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LETTER TO THE EDITOR

Methoxetamine: a novel ketamine analog and growing health-care concern

To the Editor:

Methoxetamine (MXE) is a ketamine congener that is available from online vendors. We discuss what we believe to be the first report of the abuse of this substance in a health-care setting. We also present the successful analysis of methoxetamine which can be easily purchased over the Internet.

A 32 year old male with a history of hallucinogenic drug use, presented following methoxetamine injection. Paramedics and police found the patient agitated. The patient admitted to using methoxetamine, but was unable to provide the dosage or frequency of administration. He was able to state that it was administered intramuscularly prior to his arrival. He denied any co-ingestions. On arrival to the ED (Emergency department) his temperature was 37.2 celsius, heart rate 105, blood pressure 140/95, respiration rate 16, oxygen saturation 98% room air. His capillary blood glucose measurement was 122 mg/dL. He was oriented to name and location only. He would appropriately respond to questions for a brief period, but then would appear in a dissociative state. His pupils were 6 mm and reactive with rotatory nystagmus bilaterally. He was tachycardic with clear lungs sounds bilaterally. His abdomen was soft and non-tender with normal bowel sounds. His skin was warm and dry with no rashes. His neurologic exam was normal, including no signs of clonus or rigidity. The complete blood count, basic metabolic panel were all normal. The salicylate concentration was less than 4 mg/dL and acetaminophen concentration was less than 10 mcg/mL. Serum ethanol level was less than 10 mg/dL. After an 8 h observation period, the patient had returned to his baseline mental status. He stated he purchased the methoxetamine over the Internet and that this was his first time using this substance. He stated he easily ordered the methoxetamine over the Internet and it was then delivered without incident to his home.

Methoxetamine, or 2-(3-methoxyphenyl)-2-(ethylamino) cyclohexanone, is an arylcyclohexylamine congener of ketamine and phencyclidine, or PCP.¹ Thought to be initially synthesized by an underground chemist to treat chronic pain, methoxetamine is likely manufactured in China before shipment to the UK for general distribution.² The mechanism of action likely involves NMDA receptor blockade and dopamine reuptake inhibition, although formal pharmacology has not yet been determined.

Oral, insufflation, intramuscular, rectal, and intravenous have been described as potential routes of methoxetamine administration.³ Methoxetamine is also easily accessible to the public via the Internet.^{4,5} We made two attempts to purchase the drug. The first attempt by a leading researcher in emerging drugs of abuse failed. The second attempt, made by a toxicology fellow with little presence on the Internet, secured the drug from an Internet website. Within 2 weeks, 500 mg methoxetamine arrived via registered mail with postmarks indicating the United Kingdom as the source of distribution. The methoxetamine itself was stored in a 2X2 cm silver packing material within the larger envelope. The methoxetamine was an odorless, white powder. There was no additional paperwork with the methoxetamine, including quality assurances, instruction uses, or contact information. The total cost was \$62.00.

Gas chromatography-mass spectrometry (GC-MS) of the purchased substance was identified as 2-(3-methoxyphenyl)-2-(ethylamino) cyclohexanone, or methoxetamine.⁶ A standard institutional alkaline extraction protocol was employed to determine the GC-MS profile (The University of Massachusetts Clinical Toxicology Laboratory; Agilent Technologies 5973).

There are currently no legal restrictions within the United States (U.S) prohibiting the purchase or use of methoxetamine (U.S. Drug Enforcement Agency, personal communication). Early reports from September 2010 are available on bluelight.ru. Used for the dissociative and hallucinogenic properties, users claim feelings of euphoria and enlightenment while under the influence of methoxetamine.³

Although Internet vendors state that methoxetamine is not for human consumption, the drug is clearly used for illicit purposes.^{3,7} Methoxetamine, in addition to being easily accessible, is also relatively inexpensive, with prices ranges from \$7 to \$270 US dollars for 50 mg to 10 g, respectively.^{4,5} Methoxetamine is also purported to protect against urologic pathology, since ketamine has been demonstrated as a cause of papillary necrosis, although this still requires verification.³ Similar to other substances popularized online (i.e. K2, bath salts, and benzofury), the ease of methoxetamine accessibility via the Internet and the dissemination of information with regards to use are located on numerous websites.^{3,7} This provides the framework for continued nationwide abuse potential of this novel xenobiotic.

We are concerned that this novel medication and its ease of accessibility to the public presents a new healthcare threat. These issues range from increased risk taking behavior of individuals under the influence of hallucinogens and dissociatives, as well as the increased risk of intravenous drug use infections, namely HIV. Of note, methoxetamine is a medication with no current CSA number or publications listed in PubMed or Ovid. We are in support of legislation prohibiting the future importation and use of methoxetamine into the

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U.S. We hope this report will serve to provide information pertaining to a novel xenobiotic threat to our healthcare colleagues.

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