"Bath salts" intoxication: a new recreational drug that presents with a familiar toxidrome

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ABSTRACT

It is important for emergency physicians to be aware of new psychoactive agents being used as recreational drugs. "Bath salts," which include 3,4-methylenedioxypyrovalerone (MDPV), mephedrone, and methylone, are the newest recreational stimulants to appear in Canada. There are currently more than 12 synthetic cathinones marketed as bath salts and used with increasing frequency recreationally. Although these drugs are now illegal in Canada, they are widely available online. We present a case report and discuss bath salts intoxication and its anticipated sympathomimetic toxidrome, treatment strategies, and toxicologic analysis, Treatment should not rely on laboratory confirmation. Since the laboratory identification of such drugs varies by institution and toxicologic assay, physicians should not misconstrue a negative toxicology screen as evidence of no exposure to synthetic cathinones. Illicit bath salts represent an increasing public health concern that involves risk to the user, prehospital personnel, and health care providers.

RÉSUMÉ

Il est important que les urgentologues connaissent les nouvelles substances psychoactives utilisées comme drogues à usage récréatif. Les «sels de bain», qui contiennent de la 3,4-méthylènedioxypyrovalérone (MDPV), de la méphédrone et de la méthylone, sont les tout derniers stimulants à usage récréatif qui ont fait leur entrée au Canada. Il existe actuellement plus d'une douzaine de cathinones synthétiques, qui sont vendus comme des sels de bain et qui sont de plus en plus utilisés à des fins récréatives. Bien que ces drogues soient maintenant illicites au Canada, on peut se les procurer facilement en ligne. Il y aura dans l'article un exposé de cas, suivi d'une discussion sur l'intoxication aux «sels de bain», le toxidrome sympathomimétique prévisible, les stratégies de traitement et les analyses toxicologiques. Le traitement ne devrait pas reposer sur la confirmation des résultats des examens de laboratoire. Comme l'identification de ces drogues par les laboratoires varie d'un établissement à l'autre et selon les épreuves de dosage toxicologique, les médecins ne devraient pas interpréter à tort un test de dépistage toxicologique négatif comme un signe d'absence d'exposition à des cathinones synthétiques. Les sels de bain illicites posent un problème de santé publique, qui prend de l'ampleur et qui présente des risques pour l'utilisateur lui-même, pour le personnel préhospitalier et pour les fournisseurs de soins de santé.

Keywords: bath salts, emergency, 3,4-methylenedioxypyrovalerone (MDPV), risk, toxicology, toxidrome, treatment

It is important for emergency physicians to be aware of new psychoactive agents being used as recreational drugs. "Bath salts," which include 3,4-methylenedioxypyrovalerone (MDPV), mephedrone, and methylone, are the newest recreational stimulants to appear in Canada. There are currently more than 12 synthetic cathinones marketed as bath salts and used with increasing frequency recreationally. Although these drugs are now illegal in Canada, they are widely available online. We present a case report and discuss bath salts intoxication and its anticipated sympathomimetic toxidrome, treatment strategies, and toxicologic analysis.

CASE REPORT

Prehospital events

Parents of a 21-year-old man called 911 because their son was having a "psychotic episode" after sniffing

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"bath salts." At the same time, the man himself called 911 and stated that his parents had been murdered. He had not slept for 48 hours and had spent the night opening and closing doors and turning lights on and off.

On police arrival, the man stated that his parents had been "killed and replaced" and continued to dial 911 despite the presence of police. Verbal interventions by police were disregarded, and physical contact resulted in a violent struggle. The man was described as having "superhuman strength" and was seemingly impervious to pain. He was perspiring heavily and making growling sounds and appeared to be hallucinating. Additional police officers and advanced life support paramedics were deployed, and seven police officers were required to gain physical control.

The paramedics immediately administered 10 mg of midazolam intramuscularly. The patient was restrained in a supine position with handcuffs in front of his body and transported to the emergency department (ED).

Initial ED presentation

On ED arrival, the patient's vital signs were as follows: heart rate 117 beats/min; blood pressure 128/52 mm Hg; respiratory rate 18 breaths/min; temperature 36.6°C (97.8°F); and oxygen saturation 100% on 4 L/min of oxygen by nasal prongs. A physical examination revealed no evidence of trauma. An electrocardiogram showed sinus tachycardia with normal intervals and no QT prolongation, ischemic features, or evidence of left ventricular hypertrophy.

Table 1 provides results for noteworthy initial laboratory investigations. Serum creatine kinase was elevated, peaked at 2,818 IU/L 12 hours later, and remained elevated at 1,750 U/L 24 hours after presentation. The complete blood count normalized within 12 hours, and renal function and potassium remained normal. Venous blood gas determination 30 minutes after ED arrival revealed pH of 7.35, carbon dioxide tension (pCO_2) of 37 mm Hg, HCO_3^- of 20 mm Hg, and lactate of 3.8 mmol/L (normal $<$ 2 mmol/L). The venous lactate normalized after sedation and intravenous (IV) hydration with normal saline.

Toxicology testing

Ethanol level was $<$ 2 mmol/L. The initial urine toxicologic screen was negative for cocaine, amphetamines, cannabinoids, opiates, and barbiturates but positive for benzodiazepines.

Comprehensive urine drug screening via gas chromatography/mass spectrometry (GC/MS) completed 7 hours after the patient's arrival was positive for 3,4-methylenedioxypyrovalerone (MDPV) and revealed chlorpheniramine (an antihistamine) and trazodone, which the patient had not been prescribed.

Past medical history

Past history, obtained subsequent to his initial presentation, revealed that the patient had been sniffing bath salts habitually for 1 year and had been using them continuously for 7 to 10 days. He admitted to also using benzylpiperazine, a stimulant drug with euphoric properties. When bath salts became illegal in North America, he began ordering them from China. He had been in hospital on five previous occasions for bizarre behaviour and twice held under a Mental Health Certificate with drug-induced psychosis. When abstinent from drugs, he had no psychotic features.

Table 1. Initial laboratory investigations

Test	Value	Normal range	Reference units (SI)
White blood cell count	17.2*	4–11 $\times 10^9$	$\times 10^9$/L
Neutrophils	14.5*	2–8	$\times 10^9$/l
Potassium	4.0	3.3–5.1	mmol/L
Serum CO_2	20*	21–31	mmol/L
Creatinine	85	50–120	μmol/L
Anion gap	14*	3–11	mmol/L
Osmolality	289	280–300	mmol/kg
Creatine kinase	464*	0–195	IU/L

*Abnormal.

Course in the ED

The patient remained paranoid and physically restrained because of intermittent agitation and aggression. Benzodiazepines were administered (three doses of midazolam 5 mg IV and a total of 14 mg of lorazepam IV). Three doses of haloperidol 1 mg IV were also given. Because of ongoing severe agitation, a continuous IV propofol infusion was commenced and continued for 8 hours.

Course in hospital

Twenty-four hours after his ED arrival, the patient was transferred to the psychiatry in-patient service. He was discharged 3 days later with a diagnosis of substance-induced psychosis. He had no ongoing psychiatric symptoms at discharge.

DISCUSSION

Compounds, including MDPV, mephedrone, and methylone, are colloquially known as ''bath salts'' and are the newest recreational stimulants to appear in Canada. There are more than 12 synthetic cathinones, marketed as bath salts and increasingly used recreationally. Bath salts are labeled by illicit distributors as beauty products, plant food, or pond cleaner. The original beauty product label led to the wide use of the bath salts moniker.[1,2] Distributors have skirted regulatory bodies by declaring bath salts ''not for human consumption.'' Bath salts intended for substance abuse are sold in ''headshops'' or via Internet-based companies that ship internationally. Packaging carries names such as Vanilla Sky, Purple Wave, and Red Dove. Users pay up to $75CAD for 20 to 30 g. These agents are vastly different from products intended for actual bathing or gardening sold by large-scale retailers.[1–4] Bath salts began to appear on the streets in Europe in 2007 and the United States in 2008 and are now increasingly distributed in Canada.[2,5] The first reported illicit use in Canada was in 2012 in Nova Scotia, and bath salts have now been documented in most provinces.[5,6]

Bath salts can be orally ingested, sniffed, snorted, smoked, or injected. The desired effects of euphoria, increased energy, expanded consciousness, and increased libido begin rapidly, typically last for 3 to 4 hours, and are associated with considerable adverse effects.[1,4,7–9] The duration of action is typically 2 hours or longer, although the actual half-life is difficult to ascertain due to a lack of pharmacokinetic evidence, the frequent presence of coingestants, and the possibility of undetermined contaminants.[3] Use is often continuous, with another dose taken as soon as the euphoria wanes. It is not uncommon for users to maintain a high for several days, resulting in rapid dose escalation as tolerance develops. Users and observers of bath salts have reported psychotic features with involuntary psychomotor activity, compulsive behaviour, and disturbing hallucinations. Severe self-mutilation has been reported. Underlying psychiatric disease or a history of polysubstance use can further complicate the presentation. Bath salts intoxication has been linked to significant morbidity and mortality, and the effects of intoxication present an obvious safety risk for emergency medical services (EMS) providers and law enforcement personnel.[2,3,10]

The most common synthetic cathinone found in bath salts in North America is MDPV. The closely related compounds mephedrone (4-methylmethcathinone) and methylone have also been reported but are more frequently seen in Europe.[2,4,11] Bath salts became illegal in Canada in September 2012.[6]

MDPV's mechanism of action

Bath salts are often a mixture of centrally acting synthetic cathinones combined with contaminants that may include traces of prescription drugs[1–3,7,8,12] (Table 2). Many users of bath salts attempt to mitigate any untoward psychotic features by coingesting known ''downers'' such as marijuana, heroin, narcotics, and major tranquilizers.[12,13]

Table 2. Reported constituents in bath salts and coingestants in bath salts intoxication

Reported constituents in bath salts
MDPV (3,4-methylenedioxypyrovalerone)
Mephedrone
Methylone
Caffeine
Lidocaine
Trimethoprim
Unidentifiable compounds
Reported coingestants in bath salts intoxication
Marijuana, opiates, benzodiazepines, cocaine, amphetamines
Ethanol, methadone, zolpidem, buprenorphine, tramadol, methylphenidate, chlorpheniramine, trazodone

MDPV, like other synthetic cathinones, has stimulant effects similar to those of cocaine and amphetamines. Because it is lipophilic, it crosses the blood-brain barrier, where it acts as a monoamine reuptake inhibitor and induces the release of dopamine, norepinephrine, and serotonin.[1,7,12] MDPV results in dopaminergic stimulation of the corticomesolimbic pathways, including the reward centre in the nucleus accumbens. Dopaminergic stimulation is thought to underlie the dependence, tolerance, and withdrawal syndrome. Overstimulation of D_2 receptors within the limbic system has been linked with hallucinations. It has been estimated that the central dopaminergic effect of MDPV is up to nine times greater than that of cocaine.[1,7,9]

The norepinephrine effects of MDPV are both central and peripheral, resulting in alertness, arousal, decreased fatigue, and insensitivity to pain. Stimulation of α_1 and β_1 receptors increases heart rate and causes hypertension.[1,3]

The serotoninergic activities of bath salts cause euphoria, altered perception, heightened awareness, hallucinations, and reduced appetite.[12] Alterations in perception combined with central analgesia may be responsible for the extensive self-mutilation and tolerance to pain-mediated control techniques seen in individuals with bath salts intoxication.[1,9,11]

Clinical presentation

Table 3 provides common signs and symptoms seen in bath salts intoxication. Bath salts typically present with a sympathomimetic toxidrome with altered consciousness that ranges from agitation to frank psychosis. Findings include tachycardia, hypertension, dysrhythmias, diaphoresis, mydriasis, tremor, and muscle weakness.[1,2,4] Chest pain, myocardial infarction, stroke, coma, and death have also been reported.[3,10] Behavioural changes include psychomotor activation, agitation, aggression, amnesia, and insomnia. Paranoia, delusions, and hallucinations have been reported in up to 90% of cases.[4,8,14–17] Bath salts toxicity can be difficult to differentiate from cocaine or amphetamine use, although bath salts toxicity may result in more severe psychosis and include self-injurious behaviour. A recent case of serotonin syndrome related to MDPV use suggests a larger effect on the reuptake of serotonin than initially thought.[12] Serotonin syndrome signs, such as myoclonus, diaphoresis, tremor, hyperreflexia, and hyperthermia, have all been reported in confirmed cases of MDPV use.[1,3,12] Hyperthermia has been documented and seems to relate to central dysregulation of dopamine and noradrenaline in the hypothalamus.[7,10] However, it has also been suggested that peripheral mechanisms are responsible, including an MDMA-like (3,4-methylenedioxy-*N*-methylamphetamine or "Ecstasy") uncoupling of cellular respiratory proteins and noradrenaline-mediated vasoconstriction preventing superficial cooling.[1,7,9]

Table 3. Common signs and symptoms seen in bath salts intoxication

Sympathetic
Tachycardia
Hypertension
Chest pain
Mydriasis
Psychiatric
Agitation
Combative and violent behaviour
Hallucinations
Delusions
Paranoia
Neurologic
Confusion
Seizure/tremor
Drowsiness
Myoclonus
Blurred vision

The presentation of a mixed toxidrome is likely due to the user's coingestion of "downers" such as major tranquilizers in an attempt to mitigate the psychomotor responses to bath salts.[13] In our case, GC/MS assessment revealed coingestion of an antihistamine and trazodone. For this reason, a wide range of coingestants must be considered, even as treatment is unfolding.[14,16,18–20]

Treatment

There are currently no evidence-based guidelines for treatment of bath salts intoxication; however, it is reasonable to use guidelines for sympathomimetic toxidromes and excited delirium,[1,2,4,18–20] recognizing that serotonin syndrome may also be encountered.[12] When an undifferentiated patient with a sympathomimetic toxidrome is seen, clinicians should consider the possibility of bath salts intoxication.

Bath salts users generally present to the ED after a police response for bizarre, violent, or dangerous

behaviour. Dispatch of adequate numbers of EMS providers and law enforcement personnel is prudent.[18–20] The goal of initial intervention is rapid de-escalation of agitation and sympathetic system stimulation, as with any sympathomimetic toxidrome. Physical restraint is important to protect the safety of health care providers and should be augmented with chemical restraint as rapidly as possible. Benzodiazepines are the mainstay of initial treatment, along with consideration of dissociative agents and propofol infusion.[1,3,4,13]

Similar to cocaine toxicity, the administration of β-blockers or similar agents to control hypertension is contraindicated as this may result in complications from unopposed α-adrenergic stimulation.[21] Continuous electrocardiographic monitoring, coupled with management of hyperthermia and dehydration when indicated, should be started in the field. Hospital evaluation should include the assessment and treatment of rhabdomyolysis, acidosis, dehydration, and electrolyte abnormalities.[3,10,11] Physicians should be vigilant for the possible development of serotonin syndrome.[12]

Toxicologic assessment

Initiation of treatment should not rely on laboratory confirmation. Standard urine drug toxicologic screens cannot detect bath salts. Specialized analysis for the presence of the most common cathinones using GC/MS is required if a definitive diagnosis is desired.[1,3,4] Quantitation of serum MDPV levels is not routinely performed in Canada. Requests for such levels may require involvement of a forensic laboratory.[3]

The difficulty in the toxicologic assay of synthetic cathinones rests with establishment of base levels for cutoff. If levels present in the urine are below the base level of detection for an assay, the screen will be reported as negative. Changes in chemical structures resulting from manufacturers' efforts to skirt legal limitations, as well as the presence of multiple compounds with varying side chains in the same drug portion, may confound qualitative testing.[2,5,6] The clinical response to the bath salts may last well beyond MDPV's measurable half-life, leading to an impressive clinical picture in the setting of a negative toxicologic analysis.[4] Suspicion of bath salts intoxication is sufficient to initiate treatment, and the importance of specific findings on assay are difficult to interpret because there is wide variation in the clinical response to MDPV.

Prognosis

A wide range of outcomes from bath salts toxicity have been documented. Many patients have recovered with no long-term sequelae despite severe acute medical effects, including renal failure.[1,7,8,10] However, there have been a number of deaths following MDPV consumption despite aggressive medical treatment.[3,10,11]

SUMMARY AND CONCLUSIONS

Bath salts represent new and dangerous drugs of abuse, involving intoxication that presents as a sympathomimetic toxidrome. The duration and clinical presentation of bath salts toxicity are frequently complicated by continuous dosing users, the self-administration of depressive agents, and the contamination of the compounds with prescription drugs and other contaminants. Toxicologic analysis is difficult, and a negative assay does not necessarily indicate nonexposure. Although bath salts are now illegal in Canada, these agents are widely available online and have become an increasing public health concern that involves risk to the user, prehospital personnel, and health care providers.

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