

Increased Creatinine Kinase Levels due to MDMA use without Myoglobinuria and Renal Failure

MDMA Kullanımı Sonrası Miyoglobinüri ve Böbrek Yetmezliği Olmadan Kreatin Kinaz Yüksekliği Olan Bir Olgu Sunumu

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Abstract

We report a 15-year-old boy admitted to the pediatric emergency unit with acute encephalopathy associated with an elevated serum creatine kinase (CK) level without myoglobinuria and renal failure, which was due to 3,4-Methylenedioxymethamphetamine (MDMA) toxicity and we emphasize that especially in adolescents with acute encephalopathy and an increased serum CK level, ecstasy abuse should be kept in mind as a differential diagnosis. (*Marmara Medical Journal 2012;25:41-4*)

Key Words: Increased CK level, Delirium, Ecstasy, Rhabdomyolysis, Adolescent

Özet

Akut ensefalopati ve serum kreatin kinaz yüksekliği ile başvuran adolesan hastalarda ekstazi kullanımının ayırıcı tanıda akla gelmesi gerektiğini vurgulamak amacı ile çocuk acil polikliniğine 3,4- Methylenedioxymethamphetamine (MDMA) ekstazi toksisitesine bağlı akut ensefalopati ile başvuran tetkiklerinde böbrek yetmezliği ve miyoglobinüri olmadan serumda kreatin kinaz yüksekliği tespit edilen 15 yaşında erkek olgu sunulmuştur. (*Marmara Üniversitesi Tıp Fakültesi Dergisi 2012;25:41-4*)

Anahtar Kelimeler: Artmış serum kreatin düzeyi, Deliryum, Ekstazi, Rabdomyoliz, Adolesan

Introduction

The use of 3,4 methylenedioxymethamphetamine (MDMA), also known as 'ecstasy', and other stimulant drugs with similar effects is becoming widespread all around the world¹. With the wide use of MDMA its harmful, even life threatening effects have been reported increasingly^{2,3}. MDMA is structurally related to metamphetamine and has sympathomimetic effects including tachycardia, sweating, hypertension, dilated pupils, hyperthermia and increased muscle activity, as well as euphoria, which is commonly seen within the first hour of ingestion⁴. MDMA-induced hyperthermia is commonly associated with skeletal muscle breakdown, rhabdomyolysis and renal failure^{2,5-7}. Increased levels of serum creatine kinase (CK) as a consequence of rhabdomyolysis due to MDMA use have been

reported, however, increased serum CK levels without myoglobinuria and renal failure is very unusual⁷.

A 15-year-old boy was referred to our pediatric emergency unit with acute encephalopathy due to ecstasy use, associated with a high serum CK level but without myoglobinuria and renal failure. Particularly in adolescents with acute encephalopathy and an increased serum CK level, ecstasy could be the underlying cause, so the possibility should be explored carefully.

Case Report

A 15-year-old was admitted to the pediatric emergency room with purposeless movements, meaningless speech and

Table I. Published case reports about proven MDMA intoxication

Reference	Patient number	Gender, age	Signs and Symptoms	Myoglobinuria	Renal functions	CK level (IU/l)	Treatment modalities	Serum MDMA level	Complications	Outcome
Coore JR, 1995	1	F, 18	Sweating, agitation, hyperthermia, hypotension, tachycardia, convulsions	no	Urea: 9.7mmol/L Creatinine: 204 mmol/L	170000	Dantrolene, diazepam, dopamine, dobutamine, mechanical ventilation, hemofiltration	0.246 mg/l	Renal failure, DIC, hepatic and pancreatic necrosis	Died
Mallick A. 1997	1	M, 19	Sweating, hyperthermia, obtundation, cyanosis, tachypnea, seizures	>100mg/dl	normal	42.120	Sedation with propofol, adrenalin infusion		No	Survived
Walubo A, 1999	1	M,53	Tachycardia, diaphoresis, hyperthermia, hypertension, tachypnea		BUN: 69 mg/dl Creatinine: 8.3 mg/dl	344900	Naloxone, diphenhydramine, methylprednisolone, furosamide, nitroprusside, hemodialysis, mechanical ventilation	3050ng/ml (3.05 mg/L) (NMDA)	Acidosis, DIC; renal failure, ARDS	Died
Lehmann 1995	1	M,36	Convulsion, hyponatremia, tachypnea, hyperthermia,	yes	normal	84 800	Hydration, mannitol bicarbonate dopamin with alkaline diuresis	Nontoxic level 0.013 mg/L (MDMA)	hyponatremia	Survived
Connoly 1999	1	M,29	Seizures, hyperthermia, tachycardia, coma, metabolic acidosis,	yes	Urea:20 Creatinine: 0.61mg/dl	88 000	Hydration, surface cooling, hemodialysis, mechanical ventilation		Oliguria	Survived
Eifinger 2008	1	M,8mo	Tachycardia, hypertension, sweating, seizures, hyperactivity, hyperthermia	no		1681	Rehydration, benzodiazepine	785 ng/ml (MDMA)	no	Survived

M: male, F: female, mo: month, MDMA:3,4-methylenedioxymethylamphetamine, DIC:disseminated intravascular coagulation, ARDS: acute respiratory distress syndrome, NMDA: n-methyl D-aspartate

agitation. His parents explained that these complaints occurred two days ago, he suddenly started shouting - expressions like: "they are going to stab me, they are also going to kill you" and assaulting those nearby. When he was admitted to a local hospital, intravenous Diazepam was administered, however, fever, fatigue, vomiting were observed as well as signs of acute encephalopathy. The next day, the patient was unconscious and was taken to a private psychiatry hospital. Risperidon was given intravenously with the diagnosis of acute psychotic attack, but clinical improvement was not seen and he was admitted to our hospital's emergency unit on the third day of his complaints.

His previous medical history was uneventful except for a history of acute rheumatic fever at 8 years of age. During the last year, his attendance at school had been irregular and his academic performance had gradually deteriorated .

Physical examination was normal and the patient was afebrile. Neurological examination revealed no focal sign; he could open his eyes spontaneously and with verbal stimuli. He was disorientated, he could obey simple commands partially, and he was agitated and spoke senseless and inappropriate words.

Laboratory investigations including a complete blood count, serum glucose, urea, creatinine, liver function tests, electrolytes

were within normal limits. A lumbar puncture was performed and the opening pressure was normal, no cells were detected. Cerebrospinal fluid glucose and protein levels were normal. Cranial magnetic resonance imaging (MRI) (with and without contrast) examination revealed no abnormality. Background activity on the EEG was a 4-5 Hz Theta rhythm without any abnormal discharge. The serum CK level was 1005 U/l and urine examination demonstrated no sign of myoglobinuria. In the differential diagnosis, use of any drug or substance was considered and the patient was questioned insistently. His close friend confessed that he took 3 tablets of ecstasy 5 hours before the symptoms occurred. He was treated with forced alkaline diuresis induced by intravenous fluids and bicarbonate.

After the third day of follow-up, signs of delirium were disappearing gradually and the serum CK level began to decrease dramatically (600 U/l on the fourth day, 200U/l on the fifth day).

Discussion

3,4-Methylenedioxyamphetamine (MDMA; ecstasy) is a hallucinogenic, psycho-stimulant methamphetamine derivative drug. It is commonly abused among adolescents and young adults in night-clubs, parties, concerts, even in daily life where its euphoric and stimulant-like effects can enhance social interactions and endurance. For many years, it had been accepted as a safe drug, increasing self-trust and its addictive effects were not taken into consideration^{1,8}. However, harmful, even life-threatening effects of ecstasy have been demonstrated. Nowadays, ecstasy is cheap, widely used and easy to attain so it presents a serious medical and social problem, particularly for adolescents⁹.

Studies carried out in developed countries showed that the use of this drug has been increasing each year^{10,11}. It was reported that 11% of high school students in the United States had taken ecstasy¹⁰. Studies about illegal drug use in developing countries like Turkey have been fewer and did not cover the whole population. In a study carried out in 2001 among high school students from 15 Turkish cities, it was reported that 1.6% used ecstasy in the last year and 1.2% had used it in the last one month⁵. In another study, carried out among 11,991 adolescents and young adults from different cities of Turkey, the rate of ecstasy use was found to be 2.5%. Male to female ratio was 5 and the mean age of the first trial was 13 years⁷.

MDMA is structurally related to metamphetamine and has sympathomimetic and euphoric properties. It affects the serotonergic (and to a lesser extent dopaminergic) neurons in the brain. The compound seems to cause a calcium-independent flood of serotonergic neuron release into synaptic cleft while inhibiting serotonin reuptake and this response results in euphoria and stimulus effect. The most common clinical findings of MDMA toxicity are altered mental status, tachycardia, tachypnea, profuse sweating, and hyperthermia. In addition, rhabdomyolysis, acute renal failure, cardiac collapse, malignant hyperthermia, disseminated intravascular

coagulation, cerebral infarct, and cerebral hemorrhage have been reported^{8,10-12}. Muscular hyperactivity and severe hyperthermia result from release of calcium from the sarcoplasmic reticulum and increased metabolic demands¹². Cerebral hemorrhage, hyponatremia, liver dysfunction and cardiac arrhythmias are other reported effects^{8,10,11,13}. On the other hand, cases of profound psychosis and depression (once thought to be seen only in chronic users of MDMA) have been reported after minimal use^{2,8,14}.

Severe rhabdomyolysis has mostly been reported as an early phenomenon in patients admitted with hyperprexia following ecstasy ingestion^{13,15,16}. The presented case had myoglobinuria without a history of hyperthermia or increased exercise. Our patient had signs of acute encephalopathy on admission. He was agitated and an elevated serum CK level was the only biochemical abnormality. Blood urea nitrogen (BUN) and creatinine levels were within normal limits and he did not have myoglobinuria.

Degradation of approximately 200 g of muscle can cause an increase in serum CK and the serum CK level is a sensitive biochemical indicator of rhabdomyolysis. It is an expected finding of MDMA toxicity, however most of the reported patients with rhabdomyolysis and elevated serum CK levels due to MDMA use had myoglobinuria and/or renal failure^{2,6,10,13,15,17} (Table I). The difference of this presented case from previously reported cases in the literature was the high level serum CK level without myoglobinuria and renal failure. However, cases with renal failure reported in the literature had serum CK levels higher than our case^{6,18}.

As a conclusion, in adolescents with acute encephalopathy, ecstasy use should be investigated carefully and it should be considered that these patients might have an elevated CK level due to acute rhabdomyolysis without renal failure or myoglobinuria.

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