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RESEARCH ARTICLE

"WHEN LAUGHTER GAS NO LONGER BRINGS LAUGHTER"

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Abstract

Introduction: Nitrous oxide (N2O), also dubbed the " laughing gas" or " proto," is a gas used therapeutically in the medical field. However, a recreational trend has emerged, involving the inhalation of N2O from culinary capsules or canisters.

Clinical Case: This involves a 23-year-old patient, Hospitalized for psychomotor agitation, the patient has a history of cardiac arrest following extensive inhalation of laughing gas. "The patient presented with a manic syndrome that resolved within 2 days. Biological tests returned normal results, including vitamin B12. Brain MRI revealed bilateral bi-fronto-parietal cortical cerebral atrophy. The patient underwent a neurological etiological assessment, which came back normal."

Discussion: "The majority of literature reviews on the psychiatric complications of NO2 use have indicated that the most frequent symptoms are delirium, hallucinations, and confusion. The prognosis is often favorable, with symptoms typically resolving under antipsychotic treatment.

Conclusion: The consumption of nitrous oxide is a recreational practice that is on the rise, and especially among young people. With easy access and low cost.Cases of intoxication are increasing with serious medical complications which can lead to death, regardless of the type of exposure.

Introduction:-

Nitrous oxide (N2O), also dubbed the "laughing gas" or "proto," is a gas used therapeutically in the medical field, often in an equimolar blend with oxygen, for its analgesic properties. It also finds application in the industry as a propellant or oxidizer. However, a recreational trend has emerged, involving the inhalation of N2O from culinary capsules or canisters. Initially observed primarily in festive settings, this recreational use remained sporadic(Masson, n.d., p. 1).

N2O exerts its effects on reward circuits (dopaminergic system), sedation, and anxiolysis (GABA system), as well as on the sense of well-being and pleasure (endogenous opioid pathway). Additionally, N2O hinders vitamin B12 by oxidizing its cobalt ion, preventing its binding to the enzyme methionine synthetase. Both the absorption and

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elimination of the gas through the pulmonary route are swift due to its low solubility in blood and tissues, explaining the rapid onset and disappearance of its cerebral effects after inhalation(Emmanouil & Quock, 2007, p. 3).

Discovered in 1772 by the English chemist Joseph Priestley, N2O gained notoriety as the "laughing gas" in the late 18th century. In 1792, Humphrey Davy, another English chemist, detailed its analgesic and euphoric properties. By the 1840s, it earned the moniker "laughing gas" and was showcased in fairs. In 1844, dentist Horace Wells first employed it in medicine as an anesthetic for dental extractions. Today, it is widely used as an anesthetic(n.d., p. 3).

It wasn't until 1956 that Lassen and others raised concerns about the potential suppression of bone marrow with N2O anesthesia. Since that report, various authors have delved into studies on the toxicity of N2O in medical literature(Lassen et al., 1956, p. 4).

Epidemiological data on the misuse of N2O remain scant. Recreational use of N2O has seen a recent surge, ranking 14th among the most globally consumed drugs in 2020, according to the Global Drug Survey(GDS 2020 Key Findings | Global Drug Survey, n.d.). The UK Office for National Statistics noted it as the fourth most prevalent psychoactive substance among young adults aged 16 to 24 (following alcohol, tobacco, and cannabis), with 8.7% being consumers(Drug Misuse in England and Wales - Office for National Statistics, n.d., p. 6).

While the reinforcing properties of N2O expose users to the risk of developing a usage disorder, the debate on the existence of N2O addiction persists.(Fidalgo et al., 2019, p. 7)

Clinical Case:
Identity:
This involves a 23-year-old patient, a professional chef, the second of three siblings. Hospitalized for psychomotor agitation.

The patient reports occasional nitrous oxide consumption since adolescence.5 years ago , the patient has a history of cardiac arrest following extensive inhalation of laughing gas ."2 months ago, the patient visited the psychiatric emergency department due to psychomotor agitation and irritability that lasted for 2 days with spontaneous resolution. Toxicology screening was negative, and the patient was not under the influence of laughing gas.The patient was discharged the same day from the emergency department without any treatment, with a scheduled psychiatric consultation appointment, but the patient was lost to follow-up

Upon admission, the patient was conscious, oriented, with an irritable mood, an appropriate affect, and proper attire. Speech rate and flow were accelerated, indicative of tachyphemia and tachypsychia. Thought exploration revealed a delusional syndrome with a persecutory theme, though no persecutor was identified, and the mechanism appeared intuitive. Perceptual disturbances and suicidal ideation were absent, and instinctual functions were preserved. The patient received treatment with an anxiolytic (benzodiazepine) and risperidone 2mg. Substance screening tests yielded negative results, and the biological assessment returned normal, including the vitamin B12 levels. Over the course of two days, there was a marked alleviation of psychiatric symptoms; a cerebral MRI revealed bilateral frontoparietal cerebral atrophy. The patient continued on risperidone 2mg and was transferred to the neurology department for a comprehensive biological and radiological etiological assessment, which returned normal. The patient was discharged on risperidone 2mg with close psychiatric and neurological follow-up.

Discussion:-

N2O, an inert, colorless gas with a mildly sweet smell and taste, has become popular due to its accessibility, affordability, and swift reversibility of effects, especially among young adults and minors(Gillman, 2019, p. 7).

The exact pathophysiology leading to the development of psychiatric abnormalities in N2O users remains unclear. Tym and Alexander(5) have hypothesized an increased production of nitric oxide through the activation of the presynaptic nitric oxide synthase enzyme. Nitric oxide, in turn, reacts with superoxide free radicals, forming peroxynitrite, a potent oxidant and neurotoxin. N2O's capacity to act as a non-competitive antagonist of N-methyl-D-aspartate (NMDA) may also contribute to its psychogenic properties. Chronic abuse may precipitate cobalamin deficiency when individuals with limited vitamin B12 reserves use N2O. Psychiatric sequelae are less frequently documented, with only a few case series described in the medical literature(Tym & Alexander, 2011, p. 9).

The clinical presentation of N2O use is varied.

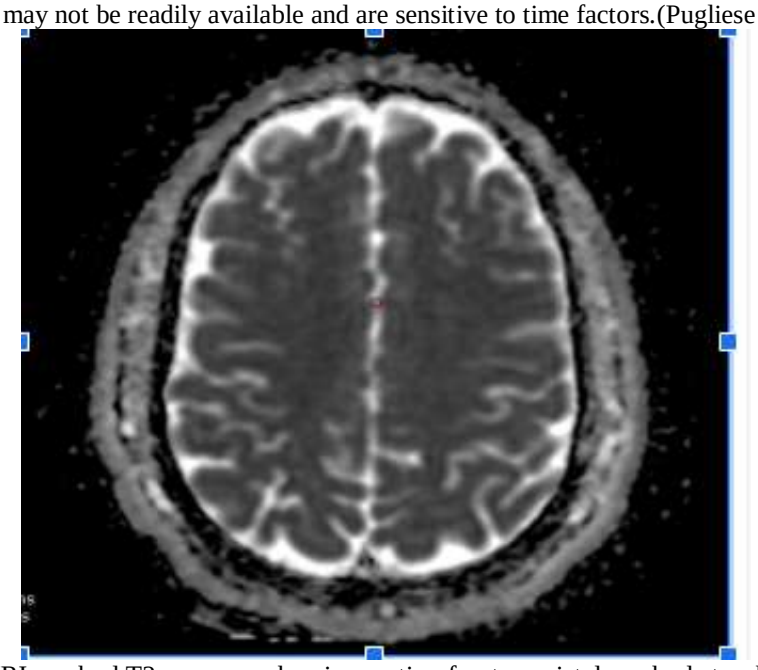
In their literature review on the psychiatric complications of N2O use (1900/2016), Amir et al. reported a total of 11 clinical cases. Among them, one presented with psychiatric symptoms (depression, hallucinations, and eventually suicide) accompanied by severe neurological complications. Hallucinations were the most common symptom at presentation (seven cases), with two cases of delusional syndrome and one case of chronic neurocognitive disorder. In the four cases where urine drug screening was reported, two tests were positive for cannabinoids, and two were negative for any abused drug. Vitamin B12 levels were low in only a few cases(Garakani et al., 2016, p. 10) .

In their retrospective study, Wan Shi Vhen et al. identified seven patients with severe N2O use who sought psychiatric emergency consultation. All these N2O users reported initiating use in adolescence or early adulthood. Most had a history of poly-substance use and mood disorders. The reasons for consultation ranged from heteroaggression and agitation to a suicide attempt for one patient, underscoring the potential danger of N2O use. Three were subsequently hospitalized due to the severity of their psychiatric symptoms. Four exhibited psychotic symptoms, with two showing negative results on their urine drug screening tests, suggesting the possibility of N2O-induced psychotic disorder(Chien et al., 2020, p. 11).

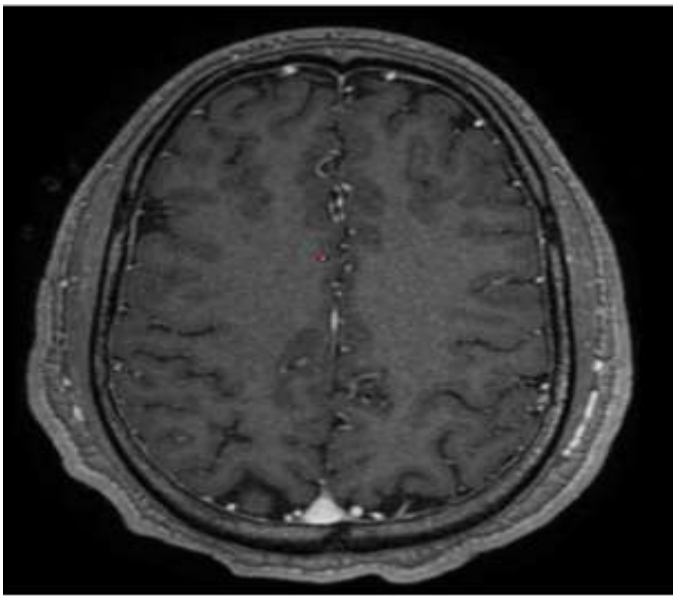
A systemic study summarized psychiatric presentations of N2O consumption, with delusions, hallucinations, and confusion being most common, aligning with the Global Drug Survey 2014, which reported a high prevalence of confusion (24.0%) and hallucinations (27.8%)

(. . Kaar SJ, Ferris J, Waldron J, et al. Up: The Rise of Nitrous Oxide Abuse. An International Survey of Contemporary Nitrous Oxide Use. J Psychopharmacol. 2016;30:395–401 - Recherche Google, n.d.; Lan et al., 2019, p. 12,13).Detecting N2O abuse poses challenges, akin to all abused substances, as quantifying the extent of N2O abuse accurately can be difficult. Patients may not fully disclose the quantity and duration of their consumption, opting to lie or deny their recreational N2O use altogether. Due to its short half-life and rapid elimination by the lungs, N2O is challenging to detect in screening tests.(14)

Given the lack of a formal screening tool for N2O abuse, it’s highly likely that N2O isn’t consistently considered as a potential cause in emergency services or medical offices. Moreover, numerous comorbid psychiatric and neurological disorders can muddle the interpretation of symptoms. Although low vitamin B12 levels may correlate with usage, these tests may not be readily available and are sensitive to time factors.(Pugliese et al., 2015, p. 15).



MRI cerebral T2 sequence showing cortico-fronto-parietal cerebral atrophy.



MRI cerebral T1 sequence showing cortico-fronto-parietal cerebral atrophy.

Conclusion:-

The consumption of nitrous oxide is a recreational practice that is on the rise, and especially among young people. With easy access and low cost.Cases of intoxication are increasing with serious medical complications which can lead to death, regardless of the type of exposure (recreational, suicidal, accidental or professional).

Finally, the education of the population, in particular via information campaigns among young people, remains a determining factor in the policy of preventing the use of psychoactive substances on the one hand, and on the other hand the use of NO2 in The treatment of resistant depression is of interest to several recent clinical trials which suggest that specific levels of No2 may be beneficial in the treatment of this disorder

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