Astronomical Use of Nitrous Oxide Associated With Stress From the COVID-19 Pandemic and Lockdown

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Studies have shown that during times of stress, such as the coronavirus disease 2019 (COVID-19) pandemic, there is a surge in substance use. Recent studies during the pandemic have shown increases in various substance use including opioids, stimulants, alcohol, and nitrous oxide (N_2O).[1–4] N_2O, listed as one of the most common substances used recreationally in the world, is an affordable legal gas and can be purchased easily.[5,6] N_2O is usually sold in cartridges as chargers for whipping cream, and it is possible to purchase thousands in bulk online with just a single transaction. An average cartridge costs approximately 70 cents, and the product is delivered right to a person's doorstep and is conveniently obtained even during the pandemic lockdown. N_2O can be inhaled directly into the mouth or by discharging nitrous gas cartridges into another object, such as a balloon. When inhaled, a calm and euphoric "high" can be felt within 10 seconds before disappearing within minutes.[5] Although this temporary high may be pleasurable, it also comes with side effects. Chronic use of N_2O irreversibly inactivates vitamin B_{12} and causes myelopathy, peripheral neuropathy,[5,7] and vitamin B_{12} deficiency[8] because inactivated vitamin B_{12} is excreted.[9] Here, we describe a patient with a history of hallucinogen use disorder, who used an astronomical amount of N_2O to cope with stress from the COVID-19 pandemic.

Case Report

A middle-aged man presented to the emergency department with tingling in his extremities and unexplained clumsiness in the past 2 weeks. He had a history of hallucinogen use disorder, periodically using psilocybin, 3,4-methylenedioxymethamphetamine, lysergic acid diethylamide, and ketamine since college. The patient initially started to use ketamine intermittently to cope with pandemic stress. Four months prior to admission, the patient could no longer obtain ketamine due to the pandemic lockdown, so he purchased N_2O online. His use escalated from 24 cans of 8-g N_2O cartridges per day to 150 cans of 8-g cartridges per day within 2.5 months. The patient attributed his escalation of N_2O use to stress induced by the pandemic lockdown, loss of his friends, and fear of loss of his business.

Two weeks prior to admission, the patient noted tingling and numbness of his hands and forearms. Ten days prior to admission, the patient stopped using N_2O, but the tingling, which he described as "like sandpaper," extended up from his feet and later throughout his trunk. He fell several times.

Upon admission, the patient was ataxic, but his motor strength and deep tendon reflexes were normal. The patient had a positive Romberg test and impaired vibration, temperature, proprioception, and light touch sensation with paresthesia from the base of his neck down. Urine toxicology screen was negative. Laboratory studies revealed hemoglobin of 13.2 g/dL, mean corpuscular volume of 95.9 fL, vitamin B_{12} of 168pg/mL, folate of 13.7 ng/mL, and ceruloplasmin of 18 mg/dL. Methylmalonic acid and homocysteine levels were elevated, and intrinsic factor blocking antibody was negative. A brain computed tomography without contrast and lumbar puncture were normal. Spinal magnetic resonance imaging showed dorsal column acute myelopathy secondary to N_2O toxicity and vitamin B_{12} deficiency. The patient received cyanocobalamin injections, and 2 months following discharge, the patient demonstrated improvement.

Discussion

During times of stress, such as in the 9/11 attacks and the economic recessions of 2008, there has been an uptick in drug use, especially among those with underlying substance use disorder (SUD).[10–12] The COVID-19 pandemic is no different. Recent studies have shown an increase in substance use among those with SUD, as evident in increases in drug-positive urine samples,[1] sales and consumption of alcohol,[2,3] and overdose deaths.[13] When one is stressed, corticotropin-releasing factor (CRF) is released.[10] Activation of CRF receptors has been hypothesized to cause behavioral changes in individuals, such as seeking more drugs under stress and triggering relapse, leading to stress-induced drug use.[14,15] For example, a study conducted among cocaine users showed that the secretion of CRF due to stress and the bodily responses to it predicted an increase in cocaine use in a 90-day period.[16] In our case, although other factors may have been involved, the patient's perception was that stress from the pandemic contributed to his increased substance use. This case adds to the importance of raising awareness of the vulnerability of patients with underlying SUD during times of stress, especially with recreationally used substances that are easy to get access to.

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