NBOMe Toxicity and Fatalities: A Review of the Literature

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NBOMe Toxicity and Fatalities: A Review of the Literature

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INTRODUCTION AND BACKGROUND

2-(4-iodo-2,5-dimethoxy-phenyl)-N-[2-methoxyphenyl)methyl]ethanamine, or 25I-NBOMe, is a “2C” ring phenethylamine and full 5HT-2A agonist first described by German chemist Ralf Heim in 2003 in his search for novel compounds with activity at the 5HT-2A receptor. Also called “Smiles,” “N-Bombs,” and “N-benzylmethoxy,” recreational use of NBOMe as a hallucinogen was first documented in the early 2010s, infused in blotter paper for oral use or a powder for nasal insufflation. NBOMe has been compared to lysergic acid diethylamide (LSD), as both drugs are 5HT-2A agonists and induce similarly altered sensorium; indeed, NBOMe is often sold as LSD. Neither NBOMe nor LSD are tested for in routine urine drug screening. Multiple NBOMe variants have been discovered, and in 2013, three NBOMe compounds, 25I, 25C, and 25B, were first categorized under the US Controlled Substances Act as Schedule I compounds.

In their review of the literature through October 2014, Suzuki et al. identified 20 cases of NBOMe toxicity, with 17 cases involving males and an average age of 20.3 years. They note that NBOMe’s toxidrome regularly includes “autonomic instability,” with the majority of individuals experiencing tachycardia (85%) and hypertension (65%), and some experiencing fever (25%) or elevated creatine kinase (45%), indicative of rhabdomyolysis. They argue that unlike LSD, which does not cause serotonin syndrome despite 5HT-2A agonism, these autonomic symptoms in NBOMe toxicity may represent a serotonin syndrome-like condition.

INTRODUCTION:
In the decade since the introduction of the novel synthetic hallucinogen NBOMe into the consumer market, this drug has become an increasingly prevalent, yet poorly understood cause of altered mental status (AMS) resulting in hospitalization.

METHODS:
In this literature review, we conducted a PubMed query for mentions of NBOMe ingestion since Suzuki et al.’s publication of their 2015 review. Among English language publications published between October 2014 and June 8, 2021, were sixteen case reports and six case series detailing a total of 42 cases of NBOMe toxicity.

RESULTS:
Notably, 26 (62%) patients experienced tachycardia, 22 (52%) had hypertension, 34 (81%) experienced hallucinations. Nine of 42 cases ended in death, including six cases of direct NBOMe toxicity, one death by suicide, and two cases of fatalities from trauma after “excited delirium.” At least seven individuals believed that they had purchased and consumed LSD.

CONCLUSION:
In their review of the literature through October 2014, Suzuki et al. identified 20 cases of NBOMe toxicity, with 17 cases involving males and an average age of 20.3 years. They note that NBOMe’s toxidrome regularly includes “autonomic instability,” with the majority of individuals experiencing tachycardia (85%) and hypertension (65%), and some experiencing fever (25%) or elevated creatine kinase (45%), indicative of rhabdomyolysis. They argue that unlike LSD, which does not cause serotonin syndrome despite 5HT-2A agonism, these autonomic symptoms in NBOMe toxicity may represent a serotonin syndrome-like condition.

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Among published cases, Suzuki et al. recorded three fatalities and eight intensive care unit admissions. This is in direct contrast to LSD, for which there have been no documented fatal overdoses and “rarely reported” true suicide attempts.

In 2014, Lawn et al. performed a large anonymous online survey of NBOMe users, recording a peak psychoactive effect of two hours after oral ingestion and 45 minutes after nasal insufflation, with duration of activity lasting 3-13 hours.

Since the publication of Suzuki et al.’s systematic review, numerous published case reports and case series have expanded the present knowledge of NBOMe toxicity and management strategies. Here, we conduct an updated review of the literature detailing cases of NBOMe ingestion and toxidrome.

**METHODS**

A PubMed query for terms including “NBOMe,” “N-bomb,” “nbomb,” and “N-benzylmethoxy” revealed 160 publications between October 2014 and June 8, 2021. Among English language publications were sixteen case reports and six case series of NBOMe toxicity, encompassing a total of 44 patients. Two cases within an included case series were excluded due to lack of presentation characteristics beyond demographic information, leaving a total of 42 cases. Extracted data included:

**Demographics and characteristics of ingestion: age, sex, and country**

**Characteristics of ingestion: NBOMe variant, analytic confirmation, presence of other substance, and source of drug**

**Toxidrome: hallucinations, agitation, duration of altered mental status (AMS), seizure, tachycardia, hypertension, hyperthermia, diaphoresis, increased muscle tone or creatine kinase, additional information, and fatality.**

**Management: use of benzodiazepines, intubation, and intensive care unit (ICU) admission.**

**RESULTS**

In demographic information (Table 1), 32 patients (76%) were male, with an average age of 20.96 years. Toxidrome (Table 2) included tachycardia in 26 (62%) patients, while 22 (52%) had hypertension, and 11 (26%) had one or more seizures. 34 (81%) experienced hallucinations and 22 (52%) experienced agitation or aggression. Management (Table 2) included treatment with benzodiazepines in 31 cases (74%), and 13 individuals (31%) required ICU-level care.

Nine (21%) cases ended in fatality, with six appearing to result from direct NBOMe toxicity, including one case labeled as “serotonin syndrome.” One fatality occurred by suicide, while two other patients...
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attempted suicide without completion. One fatality occurred after reported “excited delirium and forcible restraint” by police25, while another occurred after “blunt craniofacial trauma as a manifestation of excited delirium”10.

Additional rare but notable observations included increased muscle tone in seven patients (17%) and significantly elevated creatine kinase (CK) indicative of rhabdomyolysis in five cases (12%). One patient experienced acute vasospastic limb ischemia19.

It has been noted that NBOMe is regularly sold under the label of LSD; Suzuki et al. noted in their review that four individuals (20%) who consumed NBOMe believed that they had ingested LSD3. Our review of the literature revealed a continuation of this trend: at least nine patients (21%) believed that they had obtained and consumed LSD rather than NBOMe.

In all but one case detailing a timeline of AMS that did not end in fatality, AMS lasted less than 24 hours, the majority of AMS resolving in less than half that time. The exception occurred with one individual who experienced recurrent hallucinations over the course of 18 months28.

Table 2: Toxidrome and Management

<table>
<thead>
<tr>
<th>Toxidrome</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hallucinations</td>
<td>34 (81%)</td>
</tr>
<tr>
<td>Agitation or aggression</td>
<td>22 (52%)</td>
</tr>
<tr>
<td>Seizure</td>
<td>11 (26%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>26 (62%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>22 (52%)</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>6 (14%)</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>13 (31%)</td>
</tr>
<tr>
<td>Increased muscle tone</td>
<td>7 (17%)</td>
</tr>
<tr>
<td>Increased creatine kinase</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>Fatality</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>Use of benzodiazepines</td>
<td>31 (74%)</td>
</tr>
<tr>
<td>Intubation</td>
<td>13 (31%)</td>
</tr>
<tr>
<td>ICU admission</td>
<td>13 (31%)</td>
</tr>
</tbody>
</table>

DISCUSSION

Consistent with Suzuki et al.’s 2015 review3, the majority of recent cases of NBOMe ingestion occur in young adult males, with average age of 20.96 years old. The prior documentation of autonomic instability remains prevalent, with most individuals experiencing tachycardia and hypertension. Most individuals (81%) likewise experienced AMS with hallucinations.

Although there is no point-of-care test for NBOMe, clinical suspicion for NBOMe ingestion may prompt off-site laboratory confirmation through high performance liquid chromatography mass spectrometry3. To represent a more accurate snapshot of the types of cases that may present to the emergency department, we did not exclude unconfirmed reports of NBOMe ingestion; many institutions may not have the resources to send away samples for confirmation, while other clinicians may deem a patient’s report of ingestion as sufficient. Indeed, 29 of 42 (69%) cases were analytically confirmed, and 19 (45%) individuals ingested another substance(s) along with NBOMe. As a limitation of this review, some toxidromes were likely influenced by substances other than NBOMe.

Perhaps the most concerning finding among these 42 recent cases of NBOMe ingestion is the extremely high rate of fatality: nine of 42 (21%) cases ended in death. This represents an increase since Suzuki et al.’s documentation of 17% fatality among cases prior to 20143. Indeed, 5 of the 9 fatalities appeared to have occurred from direct NBOMe intoxication. Combined with the finding that at least 16.7% of individuals believed they had consumed LSD, which has no documentation of death from toxicity, this represents a disturbing reality. Suzuki et al. warned that “users familiar with LSD may have a false sense of security when ingesting NBOMe inadvertently”3. This warning should be reinforced: individuals purchasing what they believe to be LSD likely experience a heightened risk of decompensation and death. Clinicians interacting with individuals experiencing AMS, especially in the context of hallucinogen use, must have increased clinical suspicion for NBOMe and its potentially fatal toxidrome. This is especially true for males in late adolescence/early adulthood who have a negative UDS, and absent or limited psychiatric history. It is important to note the possibility of a bias towards publishing cases with catastrophic or unexpected outcomes: therefore, the published literature may overrepresent the true frequency of attempted suicide and fatalities.
after NBOMe ingestion. Indeed, this review only captures cases which have come to the attention of emergency or medical responders.

The labelling of NBOMe’s toxidrome as “excited delirium” in two fatal cases is alarming, especially given that one of these deaths occurred after forcible restraint by police. The term “excited delirium” was described in a 2009 white paper by the American College of Emergency Medicine to characterize an “agitated and delirious state with autonomic dysregulation” that “for some…progresses to death.” In the years since, the label has been used to justify, often post-mortem, the police restraint of agitated patients with ketamine. However, the American Medical Association stands in clear opposition to this term, as does the American Psychiatric Association, which recently published a memo noting that it “lacks any clear diagnostic criteria.” The finding of fatal restraint of an individual intoxicated with NBOMe and labeled as “excited delirium,” underlies the need for increased awareness and sensitivity to the toxidrome of NBOMe in the criminal justice system and among law enforcement.

Other serotonergic agonists like LSD are noted in some persons to cause a Hallucinogen Persisting Perception Disorder (HPPD). Our review revealed one prior case of altered sensorium appearing >24 hours after use: a 16-year-old who presented with multiple periods of hallucinations and seizure in the months following NBOMe ingestion, culminating in an episode 18 months after ingestion of progressive left-sided weakness, ataxia, facial droop, executive dysfunction and seizure activity; MRI revealed bilateral leukoencephalopathy. Given the brief time since the first synthesis of NBOMe, and the even shorter period of documented NBOMe consumption – a little over ten years – the long-term effects and clinical presentations of NBOMe remain to be understood. Therefore, the prevalence of HPPD-like symptoms remote in time from NBOMe ingestion warrants continued investigation.

Emergency clinicians and consult-liaison psychiatrists should have heightened suspicion for both recent and remote use of novel synthetic hallucinogens among patients presenting to the emergency department with AMS.

REFERENCES


### Supplemental Table 1: Case Reports of NBOMe Ingestion

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Country</th>
<th>NBOMe Variant</th>
<th>Analyt. Conf.</th>
<th>Other subcl.</th>
<th>Source</th>
<th>Demographics</th>
<th>Characteristics of Ingestion</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arndt et al.</td>
<td>2015</td>
<td>22</td>
<td>M</td>
<td>Denmark</td>
<td>25C</td>
<td>Y</td>
<td></td>
<td>Internet</td>
<td>12 hrs (death at 121 hrs)</td>
<td>Y, Y</td>
<td>Y, Y 4.9 hrs</td>
</tr>
<tr>
<td>Boulton et al.</td>
<td>2015</td>
<td>15</td>
<td>M</td>
<td>USA</td>
<td>25I</td>
<td>Not reported</td>
<td>Not reported</td>
<td>BDDT</td>
<td>Y, 24 hrs (not specified)</td>
<td>N, Y</td>
<td>Not reported</td>
</tr>
<tr>
<td>Breakwell et al.</td>
<td>2017</td>
<td>17</td>
<td>M</td>
<td>UK</td>
<td>25G</td>
<td>N</td>
<td>Not reported</td>
<td>Purchased over the internet</td>
<td>N, Y</td>
<td>Y, Y</td>
<td>Y, Y</td>
</tr>
<tr>
<td>Byed et al.</td>
<td>2016</td>
<td>19</td>
<td>M</td>
<td>Australia</td>
<td>25I</td>
<td>Y</td>
<td>Ecstasy, MRDEP</td>
<td>Bell-willed to LSD</td>
<td>Y, Y</td>
<td>Unknown, ended in death</td>
<td>Y, Y</td>
</tr>
<tr>
<td>Caesarini et al.</td>
<td>2018</td>
<td>16</td>
<td>M</td>
<td>USA</td>
<td>25I</td>
<td>Not reported</td>
<td>Not reported</td>
<td>N, Not reported</td>
<td>N, Y</td>
<td>Y, Y</td>
<td>Y, Y</td>
</tr>
<tr>
<td>Hermann-Clausen et al.</td>
<td>2017</td>
<td>42</td>
<td>M</td>
<td>Germany</td>
<td>25I</td>
<td>Y</td>
<td>DIOP</td>
<td>Accidental ingestion - not replaced - sample with 25I-NBOMe</td>
<td>Y, Y</td>
<td>&lt; 6 hrs</td>
<td>N, N, N</td>
</tr>
<tr>
<td>Boubel et al.</td>
<td>2015</td>
<td>15</td>
<td>M</td>
<td>USA</td>
<td>25I</td>
<td>Not reported</td>
<td>Not reported</td>
<td>BDDT</td>
<td>Y, 24 hrs (not specified)</td>
<td>N, Y</td>
<td>Not reported</td>
</tr>
<tr>
<td>Creagh et al.</td>
<td>2017</td>
<td>16</td>
<td>M</td>
<td>Australia</td>
<td>25B</td>
<td>Y</td>
<td>Ecstasy, MRDEP</td>
<td>Bell-willed to LSD</td>
<td>Y, Y</td>
<td>Unknown, ended in death</td>
<td>Y, Y</td>
</tr>
<tr>
<td>Cogheer et al.</td>
<td>2016</td>
<td>19</td>
<td>F</td>
<td>Canada</td>
<td>25C</td>
<td>Y</td>
<td>Cocaine, marijuana</td>
<td>Obtained at party</td>
<td>Y, Y</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Kugma et al.</td>
<td>2015</td>
<td>15</td>
<td>M</td>
<td>USA</td>
<td>25I</td>
<td>Not reported</td>
<td>Not reported</td>
<td>N, Y</td>
<td>Y, 11 hrs (14-24 hrs after ingestion)</td>
<td>Y, Y</td>
<td>Y, Y</td>
</tr>
<tr>
<td>Zygowiec et al.</td>
<td>2017</td>
<td>27</td>
<td>M</td>
<td>USA</td>
<td>25I</td>
<td>Not reported</td>
<td>Not reported</td>
<td>N, Y</td>
<td>Y, Y (11 hrs)</td>
<td>Y, Y</td>
<td>Y, Y, N</td>
</tr>
</tbody>
</table>

**NBOMe Toxicity and Fatalities: A Review of the Literature**

NBOMe ingestion cases reported in the literature are summarized in this table. The table includes authors, year, age, sex, country, NBOMe variant, analytical confirmation, other substances, source, demographics, characteristics of ingestion, and management. The table highlights variations in clinical presentation and outcomes among the reported cases. Further analysis and discussion of these cases are provided in the main text of the review. This table is intended to provide a comprehensive overview of the available literature on NBOMe toxicity and fatalities, emphasizing the need for continued research and awareness in this area.

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### Supplemental Table 2: Case Series of NBOMe Ingestion

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Cases</th>
<th>Age</th>
<th>Sex</th>
<th>Country</th>
<th>Demographics</th>
<th>Characteristics of Ingestion</th>
<th>Toxidrome</th>
<th>Management</th>
<th>Fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gee et al.</td>
<td>2016</td>
<td>10</td>
<td></td>
<td></td>
<td>New Zealand</td>
<td>10/10, 2/10</td>
<td>Not reported</td>
<td>Y Y</td>
<td>Y Y</td>
<td>0/10</td>
</tr>
<tr>
<td>Laskowski et al.</td>
<td>2015</td>
<td>2</td>
<td></td>
<td></td>
<td>USA</td>
<td>2/2</td>
<td>Not reported</td>
<td>Y Y</td>
<td>2/2</td>
<td>0/2</td>
</tr>
<tr>
<td>Kirkpatrick et al.</td>
<td>2016</td>
<td>10</td>
<td></td>
<td></td>
<td>USA</td>
<td>10/10, 8/10</td>
<td>Not reported</td>
<td>Y Y</td>
<td>Y Y</td>
<td>2/2</td>
</tr>
<tr>
<td>Chan et al.</td>
<td>2019</td>
<td>4</td>
<td></td>
<td></td>
<td>USA</td>
<td>Not reported</td>
<td>Y Y</td>
<td>Y Y</td>
<td>Y Y</td>
<td>Y Y</td>
</tr>
<tr>
<td>Hiiger et al.</td>
<td>2015</td>
<td>10</td>
<td></td>
<td></td>
<td>USA</td>
<td>10/10</td>
<td>Not reported</td>
<td>Y Y</td>
<td>Y Y</td>
<td>2/2</td>
</tr>
<tr>
<td>Shanks et al.</td>
<td>2015</td>
<td>2</td>
<td></td>
<td></td>
<td>USA</td>
<td>Not reported</td>
<td>Y Y</td>
<td>Y Y</td>
<td>Y Y</td>
<td>Y Y</td>
</tr>
</tbody>
</table>