

Use of Diethylone, a New Psychoactive Substance, Associated with Multi-system Toxicity: A Case Report of Two Patients

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Received date: Nov 02, 2017, Accepted date: Nov 16, 2017, Published date: Nov 27, 2017.

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Abstract

Introduction: New Psychoactive Substances (NPS) is a term used to describe synthetic products that may also be referred to as “designer drugs”, “research chemicals”, or “internet drugs”. As new NPS continue to emerge, drug users are exposing themselves to new chemicals with unknown effects.

Case report: We report the cases of two patients who reportedly used “Molly” and developed multi-system toxicity requiring Intensive Care Unit (ICU) admission for several days. Both patients presented with altered mental status and during their hospital course manifested neuromuscular hyperactivity and hemodynamic lability. Both patients also had neuropsychiatric symptoms lasting for days after the critical phase of their hospital course. Laboratory investigation using liquid chromatography-quadrupole time-of-flight mass spectrometry identified diethylone in the substance the patients used, and several predicted diethylone metabolites in their sera.

Discussion: Clinical effects associated with diethylone use in humans have not previously been described in the medical literature. Our cases highlight diethylone as a new NPS that can be associated with severe and prolonged toxicity.

Keywords: New Psychoactive Substances; Cathinones; Substance abuse

Introduction

New Psychoactive Substances (NPS) is a term used to describe synthetic products that may also be referred to as “designer drugs”, “research chemicals”, or “internet drugs”. The three most common types of NPS in the United States are synthetic cannabinoids, synthetic cathinones, and designer opioids [1]. The World Drug Report of 2014 reported there has been a more than two-fold increase in the number of NPS on the global market between 2009 and 2013 [2]. A total of 644 NPS have been reported by The United Nations Office on Drugs and Crime Early Warning Advisory as of December 2015, which far surpasses the 234 controlled psychoactive substances listed [3].

We report the cases of two patients who reportedly used “Molly” and developed symptoms requiring Intensive Care Unit (ICU) admission for several days. Additional investigation identified diethylone in the substance the patients used, and several predicted diethylone metabolites in their sera. Clinical effects associated with diethylone use in humans have not previously been described in the medical literature.

Case Report

Patient 1

A 44-year-old man was brought to the Emergency Department (ED) by his mother with altered mental status after he and his girlfriend had taken a drug referred to as “Molly” at an uncertain time. The patient’s mother states that he called her crying, screaming, and wanting to come to her; during the drive to the ED he complained of thirst, extreme heat, and tried to jump out of the car. Upon presentation to the ED he was noted to be variably somnolent, and appeared to be hallucinating. He complained of dizziness, and blurred vision, but denied pain. Upon the physician’s assessment, the patient became combative, and was yelling in his bed; he was given haloperidol 5 mg and lorazepam 4 mg intravenously for sedation. Initial vital signs were temperature (T) 36.7°C, blood pressure (BP) 119/87 mm Hg, pulse (P) 97 beats/min, respiratory rate (RR) 20 breaths/min, and oxygen saturation (SpO₂) 95% on room air. His initial physical exam was unremarkable except for mydriasis. His initial labs were significant only for a serum lactate of 2.72 mmol/L and a urine drug screen positive for amphetamines, benzodiazepines, and tetrahydrocannabinol. Initial CPK was 157 units/L. A CT of the head was unremarkable, as was his electrocardiogram (ECG). He was admitted to the ICU, and subsequently intubated for airway protection due a decline in his mental status.

During his hospital course, the patient developed neuromuscular hyperactivity (hyperreflexia and rigidity), hemodynamic lability, and was treated with cyproheptadine in addition to supportive care. CPK

peaked on day 5 at 442 units/L. After transfer to the floor the patient continued to have episodes of delirium and hallucinations that were treated with haloperidol. On day 11 the patient was determined to be back to his baseline, and was discharged home.

Patient 2

A 37-year-old woman presented to the ED via EMS for altered mental status; she was the girlfriend of Patient 1. She was somnolent, maintaining her airway, opened her eyes to verbal stimuli, localized to deep sternal rubs, but did not answer questions or follow commands. The rest of her physical exam was unremarkable. Initial vital signs were T 36.3°C, BP 133/80 mm Hg, P 78 beats/min, RR 18 breaths/min, and SpO₂ 99% on room air. Serum glucose measurement was 99 mg/dL. Initial serum electrolytes, renal function, and hepatic function tests were unremarkable. Initial CPK was 57 units/L. Her serum acetaminophen, salicylate, and ethanol were undetectable. Her urine drug screen was positive for amphetamines; confirmatory testing revealed methamphetamine and amphetamine, but no detectable MDMA. A chest x-ray and CT of the head were unremarkable. Her initial ECG was also unremarkable.

During her hospital course, the patient's condition worsened and she was intubated. She also developed neuromuscular findings (hyperreflexia and rigidity) and hemodynamic lability and was treated with cyproheptadine and supportive care. CPK peaked at 198 on day 4. Like Patient 1, after transfer to the floor she had episodes of delirium and delusions and was treated with haloperidol. She was discharged on day 12.

Analysis of substance and specimens

The son of Patient 2 brought in a sample of the "Molly," a fine white crystalline powder identified as the substance used by both patients. This sample, as well as the initial blood and urine specimens collected at ED presentation from each patient, were sent to the Clinical Toxicology and Environmental Biomonitoring Laboratory at the University of California, San Francisco for analysis using liquid chromatography-quadrupole time-of-flight mass spectrometry. The drug sample was found to contain diethylone (330 mg/g powder), with no detectable ethylone, methylone, MDMA, methamphetamine, or amphetamine; no other drugs or known NPS were detected in the product. Figure 1 shows the MS spectrum of diethylone detected in the sample. Neither patient's sera contained a formula match to diethylone. Patient 1's serum analysis showed formula matches to diethylone-predicted metabolites M6, M7, and M13 (Figure 2). Patient 2's serum analysis showed a formula match to M13. Details of the analytical method used to analyze the samples are published elsewhere [4].

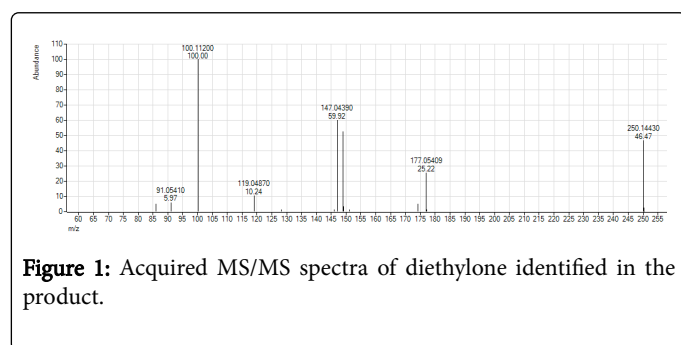


Figure 1: Acquired MS/MS spectra of diethylone identified in the product.

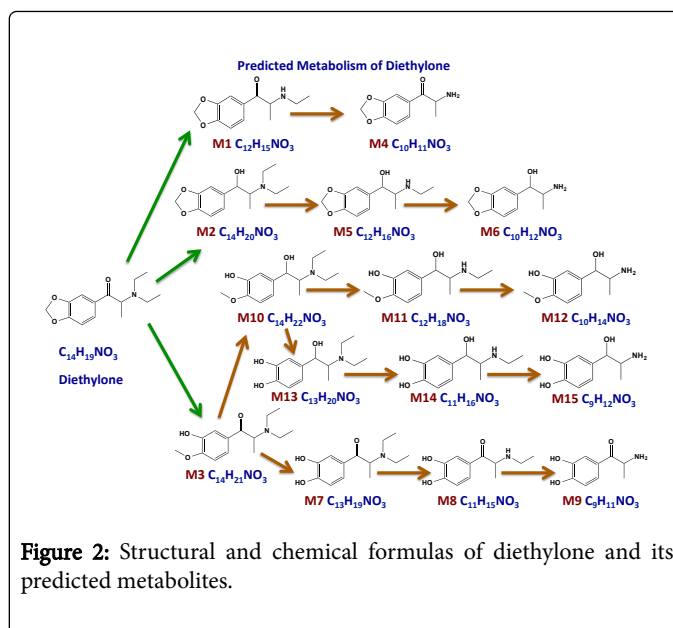


Figure 2: Structural and chemical formulas of diethylone and its predicted metabolites.

Discussion

This report summarizes the clinical effects observed in two patients who had used the new psychoactive substance diethylone. The presence of diethylone was confirmed in a sample of the drug the patients used, and predicted metabolites of diethylone were confirmed in the blood of both patients.

Diethylone (aka 5-BDDE; 3', 4'-methylenedioxy-N,N-diethylcathinone; and N-ethylethylone) by chemical structure is a substituted cathinone, and has been touted as a new designer stimulant [5]. An extensive search of both peer-reviewed and "gray" clinical literature was void of any mention of this substance in patients, reported human or animal exposures, or its effects (see supplemental material). Correspondence with the WHO's Global Synthetics Monitoring: Analysis Reporting and Trends Programme also confirmed they had not received any report of diethylone through their Early Warning Advisory on New Psychoactive Substances system as of January 2017 [6].

A review of online drug user forums only yielded mention of a few experiences with diethylone. While most reported intranasal administration, some also ingested it. Reported effects included diaphoresis, euphoria, muscle twitching, jaw clenching, diarrhea and vomiting, and mydriasis. The duration of effect was between six and thirteen hours.

Diethylone is structurally similar to the cathinones methylone and ethylone, and therefore may be expected to cause similar clinical symptoms. While there are forensic studies showing detectable ethylone and methylone found at autopsy, very few reports in the literature describe clinical features following such drug use [7,8]. After methylone use patients have been reported to return to normal within 24 hours, whereas ethylone in animal studies produces a more prolonged stimulatory effect [9,10]. One patient with confirmed methylone use was reported to have palpitations, agitation, fear, tremor, vertigo, vomiting, paresthesias, and muscle twitching; she was discharged from the ED on the same day of presentation [11].

Both case patients experienced prolonged neuropsychiatric symptoms (confusion, delusions and hallucinations) for several days. It is unclear whether diethylone use alone, use of other substances, or the treatments given during hospitalization explains this pattern. The delayed onset of rigidity, hyperreflexia and clonus observed in the patients following admission was unanticipated. The etiology of these observed neuromuscular findings is uncertain and could be related to the combination of numerous treatments the patients received (haloperidol, fentanyl, benzodiazepines, cyproheptadine, intubation, ICU admission) rather than solely due to diethylone itself.

It is not clear when the patients used diethylone prior to ED presentation. While diethylone itself was found in neither patient's sera, this is not unexpected due to metabolic transformation. Instead, predicted metabolites of diethylone were found in both patients. The substance identified as the one both took was positively identified as diethylone by laboratory analysis.

Medical toxicologists are on the frontline caring for patients who are using NPS, and new compounds are likely going to continue to emerge as drug markets evolve to outpace legislation. Our cases highlight diethylone as a new NPS that can be associated with severe and prolonged toxicity.

References

1. US DEA (2016) National Drug Threat Assessment Summary. DEA-DCT-DIR-001-17.
2. Curran HV, Wiffen P, Nutt DJ, Scholten W (2014) United Nations Office on Drugs and Crime. World Drug Report. World Health Organization. Geneva.
3. New Psychoactive Substances (NPS) Resource pack for informal educators and practitioners (2015) Ministry of Justice: 38th ECDD. Home Office and the Office for National Statistics. United Kingdom.
4. Lung D, Wilson N, Chatenet FT, LaCroix C, R Gerona (2016) Non-targeted screening for novel psychoactive substances among agitated emergency department patients. *Clin Toxicol* 54: 319-323.
5. Diethylone crystal. Hebina Higer Chemical Technology Co., Ltd. Qibin district, Xinghe street, Xinhua building, Hebi, Henan, 458030. China.
6. Personal correspondence. United Nations Office on Drugs and Crime (UNODC) (2017) – World Drug Campaign – NPS (New Psychoactive Substances). The Global SMART Programme (The Global Synthetics Monitoring: Analysis, Reporting and Trends Programme). January.
7. deRoux SJ, Dunn WA (2016) "Bath Salts" the New York City Medical Examiner Experience: A 3-Year Retrospective Review. *J Forensic Sci* 62: 695-699.
8. Lee D, Chronister CW, Hoyer J, Goldberger BA (2015) Ethylone-Related Deaths: Toxicological Findings. *J Anal Toxicol* 39: 567-571.
9. Lopez-Arnau R, Martinez-Clemente J, Carbo M, Pubill D, Escubedo E, et al. (2013) An integrated pharmacokinetic and pharmacodynamic study of a new drug of abuse, methylone, a synthetic cathinone sold as "bath salts". *Progress in Neuro-Psychopharmacology & Biological Psychiatry*; 45: 64-72.
10. Gatch MB, Dolan SB, Forster MJ (2017) Locomotor activity and discriminative stimulus effects of a novel series of synthetic cathinone analogs in mice and rats. *Psychopharmacology (Berl)* 234: 1237-1245.
11. Liakoni E, Müller S, Stoller A, Ricklin M, Liechti ME, et al. (2017) Presentations to an urban emergency department in Bern, Switzerland associated with acute recreational drug toxicity. *Scand J Trauma Resusc Emerg Med* 25: 26.