CASE REPORT

Rhabdomyolysis After Ingestion of "Foxy," a Hallucinogenic Tryptamine Derivative

GHEATH ALATRASH, DO, PHD; NAVNEET S. MAJHAIL, MD; AND JAMES C. PILE, MD

"Foxy methoxy" (chemical name, 5-methoxy-N,N-diisopropyltryptamine) is a hallucinogenic tryptamine that has been abused with increasing frequency since its appearance in the late 1990s. Like other drugs in this class, foxy frequently produces feelings of euphoria, disinhibition, and auditory as well as visual hallucinations. The drug has been linked to adverse effects, including restlessness, agitation, gastrointestinal distress, and muscle tension. In light of the relatively recent advent of foxy as a drug of abuse and given the inability of commercial toxicologic screening tests to detect the presence of hallucinogenic tryptamines, additional adverse effects seem probable. We report ingestion of foxy by a healthy 23-year-old man that resulted in rhabdomyolysis and transient acute renal failure.

***Mayo Clin Proc.* 2006;81(4):550-551**

A hallucinogenic drug analogue of N,N-dimethyltryptamine (DMT), "foxy," or "foxy methoxy" (5-methoxy-N,N-diisopropyltryptamine [5-MeO-DIPT]) has a potency 7 times greater than that of DMT.[1] 5-MeO-DIPT has been widely available over the Internet and is popular at clubs and "raves" because of its stimulant-hallucinogenic properties. The drug has recently been placed in Schedule I of the Controlled Substances Act.[2] It is available as a pill for oral ingestion and as a powder for "snorting" or smoking. We summarize what we believe is the first report of rhabdomyolysis associated with the ingestion of 5-MeO-DIPT.

REPORT OF A CASE

A healthy 23-year-old man was brought to the emergency department because of combative behavior and hallucinations. He had reportedly ingested 25 mg of 5-MeO-DIPT 30 minutes before symptom onset, which is somewhat more than the typical oral ingestion of 6 to 20 mg.[2] He later noted that a friend had ingested some of the same supply of the drug without unpleasant effects. The patient denied concurrent use of other substances and had no history of trauma, crush injury, or seizures. Initial evaluation revealed hypertension (blood pressure, 171/70 mm Hg), tachycardia (heart rate, 150/min), and tachypnea (respirations, 24/min). His oral temperature was 38.7°C. Physical examination findings were unremarkable except for agitation. The patient's urine was dark red.

Initial laboratory studies (reference ranges shown parenthetically) were notable for nonoliguric acute renal failure with a serum creatinine level of 1.7 mg/dL (0.9-1.4 mg/dL); elevated anion gap metabolic acidosis (anion gap, 44 mmol/L [10-20 mmol/L]); and a serum bicarbonate level of 9 mmol/L (22-30 mmol/L). Urinalysis was positive for heme pigment, and microscopic examination of the urine revealed numerous pigmented granular casts. The peak creatine kinase level was 38,855 U/L (30-220 U/L), with a peak myoglobin level of 13,415 mg/L (0-110 mg/L). Urine toxicology screening was negative for amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, ethanol, or phencyclidine. Rhabdomyolysis associated with 5-MeO-DIPT ingestion was diagnosed. Aggressive hydration and alkaline diuresis were initiated, with improvement in renal function and resolution of the metabolic acidosis. At hospital dismissal, the serum creatinine and creatine kinase levels were 0.9 mg/dL and 233 U/L, respectively.

DISCUSSION

Hallucinogenic tryptamines, including 5-MeO-DIPT, are derivatives of indoleethylamine (tryptamine) with substitutions on the indole ring and ethylamine side chains responsible for hallucinogenic properties. Other drugs in the class, all associated with abuse, include alpha-ethyltryptamine, alpha-methyltryptamine, DMT, and psilocybin.

5-MeO-DIPT emerged as a drug of abuse in 1999 and has been used increasingly since then. Desired effects of foxy include euphoria, visual and auditory hallucinations, loss of inhibition, and feelings of empathy for and "connectedness" to others. Adverse effects, which appear in part to be dose-related, include insomnia, restlessness, mydriasis, nausea and vomiting, diarrhea, muscle tension, and uncontrolled jaw clenching. Effects generally occur within 20 to 30 minutes of ingestion and persist for 3 to 6 hours.[2-5] The effects of foxy mimic those of 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy"), as well as those of the aforementioned hallucinogenic tryptamines that have been previously or concurrently placed in Sched-

From the Division of Medicine, Cleveland Clinic Foundation, Cleveland, Ohio. Dr Alatrash is now with the Department of Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston. Dr Majhail is now with the Department of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis.

Individual reprints of this article are not available. Address correspondence to James C. Pile, MD, at his current address: Division of Hospital Medicine, CWRU/MetroHealth Medical Center, 2500 MetroHealth Dr, Cleveland, OH 44109 (e-mail: jpile@metrohealth.org).

ule I of the Controlled Substances Act.[2] These properties appear to be mediated by central 5-HT_2 receptor agonism, with the degree of hallucinogenicity correlating with a given drug's affinity for the receptor.[6,7]

A 15-month review of the American Association of Poison Control Centers' Total Exposure Surveillance System database during 2002 and 2003 revealed 41 reported exposures to 5-MeO-DIPT, 28 of which were deemed to be "moderate" or "major."[8] Effects included agitation in 59%, hallucinations in 39%, tachycardia in 37%, and hypertension in 17%. Although often considered "safe" drugs by the teens and young adults who favor their use, recent reports of fatalities associated with the ingestion of foxy and other hallucinogenic tryptamines suggest otherwise.[5,7,9] Tanaka et al[5] reported autopsy evidence of myocardial ischemia and pulmonary hemorrhage in a 29-year-old patient who died after foxy exposure.

The diagnosis of foxy intoxication is challenging because commercially available toxicology screening tests are unable to detect hallucinogenic tryptamines, although gas chromatography/mass spectrometry–based assays have shown a high degree of sensitivity for the detection of 5-MeO-DIPT. Other methods, including high-performance liquid chromatography and nuclear magnetic resonance, also appear to reliably distinguish the various hallucinogenic tryptamines.[6,10]

Rhabdomyolysis is a known complication of multiple drugs of abuse. A recent review of 475 cases of rhabdomyolysis treated at an academic medical center revealed an association with alcohol or illicit drug intoxication in 34%.[11] Alcohol has the strongest link to rhabdomyolysis of any drug of abuse, and although this association is frequently multifactorial, an element of direct myotoxicity appears to exist. Cocaine, amphetamines, and phencyclidine have been shown to cause rhabdomyolysis through postulated mechanisms that include muscle ischemia, muscle hyperactivity, and direct myotoxicity.[12,13] Both acute and delayed rhabdomyolysis have been associated with MDMA, although the mechanism has yet to be elucidated.[14,15] We believe that our patient's rhabdomyolysis was most likely due to drug-induced muscle hyperactivity, given the apparent absence of seizures or sustained physical activity. His presentation included features of the serotonin syndrome, which has been anecdotally associated with foxy ingestion and in which 5-HT_{2A} receptor agonism appears to play a central role.[16] However, the absence of deep tendon reflex examination or assessment for clonus prevents us from confirming or refuting the presence of serotonin syndrome in this patient. A direct myotoxic effect of 5-MeO-DIPT is also possible but cannot be confirmed at this time.

CONCLUSION

5-MeO-DIPT, which along with other hallucinogenic tryptamines is an increasingly common drug of abuse, is not detected by routine toxicology screening. The possibility of intoxication with these agents should be entertained in the appropriate setting, and clinicians should be aware of the potentially serious morbidity and mortality associated with their use.

REFERENCES

1. Jacob P III, Shulgin AT. Structure-activity relationships of the classic hallucinogens and their analogs. *NIDA Res Monogr*. 1994;146:74-91.

2. Drug Enforcement Administration (DEA), Department of Justice. Schedules of controlled substances: placement of alpha-methyltryptamine and 5-methoxy-N,N-diisopropyltryptamine into schedule I of the Controlled Substances Act: final rule. *Fed Regist*. 2004;69:58950-58953.

3. Hallucinogenic tryptamines. POISINDEX® System. Vol 126 [expired 12/2005].

4. Shulgin AT, Carter MF. N, N-Diisopropyltryptamine (DIPT) and 5-methoxy-N,N-diisopropyltryptamine (5-MeO-DIPT): two orally active tryptamine analogs with CNS activity. *Commun Psychopharmacol*. 1980;4:363-369.

5. Tanaka E, Kamata T, Katagi M, Tsuchihashi H, Honda K. A fatal poisoning with 5-methoxy-N,N-diisopropyltryptamine, foxy. *Forensic Sci Int*. 2006 [Epub ahead of print].

6. Vorce SP, Sklerov JH. A general screening and confirmation approach to the analysis of designer tryptamines and phenethylamines in blood and urine using CG-EI-MS and HPLC-electrospray MS. *J Anal Toxicol*. 2004;28:407-410.

7. Sklerov J, Levine B, Moore KA, King T, Fowler D. A fatal intoxication following the ingestion of 5-methoxy-N,N-dimethyltryptamine in an ayahuasca preparation. *J Anal Toxicol*. 2005;29:838-841.

8. Wilson JM, McGeorge F, Smolinske S, Meatherall R. A foxy intoxication. *Forensic Sci Int*. 2005;148:31-36.

9. Boland DM, Andollo W, Hime GW, Hearn WL. Fatality due to acute alpha-methyltryptamine intoxication. *J Anal Toxicol*. 2005;29:394-397.

10. Spratley TK, Hays PA, Geer LC, Cooper SD, McKibben TD. Analytical profiles for five "designer" tryptamines. *Microgram J*. 2005;3:54-68. Available at: www.usdoj.gov/dea/programs/forensicsci/microgram/journal_v3/mj05_v3_1-2.pdf. Accessed February 24, 2006.

11. Melli G, Chaudhry V, Cornblath DR. Rhabdomyolysis: an evaluation of 475 hospitalized patients. *Medicine (Baltimore)*. 2005;84:377-385.

12. Richards JR. Rhabdomyolysis and drugs of abuse. *J Emerg Med*. 2000;19:51-56.

13. Allison RC, Bedsole DL. The other medical causes of rhabdomyolysis. *Am J Med Sci*. 2003;326:79-88.

14. Smith KM, Larive LL, Romanelli F. Club drugs: methylenedioxymethamphetamine, flunitrazepam, ketamine hydrochloride, and γ-hydroxybutyrate. *Am J Health-Syst Pharm*. 2002;59:1067-1076.

15. Halachanova V, Sansone RA, McDonald S. Delayed rhabdomyolysis after ecstasy use [letter]. *Mayo Clin Proc*. 2001;76:112-113.

16. Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med*. 2005;352:1112-1120.