CASE REPORT

MDMA (3,4-Methylenedioxy-Mmethamphetamine) and Cannabis Intake Resulting in Multiple Organ Failure, Hypoglycemia, Disseminated Intravascular Coagulation (DIC), and Methemoglobinemia

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Abstract

Introduction: Drug abuses have become an important part of the emergency service admissions. As a result of MDMA (3,4-methylenedioxy-methamphetamine) intake, various side effects may occur; from minor to major conditions. After using cannabis alone there appears cardiovascular symptoms, respiratory symptoms, nausea/vomiting, and neurological symptoms. We presented the MDMA and cannabis intake case which resulted in multiple major adverse events and death in the emergency department.
Case report: A nineteen-year-old male patient was brought to the emergency department with generalized tonic-clonic seizure. On admission, the patient had hypoglycemia and his urine was positive for cannabis and amphetamine. Liver, renal failure, DIC, and methemoglobinemia developed. Although he received noradrenaline and dopamine infusion due to hypotension, his hypotension deepened. During the follow-up, cardiac arrest developed and after 30 minutes of cardiopulmonary resuscitation, death was accepted.
Discussion: The current study discusses a phenomenon in which severe side effects occured after the intake of MDMA and cannabis that resulted in death. MDMA is inhibited by the CYP2D6 enzyme and is excreted renally. The presence of drugs that inhibit this enzyme, the development of kidney failure, and the genetic polymorphism of the enzyme may cause these effects.
Conclusion: In light of this study, it is concluded that the use of street drugs can cause death with many serious side effects.

Keywords: N-Methyl-3,4-methylenedioxyamphetamine, cannabis, adverse drug events

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INTRODUCTION

Drug abuses have become an important part of the emergency service admissions. But applications are rare with MDMA (3,4-methylenedioxy-methamphetamine) and cannabis intake. MDMA (3,4-methylenedioxy-methamphetamine) is a synthetic drug and is abused for its euphoric effects. As a result of MDMA (3,4 -methylenedioxy-methamphetamine) intake, various side effects may occur, from minor to major conditions. Minor situations; tachycardia, hypertension, confusion, elevated mood, mydriasis, ataxia, nystagmus, and jaw clenching (1). Major situations are; multiple organ failure secondary to rhabdomyolysis, cerebral edema secondary to hyponatremia, isolated liver failure, cerebrovascular accident, and death (1).

Cannabis is one of the most widely used psychoactive drugs (2). Cannabis affect the cardiovascular and central nervous systems due to their psychostimulant effects. Complaints of resorting to the emergency department after using cannabis alone involve cardiovascular symptoms (tachycardia, palpitations, chest pain), nausea/vomiting, anxiety, dizziness, impaired consciousness, agitation, aggression, respiratory symptoms (dyspnea, hyperventilation), panic attack, psychosis, mydriasis, seizures, and hallucinations (2,3).

Concomitant use of Cannabis/MDMA and other drugs/alcohol is also common (2). Although illicit substance use is rare, cases with multiple side effects and death are very rare after co-administration (2). We presented the MDMA and cannabis intake case which resulted in multiple major adverse events (multiple organ failure, hypoglycemia, disseminated intravascular coagulation (DIC), and methemoglobinemia) and death in the emergency department.

CASE REPORT

A nineteen-year-old male, who complained about nausea that lasted for an hour and had a generalized tonic-clonic

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seizure, was brought from a health center. The patient had no chronic disease history or regular medication for a specific disease. The patient did not have any previous illicit drug use. According to the medical history stated by the physician in this health center, the patient had a history of using one tablet of ecstasy and cannabis six hours ago before the admission there. Blood pressure 130/65 mm/Hg, pulse rate 160/min, oxygen saturation 98%, body temperature 40°C. GCS was E1M1V1. Blood glucose was measured as 49 mg/dl in admission. Therefore, intravenous 100 ml of 20% dextrose was given as a bolus and control blood glucose was 250 mg/dl afterwards. After the intravenous 80 mg propofol and 30 mg rocuronium premedication, the patient was intubated. Bilateral mydriasis was present in his pupils, and his ECG showed us sinus tachycardia.

His blood examination showed the following values: WBC count 13 600 uL, hemoglobin 17.4 g/dL, platelet 155 103 u/L (156 000 – 373 000 u/L), creatinine 2.85 mg/dL, alanine aminotransferase 92 U/L (0 – 50 U/L), aspartate aminotransferase 1039 U/L (0 – 50 U/L), gamma-glutamyl transferase 20 U/L (0 – 55 U/L), total bilirubin 0.82 mg/dl (0.3 – 1.2 mg/dl), direct bilirubin 0.17 mg/dl (0 – 0.2 mg/dL), amylase 1072 U/L (28 – 100 U/L), sodium 136 mmol/L (135 – 145 mmol/L), potassium 5.37 mmol/L (3.5 – 5.1 mmol/L), chlorine 105 mmol/L (98 – 107 mmol/L), creatinine kinase (CK) 51 165 U/L (0 – 171 U/L), INR 1.357, aPTT 37.440 sec. (26 – 37.1 sec.), PT 14.844 sec. (11.23 - 14.44 sec.), pH 7.23 (7.35-7.45), pCO_2 32 mmHg (35 – 45 mmHg), pO_2 72.7 mmHg (83 – 108 mmHg), HCO_3 14.6 mmol/L (22 – 26 mmol/L), lactate 7.8 mmol/L (0.7 – 2.5 mmol/L), oxygen saturation 97%.

Alcohol was not found in the blood and cannabis and amphetamine were positive in the urine. It was diagnosed by urine toxicological screening test (spectrophotometry). There was no abnormal finding in brain tomography and thoracoabdominal angiography.

In the follow-up of the patient with hematuria and hematemesis, control blood evaluation showed the following values: D-dimer >35.585, fibrinogen <0.5, INR 2.334, platelet 40 103 u/L, hemoglobin 11.8 g/dL; and 1-2 schistocytes were seen in the peripheral smear of the blood. The patient was diagnosed with DIC. Since the patient had active bleeding due to hematuria and hematemesis and hypotension, blood replacement was performed according to the massive transfusion protocol.

Although intravenous 10% dextrose 200 ml per hour had been given to the patient, severe hypoglycemia had continued during the follow-up period. Hence, intravenous 3 mg glucagon had been applied, and blood glucose had become stable. Since the blood pressure of the patient was 60/40 mmHg, the first infusion of noradrenaline and then dopamine infusion was started to increase blood pressure. Insufficient urine output and increased blood creatinine level were observed; therefore, continuous venovenous hemodiafiltration was started.

While the patient had been followed in the intensive care unit (ICU), intravenous 100 mg methylene blue was given to the patient due to methemoglobinemia (14.7%) caused peripheral cyanosis. While the noradrenaline infusion was increased to 2mcg/kg/h, the blood pressure had been 40/20 mmHg. So, terlipressin infusion was started at 100 mg/h; however, cardiac arrest developed afterwards during the follow-up. After 30 minutes of cardiopulmonary resuscitation (CPR), the patient had no vital response, and he was accepted as dead. The total time was about 34 hours from the admission to death.

DISCUSSION

Drug abuses have become an inseparable part of the emergency service admissions, and MDMA is one of many causes of these applications. In a study of 378 diseases, the most commonly observed findings were reported as behavioral change, hypertension, tachycardia, and hyperthermia. Rhabdomyolysis and renal failure developed less frequently, seizures in two patients, intracranial hemorrhage in three patients, and myocardial infarction in one patient had been reported [(3)]. Platelet aggregation and plasminogen activation develop after the use of MDMA. These events cause DIC, renal failure, metabolic acidosis, and hyperkalemia, respectively. This is the most common reason for the death in MDMA abusers (1). In a study by Armenia P et all, none of the patients who had hypotension had sequelae-free survival. The prognosis of the patients with low "creatinine kinase/creatinine" ratio and low body temperature was reported to be better (4). Rhabdomyolysis is required to be treated aggressively. Failure to treat it could lead to a vicious cycle resulting in multiple organ failure (5). MDMA-caused severe and persistent hypoglycemia have been explained by endogenous hyperinsulinism. MDMA-caused methemoglobinemia has also been reported as a rare event (6,7). Local anesthetics often cause methemoglobinemia. It has been reported that it is used as an additive to street drugs (cocaine and ectasy) due to its anesthetic effects (8,9).

Synthetic cannabiodes especially affect the cardiovascular and central nervous systems due to their psychostimulant effects. These effects are hypertension, arrhythmia tachycardia, arrhythmia, torsades de pointes, long QT, chest pain and acute myocardial infarction. CNS effects include seizure, ischemic, and hemorrhagic stroke. Severe respiratory system findings and acute renal failure have also been reported. Hyperthermia has also been reported [(10)]. It has been reported that half of the deaths are caused by cardiovascular side effects (10,11). In another review, it was reported that the use of cannabis increased the possibility of cardiac dysrhythmia (12).

Moreover, it has been reported that there is an interaction between the intake of MDMA, a sympamimetic agent, and the intake of phenelzine, which is a monoamine oxidase (MAO) inhibitor, and the side effects become more pronounced owing to the intake of MDMA, and toxicity occurs (9). In a similar manner, it has been shown in the literature that cannabis intake causes MAO inhibition (13).It is stated that MDMA is metabolized with CYD2P6 enzyme, and shows genetic polymorphism in individuals. This polymorphism and unique component that provides the combination of this drug have been considered as the causes of these adverse events (1). Furthermore, it has been claimed that severe hepatotoxicity due to the use of MDMA after the poor metabolism of the CYD2P6 enzyme causes death (14).

MAO inhibitors hinder cytochrome p450 enzymes (15). Cannabis intake inhibits CYP2D6 enzyme due to MAO inhibition (16). Although CYP2D6 plays a role in metabolism, the plasma half-life of amphetamine and related substances is generally dependent on the acidity of the urine, as renal excretion is the main route of elimination (17).

We think that the findings in our case may be due to the side effects of MDMA. MDMA metabolism and excretion pathway play an important role in the prolongation and exacerbation of this effect. The effect of renal excretion of amphetamines may play a role. This may be exacerbated by CYP2D6 inhibition. Genetic polymorphism of the CYP2D6 enzyme may also have a role. It can also be caused by the use of drugs that cause enzyme inhibition (e.g. methylene blue)**.** In light of the present case study, we are of the belief that it is useful to question the drugs that the patient uses constantly, to question the intake of additional substances or to pay attention to the drugs given during medical care.

CONCLUSION

This study indicated that street drugs that can often be taken together can cause serious health dangers including death and many other serious side effects.

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