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EDITORIALS

Laughter isn't always the best medicine

Recreational use of nitrous oxide is an emerging public health problem

Anita Acharya *medical student*[1], Ian Basnett *public health director*[2], Charles Gutteridge *chief clinical information officer*[3], Alastair Noyce *senior clinical lecturer*[4]

[1]Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK; [2]Public Health Department Barts Health, Barts Health NHS Trust, London, UK; [3]Department of Clinical Informatics, Barts Health NHS Trust, London, UK; [4]Preventive Neurology Unit, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK

Recreational inhalation of nitrous oxide (N_2O) is under-recognised in the UK, with potentially serious health risks. Adolescents and young adults presenting with the neurological complications of repeated N_2O use are seen regularly in east London emergency departments.[1] Greater awareness of this emerging public health problem is needed.

Nitrous oxide is a colourless gas, with minimal odour and variable taste. Inhalation of N_2O can produce a short lived, rapid onset euphoria and a dissociative effect. This is often accompanied by spontaneous laughter, hence the colloquial name "laughing gas." Historically, N_2O was inhaled as a recreational substance long before its potential use as an anaesthetic and analgesic agent was recognised.[2] Importantly, N_2O is always combined with oxygen in clinical settings to minimise the risk of hypoxia,[3] but it is inhaled neat by recreational users.

Although the clinical use of N_2O in anaesthesia has been declining in the UK and elsewhere,[4 5] its popularity as a recreational drug has increased among adolescents and young adults.[6 7] The 2017 Global Drug Survey found that it was one of the 10 most commonly used recreational drugs worldwide (excluding alcohol, tobacco, and caffeine products).[7] In a UK government survey, 8.8% of young people (aged 16-24) admitted to using N_2O in 2017-18 compared with 6.1% in 2012-13.[6 8]

The recreational use of N_2O in the UK has persisted despite the introduction of the Psychoactive Substances Act 2016, which prohibited the sale of nitrous oxide for recreational consumption.[6] The gas is sold legally for use outside healthcare, as an engine accelerant in the motor industry and as a propellant in the production of whipped cream. Small metal whipped cream chargers ("whippits") or canisters, each containing 8 g of compressed gas, are a common source of N_2O for recreational use (fig 1). Boxes of N_2O canisters are cheap and easy to buy from shops, street dealers, and social media or mainstream websites.[6] Pre-filled balloons of N_2O can also be purchased.

Nitrous oxide (N_2O) canisters (whipped cream chargers). A "cracker" device is used to pierce N_2O canisters and release the gas into balloons used for inhalation

Short and long term harms

Users of N_2O may experience dizziness, vomiting, and fainting soon after consumption. Inhalation of N_2O, particularly in enclosed environments, can lead to hypoxia and asphyxiation.[9 10] Although N_2O inhalation is rarely fatal, at least three deaths have been attributed to N_2O in the UK in each of the past five years, with eight cases in 2016.[11]

Prolonged exposure to N_2O can lead to neurological impairment from sensorimotor peripheral neuropathy and subacute combined degeneration of the spinal cord.[1 12 13] N_2O oxidises the cobalt ion in vitamin B_{12} (cobalamin), impairing its function. The mechanism of subsequent neuronal injury is not known, but one theory is that cobalamin inactivation reduces the generation of methionine, which is necessary for the methylation of myelin sheath proteins.[10 12]

In 1978, 15 cases of suspected spinal cord degeneration were reported across the US, all associated with repeated recreational or occupational N_2O exposure, mainly among dentists.[13] Between

Correspondence to: A Noyce a.noyce@qmul.ac.uk

1 November 2016 and 1 May 2017, 10 cases among recreational users were diagnosed at the Royal London Hospital,[1] and at least 10 more cases were seen the following year.

Patients with peripheral neuropathy or spinal cord degeneration can present with paraesthesia, numbness, or sensory ataxia.[1 12-14] Serum vitamin B_{12} levels can be low or normal, but raised methylmalonic acid or homocysteine concentrations indicate a functional B_{12} deficiency.[1 12] Patients presenting with neurological deficits have reported inhaling N_2O on average two to three times a week, and in large quantities (sometimes more than 100 canisters a day).[1 12]

We do not know if there is a safe level of N_2O use, but prescribing guidelines exist in the UK to limit the frequency and duration of patients' exposure to N_2O in clinical settings.[3] Nonetheless, cases have been reported of patients developing neurological problems after repeated clinical administration of N_2O for analgesia.[12 14] Neurological recovery after N_2O cessation and high dose vitamin B_{12} replacement is variable.[1 12 14]

Prolonged N_2O use can also precipitate megaloblastic changes in the bone marrow,[15] although many patients with neurological symptoms have normal mean corpuscular volume and haemoglobin levels.[1 12] Mood changes, bladder and bowel disturbance, and erectile dysfunction have also been reported after habitual N_2O use and may be particularly under-recognised.[13]

Public education

To reduce harm local authorities must publicise the adverse effects associated with frequent N_2O use and encourage users with neurological symptoms to seek early medical help. The No Laughing Matter campaign in the London Borough of Tower Hamlets is targeting antisocial behaviour and littering associated with recreational N_2O use as well as the illegal sale of N_2O.[16 17] Clinical coding and documentation of N_2O use and related symptoms in both primary and secondary care are currently inconsistent and must be improved. Systematic coding using either SNOMED CT or ICD-10 will aid patient follow-up, population health planning, and early detection of symptoms that may precede serious neurological impairment. Equally important is further research to better understand the mechanisms underlying neurological damage linked to N_2O and to quantify any potential dose threshold for harm.

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