CASE REPORT

Two cases of a prolonged excited delirium syndrome after chloromethcathinone ingestion

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ABSTRACT

Synthetic cathinones have become popular drugs of abuse. We describe our recent experience with two highly agitated patients following ingestion of the cathinone derivative chloromethcathinone, and cannabis. Both patients suffered from excited delirium syndromes that lasted for over 24 hours. Clinicians should be aware of this phenomenon, especially since routine toxicology screenings do not detect the presence of these agents.

What was known on this topic?
Very little is known about the clinical effects of the use of chloromethcathinone.

What does this add?
This report adds important clinical information about the use of chloromethcathinone. Patients could develop a prolonged excited delirium syndrome.

KEYWORDS

Excited delirium syndrome, drugs of abuse, synthetic cathinones

INTRODUCTION

The number of available new psychoactive substances (NPS) has risen dramatically in recent years. Since 2005, the European Monitoring Centre for Drugs and Drug Addition (EMCDDA) monitored more than 733 different NPS. These substances make up a broad range of drugs, including synthetic cannabinoids, stimulants, opioids, and benzodiazepines. Currently, cathinone derivatives are common among hospital presentations involving NPS.[1,2] Cathinone is one of the biologically active alkaloids found in the khat shrub. Because of their structural similarity to amphetamines, cathinone derivatives are often called 'natural amphetamines'. Similar to amphetamines, cathinone derivatives are characterised by stimulating, euphoric, and empathogenic properties.[3,4]
We describe two patients who were admitted to our hospital after the use of the cathinone derivative chloromethcathinone (CMC) which resulted in an excited delirium syndrome with prolonged psychotic symptoms. CMC use was confirmed by qualification of this drug in urine samples of both patients and in the powder substances they had in their possession. To our knowledge, this is the first case report of a prolonged excited delirium after CMC ingestion in a clinical setting.

CASE DESCRIPTIONS

Two 20-year-old Caucasian men arrived at the emergency department (ED) by ambulance. Their medical history was unknown. Both men had shown aggressive behaviour that alternated with a reduced state of consciousness before presentation. They admitted to having smoked cannabis with the possible addition of another substance about 2.5 hours prior to arrival at the hospital.

Patient 1

Patient 1 was very agitated during transport and was given 6 mg of midazolam intravenously in the ambulance. Upon arrival at the ED, he was awake, extremely anxious, and unable to cooperate; Glasgow Coma Scale (GCS) was 4-6-1. He was given an additional dose of intravenous

2.5 mg midazolam to facilitate an electrocardiogram (ECG) and blood sampling. His vital signs showed a blood pressure of 129/100 mmHg; heart rate 110 bpm, temperature 37.1°C, and a respiration rate of 18 breaths/minute with an oxygen saturation of 97% on room air. His pupils were of normal size and unresponsive to light. There were no signs of intravenous drug use. Routine blood tests were normal, including hemocytometry, electrolytes, renal function, liver enzymes, creatinine kinase, and bicarbonate. Blood alcohol levels were unmeasurably low. The ECG was normal. Qualitative analyses of drugs of abuse (Syva® RapidTest d.a.u.®, Siemens Healthcare Diagnostics Ltd., Frimley, Camberley, United Kingdom) in the urine, collected about 12 hours after admission, were positive for THC metabolite levels (cut-off 50 ng/ml) and opiates (morphine cut off 300 ng/ml), but negative for (methyl)amphetamines, methadone, benzodiazepines, and cocaine. Patient 1 was persistently anxious and extremely agitated. He developed severe myoclonus, urine retention, and respiratory depressions and required supplemental oxygen therapy. After transfer to the Medium Care Unit (MCU), he needed to be physically restrained because of combativeness. The consulting psychiatrist diagnosed a psychosis due to withdrawal of unknown drugs of abuse. He remained aggressive and highly agitated and required several doses of intravenous benzodiazepines. After 26 hours, he became calmer and started to respond to verbal instructions.

Patient 2

Patient 2 was lethargic upon arrival at the hospital with a GCS of 3-6-5. His blood pressure was 129/60 mmHg, heart rate 110 bpm, temperature 36.7°C, and he had a respiration rate of 16 breaths/minute with an oxygen saturation of 97% on room air. Physical examination, ECG, and blood test results were similar to patient 1. In his urine, collected about 12 hours after admission, only the use of cannabis was identified (Syva® RapidTest d.a.u.®). About seven hours after admission to the ED, patient 2 woke up agitated, anxious, and aggressive. He developed myoclonus, trismus, and retention of urine. After transfer to the MCU for observation, he remained aggressive and anxious and required several doses of intravenous midazolam and morphine. Patient 2 was also diagnosed with psychosis due to withdrawal of unknown drugs of abuse. In the MCU, the symptoms gradually subsided within 24 hours.

Both patients were discharged nearly two days after admission.

Both patients carried a belt bag containing three substances. One was identified as cannabis; the other two were white powders labelled 'hexen' (n-ethylhexedrone, a cathinone derivative with sympathomimetic properties) and 'speed'. Urine samples and both powders were sent for qualitative analysis using gas chromatography - mass spectrometry and liquid chromatography with diode array detection.[5,6,7] Analysis showed that both powders contained a combination of caffeine and chloromethcathinone (CMC or 'clephedrone'). CMC was also confirmed in the urine samples of both patients; caffeine or its metabolites were not detected.

DISCUSSION

We report on two patients who exhibited prolonged psychotic symptoms requiring intravenous midazolam after the use of cannabis in combination with CMC, a synthetic cathinone. To our knowledge, this is the first observation made by clinicians.

CMC is a para-substituted cathinone in which the methyl-group of methylmethcathinone (3- or 4-MMC (mephedrone)) has been substituted for a chlorine halogen. CMC was first detected on the drug market in 2014.[7]

The first cathinone derivatives were synthesised in the early 20th century. These designer drugs are popularly known as 'bath salts' and sold as 'legal highs' under a variety of names and labels. The distribution and use are difficult to control legally because they are easily modified, thereby creating new unique substances.[4] Most cathinone derivatives have sympathomimetic effects; other properties, including duration and the extent of psychoactive effects, vary, based to a large extent on functional group structure.[8] The cathinone 4-CMC was one of the five most confiscated synthetic cathinones in 2016 in Europe.[9] So far, information about the effects of CMC is based upon user experiences and observations made by the police.[7,10,11]

CMC is categorised as a methamphetamine-like cathinone. Its mechanism of action involves preferential reuptake inhibition of catecholamines and liberation of dopamine.[4] The effects reported include a sense of euphoria, increased energy, sociability and sexuality, visual and auditory hallucinations, and strong empathogenic feelings. It also seems to potentially cause bruxism, nystagmus, near syncope, dizziness, tremor, headache, apathy, psychic and somatic anxiety, jaw tension, and involuntary eye movements. The effects of CMC supposedly last for two to four hours and are considered to be dependent on both dose and route of administration.[7] Recommended care for patients exhibiting toxicity from synthetic cathinones is aimed at controlling the sympathomimetic toxidrome.[12]

Our patients showed many similarities with previous descriptions in the literature. The most prominent signs were psychomotor anxiety, aggression, and psychotic symptoms. However, some typical sympathomimetic

toxicities, such as diaphoresis and hyperthermia, were absent. Furthermore, urinary retention was observed in both patients, which is not expected after the use of stimulants. This might have been a side effect of cannabis.[13] We therefore conclude that both patients had an excited delirium that responded well to intravenous benzodiazepines. Most importantly, the effects of the intoxication lasted well over 24 hours, possibly more than 36 hours. It is possible that the co-ingestion of cannabis had a synergistic effect with regards to the psychotic symptoms.

Among the challenges for clinicians in the diagnosis of cathinone intoxication is the lack of routine toxicology screening for CMC and other synthetic cathinones. Quick assays for these compounds have not yet been developed for widespread routine hospital use. In the Netherlands, one facility provides 'send-out' testing, which is not immediately useful for practicing clinicians.[5] The performed test is not able to make a distinction between 4-CMC and 3-CMC, but as the treatment aim for both CMC variants is symptom control, this has no clinical implications.

In conclusion, the use of CMC may lead to a prolonged excited delirium syndrome requiring supportive care. These symptoms could last for 24, and up to 36 hours. Clinicians should keep cathinone derivatives in mind when evaluating substance use in young adults or in anyone presenting with unexplained aggressive behaviour. Treatment of acute intoxication involves supportive care targeting manifesting signs and symptoms. It is recommended to obtain blood and/or urine samples for toxicology screening but one should be aware that many of these compounds cannot be detected with routine toxicology screenings in hospitals.

ACKNOWLEDGEMENTS

The authors want to thank the Trimbos Institute and the Dutch National Institute of Public Health and the Environment (RIVM) for their help and for performing the analysis of our samples.

DISCLOSURES

All authors declare no conflicts of interest. No funding or financial support was received.

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