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Drug-induced psychosis and neurological effects following nitrous oxide misuse: A case report

The case of a 20-year-old female who experienced auditory and visual hallucinations after inhaling nitrous oxide she obtained legally in “whippits”—canisters used in whipped cream dispensers—highlights the need to report such adverse events to appropriate authorities so that data can be collected about the dangers associated with commercially available products and the number of misuse cases in Canada.

ABSTRACT: Nitrous oxide (N₂O) is an increasingly popular recreational drug globally. Users commonly inhale the gas from punctured canisters known as “whippits” that are designed for use in whipped cream dispensers. A surge in N₂O use has been reported in the UK, with a self-report recreational drug survey finding an increase in use from 20% in 2014 to 31% in 2017. The survey found that when nicotine, alcohol, and caffeine were excluded, N₂O was the seventh most common drug used by respondents. The accessibility

of N₂O as a consumer good contributes to misuse, as seen in the case of a 20-year-old female who presented to the emergency department complaining of visual and auditory hallucinations. The patient had no history of psychiatric or medical illness before experiencing symptoms, and results from laboratory investigations and physical examinations revealed no abnormalities. The patient reported inhaling nitrous oxide on a daily basis, however, and had recently increased her use of legally obtained whippits. A psychiatrist, a neurologist, and an addictions medicine specialist assessed the patient in consultation and agreed that her psychosis was the result of N₂O misuse. This case illustrates the need to increase awareness regarding the possible sequelae of nitrous oxide misuse and address current reporting limitations and the ease of access consumers have to nitrous oxide products.

Nitrous oxide (N₂O), commonly known as “laughing gas,”¹ has historically been used for medicinal purposes such as anesthesia, analgesia, and sedation.² It is also available as a consumer product in canisters known as “whippits” that are used in whipped cream dispensers.

An increasing number of publications and the Global Drug Survey (GDS), a self-report survey of recreational drug use, suggest N₂O is being misused by those seeking the dissociative state produced by puncturing whippits and inhaling the gas or “nanging.” The GDS found that when nicotine, alcohol, and caffeine were excluded, N₂O was the seventh most common drug used by 130 000 respondents.³

Whippits are readily available through storefront and online suppliers with no restriction on age of purchaser, medical history, quantity desired, or intended use. As long as the purchaser can pay for the product there is no barrier to obtaining whippits.

Each whippit contains 8 g of 100% N₂O, on average. The duration of action is short-lived (1 to 2 minutes)⁴ after the canister is punctured and the gas is released into an inflatable or an enclosed object for inhalation.¹

N₂O that is chemically identical to the N₂O in whippits is also sold with a drug identification number (DIN) for medicinal purposes. When used as an inhalational anesthetic, N₂O has analgesic and sedative effects. In accordance with federal legislation, N₂O is classified by Health Canada as an “ethical” product that

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“does not require a prescription, but that is generally prescribed by a medical practitioner. Ethical products are unscheduled non-prescription professional use products.”⁵

Case data

A 20-year-old female presented to the emergency department with visual and auditory hallucinations, agitation, and gait disturbance. She voiced concerns about a “transmitting” device in her throat. She believed that this device was making her legs weak and affecting her walking. She also heard voices from the device telling her to kill herself. She had come to the emergency department because she was worried for her safety.

The patient had no history of psychiatric or medical illness. She reported inhaling nitrous oxide on a daily basis. She had increased her use recently and was inhaling gas from approximately 100 whippits per day. The patient stated that she bought the canisters legally with a shopping app and showed the physician the website she used to make her purchases. She reported no other recreational or prescription drug use.

The patient was a slim and slightly built Asian female. She appeared anxious but not distressed. She was cooperative and her vital signs at triage were stable. On examination she showed no sign of head trauma. Her pupils were equal and reactive to light. Her speech and her gait were normal. Her neck was supple and her thyroid examination revealed no abnormalities. Respiratory, cardiac, and abdominal findings were unremarkable. Her neurological examination results were normal with no lateralizing sign, and her mental status exam revealed normal affect.

Laboratory investigations included an ECG that revealed normal sinus rhythm and a QTC of 399. CBC, electrolyte, blood urea nitrogen, and creatinine levels were all within normal limits. ASA, acetaminophen, and ethanol levels were normal. Her vitamin B12 level was also normal.

A psychiatrist, a neurologist, and an addiction medicine physician assessed the patient in consultation and agreed that she was psychotic as a result of N₂O misuse. The patient was kept in hospital until her symptoms resolved and she was discharged without incident.

Discussion

This case illustrates the need to consider the possible sequelae of nitrous oxide misuse (whether acute or chronic), the current reporting limitations, and N₂O accessibility issues.

Possible sequelae

Beyond symptoms of psychosis, N₂O misuse has been associated with myeloneuropathy and neurological effects, which are mentioned in a growing number of reports.^{1,2,6-8} These adverse effects can result from both acute and chronic exposure. A systematic review from 2016 that focused exclusively on N₂O misuse revealed that the users in 72 of 91 cases experienced some sort of neurological adverse effect,

Nitrous oxide can be readily obtained as a commercial product without any restrictions.

predominantly myelopathy, myeloneuropathy, and subacute combined degeneration.² Less common presentations included psychiatric symptoms as seen in our case. Additionally, 29 cases of nitrous-oxide-related death were reported.² Although the systematic review was unable to establish a dose-related toxicity because of unreliable data, the majority of cases involved the daily use of whippits.

The mechanism of these adverse effects is not well understood. N₂O is thought to be associated with low vitamin B12 levels. N₂O-induced oxidation converts vitamin B12 from a reduced to an oxidized form, which inhibits the activity of methionine synthase, leading to impairment of methylation reactions and DNA synthesis. This in turn leads to the accumulation of homocysteine.^{2,6} Clinical syndromes have been reported with both acute and chronic nitrous oxide use.

Reporting limitations

Health care providers play an important role in reporting adverse events from nitrous oxide misuse to the appropriate authorities. In the case described here it was initially difficult to

determine which authority should receive the report. When N₂O with a DIN⁵ is used for a medicinal purpose, the appropriate authority is the Canada Vigilance Program, which operates the adverse reaction online database. When the N₂O comes from a product marketed for making whipped cream, the appropriate authority is Health Canada Consumer Products and Cosmetics. A member of our health care team submitted a report to both authorities to ensure appropriate actions could be taken.

In response to our report, a Health Canada representative explained that Consumer Products and Cosmetics would document the misuse but only take further action if the N₂O canister had faults or hazards regarding its intended use, which is making whipped cream.

To our surprise, no cases of N₂O misuse have been reported to Health Canada Consumer Products and Cosmetics, and only one case of substance abuse of N₂O had been reported to the Canada Vigilance Program.

We also contacted the BC Drug and Poison Information Centre (DPIC) and learned that the provincial toxicology call centre received 14 calls regarding N₂O toxicity from misuse of whippits or similar commercial products between 2015 and 2019. Since our investigation determined that Health Canada received only one report of N₂O misuse in this period, many incidents appear to have gone unreported.

The number of N₂O cases described in the literature, the calls made to BC DPIC, and news stories of misuse⁹ all suggest that current reporting does not reflect the magnitude of the toxicity problem.

N₂O accessibility issues

Nitrous oxide can be readily obtained as a commercial product without any restrictions. In the case described here, the patient purchased canisters from a reputable online shopping website and had them shipped directly to her.

Whippits come in different sizes and can be purchased in bulk. At the time of writing, a package of 100 canisters could be purchased online for less than \$100.00 (\$1.00 per canister).¹⁰ Because the canisters are not sold for inhalation, there is no regulation that mandates

providing information on the risks or possible sequelae of N₂O misuse, nor are sellers qualified to provide this information.

Medicinal products with a drug identification number are classified by Health Canada according to different schedules that determine how accessible the product is to the public and the circumstances that require a health care provider (e.g., physician or pharmacist) to be involved in acquiring the product.¹¹ The safety and the complexity of the product and the harm the product may cause patients when used are all considered. Health Canada will reassess access to a medicinal product if new information arises, such as reports of adverse reactions, and may choose to further restrict or to ease access to the public.

Health Canada considers nitrous oxide to be an “unscheduled non-prescription professional use” product.⁵ This raises an important question: if N₂O used medicinally is deemed to require health care provider involvement, why is the purchase of N₂O used commercially not restricted in any way given the potential impact on consumers?

Summary

A case of nitrous oxide misuse by a 20-year-old female that resulted in drug-induced psychosis and neurological effects illustrates the need for clinicians to recognize N₂O as a potential substance of abuse and a possible cause of unexplained psychiatric or neurological symptoms.

In addition, this case highlights the need to report N₂O-related adverse events to appropriate authorities. The lack of N₂O misuse reports going to Health Canada means data are not

being collected about the dangers associated with commercially available products or the number of misuse cases in Canada.

Increased awareness is needed regarding N₂O toxicity and the more serious adverse drug effects that are possible. Solutions to misuse might include restricting access, adding safe-

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guards to minimize harm, and encouraging intervention from authorities to prevent product misuse. ■

Competing interests

None declared.

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