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A fatal overdose with 3,4-methylenedioxyamphetamine derivatives

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Abstract

Methylenedioxymethylamphetamine (MDMA or 'Ecstasy') is the best known of the 3,4-methylenedioxy ring-substituted amphetamines [1]. Reports of serious adverse reactions and fatalities associated with its use emphasise hyperpyrexia, profuse sweating and subsequent rhabdomyolysis, although cardiac deaths and fatal accidents whilst intoxicated are also prominent [2–5]. Other 3,4-methylenedioxy ring-substituted amphetamines are also available in the illicit market place and may have different spectra of activity [6]. We report here a case of fatal ingestion of a variety of drugs of this group.

Key words: Methylenedioxyamphetamines; Fatal poisoning; Blood concentrations pentafluoropropionic anhydride; Mass spectroscopy

1. History

A 21-year-old man attended a party where tablets which were purported to be 'Ecstasy' were available. He left the party with friends and returned home where, in company, he smoked some cannabis. His condition was described by his friends as 'normal' when they left him at 05:30 h. Some 7 h later he was found dead in his bed. At his bedside were temazepam capsules and tablets together with two different types of white tablet, neither of which appeared to have been produced by an ethical pharmaceutical manufacturer.

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Table 1
Drug concentrations in body fluids obtained at post mortem

Compound	Blood (mg/l)	Stomach content (mg/l)	Urine
Amphetamine	256 μg/l	Less than 0.1	Present
Methylenedioxyamphetamine	8.5	299	Present
Methylenedioxymethylamphetamine	2.1	96	Present
Methylenedioxyethylamphetamine	3.5	324	Present

2. Postmortem findings

Postmortem examination showed no significant external findings. Internally there was copious bloodstained froth in the airways and gross haemorrhagic oedema of both lungs. Histological examination of the lungs showed appearances typical of aspiration of gastric contents, with widespread intra-alveolar haemorrhage and oedema, areas of autolysis and bacterial overgrowth. In a few foci there was early emigration of polymorphs from capillaries, possibly suggesting a period of survival after aspiration before death. There were no other abnormal findings, in particular no evidence in the heart of myofibrillary degeneration, no evidence in the liver of an inflammatory infiltrate, and no evidence in the kidney of myoglobin casts or disseminated intravascular coagulation. Samples of brachiocephalic vein blood, urine and stomach content were obtained for toxicological analysis.

3. Toxicological analyses

Immunochemical screening of the urine gave positive results for the presence of amphetamines [7], cannabinoids and lysergic acid diethylamide. Blood, urine and stomach content gave negative results on screening for benzodiazepines [8]. No ethanol was found by head space gas liquid chromatography in blood or urine. Specific analyses of the body fluids for amphetamine and its ring-substituted derivatives was carried out by gas chromatography — mass spectroscopy [9]. The results of the quantitative analyses are shown in the table. Of the two types of non-commercial tablets found in the deceased's bedroom, one had a MDA content of ~60 mg per tablet and the other contained ~45 mg of MDEA per tablet. Whilst many illicit formulations of MDEA contain small amounts of MDMA, no MDMA was present in the MDEA tablets in this case.

4. Discussion

MDA may be produced in vivo from MDMA by *N*-demethylation. When small doses, ~50 mg, of MDMA are taken by mouth the proportion of MDA relative to MDMA in serum can be as high as 40% 4 h or so after ingestion [10]. Typically, following fatal overdose of MDMA alone much lower ratios of MDA to MDMA are found. In a patient who survives for any length of time after MDEA ingestion

one might expect to find significant amounts of MDA in blood produced by *N*-dethylation. In one case where death occurred rapidly after MDEA ingestion, no MDMA was found in blood obtained at post mortem [4]. While it is not uncommon to find small amounts of demethylated drug metabolites in stomach contents after death, presumably as a result of regurgitation of bile from the duodenum into the stomach, the substantial concentrations of MDA and MDMA found in the stomach content in this case suggest that the deceased had taken considerable amounts of MDMA and MDA as well as MDEA. The small amount of amphetamine found would be consistent with relatively small doses of amphetamine having been taken earlier in the evening.

Previous reports of fatalities following ingestion of methylenedioxyamphetamine and its *N*-alkyl derivatives have suggested that death is usually associated with central stimulant effects, such as fulminant hyperthermia and convulsions, with trauma following accidents while intoxicated by the drug and with drug induced cardiac dysrhythmias. In the present case death was the result of inhalation of gastric contents whilst intoxicated. While the inhalation could have been a primary complication of the intoxication, it would, of course, be impossible to exclude it having been precipitated by one of the other known complications, in particular by a convulsion or cardiac dysrhythmia. It is also apparent that tablets sold as 'Ecstasy' may be any one of a number of drugs or a mixture thereof.

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