Methamphetamine Intoxication in Children: A Single-Center Experience

Çocuklarda Metamfetamin İntoksikasyonu: Tek Merkez Deneyimi

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ABSTRACT

Objective: Illicit substances, especially methamphetamine, are becoming increasingly popular with adolescents in Turkey as well as around the world. Most of the studies conducted for this purpose in Turkey are survey studies. Our study therefore aimed to evaluate the clinical features and laboratory parameters of patients who applied to our hospital and were found to have methamphetamine intoxication.

Material and Methods: Patients under 18 who applied to the Ankara City Hospital Pediatric Emergency Department (PED) between August 2019 and December 2021 and were found to be positive for methamphetamine in the urine drug screening were included in the study,and their data were evaluated retrospectively.

Results: We reviewed 10 cases presenting to our PED with methamphetamine intoxication. The mean age was 16.3 ± 0.94 (14-17) and 80% of patients were male. Eight patients concealed substance use at admission. The most frequent complaints upon presentation were cardiovascular, neurological, and gastrointestinal system symptoms. Concomitant alcohol use was detected in four patients, multidrug use in one patient. No significant pathology was observed in the laboratory tests. Gastric perforation was detected in one patient with abdominal pain, and pneumomediastinum was detected in one patient with chest pain.

Conclusion: There are no specific clinical and laboratory indicators of methamphetamine intoxication, and substance abuse should be considered in all cases where a possible reason cannot explain the patient's clinical findings. Children who use alcohol should be questioned about substance abuse, care should be taken in terms of multiple substance use, and follow-up and rehabilitation plans for patients should be made accordingly.

Key Words: Alcohol, Children, Methamphetamine, Substances, Urine Drug Screening

ÖZ

Amaç: Yasa dışı uyuşturucu maddeler, özellikle de metamfetamin, dünyada olduğu gibi Türkiye'de de ergenler arasında giderek daha popüler hale gelmektedir. Türkiye'de bu amaçla yapılan çalışmaların çoğu anket çalışmalarıdır. Çalışmamız ise hastanemize başvuran ve metamfetamin intoksikasyonu saptanan hastaların klinik özelliklerini ve laboratuvar parametrelerini değerlendirmeyi amaçlamıştır.

Gereç ve Yöntemler: Ağustos 2019-Aralık 2021 tarihleri arasında Ankara Şehir Hastanesi Çocuk Acil Servisi'ne başvuran ve idrar toksik madde taramasında metamfetamin pozitif saptanan 18 yaş altı hastalar çalışmaya dahil edildi ve verileri retrospektif olarak değerlendirildi.

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Bulgular: Çalışmamızda metamfetamin intoksikasyonu saptanan 10 hastayı inceledik. Ortalama yaş 16.3 ± 0.94 (14-17)'di ve hastaların %80'i erkekti. Sekiz hasta başvuru sırasında madde kullanımını gizledi. Başvuru anında en sık kardiyovasküler, nörolojik ve gastrointestinal sistem semptomları görüldü. Dört hastada eşzamanlı alkol kullanımı, bir hastada çoklu uyuşturucu kullanımı saptandı. Laboratuvar testlerinde önemli bir patoloji gözlenmedi. Karın ağrısı olan bir hastada mide perforasyonu, göğüs ağrısı olan bir hastada pnömomediastinum tespit edildi.

Sonuç: Metamfetamin intoksikasyonunun spesifik klinik ve laboratuvar göstergeleri yoktur ve olası bir nedenin hastanın klinik bulgularını açıklayamadığı tüm durumlarda madde kötüye kullanımı düşünülmelidir. Alkol kullanan çocuklarda madde kullanımı sorgulanmalı, çoklu madde kullanımı açısından dikkatli olunmalı, buna göre hasta takip ve rehabilitasyon planları yapılmalıdır.

Anahtar Sözcükler: Alkol, Çocuk, Metamfetamin, Uyuşturucu Maddeler, İdrar Uyuşturucu Taraması

INTRODUCTION

Despite all measures that have been taken, Substance Use Disorder has steadily become more widespread in Turkey as it has around the world. Commonly given slang names such as "crystal," "fire-ice," "meth," methamphetamine is one of the most widely used narcotic after cannabis derivatives (1). Methamphetamine is a methylated analog of amphetamine that functions as a central nervous system stimulator. While carrying pharmacological properties similar to amphetamine, because of its higher lipophilicity, methamphetamine has a more powerful effect and a longer half-life. Its potential to do harm is consequently greater (2,3). It is estimated that there are about 24 million methamphetamine users worldwide (4). Its popularity has grown steadily in the last twenty years, especially in Southeast Asia, and it has surpassed heroin as the most popular illegal narcotic (4). Its easy production, low cost and comparatively better accessibility has steadily increased the use of methamphetamine in recent years (2). The exact statistics for methamphetamine use in Turkey is unknown (5). In a study by Karakukcu et al. (6), it is reported that according to laboratory findings of a reference drug screening centre in Kayseri, Turkey, amphetamine/methamphetamine has been the most commonly used substance group between 2014 and 2016. Factors such as young age, a low level of education, use of other psychoactive substances have been found to be associated with methamphetamine abuse (7).

The signs and symptoms of methamphetamine toxicity in adults are typically mydriasis, sweating, tachycardia, hypertension, chest pain, cardiac arrythmia, and myocardial infarction. Paranoia, agitation, hallucinations, and aggressive behavioral disorders are also widely noted. Adrenergic symptoms in children are similar to those observed in adults. At the same time, pediatric patients can present with symptoms such as vomiting, stomachache, agitation, irritability, and recurring stereotypic behavior. These atypical and nonspecific findings challenge the clinician in making a diagnosis and lead to further medical examinations (8,9).

The aim of this study was to assess the symptoms and findings, laboratory parameters and clinical characteristics of patients presenting at the Pediatric Emergency Department with methamphetamine intoxication.

MATERIALS and METHODS

Data belonging to patients below the age of 18 who had presented at the Ankara City Hospital Pediatric Emergency Department over the period August 2019-December 2021 and displayed a methamphetamine positive result on a panel drug urine test were evaluated retrospectively.

Urine samples for methamphetamine analysis were studied using the enzymatic immunoassay test within the first three hours of admission and positive presence in urine was confirmed using the hyphenated mass spectrometry chromatographic method. Methamphetamine use was considered positive if the level was above 1000 ng/mL.

The vital signs (temperature, pulse, blood pressure) of patients at the time of testing positive for methamphetamine in urine were extracted from the nurse's observation forms, the medical history and physical examination findings (neurological, gastrointestinal, chest pain and other systemic findings) from doctor's notes, and the laboratory results (blood glucose, blood ketones, blood gases, urea, creatinine, transaminases, coagulation parameters, ethanol levels) and imaging findings were obtained from the hospital data system. Treatments applied to patients and their clinical course were reviewed from their discharge records.

The Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM Corp., Armonk, New York, USA) was used to analyze the data. Descriptive statistics (including frequencies and means) for all variables were calculated. Results were expressed as mean ± standard deviation, frequency and percentage (%). The Kolmogorov-Smirnov test was used to examine whether the numerical variables showed normal distribution.

This study was conducted in conformity with the principles of the Declaration of Helsinki and approved by the Republic of Turkey Ministry of Health, the Ethics Committee of Ankara City Hospital Ethics Committee, and the Institutional Review Board of the Children's Hospital of Ankara City Hospital (E2-21-1141).

RESULTS

A total of 414 urine drug panel results of pediatric patients sent to laboratories over the period August 2019-December

2021 were examined. Drugs were found in the urine of a total of 25 pediatric patients. It was found that 14 of these findings indicated methamphetamine. Two patients were excluded from the study because their clinical data could not be accessed. Another two patients were excluded because it was considered that their treatment with methylphenidate due to Attention Deficit Hyperactivity Disorder may lead to false positive testing. The clinical and laboratory findings of 10 patients were ultimately reviewed.

Eight boys and two girls were taken into the study. The patients' mean age was 16.3 ± 0.94 years. While two of the patients revealed their use of drugs at their first application, evidence of drug use was found in the testing results of the remaining eight. None of the patients had a history of any previously diagnosed psychiatric disorder or of the use of any psychiatric medication. The patients more commonly presented at the emergency department for cardiovascular system (tachycardia, chest pain, hypertension), neurological system (dizziness, hallucinations), and gastrointestinal system (nausea and stomachache) symptoms. When severe poisoning findings related to methamphetamine use were examined, 80% of the patients had tachycardia, 30% had chest pain, 20% had hypertension, 20% had hallucinations, and 10% had syncope. Interestingly, hyperthermia, convulsion, delirium, hyperkalemia and metabolic acidosis were not observed in any patients. While four patients exhibited higher than normal blood ethanol levels, accompanying alcohol use was not detected in the other six. Out of the four patients who were found to be using alcohol in addition to methamphetamine, three tested positive for blood ketones while seven patients tested negative for blood ketones. The patients' blood glucose, blood gases, biochemical tests and coagulation tests did not reveal any significant pathology. Stomach perforation was found in one patient who complained of stomachache, while pneumomediastinum was detected in another case. Still another patient tested positive on the urine drug panel for marihuana and benzodiazepine. Two patients who displayed neurological symptoms at presentation but did not disclose any drug use underwent cranial computerized tomography; both results were normal. While six patients were discharged from the emergency department, two patients were followed up in the intensive care unit and two were admitted into the pediatric department for observation. The patients' complaints, symptoms, and findings at presentation, as well as their laboratory results at presentation can be seen in Table I and Table II.

Table I: Clinical symptoms of the patients

Symptoms	n (%)
Hyperthermia	0 (0)
Sweating	2 (20)
Tachycardia	8 (80)
Hypertension	2 (20)
GIS symptoms	5 (50)
Chest pain	3 (30)
Neurological findings	7 (70)
Dizziness	4 (40)
Hallucinations	2 (20)
Agitation	1 (10)
Syncope	1 (10)
Concomitant substance use	1 (10)
Concomitant alcohol intake	4 (40)

Tablo II: Laboratory test results of the patients

Parameter	Mean ± SD
Blood glucose (*mg/dL*)	92 ± 11.2
Urea (*mg/dL*)	25.7 ± 9.3
Creatinine (*mg/dL*)	0.80 ± 0.12
Uric acid (*mg/dL*)	5.3 ± 1.37
Sodium (*mEq/L*)	138.2 ± 3.6
Potassium (*mEq/L*)	3.95 ± 0.42
pH	7.39 ± 0.08
pCO2 (*mmHg*)	37.6 ± 8.6
HCO3 (*mmol/L*)	22.6 ± 2.5
Anion gap	11.3 ± 4.2
Lac (*mmol/L*)	2.5 ± 1.8
AST (U/L)	33.7 ± 18.4
ALT (U/L)	24.6 ± 15.8
INR	1.17 ± 0.14
aPTT	25.1 ± 4.1

DISCUSSION

Substance use disorder is among the most critical health problems that should be addressed because it causes severe clinical and social problems. Since methamphetamine use has recently become widespread in adolescents because it is both easily affordable and accessible, it is essential that studies are conducted with adolescent patients. Most studies on substance use in children in Turkey are survey studies; there are not enough clinical studies on substance use in children, especially in the case of methamphetamine. At the same time, there is a lack of adequate and comprehensive clinical studies on methamphetamine intoxication in children in Turkey and in the world. In this regard, we believe that our study may contribute to the pediatric literature in this area.

In the study of Gordon et al. (10), urine tests came back positive in 10 (11.8%) out of the 85 adolescent patients who presented with blunt or penetrating trauma and who had had urine drug screening. In the study of Yurtseven et al. (11), from Turkey, 131 (24%) out of the 548 adolescent patients who had urine drug screening tested positive. In a similar study by Kozer et al. (12), the frequency of positivity in urine drug screening was found to be 8% in the adolescent age group. In our study, the rate of positivity in urine screening was approximately 6%. Among the reasons behind the variability in positivity frequency

in the patients who were tested can be cited late admission to the hospital after substance abuse, the failure to take urine samples while the patient is under surveillance, and the fact that clinicians carried out more urine toxicology scans than necessary because the clinical picture caused by substance use is similar to that of many diseases.

Mild and non-specific clinical findings can be seen in methamphetamine use, as well as cardiac arrhythmia, strokes, cerebral hemorrhage, ischemic infarction, renal failure, rhabdomyolysis, coma, or even death in severe cases (18,19). Clinical findings and symptoms of methamphetamine intoxication can vary widely, depending on dose, route, duration (acute and/or chronic), and pattern of use (2). In the study by Chen et al. (20), in which the authors examined applications to the United States poison control centers between 2000 and 2019, the most common complaints were reported as tachycardia (35.5%), agitation (29.4%), hypertension (15.3%), and hallucinations/delusions (6.8%). In the study of Malasock et al.(9) in children and adolescents, the most common symptoms related to methamphetamine intoxication in the adolescent group were reported as hypertension, tachycardia, mydriasis, and GIS symptoms. In our study, the most common clinical findings were tachycardia, GIS symptoms and neurological findings. Furthermore, no significant disorder was detected in the patients' laboratory findings. No patient died in our study. The patients were discharged after a short-term follow-up, except for two patients with gastric perforation in one and pneumomediastinum in the other, both of whose blood alcohol levels were normal. Martínez-Aguirre et al. (21) found in their study that there was a trend in the methamphetamine user group to develop peptic ulcer perforation at earlier ages compared with the nonuser group, and concluded that methamphetamine use is related to ulcer perforation in age groups of younger patients. Vaghefi et al. (22) also reported a 23-year-old patient with perforated duodenal ulcer after taking methamphetamine. Although there are not sufficient clinical observational studies, several methamphetamine-associated pneumomediastinum cases, mostly following inhalation of methamphetamine have also been reported in the literature (23–25). Although spontaneous pneumomediastinum and peptic ulcer perforation are rare findings, it is essential to elicit a thorough history including illicit drug use, particularly regarding amphetamines and other stimulants. To the best of the authors' knowledge, methamphetamine intoxication accompanied by gastric perforation and pneumomediastinum has not been previously described in the Turkish literature.

In both adults and adolescents, psychoactive substance use has been found to be associated with having a psychiatric disorder and people with substance use disorders are seen to have much higher rates of comorbid mental disorders. A strong direct association between the severity of comorbidity and the severity of substance use disorders has been also found (13,14). In addition, it has been suggested that substance use may lead to psychiatric disorders (15). Gau et al. (16) found in their longitudinal study that the most significant predictive factors for substance use in adolescents included male gender, attention-deficit hyperactivity disorder, and conduct disorder. However, none of the patients with methamphetamine detected in urine tests in our study had a previously diagnosed psychiatric disease. Therefore, just as it is essential to follow up on patients with psychiatric diseases in terms of substance use risk, the close and careful follow-up of substance users is crucial in terms of the detection of additional psychiatric disease.

Substance abuse, especially methamphetamine, is becoming increasingly more common in adolescents. In addition, alcohol-substance co-use and multiple substance use are also increasing. Chen et al. (20) showed in their study that the rate of multiple-substance exposures in which methamphetamine was the first-ranked substance was 24.4 % (n=13210). Karakükcü et al. (6) found that the rate of multiple substance abuse increased significantly over the years and the most common and the second most common multiple substance usage were metamphetamine with cannabis and metamphetamine with opiate, respectively. In our study, a second substance was detected in the urine analysis of only one patient, and high blood alcohol levels were found in almost half of the patients. Thus, concomitant substance use and alcohol use should be questioned in adolescent patients admitted to the hospital; similarly, patients admitted for substance abuse should be questioned for concomitant alcohol use and multiple substance use. Rehabilitation programs should be planned based on abuse patterns.

The present study had some limitations. First, due to the retrospective nature of the study, some important unregistered information could not be obtained; including the way the patients used substance and their ECG records. Second, no blood methamphetamine concentrations were obtained. Additionally a sample size of 10 is merely enough to obtain meaningful data. Still, this study contributes meaningfully to the literature due to the dearth of pediatric studies.

CONCLUSIONS

Since there are no specific clinical and laboratory indicators of methamphetamine intoxication, substance abuse should be considered in all cases where a possible reason cannot explain the clinical findings of the patients. Children with psychiatric illness should be followed up for substance abuse; similarly, children who use illicit substances should be investigated for psychiatric illness. Children who use alcohol should be questioned about substance abuse, care should be taken in the case of multiple substance use, and follow-up and rehabilitation plans should accordingly be made for patients. In addition, multicenter clinical observational studies should be conducted

throughout the country on the use of methamphetamine in pediatric patients in Turkey, as in Europe and the USA.

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