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Original article

Possible impact of the COVID-19 pandemic on the recreational use of nitrous oxide in the Paris area, France



Possible impact de la pandémie de COVID-19 sur l'utilisation récréative du protoxyde d'azote en région parisienne

L. Dufayet^{a,b,c,d}, W. Caré^{a,e}, H. Laborde-Casterot^a, L. Chouachi^f, J. Langrand^a,
D. Vodovar^{a,b,d,*}

^a Centre antipoison de Paris - Fédération de toxicologie (FeTox), hôpital Fernand-Widal, AP-HP, 75010 Paris, France

^b Inserm, UMRS-1144, Faculté de pharmacie, 75006 Paris, France

^c Unité Médico-judiciaire, Hôtel-Dieu, AP-HP, 75001 Paris, France

^d UFR de médecine, université de Paris, 75010 Paris, France

^e Service de médecine interne, hôpital d'instruction des armées Bégin, 94160 Saint-Mandé, France

^f Centre d'addictovigilance de Paris, hôpital Fernand Widal, AP-HP, Paris, France

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ABSTRACT

Introduction. – Recreational use of nitrous oxide (N₂O) is increasing in Western countries, including France. During the COVID-19 pandemic, some authors warned that recreational N₂O use could increase further as the supply of illicit drugs was impacted by various containment measures.

Methods. – We retrospectively analyzed N₂O exposures reported to the Paris Poison Control Center (France) from 2010/01/01 to 2021/04/15. The Poison Severity Score was used to grade severity.

Results. – During the study period, 93 cases of N₂O recreational exposures were reported (male/female ratio: 1.1; median age: 20.9 years range: [14.8–49.0]). The first case was reported in 2012, 84/93 (90%) and 65/93 (70%) were reported since 2019 and March 17th 2020 (first lockdown in France) respectively. Most of the patients were symptomatic (88/93; 95%) and developed neurological symptoms (78/93; 84%). Among the fourteen patients who developed moderate to severe symptoms, eleven were reported after March 2020.

Conclusion. – Despite a marked increase in recreational N₂O exposures during the COVID-19 pandemic, the exact impact of COVID-19 on this increase remains to be determined as it was observed from 2019.

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RÉSUMÉ

Introduction. – L'usage récréatif du protoxyde d'azote (N₂O) est en augmentation dans les pays occidentaux, dont la France. Lors de la pandémie de COVID-19, certains auteurs ont averti que l'usage récréatif du N₂O pourrait encore augmenter, l'offre de drogues illicites étant impactée par les différentes mesures de confinement.

Méthodes. – Nous avons analysé rétrospectivement les expositions au N₂O signalées au Centre antipoison de Paris (France) du 01/01/2010 au 15/04/2021. Le Poison Severity Score a été utilisé pour classer la gravité.

* Corresponding author. Centre antipoison de Paris - Fédération de toxicologie (FeTox), hôpital Fernand-Widal, AP-HP, 75010 Paris, France.
E-mail address: dominique.vodovar@aphp.fr (D. Vodovar).

Résultats. – Au cours de la période d'étude, 93 cas d'expositions récréatives au N₂O ont été rapportés (rapport hommes/femmes : 1,1; âge médian : 20,9 ans plage : [14,8–49,0]). Le premier cas a été rapporté en 2012, 84/93 (90 %) et 65/93 (70 %) ont été rapportés entre 2019 et le 17 mars 2020 (premier lockdown en France) respectivement. La plupart des patients était symptomatiques (88/93; 95 %) et ont développé des symptômes neurologiques (78/93; 84 %). Parmi les quatorze patients ayant développé des symptômes modérés à sévères, onze ont été rapportés après mars 2020.

Conclusion. – Malgré une augmentation marquée des expositions récréatives au N₂O pendant la pandémie de COVID-19, l'impact exact de cette dernière sur cette augmentation reste à déterminer car elle a été observée à partir de 2019.

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1. Introduction

Recreational use of nitrous oxide (N₂O) is a growing public health problem associated with harmful effects [1–3]. The increase of the recreational use of N₂O has been reported in several western countries [1] including France [4].

During the COVID-19 pandemic, the illicit drug market was disrupted or even interrupted during lockdown periods [5]. N₂O, which is most often inhaled from cartridges/cylinders (usually through balloons) used in the food industry, remained easily, legally and cheaply available (shops, internet) during the pandemic [3]. Consistently, some authors have warned that recreational use of N₂O would increase during the COVID-19 pandemic because illicit drug users would switch to readily available products such as N₂O due to the lack of supply of illicit drugs [6].

We designed this retrospective study, based on exposure cases reported to the French National Database of Poisonings (FNPD – French Ministry of Health), to describe trends in recreational N₂O exposures in the Paris area before and during the COVID-19 pandemic.

2. Methods

Source of data: In France, eight Poison Control Centers (PCCs) respond 24/7 to the requests on toxic exposures from the public, caregivers and health authorities [7,8]. For each exposure case, data including the patient characteristics (age, weight and medical history), doses, circumstances, time from exposure to PCC call, symptoms, management and outcome are collected. In case of pediatric exposures, all patients are usually followed. When the patient is managed at home, a follow-up is made by phone, on the day after the exposure (asymptomatic patients) or until symptoms resolution (symptomatic patients). When the patient is managed at hospital, a follow-up is made by phone until discharge and the medical reporting is requested from the hospital after discharge. Cases are registered in the French National Database of Poisonings (FNPD, French Ministry of Health). The FNPD database is registered and approved by the French National Commission on Informatics and Liberty. As exposure cases are registered anonymously in the FNPD, informed consent of the patients is waived, in agreement with French law.

The COVID-19 epidemic in France: In France, the COVID-19 epidemic was officially declared on March, 2020. It led to a first strict lockdown from March 17th to May 11th, 2020, followed by various measures of lockdown until June, 2021.

Selection of data: We extracted from the FNPD and reviewed all cases involving intentional exposure to N₂O that occurred in the Paris area from 2010/01/01 to 2021/04/15. The end date corresponded to the launch of an information/prevention campaign by our Regional Health Agency on the risks associated with N₂O recreational use.

Collection of data: For each exposure, we collected the following data: demographics (age, gender), characteristics of exposure (recreational or not, frequency, amount), symptoms and outcome.

Statistical analysis: The analysis was only conducted on the recreational cases. Severity was assessed using the Poison Severity Score (PSS) that includes five severity grades, *i.e.* 0 (no symptoms related to the poisoning), 1 (minor symptoms), 2 (moderate symptoms), 3 (severe symptoms) and 4 (fatal poisoning) [9]. Results are expressed as median [interquartile range] for continuous variables and numbers (percentages) for non-continuous variables. We performed statistical analyses using GraphPad Prism[®], version 8.2.1 (GraphPad Software, San Diego, US).

3. Results

We found 98 intentional N₂O exposures; 93/98 (95%) and 5/93 (5%) were recreational and therapeutic exposures, respectively. The caller was the public and a healthcare professional in 19/93 (20%) and 74/93 (80%), respectively.

The first recreational case was reported in 2012; 84/93 (90%) and 65/93 (70%) were reported since 2019/01/01 and 2020/03/17 (first lockdown in France), respectively (Fig. 1). Median age and male/female ratio were 20.9 years [range: 14.8–49.0] and 1.1, respectively. Co-exposure was reported in 15/93 (16%) and mainly involved ethanol (*n*=6) and cannabis (*n*=5). The frequency of N₂O recreational use was poorly documented (available in 68/93; 74%). Two-thirds (61/93; 66%) of the patients reported having used N₂O recreationally several times before the call to the PCC; for 7/93 (8%) patients the call followed the first recreational use. The inhaled N₂O amount per session (available in 33/93; 35%) ranged from two to more than one hundred balloons.

Almost all patients were symptomatic at the time of the call (88/93; 94% - Table 1) and had neurologic symptoms (78/88; 90%). Five patients were asymptomatic and called the PCC after recreational exposure as they were worried about potential side effects. The most common neurologic symptoms were paresthesia (45/78; 58%), followed by headache (21/78; 27%), muscle weakness (15/78; 19%), drowsiness (12/78; 15%) and dizziness (10/78; 13%). Five patients developed persistent paresthesia and objective sensitive and motor deficit suggestive of combined degeneration of the spinal cord. Five other patients reported persistent memory impairment. Other reported symptoms were cardiovascular, respiratory, and digestive (Table 1). One case of cardiac arrest with successful resuscitation was reported in a 25 year-old man. He collapsed after consuming alcohol, poppers and N₂O at a party. No other cause beyond a hypoxic cardiac arrest was found (no evidence of methemoglobinemia) and he recovered without sequelae. Finally, 74/88 (85%), 13/88 (14%) and 1/88 (1%) were considered as PSS1, PSS2 and PSS3 respectively.

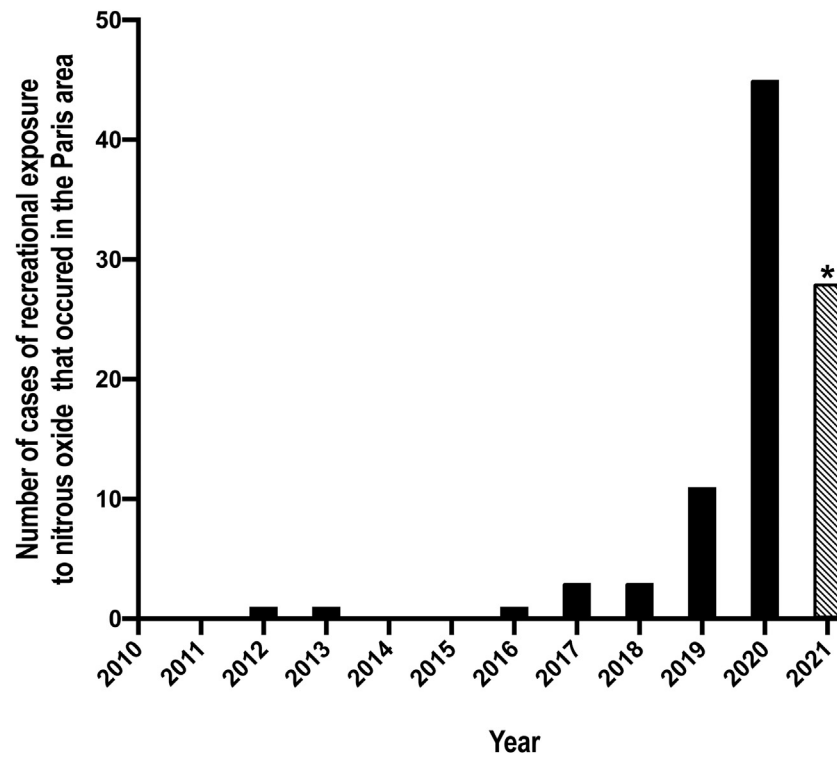


Fig. 1. Annual trends in N₂O recreational exposures reported to Paris Poison Control Center (n=93). *In 2021 data were collected until April 15th 2021.

Table 1
Reported symptoms associated with nitrous oxide recreational exposures. (PSS: Poison Severity Score).

	PSS			
Neurologic n = 78 (90%)	Minor 1 n = 74 (85%)	Moderate 2 n = 13 (14%)	Severe 3 n = 0 (0%)	n = 1 (1%)
	n = 68 (79%)	n = 10 (11%)		
	Paresthesia (n = 45)	Persistent objective sensitive and motor deficit suggestive of combined degeneration of the spinal cord (n = 5)		
	Headache (n = 21)			
	Muscle weakness (n = 15)			
	Drowsiness (n = 12)			
	Dizziness (n = 10)			
	Ataxia (n = 11)	Persistent memory impairment (n = 5)		
	Syncope (n = 6)			
	Decreased sensitivity (n = 4)			
	Confusion, agitation (n = 3)			
	Tremor (n = 3)			
	Blurred vision (n = 2)			
Brief aphasia (n = 1)				
Myoclonus (n = 1)				
Dysarthria (n = 1)				
Cardio-vascular n = 5 (5%)	n = 2 (2%)	n = 2 (2%)	n = 1 (1%)	
	Chest pain (without myocardial infarction, n = 2)	Tachycardia over 140 bpm (n = 1)	Cardiac arrest (n = 1)	
Respiratory n = 3 (3%)	n = 2 (2%)	Atrial fibrillation (n = 1)		
	Mild dyspnea (n = 1)	n = 1 (1%)		
	Mild bronchospasm (n = 1)	Prolonged bronchospasm (n = 1)		
Digestive n = 2 (2%)	n = 2 (2%)			
	Abdominal pain, nausea and vomiting (n = 2)			

All cases with known outcome (50/93; 53%) recovered with the exception of one patient who developed subacute combined degeneration of the cord and still required persistent walking aids (follow-up: five month), despite hydroxocobalamin intramuscular injections. Amongst the four other patients with similar symptoms, one recovered without sequelae in ten months and the other three were lost to follow-up.

4. Discussion

We observed a sharp increase in N₂O recreational use and associated neurological complications in the Paris area (France), since 2019 but even more in 2020 and the beginning of 2021. However, the actual impact of the COVID-19 pandemic on this increase remains difficult to interpret.

As the recreational use of N₂O seems to be increasing in developed countries, the observed increase in the Paris area may only be the reflection of this global phenomenon [6]. Moreover, the French Health Authorities published a report in July 2020 on the increase of neurological complications after N₂O recreational use between 2017–2019 [4]. The impact of such publication on the number of calls to PCCs is difficult to measure, especially in the context of the COVID-19 pandemic.

However, other evidence points to a possible “accelerating” effect of the COVID-19 pandemic on recreational N₂O use and related complications. In the study, after March 2020, three quarters of patients developed symptoms that led them to consult a doctor (49/65 of calls were from health professionals). More than three-quarters of the patients with moderate-severe symptoms were reported after March 2020. Moreover, two French neurology departments published case series of twelve and five patients, respectively, with severe neuropathy/myelopathy attributed to recreational N₂O use [10,11]. All patients were admitted from April 2020 and no previous case with a similar presentation had been admitted before. One of the neurology department was located in the Paris area but did not call our PCC; therefore those cases are not included in this series. The other was located in the East of France suggesting that this phenomenon is not limited to the Paris area. Conversely, we did not find any report from other country than France describing an increase in neurological complications attributed to the recreational use of N₂O. The annual European report on trends in illicit substances did not report any specific warnings about nitrous oxide use and harm in 2020 and 2021 [12,13].

Our PCC registry based study has limitations, related to its methodology as data are declarative, which is probably all the more true in this misuse context [14]. The number of N₂O exposure-induced complications was probably under-estimated as PCCs are not contacted for all cases of toxicant exposure. The often missing data on the N₂O consumption pattern did not allow us to conclude whether patients switched to N₂O as a substitute for other psychotropic substances (initial hypothesis), whether patients consumed more N₂O (in terms of frequency or quantity) or whether the proportion of new N₂O recreational users increased during the COVID-19 pandemic. However, in the two French case series mentioned above, most patients were recent N₂O users [10,11]. Finally, only half of the cases benefited from a follow-up and it is possible that we underestimated the severity of some complications.

5. Conclusion

We observed an increase of calls for N₂O exposures over time. This increase began as early as 2019 but was most pronounced during the COVID-19 pandemic period (2020–2021). The exact impact of the COVID-19 on this increase remains to be determined.

Disclosure of interest

The authors declare that they have no competing interest.

Author statement

Dominique Vodovar supervised the study.

Jérôme Langrand extracted the data from the French National Database of Poisonings.

Laurene Dufayet analyzed the data.

Laurene Dufayet, Weniko Care, Jérôme Langrand and Dominique Vodovar wrote the manuscript.

Hervé Laborde-Casterot and Leila Chouachi reviewed and made changes to the manuscript.

All the authors approved the manuscript in its initial and revised version.

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