

Case Report

Subarachnoid Hemorrhage and Death Following Coingestion of MDMA with Other Drugs

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Key Words

coingestion;
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Ecstasy, the popular name for 3,4-methylenedioxyamphetamine (MDMA), is a synthetic amphetamine derivative. It stimulates the sympathetic nervous system, producing serious adverse effects on the cardiovascular system. We present a 20-year-old female patient, who developed subarachnoid hemorrhage (SAH) and death following MDMA and coingestion with other drugs. She suffered from severe headache followed by vomiting, and conscious change 5 hours after an intake of 1 tablet MDMA and other drugs at a dance club. Her blood pressure was 226/164 mmHg, pulse rate 164/min, respiratory rate 30/min on arrival at our emergency department. Diffuse rales were heard over both lung fields. Both pupils' sizes were 4 mm, with sluggish reaction to light. A 12 lead electrocardiograph showed sinus tachycardia, ST depression in the inferior leads and V4 to V6 precordial leads. Laboratory findings revealed normal except a slightly raised white cell count and glucose. Arterial blood gas analysis showed pH was 7.333, with PaCO₂ 24.6 mmHg, PaO₂ 151.7 mmHg and HCO₃ 12.8 mmol/L. Chest x-ray revealed acute pulmonary edema. Urgent computerized tomography scanning of the head demonstrated SAH. Her condition continued to deteriorate, and went to deep coma and shock status. She expired on the second day although we treated aggressively.

MDMA ("Ecstasy"), a synthetic analogue of 3,4-methylenedioxyamphetamine (MDA), was first developed as an appetite suppressant in 1914, but was never marketed up to 1970.¹ It is chemically related to both hallucinogens and stimulants.² Apart from a mild amphetamine-like stimulant effect, it induces a feeling of euphoria and benevolence.³ Recently, it has become increasingly popular as a recreational drug in disco dancing clubs.⁴ MDMA use is closely tied to underground raves and dance clubs, because of strong feelings of comfort, empathy, and connection to others its users experience. Deaths following its abuse have occurred in the presence of underlying diseases such as ischemic heart disease, asthma, and cardiac conduction defects.^{1,5} We report a case of subarachnoid hemorrhage and death following MDMA and coingestion with other drugs in a young female patient.

CASE REPORT

A 20-year-old female patient was sent to our emer-

gency room by her friends because of sudden onset of headache followed by vomiting, and conscious disturbance. She had history of an intake of 1 tablet of MDMA with 2 doses of oral medication for common cold and urinary tract infection at a dance club 5 hours before. There was no personal, psychiatric, underlying medical, or traumatic history before. On arrival in the emergency department, physical examination revealed drowsy consciousness and erythematous skin rash over the whole body. The patient's glasgow coma scale was 12/15 initially. There was no neck rigidity or focal signs. Her blood pressure (BP) was 226/164 mmHg, pulse rate (PR) 164/min, respiratory rate 30/min, and temperature 36 °C. Diffuse rales were heard over both lung fields. Both pupils' sizes were 4 mm, with sluggish reaction to light. Pulse oximetry showed 95% saturation at room air status. A 12 lead electrocardiograph (ECG) showed sinus tachycardia, ST depression in the inferior leads and V4 to V6 precordial leads, and heart rate 150 beats/min. Initial management included intravenous normal saline administration and monitoring of pulse oximetry, blood

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pressure and ECG changes. The patient was treated with nifedipine 10 mg sublingually to control hypertension and given supplemental oxygen at 4 L/min via nasal prongs. Laboratory data, including hemoglobin, platelet count, sodium, potassium, cardiac enzymes, renal, and liver function values, were within normal range except for a white cell count 12,490/mL and glucose 161 mg/dL. Arterial blood gas showed pH 7.333, PaCO₂ 24.6 mmHg, PaO₂ 151.7 mmHg, and HCO₃ 12.8 mmol/L. We drew blood for routine examination and collected urine for pregnancy test and toxic drug screen. MDA, MDMA, diphenhydramine, chlorpheniramine, caffeine, and trimethoprim were detected in the patient's urine. Within a few minutes, her overall condition continued to deteriorate, and going to deep coma. She received emergent insertion of endotracheal tube (ETT) and was mechanically ventilated. CXR revealed ETT in place, and acute pulmonary edema (Fig. 1). The patient was treated with furosemide 20 mg intravenous infusion for control of acute pulmonary edema. Emergent computed tomography (CT) scanning of the head showed subarachnoid hemorrhage (SAH) (Fig. 2). After that, her BP dropped to 60/36 mmHg, and PR was 140 to 150/min. An ECG monitor showed sinus tachycardia in long lead II and heart rate 150 beats/min. The patient was treated with inotropic agents to stabilize her hemodynamics. Invasive



Fig. 1. Chest x-ray displays endotracheal tube in place, and acute pulmonary edema.



Fig. 2. A CT scan of head demonstrated subarachnoid hemorrhage.

procedure like cerebral angiography was not done because her family disagreed, and due to unstable hemodynamics. One episode of sudden asystole was noted during that night, and heart rate regained after cardiopulmonary resuscitation. An ECG monitor showed sinus tachycardia with ST depression in long lead II and heart rate 150 to 160 beats/min. The next day, the BP dropped again, to 61/28 mmHg, and the patient was unresponsive to inotropic agents and fluid resuscitation due to progressive heart failure. She then expired despite aggressive treatment.

DISCUSSION

MDMA is a synthetic analogue of MDA that was first developed as an appetite suppressant in 1914.¹ Over recent years it has been a popular recreational drug among young people, particularly at the dance parties known as "raves". It is chemically related to both hallucinogens and stimulants.² Because of its mild amphetamine-like stimulant effect and strong feelings of comfort and empathy it induces, many people use MDMA at underground raves, dances, and night clubs.^{2,3} Methamphetamine (MA) is the most important drug of abuse in Taiwan, followed by opiates. Recently, there has been an increased of ketamine and MDMA abuse in disco dancing clubs.⁴ In Taiwan, MDMA poisoning was widely re-

ported by the media as being responsible for varying degrees of toxicity observed. Many cases of MDMA-related death have been reported in the English literature,^{1,3,5-7,10} but no case was documented in the Chinese literature. Previous reports demonstrated multiple severe complications such as convulsion, fulminant hyperthermia, coma, disseminated intravascular coagulation, rhabdomyolysis, cardiac compromise, acute renal failure, fulminant hepatic failure, psychiatric disturbance, and miscellaneous toxicity associated with ingestion of MDMA (ecstasy).^{3,5-7} The epidemic use of amphetamine, cocaine and MDMA is fast replacing traditional etiological factors as the major cause of intracerebral hemorrhage (ICH) among young adults.⁸ Immediately, we got information about ingestion of MDMA from the patient's friends, and our impression was changed to MDMA-related severe clinical problems. Due to deterioration of her overall condition, she was treated with emergent insertion of ETT and mechanically ventilated. Urgent CT scanning of the head was done, revealing SAH. Some authors described development of SAH and ICH following MDMA, cocaine and amphetamine abuse.^{8,9-13} Kalant reviewed the previous literature about the variety of different side effects, including psychiatric, neurological, cardiovascular, hepatic, renal, thermoregulatory and even dental problems, indicating that patients with ecstasy-related problems may present in many parts of the health care system and not only to emergency services.⁷ McEvoy described 13 patients of ICH after amphetamine, ecstasy and cocaine abuse in young adults. Cerebral angiography demonstrated intracranial aneurysms in 6 patients, and arteriovenous malformations in 3.¹⁰ After ingestion of MDMA, however, it is possible that there is an acute sympathetically mediated surge in blood pressure which causes the aneurysm to rupture.^{7,8} It is also possible that rupture of vessels that are already weakened by congenital anomaly or pre-existing disease due to this drug directly surges in blood pressure.¹³ Arteriography should be part of the evaluation of young patients with nontraumatic ICH.⁸ We well discussed with her family doing another procedure like cerebral angiography, but they disagreed with doing it. Besides MDA and MDMA, other drugs were detected in our patient's urine. This was due to her previous intake of these drugs for common cold and urinary

tract infection, which was confirmed by her family. In our patient, development of SAH may be due to underlying vasculitis or ruptured intracranial aneurysms and arteriovenous malformations. MDMA increased release of noradrenaline and dopamine, especially noradrenaline that is responsible for hypertension, with a consequent risk of ruptured blood vessels and internal hemorrhage, and tachycardia, with a consequently increased cardiac workload and a resulting risk of heart failure.⁷ Kalant stated that many of fatal cases had lung edema, which is a sign of heart failure.⁷ In our case, cardiogenic shock and heart failure lead to death. Yeh reported that chlorpheniramine attenuated and diphenhydramine had no effect on MDMA-induced hyperthermia.¹⁴ Most MDMA and related drugs are sold mixed with caffeine, sugar, and polyols (such as mannitol).¹⁵ So, caffeine was detected in her urine. MDMA ingestion could result in severe intoxication and even death, especially when combined with other psychoactive drugs (e.g. opiates, cocaine).¹⁵

In conclusion, MDMA-induced sudden death may occur, especially after mixed use with other drugs and/or alcohol. We emphasize the importance of taking a full drug history, including the possible abuse of illicit drugs, and toxicological screening of urine and serum in patients with nontraumatic ICH and SAH. Obtaining detailed history of the drug taken and its content or dose is difficult, but it is important for emergency physicians.

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