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CASE REPORT

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Deaths associated with MBDB misuse

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Abstract The use of phenethylamines in the dance scene is now well established. Apart from amphetamine, the commonest phenethylamine encountered in clinical and forensic settings is 3,4-methylenedioxymethamphetamine (MDMA) commonly known as ecstasy. Other phenethylamines, which have similar effects are encountered, such as 3,4-methylenedioxyethylamphetamine (MDEA) and their use has resulted in death. We report two deaths associated with another less commonly encountered member of the group, N-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB), also known as Methyl-J and Eden.

Key words N-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine · MBDB Ecstasy · Eden Death

Introduction

In 1988 a music movement entered the culture of the UK [1]. Brought from Ibiza, it was accompanied by the use of ecstasy and was commonly known as the "rave" or "acid house" scene. The participants characteristically danced for long periods to repetitive music and took the drug ecstasy, a term which was traditionally used to mean the substance 3,4-methylenedioxymethamphetamine (MDMA). MDMA is a member of the group of drugs known as ring substituted phenethylamines. In the UK all these substances have been subject to the 1971 Misuse of Drugs Act since 1977, when all compounds structurally derived from N-alkyl-a-methylphenethylamine were classified as class A drugs, the most restrictive classification, which carries the most draconian penalties for possession and supply. This group also includes 3,4-methylenedioxyethylamphetamine (MDEA) and 3,4-methylenedioxyamphetamine (MDA). The tablets that are sold as ecstasy often have sophisticated logos such as "doves", "£" or "$" signs or commercial logos. The external appearance of the tablet is not a reliable guide to its content; tablets of the same appearance may contain quite different compounds from week to week [1,2]. The user hopes the tablet contains MDMA, but other phenethylamines, such as MDEA and MDA may be present, along with amphetamines, caffeine, ephedrine and pseudoephedrine, paracetamol, aspirin, ketamine or no active compounds. Recently N-methyl-1-(3,4-methylenedioxyphenyl)-2-butanamine (MBDB), also known as Methyl-J and Eden, has been encountered. We report two deaths associated with its misuse.

MBDB is the N-methyl homologue of BDB and is the alpha-ethyl analogue of MDMA. BDB is the principle metabolite of MBDB, but may also be encountered in tablets containing MBDB. BDB is also known as J, hence Methyl J for MBDB.

Case reports

Case 1

A 19-year-old female attended a nightclub. She was believed to have taken amphetamine powder and a tablet of ecstasy between 1915 hours and 2115 hours. At approximately 0200 hours she began to behave aggressively and had difficulty in speaking and standing. Shortly after this she was taken home by her friends and laid on a sofa. At 0717 hours an ambulance was called as she was fitting. She was found to be in cardiac arrest. She was conveyed to the local hospital, but despite further resuscitation she died at 0830 hours. Post-mortem examination revealed an oedematous brain and subsequent neuropathological examinations did not identify any localised pathology. There was pulmonary congestion and patchy intra-alveolar haemorrhages. Subendocardial haemorrhage was present in the aortic outflow tract. The liver, spleen and kidneys were markedly congested. Histology of the heart showed extensive contraction band necrosis. The kidneys and spleen were congested. No individual hepatocyte necrosis was seen in the liver, but neutrophils were present in the sinusoids. No myoglobinuria was identified and skeletal muscle appeared normal as did the remaining organs. No pre-existing disease was identified.

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Blood, urine and stomach contents were submitted for toxicological examination. This revealed the presence of amphetamine in the blood at a concentration of 2.1 mg/l and in stomach contents at a concentration of 9 mg/l. MBDB was present in the blood at a concentration of 0.435 mg/l and in the stomach at a concentration of 5.2 mg/l. BDB was present in the blood at a concentration of 0.106 mg/l and in the stomach at a concentration of less than 1 mg/l.

Case 2

The body of a 33-year-old man was found at the foot of a multistorey car park. He had a previous history of attempted suicide but was not known to misuse alcohol or other illicit drugs. Postmortem examination revealed multiple external and internal injuries entirely in keeping with a fall from a height. There was no evidence of an assault. No pathological process was identified on histological examination. The bladder was empty, but peripheral blood was submitted for toxicological examination. This revealed a blood ethanol of 15 mg/100 ml. The only other significant finding was the presence of MBDB at a concentration of 1.2 mg/l. BDB was not detected. Analysis for LSD was not performed.

Toxicological methodology

Urine samples submitted for screening for misused drugs are, *inter alia*, screened using the EMIT Amphetamine group assay with a cut off for dexamphetamine of 0.3 mg/l. (Dade Behring Diagnostics UK Milton Keynes). Using blank urine spiked with MBDB, this assay has a cut off for MBDB of about 10 mg/l. This appears to be of the same order as that of the EMIT DAK monoclonal amphetamine/methamphetamine assay, which has been reported as being capable of detecting MBDB and its metabolite in urine 4 h post a 100 mg dose of MBDB in a volunteer [3]. Any sample yielding a positive or borderline result is subject to further screening by GC/MS.

Discussion

In their book PIHKAL, Shulgin and Shulgin [4] describe the effects of taking 210 mg of MBDB, followed by a further 70 mg, as very much like MDMA. Overall users would appear to prefer MDMA, as MBDB induces less spontaneity, warmth and clear intimacy associated with of use of MDMA. The recommended dosage for recreational use in PIHKAL was 180–210 mg of MBDB, which is higher than for MDMA, which was 80–150 mg. In the UK around 60% of tablets sold as ecstasy have contained MDMA, characteristically the majority contained around 80–140 mg of MDMA, but this varies from time to time. Around 20% contained MDEA and 10% have contained MBDB [1].

Deaths associated with MDMA and MDEA misuse were first reported in the USA in the 1980 s [5,6]. Reports of ecstasy use and deaths followed in the UK and other European countries. Deaths in the USA were associated with pre-existing disease or accidents, but the first deaths in the UK were due to heat-stroke [2, 7–18]. Ring substituted phenethylamines are known to alter thermoregulation and their use at raves and other dances appeared to be an important component in the UK deaths. Hepatitis, fibrosis and fulminant liver failure were also identified [19–25]. Cases of water intoxication, some fatal, were also encountered [2, 26–27]. The mechanism of injury to the liver remains unknown, but MDMA has been shown to cause inappropriate secretion of anti-diuretic hormone (ADH), which may play a significant role in water intoxication [28].

As MBDB has a similar action to MDMA, it is likely to be as potentially dangerous as MDMA and MDEA. In the first case, amphetamine was present in the largest concentration, but MBDB may have had an additive effect. Whether amphetamine and MBDB was ingested separately or together, or whether the compounds were in the same tablet is uncertain. Both were present in the stomach. The specific mechanism of death in this case could not be ascertained. No histological features of heat-stroke were identified and no body temperature was recorded. A cardiac arrhythmia is a possible cause of death and both amphetamines and other phenethylamines are capable of inducing a malignant arrhythmia.

We first encountered MBDB in post-mortem blood in January 1996, in a young man who died of methadone poisoning. It remains a rare finding in our clinical toxicological practice. In the last 3 years, 23,797 drug screens have been performed on 6588 persons. MBDB was identified in only one case involving a 28-year-old female, who was a known drug misuser. Methadone, MDMA and MDA were also detected in the urine. In comparison there were 62 urine samples that contained MDMA, MDEA and/or MDA. MBDB has been identified in ecstasy tablets in Italy and in a non-fatal case from Sweden [29,30].

The exact role of MBDB in people dying of trauma, as in the second case, is unclear, but as phenethylamines may induce hallucinations, its direct involvement cannot be excluded. Furthermore the role of these substances in serotonin metabolism and the possible depressive effects suggests a role in some suicides.

The use of phenethylamines change and investigators need to be aware of possible variations in drug culture. Local production will inevitably vary and drugs sold as ecstasy will vary. A recent report from South Australia [31] recorded the deaths of six people from paramethoxyamphetamine (PMA), which caused deaths in a similar manner to other phenethylamines, but has not been seen in our department. All phenethylamines appear to have the potential to cause harm. Their use cannot be claimed to be safe.

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