LESSONS FROM PRACTICE

Death and paramethoxyamphetamine — an evolving problem

Case reports

Case 1: A 22-year-old man complained that he was "burning up" and collapsed after ingesting drugs at a friend's house. He died soon afterwards at a local hospital, despite attempts at resuscitation. His core temperature was 42°C. At autopsy there was evidence of coagulopathy, with scattered bruises, intra-alveolar haemorrhage, and haemorrhagic pleural effusions, ascites and stomach contents. Toxicological blood analysis revealed a lethal level of PMA (1.3 mg/L), together with 0.02 mg/L of MDMA and 0.21 mg/L of methylamphetamine. No alcohol was detected in the blood.

Case 2: An 18-year-old man died at his home after ingesting a number of "ecstasy" tablets over five hours, both at a dance club and at home. Two hours after death the core temperature of the body was 39°C. Autopsy revealed focal pericardial haemorrhage, pulmonary congestion and renal tubular necrosis. Toxicological blood analysis showed a lethal level of PMA (1.7 mg/L), with 0.1 mg/L of MDMA and 0.06 mg/L of methylamphetamine. No alcohol was detected in the blood.

Case 3: A 19-year-old man died in hospital 40 hours after being brought to the emergency department in respiratory arrest with a body core temperature of 41.6°C. He had taken "two or three capsules" of street drugs of an uncertain nature, both at a "rave" party and then at a friend's home the following day. According to witnesses, he had been advised to take PMA for an enhanced effect after taking MDMA. Laboratory investigations revealed evidence of rhabdomyolysis, with a serum myoglobin level of 328 960 g/L (normal level, < 150 g/L), disseminated intravascular coagulation and marked hyperkalaemia (7.7 mmol/L; normal range, 3.5–5.0 mmol/L).

At autopsy there was evidence of coagulopathy, with epicardial petechiae, pulmonary haemorrhage, haemorrhagic gastric and intestinal contents, and haemorrhagic serous cavity effusions. There was also oedema and necrosis of skeletal muscle and renal tubular necrosis. Toxicological blood analysis revealed a lethal level of PMA (0.98 mg/L), with 0.32 mg/L of MDMA. No alcohol was detected in the blood. Analysis of capsules found with the patient revealed PMA with no other amphetamine derivatives.

Death from amphetamine use is a well recognised occurrence, with most reported fatalities involving the use of 3,4-methylenedioxymethamphetamine (MDMA, or "ecstasy"). In 1998, a series of six cases of death due to an unusual amphetamine drug, paramethoxyamphetamine (PMA), was reported in South Australia.[1] The only other comparable report of deaths due to PMA was that of nine deaths in Ontario, Canada, in the early 1970s.[2] In 1998, our group warned that, although PMA substitution for MDMA appeared at the time to be a local Australian problem, there was a possibility that the manufacture and sale of PMA could occur in other countries. Unfortunately, this prediction has been proved accurate, with recent reports of PMA-related deaths in the United States, Europe and Canada.[3-5]

Initially, it was assumed that PMA was created as a contaminant during the synthesis of MDMA and was being disguised and substituted for MDMA by local dealers attempting to offload the drug.[1,6,7] However, this is now considered unlikely, as the chemical precursors of PMA and MDMA are different,[3,4] and information received concerning Case 3 (described here) suggests that capsules containing only PMA are being marketed specifically to augment the effects of MDMA. This is an extremely dangerous development, as it is well recognised that PMA has a much greater propensity to produce adverse effects than other ring-derivative amphetamines.[6]

Death in each of the cases described here was due to PMA toxicity with hyperthermia. PMA levels of higher than 0.3 mg/L and MDMA levels higher than 0.6 mg/L have been found in cases where deaths were attributed to these drugs.[1]

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Lessons from practice

- Amphetamine ingestion is now not only occurring at dance clubs, but also in the home.
- Paramethoxyamphetamine (PMA), which has much more serious adverse effects than other ring-derivative amphetamines, continues to be sold in South Australia.
- PMA is now being marketed and supplied independently as a follow-on drug to methylenedioxymethamphetamine ("ecstasy").

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