Toxicity from the NPS N-Methyl-Cyclazodone with Laboratory Confirmation - A Dance Befitting St. Vitus

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Authors:

Jack Basile[1], Joan Nolan[2], Alex Krotulski[3], Kevin Osterhoudt[2]

Institutions:

[1]Penn State Health, Reading, PA, [2]Poison Control Center at Children's Hospital of Philadelphia, Philadelphia, PA, [3]The Center for Forensic Science Research and Education, Willow Grove, PA

First Author:

Jack Basile, DO
Penn State Health
Reading, PA

Co-Author(s):

Joan Nolan, RN
Poison Control Center at Children's Hospital of Philadelphia
Philadelphia, PA
Alex Krotulski, PhD
The Center for Forensic Science Research and Education
Willow Grove, PA
Kevin Osterhoudt, FAACT, MD, MS
Poison Control Center at Children's Hospital of Philadelphia
Philadelphia, PA

Presenting Author:

Kevin Osterhoudt, FAACT, MD, MS
Poison Control Center at CHOP
Wayne, PA

Abstract:

Background:
Stimulants and purported nootropic, or "smart drug" chemicals, that are not internationally controlled,

comprise part of a wide range of drug analogs that are collectively regarded by the clinical toxicology community as Novel Psychoactive Substances (NPS). We report clinical features of a case of self-administration of a particular stimulant NPS, N-methyl-cyclazodone, to add to the establishment of its toxicological profile.

Case Report:

A 38-year-old man sought evaluation for uncontrollable body movements and palpitations. He reported that he had been self-treating his attention deficit disorder for 5 days with N-methyl-cyclazodone; he purchased "pure" powder online and had consumed a total of ~5g mixed in water. He also had prescriptions for fluoxetine and aripiprazole for bipolar disorder. The man was noted to be inattentive, restless, tremulous, and to have choreiform movements of his entire body. His heart rate was 110/min, blood pressure 150/90mmHg, and respiratory rate 24/min. His pupils were dilated but reactive to light. An ECG displayed sinus tachycardia with QRS interval 140msec and QTc 526msec. A urine drug immunoassay was negative for amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, opiates and phencyclidine; serum ethanol testing was negative. He was given IV crystalloid to achieve vascular euvolemia, and lorazepam for his movement disorder and autonomic hyperactivity; two ampules of sodium bicarbonate were given with shortening of the widened QRS, and magnesium was supplemented. Serum chemistries were notable for a creatine kinase (CK) of 2954U/L and an alanine aminotransferase (ALT) of 104U/L; creatinine was normal. With supportive care his symptoms resolved by hospital day 3 and his serum CK and ALT was trending downward. Liquid chromatography high resolution mass spectrometry testing confirmed the drug cyclazodone, an expected metabolite of N-methyl-cyclazodone, in the urine. No unexpected drugs were identified in the sample; specifically, no pemoline or 4-methylaminorex were found.

Discussion:

The oxazolidine derivative cylazodone is a centrally acting dopaminergic stimulant drug. It was developed in the 1960s and has chemical similarity to pemoline and aminorex, and it appeared in the online research chemical market in 2017. Cyclazodone is not currently approved by the U.S. Food & Drug Administration; despite its online sale and the presence of online testimonials of human consumption little is documented regarding its observed toxic effects. Cyclazodone use appears uncommon as it was not listed in the 2022-Quarter 1 NPS Stimulants Trend Report of the Center for Forensic Science Research and Education. The related drug pemoline became a schedule IV controlled substance in the U.S. after clinical reports of associated liver damage in children. Pemoline toxicity has also been associated with choreoathetosis and rhabdomyolysis.

Conclusion:

We present a case of user-reported N-methyl-cyclazodone use, with laboratory confirmation of cyclazodone, remarkable for associated hyperadrenergic vital signs, choreoathetoid movements, sodium bicarbonate-responsive QRS interval prolongation, and rhabdomyolysis with hepatic aminotransferase elevation. Contribution from, or interaction with, prescribed fluoxetine or aripiprazole cannot be excluded, but the toxic syndrome witnessed with cyclazodone was similar to toxicity described with the related drug pemoline.

Topic:

Drugs of Abuse, Ethanol, Addiction Medicine