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Long-Acting Methylphenidate Toxicity: A Case Report

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ÖZET:

Uzun etkili metilfenidat toksisitesi: Bir olgu sunumu

Metilfenidat, dikkat eksikliği hiperaktivite bozukluğu (DEHB) ve davranım bozuklukları tedavisinde yer alan bir psikostimülandır. Metilfenitat toksisitesinde, bilinç kaybı, letarji, epileptik nöbet, psikotik belirtiler gibi nöropsikiyatrik belirtiler ve taşikardi, hipertansiyon, hipertermi gibi kardiyovasküler yan etkilerin görülebileceği bildirilmiştir. Bu olgu sunumunda, özkıyım amaçlı 486 mg MFD alan ve bir ergenin klinik tablosu tartışılmıştır.

Anahtar sözcükler: metilfenidat, dikkat eksikliği hiperaktivite bozukluğu, toksisite

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ABSTRACT:

Long-acting methylphenidate toxicity: a case report

Methylphenidate is a psychostimulant that is used in the treatment of attention deficit hyperactivity disorder and behavior disorders. Neuropsychiatric symptoms like loss of consciousness, lethargy, seizures and psychotic symptoms, and cardiovascular side effects like tachycardia, hypertension and hyperthermia have been reported in methylphenidate toxicity. In this case report, the clinical manifestations of an adolescent having taken 486 mg methylphenidate in a suicide attempt are discussed.

Keywords: methylphenidate, attention deficit hyperactivity disorder, toxicity

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INTRODUCTION

Methylphenidate (MPH) is a psychostimulant which is used in treatment of attention deficit hyperactivity disorder (ADHD) and behavior disorders. Anorexia, nervousness, restlessness, headache, insomnia, abdominal pain and nausea are the most commonly reported side effects of MPH[1]. While anorexia and insomnia are dose-dependent side effects, others are not dose-dependent[2]. Neuropsychiatric symptoms like loss of consciousness, lethargy, seizures, agitation and psychotic symptoms[3,4], and cardiovascular side effects like tachycardia, hypertension and hyperthermia have been reported in MPH toxicity[5-7]. In a side effect analysis covering the years between 1993 and 1999, MPH toxicity was observed to be mostly associated with tachycardia, agitation/irritability and hypertension[8]. In a study investigating MPH toxicity and abuse between 2002 and 2010 via the oral, intranasal, intravenous, and intra-arterial routes, MPH intake via the oral route was detected in 9 out of 14 cases, and the dose was reported to be 30-400 mg[9]. Tachycardia,

hypertension, agitation, and hallucinations were reported in one case of a person who ingested 270 mg MPH with suicidal intention; disorientation was reported in a 33-year-old subject who took 300-400 mg MPH; multiple drug abstinence symptoms were reported in a patient who ingested 320 mg of the drug[9]. However, this study did not include data about plasma levels and type of MPH used.

In this paper, the clinical manifestations of an adolescent having taken 486 mg MPH in a suicide attempt are discussed.

CASE

The case was an 18-year-old male patient who had been followed for ADHD for 5 years and who had been using MPH 54 mg and risperidone 1 mg daily for approximately 2 years. He ingested 9 MPH pills following a quarrel with his mother at home and was brought to the emergency department by his family. At the first assessment, there were no neurological and psychiatric symptoms except psychomotor agitation. Patients' orientation was normal. Glasgow coma scale score was 15, arterial blood pressure was 150/110 mmHg, heart rate was 145 bpm, respiratory rate was 20/min, body temperature was 36.8°C. His blood glucose was 153 mg/dl, blood urea 20.5 mg/dl, creatinine 0.81 mg/dl, sodium (Na^+) 141.7 mmol/L, potassium (K^+) 3.89 mmol/L, chloride (CL) 102.7 mmol/L, calcium (Ca) 9.2 mg/dl, ALT 16.8 U/L, AST 22.1 U/L, GGT 16.3 U/L. Urinary ecstasy, cannabinoids, barbiturate, benzoylecgonine, and phencyclidine were not detected and amphetamine was found to be 4.6 (normal range: 0-1000)ng/ml. Electrocardiography was uneventful with the exception of sinus tachycardia. The patient's height was 182 cm, weight was 86.5 kg and BMI was 26. Plasma MPH level was measured to be 48.09 ng/ml (normal range: 13-22 ng/ml) a couple of hours following MPH intake. Risperidone was measured to be 4.72+3.42 ng/ml (normal range: 20-60 ng/ml).

He was given activated carbon in the emergency room and 25 mg metoprolol for tachycardia. His arterial blood pressure was 150/90 mmHg and the heart rate was 115 bpm one hour later. Metoprolol was discontinued 24 hours later as his vital signs became normal. On day 6, his plasma MPH level was 0.5 ng/ml.

DISCUSSION

Slow release MPH toxicity shows signs similar to amphetamine-like drug toxicity[10]. Side effects due to central nervous system stimulation like agitation, mydriasis, tachycardia, hypertension and nausea may arise in addition to mydriasis, tachycardia, hypertension and nausea due to sympathomimetic effects[7]. Reports of long-acting MPH toxicity are limited to case reports in the literature. In a review study investigating MPH toxicity between 2002 and 2003, long-acting MPH toxicity was encountered in 58 cases (maximum dose 4 mg/kg) and minor side effects or no side effects were reported[7]. However, this study did not report plasma MPH levels.

Özdemir et al. (2010) reported the case of a 17-year-old patient who ingested 270 mg of long-acting methylphenidate for suicidal purposes and did not develop any toxicity reactions except tachycardia; he was discharged from the hospital after a 12-hour follow-up[11]. One study reported that a 3-year-old patient accidentally ingested 108 mg of long-acting methylphenidate and developed restlessness[12]. Murat et al. (2013) reported that a13-year-old boy took 1350 mg of long-acting MPH in a suicide attempt and did not develop life-threatening symptoms, but emergency medical intervention was necessary. Our case did not experience any life-threatening symptoms.

In this case, the patient ingested 486 mg of long-acting MPH for suicidal purposes. He developed restlessness, sinus tachycardia and hypertension as side effects. While Goodman et al. reported that hepatotoxicity was associated with the use of methylphenidate[13], in the presented case the liver enzymes were normal.

Activated carbon administration is recommended in MPH intoxication within 3 hours following drug ingestion[1]. Elevation of MPH plasma levels is considered to be preventable

through activated carbon administration. Beta-blockers, alpha-adrenergic antagonists and calcium channel blockers are recommended in case of hypertension development in MPH intoxication cases[5]. This patient was administered 25 mg of metoprolol considering a blood pressure of 150/90 mmHg; the metoprolol treatment was discontinued as the blood pressure declined to 120/80 mmHg after 24 hours.

It has been reported that the plasma drug concentration in MPH intoxication cases is not to be associated with a clinical condition[5]. The main cause of this condition is considered to be the fact that long-acting MPH releases 22% of the active ingredient within the first 4 hours and the remaining within 4-12 hours due to the osmotic release oral system (OROS)[2]. However, case reports about high dose long-acting MPH suggest a relationship between the plasma level of the drug and toxic symptoms. For example, visual hallucinations, agitation, hypertension, and sinus tachycardia developed in a 14-year-old who ingested 1134 mg of long-acting MPH for suicidal purposes[6]. The plasma MPH level of this case was 107 ng/ml. As side effects, hallucinations were reported in addition to sinus tachycardia and hypertension. In our case, Methylphenidate plasma level was 48.09 ng/ml, and side effects were tachycardia, hypertension, and restlessness. The likelihood of a relationship between plasma MPH level and toxicity is considered. However, high dose long-acting MPH ingestion is regarded to be non-fatal and not to cause addiction despite leading to some toxic symptoms. In addition, it was considered that activated carbon administration should not be neglected if less than 3 hours has passed as toxic symptoms may be related to the dose.

Finally, suicidal ideation is a less common adverse effect in patients treated with MPH. It is advisable to follow up for depressive symptoms in patients using MPH.

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