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CASE REPORT

PATHOLOGY/BIOLOGY

Tarini Fernando,[1] M.B.B.S.; John D. Gilbert,[2] F.R.C.P.A.; Christine M. Carroll,[2] B.Sc.; and Roger W. Byard,[1,2] M.D.

Ecstasy and Suicide

ABSTRACT: Deaths due to the ring-derivative amphetamines are not common and are usually accidental involving dehydration and hyperthermia. Suicides from 3,4-methylenedioxymethamphetamine (MDMA) and related ring-derivative amphetamines overdose are rare. A 15-year-old female who had a history of depression and previous suicide attempts was found dead with a suicide note. Toxicology demonstrated lethal serum concentrations of MDMA (9.3 mg/L), with 34 mg/kg of MDMA in the liver, 2.4 mg/L in the urine, and 530 mg/kg in the stomach. The cause of death was MDMA toxicity, the manner suicide. While MDMA may be detected in victims in other drug-related or traumatic deaths, it is only rarely used in isolation in suicide, with a predominance in the 21- to 25-year-old range. Despite the rarity of such events, the possibility of a nonaccidental manner of death should be considered when high levels of MDMA and associated amphetamines are found at autopsy.

KEYWORDS: forensic science, ecstasy, MDMA, death, suicide, hyperthermia

"Ecstasy" is the street name for the ring-derivative amphetamine 3,4-methylenedioxymethamphetamine (MDMA) (1), an hallucinogen that induces physical and psychological effects such as increased alertness, sensory perception, physical endurance, and sexual arousal, along with sense of empathy for others and a feeling of euphoria (2,3).

Deaths associated with the ring-derivative amphetamines are uncommon and are usually accidental (4). Following the suicide of an adolescent female who had deliberately taken a large quantity of MDMA, the literature was reviewed for similar cases to determine the extent of the problem and whether there were any features common to the victims.

Case Report

A 15-year-old female who had been at home alone was found dead on her bedroom floor by her mother. She had last been seen alive 5 h before. There was a history of depression with episodes of self-harm and two previous suicide attempts the previous year, which were precipitated by the break up of a relationship with her boyfriend. The first suicide attempt involved the ingestion of metoclopramide and antibiotic tablets; the second episode involved the ingestion of sodium valproate (prescribed for another family member). At the scene, a suicide note addressed to her ex-boyfriend was found, with "goodbye" messages on her cell phone, and a fragment of a tablet on the floor.

An autopsy was performed 60 h after death. At autopsy, there were no significant injuries, with multiple superficial linear scars over the lateral aspect of the right upper thigh in keeping with the history of self-harm. Tablet residues were found in the stomach. There were no natural diseases present that could have caused or contributed to her death. Histology showed edema and congestion of the lungs with equivocal changes of early neuronal hypoxic-ischemic changes in Sommer's sector of the hippocampus. Contraction band necrosis within the myocardium was not identified. Toxicological analyses revealed lethal blood concentrations of MDMA and its metabolite 3,4-methylenedioxyamphetamine (MDA) of 9.3 and 0.28 mg/L, with 34 and 0.9 mg/kg of MDMA and MDA in the liver, respectively. There was also 530 mg/kg of MDMA in the stomach and 2.4 and 0.2 mg/L of MDMA and MDA, respectively, in the urine. Toxic levels of caffeine were also found with levels of 25 mg/L, 8.4 mg/L, 25 mg/kg, and 550 mg/kg in the blood, urine, liver, and stomach. There was no alcohol detected or other common prescription and nonprescription drugs. The cause of death was MDMA toxicity, the manner suicide.

Discussion

MDMA has been used recreationally since the 1980s and is the second most commonly used illicit drug in Australia after cannabis and is often associated with the dance club scene (5,6). The effects of MDMA begin within *c.* 30 min of ingestion and last for 4–6 h. Peak plasma concentrations occur *c.* 2 h after oral intake, and metabolism occurs within the liver through the P450 system (the main enzyme being CYP2D6) (1,7), with almost 65% of the dose excreted unchanged. MDMA has a long half-life of 8 h, and the major metabolite (MDA) is still pharmacologically active, increasing the duration of action (8,9). It may be difficult to determine at what concentration MDMA toxicity occurs, as the adverse effects are not necessarily dose dependent (10). While in most cases of MDMA toxicity or fatality, the plasma levels range from 0.5 to 10 mg/L (11), individual susceptibility occurs, possibly linked to debrisoquine hydroxylase (CYP2D6) deficiency (1). CYP2D6, a member of the cytochrome P450 superfamily, is absent in 5–9% of Caucasians. Such deficiencies may result in deaths from lower doses because of either decreased demethylation of MDMA or idiosyncratic reactions causing cardiac dysrhythmias (12). Inhibition of

[1]Discipline of Anatomy and Pathology, The University of Adelaide, Frome Road, Adelaide, SA 5005, Australia.
[2]Forensic Science SA, 21 Divett Place, Adelaide, SA 5000, Australia.

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CYP2D6 by other illicit or prescribed drugs may also decrease the clearance of amphetamine derivatives (1).

Many ecstasy tablets contain 80–120 mg of MDMA (13); however, the amount of MDMA varies given the lack of control over the composition of street drugs. Other amphetamine derivatives that may be present include *N*-methyl-L-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB or "Eden"), MDA, 3,4-methylenedioxyethylamphetamine (MDEA or "Eve"), and paramethyoxyamphetamine (PMA). The latter drug has a street name of "death" and is associated with a higher rate of lethal events (1,14). In addition, tablets often contain contaminants such as caffeine, ketamine, and pseudoephedrine (1). The toxic levels of caffeine in the reported case were most likely due to this. Given these levels, it is also possible that caffeine toxicity may have contributed to the terminal episode by exacerbating cardiotoxic effects (15,16).

Deaths from ecstasy are most often accidental involving a variety of mechanisms. Hyperthermia may occur because of an MDMA-induced increase in central nervous system serotonin levels resulting in rhabdomyolysis, renal failure, and disseminated intravascular coagulation (1,17). Profuse sweating may lead to hyponatremia, which is often exacerbated by the ingestion of large amounts of water in an attempt to cool down. This may also be contributed to by inappropriate antidiuretic hormone release, the cause of which is unknown in MDMA users (18). Hyponatremia may cause lethal cerebral edema. MDMA also induces an increase in noradrenaline levels, sometimes causing malignant hypertension with intracerebral hemorrhage or cardiotoxicity (5,19).

Suicide relying on MDMA and/or other related ring-derivative amphetamines in isolation appears to be quite rare (20–23). More common is the finding of nonlethal levels of these drugs in traumatic deaths such as hanging or in association with other drugs such as methadone, ketamine, or insulin that have been used to terminate life (5,8,24,25).

Suicide methods are governed by accessibility and also by an understanding of the potential lethality of a particular action or substance (26,27). This may explain the low rate of ecstasy ingestion in isolation as a means of suicide, as widespread use with only rare adverse reactions may have led to a belief that it is not sufficiently toxic to reliably cause death. A lack of understanding of substance lethality, particularly in the young, was demonstrated in the reported case with antibiotics being taken in a previous suicide attempt. The rate of ecstasy use in failed suicide attempts is even more difficult to determine because of great variability in the reporting of such events. Chronic use of MDMA has been shown to lead to severe depression with suicidal ideation because of serotonergic neurotoxicity (28).

Other reasons for death following MDMA ingestion include trauma associated with falls and motor vehicle accidents from impaired judgment with increased risk taking, factors which may also come into play in MDMA-related homicides (5). Substitution of MDMA with more lethal ring-derivative amphetamines such as PMA may also increase the rate of adverse events (1). Finally, there may also be an increased incidence of lethal cardiovascular disease with a higher rate of atherosclerosis (5) and the occurrence of dilated cardiomyopathy (18,29). Myocardial infarction and aortic dissection have also been found in MDMA users (5).

The rarity of suicide using MDMA suggests that users remain unaware of the potentially lethal effects of overdosage. However, when high levels of MDMA and associated amphetamines are found at autopsy with no other drugs or alcohol, the possibility of a nonaccidental manner of death should be considered.

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Additional information and reprint requests:
Prof. Roger W. Byard, M.D.
Discipline of Anatomy and Pathology
Level 3 Medical School North Building
The University of Adelaide
Frome Road
Adelaide
SA 5005
Australia
E-mail: roger.byard@sa.gov.au