

## CASE REPORT

# Arytenoid swelling due to inhalation frostbite injury after the recreational use of nitrous oxide

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**Keywords** - Nitrous oxide, recreational, abuse, frostbite, airway, inhalation injury

## Abstract

In this case report, we present a patient with a potentially life-threatening airway obstruction after the recreational use of nitrous oxide. The patient initially presented with a globus sensation and hoarse voice. Flexible nasal endoscopy showed severely swollen arytenoids not responding to treatment with progression over time. After two days of mechanical ventilation the patient was extubated and discharged home without permanent disability. When confronted with patients with complaints of the throat after nitrous oxide abuse, we recommend flexible nasal endoscopy to identify potential airway compromise.

## Introduction

Nitrous oxide (N<sub>2</sub>O) or laughing gas is a stable, colourless, non-flammable gas with a lightly sweet taste. It has been in use in medical practice since the 19th century as an anaesthetic. However, since its discovery it has also been used as a recreational drug for its euphoric effects. It is typically inhaled from balloons which in turn are filled using 'whippits' (non-refillable steel bulbs) or larger professional canisters.<sup>[1]</sup> In the recreational use of nitrous oxide, inhaling the gas from a balloon acts as a safety measure against hypoxic injury. The balloon will be dropped if the user loses consciousness. New EU legislation, introduced in 2016, made it easier to sell nitrous oxide. Nowadays, nitrous oxide can be legally sold for a variety of uses. It is no longer considered a medical drug. Over the last few years, the recreational use of nitrous oxide has become increasingly popular, particularly among young clubbers.<sup>[1]</sup> The 2018 global drug survey found that 11.9% of respondents had used nitrous oxide in the past year as opposed to 6.3% in 2013. In the Netherlands, the 12-month prevalence of nitrous oxide use amongst respondents increased from 26.5% in 2014 to 34.1% in 2017, with a lifetime prevalence of 44.2% in 2017. Nitrous oxide is considered to be a relatively safe drug by users with

just a handful of reports describing adverse events. In general, these adverse events follow excessive use or misuse. The most commonly reported adverse events after excessive use of N<sub>2</sub>O are neurological symptoms due to a functional vitamin B12 deficiency.<sup>[2]</sup> Misuse or accidents during recreational use most commonly involve inhalation directly from the tank or frostbite injury to hands or legs from the rapid cooling of the tank. In this case report, we present a patient with odynophagia and vocal cord swelling after the recreational use of nitrous oxide.

## Case

A 16-year-old male with a past medical history of Crohn's disease presented to the emergency department of our hospital with odynophagia after the recreational use of nitrous oxide. During inhalation from a balloon he felt a sharp pain in his throat. Subsequently, he dropped the balloon and the ice-cold nitrous oxide spilled and caused burns to his arm. In the past few weeks he had regularly used nitrous oxide, always by directly inhaling it from a balloon. He had not had odynophagia before. He had not used any other substances. He presented approximately an hour after inhalation of the nitrous oxide. At presentation, his voice was hoarse and he had a globus sensation without an inspiratory stridor or dyspnoea. After the initial sharp pain, he was pain-free. No supplemental oxygen was needed to maintain a saturation of more than 95% and his breathing was regular and calm. Inspection of his oral cavity revealed no abnormalities. No signs of pneumomediastinum or emphysema were found during physical and radiological examination and the patient had no neurological symptoms such as weakness or numbness in his limbs. Laboratory analysis revealed no abnormal values. Because of the severe hoarseness and progressive globus sensation, the ENT consultant was asked to perform a flexible nasal endoscopy to identify airway compromise. Flexible nasal endoscopy showed severely swollen arytenoids and vocal cords,

as seen in thermal injury of the larynx. The nasopharynx and oropharynx appeared normal. Treatment was started with dexamethasone and nebulised adrenaline but at re-examination no decrease in swelling was seen. Because progressive swelling was feared, with airway compromise, endotracheal intubation was performed by the anaesthesiologist in the operating room using a small tube (size 7) in relation to the size of the patient and he was transferred to the intensive care unit. No antibiotics were started since no invasive lesions were seen. He was sedated and supported by mechanical ventilation with 5 cm H<sub>2</sub>O PEEP and a FiO<sub>2</sub> of 0.3. No haemodynamic support was needed. The burns on his arm were classified as first-degree burns. Flexible nasal endoscopy on day 1 showed progressive swelling and oedematous mucosa surrounding the tube with no clear view of the larynx. A chest X-ray showed no abnormalities. Re-examination on day 2 revealed decreased swelling. During the cuff-leak test, an air leak could be heard and he was successfully extubated shortly afterwards. He was discharged from the ICU and sent home the next day without permanent injury.

**Table 1.** Clinical manifestations of nitrous oxide abuse. Sequela marked with an \* were described after abuse from high pressurised nitrous oxide containers

Organ system	Clinical manifestations
Central nervous system	Myelopathy or acute demyelinating neuropathy mimicking Guillain-Barré syndrome <sup>[12]</sup> Myeloneuropathy, subacute combined degeneration of the spinal cord, peripheral neuropathy or polyneuropathy <sup>[2]</sup> Ischaemic stroke <sup>[13]</sup> Cognitive impairment <sup>[14]</sup> Toxic encephalopathy <sup>[15]</sup>
Pulmonary	Asphyxia (when used in closed spaces) <sup>[1]</sup> Emphysema*, frostbite of the oropharyngeal region * <sup>[2]</sup> Pneumomediastinum* <sup>[16]</sup>
Cardiovascular	Acute ST-elevation myocardial infarction <sup>[17]</sup> Pneumopericardium* <sup>[18]</sup>
Haematological	Megaloblastic anaemia <sup>[1]</sup> Haemolytic anaemia and leukopenia <sup>[19]</sup> Arterial occlusion, cerebral infarction <sup>[20]</sup> Deep venous thrombosis, pulmonary embolism <sup>[20,21]</sup> Pancytopenia <sup>[14]</sup>
Other	Variation of psychiatric symptoms <sup>[2]</sup> Fainting, accidents caused by loss of consciousness <sup>[22]</sup> Skin hyperpigmentation <sup>[14,23]</sup>

## Discussion

Nitrous oxide is a relatively safe anaesthetic and its recreational use is regarded as safe by its users, with a reported injury rate of 2%.<sup>[1]</sup> However, multiple articles have been published addressing the dangers of nitrous oxide. A systematic review published in 2016 identified 52 cases of abuse resulting in low vitamin B12 levels with neurological symptoms after chronic use. Other medical sequelae include pneumomediastinum, emphysema, frostbite to the oral cavity and pulmonary infiltrates.<sup>[2]</sup> The medical sequela described after the abuse of nitrous oxide are outlined in *table 1*.

Frostbite injury occurs through direct cellular damage and vascular stasis. After thawing, rapid intracellular influx of water causes swelling and oedema with further tissue death from cellular apoptosis progressing two to eight hours after exposure.<sup>[3]</sup> Burn and freezing injuries produce similar degrees of tissue destruction and progression of oedema will occur up until 24 hours after the injury.<sup>[4,5]</sup>

Misuse, using nitrous oxide directly from a canister, has been described to result in frostbite injury to the hands, face and airway.<sup>[6,7]</sup> Frostbite injuries from direct contact mainly occur when larger tanks or canisters are used, mainly because larger tanks tend to cool down more due to prolonged use. As the gas is stored in liquid form under pressure, the temperature of the gas released will be as low as its boiling point (-88°C).<sup>[8]</sup> Frostbite injuries commonly affect the hands and inner thighs when balloons are filled from larger tanks. Direct inhalation from a tank can result in frostbite injury to the airway and airway obstruction.<sup>[9-11]</sup> The use of a balloon as a delivery device should prevent this by collecting the nitrous oxide in its gaseous form. The time between filling the balloon and inhaling should warm it enough to prevent frostbite injury.

When patients present with frostbite injury of the larynx, we recommend to re-assess when further swelling is suspected and after the first 24 hours. Consider early intubation when signs of a narrowed airway are present or when, based on the mechanism of injury or endoscopic view, an increase in oedema is expected which might compromise the airway. Although we strongly suspect that the injuries sustained by the young man described in this case report were related to frostbite, we cannot rule out the possibility that these injuries were caused by a chemical or allergic reaction. A chemical injury, however, was unlikely since the patient and his friends had been regularly using nitrous oxide from the same manufacturer and from the same canister before these injuries occurred. The use of contaminated nitrous oxide cannot be ruled out. An allergic reaction was also unlikely since the patient had been a regular user, the swelling occurred after a sharp pain and he did not show any other signs of an allergic reaction (i.e. no rash, no hypotension). In addition, allergic reactions to nitrous oxide have not been described.

To the best of our knowledge, we have described the first case

of a compromised airway after the recreational use of nitrous oxide by direct inhalation from a balloon, the current 'gold standard' of nitrous oxide abuse. The recreational use of nitrous oxide has increased significantly since the introduction of new EU legislation in 2016 no longer classifying nitrous oxide as a controlled drug. Nowadays, 2- to 50-litre canisters can be easily purchased online.

Although the incidence of reported injuries and intoxications are still relatively low, we expect that with the increase in nitrous oxide abuse, injuries related to nitrous oxide will become more frequent. Professionals in emergency medicine, anaesthesiology and intensive care medicine are nowadays more likely to deal with injuries related to and side effects from nitrous oxide. Therefore, they should be familiar with the potential dangers. When a patient presents with a sore throat, globus sensation, hoarseness or breathing difficulties after inhaling nitrous oxide, flexible nasal endoscopy should be promptly considered to identify soft tissue injury which might lead to airway obstruction over time.

### Disclosure

All authors declare no conflict of interest. No funding or financial support was received.

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