Case Report
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Survival Despite Severe Hyperthermia and Multi-Organ System Dysfunction Following Week-long Use of an MDPV Containing "Stain Remover"

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Abstract

Synthetic amphetamine and cathinone analogs are sympathomimetic hallucinogens that can cause significant toxicity. Hyperthermia in the setting of sympathomimetic overdose is typically associated with a high mortality. We report a case of neurologically intact survival after extreme hyperthermia in the setting of a sympathomimetic overdose. A 29 year-old male ingested a methylenedioxypyrovalerone "stain remover" and exhibited excited delirium and severe sympathomimetic effects. Multi-organ system toxicity included severe hyperthermia, acidosis, hypoglycemia, intracranial hemorrhage, status epilepticus, myocardial infarction, hypotension, rhabdomyolysis, acute renal failure, acute hepatic injury, and coagulopathy. With aggressive cooling, intravenous fluids, benzodiazepine use, peripheral vasopressors, and hemodialysis, he had a good neurologic outcome at the time of discharge after a 17-day hospital course. Despite a high mortality rate with severe hyperthermia, this case suggests that patients with toxin-induced multi-system organ dysfunctionand associated hyperthermia may recover with early aggressive supportive care.

Keywords: drugs of abuse; hyperthermia; methylenedioxypyrovalerone

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1. Introduction

Synthetic cathinones are stimulant hallucinogens often marketed as household products "not for human consumption" in order to avoid prosecution. The synthetic cathinone methylenedioxypyrovalerone (MDPV) is a common constituent of these products and has been associated with delirium, hyperactivity, sleeplessness, auditory and visual hallucinations, anxiety and anorexia[1]. Hyperthermia in the setting of stimulant toxicity markedly increases morbidity and mortality[2]. We present a case of recovery after severe hyperthermia and multi-organ dysfunction following MDPV use.

Case Report

A 29 year-old male presented to an emergency department (ED) with agitation and altered mental status. Emergency medical services (EMS) found him underneath his house stating that he was digging for wires that he thought were shocking him. He became combative toward police and EMS and had to be physically restrained. En route to the ED he developed a decreased level of alertness, with respiratory depression on arrival. Initial vital signs included heart rate of 190 beats per minute (bpm), temperature of 103° F (39.4° C), and systolic blood pressure of 50 mmHg. Physical exam included mydriasis with nonreactive pupils, diaphoresis and Glasgow Coma Score (GCS) of 3.

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In the ED, the patient was intubated without requiring sedatives or paralytics and he received three liters of crystalloid for persistent hypotension. The rectal temperature increased to 109.2° F (42.9° C) and cooling was continued with cooling blankets and intravenous fluids. Computed tomography of the head revealed an intracranial hemorrhage. The patient subsequently had multiple generalized seizures over several hours that were treated with multiple 2 mg lorazepam boluses and subsequent lorazepam infusion at 1 mg/hour.

The initial serum sodium was 152 mmol/l, potassium 5 mmol/l, chloride 111 mmol/l, bicarbonate 18 mmol/l, blood urea nitrogen 20 mg/dl, glucose 46 mg/dl and calcium 10.2 mg/dl. Serum lactate was 14.7 mmol/L with an arterial pH of 7.26. Acetaminophen, salicylate, and ethanol concentrations were non-detectable. Urine drug screen for drugs of abuse was negative.

Creatine kinase was 693 IU/L initially, peaked at 347,800 IU/L on hospital day three, and was treated with intravenous crystalloids and alkalinization. Initial creatinine was 2.8 mg/dL and peaked at 10.1 mg/dL on hospital day five with associated oliguria, prompting the initiation of hemodialysis. The initial AST/ALT were 49 and 60 units/L respectively. On hospital day two AST peaked at 11,970 units/L and ALT at 8019. Total bilirubin peaked at 9.2 mg/dl on day three. Ammonia peaked at 82 μmol/L and decreased to 40 μmol/L on hospital day seven. Coagulopathy developed with a peak INR of 7.7 on hospital day three. The platelet nadir was 27,000/microliter and improved to 75,000/microliter by hospital day seven. On hospital day three the patient received four units of fresh frozen plasma and two units of platelets.

Other organ system dysfunction included myocardial infarction with a peak troponin of 38.59 ng/ml on day two of admission. The presenting rhythm was a narrow complex tachycardia and on hospital day one there were brief runs of non-sustained ventricular tachycardia. Hypotension initially improved with intravenous crystalloid, though a phenylephrine infusion was started on day two and discontinued on day three.

With resuscitation the heart rate decreased to 160 bpm and systolic blood pressure improved to 100 mmHg. Cooling measures were continued for twelve hours until the rectal temperature reached 98.7°F (37.1° C); after this point the patient remained normothermic. The intracranial hemorrhage was treated non-operatively and did not require mannitol or hypertonic saline. He was extubated on hospital day eight and was following commands at that time.

The patient's family was able to locate and provide the ingested substance. It was in a container labelled "White Girl," and was advertised as a household furniture cleaner and stain remover. By report, the patient had been using it every day for approximately a week. The toxicology laboratory at our institution performed comprehensive testing on the product and identified MDPV. The patient was discharged on hospital day 17. He still required hemodialysis at the time of discharge from the hospital but was neurologically intact. He was lost to follow-up after discharge.

2. Discussion

Phenethylamine and cathinone analogs are stimulant drugs of abuse, often disguised as commercial products such as "bath salts" and sold over the internet or at convenience stores. As the term bath salt became associated with illicit drug use, these stimulants began to be marketed as other products, including scratch removers, plant food and stain removers. These products are often labeled "not for human consumption" in order to avoid regulation. As specific active ingredients in these products became illegal based on state and federal actions, new unregulated congeners have been used. Some products with similar or even identical names might contain different ingredients over time or in different geographic locations.

Pyrovalerone was first synthesized in the 1960s, and in the 1970s it was utilized as a psychostimulant to treat lethargy and chronic fatigue[3]. Because of abuse and dependency it was eventually withdrawn from the market[3]. Newer cathinone analogs found in many stimulant hallucinogen products include: mephedrone, methylone, and MDPV.

MDPV was the chief substance detected in blood and urine from patients hospitalized for bath salts overdose in the US[1]. It has been marketed on the internet and in convenience stores under names such as "White Horse" and "Cloud Nine". Intoxication with MDPV has been reported to cause delirium, hyperactivity, sleeplessness, auditory and visual hallucinations, anxiety and anorexia[1]. Vital sign abnormalities may include hypertension, hyperthermia and tachycardia[4]. MDPV use has been associated with psychosis, agitation, rhabdomyolysis, myocardial infarction, and death[5].

The mechanism of action of MDPV includes a cocaine-like dopamine and norepinephrine, and to a

lesser extent serotonin, reuptake inhibition with a rapid onset of toxicity[6,7].When compared to the prototypical monoamine transporter blocker cocaine in animals, MDPV is a 50-fold more potent uptake blocker at the dopamine transporter, 10-fold more potent at the norepinephrine transporter, and 10-fold less potent at the serotonin transporter[8]. Other synthetic cathinones including mephedrone and methylone act more like amphetamines in that they are non-selective transporter substrates that stimulate the non-exocytic release of dopamine, norepinephrine and serotonin, whereas MDPV is a pure catecholamine-selective transporter blocker like cocaine[8].

The proposed mechanism of sympathomimetic-mediated hyperthermia is impaired sweating and cutaneous vasodilation (the major autonomic adjustments to thermal stress) and heat perception[9]. The loss of autonomic self-regulation may be directly related to the dysregulation of dopaminergic pathways in states of excited delirium[10]. Deaths related to Excited Delirium Syndrome have been observed with mephedrone, methylenedioxymethamphetamine, cocaine, amphetamine and to a lesser extent, MDPV[8,10].

Hyperthermia generally portends a worse prognosis in stimulant overdoses. In one study, substituted amphetamine toxicity with temperatures of >104.9 °F had mortality rates of ~50%[2]. In a case series from the ToxIC registry, the only patient who died had a temperature of >104 °F[5]. The majority (67%) of patients in this study had a temperature of 96.1-100 °F, 21% had 100.1-102°F, 1 had 102.1-104 °F, and 1 had >104 °F. Our case is unique in that the patient survived with neurologic recovery after a rectal temperature of 109.2 °F. While recovery from multi-system organ dysfunction has been reported after MDPV intoxication with temperatures as high as 106.3 °F[11], temperatures this high are typically associated with high mortality[10,12].

This case suggests that patients with suspected cathinone associated severe hyperthermia and multi-organ system failure treated aggressively with supportive measures can recover. Severe hyperthermia, while associated with higher mortality, does not universally preclude survival in patients with MDPV use.

3. Conflict of Interest

None Declared

4. References

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