Nitrous Oxide Occupational Exposure in Conscious Sedation Procedures in Endoscopic Ambulatories: A Pilot Retrospective Observational Study in an Italian Hospital

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Research

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Title

Nitrous oxide occupational exposure in conscious sedation procedures in endoscopic ambulatories: a pilot retrospective observational study in an Italian hospital

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Background:

Nitrous oxide is widely used to induce sedation; however, its use outside of operating rooms – such as in ambulatory rooms – is not properly controlled by norms. In the lack of supervision, there is a chance of workplace exposures for the operators engaged in the outpatient use of nitrous oxide. The aim of this research is to assess nitrous oxide exposure in gastroenterology outpatient settings.

Methods:

We performed an observational study with a first step marked by nitrous oxide environmental testing in a gastroenterology outpatient care where colonoscopies were practiced; environmental research was supported by biological monitoring with urinary N2O analysis in exposed operators. The research was conducted in the absence and then in the presence of a collective security device (Niki mask).

Results:

The study was rolled out in 10 sessions of day shift procedures, totaling 4105 samples. The average nitrous oxide concentration in the environment was 27.58 (SD 1.76) and 449.59 (SD 35.29), respectively with and without Niki Mask; the distribution of gases in the environment under investigation was not homogeneous (Anova test p.001). Biological testing revealed a substantial rise in urinary concentration of 8.97 (p.001) between the start and the end of the shift, and the use of the Niki mask was effective (p=.003).

Conclusions:

The exposure levels reported in environmental sampling exceed the limits of 50 ppm (the value set for operating rooms in Italy) as well as the value of 25 ppm (NIOSH threshold value), indicating a significant issue in the outpatient use of nitrous oxide. It is evident that technical measures are needed to contain the occupational risk from Nitrous oxide exposure outside of operating rooms, and that even the basic use of Niki masks would not be sufficient to minimize professional exposure and protect workers; for the exposure results detected in this research, it is also plain that exposures must be subject to health surveillance.

Keywords: occupational medicine, nitrous oxide, toxicology, operators exposure, anesthetic gas

Background

Sedation is an integral feature of any gastrointestinal endoscopic treatment since it helps gastroenterologists to relieve patient anxiety and distress while optimizing the endoscopic exam's result [1]. Nitrous oxide gas, as well as benzodiazepines and opioids, can be used to induce conscious sedation [2].

Multiple research and reviews have thoroughly defined esophagogastroduodenoscopy (EGD) or upper endoscopy sedation monitoring. A basic diagnostic EGD is a reasonably fast treatment that only involves 30 minutes of sedation. Sedation may be given for diagnostic upper EGD with either mild sedation or controlled anesthesia treatment (MAC) with [3,4]. Nitrous oxide-sedation is also a safe and reliable alternative for patients undergoing digestive endoscopy [5,6,7].

The use of moderate to deep sedation is becoming more common, which can be difficult for both anesthesiologists and gastroenterologists [8]. While deeper sedation helps gastroenterologists to conduct more complex procedures, there is a risk of multiple cardiopulmonary complications, particularly in high-risk patients [8,9,10].

Nitrous oxide has proved clinical efficacy, but at such ambient levels, it may pose a health threat to medical professionals who are chronically exposed.

The study seeks to detect the critical issues with the use of this anesthetic gas in ambulatory settings (outside of surgical rooms); the study aims to analyze the exposure conditions of health professionals engaged in these diagnostic procedures; one of the major issues in nitrous oxide conscious sedation is the definition of reference values in ambulatory rooms that are not comparable to those established in operating rooms; to this end, it should be noted that current legislation in Italy establishes environmental criteria for the use of N2O in operating rooms but no specific references for outpatient settings .

In terms of occupational toxicology, the most important factor is obviously persistent exposure to N2O; literature cites numerous findings that correlate chronic exposure to nitrous oxide with the onset of adverse effects on workers exposed to dental procedures. The most often reported side effects are: an increase in the rate of spontaneous abortion, infertility and reproductive difficulties, congenital anomalies and fetal growth delay; an increase in the incidence of cancer in the uterine cervix and kidney, liver diseases; adverse effects on bone marrow function and immune system, generalized neurological disorders and psychomotor dysfunction [11,12,13,14,15,16].

Occupational exposure may trigger nausea, irritability, and headache [17,18], as well as liver, renal, and hematopoietic system defects [19,20], and neurobehavioral shifts [21]. Furthermore, exposure to waste anesthetic gases is linked to an increased occurrence of abortion/miscarriage [22,23], decreased fertility [24], and birth defects, which are particularly linked to N2O [25]. Chronic exposure can also affect DNA [26].

The study's goal, in addition to evaluating staff occupational exposure, is to assist the scientific community in determining the reference environmental values specific for endocrinology ambulatories that use nitrous oxide, with a focus on the pediatric background.

The study's key endpoint measures was associated with the determination of nitrous oxide environmental and biological concentrations during gastrointestinal endoscopic sessions. These tests are taken to monitor the degree of anesthetic gas exposure among operators and to investigate the effectiveness of the preventive system (structure/implant features, anesthesia devices, work procedures, and human factors).

2 Methods

The study is made up of two parts: the first focuses on the interpretation of data obtained from N2O environmental monitoring, while the second is centered on biological monitoring data from exposed operators.

The environmental concentrations of nitrous oxide were detected using an instrument during four months for a total of 10 surveys. The instrument used for gas analysis is the photoacoustic spectrometer Innova-B&K (Brüel & Kjær, Denmark) “Multi-gas monitor model 1312” and Innova-B&K (Brüel & Kjær, Denmark) “Multi-sampler model 1309”. Measurements were performed using the instrument for the whole outpatient session. The measuring probes were placed in five different point in the ambulatory (Figure 1).

The environmental monitoring surveys were divided into two sessions: the first, in which patients were sedated with an O2/N2O mixture delivered without the use of an evacuation system, and the second, in which patients were sedated with the same O2/N2O mixture, but with the assistance of a mobile double mask evacuation system of type "NIKI 2002 Airnova" capable of intercepting the anesthetic gases that come out.

A descriptive study design was used to assess gas concentrations in a hospital's gastroenterology ambulatories. For environmental sampling results, the Shapiro-France analysis was used to measure data dissemination. The data was then stratified using the categorical variable relating to the use of the Niki mask. The t-Student parametric test was then used to analyze the averages in relation to the variable of Niki mask use; The ANOVA variance test was used instead for the study of the averages of the environmental levels of N_2O at the respective sample points, with the averages above two being corrected with the Bonferroni's test.

The study's participants were a team of health professionals who serve in the gastroenterology ambulatory for each colonoscopy session; the team included one gastroenterologist and one nurse. An operator with the qualification of prevention technician was interested in the environmental analysis and the preparation of urinary samples; biological sampling was performed on their urine for the biological analysis. The environmental data and urinary samples were analyzed in validated laboratories.

The samples were then analyzed in laboratory, by means of a Thermo Trace GC Ultra with Polaris Q Mass Spectrometer GC/MS System (IET-International Equipment Trading Ltd., Mundelein, Illinois, USA), and Thermo Direct Probe Controller (IET-International Equipment Trading Ltd., Mundelein, Illinois, USA). After urine sampling an immediate transfer of a urine aliquot to a hermetically sealed tube was therefore performed very quickly ($t < 1$ minute) so that the vapors loss was negligible ($< 5\%$). The urines were then acidified with sulfuric acid (200 μl of H_2S04 9N as antimicrobial agent) and stored for more than 24 h. Collection was performed in environments free of pollution due to anesthetic gases. The vials, appropriately labeled, were transported to the laboratories, through a thermostatic thermal bag and stored at 4 °C up to the analysis.

A descriptive analysis of the N_2O concentrations of urine was performed. Due to the limited sample size, data distribution analysis was performed using the Shapiro-Wilk test. The t-test was thus used to compare the urinary concentration averages of N_2O for doctors and nurses at time 0 (start of shift), and the same was repeated at time 1. (end of shift). The t-test was also used to analyze N_2O averages between time T0 and T1 in participants who wore Niki masks and those who did not. Statistical significance was determined by $p<.05$ values.

3 Results

The endoscopists and nurses engaged in the outpatient diagnostic procedure were hired for the study; the observation period lasted 10 days, and 48 patients were treated; diagnostic services were conducted during day shifts between 06:57 and 18:23.

3.1 environmental analysis (Study 1)

The N2O levels in the environment were first stratified in order to compare the conditions under which N2O is used without any emission control mechanism and then with the use of the control mechanism (Niki mask).

For a total of 10 days of observation, 4105 sequential samples were collected for each of the five detection stations; having discovered values well above the exposure limits (50ppm) in the absence of the use of containment mechanisms (Niki mask), it was decided to discontinue the experimentation in this way and continue only for samples with the use of Niki mask as a principle of safeguarding. We obtained 374 environmental determinations without using the Niki mask and 3731 with using this mask.

The average environmental concentration of N2O in the air was 27.58 (SD 1.76) in the presence of Niki mask and 449.59 (DS 35.29) without the use of Niki. The difference in averages (with and without Niki) detected was largely significant ($p<.001$).

As mentioned - the environmental samplers - in the room were placed in five different places; the average concentrations at the individual points were determined (Table 1) noting a significant difference ($p<.001$) between the points even if with a low strength (F16.42) and an R2 supporting the model only of .017.

Table 1- Average concentrations at different points

Sampling point	number	Average	S.D.
1-Niki	749	40.00	85.47
	75	436.52	329.59
2- head-window	748	23.59	43.23
	75	518.77	416.95
3- head door	747	26.57	46.19

	75	424.73	308.18
4- stabilized door	746	18.33	32.06
	75	446.06	319.51
5- access	741	29.40	49.59
	73	421.11	348.20
Totale	3731	27.58	54.87
	373	449.59	346.62

According to the Threshold Limit Value in the measurements in which the Niki mask was used, the levels set by NIOSH (25ppm) were exceeded 982 times, the levels set by Italian law for 'new' operating rooms (50ppm) 645 times and those for 'old' operating rooms (100ppm) 288 times.

There was a huge variation in environmental concentrations of N2O at the different sample points (Table 2), implying that the lack of specific mechanisms for handling air flows and modifications causes areas of greater concentration and, as a result, greater professional exposures to anesthetic gases.

Table 2- Test Comparison of N2O concentration (in ppm) and sampling points (with * significant values, p<.05)

	1-Niki	2-head-window	3-head door	4- stabilized door
2- head-window	-16.41* p<.001			
3- head door	-13.43* p<.001	2.98 p=1.00		
4- stabilized door	-21.67* p<.001	-5.26 p=.62	-8.24 p=.03*	
5-access	-10.60* p<.001	5.82 p=.39*	2.84* p<.001	11.08* p<.001

3.2 Biological monitoring (Study 2)

There was no discrepancy in urinary concentrations between doctors and nurses when the two classes of operators were examined. The exposure group (nurses and doctors) was then viewed as a single sample with a total of 16 determinations at T0 and 16 determinations at T1

The urine concentration averages of NO2 were analyzed, and the substantial reduction of urinary concentrations in those exposed to NO2 in the two groups compared: with Niki we obtained at T0 time and with the use of the mask a value of 1.17 (SD 2.32) and at T1 time a value of 10.14 (SD 3.78); without the mask the average at T0 time was of 1.01 (SD .39) and at T1 time was of 77.49 (SD 66.17); the protective effect of the Niki mask was then detected (p=.003).

The concentration variation at the start and end of the shift was relevant (p.001), with an average at T0 of 1.17 (SD 2.32) and at T1 of 10.14 (SD 3.77). (tab3).

4 Discussion

The first interesting finding from this research is that using anesthetic gases in conditions other than operating rooms exposes operators to a risk that exceeds the maximum values set by international agencies such as NIOSH (25 ppm, which is equal to 30 mg/m3 [27,28]).

However, in an Italian context, there are limits on the environmental concentration of nitrous oxide that are controlled by specific provisions; Memorandum No 5 of 14 March 1989 of the Ministry of Health sets as the reference limit value for operating rooms the threshold of 50 ppm (91 mg/m3) – which rises to 100 ppm for operating rooms that were already in existence at the time of Memorandum.

This research, in addition to discussing a topic not addressed by Italian regulations or national standards on N2O, highlights a professional field – ambulatory where medical gases are used – where operators are exposed to workplace hazards, revealing a deficiency in the health professionals' prevention and safety framework. Despite the limited sample size, the end-of-shift urinary concentration was observed to be 77.49 and 10.14 mg/l without and with a Niki mask, respectively, against an exposure limit of 27 mg/l.

To be able to use a facility as a safe room for the use of anesthetic gases, mechanisms for reducing emissions and/or air exchange systems that can guarantee compliance with anesthetic gas exposure values must be provided. The use of the Niki Mask tested in this study seems to be a useful intervention to satisfy the reduction of environmental concentrations of N2O below the expected values in the operating rooms; however, it should be noted that the average concentration is still higher than the values set for occupational exposures (NIOSH) of 25 ppm, and hence additional containment systems should be studied.

There was no noticeable variation in N2O exposure between doctors and nurses, which was most likely due to their location in the room being near the same area examined by the sampler. In this regard, it is also worth noting that in the absence of complex air collection and control systems, there are areas of higher N2O aggregation and areas with lower concentrations.

A final comment should be taken on the health surveillance of the operators involved, including the fact that it is noted that these operators, as well as counterparts working in the operating rooms, would join the health surveillance program for exposure to anesthetic gases.

The samplers were put in five different points as stated in the room; the average concentrations at the individual points were calculated (Table 3) and then a comparison between the averages and the Variance test (ANOVA) was performed, revealing a substantial difference (p.001) between the points despite a low intensity (F16.42) and an R2 supporting the model of just .017.

Table 3- Comparison of N_2O urine concentration averages

	Observations	Mean	S.E.	S.D.	95% C.I.	p-value
Operators T1	16	10.14	.94	3.78	8.13 / 12.15	
Operator T0	16	1.17	.58	2.32	-.06 / 2.41	
Difference	16	8.97	.88	3.53	7.09 / 10.85	p<.001
Comparison of N_2O urine concentration averages without the use of Niki mask						
Operators T1	4	77.49	33.09	66.17	-27.80 a 182.79	
Operator T0	4	.62	.26	.52	-.21 a 1.45	
Difference	4	76.87	33.00	66.00	-28.13 a 181.88	p=.10

The study appears to be rigorous in terms of what has been discovered in the context of environmental monitoring, with the number of measurements and sample size appearing large enough to show that outpatient environments need structural actions to minimize the workplace exposures of the operators involved; The section on biological monitoring seems to be interesting in terms of providing scientifically valid support for the assumption that outpatient exposures of healthcare professionals are at risk of N2O exposure, but the small size of the observed sample should be noted, as should the need to expand the study to larger populations in order to provide greater consistency to the data collected in relation to the environmental monitoring.

5 Conclusion

The current study's findings lead to the need to deepen and enforce technical guidelines, requirements, and systems for the use of N2O in ambulatory settings; in the Italian setting, it is apparent that law enforcement needs to properly identify the technical standards and exposure limit of N2O outside the operating room.

This study emphasizes the importance of implementing additional precautions for operators who are exposed to endoscopic procedures in ambulatory facilities.

Finally, the authors would consider using nitrous oxide in conjunction with a gas scavenging device to reduce the operators' exposure.

This study also reveals that measuring the gas scavenging system is insufficient to secure operators, who would need to undergo health surveillance measures to track the medium to long-term effects.

The authors intended to add to the debate over the concept of reference standards for nitrous oxide environmental concentrations by highlighting the lack of specific regulatory limits for medical procedures involving nitrous oxide in facilities other than operating rooms.

Abbreviations

Esophagogastroduodenoscopy (EGD); monitored anesthesia care (MAC); National Institute for Occupational Safety and Health (NIOSH); biological exposure index (BEI)

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate:

Not applicable. All methods were carried out in accordance with the relevant guidelines and regulations and approved by the institution where they were applied. The data is completely anonymous with no personal information being collected and the data are limited to topics that are strictly within the professional competence of the participants. The collection of data was carried out in accordance with national legislation on safety and health at work. According to the legislation the Employer must investigate the issues of research (ethical issues and implications for occupational well-being) in order to meet all legal obligations. Among the obligations of the employer there is also that of having to communicate and transmit to the company representations the data of the investigations carried out after having made them anonymous. Workers, within their employment relationship, contractually authorize the processing of privacy and consent to all procedures useful for the fulfilment of legal obligations in the field of health and safety at work. For what said there is no need for further approval by an Ethics Board; the absence of any further evaluation by the Ethics Committee is also due to the fact that research topics do not require either diagnostic or therapeutic intervention by any subject.

Consent for publication

Not applicable.

Competing interests

There are no financial conflicts of interest related to the material presented.

Authors' contributions

UM was responsible for the urine analyses and their interpretation and was involved in the conception and design of the study, data analysis and interpretation, manuscript writing and final approval of the manuscript;

IB was involved in the conception and design of the study, data analysis and interpretation, manuscript writing and literature review

RP was involved in the design of study and data analysis

RB was involved in data analysis, manuscript writing and literature review

PES was involved in the design of study and data analysis

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Figures

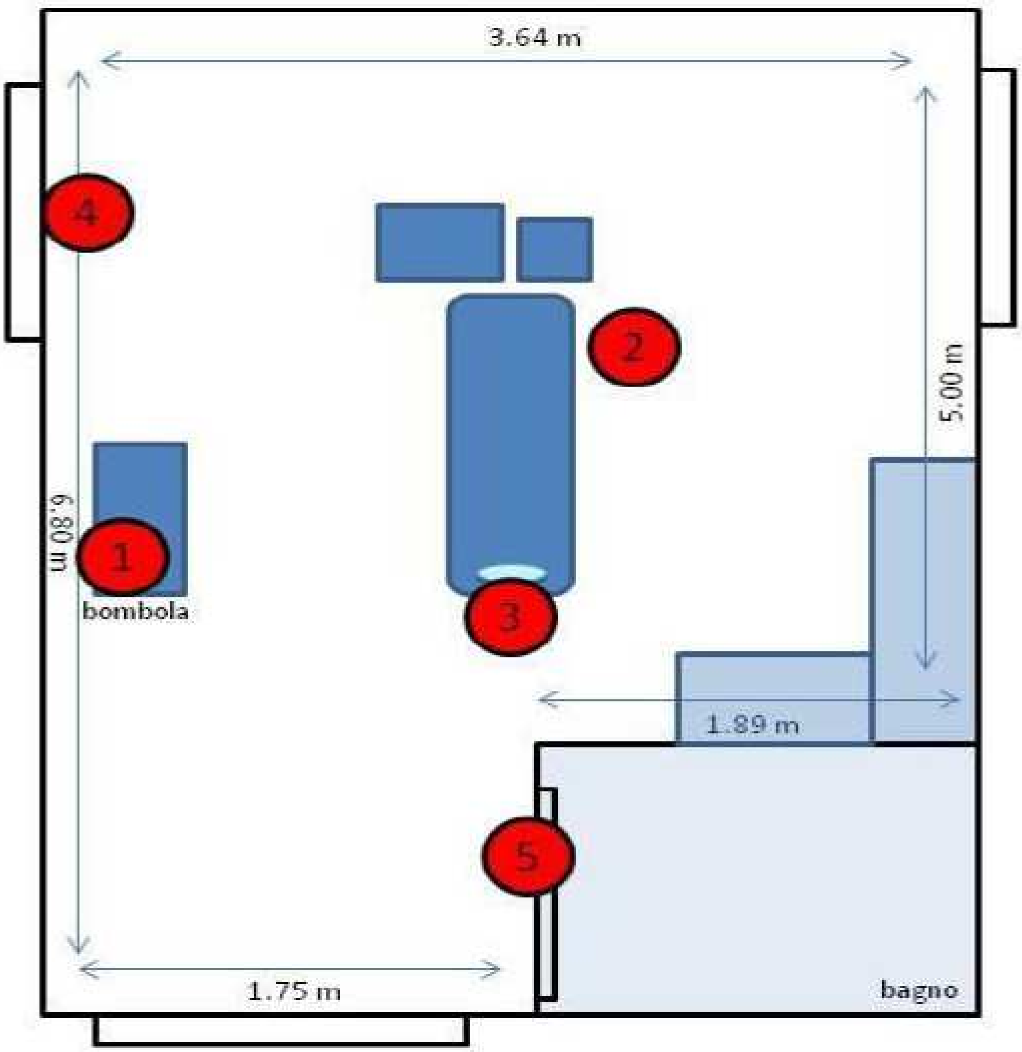

Figure 1

The measuring probes were placed in different point (1=Niki; 2=head-window; 3 head-door; 4= stabilized door; 5=access)