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Nitrous oxide in dental surgery

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This chapter will focus on the use of nitrous oxide–oxygen inhalational sedation with dental treatment or oral surgery procedures. Desirable properties for sedation systems in dentistry will be listed, the rationale and background for inhalational sedation related to dental treatment will be commented upon, with the emphasis being on several investigations that have shown superior effects of nitrous oxide–oxygen sedation compared to other methods.

Both general and local indications as well as contra-indications/cautions for the use of nitrous oxide–oxygen sedation in the dental surgery setting will be presented. A review of the clinical setting and procedures, including clinical and subjective signs of the correct level of sedation, will be presented, as well as definitions and data for acceptance and side effects.

Occupational hazards of the use of nitrous oxide–oxygen sedation in dental surgeries will be evaluated, and recommendations for minimizing the risks of chronic exposure to nitrous oxide for the health care personnel involved will be presented, with suggestions for further research priorities.

Key words: N_2O; sedation; dentistry; oral surgery; side effects; occupational hazard.

Dental treatment often includes painful or annoying procedures as well as the handling of patients who are anxious and apprehensive. The prevalence of marked dental anxiety in the general population is in the region of 4–7%.[1] The major proportion of dental patients can be treated painlessly and with little or no discomfort or fear, by the use of adequate local analgesia, modern equipment, careful patient management and good technical skill. However, a considerable group, e.g. anxious and apprehensive children, patients with mental retardation, physical handicaps and/or chronic diseases and those with an extreme fear of dental procedures, will still constitute a problem. Furthermore, dental treatment of patients in whom local anaesthesia will represent risks, e.g. patients with bleedings disorders, or where local anaesthesia will be inadequate in alleviating pain, may require other methods of controlling pain and anxiety. These methods include pre-operative oral, rectal, or intravenous sedation, nitrous oxide–oxygen inhalational sedation, and treatment under general anaesthesia, hypnosis, or audio-analgesia.

The British General Dental Council has defined conscious sedation as:

> A technique in which the use of a drug, or drugs produces a state of depression of the central nervous system enabling treatment to be carried out, but during which communication can be maintained and the modification of the patient's mind is such that the patient will respond to command throughout the period of sedation. Techniques used should carry a margin of safety wide enough to render unintended loss of consciousness unlikely.

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The desirable properties of an efficacious method of controlling pain and anxiety in dentistry are:

- Rapid onset.
- Rapid elimination.
- Ease of administration.
- Minimum interference with dental procedures.
- Easily controllable dose/response relationship.
- Safety for patient and operators.
- Freedom from hangover.
- Low cost.

Nitrous oxide (N_2O)–oxygen sedation meets almost all of these requirements and has, therefore, been used for years in many countries, including the USA and Great Britain. In Scandinavia, dentists in Denmark have used N_2O–oxygen sedation since 1955 and in Sweden since 1978. In Norway dentists were first authorized by the National Health Authorities to use N_2O–oxygen sedation in 1988.

N_2O–oxygen sedation may be defined as a state of sedation with different degrees of analgesia, caused by breathing a mixture of N_2O–oxygen in a conscious patient with adequate laryngeal reflexes.

INDICATIONS

A number of categories of patients need sedation to be able to tolerate dental treatment. N_2O–oxygen sedation has some advantages over sedation via other routes of administration:

- An easy titration of effect.
- Insignificant hangover effects.
- Tolerated well by patients.

However, the disadvantages of N_2O–oxygen sedation include:

- Expensive equipment: gas machine and scavenging system.
- The need for full co-operation from the patient.
- Possible occupational hazards to personnel.

The administration of 40% N_2O and 60% oxygen has been shown to significantly improve patient behaviour and to alter physiological indicators in children undergoing restorative dental treatment, compared to the use of 100% oxygen.[2] A mixture of 50% N_2O and 50% oxygen has also been found to elevate the temperature stimulus threshold, supporting a definite but modest analgesic action, which is believed to facilitate general dental treatment.[3] Anxiety scores of children treated for anxiety related to dental treatment with N_2O have been reported to be significantly lower than for those treated in a behavioural management group.[4] N_2O has further been found to reduce relapse of dental fear when used in combination with behavioural therapy.[5] Patients undergoing restorative dental treatment have shown significant post-treatment reduction in indicators of anxiety: sweating, palpitations, restlessness, dry mouth, muscular tension, nausea, loss of appetite, upset stomach and particularly irritability, when treated under N_2O–oxygen sedation compared with controls. Patients' memory of the dental procedures was also found to be significantly reduced.[6] Treatment with N_2O has shown advantages over non-pharmacological methods, such as applied relaxation and cognitive therapy, for post-operative emotional distress symptoms and dental fear.[7] A British study demonstrated that 53 out of 61 (87%) children referred for extraction under general anaesthesia could successfully be treated with N_2O–oxygen inhalation sedation with local anaesthetic.[8]

The use of N_2O–oxygen has not proven to be effective in enhancing the effects of oral sedation with diazepam in very young (<3 years) children in conjunction with dental treatment.[9] N_2O has, however, been reported to deepen sedation as an adjunct to an oral narcotic regimen (chloral hydrate, meperidine or hydroxyzine pamoate) with minimal alteration in physiological parameters.[10]

Conscious sedation with N_2O and oxygen has, in several studies, been found to be clinically successful in dentistry and oral surgery, acceptable to both children and adults, and cost effective, especially compared to treatment under general anaesthesia.[11–14]

General indications for N_2O–oxygen sedation in dentistry

Adults

- Fear, anxiety and apprehension of dental treatment.
- Fear of needle injections.
- Decreased tolerance to dental treatment.
- Patients with muscular disorders with spasm or tremor.
- Patients with a pronounced gag reflex.
- Mentally retarded patients; must be able to co-operate.

Children

- Minimum age approximately 4 years.
- Must be able to co-operate with nose breathing.

Local indications

- Dental treatment.
- Minor oral surgery in conjunction with local anaesthesia.
- Special procedures, e.g. removal of intermaxillary fixation devices (arch-bars).

Contra-indications/cautions for N_2O sedation

N_2O is known to interfere with B_{12} or folate metabolism and this may be of clinical significance with this form of sedation.[15] Patients on anti-folate medication (e.g. methotrexate) should not be exposed to N_2O sedation.[16] Sickle-cell disease and exposure to N_2O may cause a risk of neuropathia.[17] Poorly controlled asthma, chronic obstructive pulmonary disease (COPD) etc, may represent problems in relation to oxygen toxicity. Increased gas pressure by diffusion into closed spaces may cause problems in relation to middle ear infections, recent ear-nose-throat (ENT) surgery and diaphragmatic hernias.[18] Neuromuscular disorders, e.g. myasthenia gravis and multiple sclerosis, may present problems since sedation theoretically may depress the muscular activity of an affected patient below a critical level. Teratogenic effects of N_2O have been demonstrated in mice,[19] especially when exposed during organogenesis,[20] and have not been ruled out in humans,[21] hence exposure to N_2O should be avoided during pregnancy and especially in the first trimester.

A clinical picture has been described of central anti-cholinergic blockade induced by N_2O.[22] This picture includes, among others, hallucinations, and caution should be taken with psychotic patients. One report concluded that the use of N_2O was associated with a higher incidence of isorhythmic atrioventricular dissociation in response to a commonly used local anaesthetic solution in dentistry: lidocaine with epinephrine.[23] It may be that this combination should be avoided in predisposed patients. However, N_2O seems to be unlikely to cause severe myocardial ischaemia in a high proportion of patients.[24] Patients with symptomatic coronary artery disease should, however, not be treated in the dental ambulatory setting with the standard level of monitoring. Caution should be taken with the use of midazolam combined with N_2O–oxygen sedation in children, since the level of sedation may be difficult to control.[25] Enlarged tonsils and premedication with midazolam[26] or chloral hydrate[27] may cause upper airway obstruction. These combinations should be avoided.

Some procedures in the oral cavity may interfere with the administration of gas via the nose mask. Peri-apical surgery of the frontal maxilla and incision and drainage of intra-oral abscesses may represent such problems, by direct interference with the nose mask and the need to secure the airway, respectively.

Contra-indications/cautions for use of N_2O–oxygen sedation in the dental surgery

General contra-indications

- Acute upper airway infections.
- Lower respiratory acute or chronic conditions.
- Severe forms of systemic diseases.
- Psychotic patients.
- Myasthenia gravis.
- Multiple sclerosis.
- Sickle-cell disease.
- Diaphragmatic hernia.
- B_{12} or folate deficiency/disorders.
- Anti-folate medication.
- Pregnancy.

Local contra-indications

- Dental procedures that may interfere with the use of a mask, e.g. peri-apical surgery in the maxillary front region.
- The need for securing the airway, e.g. with incision of intra-oral abscess.
- Mouthbreathers.
- Unable to co-operate.

CLINICAL SETTING

The N_2O–oxygen gas mixture is administered to the patient via a nasal mask that has a ‘double’ design with an inner space to deliver the gas mixture to the patient. The

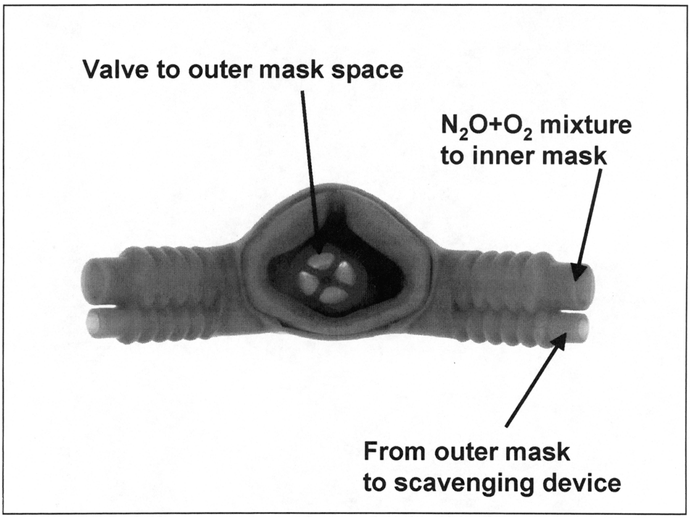

Figure 1. Inner aspect of a typical nose mask for the delivery of a nitrous oxide–oxygen mixture.

outer space is connected to the inner via a one-way valve, and leads the exhaled air to the connected scavenging suction device (Figure 1). These masks come in varying sizes and should be individually fitted to the patient to minimize gas leaks into the operating room. In addition to the scavenging device connected to the nasal mask, another local exhaust device is applied in the field of treatment directly over the patient's mouth. This device removes inadvertently exhaled gas mixture from the patient (Figure 2).

The device for administering the anaesthetic is designed to enable the operator to vary the N_2O concentration from 0% up to a defined maximum of 60–70%, according to the relevant national regulation. The machine is blocked to prevent any further increase in N_2O concentration. There is also the possibility of delivering a 100% oxygen flush. Most gas machines are small (Figure 3) and easily accommodated in dental surgeries.

The most important requirements for the equipment include:

- A fail-safe system to cut off N_2O flow if the oxygen pressure drops.
- An emergency air inlet valve.
- A secured minimum oxygen concentration of 30–40%.
- No rebreathing.
- The ability to deliver a flow rate of at least 8 l/min.
- It should comply with the defined maximum breathing resistance.
- It should be equipped with a scavenging system.
- There should be colour coding of gas connectors.

Clinical procedure

Restrictions on food and fluid intake pre-operatively have arbitrarily been set to 4 and 2 h, respectively. Restrictions are suggested for safety reasons, since gag reflexes may be reduced; there is, however, no documentation of needs. Patients should preferably be monitored using pulse oxymetry.

- Patients are pre-oxygenated with 100% oxygen for 5 min or until a reading of $\geqslant$ 99% oxygen saturation is obtained.

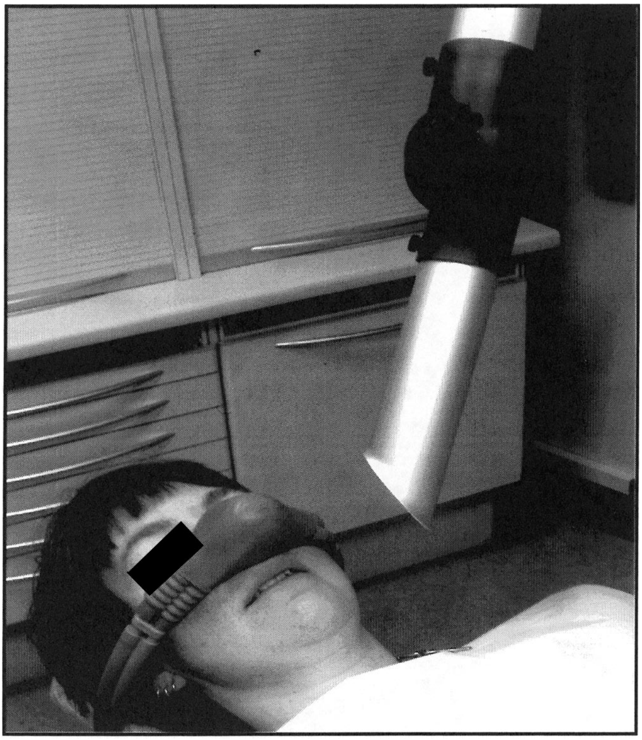

Figure 2. In addition to having a scavenging system to evacuate exhaled air from the nose mask, a local exhaust system is also recommended for the evacuation of gas leaks.

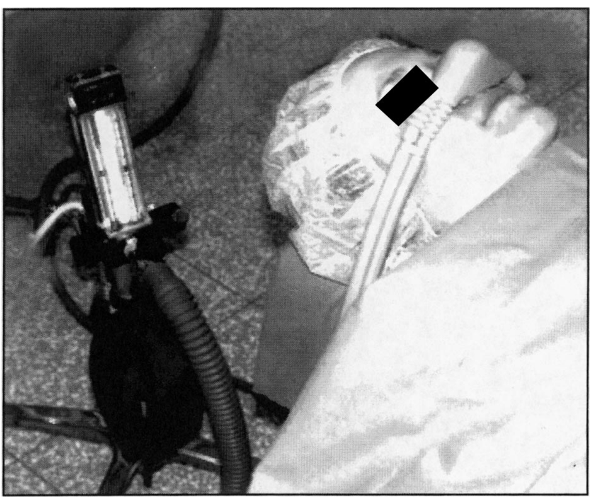

Figure 3. This figure shows a Porter MXR machine for the delivery of a nitrous oxide–oxygen mixture via a nose mask to the patient.

- Gas flow rate is manually adjusted to match the patient's tidal volume.
- The percentage of N_2O is increased gradually, starting at 10% and with a 10% increase approximately every 1 min.
- The maximum percentage of N_2O needed, typically 45–55%, is clinically assessed by monitoring the patient's level of sedation.

Clinical signs of correct level of sedation

Clinical signs of the correct level of sedation are:

- Intact response to verbal command.
- Awake, eyes open.
- Relaxed and comfortable.
- General reduction of spontaneous movements.
- Mouth is kept open on request.
- Normal laryngeal reflex.
- Reduction of gag reflex.
- Normal blood pressure, heart rate, respiratory rate, skin colour and oxygen saturation level.

Subjective symptoms

The subjective symptoms experienced by patients have been described by Kaufman et al (Table 1).[28]

Other descriptions of subjective sensations include:

- Paraesthesia of fingers, mouth, feet, tongue or over whole body.
- Feeling of warmth.
- Dreaming.
- Indifference to passage of time and surroundings.
- Mild euphoria.
- Physical and mental relaxation.
- Enhanced hearing.

Table 1. Prevalence of sensory experiences induced by a mixture of 35% nitrous oxide/65% oxygen that are significantly different from those induced by oxygen alone, in 44 patients.

Sensation	%
Heaviness	80
Relaxation	66
Tingling in hands	59
Diminished sound	55
Tinnitus	55
Lip or tongue tingling	50
Smell sensation	50
Taste sensation†	43
Blurred vision	37
Shivering	30

†Sweet, salty and sour dominated the taste sensations, while bitter was almost entirely absent.
Source: adapted from Kaufman et al.[28]

- Lower awareness of pain.
- A sense of floating or drifting, detachment.

However, one study was unable to confirm the assumption of enhancement of hearing, when inhaling low concentrations (10–20%) of N_2O.[29]

Once sedated, local anaesthesia is administered according to a planned procedure. Ordinary dental procedures, e.g. the preparation of cavities and cleaning of teeth, can often be performed without local anaesthesia. On completion of the procedure, the patients are given 100% oxygen for 5 min to avoid diffusion hypoxia. One study has, however, shown no differences in oxygen saturation levels between two groups of children when terminating N_2O–oxygen sedation with 100% oxygen compared to immediately breathing room air.[30] Patients are observed in the clinic for 30 min after the termination of gas administration.

Compared to midazolam-induced sedation, N_2O–oxygen sedation does not seem to impair the ability to perform higher cognitive tasks and, thus, patients receiving N_2O sedation can resume normal activities in the post-operative period.[31] Also the use of N_2O–oxygen analgesia for sigmoidoscopy has been shown not to impair driving ability.[32] However, patients are still, pending further documentation, advised to refrain from activities that demand a special level of alertness, e.g. driving, for the rest of the day.

ACCEPTANCE OF THE SEDATION PROCEDURE

Acceptance is usually evaluated by the dentist/surgeon according to the reactions of the patient and the ability of the patient to receive the planned treatment. Acceptance rates of 72–93% for dental treatment under N_2O sedation have been reported.[12–14,33,34] The most powerful predictors of acceptance are health status[33] or American Society of Anesthesiologists (ASA) category.[14] Breaking previous dental appointments has also been identified as a predictor of negative response to N_2O–oxygen sedation.[35]

SIDE EFFECTS

Mild side effects, such as nausea and vomiting, have been reported in 4–10% of cases[12–14,33,34]; however, potentially serious complications have been reported in only 0.7% of cases.[33]

Increased complication rates, predominantly those for nausea and vomiting, have been associated with the use of N_2O concentrations above 50%, procedures of more than 2 h duration[36] and use in young patients (Table 2). However, N_2O in combination with halothane or propofol has not been found to increase the incidence of post-operative vomiting in children.[37] Increased odds ratios (OR) for complications and/or reduced acceptance are associated with ASA class 2 patients (OR = 7.7 compared to class 1) and patients with fear/apprehension (OR = 3.3–4.3).[14]

HAZARDS TO DENTAL PERSONNEL ASSOCIATED WITH THE USE OF N_2O IN THE DENTAL SURGERY

Chronic exposure to N_2O has been associated with reproductive, haematological, immunological, neurological, liver and kidney disorders. A study of the morphology of

Table 2. Prevalence (%) of mild complications in 241 sessions of nitrous oxide–oxygen sedation with oral surgery.

Type	Intra-operative %	Post-operative %
Nausea	2.9	1.2
Restlessness	1.7	0.0
Vomiting	0.4	0.8
Headache	0.0	0.4
Total	5.0	2.4

Source: Reproduced from Berge[14], with permission.

the bone marrow of 21 dentists who habitually used N_2O in their surgeries showed that occupational exposure to N_2O might cause depression of vitamin B_{12} activity resulting in measurable changes in the bone marrow.[38] Reduced fertility has been found in female dental assistants who were exposed to high levels of unscavenged N_2O.[39] The effect required more than 4 h of weekly exposure. Increased rates (relative risk (RR = 2.6) of spontaneous abortions have also been demonstrated among female dental assistants exposed to unscavenged N_2O for an average of more than 3 h/week, while this effect was not found when scavenging equipment was used.[40] An increased risk of spontaneous abortion among the wives of male dentists, and nearly doubled rates of liver diseases among dentists and chair-side assistants who were exposed to N_2O, have been reported.[41]

The US Occupational Safety and Health Administration has established a recommended exposure limit of 25 parts per million (ppm) N_2O during administration, based on the prevention of adverse reproductive and psychomotor health effects. N_2O concentrations of up to 3500 ppm have been reported from unscavenged dental surgeries.[42] Even with the use of active scavenging, a considerable pollution of N_2O has been reported with inhalational sedation for paediatric exodontia, even though staff exposure to N_2O was within the national occupational exposure standards.[43] Over short periods peak concentrations that are far above the recommended levels have been detected in dental theatres and community dental clinics that regularly use inhalational sedation.[44] A study from Nebraska, USA found exposure levels for dentists and dental assistants of 97 and 59 ppm, compared to the recommended 25–50 ppm.[45] Predictors of N_2O exposure were minutes of use, frequency of use, number of operating rooms equipped, education of staff on N_2O related health risks and the operation of scavenging systems according to recommendations. A thermocamera study has shown a positive effect of a local exhaust system ensuring minimal exposure when N_2O leaks contaminate the air in the dentist's and chair-side assistant's breathing zone.[46]

N_2O gas in room air may come from several sources:

- Equipment leaks.
- Leaks around the periphery of poorly fitting nasal masks.
- Exhaled air from patients during mouth-breathing and talking.
- Inadequate scavenging.
- Inadequate general ventilation in the operating theatre, either a lack of air exchange or recirculation of contaminated room air.

Correction of these sources of N_2O in room air may reduce the quantity of N_2O inhaled by the operators by as much as 97%.[47]

Practice points

- observe possible contra-indications
- evaluate possible alternatives
- mask should not interfere with planned treatment
- patient must be able to co-operate by breathing through the nose during treatment
- thorough information should be given to the patient on the sedation procedure
- apply pulse oximetry
- apply pre- and post-oxygenation
- gradually increase the gas concentration
- maximum N_2O concentration should be set to 65%
- be prepared for side effects
- observe the patient in the surgery for approximately 30 min after completion of the procedure
- advise patient to refrain from demanding activities (e.g. driving) for the rest of the day
- apply scavenging systems
- regularly monitor the operating room for gas leaks

The following practice points have been adapted from Howard[48]

- assess room ventilation to ensure that there is adequate air exchange
- evaluate the air exchange rate, the location of fresh air inlets and the ventilation system exhaust. In order to obtain gas concentrations of less than 25 ppm, an exchange rate of room air of 10 exchanges/h is recommended[49]
- a daily inspection of equipment, with a special emphasis on possible gas leaks, should be carried out
- the scavenging system should always be used when administering gas. A flow rate of at least 45 l/min should be used
- the patients should be instructed to refrain from talking and mouth-breathing
- gas flow should be adjusted according to tidal volume to prevent the reservoir bag from becoming overfilled
- a properly sized mask should be used and care taken to ensure that there are minimal leaks around the mask
- the session should be completed with 100% oxygen breathing for 5 min with ongoing scavenging
- there should be a periodic inspection schedule for equipment
- there should be periodic personal sampling of dental personnel

SUMMARY

Desirable properties for sedation systems that are intended for use with dental treatment/oral surgical procedures include a wide safety margin, no interference with treatment, an easily controllable titration of both effect and administration, a rapid onset and elimination and low environmental/occupational hazards. Nitrous oxide (N_2O)–oxygen inhalational sedation meets most of these criteria and has been widely in use for a long time in several countries.

As many as 7% of the population may have some form of fear or anxiety related to dental treatment. There is substantial evidence that these patients will benefit markedly

Research agenda

The following points have been adapted from American Dental Association (ADA) council of scientific affairs; ADA council on dental practice[50]

- an evaluation of the advantages of using nitrous oxide (N_2O) in combination with other sedative drugs needs to be undertaken
- a cost comparison analysis of various methods of fear and apprehension control in dental patients is needed
- efficacy studies of scavenging systems, ventilation systems and air exchange systems for dental surgeries are required
- there is a need for the development of equipment for monitoring N_2O exposure
- the possible cognitive effects of exposure to low levels of N_2O need to be studied
- prospective studies of the long-term health effects of chronic low-level exposure to N_2O in dental health personnel are needed
- the biological mechanisms responsible for adverse health effects need to be investigated
- large-scale clinical studies are needed to evaluate:
  - the validity of limitations and safe use in patients with various types of medical conditions
  - the prevalence, and severity, of side effects and the safety of N_2O use

from sedation with N_2O–oxygen and that this form of sedation has advantages over other methods of controlling fear and anxiety. The advantages of N_2O relate especially to its rapid onset and elimination. Recommended contra-indications are predominantly related to the clinical setting in the dental surgery, with the corresponding level of monitoring, and include acute upper and lower airway conditions, severe systemic conditions, early pregnancy and mask interference with the dental procedure. Clinical procedures have been developed on the basis of theoretical considerations and experience. The background for recommendations of pre- and post-operative restrictions has not yet been confirmed, but since clinical studies are scarce so far, recommendations will be maintained until there is further evidence. Acceptance rates are around 90% and side effects are mild and few: predominantly nausea and vomiting. Bearing in mind the wide use of N_2O–oxygen sedation, serious side effects seem to be extremely rare, indicating an excellent safety record.

Occupational hazards, primarily of a reproductive and hepatic nature, for chronic exposure to N_2O in the dental surgery setting, have been documented. However, a marked positive effect for scavenging and local exhaust systems on the local concentration of N_2O has also been shown. Research priorities include the improvement of the effects of scavenging systems and a more accurate determination of the occupational hazards related to low level exposure.

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