New Drugs of Abuse and Withdrawal Syndromes

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KEYWORDS

• NBOMe • Amphetamine • Synthetic cannabinoid • Drug withdrawal • Drug abuse

KEY POINTS

- New drugs of abuse are emerging at an exponential rate. As law enforcement attempts to ban these legal highs, new chemicals are used to replace those that are prohibited.
- Newer drugs, such as NBOMe, synthetic cannabinoids, share mechanisms of action with already existing drug classes but can have atypical or severe clinical presentations.
- It is important to recognize substance use disorders when they are encountered in the emergency department. Careful consideration should be given about how to approach the patient with substance use disorder so that they can be transitioned to the appropriate outpatient treatment.
- The first priority when evaluating a patient with suspected intoxication is ensuring safety of staff and other patients, after which one should ensure the patient has a protected airway.
- Management is guided by the patient's symptoms, and basic laboratory test results, including creatinine levels, complete blood count (CBC), and liver function tests, can help diagnose end-organ damage. Midazolam may be the fastest therapeutic option to sedate patients.

NBOMe

A new group of phenethylamine derivatives called NBOMe have gained popularity among new drugs of abuse. These are phenethylamine derivatives of the 2C class of hallucinogens and include 25I-NBOMe, 25C-NBOMe, and 25B-NBOMe.[1–3] One of the most common within the NBOMe group is 25I-NBOMe, which has emerged in the designer drug market as a legal replacement for lysergic acid diethylamide

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(LSD) or even sold as LSD in the illicit drug market. It is referred to by street names, including BOM-CI, INBMeO, Holland Film, Legal Acid, N-Bomb, N-boom, NE-BOME, Smiles, Solaris, and 25-I.[4]

25I-NBOMe is the most common of the synthetic derivatives of the classical serotonergic hallucinogen 2C-I. Both are shown in **Fig. 1** for comparison. This name comes from the *N*-benzylmethoxy substituent.[5] The chemical shorthand for methoxy is OMe. Functional activity studies suggest that 25I-NBOMe is a full agonist at the 5-hydroxytryptamine (5-HT) 2A receptor. The addition of the *N*-2-methoxybenzyl group has been shown to increase binding affinity and potency when compared with 2C-I. Stimulation of this receptor is essential for the hallucinogenic effects described for drugs such as NBOMe and LSD.[6,7] The hallucinogenic effects of 25I-NBOMe have been studied in mice by observing head-twitch behavioral response (HTR). HTR functions as a surrogate marker of the hallucinogenic effect of 5-HT_{2A} receptor activation in humans.[8] This study found that 25I-NBOMe induces HTR in mice that is dose dependent and significant when compared with controls.[9]

The routes of administration for 25I-NBOMe may include sublingual, buccal (especially blotter paper; **Fig. 2**), nasal (insufflation and absorption of liquid solutions), oral, injection (intravenous and intramuscular), rectal, and inhalation.[3] The available information suggests that a range of doses are used, which in part depends on the route of administration. Blotters are the most noted method of administration, and doses may range from high microgram to low milligram levels. LSD is commonly taken sublingually in form of blotters and is one of the reasons that 25I-NBOMe is marketed as LSD in the drug market.[10]

The NBOMe compounds are highly potent 5HT_{2A} receptor agonists and α-adrenergic receptor agonists, accounting for their serotonergic and sympathomimetic symptoms. The 5-HT_{2A} receptor has been closely linked to behaviors including working memory, cognitive processes, and affective disorders such as schizophrenia. These receptors are believed to mediate the primary effects of hallucinogenic drugs such as 25I-NBOMe. Given the relationship at the 5-HT_{2A} receptor, there is concern for potential interaction with other substances that act on the serotonergic system, such as selective serotonin reuptake inhibitors and serotonin and norepinephrine (NE) reuptake inhibitors. Symptoms such as tachycardia, hypertension, hyperthermia, muscle rigidity, and convulsions should be monitored, as development of serotonergic toxicity can be a possibility in these patients. **Table 1** lists various effects noted with the drug.[3,4,11,12] The detection of 25I-NBOMe has been shown by gas chromatography and liquid chromatography coupled with mass spectrometry.[13,14]

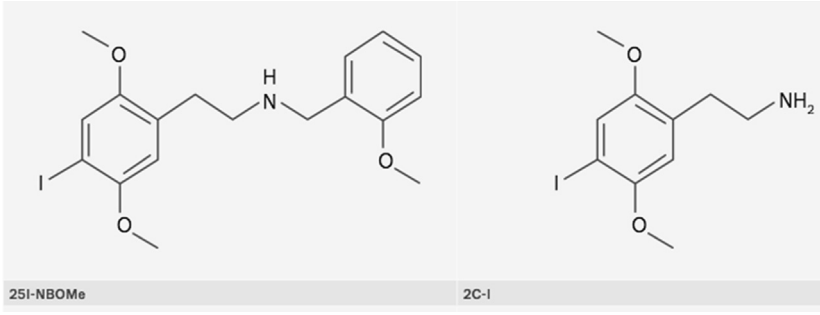

Fig. 1. Molecular structures of 25I-NBOMe and 2C-I. (*From* EMCDDA-Europol. EMCDDA–Europol Joint Report on a New Psychoactive Substance: 25I-NBOMe. 2014. Available at: http://www.emcdda.europa.eu/. Accessed March 27, 2014.)