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Toxicities associated with NBOMe ingestion, a novel class of potent hallucinogens: A review of the literature

Joji Suzuki, MD[1,2], **Michael A. Dekker, DO**[3], **Erin S. Valenti, MD**[2,4], **Fabiola A. Arbelo Cruz, BA**[5], **Ady M. Correa, BS**[5], **Justin L. Poklis, BS**[6], and **Alphonse Poklis, PhD**[7]

[1]Department of Psychiatry, Brigham and Women's Hospital, 75 Francis St, Boston, MA

[2]Harvard Medical School, 25 Shattuck St, Boston, MA

[3]Southern Arizona VA Healthcare System, 3601 S. 6th Ave, Tucson, AZ

[4]Harvard Longwood Psychiatry Residency Training Program, 330 Brookline Ave, Boston, MA

[5]Ponce School of Medicine and Health Sciences, 388 Zona Ind Reparada 2, Ponce, PR

[6]Department of Pharmacology and Toxicology, Virginia Commonwealth University, Box 98-0613 MCVH/VCU Station, Richmond, VA

[7]Department of Pathology, Virginia Commonwealth University, Box 98-1065, MCVH/VCU Station, Richmond, VA, Richmond, VA

Abstract

Objective—A new class of synthetic hallucinogens called NBOMe has emerged as drugs of abuse. Our aim was to conduct a systematic review of published reports of toxicities associated with NBOMe ingestion.

Methods—We searched the PubMed for relevant English language citations that described adverse effects from analytically confirmed human NBOMe ingestion. Demographic and clinical data were extracted.

Results—Ten citations met criteria for inclusion, representing 20 individual patients. 25I-NBOMe was the most common analog identified, followed by 25B-NBOMe and 25C-NBOMe. Fatalities were reported in 3 (15%) cases. Seven (35%) were discharged after a period of observation, while 8 (40.0%) required admission to an intensive care unit. The most common adverse effects were agitation (85.0%), tachycardia (85.0%), and hypertension (65.0%). Seizures were reported in 8 (40.0%) patients. The most common laboratory abnormalities were elevated creatine kinase (45.0%), leukocytosis (25.0%), and hyperglycemia (20.0%).

Corresponding author: Dr Suzuki, Department of Psychiatry, Brigham and Women' Hospital, 75 Francis St, Boston, MA 02115. jsuzuki2@partners.org. Telephone 617-732-5752. FAX 617-738-1275.

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Conclusion—NBOMe ingestion is associated with severe adverse effects. Clinicians need to have a high index of suspicion for NBOMe ingestion in patients reporting the recent use of hallucinogens.

Keywords

NBOMe; 25I; 25B; 25C; LSD; hallucinogens

Introduction

A novel class of synthetic hallucinogens called NBOMe has recently emerged as new substances of abuse[1–3]. NBOMes are N-benzylmethoxy derivatives of the 2C family of hallucinogens (i.e. 2C-I, 2C-B, and 2C-C), initially synthesized for research purposes as a potent 5HT2A receptor agonist[4]. NBOMes are sold with names such as “Smiles”, “N-Bombs”, or by their shortened chemical name “25I” “25B” and “25C” [5]. Similar in structure to mescaline, the 2C family of hallucinogens are phenylethylamines with methoxy substitutions at the 2- and 5-positions, and a substitution at the 4-position often consisting of a halogen (i.e. chlorine, bromine, iodine). These compounds produce effects common to all hallucinogens that are 5-HT2A receptor agonists, ranging from mild to profound alterations in cognition and affect, powerful sensory and somatic effects, and mystical experiences[6–8]. However, compared to previous 2C compounds, NBOMes have a significantly higher affinity at the 5-HT2A receptor[9,10]. As a consequence, sublingual doses as low as 50μg may produce psychoactive effects[3].

While only a few human pharmacologic studies have been conducted on these drugs, reports of adverse effects from human NBOMe ingestion have begun to appear in the scientific literature since 2013[9,12–21]. In this report, we aimed to systematically review analytically confirmed cases of NBOMe-related toxicities.

Methods

Relevant scientific articles were identified from MEDLINE (PubMed) database through October 2014 using medical subject headings “N-benzylmethoxy”, “NBOMe”, “25I”, “25B”, “25C”, and “N-bomb”. Inclusion criteria were those citations that: 1) were in English language, 2) described human ingestion of NBOMe, and 3) analytically confirmed the presence of NBOMes. One author (JS) conducted the initial search of the electronic database, which was followed by the other authors (MD, EV, FC, AC) conducting additional searches and assessment of relevant citations. References from the identified publications were also reviewed to identify other citations. The following data were extracted: the product(s) consumed by the patient, analytically confirmed product(s), quantitative analysis of confirmed product(s), patient demographics and known characteristics, toxic effects, clinical management, and outcomes.

Results

Twelve citations were identified, but 2 were excluded (one was not in English, and the other did not analytically confirm the presence of NBOMe). In addition, in one of the citations

that reported 4 cases of NBOMe toxicity, 1 case was excluded as the presence of NBOMe was not analytically confirmed[18]. In total, 10 citations met criteria for inclusion, representing 20 individual patients. The extracted data are summarized in Table 1.

Seventeen (85%) patients were male, with an average age of 20.3 (range 15 to 31). Seven (35.0%) reported a prior history of marijuana use, 3 (15.0%) with prior history of MDMA use, and 1 (5.0%) each for the prior use of LSD, amphetamines, and cocaine. Depression was reported in 1 (5.0%) case.

Of the 20 cases identified, fatalities were reported in 3 (15%). Seven (35%) were discharged after a short period (<15 hours) of observation, while 8 (40.0%) required admission to an intensive care unit. One (5%) required surgery to correct a self-inflicted stab wound. The most common adverse effects were agitation (85.0%), tachycardia (85.0%), hypertension (65.0%), dilated pupils (55.0%), delirium (40%), hallucinations (40%), seizures (40.0%), tachypnea (25.0%), and fever (25.0%). The most common laboratory abnormalities were elevated creatine kinase (45.0%), leukocytosis (25.0%), hyperglycemia (20.0%), transaminitis (15.0%), and elevated creatinine (10.0%). Of note, the adverse effects and laboratory abnormalities noted above were not investigated in every case. Routine urine toxicology testing was negative in the majority of cases, with marijuana metabolites being identified in only 3 (15.0%) cases.

Eight (40.0%) patients consumed what they thought were NBOMe compounds. Six (30.0%) thought they ingested 2C-B, 4 (20.0%) thought they ingested LSD or a related drug, and it was unclear what the remaining 2 (10.0%) thought they ingested. The most common route of ingestion was by mouth, reported by 9 (45.0%). Of those ingesting it by mouth, 4 (20%) reported swallowing the substance, 3 (15%) were through the sublingual route, and 2 (10%) did not specify whether it was swallowed or taken sublingually. Three (15%) reported insufflating the compound, and 1 (5%) reported the intravenous route. Three (15%) reported either the oral or insufflation route. The route of administration remained unreported in 3 cases (15%).

The presence of 25I-NBOMe was confirmed in 17 cases (85.0%), while 25B-NBOMe, 25C-NBOMe, 25H-NBOMe, and 2C-I were confirmed in 3 (15.0%), 2 (10.0%), 1 (5.0%), 5 (25.0%) of the cases, respectively. The mean urine and serum concentrations of 25I-NBOMe were 15.3ng/ml and 0.49ng/ml, respectively. Urine concentrations for 25I-NBOMe ranged from 2.0 to 36.0ng/ml, while serum concentrations ranged from 0.034 to 0.75ng/ml. Urine and serum concentration for 25B-NBOMe, reported in only 1 case, were 1.9ng/ml and 0.18ng/ml, respectively. In the only case where 25H-NBOMe was found, the urine concentration was 0.9ng/ml.

Discussion

The abuse of hallucinogens remains an important public health issue in the United States, with the prevalence of past month hallucinogen use reported to be 1.2 million in 2010[22]. The number of new initiates for hallucinogens increased significantly from 200,000 in 2003 to 377,000 in 2010, despite a corresponding decline in the perceived availability of LSD and

other hallucinogens during the same time period[22,23]. Additionally, the Drug Abuse Warning Network indicates the number of LSD and other hallucinogen-related emergency room visits almost doubled from 5,296 cases in 2004 to 10,607 cases in 2009[24]. In this context, the introduction of a potent synthetic hallucinogen with little pharmacologic data on human effects is a major public health concern.

Our study results indicate that the typical profile of a NBOMe user who experiences adverse effects is a young male who is a regular user of marijuana and other substances. NBOMe ingestion often presented as a toxidrome that began shortly after ingestion, characterized by prominent neuropsychiatric effects (agitation, delirium, perceptual disturbances, seizures) and autonomic instability (tachycardia, hypertension, diaphoresis, and dilated pupils), ranging in severity from mild to severe. Once brought to medical attention, majority of patients recovered, but a substantial number required extended stays in the ICU requiring ventilatory support. These are effects similar to toxidromes reported in users of synthetic cathinones ("bath salts"), PCP, MDMA, anticholinergics, cocaine, and other stimulants, where agitation and cardiovascular effects are prominent[25–28]. These findings also resemble prior reports of NBOMe toxicity that remained analytically unconfirmed. For example, in a study of 25 cases of NBOMe ingestion reported to the Texas poison control center in 2012 and 2013, 88% were male with a mean age of 17 (range 14–25). Tachycardia (52.0%), agitation (48.0%), and hallucinations (32.0%) were most commonly noted, with 2 (8.0%) fatal outcomes[29]. Considering the short period of time that NBOMes have been on the black market, the accumulating reports of fatalities and serious adverse effects are of considerable concern.

Most drug ingestions lead to time-limited reactions that resolve once the substance is cleared from the body. Prolonged reactions become more common in overdoses or in binge usage, where protracted psychotic reactions or end-organ damage may occur. Yet, it is still concerning that 40% of the patients reported here required admission to an intensive care unit for management. This may suggest the possibility that these cases represent massive overdoses, that NBOMes have long-acting active metabolites, or that NBOMes are particularly prone to cause such toxic effects regardless of dose. Given that NBOMes are potent 5-HT2A agonists, and that agonism at the 5-HT2A receptor contributes substantially to the development of serotonin syndrome[30], the adverse effects seen may represent severe cases of serotonin syndrome. However, the relative paucity of neuromuscular findings common in serotonin syndrome (i.e. hyperreflexia, tremors, clonus) may argue against this diagnosis[30].

Many of the patients were noted to be behaving aggressively towards others, and one patient stabbed himself as a suicide attempt. In the 2 fatal cases described by Walterscheid et al, both patients suffered violent deaths, as evidenced by the numerous contusions and hemorrhages found at autopsy[19]. These reactions are also similar to the aggressive behaviors sometimes seen in synthetic cathinone ingestions[31]. However, these violent reactions to ingestion of synthetic cathinones, PCP or psychostimulants are often idiosyncratic[32], and it remains to be elucidated if NBOMes users are more prone to violent reactions.

Without knowing the actual dose ingested, it is difficult to ascertain if the adverse effects are dose dependent. Due to the extreme potency of this class of drugs, it is possible that individuals in this review had ingested much larger quantities of NBOMe than intended. The psychoactive dose can be as low as 50μg[3], making it impossible to correctly identify an appropriate dose with the naked eye. For example, a 5mg dose, equivalent to 25–50 times the psychoactive dose, would appear no larger than a single grain of kosher salt[33]. Additionally, it remains unclear if the route of ingestion plays any significant role in producing adverse reactions. Even those individuals taking NBOMe through the oral route experienced seizures and prolonged hospital stays. For example in the case series reported by Hill and colleagues, six individuals presumably ingested the same material from the same batch that was mislabeled as 2C-B. Nevertheless, one individual experienced a marked agitated delirium requiring several days of intensive care treatment, even though he ingested it orally[17]. The five others, two of whom insufflated the material, were treated and discharged relatively quickly after treatment with benzodiazepines. The individual that injected the drug intravenously experienced a significantly prolonged hospital course with many medical complications including ARDS, pulmonary abscess, and anuria. This may suggest that the intravenous route is especially hazardous.

The overall prevalence of NBOMe in the general population is likely to be small, but it may be gaining popularity in certain populations. In an online survey of 22,289 individual drug users, 39.4% reported ever using LSD, while 2.6% reported any NBOMe use. The most commonly reported NBOMes were 25I-NBOMe (2.0%), followed by 25B-NBOMe (1.2%) and 25C-NBOMe (0.8%). Highlighting the relatively brief period in which NBOMes have been available, the vast majority (93.5%) reported the first use on NBOMe in 2012 or later. In regards to the source of the drug, the majority reported obtaining the drug from a website (41.7%) or from a friend (39.7%), while only a minority from a dealer (15.9%). Users from this survey noted that peak psychoactive effects appear approximately 2 hours after oral ingestion, or 45 minutes after insufflation. Duration of effect was noted to range from 3 to 13 hours.

Similar to LSD, NBOMes are often sold on a blotter paper, which are small pieces of paper infused with the drug. Blotter papers are often adorned with unique artwork or colorful designs to indicate a particular brand or drug[33]. Of great concern are reports that NBOMes are sold as LSD, not only because NBOMe produce similar psychological and somatic effects as LSD, but because the potency of NBOMes allow the use of blotters. Most other drugs of abuse are psychoactive at much higher doses (typically >10mg), making it difficult to contain a single dose on a blotter paper. Masquerading of NBOMe as LSD has an important consequence. Adverse reactions to LSD have been well described, with “bad trips” being a common time-limited adverse reaction that responds well to reassurance and benzodiazepines[34]. Suicide attempts while intoxicated on LSD have been rarely reported, and no fatal cases of overdoses from LSD have been reported[6,7,34]. Indeed, despite its potent agonism at the 5-HT2A receptor, no clear case of serotonin syndrome has been reported in the 50 years that this compound has been used and misused[35]. Therefore, users familiar with LSD may have a false sense of security when ingesting NBOMe inadvertently. Indeed, our review indicated that 4 (20%) of the patients thought they had ingested LSD, and two of those patients died, while another patient attempted suicide.

Patients in this review were generally managed with intravenous fluids and benzodiazepines, and mechanical ventilatory support where indicated. This is in line with recommended management strategies for drug ingestions leading to toxic reactions, including serotonin syndrome, where the aggressive use of sedatives to reduce the agitation is paramount[26,30]. As such, even though no guidelines exist at this time, it appears that NBOMe ingestions should be managed using a similar approach. Therefore, the use of 5-HT2 antagonists may be an option to consider, particularly in those patients who are at least moderately ill[30]. Indeed in this review, one patient did receive cyproheptadine as part of the management[17]. The cases presented here provided minimal clinical information after the initial autonomic and neuromuscular issues resolved, suggesting patients generally did not present with persistent dysphoria, anxiety, paranoia, psychosis, delusions, or perceptual disturbances. However, given that these types of reactions can be seen following drug ingestions, it may be prudent to monitor for such persistent reactions and be prepared to provide antipsychotic medications.

In November of 2013, the Drug Enforcement Agency placed all three NBOMe analogs (25I, 25B, 25C) into schedule 1, making it illegal to manufacture, distribute, import/export, research, or possess these compounds[36]. A number of US states have also enacted laws to schedule these compounds, including Arkansas, Florida, Georgia, Louisiana, and Virginia[37]. Nine other countries are known to have enacted laws to control these substances, including Australia, Brazil, Denmark, Israel, Latvia, Russia, Slovenia, Sweden, and United Kingdom[2,37].

Presently NBOMes are not part of routine drugs of abuse screens available in hospital or other clinical laboratories. There are no rapid immunoassay screening tests or point of care devices which can detect the presence of NBOMes in urine specimens. Testing NBOMes in serum specimens is beyond the capabilities of all but perhaps a few hospital based laboratories. Presently, a few commercial reference laboratories offer a qualitative screen to identify the presence of 25I-NBOMe, 25C-NBOMe and 25B-NBOMe in blood, serum or urine. All published procedures for NBOMe analysis in biological samples utilize high performance liquid chromatography mass spectrometry (HPLC/MS) or HPLC/MS/MS. 25I-NBOMe has been identified in plasma[17], urine[16,17,19] and postmortem heart blood[19] in cases of severe intoxication. Validated HPLC/MS/MS methods have been published for detection and quantification of 25I-NBOMe in serum[13,38], urine[38] and numerous postmortem fluids and solid tissues[14]. Additionally, validated quantification methods are available for 25C-NBOMe in serum[38] and urine[20,39], 25B-NBOMe in serum[15] and urine[15,20] and an additional six NBOMe derivatives in urine[39]. Serum specimens for NBOMe testing should be collected in the classic red top or gray top blood tubes. Gold top or tiger top tubes with clot activator and thixotropic serum separator gel should not be used for NBOMe specimens. All specimens should be stored refrigerated. When sending serum tubes and/or urine containers off site for testing, they should be double bagged in zip lock bags in the event of leakage and shipped overnight with “cold packs”.

Clinical suspicion should remain high for a possible NBOMe ingestion in patients presenting with recent use of hallucinogens, especially LSD or the hallucinogens in the 2C family. If possible, analytic confirmation should be obtained. Management of NBOMe

ingestion should include aggressive fluid repletion and sedation using benzodiazepines. Patients should be made aware of the potential for ingesting NBOMes even if they feel confident about the source. As a harm reduction strategy, users should be advised against using hallucinogens alone without a sober sitter, avoiding “eye-balling” the dose due to overdose risk, and avoiding insufflating or injecting NBOMes. If a substance that may be NBOMe is found on a patient by a clinician, gloves should be used to avoid any direct contact and to take extreme caution to avoid inadvertent exposure—i.e. touching the mouth after handling the substance. In addition, caution should be exercised handling NBOMe powder to avoid making the compounds airborne.

NBOMes are a novel class of potent 5-HT2A agonist hallucinogens, with accumulating evidence for users suffering severe adverse effects. In severe cases, death can occur even after ingesting a single dose. Limited data on human use of NBOMes precludes the ability to predict which users will develop these severe reactions, and as such both clinicians and patients need to be educated about the potential dangers. Additional research is needed to further evaluate the effects associated with NBOMe ingestion in humans.

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Table 1

Summary of published reports of toxic effects of NBOMe ingestion in humans.

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
Armenian and Gerona 2014 (12)	1	3 hits of "acid" on blotter paper taken sublingually or orally	25C-NBOMe, 25I-NBOMe	not quantified	24 Caucasian F with "many" prior LSD use	**Neuropsychiatric:** Agitated delirium **Autonomic:** Tachycardia 140bpm, tachypnea 32/min; pupils 5mm; skin was moist and hot to the touch **Others**: Not reported **Laboratory abnormalities**: Not reported **Routine urine toxicology**: Not reported	IV fluids and lorazepam, and full recovery within 10 hours of ingestion.
Hill, et al. 2013 (17)	7	Intravenous injection of "3ml" of 25I-NBOMe	25I-NBOMe, 2C-I, amphetamine (trace), methamphet-amine (trace)	not quantified	29 M	**Neuropsychiatric:** Seizures, severe agitation, aggression, self injurious behavior, myoclonus **Autonomic:** tachycardia 160bpm, hypertension 187/171mmHg, tachypnea 58/min, temp 102.2F, dilated pupils **Other:** Anuria, ARDS, pulmonary abscess, loss of corticomedullary differentiation of renal parenchyma **Laboratory abnormalities**: serum pH 7.2, WBC 23.5 $\times 10^9$/L, CK 15424 U/L, ALT 121 U/L **Routine urine toxicology**: not reported	Intubation and ventilation, and intravenous sedation with propofol and midazolam and vasopressor support. Percutaneous tracheostomy on day 18. Producing urine on day 27, and discharged from ICU on day 38. Normalized renal function by discharge on day 43.
		1 cap of "2C-B" taken orally	25I-NBOMe, 2C-I, amphetamine (trace), methamphet-amine (trace)	not quantified	20 M with history of depression	**Neuropsychiatric:** Seizures, agitation	Initially given diazepam, then intubated, and pressure-control ventilation commenced,

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
						Autonomic: Tachycardia 126bpm, hypertension 170/90mmHg, tachypnea 24/min, temp 101.2F **Others**: sustained clonus, ocular clonus, nystagmus, urinary retention, serotonin syndrome **Laboratory abnormalities**: serum pH 7.3, peak CK 550 U/L on day 1 **Routine urine toxicology**: not reported	maintaining anesthesia with infusions of propofol, midazolam, lorazepam, cyproheptadine, and serotonin antagonist. Extubated on day 3, and discharged at Day 5.
		Insufflated a “small amount” of “2C-B”	25I-NBOMe, amphetamine (trace), methamphet-amine (trace)	not quantified	19 M with regular cannabis use	**Neuropsychiatric:** Auditory and visual hallucinations, derealization, and severe agitated with aggression **Autonomic:** tachycardia 110bpm, hypertension 138/100, dilated pupils to 9mm reactive to light **Others**:None **Laboratory abnormalities**: WBC 18.9×10^9/L, CK 326 U/L **Routine urine toxicology**: not reported	Diazepam to control agitation. Discharged 15 hours after ingestion.

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
		Insufflated an unknown quantity of “2C-B”	25I-NBOMe, amphetamine (trace), methamphet-amine (trace)	not quantified	22M	**Neuropsychiatric:** Seizure, agitation, visual hallucination, **Autonomic:** tachycardia 104bpm, dilated pupils **Others**: Nausea, dizziness **Laboratory abnormalities**: peak CK 633 U/L on day 1 **Routine urine toxicology**: not reported	Diazepam to control agitation. Discharged 15 hours after ingestion.
		Insufflated 100mg of “2C-B”	25I-NBOMe, amphetamine (trace), methamphet-amine (trace)	Not quantified	21 M with history of asthma	**Neuropsychiatric:** Severe agitation, aggression, hallucinations **Autonomic:** tachycardia 160bpm, hypertension 150/80mmHg, temp 101.1F, dilated pupils **Others**: None reported **Laboratory abnormalities**: WBC 11.1×10^9/L, CK 598 U/L **Routine urine toxicology**: not reported	Diazepam, lorazepam, and haloperidol to manage agitation. Discharged 15 hours after ingestion.
		One capsule of “2C-B” taken orally	25I-NBOMe, 2C-I, amphetamine (trace), methamphet-amine (trace)	not quantified	20 M with regular user of amphetamine and MDMA	**Neuropsychiatric:** Visual hallucinations **Autonomic:** Tachycardia 131bpm, hypertension 132/67, dilated pupils **Others**: palpitations, ankle clonus **Laboratory abnormalities**:none **Routine urine toxicology**: not reported	Hallucinations resolved, and discharged 15 hours after ingestion.
		One capsule of “2C-B” taken orally	25I-NBOMe, 2C-I, amphetamine (trace), methamphet-amine (trace)	not quantified	20 M with regular cocaine, cannabis, and MDMA use	**Neuropsychiatric:** Visual and auditory hallucinations **Autonomic:** tachycardia 125bpm,	Hallucinations resolved, and discharged 15 hours after ingestion.

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
						hypertension 154/90, dilated pupils, diaphoresis, clammy skin hypertension 154/90, dilated pupils, diaphoresis, clammy skin hypertension 154/90, dilated pupils, diaphoresis, clammy skin **Others**: Palpitations **Laboratory abnormalities**: None **Routine urine toxicology**: not reported	
Kelly et al. 2012 (18)	3	Unknown quantity of "25I-NBOMe" ingested either by mouth or insufflated	25I-NBOMe	Urine concentration: 2ng/ml	Male age 18–19	**Neuropsychiatric:** Agitated delirium **Autonomic:** Tachycardia 122bpm **Others**: Not reported **Laboratory abnormalities**: Glucose 239mg/dL **Routine urine toxicology**: Caffeine	Did not require mechanical ventilation, and outcome of hospitalization not described
		Unknown quantity of "25I-NBOMe" ingested either by mouth or insufflated	25I-NBOMe	36ng/ml	Male age 18–19	**Neuropsychiatric:** Seizure, agitated delirium **Autonomic:** Tachycardia 153bpm; hypertension 148/49 mmHg **Others**: Not reported **Laboratory abnormalities**: Glucose 292mg/dL **Routine urine toxicology**: Caffeine	Required intubation and mechanical ventilation, and outcome of hospitalization not described
		Unknown quantity of "25I-NBOMe" ingested either by mouth or insufflated	25I-NBOMe	28ng/ml	Male age 18–19	**Neuropsychiatric:** Seizure activity, agitated delirium **Autonomics:** Tachycardia 184bpm **Others**: Rhabdomyolysis, renal failure. **Laboratory abnormalities**: CK 30,000U/L **Routine urine toxicology**: Caffeine, nicotine	Required intubation and mechanical ventilation, and developed renal failure from rhabdomyolysis requiring hemodialysis. Outcome of hospitalization not described

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
Poklis et al., 2013 (15)	1	Unknown quantity of “25B” taken through unknown route	25B-NBOMe	serum concentration: 0.180ng/ml urine concentration: 1.9ng/ml	19 M with no known prior history of alcohol or drug use, or psychiatric illness	**Neuropsychiatric:** Status epilepticus, agitation; diaphoresis with facial cyanosis **Autonomic:** fever up to 104F; tachycardia 152bpm, hypertension 145/90mmHg, tachypnea 22rpm **Others:** purpuric rash on forehead; rhabdomyolysis **Laboratory findings**: initial blood gas pH 6.9 and pCO2 89mmHg, glucose 286mg/L, potassium 5.9mEq/L, creatinine 1.6 mg/dL, WBC 26.1×10^9/L, peak CK 11,645 on day 5 **Routine urine toxicology**: THC	Seizure control with multiple doses of lorazepam and dilantin loading, and ventilator support with propofol and midazolam. Extubated on day 3, and was fully alert and oriented by day 6.
Poklis, et al., 2014 (14)	1	One blotter of “acid” taken sublingually or orally	25I-NBOMe	serum concentration: 0.405ng/ml urine concentration: 2.8ng/ml	19 M with no known prior history of alcohol or drug use, or psychiatric illness	**Neuropsychiatric:** delirium **Autonomic:** Not described **Others:** Not described **Laboratory findings**: Not performed **Routine urine toxicology**: Negative	Fell or jumped from apartment balcony. Pronounced dead at the scene. **Autopsy findings**: Multiple blunt impact injuries, lacerations to heart, aorta, liver, spleen. Multiple skull fractures, subdural and subarachnoid hemorrhages and cortical contusions and axonal injury. Heart blood and ocular fluid negative for common drugs of abuse including targeted analysis for LSD and volatile drugs.
Rose, et al. 2013 (13)	1	Unknown quantity of “25I-NBOMe” taken through unknown route	25I-NBOMe	serum concentration: 0.76ng/mL	18 M	**Neuropsychiatric:** Severe agitation, aggression and hallucinations **Autonomic:** tachycardia 138bpm. Hypertension 150–170/110, pupils 6–7mm **Others**: None	IV fluids and lorazepam then admitted to the ICU. Patient remained agitated, requiring restraints in addition to continued lorazepam infusion and dexmedetomidine. Over the next 24 h, patient continued to have episodes of aggressiveness and was started on oral ziprasidone treatment.

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
						Laboratory abnormalities: Renal disposition not **Laboratory abnormalities**: Potassium 2.8 mEq/L, creatinine 1.4mg/L, glucose 192mg/dL, WBC 18,200 U : Potassium 2.8 mEq/L, creatinine 1.4mg/L, glucose 192mg/dL, WBC 18,200 U : Potassium 2.8 mEq/L, creatinine 1.4mg/L, glucose 192mg/dL, WBC 18,200 U : Potassium 2.8 mEq/L, creatinine 1.4mg/L, glucose 192mg/dL, WBC 18,200 U : Potassium 2.8 mEq/L, creatinine 1.4mg/L, glucose 192mg/dL, WBC 18,200 U **Routine urine toxicology**: THC	
Stellpflug et al. 2013 (16)	1	Unknown quantity of "25I-NBOMe" taken sublingually	25I-NBOMe, 25H-NBOMe, 2C-I	urine concentration: 25I-NBOMe:7.5ng/mL 25H-NBOMe: 0.9ng/mL 2C-I: 1.8ng/mL	18 F with moderate alcohol use and regular marijuana use	**Neuropsychiatric:** seizure, agitated delirium; pressured speech, hyperreflexia **Autonomic:** tachycardia 145bpm; hypertension 145/100mmHg, cutaneous flushing, pupils 7–8mm minimally reactive **Laboratory abnormalities:** fingerstick blood glucose 11.82 mmol/L, others not done **Routine urine toxicology**: not reported.	Improved with IV fluids and lorazepam, discharged after 5 hours of observation
Suzuki et al 2014 (21)	1	2 hits of "LSD" taken sublingually	25I-NBOMe	Serum concentration: 0.034ng/ml	18 Asian M with history of marijuana use	**Neuropsychiatric:** visual hallucinations, suicide attempt by stabbing self in neck and chest **Autonomics:** hypertension 140/84mmHg, tachypnea 20/min, dilated pupils 5mm **Others:** 12cm stab wound in anterior neck, two 8cm stab wounds in right lateral neck, and a 2cm penetrating stab wound to left anterior chest wall. Chest x-ray showing left pneumothorax and pleural effusion	Arrived in ED 11 hours after ingestion, alert and oriented. No longer under the influence but anxious. After insertion of chest tube, sent to operating room for wound exploration and closure. Suicidal ideation resolved, and transferred to an inpatient psychiatric unit 3 days after admission.

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
						Laboratory abnormalities **Laboratory abnormalities** : All within normal limits **Routine urine toxicology**: THC	All within normal limits
Tang et al. 2014 (20)	2	One pill of "NBOMe" taken orally	25B-NBOMe	not quantified	17 Caucasian M with history of recreational cannabis use	**Neuropsychiatric:** Seizure, agitated delirium **Autonomic:** tachycardia 140bpm, hypertension 215/94mmHg **Laboratory abnormalities**: peak CK 11066 U/L on Day 1, ALT 463 U/L, AST 492 U/L **Routine urine toxicology**: not reported	IV diazepam for seizure control then intubated with midalozam and rocuronium infusion.Fully conscious 12 hours after admission, and discharged on day 5.
		Half a packet of "Holland film" taken sublingually	25B-NBOMe, 25C-NBOMe	not quantified	31 Asian M with history of "substance abuse"	**Neuropsychiatric:** Agitated delirium **Autonomic:** Tachycardia 162bpm, hypertension 160/123mmHg, Fevers 39.6C, diaphoresis, pupils 5mm **Others:** elevated troponin and lactate; rhabdomyolysis; impaired renal function; transaminitis **Routine urine toxicology**: not reported	IV lorazepam, ice packs for physical cooling. Insisted on leaving hospital on day 3.
Walterscheid et al. 2014 (19)	2	2 hits of "acid" taken through unknown route	25I-NBOMe	not quantified	21 M with daily marijuana use	**Neuropsychiatric:** Hallucinations, severe agitation, aggression **Autonomic:** Not described **Others**: None reported **Laboratory abnormalities**: Not reported	Unresponsive in vehicle. Pronounced dead at the scene. **Autopsy findings**: Numerous scattered, linear, and confluent contusions and ecchymoses of the face, head, chest, back, arms, and legs; few petechial hemorrhages on the palpebral surfaces on the conjunctivae; hemorrhage in subcutaneous corresponding to cutaneous

Reference	N	Product consumed by user	Analytically confirmed product(s)	Quantitative Analysis of product consumed	Patient Characteristic	Effects	Management and outcomes
		"Unknown clear liquid" taken through unknown route	25I-NBOMe, THC (trace)	not quantified	15Caucasian F with marijuana and MDMA use	**Routine urine toxicology**: Not reported **Routine urine toxicology**: Not reported **Neuropsychiatric:** Agitation **Autonomic:** asystole, rectal temp 103.8F **Others**: Not reported **Laboratory abnormalities**: Not reported **Routine urine toxicology**: Not reported	contusions; hematomas in back and shoulder; lung parenchyma moderately congested and edemetous Found screaming in tent, and transferred to hospital. Pronounced dead on arrival. **Autopsy findings**: Numerous areas of abrasion and contusion over shoulders and upper extremities, left hip, right buttock, and left thigh and shins. Subscapular hemorrhages in frontal, parietal and occipital regions. Copious amounts of white foam in trachea and bronchi.