

# MDMA Toxicity Presenting with Severe Hyperpyrexia: A Case Report

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## ABSTRACT

*Ingestion of even small amounts of MDMA ('ecstasy') by a small subset of the population may result in a potentially fatal clinical syndrome of severe hyperpyrexia, cardiovascular collapse, coagulopathy, rhabdomyolysis and multiple organ failure. Rapid and aggressive temperature control is of utmost importance in the management of these patients.*

*We report a case of MDMA toxicity presenting with severe hyperpyrexia (43°C) who survived after a rapid reduction in temperature to 36°C within 60 minutes following active surface cooling, cooled (approximately 4°C) intravenous solutions, urinary and gastric lavage solutions and replacement fluids for continuous veno-venous diafiltration. (Critical Care and Resuscitation 1999; 1: 368-370)*

**Key words:** MDMA, ecstasy, rhabdomyolysis, hyperthermia, acute renal failure

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The 'designer' compound 3,4 methylenedioxymethamphetamine (MDMA), also known as 'ecstasy', is an increasingly used 'recreation' drug. Chemically related to amphetamine, it has both stimulant and hallucinogenic effects, and appears to induce a state of euphoria and well-being when ingested. Although it is often perceived as being a 'safe' drug, use of MDMA is associated with significant morbidity and mortality, largely attributable to profound disturbances in thermoregulation.<sup>1,2</sup> A case of MDMA ingestion associated with severe hyperthermia, rhabdomyolysis and acute renal failure is reported.

## CASE REPORT

A 29 year old male presented to the emergency department with sudden onset of generalised seizures. Accompanying friends stated that he had ingested 2 ecstasy tablets with 750mL of spirits approximately 12 hours prior to presentation. Five hours before his admission he took another ecstasy tablet and was noted to become hyperactive and agitated. Generalised tonic-clonic seizures commenced approximately 30 minutes before his admission.

On examination his core temperature was 43°C, systolic blood pressure 76 mmHg, heart rate 160 beats per minute and respiratory rate was 28 per minute. The patient was mottled, cyanosed, and cool peripherally with laboured respirations. He had generalised muscular rigidity and a Glasgow coma score of 3. The tonic-clonic seizure activity noted during transport to hospital was not evident on admission.

The patient was sedated and paralysed with 200 mg of thiopentone and 80 mg of rocuronium, and was intubated and ventilated. Cooling was immediately commenced using 1 L of intravenous 0.9% saline (cooled to approximately 4°C) and ice packs applied to axillae, groin, thorax and abdomen. He was transferred to the critical care unit where the surface cooling continued using surface ice packs and alcohol with fans to enhance evaporation. A further 2 L of intravenous fluids (1 L of dextrose 5% and 1 L of 0.9% saline cooled to approximately 4°C) were administered and cold fluid lavages via the indwelling urinary catheter and nasogastric tube were performed. Continuous veno-venous haemofiltration with replacement fluids cooled to approximately 4°C were also commenced. He was

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sedated with a thiopentone infusion (200 mg/hr) and paralysed using vecuronium (2 - 4 mg hourly as required) and was given phenytoin 1 g intravenously on admission with 300mg i.v. daily thereafter. Lincomycin (600 mg i.v. 8-hourly) was commenced for right lower lobe aspiration. Within one hour of admission to hospital his temperature was 36°C and was maintained to less than 37.3°C over the next 48 hours.

The initial post intubation blood gas revealed a pH of 7.10, HCO<sub>3</sub><sup>-</sup> 13 mmol/L, PCO<sub>2</sub> 41 mmHg, PO<sub>2</sub> 135 mmHg and a lactate of 15 mmol/L. The laboratory investigations revealed a plasma sodium of 140 mmol/L, potassium of 5.3mmol/L, creatinine of 0.226 mmol/L, white cell count of 29x10<sup>9</sup>/L (marked neutrophilia, left shift and toxic changes) with the remaining electrolytes, liver function tests, creatine kinase (CK), platelet count, INR and APTT being within normal limits.

A pulmonary artery catheter was inserted which revealed a central venous pressure of 8 mmHg, pulmonary artery occlusion pressure 12 mmHg, cardiac index 4.6 L/min/m<sup>2</sup> and systemic vascular resistance index of 1186 dyne.sec.cm<sup>5</sup>/m<sup>2</sup> on an adrenaline infusion to maintain a mean arterial pressure (MAP) of 70 mmHg or greater. The patient remained in sinus rhythm at a rate that varied between 140 to 160 beats per minute. A cerebral CT scan performed shortly after admission showed effacement of right sided sulci but no focal abnormality. An intracranial pressure monitor was inserted and recorded pressures varying between 17 to 27 mmHg. A jugular venous bulb oximetry catheter was inserted into his right internal jugular vein which revealed saturations ranging between 65% to 75% during the following 48 hours. Intracranial pressure readings decreased to 8 mmHg with increased sedation and intravenous mannitol 0.25 g/kg and 20 mL of 20% sodium chloride. The cerebral perfusion pressure was maintained between 65 and 80mmHg with a combination of intravenous adrenaline and noradrenaline. The plasma CK peaked at 88000 U/L on day 2 of admission.

He remained oliguric with a urine output varying between 10 to 15 mL/hr and the plasma urea and creatinine increased to 20 mmol/L and 0.61 mmol/L respectively, despite continuous veno-venous haemodiafiltration. Inotropic support was successfully weaned and ceased by day 2 of admission. The neurological state improved and he was uneventfully extubated on day 4. Continuous renal replacement therapy was converted to intermittent haemodialysis and he was discharged neurologically intact on day 7 to the general wards where he required intermittent haemodialysis for a further 3 weeks. A renal review of the patient 3 months post admission, revealed normal plasma urea and creatinine concentrations.

## DISCUSSION

Ecstasy (MDMA) is taken to induce a feeling of euphoria, well-being and increased self awareness. *In vitro* and *in vivo* animal studies suggest that it acts by causing an initial release of serotonin followed by inhibition of inactivation and reuptake of serotonin with possible subsequent depletion of neuronal stores. Dopamine appears to be also affected, but to a lesser extent. Findings in non-human primates demonstrate a long-lasting loss of serotonergic neurons which in some brain regions appears to be permanent.<sup>3</sup> Recent studies in human subjects suggest that MDMA use may lead to long term and possibly permanent serotonergic neuronal injury.<sup>4</sup>

Ecstasy is readily absorbed from the gastrointestinal tract with an onset of action within 30 - 60 minutes of ingestion. The peak effects usually last for 4 to 6 hours but may occasionally last for 8 hours or more. The acute adverse effects range from the mild (and probably largely unreported) symptoms of tremor, headache, excessive sweating, blurred vision and muscle cramps (especially jaw muscles), to the severe and potentially fatal clinical picture of hyperthermia, seizures, rhabdomyolysis, disseminated intravascular coagulation, multiorgan failure and death.

Although the use of MDMA is widespread, with up to 24% - 39% of American college students using it on at least one occasion,<sup>5</sup> the incidence of severe life-threatening reactions remains relatively small and sporadic. What predisposes certain people to develop overwhelming hyperthermia with all its complications remains unclear? Many of these fatal, or near fatal cases of MDMA intoxication have been associated with low doses of MDMA, and an overdose with much larger doses of MDMA is not necessarily associated with any life-threatening events. Susceptibility to the toxic effects of ecstasy may reflect genetic or metabolic predisposition. Another possible explanation is that severe reactions are secondary to impurities in the MDMA tablet; however, this theory has not received widespread support. Certainly the use of MDMA in the conditions of high ambient temperatures with prolonged muscle activity, which occur at 'rave' parties, appears to predispose to severe reactions, especially when complicated by inadequate or unsuitable fluid replacement.<sup>6</sup>

Initial management of severe MDMA toxicity should be directed at assessment and stabilisation of airway, breathing, circulation and temperature. Peak temperature and duration of hyperpyrexia have in the past predicted poor outcome in these patients.<sup>7</sup> Rapid treatment of hyperthermia in MDMA toxicity is important, which includes intravenous rehydration, and surface and core cooling. The application of cold ice packs to the skin

surface of the groin and axillae (where large arterial vessels lie close to the surface) and cold intravenous fluids are useful in rapidly reducing the body temperature. These manoeuvres may be followed by cold nasogastric, bladder and peritoneal lavage. Continuous veno-venous haemodialysis or haemofiltration with cold replacement fluids is also effective. Reduction in heat generation may be necessary with sedation and intubation with or without muscular paralysis. The role of dantrolene in the management of MDMA associated hyperpyrexia remains unclear and is not routinely used.<sup>8,9</sup>

Haemodynamic instability frequently accompanies severe reactions to MDMA. Our patient was hypotensive and required inotropic support for the initial 24 hours; however, malignant hypertension may be the predominant haemodynamic feature either, as a primary problem, or as a reflection of raised intracranial pressure. Seizure activity may occur as a result of hypertension, cerebral oedema or as a result of an intracerebral event such as intracranial haemorrhage. Hyponatraemia with MDMA ingestion has been described as a result of ingestion of large amounts of water as fluid replacement, especially in the setting of 'rave' parties and may also be responsible for the seizure activity.<sup>10,11</sup>

Rhabdomyolysis associated with MDMA toxicity may respond in milder cases to intravascular fluid loading, with or without mannitol and urinary alkalinisation. More severe rhabdomyolysis may require haemodialysis especially if associated with acute tubular necrosis complicated by hypotension. Hepatic injury post MDMA ingestion did not occur in our patient although it has been well described. While most patients recover spontaneously, some cases progress to fulminant liver failure and death or require urgent transplantation.<sup>12</sup> Fulminant liver failure post ingestion of MDMA has been described both in association with hyperpyrexia and multi-organ failure, and also independently of hyperpyrexia.<sup>13</sup>

Our patient demonstrated a typical severe reaction to MDMA with features of severe hyperpyrexia (being the highest temperature so far reported in a patient who survived), haemodynamic instability, rhabdomyolysis, acute renal failure and central nervous system involvement. In addition to the haemodynamic control and organ support, immediate rapid control of

hyperpyrexia in the management of MDMA toxicity is a priority. We feel this approach contributed significantly to the favourable outcome in this patient.

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