long-term follow-up of such patients with OP.

Keywords: emergency, organophosphate, magnesium, neutrophil lymphocyte ratio

Özet

Amaç: Bu çalışmada acil servise başvuran organofosfat zehirlenmesi (OP) ile başvuran hastalarda morbidite ve mortalitenin ciddiyetinin belirlenmesinde magnezyum, nötrofil / lenfosit oranlarının (NLR) prediktif değerini araştırmak amaçlanmıştır.

Gereç ve Yöntem: Bu çalışma 2010-2015 yılları arasında OP ile acil servise başvuran 18 yaş üstü hastaların tıbbi kayıtları retrospektif taranarak yapıldı. Hastaların Demografik özellikler, tıbbi öykü, laboratuvar bulguları ve Glasgow Koma Skalası (GKS) skorları kaydedildi.

Bulgular: 91 erkek ve 62 kadın 153 hastanın verileri değerlendirildi. OP'li hastalarda magnezyum, hemoglobin, hematokrit, lökositoz, trombosit, potasyum, kalsiyum, glukoz, alanin aminotransferaz (ALT), troponin ve mortalite değişiklikleri arasında anlamlı bir ilişki bulunmadı (p > 0.05). Laktat dehidrojenaz artışı (LDH) (p = 0.004), düşük lenfosit sayısı (p = 0.003), azalmış kolinesteraz (p = 0.001), yüksek NLR düzeyi (p = 0.002), GKS (p < 0.001) mekanik ventilatör (MV) gereksinimi (p < 0.001), yaş (P = 0.009), vazopressör tedavisi (p < 0.001) ve mortalite arasında anlamlı bir ilişki vardı.

Sonuç: Magnezyum düzeyleri ile prognoz arasında anlamlı bir ilişki bulunamamıştır. OP'li hastalarda düşük lenfosit sayısı, azalmış kolinesteraz, LDH ve NLR artışı mortalite ile anlamlı olarak korele idi. Rutin hemogramlardaki parametrelerden biri olan artmış NLR oranı, OP hastalarının uzun süreli takibi hakkında hekimlere bilgi verebilir.

Anahtar kelimeler: acil, organofosfat, magnezyum, nötrofil lenfosit oranı

Introduction

Organophosphate compounds are widely used in agriculture¹ and poisoning with these compounds is more common in developing countries such as our country, Turkey, although it is also known to be a major problem in industrialized countries^{2,3}. Poisoning can occur accidentally in agricultural areas, in industry, in animal husbandry or due to contaminated food, and may also occur in suicide⁴. It is reported that three million people in the world are poisoned with pesticides every year and nearly 200,000 of these die⁵. Orga-

nophosphate poisoning (OP) is frequently seen in Turkey in accidental poisoning or suicides. Poisoning with these chemicals affects all vital functions and requires early diagnosis and treatment^{6, 7}.

In recent years, in addition to clinical tests in which the neutrophil/lymphocyte ratio (NLR) is used as an inflammatory marker, the relationship of the NLR with many diseases has been investigated. The basis of these studies is the physiologic response of leukocytes to stimuli, the increase in the neutrophil count, and the relative decrease in lymphocyte counts associated with neutrophilia8. The NLR is frequently used as a prognostic factor in cardiovascular system diseases. An increase in the NLR in patients undergoing cardiovascular interventions was found to be an indicator of poor prognosis. Similarly, there are studies that showed an increase in the NLR could be associated with increased mortality in acute coronary syndrome^{9, 10}. In some studies, the NLR was found to be useful for predicting prognosis in some types of cancer^{9, 11}. As we guess that as a result of OP, inflammation begins in the body, the severity of the poisoning will be in correlation with the severity of the inflammatory process, and that there will be significant changes in NLR. In this study, we aimed to investigate the predictive value of the NLR in determining the severity of morbidity and mortality in patients with OP admitted to the emergency department.

It is stated that organophosphates cause acetylcholine (Ach) accumulation in synapses by irreversibly inhibiting the acetylcholinesterase enzyme (AchE)^{12,13}, and that the clinical presentation is caused by the excessive stimulation of nicotinic and muscarinic cholinergic receptors with Ach in central nervous system, in the autonomic nervous system, and at neuromuscular junctions^{12, 13}. It is reported that the stimulation of muscarinic receptors causes myosis (<3 mm), bradycardia, and increased bronchial secretion, and the stimulation of nicotinic receptors causes fasciculation in muscles, cramps, weakness in respiratory muscles, seizures and loss of consciousness¹².

The diagnosis of OP is based on clinical findings and the level of cholinesterase in the serum. The treatment includes administering drugs including atropine and oxime and supportive care. However, atropine and oximes used in the treatment of OP may be insufficient to reduce morbidity and mortality in some cases. The mortality rate in OP can reach up to 30%⁶. We aimed to investigate the predictive value of NLR) in determining the severity of morbidity and mortality in patients with OP admitted to the emergency department.

Materials and Methods

This retrospective study was approved by the local ethics committee (Number: 2016/496). The study was performed by scanning the medical records of 153 patients who were

diagnosed as having OP in the Emergency Medicine Clinic between January 2010 and January 2016. Patients aged under 18 years, pregnant females, and those with previously known cardiac disease were excluded from the study. Demographic characteristics, medical history, vital signs, laboratory findings, hospitalization and intensive care unit stay durations, mechanical ventilator and vasopressor requirements, mortality rates, and Glasgow Coma Scale (GCS) scores of the patients were recorded. The Statistical Package for the Social Sciences (SPSS) for Windows Ver. 15.0 (SPSS Inc, Chicago, IL) was used for statistical analyses of the data. Descriptive statistics were presented as mean±standard deviation, median (min-max), frequency distribution, and percentage. The normality of distribution of the variables was evaluated with visual (histogram and probability plots) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. For variables that did not have normal distribution, the Mann-Whitney U test was used to search for the relation between two independent variables, and the Kruskal Wallis test was used to investigation relations between three independent variables. When a significant difference was detected between three independent groups, Bonferroni correction was used to determine the source of the difference. The relationship between the variables was evaluated using the Spearman's correlation test. P<0.05 was considered as statistically significance.

Results

Ninety-nine of the 153 patients included in the study were males (59.5%) and 62 were females (40.5%). The mean age of the males and females was 43.10±18.41 and 40.32±17.27 years, respectively, and the age range was 18-82 years. When we examined the routes of OP, in male patients it was observed that 40 had OP by ingestion, 40 by inhalation, and 11 through skin exposure, and in female patients 34 had had OP by ingestion, 21 had OP by inhalation, and 7 through skin exposure. Thirty-two males and 23 females had OP in suicide attempts. Fifty-nine males and 39 females were had OP accidentally. When the clinical findings of the patients were examined at admission to the emergency room, 92 (60.1%) patients had nausea, 66 (43.1%) vomiting, 14 (9.2%) abdominal pain, 32 (20.9%) shortness of breath, 17 (11.1%) dizziness, 10 (6.5%) diarrhea, 11 (7.2%) headache, 13 (8.5%) burning and redness in the body, 18 (11.8%) confusion, 8 (5.2%) coma, 1 (0.7%) hemoptysis, and 1 (0,7) chest pain.

Complete blood count findings of the patients were as follows: the mean leukocyte value was $8.8\pm2.86\times10^3/uL$ (min-max: 3.9-19.2x10³/uL), the mean hemoglobin value was 13.2 ± 1.9 g/dL (min-max: 8.1-17.5 g/dL), the mean hemotocrit value was $39.2\pm5.03\%$ (min-max: 26.7-50.9%), the mean neutrophil value was $6.2\pm2.9\times10^3/uL$ (min-max:

1.54-17.3 x10³/uL), the mean lymphocyte value was 1.8 \pm 0.8 x103/uL (min-max: 0.34-4.62x10³/uL), and the mean platelet (PLT) value was 234.9 \pm 80.02x10³/uL (min-max: 26.7-50.9x10³/uL). There was a significant correlation between low lymphocyte counts and mortality (p=0.003). There was a significant correlation between high NLR and mortality (p=0.002) (Table 1).

Discussion

No significant relationship determined between magnesium levels and prognosis. In this article want to take attention to predictivity between NLO and organophosphate poisoning.

To the best of our knowledge, there are no studies on the effects of NLR on prognosis in OP. In our study, the effect of NLR on mortality and prognosis was investigated. A significant correlation was found between NLR and mortality and prognosis.

Recently, lymphocytopenia and NLR have been noted as an independent predictor in a wide conditions ranging from oncologic diseases to cardiovascular system diseases. Tamhane et al.¹⁰ showed that a high NLR was correlated with intra-hospital and 6 months mortality and reinfarction, and also increased incidence of stroke. The NLR is frequently used as a prognostic factor in cardiovascular system diseases. Increased NLR in patients undergoing cardiovascular interventions was shown as an indicator of poor prognosis. Similarly, an increased NLR was found correlated with increased mortality in acute coronary syndrome in some studies9, 10. Goodman et al. showed that the NLR was more sensitive than white blood cell (WBC) counts in appendicitis¹⁴. Neutrophilia was found correlated with acute decompensated heart failure in patients with acute myocardial infarction, and together with relative lymphopenia, they were good markers of mortality in heart failure¹⁵. The NLR is considered to be indicative of subclinical inflammation¹⁶. In some studies, the NLR was found to be useful for predicting prognosis in some types of cancer¹¹.

The low number of lymphocytes in colorectal tumors is associated with poor prognosis because the presence of T-lvmphocytes in a tumor is indicative of a significant immune response against the lesion. It was shown that the NLR was a good prognostic factor in determining mortality in colorectal and ovarian cancers¹¹. In a study by Buck et al., complete blood counts from peripheral blood samples were measured at 24 hours in patients who were diagnosed as having ischemic stroke. It was shown that high peripheral leukocyte and neutrophil numbers were associated with the existing ischemic infarct volume. In that study, no relation was found between the number of lymphocytes and infarct volume¹⁷. In addition to infectious diseases, the NLR has been investigated in metabolic syndrome, chronic obstructive pulmonary disease, end-stage renal failure, subdural hemorrhage, Behcet's disease, malignancy, and keratoconjunctivitis¹⁸⁻²⁰.

Table 1. The relationship between the NLR, lymphocyte count, and mortality

Parameter	Discharge	Ex	Р
			value
Lymphocyte, mean±SD	1.92±0.79	0.83±0.38	0.003
NLR, median (IQR)	2.81 (2.74)	9.24 (11.96)	0.002

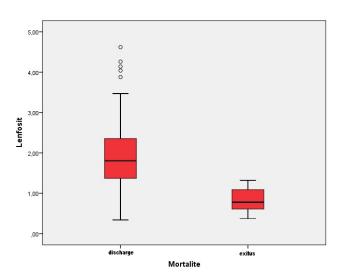


Figure 1. Boxplot showing the relationship between lymphocyte count and mortality

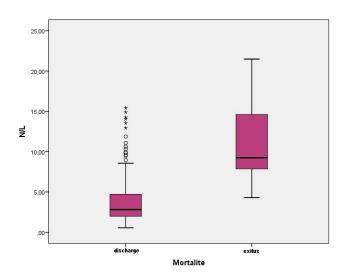


Figure 2. Boxplot showing the relationship between NLR and mortality

In our study, we found increased NLR and low lymphocyte counts in patients with OP. In the literature, we found no information about the use NLR in OP; therefore, comparisons were made with the use of NLR in other diseases to show the inflammatory process and prognosis. We concluded that prognosis is worse in patients with an increased NLR and low lymphocyte count, and these patients should be followed up for longer. These findings should be validated by future studies because there are no similar studies in the literature.

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Orginal Article

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Acil Servise Parasetamol İntoksikasyonu Nedeniyle Başvuran Hastaların Değerlendirilmesi

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Abstract

Objective: We aimed to evaluate the demographical and clinical variations and treatment and complications of the patients admitted to emergency department (ED) with paracetamol intoxication.

Materials and Methods: This is a retrospective study. Patients who were diagnosed as paracetamol intoxication at the ED of Keçiören Health Research and Application Center Hospital included into the study. Patients with missed data, pregnant patients and patients with drug intoxications other than paracetamol were excluded. Statistical analysis was performed using the Statistical Package for the Social Sciences version 16.0. P-value less than 0.05 was considered statistically significant.

Results: Fifty-five patient included into the study. Mean age of the patients was 34±12 years and 63.6% of them were female. The amount of paracetamol ingested was 11.02±4.04 gr and fourth hour paracetamol level was 28.8 µg/dl (IQR 25-75: 12.5-41.7). There was a statistically significant weak correlation between the amount of paracetamol ingested and the blood paracetamol level of the patients (r=0,475 ve p=0,04). Liver function tests of the patients were elevated during the follow up and that was statistically significant (p<0.05).

Conclusion: According to the results despite of more than half of the patients ingested paracetamol at toxic doses, at most of them severity of intoxication was mild. Levels of the liver function tests of the patients could increase at paracetamol intoxication compared to baseline levels.

Keywords: paracetamol, intoxication, liver function tests

Özet

Amaç: Bu çalışmada, acil kliniğine parasetamol intoksikasyonu nedeniyle başvuran hastaların; demografik, klinik değişkenleri, tedavileri ve komplikasyonlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Bu çalışma retrospektif bir çalışmadır. Keçiören Sağlık Araştırma ve Uygulama Merkezi Hastanesi acil kliniğinde parasetamol intoksikasyonu tanısı alan hastalar çalışmaya dahil edildi. Verileri eksik olanlar, gebeler, parasetamol dışı ilaçlarla zehirlenen hastalar çalışma dışı bırakıldı. Verilerin analizi SPSS 16 programında yapıldı. p<0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışmaya 55 hasta dahil edildi. Hastaların yaş ortalaması 34±12 yıl olup, %63,6'sı kadındı. Hastaların aldıkları parasetamol miktarı 11.02±4.04 gr ve dördüncü saat parasetamol düzeyleri 28.8 µg/dl (IQR 25-75: 12.5-41.7) olarak bulundu. Hastaların aldıkları parasetamol miktarı ile kan parasetamol düzeyi arasında istatistiksel anlamlı zayıf düzeyde korelasyon saptandı (r=0,475 ve p=0,04). Hastaların takip süresince bakılan karaciğer fonksiyon testlerinde artış saptandı ve bu fark istatistiksel olarak anlamlıydı (p<0.05).

Sonuç: Çalışma bulgularımıza göre hastalarımız yarıdan fazlası toksik doz parasetamol almış olmasına rağmen büyük bir kısmında zehirlenme şiddetinin hafif olduğu görülmüştür. Parasetamol zehirlenmelerinde hastaların karaciğer fonksiyon testlerinde başlangıç değerlerine göre artış olabilmektedir. Anahtar kelimeler: parasetamol, zehirlenme, karaciğer fonksiyon testleri

Giriş

Parasetamol, güvenirliği, etkinliği ve ucuzluğu ile en sık kullanılan ağrı kesici ve analjeziktir. Yaygın kullanımı ve kolay ulaşılması sebebiyle parasetamol intoksikasyonu sık bildirilen intoksikasyonlardan biridir. Amerika Zehir Kontrol Merkezi'nin raporuna göre her yıl 100.000'nin üzerinde parasetamol zehirlenmesi bildirilmekte, 50.000 acil servis başvurusu ve yılda 10.000 hastaneye yatış meydana gelmektedir¹. Son dönemlerde Parasetamol kullanım sıklığının artmasıyla beraber, parasetamol aşırı doz alımları ve buna bağlı karaciğer toksisitesi ve ölüm oranlarında da artış görülmektedir². Parasetamol intoksikasyonu, hepatoselüler nekroza neden olarak, sadece Amerika Birleşik Devletleri'nde yıllık yaklaşık 500 ölümden sorumludur. Toksik doz Parasetamol alımlarında sık olarak hepatotoksite gelişse de renal yetmezlik, metabolik asidoz, koagülopati, ensefalopati ve rekürren gastrointestinal sistem semptomları da görülebilir. Parasetamol oral alındıktan sonra karaciğerde sitokrom p450 enzim sistemi tarafından toksik metaboliti olan N-acetyl-p-benzoquinonimine (NAB) dönüştürülür ve endojen glutatyon ile detoksifiye edilir. Yüksek doz alımlarda glutatyon depoları azalır ve toksik metabolitler detoksifiye edilemediği için karaciğer toksisitesi meydana gelir. N-Asetilsistein (NAS) bir glutatyon öncülüdür. Parasetamolün toksik metabolitlerinin hepatik makro moleküllere bağlanmasını önler ve azalmış glutatyon depolarını tazeler. NAS antioksidan mekanizmalarla da hepatik nekrozu azaltır. Akut parasetamol zehirlenmesinde; alımı takiben ilk 8 saat içerisinde uygulanan NAS'in toksisitesi gelişmesini büyük oranda önlediği bildirilmektedir¹⁻⁴.

Günümüzde özkıyım amaçlı toksik doz parasetamol alımları acil kliniklerinde sık görülmektedir. Bütün intoksikasyon olgularında olduğu gibi parasetamol intoksikasyonlarının ilk değerlendirme yeri acil servislerdir ve özellikle toksik doz alımlarda başlangıç tedavisi hayati önem taşımaktadır^{1, 2}. Bu nedenle acil doktoru, parasetamol toksisitesinin klinik bulguları ve tedavi protokollerine hâkim olmalıdır.

Biz bu çalışmada; acil servisimize parasetamol intoksikasyonu nedeniyle başvuran hastaların demografik, klinik değişkenleri, tedavileri ve komplikasyonlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem

Bu çalışma retrospektif bir çalışmadır. 01.01.2015-31.05.2018 tarihleri arasında Keçiören Sağlık Araştırma ve Uygulama Merkezi Hastanesi acil servisine başvuran; X60 ICD kodu (opioid olmayan analjezikler, antipiretikler ve antiromatizmallere maruz kalma ve kasıtlı olarak kendine zarar verme) girilen, otomasyon sisteminden ve hasta dosyalarından parasetamol zehirlenmesi olduğu tespit edilen 18 yaş ve üzeri hastalar çalışmaya dahil edildi. Verileri eksik olanlar, gebeler, parasetamol dışı ilaçlarla zehirlenen hastalar çalışma dışı bırakıldı.

Olguların demografik bilgileri, vital bulguları, aldıkları parasetamol miktarı, ek ilaç alımları, nazogastrik/orogastrik irrigasyon, aktif kömür uygulanıp uygulanmadığı, kan parasetamol düzeyleri, hastane sonlanımları, başvurularında ve acil serviste takip süresince bakılan tam kan sayımı ve biyokimyasal değerleri kaydedildi.

Akut alımlarda; 200 mg/kg'ın üzeri veya 10 gr üzeri alım, tekrarlayan alımlar için 24 saatte 10 gr ya da 200 mg/ kg üzeri alımlar toksik alım olarak kabul edildi.

Kliniğimizde NAS tedavisi IV veya oral olarak parasetamol zehirlenme protokollerine uygun olarak verilmektedir. Hastaların aldıkları tüm tedaviler çalışma formlarına kayıt edildi.

İstatiksel Analiz

Verilerin analizi SPSS for Windows 16 paket programında yapıldı. Kesikli ve sürekli sayısal değişkenlerin dağılımının normal dağılıma uygun olup olmadığı Kolmogorov Smirnov testi ile araştırıldı. Tanımlayıcı istatistikler kesikli ve sürekli sayısal değişkenler için median (minimum-maksimum) şeklinde, kantitatif veriler gözlem sayısı ve yüzde (%) olarak gösterildi. Kategorik değişkenler Ki-kare ile sürekli değişkenler ise Mann Whitney U testi ile değerlendirildi. Alınan parasetamol miktarı ile kan parasetamol düzeyi arasında istatistiksel olarak anlamlı korelasyon olup olmadığı Spaerman korelasyon testiyle araştırıldı.

p<0.05 istatistiksel olarak anlamlı kabul edildi.

Bulgular

Çalışma boyunca 753 hasta dosyası tarandı. 62 hastanın parasetamol aldığı tespit edildi. 7 hastanın verileri eksik olduğu için çalışma dışı bırakıldı ve sonuçta 55 hasta çalışmaya dahil edildi. Hastaların 35'i (%63.6) kadın, 20'si (%36.4) erkek ve yaş ortalamaları 34 ± 12 'di. Hastaların aldıkları parasetamol miktarı ortalama (standart sapma) 11.02±4.04 gr ve dördüncü saat parasetamol düzeyleri 28.8 µg/dl (medyan, IQR 25-75: 12.5-41.7) olarak bulundu. Hastaların %56.4'ü toksik doz alımdı. Hastalarımızın hiçbirinde mortalite gelişmedi ve transplantasyon ihtiyacı olmadı. Hastalara ait demografik veriler Tablo 1'de gösterildi.

Hastaların aldıkları parasetamol miktarları ile kan parasetamol düzeyi arasında istatistiksel olarak anlamlı aynı

Tablo 1. Hastaların demografik verileri

Cinsiyet n (%)	35 (%63.6)
Kadın	
Yaş ortalama± standart sapma	34±12
Ek ilaç alımı n (%)	27 (%49.1)
Alınan ek ilaçlar n (%)	
Analjezik	13 (%23.6)
Antibiyotik	3 (%5.5)
Asetil salisilik asit	3 (%5.5)
Diğer	8 (%14.5)
Mide lavajı yapılması n (%)	30 (%55.6)
Parasetamol miktarı gr ortalama± standart	11.02±4.04
sapma	
Toksik doz alan hasta sayısı n (%)	31 (%56.4)
4. saat parasetamol düzeyi medyan µg/dl	28.8 (12.5-41.7)
(IQR 25-75)	
Vital bulgular ortalama± standart sapma	
Sistolik tansiyon mm/Hg	123.5 ± 15
Diastolik tansiyon mm/Hg	73.5±7.9
Nabız /dakika	84.2±14.5
N-asetil sistein verilmesi n (%)	18 (%32.7)
Hasta sonlanımı (%)	
Taburcu	35 (%63.6)
Servise yatış	13 (%23.6)
Yoğun bakıma yatış	7 (%12.7)

IQR: Inter quartile range

yönlü zayıf düzeyde korelasyon saptandı (r=0,475 ve p=0,04) (Tablo 2).

Hastaların karaciğer fonksiyon testleri değerlendirildiğinde, takipte bakılan Alanin Amino Transferaz (ALT), Aspartat Transaminaz (AST) ve International Normalized Ratio (INR) değerlerinde, ilk bakılan değerlerine göre artış saptandı ve bu farklar istatistiksel olarak anlamlıydı (sırasıyla p=0.002, p=0.019, p=0.003). Hastalara ait laboratuar değerleri Tablo 3'de verildi.

Tartışma

Acil servise parasetamol intoksikasyonu nedeniyle başvuran hastaların demografik verileri, tedavileri ve komplikasyonlarını değerlendirdiğimiz bu çalışmamızda iki sonuç elde ettik.

Birinci sonucumuz, hastaların çoğunun verilerinde toksik doz parasetamol doz aldığı görülse de hastaların aldıkları miktar ile kan parasetamol düzeyleri arasında zayıf bir korelasyon mevcuttu.

İkinci sonucumuz, hastaların karaciğer fonksiyon testlerinde başlangıç değerlerine göre artış platelet sayılarında azalma görüldü. Bu durum, parasetamolün karaciğerde subklinik, hücresel düzeyde etkilenmeye neden olduğunu gösterebileceğini düşünüyoruz.

Ateş düşürücü ve ağrı kesici etkileri olan parasetamol, tek başına veya nezle-grip ilaçlarıyla birlikte olacak şekilde sık kullanılmakta ve buna paralel olarak doz aşımı veya özkıyım amaçlı çok miktarda alınmasına bağlı yan etkilerine acil servislerde sık karşılaşılmaktadır⁵. Çalışmamızda hastalarımızın hepsi özkıyım amaçlı parasetamol almıştı. Özkıyım amacıyla ilaç alımına bağlı zehirlenmelerin büyük çoğunluğu 15-35 yaş arasındaki kadınlar oluşturmaktadır^{6,7}. Hastalarımızın yaşı ve cinsiyetleri literatür ile benzerdi. Hastaların yaklaşık yarısına mide lavajı yapılamadığı görüldü. Bu durum hastaların acil servise daha geç sürelerde başvurduğunu göstermektedir.

Parasetamol zehirlenmeleri düşük dozlarda zararsız iken, yüksek dozlarda ölümcül olabilmektedir¹. Parasetamol analjezik etkisi 10 mcg/ml, antipiretik etkisi 18 mcg/ml düzeyindeki kan konsantrasyonunda ortaya çıkar. Tek seferde 200mg/kg'ın üzeri veva 10 gr üzeri parasetamol alımı, tekrarlayan alımlar içinse 24 saatte 10 gr ya da 200 mg/kg üzeri toksik alım olarak kabul edilmektedir. Tek bir seferde belirgin toksisite genellikle 200 mg/kg ve üstü dozlarda ortaya çıktığı bildirilmiştir². Hastalarımızın verileri incelendiğinde yarıdan fazlasının toksik doz parasetamol aldığı görüldü. Ancak hastaların parasetamol miktarları ile 4. saat parasetamol düzevleri arasında zavıf bir ilişki mevcuttu, daha önce bildirilen çalışmalarda alınan parasetamol miktarı ile ölçülen serum konsantrasyonu arasında bir korelasyon bulunamadığı gösterilmiştir^{8,9}. Ayrıca bu durum hastalarımızın tamamının özkıyım amaçlı ilaç içen hastalardan oluşması ve içinde bulundukları bu psikolojik açıdan sıkıntılı durumda verdikleri anamnezin güvenilirliğinin azalmasından da kaynaklanmış olabilir.

Parasetamol miktarı	r	р	
Kan parasetamol düzeyi	0,475	0,04	

Tabl	o 3.	Hasta	ların	bazı	la	boratuvar	değerl	leri
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Medyan IQR	Başlangıç	Takip değerleri	р		
(25-75)	değerleri				
Platelet	208 (182-246)	252 (228-285.2)	0.002		
AST	16.5 (14-33)	22 (19-29)	0.002		
ALT	14 (13-29)	17 (14-22)	0.019		
INR	1.19 (1.17-1.31)	1.1 (1.03-1.18)	0.003		
ALT: Alanin Amino Transferaz, AST: Aspartat Transaminaz, INR:					
Internasyonel Normalized Ratio IQR: Inter quartile range					

Parasetamol aşırı doz alımıyla acil servise başvuran hastaların başvuru anındaki rutin laboratuar tetkiklerinin toksisitenin ciddiyet hakkında bilgi vermediğini görülmüştür. Bu konuda literatür incelendiğinde çalışmamıza benzer şekilde başvuru anındaki laboratuar tetkikleri ile akut parasetamol intoksikasyon ciddiyeti arasında ilişki gösterilememiştir^{9, 10}. Trombositlerin parasetamol zehirlenmelerinde von Willebrand faktörü aracılığıyla karaciğer harabiyetini artırdığı bilinmektedir¹¹. Parasetamol intoksikasyonlarında karaciğer ve böbrek fonksiyonlarında bozulmanın yanında platelet fonksiyonlarının inhibisyonu üzerinden koagülasyon bozukluğu görülebilmektedir¹². Shorr ve ark.'nın parasetamolün platelet agregasyonunu engelleyici etkisini laboratuar ortamında göstermesinin ardından Niemi çalışmasında bu etkiyi sağlıklı gönüllülerde ortaya koymuştur^{13,14}. Bizim sonuçlarımıza bakıldığında hastaların başvuru anında alınan sonuçlara göre takipte alınan platelet sayılarında azalma tespit ettik. Ancak hastalarımızda herhangi bir kanama komplikasyonu gelişmedi. Bu durum hastalarımızın zehirlenme ciddiyetinin hafif olmasından kaynaklanmış olabileceğini düşünüyoruz.

Benzer durum karaciğer sentez fonksiyon göstergelerinden birisi olan INR için geçerlidir. Literatürde, hepatik hasarı göstermesi bakımından INR daha sensitif olduğunu vurgulayan yayınlar mevcuttur fakat bu oranın da hepatotoksisite riskini erken tahmin etmeden ziyade, karaciğer sentez fonksiyonunun düzelmesini gösterme bakımından daha kullanışlı olduğu vurgulanmıştır¹⁵. Whyte ve arkadaşlarının çalışmasında karaciğer hasarı olmaksızın INR yüksekliği olduğunu bildirmişlerdir¹⁶. Bizim hastalarımızda da benzer şekilde takip INR değerlerinde artış tespit ettik.

Parasetamol zehirlenmelerinde karaciğer fonksiyon testleri genellikle alımdan 24 saat sonra artmaya başlar¹⁷. Son dönemde yayınlanan çalışmada, acil servis başvurusunda bakılan AST'nin 50 IU/L'nin üzerinde olmasının hepatik hasarı göstermede; sensitivitesi %79.5, spesifitesi %82.6 bulunmuştur. Ancak bu çalışmada başvuru anında bakılan AST'nin mortalite tahmini veya karaciğer transplantasyonunu belirlemede kullanışlı olmadığı vurgulanmıştır¹⁸. Karaciğer hasarının ciddiyetini göstermede geleneksel bir marker olan ALT ise genelde AST'ye göreceli olarak daha yavaş yükselmektedir¹⁷. Çalışmamızda hem AST ve ALT düzeylerinde başvuru anına göre takip değerlerinde artış saptadık ve bu fark istatistiksel olarak anlamlıydı.

Parasetamol toksik doz aşımı olan hastalarda NAS tedavisin mümkün olan en kısa sürede başlanması önemlidir. İntravenöz NAS tedavisinin kısa zamanda yüksek kan konsantrasyonuna ulaşma, tedavi süresinin kısa olması, hasta uyumunun daha iyi olması, bilinç kapalı hastada uygulanabilmesi olumlu yönleri iken, ürtikeryal reaksiyon, ciddi anaflaksi gibi yan etkileri de mevcuttur¹⁹. Çalışmamızda sadece 18 hastaya intravenöz NAS uygulanmış olup herhangi bir yan etki gözlenmemiştir.

Kısıtlılıklar

Çalışmamız öncelikli olarak retrospektif bir çalışma olması nedeniyle hastaların dosya kayıtları üzerinden verilere ulaşılmıştır. Çalışmamızda hastaların ilaç alımını takiben hastaneye başvurusu arasında geçen zamanın değerlendirilememiş olması diğer bir kısıtlılıktır. Hastalarımızın çoğunun zehirlenme bulguları hafiftir.

Sonuç

Çalışma bulgularımıza göre hastalarımızın aldıkları parasetamol miktarı ile kan düzeyleri korele değildir. Hastalarımızın yarıdan fazlası toksik doz parasetamol almış olsa da büyük bir kısmında zehirlenme hafif şiddette olup sonuçlarımız ağır zehirlenme olgularına genellenemez. Parasetamol zehirlenmelerinde hastaların karaciğer fonksiyon testlerinde başlangıç değerlerine göre artış olabilmektedir. Bu durum, parasetamolün karaciğerde hücresel düzeyde etkilenmeye neden olduğunu gösterebilir.

Çıkar Çatışması

Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

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Original Article

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Demographic and Clinical Characteristics of Carbon Monoxide Poisoning: Data Between 2014 and 2018 in Erzurum

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Abstract

Objective: This report describes the epidemiology and analyses the clinic status, treatment, morbidity of carbon monoxide intoxication cases in a university hospital. Furthermore, the results of blood tests of cases mentioned in this study were evaluated in detail.

Materials and Methods: In this retrospective study, patients diagnosed with toxic effects of carbonmonoxide were evaluated between years 2014-2018. The data extracted from the patients' files included seasonal variation, age, gender, underlying comorbidities, smoking and alcohol abuse history, vital parameters, clinical manifestations and source of poisoning, laboratory and imaging records, treatment and outcome.

Results: A total of 653 patients were included in the study. Admissions during the winter was found to be higher that other seasons with a significant difference (p < 0.001). The most frequent symptoms were headache (%62.3), nausea (%42.3), sudden loss of consciousness (%15.9) and dizziness (%12.1). Lactate levels were positively correlated with carboxyhemoglobin values (r= 0.257, p < 0.001) and troponin I levels (r= 0.267, p < 0.001). A blood lactate concentration >2 mmol/L was associated with %40 sensitivity and %75 specificity for predicting hyperbaric oxygen therapy requirement. Hyperbaric oxygen therapy group had a longer hospitalization period, which was statistically significant (mean difference -0.98; 95% CI = -1.38, -0.57) (p < 0.001).

Conclusion: Emergency medicine clinics are fighting almost alone in carbonmonoxide poisoning cases. Now it is required to develop new perspectives in these cases. Lactate can be used safely in the management of patients as an option.

Keywords: carbonmonoxide, intoxication, lactate, poisoning

Özet

Amaç: Bu çalışma bir üniversite hastanesine, karbonmonoksit zehirlenmesi tanısı ile başvuran vakalarının klinik durumunu, tedavisini ve morbiditesini analiz etmeyi ve epidemiyolojik verilerini tanımlamayı amaçlamaktadır. Ek olarak, bu çalışmada belirtilen vakaların kan testlerinin sonuçları ayrıntılı olarak değerlendirilmiştir.

Gereç ve Yöntem: Bu retrospektif çalışmada, 2014-2018 yılları arasında karbonmonoksitin toksik etkileri tanısı alan hastalar değerlendirildi. Hastaların dosyalarından elde edilen veriler arasında yaş, cinsiyet, altta yatan komorbiditeler, sigara kullanımı, alkol kötüye kullanımı öyküsü, vital bulgular, klinik belirtiler, laboratuvar ve görüntüleme sonuçları, tedavi, sonuç, zehirlenme kaynağı ve mevsimsel değişken yer alıyordu.

Bulgular: Çalışmaya toplam 653 hasta dahil edildi. Kış mevsiminde yapılan başvuruların diğer mevsimlere anlamlı olarak daha yüksek olduğu tespit edildi (p <0.001). En sık görülen semptomlar baş ağrısı (% 62.3), bulantı (% 42.3), ani bilinç kaybı (% 15.9) ve baş dönmesi (% 12.1) idi. Laktat seviyeleri ile karboksihemoglobin değerleri (r = 0.257, p <0.001) ve troponin I düzeyleri (r = 0.267, p <0.001) arasında pozitif korelasyon gösterildi. > 2 mmol / L'lik bir kan laktat konsantrasyonu, hiperbarik oksijen tedavisi ihtiyacını öngörmek için% 40 hassasiyet ve% 75 özgüllük ile ilişkilendirildi. Hiperbarik oksijen tedavisi grubu daha uzun bir hastanede kalış süresine sahipti, bu durum istatistiksel olarak anlamlıydı (ortalama fark -0.98;% 95 CI = -1.38, -0.57) (p <0.001).

Sonuç: Acil tıp klinikleri karbonmonoksit zehirlenmesi vakalarında neredeyse tek başına savaşmaktadır. Bu nedenle yeni bakış açılarına ihtiyaç vardır. Laktat, hastaların yönetiminde bir seçenek olarak güvenle kullanılabilir.

Anahtar kelimeler: karbonmonoksit, intoksikasyon, laktat, zehirlenme

Introduction

Carbon monoxide (CO) toxicity is common in Turkey, especially in eastern cities. Carbon monoxide is an odorless gas which is formed from insufficient burning of organic substances. It is usually emitted through domestic or industrial media that require fuel-burning such as water and gas heaters, cooking equipment, motor vehicles, gas-powered furnaces, portable generators and processes like charcoal burning¹. In our country, especially in winter months, CO intoxication

cases increase with the use of chimney stoves, barbecues and water heaters in small areas with insufficient ventilation². Considering the developed countries, suicide attempts take the first place in the list of causes of CO intoxication.

The symptoms of CO intoxication are non-specific. Patients often do not understand that they are exposed to CO. Common symptoms of exposure include headache, dizziness, fatigue, nausea, vomiting, and chest pain³. Mild exposure to CO causes headache, myalgia or dizziness, whereas severe exposure will result in confusion, loss of consciousness or death.

Carbon monoxide forms carboxyhemoglobin (COHb), which has an affinity for hemoglobin 250 times greater than its affinity for oxygen; therefore, even low amounts of inhaled CO can cause severe tissue hypoxia⁴. The main reason for the lethal mechanism of intoxication is tissue hypoxia. Survivors of severe CO intoxication may experience cardiac damage and acute neurological pathologies depending on the duration of exposure.

The most important clue to determine the severity of CO intoxication is the clinical condition of the patient. However, if the patient has no evidence of CO exposure in his/her history, this will be inconclusive. Therefore, the final diagnosis requires clinical acumen and a high index of suspicion coupled with epidemiological data, thoughtful clinical examination as well as patient COHb levels, which remains the mainstay for the diagnosis⁵. The main reason why COHb levels alone are insufficient in diagnosis is that the patients' clinical situation at admission is not always consistent with COHb levels. This situation can be explained by the contact with normal atmospheric oxygen after leaving the environment of intoxication and the elimination of COHb during the time of arrival to the hospital6. Therefore, the addition of different laboratory parameters (such as pH, lactate and troponin) to the process of evaluating the severity of intoxications is a guide for clinicians in emergency medicine practice.

Treatment of CO intoxication begins with inhalation of a high concentration oxygen and aggressive supportive care. Hyperbaric oxygen therapy (HBOT) accelerates the dissociation of CO from hemoglobin and may prevent delayed neurologic sequelae^{7,8}.

In our country, the most important clinic in the diagnosis and treatment of cases related to CO intoxication is the emergency medicine clinic. The articles, in which the features of CO intoxication cases and their clinical courses after the admission to the emergency clinic are compiled, constitute easily accessible sources for every doctor. This report describes the epidemiology and analyses the clinic status, treatment, morbidity of CO intoxication cases in a university hospital in Erzurum from 2014 to 2018. Furthermore, the results of blood tests of CO intoxication cases mentioned in this study were evaluated in detail. Based on this data, the usability of blood lactate levels in the emergency services for the diagnosis and treatment of CO intoxication was investigated.

Materials and Methods

The population of this retrospective study included all adults and children who were admitted to the Department of Emergency Medicine of Erzurum Atatürk University with suspected CO intoxication during the years 2014-2018. The study was approved by the Ethics Committee of the same institution. The patients who were diagnosed with 'Toxic effect of carbon monoxide (T58)' were identified through the computerized medical and laboratory records of the hospital. The data extracted from the patients' files included seasonal variation, age, gender, underlying comorbidities, smoking and alcohol abuse history, vital parameters, clinical manifestations and source of intoxication, laboratory and imaging records, treatment and outcome. The application seasons of patients were defined as spring (March, April, and May), summer (June, July, and August), autumn (September, October, and November), and winter (December, January, and February). On admission to the emergency department, blood samples were obtained from patients; blood gas analysis and white blood cell (WBC) and hemoglobin (Hg) counts were done in heparinized tubes, and troponin I, creatinine, creatine kinase (CK) and creatine kinase-MB (CK-MB) levels were measured in anticoagulant tubes. From blood gas analysis, values for pH, bicarbonate, COHb and lactate were evaluated. Mortality was evaluated as mortality during hospitalization. According to COHb level, the patients with 0% -25% COHb were classified as 'mild exposure' (Group 1), 25%-40% were classified as 'moderate exposure' (Group 2), and 40% and above were classified as 'severe exposure' (Group 3).

Statistical analysis

In the statistical evaluation of the data, IBM Statistics 20.0 (SPSS) statistical package program was used. The baseline patient characteristics are presented as frequencies for categorical variables and as medians and interquartile ranges for continuous variables. For continuous variables, Student's t-test or the Mann-Whitney test was used for two group comparisons according to normality, which was tested using the Shapiro-Wilk test. For categorical variables, the Chi-Square test was used. The Spearman correlation analysis was used to evaluate the relationship between laboratory parameters. Receptor operating characteristic (ROC) analysis was used to determine the diagnostic value and cut-off value of lactate levels in predicting HBO treatment status of poisoned patients. In the obtained ROC curve, the Area under the curve (AUC) value is close to 1, indicating that the value of the test is high. Results were evaluated at 95% confidence interval and p < 0.05 at significance level.

Results

A total of 653 patients were included in the study. %56.2 of the cases is female and %43.8 of the cases is male. In addition to the fact that the average age of the people who were the subject of the cases was 37.2 ± 0.7 , the adults (18 years and older) constituted %92.6, while the children and adolescents constituted %7.4. The basic data of the cases are summarized in Table 1. The time interval between exposure and admission to the hospital was calculated to be 5.7±0.3 hours in average. It was found out that the patients in the 337 of the cases (%51.6) had applied to the hospital during the winter months and 159 (%24.3) in spring (Fig 1). The number of cases admitted during the winter was found to be higher than the number of those admitted in the other season with a significant difference (p < 0.001). The CO sources that caused intoxication are listed in Table 2. The rate of most frequent comorbid conditions in the patients who were included in the study were hypertension with % 6.3, chronic obstructive pulmonary disease with %2.1, coronary artery disease with %1.4 and diabetes with %1.4. A history of smoking and alcohol abuse was present in the %18.4 and %0.9 of the patients respectively. The most frequent symptoms were headache (%62.3), nausea (%42.3), sudden loss of consciousness (%15.9) and dizziness (%12.1). In 16 of the patients, there was altered level of consciousness. In terms of suspected cardiac complications, four of them reported palpitation, while eight reported chest pain.

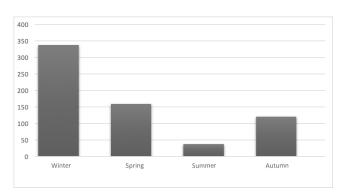


Figure 1. Number of patients approaching emergency department in all years according to seasons.

During the laboratory analyses, the average COHb level was calculated to be 11.5 ± 0.4 . Among the patients, 563 of them had Group 1, 81 of them had Group 2 and 8 of them had Group 3 of COHb level. No significant difference was found between measured COHb levels and demographic characteristics of the patients like age and gender (p>0.05). This is the same for the other evaluated laboratory parameters (WBC, Hg, troponin I, creatinine, CK; CK-MB and lactate). The difference between the lactate levels of Group 1 and Group 2 was statistically significant (mean difference -1.02; 95% CI = -1.43, -0.61) (p <0.001). Moreover, lactate levels were positively correlated with COHb values (r= 0.257, p < 0.001) and troponin I levels (r=0.267, p<0.001).

It was found out that oxygenotherapy had been administered in all the cases, while HBOT had been provided in 352 of them (%53.9). The average COHb level in those ad-

Table 1. Baseline characteristics of the stud	ly po	pulation.
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Variables	Mean + SD or median (IQR) of All Patients		
Age	37.2 ±0.7		
Systolic blood pressure (mm Hg)	125 (115-	136)	
Diastolic blood pressure (mm Hg)	75 (67-8	2)	
Pulse (beats/min)	86.6 ±0.6		
Respiratory rate (breaths/min)	16 (15-1	8)	
Oxygen saturation (%)	96 (94-9	8)	
Temperature (°C)	36.5 (36.2	-36.7)	
COHb (%)	11.5 ±0.4		
Hb (g/dL)	14.2 ±0.8		
WBC (count, /mm ³)	9.4 (7.7-1	1.8)	
Creatinine (mg/dL)	0.7 (0.6-0).9)	
CK (IU/L)	116 (79-1	71)	
CK-MB (IU/L)	21 (16-2	8)	
Troponin I (ng/mL)	0.010 (0.00	-0.016)	
Lactate (mmol/L)	1.6 (1.2-2	2.3)	

Abbreviations: COHb, carboxyhemoglobin; Hb, hemoglobin; WBC, white blood cell; CK, Creatine kinase

ministered HBOT was 13.9±0.6 and the lactate level was 2.1±0.1. We developed a ROC curve to investigate the value of lactate levels in predicting HBO treatment status of poisoned patients. AUC for lactate was calculated as 0.577 (95% confidence interval, 0.53, 0.62; p <0.001). A blood lactate concentration > 2 mmol/L was associated with %40 sensitivity and %75 specificity for predicting HBOT requirement. In the follow-up of the patients, those administered HBOT had a longer hospitalization period compared to the others, which was statistically significant (mean difference -0.98; 95% CI = -1.38, -0.57) (p <0.001). Distribution of clinics where patients were admitted and referred are demonstrated in Figure 2.

Discussion

As there are lots of various systems that are used in daily life and emit CO, the population of intoxication is extremely large. The different age groups may be affected negatively from CO. However, the average age calculated in our study indicates that the frequency of the mid-thirties is higher. This is compatible with the literature⁹.

Being in an indoor environment not ventilated enough during the fuel consumption for heating is the most common reason for intoxication¹⁰. Therefore, the number of cases encountered increases during the winter months. We found that during the winter, there was a higher percentage of CO intoxication than during the other seasons. Furthermore, we found that intoxication were most likely to be caused by the use of warming stoves and water heaters in accordance with similar literature¹¹. The clinical findings of CO intoxication are highly variable. Headache, as expressed in many studies, is a common early symptom of CO intoxication^{12,13}. Among the CO intoxication cases investigated in our study, the most common symptom was headache, followed by nausea and sudden loss of consciousness. The symptoms, signs, and prognosis of acute CO intoxication correlate poorly with the level of COHb measured at the time of arrival at the hospital. Although a history of CO exposure was present among all the cases in our study, the average COHb levels were found to be lower than the studies in the literature^{11,14}. This situation can be related to the fact that the time interval and admission to the hospital was long in the cases of this study. The low levels of COHb themselves did not change our clinical approach towards the patient. As COHb levels alone are not conclusive enough in the diagnosis and treatment, there are some studies that examine the lactate levels in the intoxications due to these levels' relation to tissue hypoxia. The debates about the blood lactate measurements' contribution to CO intoxication are still ongoing. In our study, we found that the lactate levels of the patients correlated with COHb and troponin I levels. Besides, among the exposure groups, it was found that the lactate levels were higher in Group 2 than Group 1 with a significant difference.

The role of HBOT in the management of CO toxicity

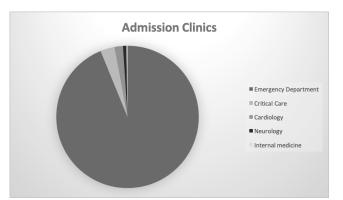


Figure 2. Clinics where patients were admitted and referred.

remains controversial. Clinical Policies Subcommittee of the American College of Emergency Physicians emphasizes that hyperbaric oxygen is a therapeutic option for CO poisoned patients, although its use cannot be mandated¹⁷. In our study, we found that approximately half of CO intoxication cases had received HBOT. This rate is higher than previous studies, and we believe that the differences in the clinical presentation of the patients may be the main cause of this¹. In addition, we found that lactate levels were higher in HBOT group than in other cases. Increased tissue hypoxia in the patients receiving HBOT has been an indicator of the suitability of treatment choice.

In our study, there are some limitations. Only the cases whose data is complete were included in the study, making the sum of the patients few. Furthermore, the data belongs to one region and clinic. Consequently, regional differences are not included in the study. If a similar, but multicentered, study is conducted, it may represent the data of CO intoxication in our country better.

Conclusion

The main reason of CO intoxication cases in our country is the heating systems used in winter months. Raising the public awareness public about CO intoxication and seriousness and taking necessary precautions will reduce the number of

Table 2. Sources of Carbon Monoxide in Intoxicated Cases

Sources	Patients (%)
Stove	70
Water Heater	7.2
Natural Gas	4.6
Fires	3.8
Tandoor Smoke	3.7
Exhaust Fumes	2.1
Gas Cylinder	1.1
Other	0.2

cases. Emergency medicine clinics are fighting almost alone in CO intoxication cases. Now it is required to develop new perspectives in these cases. Lactate measurements can be used safely in the management of patients as an option to facilitate our diagnosis and treatment.

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Original Article

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The Evaluation of Blood Glucose and pH Levels on The Patients Who Attempt Suicide With Drug Overdose

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Abstract

Objectives: Throughout the history of humanity, suicides in all societies are not only a matter of concern to the psychiatrists, but also have economic, cultural and social aspects. The World Health Organization divides the suicides into completed suicides and suicide attempts and determines that the completed suicides result in deaths. Suicide attempts are all non-lethal voluntary attempts to destroy, harm, and poison oneself.

Materials and Methods: Our study was done retrospectively in the emergency department of Faculty Hospital at Atatürk University. The files of the intoxication patients who applied to our hospital between 01.01.2010 and 31.12.2011 were examined. The patients who applied to our hospital after taking pills for suicidal reasons were included in the study. In addition to demographic data such as age, gender, marital status, these patients were classified according to the drugs they took like psychiatric drugs (antidepressant, anxiolytic) and analgesic (paracetamol, NSAID) and antibiotic drugs. Psychiatric diagnose, Glasgow coma score, blood pH at the time of presentation, glucose and hospitalization time(less than 1 day, more than 1 day) were registered.

Results: From the file scan, the data of a sum of 234 patients was reached. 69.7% (n = 163) of the patients were female. The mean age of the patients was 24.64 (\pm 9.463). According to marital status, 75 (32.1%) of the patients were married, 150 (64.1%) were single, 5 were widow (2.1%) and 4 (n = 1.7) patients were engaged. According to the drugs they used for suicide, there were 72 (30.8%) patients who used psychiatric drugs and 83 (35.5) patients who used analgesics and antibiotics. The number of patients that were hospitalized above 24 hours was 38 (16.2%). In the statistical analysis, there was no significant difference between GCS, pH and Glucose values of the patients who committed suicide with Psychiatric and Antibiotic-Analgesic drugs (p> 0.05). Similarly, there was also no significant difference between hospitalization times (p> 0.05).

Conclusion: As a result of our study, it was found that the patients that committed and attempted suicide were under 30 years old and mostly women. Considering the drugs used for suicidal purposes, no difference could be detected between the use of analgesic-antibiotics and psychiatric medication on blood parameters and GCS.

Keywords: suicide attempts, drug overdose, glucose, ph, blood analyzes

Özet

Giriş: İnsanlık tarihi boyunca bütün toplumlarda her zaman görülen intihar sadece ruh hekimlerini ilgilendiren bir sorun olmayıp ekonomik, kültürel ve toplumsal yönleri vardır. Dünya Sağlık Örgütü, intiharları gerçek intiharlar ve intihar girişimleri olarak ikiye ayırarak gerçek intiharları ölümle sonuçlananlar olarak belirlemektedir. İntihar girişimleri ise bireyin kendisini yok etmek, zarar vermek, zehirlemek amacıyla gerçekleştirdiği intihara yönelik, ölümcül olmayan tüm istemli girişimlerdir.

Gereç-yöntem: Çalışmamız Atatürk Üniversitesi Tıp Fakültesi hastanesi Acil servisinde retrospektif olarak yapılmıştır. Çalışmamız için 01.01.2010-31.12.2011 tarihleri arasında hastanemize başvuran intoksikasyon hastalarına ait dosyalar incelenmiştir. Çalışmamız içinde belirlenen tarih aralığında hastanemize ilaç içme sonrası başvuran hastalar dahil edilmiştir. Bu hastaların yaş, cinsiyet, medeni durum gibi demografik verilerine ek olarak aldığı ilaçlarda psikiyatrik ilaçlar(antidepresan, anksiyolitik) ve analjezik(parasetamol, NSAİD) ve antibiyotik ilaçlar olarak gruplandırılmıştır. Hastanede yattığı süre içerisinde psikiyatri konsültasyonu sonrası aldığı psikiyatrik tanı, Glasgow koma skoru, başvuru anı kan ph, glikoz ve hastanede kalış süresi (1 günden az, 1 günden çok olmak üzere) kayıt altına alınmıştır.

Bulgular: Dosya taramasından toplam 234 hasta verisine ulaşıldı. Hastaların %69,7'si (n=163) kadın cinsiyette idi. Hastaların yaş ortalaması 24,64(±9,463). Medeni durumlarına göre hastaların 75 tanesi (%32,1) evli, 150 tanesi (%64,1) bekar, 5 kişi dul (%2,1) ve 4 (n=1,7) hasta ise nişanli idi. Hastaların intihar amaçlı kullandıkları ilaçlara göre psikiyatrik ilaç kullanan 72 (%30,8), analjezik ve antibiyotik kullanan 83 (35,5) hasta vardı. Hastalardan 24 saat üzerinde hastanede yatan hasta sayısı 38 (%16,2) idi. Yapılan istatistiksel analizde psikiyatrik ve Antibiyotik-Analjezik ilaçlar ile intihar eden hastaların GKS, PH ve Glikoz değerleri arasında anlamlı fark yoktu. (p>0,05) aynı şekilde aldıkları ilaç çeşidine (psikiyatrik, analjezik-antibiyotik) göre hastanede yatma süreleri arasında da anlamlı fark yoktu(p>0,05).

Tartışma: Çalışmamızın sonucunda intihar ve intihar girişimi olan hastalarda; kadınların çoğunlukta olduğu ve hastalarımızın çoğunun 30 yaşın altında olduğu bulundu. İntihar amaçlı kullanılan ilaçlar göz önüne alındığında analjezik-antibiyotik ile psikiyatrik ilaç alınmasının, kan parametreleri ve GKS üzerinde bir fark tespit edilememiştir.

Anahtar Kelimeler: intihar girişimi, ilaç overdoz, glukoz, ph, kan analizi

Introduction

Throughout the history of humanity, suicides in all societies are not only a matter of concern to the psychiatrists, but also have economic, cultural and social aspects^{1,2}. The World Health Organization divides the suicides into completed suicides and suicide attempts and determines that the completed suicides result in deaths. Suicide attempts are all non-lethal voluntary attempts to destroy, harm, and poison oneself². Many psychosocial risk factors are considered to contribute to the suicide risk. Suicide risk also increases in situations such as marriage problems, unemployment, low socioeconomic status, living alone, migration history, stress-ful life, death of a relative, job loss and detention^{3, 4}. Drug intoxication is one of the reasons for admission to emergency services. Drug intoxications often occur as a result of accidental ingestion in children and suicide in adults. Although it is one of the common problems encountered in emergency services in our country, it is very difficult to reach a reliable morbidity and mortality statistics⁵.

Toxicology is divided into three main sub-branches as industry, economic and forensic toxicology. Industrial toxicology examines the harmful effects of chemical pollutants in air and water, and also discusses the existing pollutants at the work and home. Economic toxicology examines chemicals in drugs, food additives, cosmetics, fertilizers and veterinary drugs. Forensic toxicology, in particular, investigates the medical aspect of cases that result in death or serious injury. Drugs are used for healing, while poisons are used for killing. However, if an overdose is the case, this generally means that the drug is used as poison. Suicide is the most common form of death due to intoxication. Cyanide, arsenic and other toxic substances are common, but the cause of suicides is most commonly prescribed drugs. People who have psychiatric disorders can easily access drugs that can be lethal when taken in large amounts to deal with the symptoms of these diseases⁶.

In our study, the patients who had taken high doses of drugs used for medical purposes and received inpatient treatment in our hospital afterwards, were examined. Changes in blood biochemistry and Glasgow coma scores were examined according to the medications taken by the patients.

Materials and Methods

Our study was done retrospectively in the emergency department of Medical Faculty Hospital at Atatürk University. The files of the intoxication patients who applied to our hospital between 01.01.2010 and 31.12.2011 were examined. The hospital in which our study is performed is a central hospital providing third step health services in eastern Anatolia. The patients who were admitted to our hospital after taking drugs for suicidal reasons at aforementioned date range were included in this study. In addition to demographic data such as age, gender, marital status, these patients' drugs were classified according to the drugs like psychiatric drugs (antidepressant, anxiolytic) and analgesic (paracetamol, NSAID) and antibiotic drugs. During their stay in the hospital, psychiatric diagnosis after psychiatric consultation, Glasgow coma score, blood pH at admission time, glucose and hospital stay time (less than 1 day, more than 1 day) were registered.

Descriptive statistics were reported as proportions for categorical data and as mean \pm standard deviation for continuous numeric variables. We performed a series of uni-

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variate analyses using the independent t test for numeric variables and the Chi-square test for categorical variables. In defining independent variables, we accepted p<0.05 in univariate analyses as the numbers in each groups were sufficient. The statistical analysis was performed using SPSS software (released 2011; IBM SPSS Statistics for Windows, Version 20.0, IBM Corp., Armonk, NY).

Results

From the file scan, the data of a sum of 234 patients was reached. 69.7% (n = 163) of the patients were female. The ages of the patients ranged from 14 to 88 and the mean was 24, 64 (\pm 9,463). According to the marital status, 75 (32.1%) of the patients were married, 150 (64.1%) were single, 5 were widowed (2.1%) and 4 (n = 1.7) patients were engaged. According to the drugs they used for suicide, there were 72 (30.8%) patients who used psychiatric drugs and 83 (35.5) patients who were using analgesics and antibiotics. The classification of the patients according to their diagnosis after psychiatric consultation is summarized in Table-1.

The number of patients that were hospitalized above 24 hours was 38 (16.2%). Their classification according to Glasgow coma score and blood parameters of patients are shown in Table-2.

Table 1. Classification of the patients according to their diagnosis after psychiatric consultation

	Number (n)	Percentage (%)
No psychiatric diagnosis	143	31,1
Impulsive Suicide	67	28,6
Major depressive disorder	20	8,5
Obsessive compulsive disorder	2	0,9
Bipolar	1	0,4
Psychosis	1	0,4
Total	234	100

In the statistical analysis, there was no significant difference between GCS, PH and Glucose values of the patients who committed suicide with Psychiatric and Antibiotic-An-

Table 2. Classification of patients according to blood parameters and Glasgow coma score

	N	Minimum	Maximum	Mean	Standard deviation
GCS	234	3	15	14,18	2,559
PH	195	6,85	7,62	7,39	0,077
Glucose	219	67,7	442	110,67	41,40

algesic drugs (p> 0.05). Similarly, there was no significant difference between hospitalization times according to the type of medicine they took (p> 0.05).

Discussion

The cause of suicide varies from one individual to another. Generally, there is a motive of frightening their relatives, punishment, anger or a need escape for intense shame.

Crisis situations involving parasuicide risks are closely related to negative and stressful life events. Volant stated that the feeling of exhaustion and depressions that lead to the suicidal tendencies were observed in women. According to Volant, poverty and low education level as well as their inability to integrate with the society have a significant impact on the emergence of women's depression⁷. The suicide rate for men is more than women in all regions in Turkey. It is seen that female suicides are more than male suicides in South East Anatolia Region⁸. Şenol and his friends found female / male ratio as 1/7 in their studies in Kayseri⁹. In a study by Ambade and his friends, the rate of deaths from suicide was found to be 62.5% for men, 37.5% for women and 1.7: 1 for ratio¹⁰. Women's suicide rate in China is 25% higher than in men¹¹. This situation is similar in our study.

Suicide prevalence is the highest in the males over 45 years of age. After the age of 55, it was observed that the number of completed suicides had increased. The number of suicide attempts in older men is low, but the rate of completed suicide is high. Suicide attempts are common in the patients with psychiatric disorders. They are observed between the ages of 20 and 40 in the patients with mood disorders. They are seen in all ages between childhood (5-6 years) to 50 years of age (rarely older) in bipolar patients^{12, 14}. In major depression, suicide is more common in all ages, but is usually more common in those who are 30 to 40 years¹⁵. The suicides in Turkey show a density of ages 15-24 and ages 25-34. While the women of 15-24 years old and younger than 15 years old have a higher rate, males have higher rate in other age group⁸. This situation is similar in our study.

In the United States, the rate of suicide in the married is 11/100000, while the rate of unmarried people is almost twice as much. Being a man raises rates here. The proportion of suicide in the divorced men is 69/100000, whereas it is 18/100000 in the divorced women, which is lower. The majority of individuals who attempt suicide in Europe are single, widowed or alone¹⁶. In a study, the rate of divorced or separated people is 11 times higher than those without risk¹⁷. Divorce rates are less common in the eastern part of our country than the western part. The highest suicide rate in our country is seen in the Aegean region¹⁸. In our study, the majority of those who attempted suicide are single.

In our study, our patients who attempted suicide with medications used for psychiatric purposes consist of approximately 30%. This situation is an indication of the use of these drugs by the patients themselves or someone from their family. After all, the people with psychiatric disorder or who have someone with one are more prone to suicide. Among the patients, 35% of the drugs used for suicide were analgesics and antibiotics.

This ratio was also expected to be high. Analgesic and antibiotic groups are the most commonly used drugs in households. In our study, we investigated the effect of psychiatric medication and analgesics-antibiotics on the blood parameters of patients. GCS score was also evaluated. As a result of this study, no difference was found between these drugs.

Conclusion

As a result of our study, it was found that patients that committed and attempted suicide were mostly women and under 30 years old. Considering the drugs used for suicidal purposes, no difference could be detected between the use of analgesic-antibiotics and psychiatric medication on blood parameters and GCS.

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Original Article

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Demographic Analysis of Suicide Victims Presenting to The Emergency Department with Drug-induced Intoxication

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Abstract

Objective: To investigate the demographic data of patients who applied to our clinic with suicide attempt between the years 2014 and 2016.

Materials and Methods: The patients with suicidal attempt were analyzed retrospectively. The demographic characteristics of the patients such as gender, age, marital status, residence address and the way of suicide attempt, occupations, educational status and treatment modalities in emergency department were examined and discussed.

Results: A total of 79 patients were included in the study. The mean age of the study group was 25.2 years and the standard deviation was 9.2. Fourty two of the patients (53.2%) used more than one type of drugs and 37 patients (46.8%) used single drug. At the emergency medicine follow up, 81% (n: 64) of the patients were applied gastric lavage as well as active charcoal and IV drip, while gastric lavage and active charcoal was applied to 3.8% (n: 3), only gastric lavage was applied to 2.5% (n: 2). Patients with IV drip and active charcoal combined were 5.1% (n: 4) and also only IV drip was applied to 5.1% (n: 4).

Conclusion: It is clear that the first attempts are very important in psychological and physiological aspects. Although there is not enough study, these units in which emergency interventions are carried out are units that may have serious effects on survival rates.

Keywords: demographics, drug Intoxication, suicide.

Özet

Amaç: Bu çalışmanın amacı 2014 - 2016 yılları arasında kliniğimize intihar girişimi ile başvuran hastaların demografik verilerini araştırmaktır.

Gereç ve Yöntem: İntihar girişimi olan hastalar geriye dönük olarak incelendi. Hastaların cinsiyet, yaş, medeni hal, ikametgah adresi, intihar girişim şekli, meslek, eğitim durumu ve tedavi yöntemleri gibi demografik özellikleri incelenmiş ve tartışılmıştır.

Bulgular: Çalışmaya toplam 79 hasta dâhil edildi. Çalışma grubunun yaş ortalaması 25.2, standart sapma 9.2 idi. Hastaların 40'ı (% 53,2) birden fazla ilaç türü, 37'si (% 46,8) tek tip ilaç kullanmıştı. Acil servis takiplerinde hastaların% 81'ine (n: 64) gastrik lavaj, aktif kömür ve IV tedavi birlikte verilmişti, % 3.8'ine (n: 3) gastrik lavaj ve aktif kömür, % 2.5'ine (n: 2) sadece gastrik lavaj ve % 2.5'e (n: 2) ise yalnızca aktif kömür uygulanmıştı. IV terapi ve aktif kömür birlikte alanların oranı % 5.1 (n: 4) ve sadece IV terapi alanların oranı %5.1'di (n: 4).

Sonuç: İlk intihar girişimlerinin psikolojik ve fizyolojik açıdan çok önemli olduğu açıktır. Yeterli çalışma olmamasına rağmen, ilk müdahalelerinin yapıldığı acil servisler, hayatta kalma oranları üzerinde ciddi etkileri olabilecek yerlerdir.

Anahtar Kelimeler: intihar, ilaç zehirlenmesi, demografik analizler

Introduction

A suicide attempt can occur in the normal population and also in people with a psychiatric disorder and may sometimes be fatal. The occurrence of a high number of cases requires studies to be carried out on this issue and prevention of suicidal attempts by protecting risk groups.

In order to contribute to these studies, we aimed to investigate the demographic data of patients who applied to our clinic with suicide attempt between 2014-2016.

Materials and Methods

This study was carried out between 2014 and 2016 in Erzurum Atatürk University Faculty of Medicine, Department of Emergency Medicine with the examination of patients that attempts suicide. 79 patients were included in this study and their demographic characteristics such as educational status, occupations, ways of suicide attempt and treatment modalities were discussed.

Results

77.2% (n: 61) of the cases were female. The youngest of the individuals were 16 years old and the oldest was 64 years old. The mean age of the study group was 25.2 years and the standard deviation was 9.2 [mean: 25,2, SD:9,2]. While the marital status of 45.6% (n: 36) of all cases was married, 51.9% (n: 41) were single, and one of the remaining 2 were widowed and one was divorced. 54.4% of the cases (n: 43) were living in the city center while 15.2% were living in the district and 10.1% were living in the rural areas. 20.3% (n: 16) patients were referred from out of the city. The occupations of the cases are given in table 1. In Table 1, the group with no occupation was grouped as "other" and these cases accounted for 57% (n: 45) of the study group.

Of the 79 patients who had committed suicide with drugs, 53.2% (n: 42) used more than one type of drugs and 46.8% (n: 37) used single drug. When we look at the education level of the patients that included in this study, 19 people were graduated from university and 19 people were graduated from high school and 26 people were primary school graduates. While 4 people had literacy, 11 people had not literacy.

Patients were also evaluated in terms of treatment in the emergency department. 81% (n: 64) of the patients were applied gastric lavage as well as active charcoal and IV drip, while gastric lavage and active charcoal was applied to 3.8%

(n: 3), only gastric lavage was applied to 2.5% (n: 2) and only active charcoal was applied to 2.5% (n: 2). Patients with IV drip and active charcoal combined were 5.1% (n: 4) and also only IV drip was applied to 5.1% (n: 4).

Discussion

The suicide attempt of a person is caused by many factors, both socially and psychological. The complex nature of the suicide pattern leads to research and, consequently, to study on measures. The fact that it can result in death forces this situation to accept that it is a social phenomenon. In Turkey, women constitute more suicide case both in terms of number of attempts and in terms of mortality¹. Bercz and Bercz's friends found that suicide rates were 3 to 4 times higher in males than females².

A study by Gönenç showed that suicide attempts were more frequent in singles with a rate of 56.3%. Also in our study group, suicide of singles was similar with 51.9%³. In the study which Acar examined the suicide cases who applied to the emergency room, it is stated that the suicides were mostly the single individuals (50%), however, it is stated that a significant percentage of married people (31%)

Occupation						
	Frequency	Percent	Valid Percent	Cumulative Percent		
Valid Driver	2	2,5	2,5	2,5		
Bank staff	2	2,5	2,5	5,1		
Military staff	4	5,1	5,1	10,1		
Secretary	3	3,8	3,8	13,9		
Worker	4	5,1	5,1	19,0		
Teacher	2	2,5	2,5	21,5		
Craft	5	6,3	6,3	27,8		
Midwife	3	3,8	3,8	31,6		
Veterinary	2	2,5	2,5	34,2		
Farmer	2	2,5	2,5	36,7		
Security guard	1	1,3	1,3	38,0		
Accountant	2	2,5	2,5	40,5		
Medical Stuff	1	1,3	1,3	41,8		
Unqualified worker	1	1,3	1,3	43,0		
Other	45	57,0	57,0	100,0		
Total	79	100,0	100,0			

Table 1. Occupational distribution of patients with suicide attempt

applied to the emergency department due to suicide, too⁴. In another study, the risk of suicide was found to be 11 times higher in divorced or separated individuals⁵. In our study, as seen in many studies, more than half of those who commit suicide are younger than 35 years^{6,7}. In accordance with the literature, a study carried out in our country reports that 59% of suicide cases applied to the emergency department are in the 16-24 age group⁸. In our study, 50 patients (63.4%) were in this age group. In another study, the age range of the most suicide cases applied to the emergency department has been reported to vary between 25-34⁹.

Conclusion

Suicide cases are frequently admitted to emergency services and 112 ambulance service. It is clear that the first attempts are very important in psychological and physiological aspects. Although there is not enough study, these units in which emergency interventions are carried out are units that may have serious effects on survival rates.

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Original Article

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Demographic and Clinical Features Of Applications To The Emergency Service For Suicide Attempts

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Abstract

Introduction and Objectives: Parasuicide is an important health problem which frequently occupies our emergency services and shows the possibility of future suicides. The investigation of the epidemiological and clinical features of parasuicidal patients in our region will guide us in approaching these patients.

Method: Adult parasuicidal patients who were admitted to our emergency department in 45 months were examined according to their gender, the way they came from the inside/outside of Erzurum province, the suicide form, the application season and complaints for the patients who were intoxicated with medication. In the groups, the parameters which were found to be significant with x2, t test or Mann Whitney U test were examined by multivariate analysis.

Results: A total of 533 patients, 66.8 percent of whom were females, were more likely to have suicide attempts in married women and single men. Antidepressant intoxication is higher in females, while salicylate and alcohol intake is higher in males. Aggressive suicides are more common in males and non-aggressive suicides are more common in females. Patients referred from outside the province of Erzurum are usually patients with organophosphate poisoning and loss of consciousness. Suicidal attempt is most commonly seen in the spring. While the rate of attempted suicide was higher in spring with antidepressant drug; In the summer, the rate of attempting suicide by taking organophosphate is high.

Conclusion: There are significant differences in the parasuicidal patients admitted to our emergency department according to the grouping mentioned in the methods. These data will provide guidance for treatment planning and follow-up in ED.

Keywords: suicide attempt, turkey, overdose, intoxication, aggressive, suicide intent

Özet

Amaç: Parasuisid acil servislerimizi sıkça meşgul eden ve ileride gerçekleşecek suisid ihtimalini gösteren önemli bir sağlık sorunudur. Bölgemizdeki parasuisid hastalarının epidemiyolojik ve klinik özelliklerinin incelenmesi bize, bu hastalara yaklaşımda yol gösterecektir.

Gereç ve Yöntem: Acil servisimize 45 ayda gelen yetişkin parasuisid hastaları kesitsel olarak cinsiyetlerine, Erzurum il sınırı içi/dışından gelmelerine, intihar şekline, başvuru mevsimine ve ilaçla zehirlenen hastalar da şikayetlerine göre incelenmiştir. Gruplarda x2, t testi veya Mann Whitney U testi ile anlamlı görülen parametreler mutivarite analizle incelenmiştir.

Bulgular: Yüzde 66,8'i bayan olan toplam 533 hastanın incelenmesinde, evli kadınlarda ve bekâr erkeklerde intihar girişimlerinin daha fazla olduğu görülmüştür. Antidepresan ile zehirlenme bayanlarda, salisilat ve alkol alımı ise erkeklerde daha yüksektir. Agresif suisidler erkeklerde, agresif olmayan suisidler ise bayanlarda daha sık görülmektedir. Erzurum il dışından sevk edilen hastalar genellikle organofosfat zehirlenmesi olan hastalar ve şuur kaybı olan hastalardır. İntihar girişimi anlamlı olarak en sık ilkbaharda görülmektedir. İlkbaharda antidepresan ilaç alarak intihara teşebbüs oranı fazla iken; yazın organofosfat alarak intihar girişiminde bulunma oranı fazladır.

Sonuç: Acil servisimize başvuran parasuisid hastalarının metodlarda değinilen gruplandırmaya göre incelenmesinde önemli farklılıklar göze çarpmaktadır. Acil serviste tedavi ve takibin planlamasında bu veriler yol gösterici olacaktır.

Anahtar kelimeler: intihar girişimi, türkiye, doz aşımı, zehirlenme, agresif, intihar amacı

Introduction

Throughout the history of mankind, the suicidal attempt in all societies is not only a matter of concern to psychiatrists, but also has economic, cultural and social aspects^{1,2}.

World Health Organization defines suicide in two groups as committed suicide and attempted suicide. Committed sui-

cides result in death according to definition of WHO³⁻⁵. Suicide attempts are all non-lethal voluntary attempts to destroy, harm, poison themselves². Sociodemographic risk factors of suicide include male gender, unemployment, poverty, being single, divorced, widowed or separate living and puberty^{6,7}. There are reports that the level of education is low in the groups showing suicide attempts^{8,9}.

Corresponding Author: Sultan Tuna Akgöl Gür **e-mail:** sultantuna@hotmail.com **Received:** 28.11.2018 • **Accepted:** 11.01.2019 ©Copyright 2018 by Emergency Physicians Association of Turkey - Available online at www.ejtoxicology.com Depression in societies causes changes in suicide rates. Emile Durkheim, in his classic work which was published more than a century ago, is known to examine suicide in three ways based on the effect of social change and social integration levels¹⁰:

- 1- **Egoistic suicides:** It is defined as the suicide incident that occurs when social ties are loose and when the individual feels lonely, due to the lack of integration with the social environment of the individual.
- 2- **Benevolent (Altruistic) suicides:** Individual life is strictly regulated by customs, traditions and habits, and it means that they kill a person when the commandments (whether religious or political nature) of the community require it.
- 3- Normless (Anomic) suicides: It is described that the change in the structure of the society as causing the chaos by disrupting the living conditions and moral values of the individual. This is due to social instability, which leads to moral instability and loss of the norms we are familiar with.

In our country, commited suicides occurs in females between first 15-24 years and in males first 15-34 years of life according to Turkey Statistics Institute¹¹. Rates of suicide are 3,5 times higher in males than females in all over the world. However, suicide attemptions are 4 times higher in females than males¹².

Education level is most important indicator amongst socio-economical level¹³. Risk factors are low socio-economical level, low education level, low income, and poor life conditions¹⁴. Rates of sucide are higher in unemployed individuals than employed ones. Suicide rates increase during economical crisis and in the period of higher unemployment rates and decreases during good economical state end war times, contrarily¹⁵. Behaviours of parents are directly linked to character, personality, psychopathology and orientation of the offspring¹⁶⁻¹⁸.

Altough rates may vary in different countries, most preffered three methods of suicide are self-intoxicatin by drugs (analgesics, antibiotics, antidepressants, antihistamines and corrosive drusgs), self-hanging and shooting by gunshot¹⁹.

One chooses easily recruitble substances for a painless death. Suicidal ones uses the materials most easy to reach to die, for instance drugs in urban, insectisides in rural areas.

Altough poisoning by accident is common in other countries, drug intake for suicide is more common in developed countries. Insectisides and organophosphates are becoming more problematical in developing countries^{20,21}. Parasetamol is most common drug in England but alcohol and psychatric drugs are more common in Finland²⁰.

Alcohol usage is 2 times higher in males than females. Alcohol levels are 4,9 times higher in the cases of suicide by gunshot²²⁻²⁴. Both genders are more prone to sucide during months of may and june, additionally another peak is seen in females during october²⁵. Among the methods of suicide attempt in patients admitted to our hospital include drug intake, gunshot injuries, hang oneself, high jump, self-mutilation with a sharp object, jumping infront of a vehicle, self-burning, exposure to toxic substances and other methods. In this study; We aim to evaluate the patients who applied to our emergency department due to suicide attempt in terms of demographic characteristics (age, gender, race, religion, education, occupation, marital status, geographic factors), cost, the problem that caused suicide and the method used.

Material and Method

It was planned to include patients aged 16 years and over who were admitted to the Emergency Service of the Academic Emergency Department of Atatürk University Faculty of Medicine, between May 2008 and January 2012. Non-suicidal drug intoxications and accidental injuries and accidents were excluded from the study. During the first admission and follow-up, registration of medical interventions, consultations, follow-up and treatment clinics, psychiatric support and psychiatric diagnoses and calculation of the time from initial presentation to diagnosis and biochemical data of this process, were planned.

After the first admission and evaluation of the patients who applied to the emergency service with suicide attempt, the demographic data of the patients, complaints, symptoms and findings, the psychosocial status before the suicide attempt, the reason of attempted suicide and the method of suicide, if a drug and /or toxic substance selected for suicide where they provided it, medical and social histories were planned to be taken from patients or their relatives.

This study is a cross-sectional study of 533 parasuicid cases admitted to our emergency department between May 2008 and January 2012 (45 months). An informed consent form was obtained from each patient regarding the study, agreeing to participate in the study. For statistical analysis, SPSS.19 (Statistical Package for Social Sciences) for Mac (SPSS Inc., Chicago, IL, USA) program was used when evaluating the calculated data. Averages were shown with standard deviations. Statistical analysis of categorical variables was done by "chi-square" test and numerical variables were analyzed by "t test" and Mann Whitney U test. The data were divided into groups and logistic regression analyzes were performed. Results were accepted as significant at p <0.05 level.

Results

Of the 533 patients included in the study, 66.8% (n = 356) were female, and the average age of all patients was 25.7 ± 9.9 (minimum 14, maximum 88). The distribution of the patients who applied to our emergency department according to years is given in the table. In 2009-2010-2011, there was no difference according to gender among the applicants for suicide attempt in the emergency department (P> 0.05).

Patients attempting suicide by taking antidepressants were significantly higher in women than men (30.9% to 19.8%; P = 0.007) and ethanol intake was significantly higher in men than in women (4.5% to 0.6%; P = 0.002) (Table: 1).

There are also significant differences in sociocultural characteristics of patients by gender. It was found that women were generally less educated than men (Table 2). Parasuisid rates increase in the case of being married in females (42.4% vs. 32.2%) and in males in the case of being single (67.8% vs. 57.6%) (P = 0.023) (Table 2). The employment status of patients admitted to the emergency department according to gender reflects the general employment situation of eastern and northeastern Anatolia and being unemployed is significantly higher in females than males (63.5% to 31.6% P = 0.001) (Table 2).

Discussion

In our study, the majority of patients who attempted suicide are young married or single housewives and these patients are char-

Table 1. Examination of the drugs taken by patients acco	or-
ding to gender	

Drug	Female	Male	Р
Drug	n (%)	n (%)	1
Organophosphate	41	20	0,533
intake	(%11,5)	(%11,3)	,
Antidepressant	110	35	0,007
intake	(%30,9)	(%19,8)	
Analgesic intake*	73	35	0,843
	(%20,5)	(%19,8)	
Antihypertensive	14	12	0,151
intake	(%3,9)		
Salicylate intake	9	10	0,067
	(%2,5)		
Paracetamol intake	67	24	0,128
	(%18,8)	(%13,6)	
Antibiotic intake	52	16	0,070
	(%14,6)		
Other medication	212	92	0,096
intake	(%59,6)	· /	
Ethanol in blood	2	8	0,002
	(%0,6)	(%4,5)	
TCA in urine	16	4	0,201
	(%4,5)		0.100
THCB in urine	5	6	0,129
D 1' · · ·	(%1,4)		0.005
Benzodiazepine in urine	9	2	0,285
D (1' '	(%2,5)		0.(27
Paracetamol in urine	24 (%6,7)	10 (%5,6)	0,627
	(/00,/)	(705,0)	

acterized by low educational status. In some studies from our country, "a similar relationship was found" also encountered in the patient group^{26,27}. We thought that the feudal way of life in our region caused social pressure on women and women were not able to decide about their lives, so women could not find a way out and expressed their helplessness through suicidal behavior. In addition, this situation may be explained by some biological differences between women and men, as well as the differences in coping ways used by men and women. It also supports the idea that women are more affected by the events they experience than men and that women are more open and comfortable than men in terms of asking for help²⁸.

In general, it may be based on socio-cultural reasons such as family incompatibility, low literacy rate, difficulties or prevention of girls having education, immigration from rural to urban, forced marriage in early age, marriages based on religious wedlock, social changes, rapid role changes, the fact that young girls cannot tolerate their own realities in a patriarchal society as a result of their contradiction with a different culture presented by media.

Suicidal attempt rates of married people are lower than singles, suggesting that marriage is a strong preventive against suicide. In a study conducted at Erciyes University in Kayseri, suicide was found to be more prevalent in single men and married women in accordance with our findings²⁹. While marriage increases the responsibilities and roles of a woman, it seems to be an institution that causes less change in the basic factors of life of a man in our country. Our data also show that women's suicide attempts increased by marriage, which could explain this situation.

Conclusion

With the social and economic changes experienced in and around Erzurum province, it can be predicted that suicidal behavior will increase and will continue to increase and it will be a serious public health problem over time. In our study, we found that suicidal attempts were more common in married women and single men. As a result of our study, in patients with suicide and suicide attempt; women were in the majority and most of our patients were under 30 years of age. In suicide and suicide attempt methods, drug intake was found mostly.

The existence of sociological, biological and psychological aspects of suicide and suicide attempts and eliminating the risk factors associated with them are vital to prevent suicide attempts. In our emergency service when we encountered a patient who attempted suicide; the health care personnel should provide the patient with adequate and appropriate time, try to understand the patient, and gain the patient's trust by acting calmly and carefully. The condition of patients who attempted suicide should be informed to their family.

Sociocultural characteristic		Female n (%)	Male n (%)	Р
Education	Not literate	39 (%11)	1 (%0,6)	<0,0001
	Literate	26 (%7,3)	6 (%3,4)	
	Primary education	113 (%31,7)	63 (%35,6)	
	High school	112 (%31,5)	78 (%44,1)	
	University	63 (%17,7)	28 (%15,8)	
	Unknown	3 (%0,8)	1 (%0,6)	
Marital Status	Married	151 (%42,4)	57 (%32,2)	0,023
	Single	205 (%57,6)	120 (%67,8)	
Employment status	Employee	31 (%8,7)	72 (%40,7)	0,001
	Unemployed	226 (%63,5)	56 (%31,6)	
	Student	92 (%25,8)	36 (%20,3)	
	Unknown	7 (%2)	13 (%7,3)	

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Aluminum Phosphide Intoxication

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Abstract

Phosphine gas is a gas that is frequently used as rodenticide and insecticide due to its high diffusion capacity and the absence of residues in agricultural products. Since this gas is highly toxic, it is found in our country as aluminum phosphite tablets impregnated with clay, these tablets emit phosphine gas when they meet with the moisture in the air or gastric hydrochloric acid. Mortality rates in aluminum phosphite intoxications are 40-80% depending on the exposure dose. There is no control mechanism in the supply of aluminum phosphide tablets which are so dangerous and no information is given about the serious conditions that may occur during the use of these tablets. A 2 month old baby, whose family practiced drying pepper-eggplant, was reported to have been exposed to phosphine gas by inhalation, admitted to hospital with vomiting and cyanosis and lost his life within 24 hours. We present our case, who lost his life due to erroneous usage of aluminum phosphite, with additional emphasis on early diagnosis, treatment and gathering sample for toxicologic analysis, with corresponding forensic and medical documents.

Keywords: aluminum phosphide, autopsy, toxicology, intoxication

Özet

Fosfin gazı difüzyon kapasitesinin yüksek olmasından ve tarımsal ürünlerde kalıntı bırakmamasından dolayı rodentisit ve insektisit olarak sıklıkla kullanılan bir gazdır. Bu gaz oldukça toksik olduğundan preparat olarak kile emdirilmiş alüminyum fosfit tabletleri olarak ülkemizde bulunmakta, bu tabletler havadaki nem ya da mide de hidroklorik asit ile karşılaştığında fosfin gazı ortaya çıkmaktadır. Maruz kalınan doza bağımlı olarak alüminyum fosfit intoksikasyonlarında mortalite oranları %40-80 olarak belirtilmiştir. Bu kadar tehlikeli olan alüminyum fosfit tabletlerinin temininde ülkemizde herhangi bir kontrol mekanizması olmadığı gibi bu tabletlerin kullanımı sırasında oluşabilecek ciddi durumlar hakkında herhangi bir bilgilendirme de yapılmamaktadır. Ailesi biber-patlıcan kurutuculuğu yapan 2 aylık bebeğin inhalasyon yoluyla fosfin gazına maruz kaldığı, kusma ve morarma şikayetleriyle hastaneye kaldırıldığı ve 24 saat içerisinde hayatını kaybettiği bildirilmiştir. Bilinçsiz kullanılan alüminyum fosfite bağlı gelişen intoksikasyon sonucu hayatını kaybeden olgumuzu erken tanı-tedavinin ve toksikolojik inceleme için örnek alımının önemi vurgulanarak adli ve tıbbi belgeler eşliğinde sunuldu

Anahtar kelimeler: alüminyum fosfit, zehirlenme, otopsi, toksikoloji

Introduction

Aluminum phosphite tablets are frequently used to protect stored agricultural products from rodents and insects¹. The most common cause of aluminum phosphite poisoning is suicide attempts and it is followed by accidental intoxications. This preparation has recently been identified as one of the most commonly used agents in suicide attempts in Iran². Likewise, in a study conducted in India; organophosphate poisonings were found to be the most common cause of poisoning cases until 1982, while aluminum phosphite poisoning became the most common factor in the period after 1982³. As a result of a series of chemical reactions after aluminum phosphide tablets come into contact with air or encounter with gastric acid; highly toxic phosphine gas occurs. Phosphine gas in general inhibits cytochrome c enzyme, disrupts the use of oxygen at the cellular level and causes an increase in free oxygen radicals. This may result in multiple organ failure and death⁴⁻⁵. Despite good ICU follow-up, the mortality rate is high in the patients who are admitted to the hospital late and the exposure dose is high and this ratio is 40-80% in the literature⁶⁻⁷.

We will present a 2-month-old infant case who was exposed to intoxication as a result of unconsciously used aluminum phosphide tablets in the presence of autopsy reports, forensic and medical documents.

When the forensic and medical documents of the patient was examined; it was seen that the 2-month old baby was admitted to hospital with vomiting and bruising. It was learned that the baby's family were making dry eggplant and pepper trade. They put pesticide (aluminum phosphite) tablets just twenty four hours ago onto the dried vegatables with fumigation purposes in the room next to the room where they slept. It was learned that the baby was vomited within 5-6 hours after the tablets were placed and then he was put to sleep by his mother. It was learned that the baby's father had resistant vomiting starting in a few hours after putting the tablets and that he was admitted to hospital and received treatment for intoxication. Twelve hours after the administration of the tablets, it was reported that the baby was admitted to the hospital after the bruising. It was reported that cardiac arrest developed shortly after admission and the baby died at the second hour of admission.

In the crime scene review; it was reported that there was a smell similar to intense garlic smell at home. It was seen that there were dry vegetables next to the room where the beds were located, and it was also recorded that "Dephos" written packaging was found on the floor of the room where those vegetables were dried.

In the baby's autopsy report; no prominent pathology was detected other than single petechial hemorrhage in the scalp, on the surface of the heart and in the lungs. Blood, urine and adipose tissue samples were taken for toxicological examination and tissue samples were taken for histopathological examination. In toxicological examination; no substances in the systematics of the Chemical Specialized Department of Forensic Medicine Institute (including pesticides) were found. Histopathological examination revealed no special features other than intraalveolar fresh hemorrhage. As the exact cause of death could not be determined; it was reported that the Council of Forensic Medicine should be consulted by the First Specialized Board of Council of Forensic Medicine.

In the case of the the First Specialized Board of Council of Forensic Medicine; the death of the infant was recorded to be as a result of exposure to an unpredictable toxic substance (insecticide) when macroscopic and histopathological findings in the autopsy of the baby, crime scene investigation and baby's father to be treated with the diagnosis of poisoning were taken all together.

Discussion

Deaths due to aluminum phosphide poisoning are frequently reported in Iran and India²⁻⁴. These deaths in the US and Europe are very rare due to the limitation of the use of this preparation and the conscious about its use. In our country, although not as frequent as Iran and India, aluminum phosphide poisoning cases are reported ¹³.

Phosphin gas, which is quite toxic, is frequently used as an effective insecticide because it disrupts the developmental stages of all living things in the environment at various levels⁸. It is found in our country as aluminum phosphite tablets impregnated with clay as a gas preparation. When these tablets encounter atmospheric or gastric acid, phosphine gas is produced by a series of chemical reactions^{5, 9}.

Phosphine gas is colorless and odorless in its natural form. In commercial forms, it has the smell of rotten fish or garlic with some additives¹⁰. In our case, it was reported that there was intense garlic smell at home.

The most important factors affecting mortality and morbidity in aluminum phosphite poisoning are the amount of intake, the mode of administration (inhalation-oral) and time of hospital admission¹¹. Symptoms of poisoning include nausea, vomiting, restlessness, abdominal pain, palpitations, refractory shock, cardiac arrhythmias, pulmonary edema, shortness of breath, cyanosis and sensory changes⁷⁻⁹. Cardiovascular collapse, ARDS (acute respiratory distress syndrome) and neurological complications are expected in the early period. Rarely, DIC (Disseminated Intravascular Coagulopathy), pancreatitis, hypoglycemia and multiple organ failure findings are observed. The main step of treatment is the early application to the health institution and the intensive care support¹¹. In our case; Cardiovascular collapse and cardiac arrest were developed in a short time after the baby was brought to the hospital with cyanosis, vomiting and poor general condition. We think that high exposure as inhaler and late detection of poisoning by family had strongly contributed to the death of baby.

In our country, aluminum phosphite exposure is generally caused by suicide, but rarely by accident. Because clinical findings are non-specific, anamnesis is important in diagnosis¹¹. In a case report of Demir et al.¹², 20-year-old patient who drunk aluminum phosphate with suicide purpose; no significant features were found in the autopsy. The toxicological analysis revealed high levels of aluminium in gastric fluid and sulfonic acid in muscle samples. In the autopsy of our case; no obvious pathology was found except single petechial hemorrhage in the scalp, heart surface and lungs, and toxicological examination revealed no insecticides in blood, urine and adipose tissue. The fact that the age of our case was very small (2 months), the exposure was through inhalation and not taking sample for toxicological examination from lung tissue prevented the determination of the factor. When the findings in the investigation of the crime scene, the baby's autopsy findings, the application of father a few hours before the baby to the hospital with signs of intoxication and the anamnesis given by the family were evaluated together; we believe the death of the baby was due to aluminum phosphite poisoning.

Conclusion

The investigation of the crime scene, taking the appropriate samples and specifying these examples in detail are very important. In this case, it will be possible to perform a specific study and be able to diagnose the exact diagnosis. In addition, it is important to know the systematics of the toxicology laboratory, the factors which have been studied, and to ensure the specific study of the agent if necessary. If the appropriate sample was taken from the scene and work could be done for the suspected agent, the exact cause of death could be mentioned.

As a result of the unconscious and carelessly use of aluminum phosphite in the living area and late application to the health institution caused the death of a 2-month-old baby in our case report.

Restriction of aluminum phosphite procurement, strict control of its use and making necessary warnings when given to the user will reduce aluminum phosphite intoxications and related mortality and morbidity.

Intoxication should be kept in mind in the presence of similar symptoms that occur suddenly in more than one person living in the same household. Health institutions should be consulted as soon as possible and health workers should be informed.

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Multiple Organ Failure Due to Fungal Intoxication; Case Report

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Abstract

A 35-year-old female patient was admitted to our hospital with organ failure due to excessive consumption of wild mushrooms. She had a medical history of previous tuberculosis and, in accordance with it, a destructed lung. Hepatorenal syndrome and encephalopathy clinics were established. The patient's clinical findings related to fungal intoxication declined with penicillin G and supportive fluid electrolyte treatment, however, the patient died from ARDS due to her destructed lung. Fungal intoxication may be asymptomatic throughout the incubation period. Health care professionals should consider that fungal intoxication may also occur in patients admitted with asymptomatic symptoms due to seasonal conditions and nutritional habits.

Keywords: fungus, intoxication, multiple organ failure

Özet

35 yaşında kadın hasta, yabani mantar tüketimi sonrası organ yetmezliği ile hastanemize başvurdu. Tıbbi özgeçmişinde, tüberkülozun ve buna bağlı destrüktif akciğer hastalığı hikâyesi vardı. Hastada hepatorenal sendrom ve ensefalopati'yle ilişkili klinik bulgular mevcuttu. Hastanın mantar intoksikasyonu ile ilgili klinik bulguları penisilin G ve destekleyici sıvı elektrolit tedavisi ile azaldı, ancak hasta dekstrüktif akciğere bağlı gelişen ARDS nedeniyle hayatını kaybetti. Mantar zehirlenmesi inkübasyon süresi boyunca asemptomatik olabilir. Sağlık profosyonelleri, mevsimsel koşullar ve beslenme alışkanlıkları nedeniyle riskli hastalarda asemptomatik olsalar bile mantar zehirlenmesini düşünmelidir.

Anahtar Kelimeler: mantar, zehirlenme, multipl organ yetmezliği

Introduction

Turkey, with its suitable ecological conditions, is a country rich in diversity of fungal species. Mushroom is a protein-rich food source. Especially in spring and autumn, mushrooms cultivate more after periods of ample precipitation and poisoning cases are more common in these periods. In areas with low socio-economic conditions, it is also common to consume mushrooms after gathering from their habitat^{1,2}.

It is known that there are approximately 5000 fungus species around the world and only 200-300 are safe for consumption. Among the known, 100 fungus species are found to be toxic and 10 species to be lethal. It is not known whether other fungus species are edible or poisonous³.

Mushroom species in our country are consumed very often for nutrition purposes. We aimed to present a patient who was poisoned as a result of consuming the mushrooms collected from the environment with repeated meals every day for natural nutrition. This patient also developed multiple organ failure due to late diagnosis.

Case Report

A 35-year-old female patient applied to an external center because of abdominal pain, nausea and vomiting that started three days ago; but afterwards, the patient was admitted to our hospital with deterioration of general condition, confusion and the development of acute renal failure. In her history, it was learned that her complaints started one week before she was admitted to the hospital and that she ate mushrooms she collected from the environment every day for about fifteen days. She had a history of tuberculosis 4 years ago. She had respiratory distress when she was admitted. Because of mixed acidosis in the arterial blood gas analysis (ABG) and high liver enzymes in the biochemical analysis; the patient was transferred to the general intensive care unit (ICU). Her general condition was bad and she had confusion, tachypnea, dyspnea, hypotension and low sPO₂ (78%). Physical examination with oscultation revealed bilateral rhonchus in the lung zones. Because of the destructed lung tissue detected in computed tomography (CT) image due to previous tuberculosis, non-invasive mechanical ventilation support was initiated, since it was thought that there might be extubation difficulties. However, with her advanced confusion (GCS: 8) the patient underwent orotracheal intubation and mechanical ventilation.On arrival, her workup results were as following: AKG pH:6,94, PO2: 70,6mmHg, PCO2:81,8mmHg, HCO3:17,8, BE:-15,7, Lactate:9,2, SO2:78,8%, INR 3,20, PT: 34,9sec, urinary hematuric, D-Dimer :11400, WBC on hemogram:21,8 103mm3, Hb:12,5 g/dl, PLT:238,10³mm³, CRP:3,28 mg/dl, BUN:77mg / dl, Creatinine: 1,08mg /dl, ALT:1401U /L, AST:2600 U /L, Alb:2,9 g / dl. According to the results and the story, the patient was thought to have multiple organ failure due to fungal poisoning. Penicillin G infusion was initiated with 1 million units/hour/24 hours with supportive therapy in the ICU. Gastric lavage and bowel decontamination were not performed due to late period. During the treatment process, patient's liver and kidney failures and encephalopathy were improved and her consciousness was recovered. Respiratory support was continued in this process. Weaning from mechanical ventilation was applied. The patient was extubated on the seventh day of intubation. However, one day after the extubation, the patient was re-intubated because of the destructed lung. The patient, who could not meet the extubation criteria during the next intensive care unit period, died due to ARDS on the 21st day of hospitalization.

Discussion

Fungal intoxication is caused by the oral administration of many different toxic substances⁴. Consumption of uncultivated wild mushroom species instead of known edible mushroom species as a consequence of physical similarity plays a major role in toxicity. In addition, it has been reported that toxicity develops as a result of consciously ingestion for psychoactive effects, use for suicide or murder purposes and accidental ingestion, especially in pediatric patients^{2,3}.

Toxicity occurs with various clinical findings depending on the species being consumed, the amount of consumption, the season the mushroom is being consumed, the geographical location of the mushroom, the cooking method and the individual's response². Amanita species (Amanita phalloides) are responsible for 90-95% of the fungal intoxications associated with death. Amatoxins (900 dalton proteins) are primarily alpha and beta groups, thermostable and dialyzable octapeptides and bind to the 140 kd sub-unit of RNA polymerase II, in order to compete for mRNA synthesis. These toxins are highly potent and are lethal at a dose of 0, 1-0,3 mg/kg. Amatoxins are resistant to cooking and freezing.Toxins can cause poisoning even when frozen¹.

The early diagnosis of Amanita phalloides intoxication is very important, but usually atypical onset symptoms lead to skipped cases⁵. Intoxication may be asymptomatic throughout the incubation period. Afterwards, gastrointestinal symptoms such as nausea, vomiting, abdominal pain, diarrhea and, in accordance with these, severe dehydration may develop.

Liver is the target organ for Amanita phalloides intoxication; acute liver failure occurs with a sudden increase in aminotransferase and bilirubin. Hepatic coma, coagulation disorders and renal failure occur with hepatic failure. The central nervous system is also affected by toxicity and changes in consciousness develop^{5, 6}. Renal failure in patients depend on the toxic effect of hepatorenal syndrome and alpha-amanitis direct effect on the kidneys¹. In general, gastroenteritis and central nerve system findings are temporary. Liver failure can be fatal with the need for transplantation. These clinical pictures were also formed in our patient.

The early diagnosis of Amanita phalloides intoxication is very important, but usually atypical onset symptoms lead to skipped cases⁵.

In our case, asymptomatic gastrointestinal system findings were the first reason for admission and toxicity was overlooked, because the complete history could not be obtained. On the third day of admission to the external center, the patient was admitted to our hospital with multiple organ failure.Since asymptomatic fungal intoxication cases were very common in our hospital and the patient had encephalopathy due to liver failure, history of fungal ingestion was included in the questioning of the history and the family transferred the information after interrogation.

In treatment, stabilization of vital signs is the main objective; firstly, intestinal decontamination, and activated charcoal and intravenous fluid treatments are applied to prevent amatoxin absorption. To our patient, gastric lavage and activated charcoal were not applied because of the late period. Diuresis and biliary drainage were injured for toxin elimination. As supportive treatment, plasmapheresis, Molecular Adsorbent Recirculating System (MARS)⁷ and fractionated plasma separation and absorption (FPSA)⁸ can be considered to be administered in the first 36-48 hours after ingestion. However, clinical data are limited on this regard. In addition, diuresis and biliary drainage can increase the elimination of amatoxins and provide sufficient therapeutic effect⁵. Since our patient had renal failure, appropriate fluid treatment was initiated.

Controversial results with regard to the therapeutic efficacy associated with potential antidotes, including benzylpenicillin, N-acetylcysteine and silymarin, are available in publications. These antidotes are known to provide some degree of success and are recommended for use by some national poison centers. To our patient, we applied penicillin G infusion, despite being in the late period⁵.

In addition, polimoxin B antidotes and traditional Chinese medicine glossy Ganoderma decoction (GGD) are considered novel therapeutic agents that promise to prevent toxin-induced liver damage⁵.

Liver transplantation is accepted as the only approach to increase survival rate in fulminant liver failure due to fungal intoxication⁹.

Conclusion

Despite successful treatment with hepatorenal syndrome and encephalopathy due to fungal intoxication, the patient died due to the existing destructive lung.Health care professionals should consider that fungal intoxication may be present in patients applying with asymptomatic symptoms depending on seasonal conditions and nutritional habits. This may allow the table to be resolved without aggravation.

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A Dystonia Case Due to Metoclopramid Usage

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Abstract

Metoclopramid is the dopamine receptor antagonist. It has been used widely as antiemetic agent. This drug enters the blood-brain barrier and causes extrapyramidal symptoms such as Parkinsonism, malign neuroleptic syndrome, akathisia, tardive dyskinesia and acute dystonic reaction. Our case is a 17-year-old female, who took 3x10 mg metoclopramid for the purpose of treatment for three days and applied to our emergency service with the involuntary spasm in the neck and both arms.

Keywords: Metoclopramide, acute dystonic reaction, adolescent

Özet

Metoklopramid, bir dopamin reseptörü antagonistidir. Antiemetik ajan olarak yaygın olarak kullanılır. Bu ilaç kan-beyin bariyerini geçerek ve Parkinsonizm, malign nöroleptik sendrom, akatizi, tardif diskinezi ve akut distonik reaksiyon gibi ekstrapiramidal semptomlara neden olur. Olgumuz, üç gün boyunca tedavi amacıyla 3x10 mg metoklopramid kullanan ve boyun ve her iki kolda istemsiz spazmla başvuran 17 yaşında kadın hastadır.

Anahtar Kelimeler: Metoklopramid, akut distonik reaksiyon, adolesan

Introduction

Dystonia is a neurological disorder which is characterized by posture disorder caused by repetitive, bending, strong involuntary muscle contractions. Acute dystonic reaction manifests itself with muscle contractions, opistotonus, tortikollis, oculogyric crisis, dysarthria, trismus especially on the face, neck and back muscles¹. Metoclopramide is the most dystonic drug among antiemetics². Metoclopramide is an effective and commonly used antiemetic, acts as dopamine-2 receptor antagonist, inhibits both central and peripheric effects of apomorphine³. Its effect is emerging in 1-3 minutes when given intravenously, within 15-20 minutes when given orally. Its half life is four hours⁴. Most common extrapyramidal adverse reactions due to metoclopramide use are, parkinsonism, tardive dyskinesia, neuroleptic malignant syndrome, akathisia and acute dystonic reaction^{5,6}. In this article, we present a case with acute dystonic reaction associated with metoclopramide. It was intended to draw attention to the diagnosis and treatment of extrapyramidal symptoms and, in particular, acute dystonic reaction and the detailed evaluation of the differential diagnosis in emergency departments.

Case Report

A 17-year-old female patient presented to Başkent University Istanbul Research and Practice Hospital Emergency Department due to sudden, involuntarily contraction of neck and both arms, and backward shifts of eyes. From the patient history, it was determined that a nasal spray containing Oxymetazoline HCl (four times a day), a tablet containing Ibuprofen and Pseudoephedrine HCl (three times a day), a throat spray containing Benzidamine HCl, and Chlorhexidine Gluconate (four times a day) and a tablet containing Metoclopramide (three times a day) were prescribed 3 days prior due to complaints of nausea and cold symptoms. In the first evaluation of the patient, her general condition was anxious, agitated, conscious, cooperative and oriented, with GCS: 15. On physical examination, her temperature was 37.3°C, blood pressure 125/75 mmHg, pulse 102 / min and respiratory rate was 22 / min. Pupils isochoric, with both direct and indirect light reflexes present. In laboratory examinations, complete blood count and biochemical values were found to be normal. Blood gas pH: 7.4, lactate: 1.4, base excess -0.9. From the patient history and the first evaluation, it was learned that she had been using the medications prescribed for treatment regularly for 3 days only, did not have any health problems and did not use any drugs prior. Motor examination and muscle tone were normal and there was no rigidity determined. The deep tendon reflexes were equal and normoactive in all four extremities. Extrapyramidal system examination revealed hyperextension in the neck, dystonic movements in the arms and an ocular gait. Other system examinations of the patient were considered normal. Due to the absence of a similar complaint, the acute dystonic reaction was thought to have developed due to use of metoclopramide. 5 mg biperidene was administered to the patient intravenously. Symptoms disappeared within approximately one hour after injection. However, 10 mg Diazepam was administered intravenously as the patient agitation continued. The patient was discharged after six hours of follow-up and referred for control to the neurology outpatient clinic the next day. It was found that the patient's physical examination was completely normal and the patient's symptoms did not recur and the patient was advised not to use any medications in this group again.

Discussion

Antipsychotics, antidepressants and metoclopramide, used as an antiemetic in particular, are among the main drugs causing acute dystonic reaction. In addition, antihistamines, decongestants, expectorants, antipyretics along with the use of codeine, cocaine, carbamazepine, phenytoin, chlorokine and diazepam have been reported to cause the development of an acute dystonic reaction^{6,7}. Metoclopramide is an antiemetic dopamine agonist commonly used in gastroesophageal reflux disease, nausea due to chemotherapy, respiratory infections and gastroenteritis in children. This drug is metabolized in the liver and excreted in the urine. Therefore, dose adjustment should be done in patients with liver and renal failure and these problems should be queried before the prescription of this drug. Our case was a 17-year-old female adolescent and had no liver and kidney problems. The extrapyramidal side effects of metoclopramide (tardif dyskinesia, Parkinson's disease, akathisia, malignant neuroleptic syndrome and acute dystonia) develop due to dopamine receptor antagonism in basal ganglia and disappear within 24 hours after the discontinuation of the drug⁸. The acute dystonic reaction seen in 0.5-1% of patients treated with metoclopramide, manifests itself especially with contractions in the face, neck and back muscles, opistotonus, torticollis, oculogyric crisis, dysarthria, trismus. The frequency is not related to gender and age^{1,9}. These drug-related effects are not only dose-dependent (they develop more in those receiving doses greater than 0.5 mg / kg), but may also be idiosyncratic due to individual factors. However, there are

studies that indicate that side effects occur more frequently when the recommended dose is exceeded and cumulative effects occur in repeated doses. In our case, the patient was admitted to our clinic with a total of 90 mg metoclopramide over a course of 3 days. It has been reported that Patients with acute dystonic reaction may receive different diagnoses such as encephalitis, hypocalcemia, seizures, convulsion, insect bite and tetanus¹⁰. Such misdiagnoses can cause a loss of time on the one hand, and on the other hand the use of unnecessary drugs for treatment.

Conclusion

In conclusion, for every patient with involuntary movements in the neck and/or arms presenting to the the emergency department, the emergency physician should definitely consider acute distonic reaction in a differential diagnosis. The use of anti-emetics, in particular the use of metoclopramide, should be queried.

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