Use of Nitrous Oxide for Pediatric Dental Patients

Latest Revision

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Purpose

The American Academy of Pediatric Dentistry (**AAPD**) recognizes nitrous oxide/oxygen inhalation as a safe and effective technique to reduce anxiety, produce analgesia, and enhance effective communication between a patient and health care provider. The need to diagnose and treat, as well as the safety of the patient and practitioner, should be considered before using nitrous oxide. By producing this guideline, the AAPD intends to assist the dental profession in developing appropriate practices in the use of nitrous oxide/oxygen analgesia/anxiolysis for pediatric patients.

Methods

These recommendations were developed by the Council on Clinical Affairs and adopted in 2005. This document is a revision of the previous version, last revised in 2013. The revision is based on a review of the current dental and medical literature related to nitrous oxide use. A search was conducted using the database of PubMed®/MEDLINE with the parameters: nitrous oxide [Mesh] OR nitrous oxide reductase [Supplementary Concept], publication date from January 1, 2012; humans; child: birth-18 years. Thirty-nine articles met these criteria, and applicable articles were chosen and added to the references from the previous document. Additionally, the American Dental Association's *Guideline for the Use of Sedation and General Anesthesia by Dentists*[1] and the American Dental Association's *Oral Health Topics – Nitrous Oxide Dental Best Practices for Nitrous Oxide-Oxygen Use*[2] were reviewed. When data did not appear sufficient or were inconclusive, recommendations were based upon expert and/or consensus opinion by experienced researchers and clinicians.

Background

Dentists have expertise in providing anxiety and pain control for their patients. While anxiety and pain can be modified by psychological techniques, in many instances pharmacological approaches are required.[1] The outcome of pharmacological approaches is variable and depends upon each patient's response to various drugs. The clinical effect of nitrous oxide/oxygen inhalation, however, is more predictable among the majority of the population. When used for analgesia/anxiolysis, nitrous oxide/oxygen inhalation allows for diminution or elimination of pain and anxiety in a conscious patient, while entailing minimum risk.[3] The patient responds normally to verbal commands.[4] All vital signs are stable, there is no significant risk of losing protective reflexes, and the patient is able to return to preprocedure mobility. In children, analgesia/anxiolysis may expedite the delivery of procedures that are not particularly uncomfortable, but require that the patient not move.[3] It also may allow the patient to tolerate unpleasant procedures by reducing or relieving anxiety, discomfort, or pain. Furthermore, it increases reaction time and reduces pressure-induced pain, but does not affect pulpal sensitivity, as shown in a double blind, crossover study.[5]

Nitrous oxide is a colorless and virtually odorless gas with a faint, sweet smell. It is an effective analgesic/anxiolytic agent causing central nervous system (**CNS**) depression and euphoria with little effect on the respiratory system.[6,7] Nitrous oxide has multiple mechanisms of action. The analgesic effect of nitrous oxide appears to be initiated by neuronal release of endogenous opioid peptides with subsequent activation of opioid receptors and descending gamma-aminobutyric acid type A (**GABAA**) receptors and noradrenergic pathways that modulate nociceptive processing at the spinal level. The anxiolytic effect involves activation of the GABAA receptor either directly or indirectly through the benzodiazepine binding site.[8,9] Nitrous oxide has rapid uptake, being absorbed quickly from the alveoli and held in a simple solution in the serum. It is relatively insoluble, passing down a gradient into other tissues and cells in the body, such as the CNS. It is excreted quickly from the lungs. Nitrous oxide causes minor depression in cardiac output while peripheral resistance is slightly increased, thereby maintaining the blood pressure.[5] This is of particular advantage in treating patients with cerebrovascular system disorders.

Nitrous oxide is absorbed rapidly, allowing for both rapid onset and recovery (two to three minutes). It causes minimal impairment of any reflexes, thus protecting the cough reflex.[6] It exhibits a superior safety profile with no recorded fatalities or cases of serious morbidity when used within recommended concentrations.[10-13]

The decision to use nitrous oxide/oxygen analgesia/anxiolysis must take into consideration alternative behavioral guidance modalities, the patient's dental needs, the effect on the quality of dental care, the patient's emotional development, and the patient's physical considerations. Nitrous oxide generally is

ABBREVIATIONS

AAPD: American Academy Pediatric Dentistry. **CNS:** Central nervous system. **GABAA:** Gamma-aminobutyric acid type A. **L/min:** Liters per minute.

acceptable to children and can be titrated easily. Most children are enthusiastic about the administration of nitrous oxide/oxygen; many children report feeling a tingling or warm sensation.[14] Objectively, children may appear with their hands open, legs limp, and a trancelike expression.[14] For some patients, however, the feeling of losing control may be troubling, and children with claustrophobia may find the nasal hood confining and unpleasant.[15]

Nitrous oxide has been associated with bioenvironmental concerns because of its contribution to the greenhouse effect.[16] Nitrous oxide is emitted naturally by bacteria in soils and oceans; it is produced by humans through the burning of fossil fuels and forests and the agricultural practices of soil cultivation and nitrogen fertilization. Altogether, nitrous oxide contributes about five percent to the greenhouse effect.[17,18] However, only a small fraction of the total nitrous released into the atmosphere (0.35 to two percent) is actually the result of medical applications of nitrous oxide gas.[18]

The objectives of nitrous oxide/oxygen inhalation include:

1. reduce or eliminate anxiety.
2. reduce untoward movement and reaction to dental treatment.
3. enhance communication and patient cooperation.
4. raise the pain reaction threshold.
5. increase tolerance for longer appointments.
6. aid in treatment of the mentally/physically disabled or medically compromised patient.
7. reduce gagging.
8. potentiate the effect of sedatives.

Disadvantages of nitrous oxide/oxygen inhalation may include:[6]

1. lack of potency.
2. dependant largely on psychological reassurance.
3. interference of the nasal hood with injection to anterior maxillary region.
4. patient must be able to breathe through the nose.
5. nitrous oxide pollution and potential occupational exposure health hazards.

Recommendations

Indications for use of nitrous oxide/oxygen analgesia/anxiolysis include:

1. a fearful, anxious, or obstreperous patient.
2. certain patients with special health care needs.
3. a patient whose gag reflex interferes with dental care.
4. a patient for whom profound local anesthesia cannot be obtained.
5. a cooperative child undergoing a lengthy dental procedure.

Review of the patient's medical history should be performed prior to the decision to use nitrous oxide/oxygen analgesia/anxiolysis. This assessment should include:

1. allergies and previous allergic or adverse drug reactions.
2. current medications including dose, time, route, and site of administration.
3. diseases, disorders, or physical abnormalities and pregnancy status.
4. previous hospitalization to include the date and purpose.
5. recent illnesses (e.g., cold or congestion) that may compromise the airway.

Contraindications for use of nitrous oxide/oxygen inhalation may include:

1. some chronic obstructive pulmonary diseases.[19]
2. current upper respiratory tract infections.[20]
3. recent middle ear disturbance/surgery.[20]
4. severe emotional disturbances or drug-related dependencies.[20]
5. first trimester of pregnancy.[21]
6. treatment with bleomycin sulfate.[22]
7. methylenetetrahydrofolate reductase deficiency.[23]
8. cobalamin (vitamin B12) deficiency.[9]

Whenever possible, appropriate medical specialists should be consulted before administering analgesic/anxiolytic agents to patients with significant underlying medical conditions (e.g., severe obstructive pulmonary disease, congestive heart failure, sickle cell disease[24], acute otitis media, recent tympanic membrane graft[25], acute severe head injury[26]). In addition, consultation with the prenatal medical provider should precede use of nitrous oxide/oxygen analgesia/anxiolysis during pregnancy.[27]

Technique of nitrous oxide/oxygen administration

Nitrous oxide/oxygen must be administered only by appropriately licensed individuals, or under the direct supervision thereof, according to state law. The practitioner responsible for the treatment of the patient and/or the administration of analgesic/anxiolytic agents must be trained in the use of such agents and techniques and appropriate emergency response.

Selection of an appropriately sized nasal hood should be made. A flow rate of five to six litres per minute (**L/min**) generally is acceptable to most patients. The flow rate can be adjusted after observation of the reservoir bag. The bag should pulsate gently with each breath and should not be either over- or underinflated. Introduction of 100 percent oxygen for one to two minutes followed by titration of nitrous oxide in 10 percent intervals is recommended. During nitrous oxide/oxygen analgesia/anxiolysis, the concentration of nitrous oxide should not routinely exceed 50 percent. Studies have demonstrated that gas concentrations dispensed by the flow meter vary significantly from the end-expired alveolar gas concentrations; it is the latter that is responsible for the clinical effects.[28,29] To achieve sedation, clinicians should keep the patient's talking and mouth breathing to a minimum, and the scavenging vacuum should not be so strong as to prevent adequate ventilation of the lungs with

nitrous oxide.[30] A review of records of patients undergoing nitrous oxide-oxygen inhalation sedation demonstrated that the typical patient requires from 30 to 40 percent nitrous oxide to achieve ideal sedation.[31] Nitrous oxide concentration may be decreased during easier procedures (e.g., restorations) and increased during more stimulating ones (e.g., extraction, injection of local anesthetic). One study found that there was no benefit to continuous administration of nitrous oxide after profound anesthesia had been achieved.[32] During treatment, it is important to continue the visual monitoring of the patient's respiratory rate and level of consciousness. The effects of nitrous oxide largely are dependent on psychological reassurance.[33] Therefore, it is important to continue traditional behavior guidance techniques during treatment. Once the nitrous oxide flow is terminated, 100 percent oxygen should be administered until the patient has returned to pretreatment status.[34] The patient must return to pretreatment responsiveness before discharge.

Monitoring

The response of patients to commands during procedures performed with analgesia/anxiolysis serves as a guide to their level of consciousness. Clinical observation of the patient must be performed during any dental procedure. During nitrous oxide/oxygen analgesia/anxiolysis, continual clinical observation of the patient's responsiveness, color, and respiratory rate and rhythm must be performed. Spoken responses provide an indication that the patient is breathing.[3] If any other pharmacologic agent is used in addition to nitrous oxide/oxygen and a local anesthetic, monitoring guidelines for the appropriate level of sedation must be followed.[4]

Adverse effects of nitrous oxide/oxygen inhalation

Nitrous oxide/oxygen analgesia/anxiolysis has an excellent safety record. When administered by trained personnel on carefully selected patients with appropriate equipment and technique, nitrous oxide is a safe and effective agent for providing pharmacological guidance of behavior in children. Acute and chronic adverse effects of nitrous oxide on the patient are rare.[35] The most common adverse effects, occurring in 0.5-1.2 percent of patients, are nausea and vomiting.[36,37] A higher incidence is noted with longer administration of nitrous oxide/oxygen, fluctuations in nitrous oxide levels, lack of titration, increased concentrations of nitrous oxide, and a heavy meal prior to administration of nitrous oxide.[6,29,30] Fasting is not required for patients undergoing nitrous oxide analgesia/anxiolysis. The practitioner, however, may recommend that only a light meal be consumed in the two hours prior to the administration of nitrous oxide.[38]

Studies have reported negative outcomes associated with use of nitrous oxide greater than 50 percent and as an anesthetic during major surgery.[39,40] Although rare, silent regurgitation and subsequent aspiration need to be considered with nitrous oxide/oxygen sedation. The concern lies in whether pharyngeal-laryngeal reflexes remain intact. This problem can be avoided by not allowing the patient to go into an unconscious state.[41] Diffusion hypoxia can occur as a result of rapid release of nitrous oxide from the blood stream into the alveoli, thereby diluting the concentration of oxygen. This may lead to headache, disorientation, and nausea and can be avoided by administering 100 percent oxygen once the nitrous oxide flow is terminated.[6] While the standard recommendation is to administer 100 percent oxygen at the end of the procedure, several studies have questioned the necessity for this step in nitrous oxide protocols in healthy patients.[42-45]

Documentation

Informed consent must be obtained from the parent and documented in the patient's record prior to administration of nitrous oxide/oxygen. The practitioner should provide instructions to the parent regarding pretreatment dietary precautions, if indicated. In addition, the patient's record should include indication for use of nitrous oxide/oxygen inhalation, nitrous oxide dosage (i.e., percent nitrous oxide/oxygen and/or flow rate), duration of the procedure, and post treatment oxygenation procedure.

Facilities/personnel/equipment

All newly installed facilities for delivering nitrous oxide/oxygen must be checked for proper gas delivery and fail-safe function prior to use. Inhalation equipment must have the capacity for delivering 100 percent, and never less than 30 percent, oxygen concentration at a flow rate appropiate to the child's size. If nitrous oxide/oxygen delivery equipment capable of delivering more than 70 percent nitrous oxide and less than 30 percent oxygen is used, an inline oxygen analyzer must be used. Additionally, inhalation equipment must have a fail-safe system that is checked and calibrated regularly according to the practitioner's state laws and regulations.[46] The system components, including the reservoir bag, should be inspected routinely for cracks, wear, and tears. If detected, repairs should be made immediately. Pressure connections should be tested for leaks when delivery system is turned on and each time a tank is changed. Consult state and federal guidelines regarding storage of compressed gas tanks. Additional locks at the tanks or mixer/delivery level are available from many manufacturers to deter individuals from accessing nitrous oxide inappropriately.[46] The equipment must have an appropriate scavenging system to minimize room air contamination and occupational risk.

The practitioner who utilizes nitrous oxide/oxygen analgesia/anxiolysis for a pediatric dental patient shall possess appropriate training and skills and have available the proper facilities, personnel, and equipment to manage any reasonably foreseeable emergency. The practitioner is responsible for managing the potential complications associated with the intended level of sedation and the next deeper level. Therefore, because moderate sedation may occur, practitioners should have the appropriate training and emergency equipment to manage this.[4,34] Training and certification in basic life support are

required for all clinical personnel. These individuals should participate in periodic review of the office's emergency protocol, the emergency drug cart, and simulated exercises to assure proper emergency management response.

An emergency cart (kit) must be readily accessible. Emergency equipment must be able to accommodate children of all ages and sizes. It should include equipment to resuscitate a nonbreathing, unconscious patient and provide continuous support until trained emergency personnel arrive. A positive-pressure oxygen delivery system capable of administering greater than 90 percent oxygen at a 10 L/min flow for at least 60 minutes (650 L, "E" cylinder) must be available. When a self-inflating bag valve mask device is used for delivering positive pressure oxygen, a 15 L/min flow is recommended. There should be documentation that all emergency equipment and drugs are checked and maintained on a regularly scheduled basis.[4] Where state law mandates equipment and facilities, such statutes should supersede these recommendations.

Occupational safety

In the medical literature, long-term exposure to nitrous oxide used as a general anesthetic has been linked to bone marrow suppression and reproductive system disturbances.[10,49-51] However, it has been shown that appropriate scavenging is effective in reducing these reproductive system effects.[21,52] In an effort to reduce occupational health hazards associated with nitrous oxide, the AAPD recommends exposure to ambient nitrous oxide be minimized through the use of effective scavenging systems and periodic evaluation and maintenance of the delivery and scavenging systems.[53-55] Clinicians should try to minimize the patient's talking and mouth breathing during nitrous oxide administration to prevent expired gas from contaminating the operatory.[30]

References

1. American Dental Association. Guideline for the use of sedation and general anesthesia by dentists. 2016. Available at: "http://www.ada.org/en/~/media/ADA/Education%20and%20Careers/Files/ADA_Sedation_Use_Guidelines". Accessed June 29, 2018.
2. American Dental Association. Oral Health Topics – Nitrous oxide: dental best practices for nitrous oxide-oxygen. Available at: "https://www.ada.org/en/member-center/oral-health-topics/nitrous-oxide". Accessed June 29, 2018. (Archived by WebCite® at: "http://www.webcitation.org/70XToIYQm")
3. Apfelbaum JL, Gross JB, Connis RT, et al. Practice guidelines for moderate procedural sedation and analgesia 2018: A report by the American Society of Anesthesiologists Task Force on Moderate Procedural Sedation and Analgesia, the American Association of Oral and Maxillofacial Surgeons, American College of Radiology, American Dental Association, American Society of Dentist Anesthesiologists, and Society of Interventional Radiology. Anesthesiology 2018;128(3): 437-79.
4. Coté CJ, Wilson S, American Academy of Pediatric Dentistry, American Academy of Pediatrics. Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnosis and therapeutic procedures: Update 2016. Pediatr Dent 2016; 38(4):E13-E39.
5. Groenbaek A, Svensson P, Vaeth M, Hansen I, Poulsen S. A placebo-controlled, double-blind, crossover trial on analgesic effect of nitrous oxide-oxygen inhalation. Int J Paediatr Dent 2014;24(1):69-75.
6. Paterson SA, Tahmassebi JF. Pediatric dentistry in the new millennium: 3. Use of inhalation sedation in pediatric dentistry. Dent Update 2003;30(7):350-6, 358.
7. Saxen M. Pharmacologic management of patient behavior. In: Dean JA, ed. McDonald and Avery's Dentistry for the Child and Adolescent. 10th ed. St. Louis, Mo.: Elsevier; 2016:9-18.
8. Emmanouil DE, Quock RM. Advances in understanding the actions of nitrous oxide. Anesth Prog 2007;54 (1):9-18.
9. Sanders RDB, Weimann J, Maze M. Biologic effects of nitrous oxide: A mechanistic and toxicologic review. Anesthesiology 2008;109(4):707-22.
10. Foley J. A prospective study of the use of nitrous oxide inhalation sedation for dental treatment in anxious children. Eur J Paediatr Dent 2005;6(3):21-7.
11. Holyroyd I. Conscious sedation in pediatric dentistry: A short review of the current UK guidelines and the technique of inhalational sedation with nitrous oxide. Paediatr Anaesth 2008;18(1):13-7.
12. Lyratzopoulos G, Blain KM. Inhalation sedation with nitrous oxide as an alternative to dental general anesthesia for children. J Public Health Med 2003;25(4):303-12.
13. Wilson S, Gosnell E. Survey of American Academy of Pediatric Dentistry on nitrous oxide and sedation: 20 years later. Pediatr Dent 2016;38(5):385-92.
14. Houpt M, Limb R, Livingston R. Clinical effects of nitrous oxide conscious sedation in children. Pediatr Dent 2004;26(1):29-36.
15. Wilson S. Management of child patient behavior: Quality of care, fear and anxiety, and the child patient. J Endod 2013;39(3s):S73-S77.
16. Yasny J, White J. Environmental implications of anesthetic gases. Anesth Prog 2012;59(4):154-8.
17. Levering NJ, Welie JVM. Current status of nitrous oxide as a behavior management practice routine in pediatric dentistry. J Dent Child 2011;78(1):24-30.
18. McGain F. Why anaesthetists should no longer use nitrous oxide. Anaesth Intensive Care 2007;35(5):808-9.
19. Duncan GH, Moore P. Nitrous oxide and the dental patient: A review of adverse reactions. J Am Dent Assoc 1984;108(2):213-9.
20. Clark MS, Brunick AL. N_2O and its interaction with the body. In: Handbook of Nitrous Oxide and Oxygen Sedation. 4th ed. St. Louis, Mo.: Elsevier Mosby; 2015: 90-8.

21. Rowland AS, Baird DD, Shore DL, Weinberg CR, Savitz DA, Wilcox AJ. Nitrous oxide and spontaneous abortion in female dental assistants. Am J Epidemiol 1995;141 (6):531-7.
22. Fleming P, Walker PO, Priest JR. Bleomycin therapy: A contraindication to the use of nitrous oxide-oxygen psychosedation in the dental office. Pediatr Dent 1988; 10(4):345-6.
23. Selzer R, Rosenblatt D, Laxova R, Hogan K. Adverse effect of nitrous oxide in a child with 5, 10-methylene-tetrahydrofolate reductase deficiency. N Engl J Med 2003;349(1):45-50.
24. Ogundipe O, Pearson MW, Slater NG, Adepegba T, Westerdale N. Sickle cell disease and nitrous oxide-induced neuropathy. Clin Lab Haematol 1999;21(6): 409-12.
25. Fish BM, Banerjee AR, Jennings CR, et al. Effect of anaesthetic agents on tympanometry and middle-ear effusions. J Laryngol Otol 2000;114(5):336-8.
26. Moss E, McDowall DG. ICP increase with 50% nitrous oxide in oxygen in severe head injuries during controlled ventilation. Br J Anaest 1979;51(8):757-61.
27. American Academy of Pediatric Dentistry. Oral healthcare for the pregnant adolescent. Pediatr Dent 2017;39 (6):221-8.
28. Klein U, Robinson TJ, Allshouse A. End-expired nitrous oxide concentrations compared to flowmeter settings during operative dental treatment in children. Pediatr Dent 2011;33(1):56-62.
29. Klein U, Bucklin BA, Poulton TJ, Bozinov D. Nitrous oxide concentrations in the posterior nasopharynx during administration by nasal mask. Pediatr Dent 2004;26(5): 410-6.
30. Malamed SF. Inhalation sedation: Techniques of administration. In: Sedation: A Guide to Patient Management. 6th ed. St. Louis, Mo.: Mosby Elsevier; 2018:227-52.
31. Malamed SF, Clark MS. Nitrous oxide-oxygen: A new look at a very old technique. J Calif Dent Assoc 2003; 31(5):397-403.
32. Guelmann M, Brackett R, Beavers N, Primosch RE. Effect of continuous versus interrupted administration of nitrous oxide-oxygen inhalation on behavior of anxious pediatric dental patients: A pilot study. J Clin Pediatr Dent 2012;37(1):77-82.
33. Clark MS, Brunick AL. N_2O/O_2 sedation in pediatric dentistry. In: Handbook of Nitrous Oxide and Oxygen Sedation. 4th ed. St. Louis, Mo.: Elsevier Mosby; 2015: 164-86.
34. Clark MS. Contemporary issues surrounding nitrous oxide. In: Malamed SF, ed. Sedation: A Guide to Patient Management. 6th ed. St. Louis, Mo.: Mosby Elsevier; 2018:253-63.
35. Donaldson D, Meechan JG. The hazards of chronic exposure to nitrous oxide: An update. Br Dent J 1995; 178(3):95-100.
36. Kupietzky A, Tal E, Shapira J, Ram D. Fasting state and episodes of vomiting in children receiving nitrous oxide for dental treatment. Pediatr Dent 2008;30(5):414-9.
37. Galeotti A, Garret Bernardin A, D'Anto V, et al. Inhalation conscious sedation with nitrous oxide and oxygen as alternative to general anesthesia in precooperative, fearful, and disabled pediatric dental patients: A large survey on 688 working sessions. Biomed Res Int 2016;2016:7289310.
38. Hosey MT. UK National Clinical Guidelines in Paediatric Dentistry. Managing anxious children: The use of conscious sedation in paediatric dentistry. Int J Paediatr Dent 2002;12(5):359-72.
39. Schmitt EL, Baum VC. Nitrous oxide in pediatric anesthesia: Friend or foe? Curr Opin Anaesthesiol 2008;21 (2):356-9.
40. Zeir JL, Doescher JS. Seizures temporarily associated with nitrous oxide administration for pediatric procedural sedation. J Child Neurol 2010;25(12):1517-20.
41. Hogue D, Ternisky M, Iranour B. The response to nitrous oxide analgesia in children. ASDC J Dent Child 1971;38(2):129-33.
42. Dunn-Russell T, Adair S, Sams DR, Russell CM, Barenie JT. Oxygen saturation and diffusion hypoxia in children following nitrous oxide sedation. Ped Dent 1993;16(2): 88-92.
43. Quarnstrom FC, Milgrom P, Bishop MJ, DeRouen TA. Clinical study of diffusion hypoxia after nitrous oxide analgesia. Anesth Prog 1991;38(1):21-3.
44. Khinda V, Bhuria P, Khinda P, Kallar S, Brar G. Comparative evaluation of diffusion hypoxia and psychomotor skills with or without postsedation oxygenation following administration of nitrous oxide in children undergoing dental procedures: A clinical study. J Indian Soc Pedod Prev Dent 2016;34(3):217-22.
45. Clark MS, Brunick AL. Anatomy and physiology of respiration and airway management. In: Handbook of Nitrous Oxide and Oxygen Sedation. 4th ed. St. Louis, Mo.: Elsevier Mosby; 2015:84-6.
46. Donaldson M, Donaldson D, Quarnstrom F. Nitrous oxide-oxygen administration: When safety features are no longer safe. J Am Dental Assoc 2012;143(2):134-43.
47. Chrysikopoulou A, Matheson P, Miles M, Shey Z, Houpt M. Effectiveness of two nitrous oxide scavenging nasal hoods during routine pediatric dental treatment. Pediatr Dent 2006;28(3):242-7.
48. Freilich MM, Alexander L, Sandor GKB, Judd P. Effectiveness of 2 scavenger mask systems for reducing exposure to nitrous oxide in a hospital-based pediatric dental clinic: A pilot study. J Can Dent Assoc 2007;73(7):615.
49. Corcetti M, Serwint JR. Inhalants. Pediatr Rev 2008; 29(1):33-4.
50. Lehmberg J, Waldner M, Baethmann, Eberhard UHL. Inflammatory response to nitrous oxide in the central nervous system. Brain Res 2008;1246:88-95.

51. Luhmann JD, Kennedy RM. Nitrous oxide in the pediatric emergency department. Clin Pediatr Emerg Med 2000;1(4):285-9.
52. Rowland AS, Baird DD, Shore DL, et al. Reduced fertility among women employed as dental assistants exposed to high levels of nitrous oxide. N Engl J Med 1992;327(14): 993-7.
53. American Academy of Pediatric Dentistry. Policy on minimizing occupational health hazards associated with nitrous oxide. Pediatr Dent 2018;40(6):104-5.
54. Rademaker AM, McGlothlin JD, Moenning JE, Bagnoli M, Carlson G, Griffin C. Evaluation of two nitrous oxide scavenging systems using infrared thermography to visualize and control emissions. J Am Dent Assoc 2009; 140(2):190-9.
55. National Institute for Occupational Safety and Health. Control of nitrous oxide in dental operatories. 1996. Available at: "https://www.cdc.gov/niosh/docs/hazard-control/hc3.html". Accessed July 6, 2018. (Archived by WebCite® at: "http://www.webcitation.org/71Ttkr5Tm")