Effect of Continuous versus Interrupted Administration of Nitrous Oxide-Oxygen Inhalation on Behavior of Anxious Pediatric Dental Patients: A Pilot Study

Guelmann M * / Brackett R ** / Beavers N *** / Primosch RE ****

Objective: The purpose of this study was to determine the effect of interrupted administration of nitrous oxide (N_2O) inhalation, after obtaining profound local anesthesia, on the behavior of mild to moderately anxious pediatric patients during routine restorative dentistry. **Study Design:** Healthy children, 5 to 8 years old, requiring nitrous oxide/oxygen inhalation sedation and bilateral mandibular restorative treatment performed in two sequential appointments under local anesthesia were recruited for this study. After profoundness of the local anesthesia was confirmed, the subject was randomly assigned to either Protocol A $(50\% N_2O / 50\% O_2)$ or Protocol B $(100\% O_2)$ and restorative dental care was completed. On the second appointment, the subject was assigned to the alternate protocol. **Results:** Hemoglobin oxygen saturation remained constant with no episodes of oxygen desaturation recorded. There were no statistically significant differences (P > .05) in pulse rate or behavior change noted between the two protocols. **Conclusion:** The implication of this pilot study was significant in consideration of the desire to minimize chronic exposure to ambient nitrous oxide and its potential health hazards to the dental team. These findings challenge the traditional practice of N_2O maintenance throughout the dental appointment.

Keywords: nitrous oxide, inhalation, sedation, behavior management J Clin Pediatr Dent 37(1): 77–82, 2012

INTRODUCTION

eighty five percent of pediatric dentists used nitrous oxide-oxygen inhalation in their offices¹ and this practice has been well accepted by most children.² The inhalation of low to moderate concentrations of nitrous oxide in combination with oxygen effectively relieves dental anxiety and has been shown to alter pain perception.³-4 Furthermore, the use of nitrous oxide-oxygen inhalation has demonstrated lasting benefits by increasing coping skills for pediatric patients on subsequent visits.⁵

The avoidance of pain by the successful delivery of profound local anesthesia is a crucial aspect in managing child

- * Marcio Guelmann, DDS, Associate Professor, Department of Pediatric Dentistry, University of Florida.
- ** Ryan Brackett, DDS, Senior Resident, Department of Pediatric Dentistry, University of Florida.
- *** Nathan Beavers, DMD, Senior Resident, Department of Pediatric Dentistry, University of Florida.
- **** Robert E. Primosch, DDS, MS, MEd, Professor, Department of Pediatric Dentistry, University of Florida.

Send all correspondence to: Dr. Robert E. Primosch, Department of Pediatric Dentistry, College of Dentistry, P.O. Box 100426, Gainesville, FL 32610-0426

Phone: (352) 273-7631 Fax: (352) 273-3135

E-mail: rprimosch@dental.ufl.edu

behavior in the dental office. Inadequate local anesthesia was reported in approximately 12% of all pediatric dental patients, increasing the need for supplemental analgesia and alteration of the anxiety response.6 Nitrous oxide-oxygen inhalation even at 10% N₂O, has been shown to reduce significantly the heart rate during local anesthetic delivery.³ The same study showed that the heart rate decreased during the operative phase of treatment, but only with concentrations at 50% nitrous oxide. The administration of 35-50% nitrous oxide-oxygen prior to and during local anesthesia for dental treatment was a highly accepted and often practiced behavior modification technique for anxious pediatric patients.^{2,7,8} For restorative procedures, after profound anesthesia and rubber dam isolation were obtained, traditional practice dictated that the nitrous oxide concentration be maintained at the desired level or reduced slightly.9 Many contemporary textbooks supported the continuous administration of nitrous oxide throughout the duration of the dental appointment.7,10-12 With the awareness of the potential health hazards to the dental team exposed to chronic ambient nitrous oxide levels in the dental operatory, 13,14 published guidelines advocated careful monitoring and reduction in ambient nitrous oxide levels. 15,16

In 2005, the American Academy of Pediatric Dentistry (AAPD) introduced guidelines for the administration of nitrous oxide inhalation.¹⁷ According to these guidelines, a flow rate of 5 to 6 L/min was generally recommended; adjusted after observation of the reservoir bag which should

pulsate gently with each breath and should not be either over- or underinflated. For the induction phase, 100% oxygen was administered for 1 to 2 minutes followed by rapid titration of nitrous oxide. The concentration of nitrous oxide should not exceed 50%; it may be decreased during less stimulating procedures (eg, restorations) and increased during more stimulating ones (eg, extraction, injection of local anesthetic). Visual monitoring of the patient during treatment with N2O inhalation was important and included observation of the patient's respiratory rate and level of consciousness. Once the dental procedure was terminated, 3 to 5 minutes of 100% oxygen must be delivered at the end of the treatment while scavenging exhaled nitrous oxide. An alternative to the titration induction, known as the rapid induction technique, consisted of the immediate administration of 50% nitrous oxide without any titration steps. 10,12 This method was safely utilized in previous clinical trials with young children.18-20

In mild to moderately anxious children, after establishment of profound local anesthesia, the need for continuous administration of nitrous oxide-oxygen inhalation to control anxiety and maintain desired behavior has not been tested. However, it has been suggested that 100% oxygen may be administered if behavior problems related to local anesthetic administration alone have been overcome.7,12 While profound anesthesia can be confirmed, the noise and vibration from the dental instruments, as well as the duration of the dental appointment, may influence displayed child behavior and promote continued use of nitrous oxide inhalation throughout the appointment. Therefore, the purpose of this study was to determine the effect of interrupted administration of nitrous oxide inhalation, after achievement of profound local anesthesia and rubber dam placement (two stimulating events), on the behavior of mild to moderately anxious pediatric dental patients during the subsequent tooth preparation and restoration phases of the appointment. Stated in another way, the goal of this study was to determine if the traditional practice of continuous administration of nitrous oxide-oxygen inhalation throughout the appointment was necessary to assure continued patient cooperation (reduced anxiety or if interrupted administration (discontinuation of delivery) after the achievement of profound local anesthesia would be just as effective, permitting reduced chronic exposure of the dental team to potentially hazardous ambient nitrous oxide levels.

MATERIALS AND METHOD

Healthy children, 5 to 8 years old, with displayed anxiety and no previous dental experience, requiring nitrous oxide/oxygen inhalation sedation and bilateral mandibular restorative treatment to be performed in two sequential appointments under local anesthesia were recruited for the study. Subjects were recruited from the pool of patients attending the University's Pediatric Dental Clinic. To meet the selection criteria, patients needed to have bilateral mandibular molars requiring similar restorative care complexity with local anesthesia, but having no dental extrac-

tions. The procedures, possible discomforts or risks, as well as possible benefits were explained fully to the subjects and their parents and informed consent was obtained. The study was approved by the University's Institutional Review Board.

Prior to each trial, the subject received an airway patency assessment to verify the absence of upper respiratory infection and to confirm that the subject was able to breathe easily through the nose. After parental separation, the child was brought to the dental operatory and placed in a supine position in a dental chair. A mixture of 50% nitrous oxide and 50% oxygen was delivered by rapid induction technique for 5 minutes through a portable nitrous oxide unit (MRX, Porter Instrument Co., Hatfield, PA) at a flow rate of 4-6 L/min, adjusted by the degree of reservoir bag expansion. A scavenging system with a child-sized nasal hood (Porter Brown Double Scavenging Mask, Porter Instrument Co., Hatfield, PA) was employed at a 45 L/min evacuation rate as recommended.^{15,16} If during the course of treatment, operator assessment determined the patient had become over-sedated (including loss of consciousness or sleep) or was undersedated due to displayed anxious behavior, the N₂O concentration was adjusted accordingly and recorded by the evaluator/recorder.

A pulse oximeter probe was attached to the index finger and physiologic measurements (pulse rate and hemoglobin oxygen saturation) were continuously monitored from the pulse oximeter (Criticare System, Waukesha, WI) and periodically recorded by the evaluator/recorder. Baseline values were recorded for the first minute and then readings were taken subsequently at the end of each minute interval of treatment from the tabular trend display on the monitor. The subject's behavior was assessed using the Ohio State University Behavior Rating Scale (OSUBRS).²¹ These ratings based upon an ordinal scale were mutually exclusive and only the highest rating was recorded as a global assessment of behavior displayed for each minute. The categories' codes were:

Q – for quiet behaviors with no movement;

C – for crying behaviors with no struggling;

M – for movement behaviors with struggling only, no crying;

S – for both crying and struggling disruptive behaviors.

Movement was further classified as to whether it interfered with treatment or not.

No procedures were performed during the initial 5 minutes of rapid induction to establish baseline physiologic and behavioral levels.

After approximately 5 minute administration of nitrous oxide and evidence of its desired effect, a 2" x 2" sterile gauze was used to dry the local anesthesia injection site and 20% benzocaine topical anesthetic gel (Hurricaine®, Beutlich Pharmaceuticals, Waukegan, IL) was applied with a cotton-tip applicator for 45 seconds prior to local anesthesia delivery. An inferior alveolar nerve and long buccal nerve blocks were then performed with an aspirating syringe using a 27-gauge needle at a slow-flow rate (1-2 minutes) to

minimize discomfort. The total volume and type of anesthetic solution used was 1.8ml of a 2% lidocaine (36mg) with 1:100,000 epinephrine. After 5 minutes, profoundness of anesthesia was checked by firmly pressing the tip of a dental explorer to the buccal mucosa of the treated side between the mandibular lateral incisor and canine as described by Ellis and co-workers.²² If discomfort was reported, supplemental anesthesia was administered, not exceeding 4.4 mg/kg body weight, until profound anesthesia was confirmed by the test described above. A mouth prop was placed and rubber dam isolation obtained.

At this point, the operator adjusted the concentration of the nitrous oxide to the randomized condition, either 50% N_2O/O_2 (Protocol A) or 100% O_2 (Protocol B), leaving both the patient and evaluator/recorder blinded. Any disruptive behavior displayed by the child that required physical restraint would result in the termination of data collection. For the second appointment, the alternate protocol was provided. This double blind, cross-over study design allowed each subject to serve as his/her own control. At the end of the dental procedure, the operator notified the evaluator and 100% O_2 was administered for an additional 3-5 minutes before releasing the patient.

Preoperative data collected in an excel spreadsheet included subject code #, date, age (months), gender, group # (appointment # and protocol). Intraoperative data collection included lidocaine dose (mg), pulse rate (beats/min), hemoglobin oxygen saturation (%) and time (minutes). Individual treatment phases were defined as: Phase I (topical anesthesia, local anesthesia, local anesthesia test, mouth prop placement and rubber dam isolation), Phase II (tooth preparation) and Phase III (tooth restoration) with overall behavior for each phase based on the percent OSUBRS.

RESULTS

Seventeen patients with a mean age of 6.75 years (81 months, range= 63 to 106) were treated. At the first visit, Protocol A was used 9 times, while Protocol B was used 8 times. Operator 1 (RB) performed restorative treatment on 6 children while operator 2 (NB) treated 11 children. A composite of each trial's data are displayed in Table 1.

Hemoglobin oxygen saturation remained constant with no desaturation episodes (> 5% decrease from baseline) recorded. No statistically significant differences (P > .05) in pulse rate or behavior change were noted between the protocols during either the tooth preparation or restoration phases. (Table 2) Supplemental local anesthesia was given for three visits, two occurrences with the same patient. The mean duration in minutes for each phase were: Phase I (19.4), Phase II (6.6 minutes) and Phase III (6.3).

DISCUSSION

In the present study, all subjects had not been previously exposed to nitrous oxide/oxygen inhalation and had no previous dental experience. The rapid induction technique usually took approximately 3–5 minutes to achieve the desired effect of relative analgesia. No procedures were performed

during the initial 5 minutes to establish baseline physiologic and behavioral levels. Houpt et al.2 observed that open hands (90%), limp legs (81%) and facial smile (66%) were the most common signs children demonstrated after 5 minute exposure to 50% nitrous oxide inhalation. In his study, a vast majority of children reported feeling different (86%), feeling good (70%) and with an overwhelming number reporting a pleasant experience (95%). Physical sensations such as tingling of the fingers and warm feeling were reported for less than 50% of the study's patient population. These signs marked the stage when the analgesic effect of nitrous oxide in children can be observed4 and was known as relative analgesia.23 Carnow identified these signs as the "drift" stage where the relative analgesia plateau of euphoria and a sensation of floating or drifting were expressed by the patient.²⁴ After waiting five minutes, all subjects exhibited the signs of relative analgesia described above. No patient resistance or need to apply physical restraint was observed in Phase I, further confirming that the subjects achieved relative analgesia prior to the administration of local anesthesia.

No significant physiologic changes in pulse rate or hemoglobin oxygen saturation occurred during the study. This finding was in agreement with McCann et al.21 who were unable to demonstrate significant differences in physiological parameters while using 50% nitrous oxide inhalation in sedated pediatric dental patients. They reported that the administration of 50% nitrous oxide inhalation produced only a tendency to decrease pulse rate when compared to 100% oxygen inhalation alone and hemoglobin oxygen saturation remained constant with no episodes of desaturation. Similar results were obtained when 40% nitrous oxide inhalation given to non-sedated pediatric dental patients produced no significant effect on the development of hypoxemia.8,25 The concurrent use of oxygen with nitrous oxide inhalation likely contributed to this finding. Oxygen supplementation via nitrous oxide/oxygen inhalation was shown to prevent decreases in hemoglobin oxygen saturation, even in the presence of apnea and hypoventilation, during pediatric dental sedation.²⁶ The use of supplemental oxygen administration during pediatric dental sedation was advocated to decrease the risk of hypoxemia and its beneficial use was supported in several other animal²⁷ and human²⁸⁻³⁰ sedation studies. Other studies implied that sedated children receiving nitrous oxide-oxygen inhalation were at greater risk for hypoventilation and airway obstruction when nitrous oxide was delivered by full face mask rather than a nasal hood.31,32 In those reported studies, significant elevations in end-tidal carbon dioxide (>45), indicating hypoventilation, were produced in sedated children receiving 50% nitrous oxide prior to general anesthesia. Evidence of safe outcomes have been obtained when this concentration was used at medical settings to obtain analgesia during emergency and painful procedures with no adverse effects reported.33,34

The unchanged physiological parameters observed and lack of disruptive behavior displayed may indicate that the patient selection was bias. Patient selection was performed, however, by an experienced operator who, during an initial

Table 1. Composite Data

		Phase I				Phase II				Phase III			
	Protocol	Pulse Rate	Beh.	Move.	Dur. (min)	Pulse Rate	Beh.	Move.	Dur. (min)	Pulse Rate	Beh.	Mov.	Dur. (min)
1	А	87	Quiet	1	4	92	Quiet	1	9	91	Quiet	2	27
	В	83	Quiet	1	4	92	Quiet	1	6	91	Quiet	2	12
2	А	89	Quiet	1	5	92	Quiet	1	9	88	Quiet	1	27
	В	95	Quiet	1	5	98	Quiet	1	5	95	Quiet	1	42
3	А	96	Quiet	1	5	101	Quiet	1	5	101	Quiet	1	12
	В	98	Quiet	1	5	108	Quiet	1	5	99	Quiet	1	23
4	А	100	Quiet	1	5	99	Quiet	1	6	96	Quiet	1	21
	В	110	Quiet	1	5	108	Quiet	1	6	107	Quiet	1	14
5	А	73	Quiet	1	6	80	Quiet	1	6	81	Quiet	2	28
	В	81	Quiet	1	5	87	Quiet	1	6	93	Quiet	2	28
6	Α	93	Quiet	1	5	95	Quiet	1	7	98	Quiet	1	22
	В	95	Quiet	1	5	90	Quiet	1	4	95	Quiet	1	24
7	А	104	Quiet	1	5	100	Quiet	1	4	101	Quiet	1	18
	В	94	Quiet	1	4	91	Quiet	1	4	90	Quiet	1	17
8	А	86	Quiet	1	3	93	Quiet	1	5	84	Quiet	2	16
	В	83	Quiet	1	5	87	Quiet	1	5	74	Quiet	1	29
9	А	93	Quiet	1	5	92	Quiet	1	5	90	Quiet	1	24
	В	82	Quiet	1	5	92	Quiet	1	5	94	Quiet	1	21
10	А	100	Quiet	1	13	99	Quiet	1	11	104	Quiet	1	18
	В	95	Quiet	1	9	99	Quiet	1	10	102	Quiet	1	14
11	А	75	Quiet	1	8	74	Quiet	1	9	78	Quiet	1	14
	В	109	Quiet	1	7	103	Quiet	1	8	102	Quiet	1	13
12	А	90	Quiet	1	7	88	Quiet	2	10	84	Quiet	2	15
	В	77	Quiet	1	13	77	Crying	2	8	72	Crying	2	19
13	А	88	Quiet	1	10	91	Quiet	1	7	88	Quiet	1	12
	В	98	Quiet	1	11	93	Quiet	1	8	93	Quiet	1	30
14	А	87	Quiet	1	13	84	Quiet	2	11	80	Quiet	1	12
	В	83	Quiet	2	11	82	Quiet	1	7	78	Quiet	1	13
15	А	79	Quiet	1	5	82	Quiet	1	8	92	Quiet	1	19
	В	67	Quiet	1	5	75	Quiet	1	6	83	Quiet	2	8
16	А	75	Quiet	1	4	78	Quiet	1	4	74	Quiet	1	21
	В	74	Quiet	1	5	77	Quiet	1	6	75	Quiet	1	20
17	А	70	Quiet	1	5	76	Quiet	1	5	78	Quiet	2	15
	В	82	Quiet	1	5	90	Quiet	1	5	89	Quiet	1	13

Protocol: A—Nitrous oxide/oxygen delivered in all phases; B – Nitrous oxide /oxygen delivered in Phase I, 100% oxygen delivered in Phase II & III Pulse Rate: beats/min; Beh.: Behavior using OSUBRS²¹; Dur.: Duration

Movement: None (1), Not interfering with treatment (2), Interfering with treatment (3)

Tooth Preparation (Phase II) Tooth Restoration (Phase III) Protocol A **Protocol B** Protocol A **Protocol B** Variable P-value P-value 50% N₂O/O₂ 100% O₂ 50% N₂O/O₂ 100% O₂ Pulse Rate .74 90 .74 90 89 89 Quiet Behavior .96 .94 .50 .93 .94 .40 Crying Behavior 0 0 0 .02 Struggling Behavior .04 .06 .50 .07 .04 .40

Table 2. Physiologic and Behavioral Changes After Obtaining Profound Local Anesthesia

clinical examination and according to the displayed anxious behavior, determined those recruited children would benefit from the administration of nitrous oxide inhalation. The beneficial effect of the continuous administration of 50% nitrous oxide on more challenging children with higher levels of anxiety needs to be investigated further.

The OSUBRS used in this study was confirmed by its authors to be well correlated to the original and more complex rating scale. Using this scale, sedated pediatric dental patients displayed decreased crying and struggling behavior and increased quiet behavior with 50% nitrous oxide compared to 100% oxygen inhalation. The results of the present study using 50% nitrous oxide inhalation with scavenging in non-sedated children supported the findings of these prior investigations with sedated children undergoing routine dental care.

CONCLUSIONS

The following conclusions can be drawn for this study:

- No physiologic and behavioral changes were found during the delivery of routine restorative dentistry in young pediatric patients after profound local anesthesia was confirmed.
- When mild to moderately anxious pediatric patients received routine dental treatment, no beneficial effect was found for continuous administration of nitrous oxide inhalation after confirming the achievement of profound local anesthesia.
- Further studies with multiple operators using a larger sample size of more severely anxious children requiring greater complexity of invasive dental procedures were necessary to confirm the results of the present study.

REFERENCES

- Wilson S. A survey of the American Academy of Pediatric Dentistry membership: nitrous oxide and sedation. Pediatr Dent, 18: 287–293, 1996.
- Houpt MI, Limb R, Livingston RL. Clinical effects of nitrous oxide conscious sedation in children. Pediatr Dent, 26: 29–36, 2004.
- Everett GB, Allen GD. Simultaneous evaluation of cardiorespiratory and analgesic effects of nitrous oxide-oxygen inhalation analgesia. J Am Dent Assoc, 83: 129–133, 1971.
- Hammond N, Full C. Nitrous oxide analgesia in children's perception of pain. Pediatr Dent, 6: 238–242, 1984.

- Nathan JE, Venham LL, West MS, Werboff J. The effect of nitrous oxide on anxious young pediatric patients across sequential visits: a double blind study. J Dent Child, 55: 220–30, 1988.
- Nakai Y, Milgrom P, Mancl L, Coldwell SE, Domoto PK, Ramsay DS. Effectiveness of local anesthesia in pediatric dental practice. JADA, 131: 1699–1705, 2000.
- Clark M, Brunick A. Technique for nitrous oxide/oxygen administration (Chapter 13), In Handbook of Nitrous Oxide and Oxygen Sedation. St. Louis: CV Mosby; 127–145, 1999.
- Primosch RE, Buzzi IM, Jerrell G. Effects of nitrous oxide-oxygen inhalation with scavenging on behavioral and physiological parameters during pediatric dental treatment. Pediatr Dent, 21: 417–420, 1999.
- Henry RJ, Primosch RE, Courts FJ. The effects of various dental procedures and patient behaviors upon nitrous oxide scavenger effectiveness. Pediatr Dent,14: 19–25, 1992.
- Primosch RE: Nitrous oxide-oxygen inhalation. In: Mathewson RJ and Primosch RE. Fundamentals of Pediatric Dentistry. 3rd ed. Chicago: Ouintessence Publishing Co.; 186–196, 1995.
- Dock M, Creedon RL. Pharmacologic management of patient behavior.
 In: McDonald RE, Avery DR, Dean JA. Dentistry for the Child and Adolescent. 8th ed. St. Louis: CV Mosby, 285–311, 2004.
- Wilson S, Vann WF, Dilley DC. Pain reaction control: sedation. In: Pinkham JR, Casamassimo PS, Fields HW, McTigue DJ, Nowak AJ. Pediatric Dentistry: Infancy Through Adolescence. 4th ed. St. Louis: Elsevier Saunders; 116–129, 2005.
- Clark M, Brunick A. Potential biohazards for health personnel with chronic exposure to nitrous oxide (Chapter 17), In Handbook of Nitrous Oxide and Oxygen Sedation. St. Louis: CV Mosby; 169–182, 1999.
- 14. Howard WR. Nitrous oxide in the dental environment: assessing the risk, reducing the exposure. J Am Dent Assoc 128:356-60, 1997.
- American Dental Association, Council on Scientific Affairs. Nitrous oxide in the dental office. J Am Dent Assoc, 128: 364–65, 1997.
- American Academy of Pediatric Dentistry. Policy on minimizing occupational health hazards associated with nitrous oxide. Reference Manual, 32: 65–66, 2010.
- American Academy of Pediatric Dentistry. Guidelines on use of nitrous oxide for pediatric dental patients. Reference Manual, 32: 163–166, 2010.
- Houpt MI, Koenigsberg SR, Weiss NJ, Desjardins PJ. Comparison of chloral hydrate with and without promethazine in the sedation of young children. Pediatr Dent, 7: 41–46, 1985.
- Houpt MI, Sheskin RB, Koenigsberg SR, Desjardins PJ, Shey Z. Assessing chloral hydrate dosage for young children. J Dent Child, 52: 364–369, 1985.
- Houpt MI, Kupietzky A, Tofky NS, Koenigsberg SR. Effect of nitrous oxide on diazepam sedation of young children. Pediatr Dent, 18: 236–241, 1996.
- McCann W, Wilson S, Larsen P, Stehle B: The effects of nitrous oxide on behavior and physiological parameters during conscious sedation with a moderate dose of chloral hydrate and hydroxyzine. Pediatr Dent, 18: 35–41, 1996.
- Ellis RK, Berg JH, Raj PP. Subjective signs of efficacious inferior alveolar nerve block in children. J Dent Child, 57: 361–5, 1990.

- Langa H. Relative Analgesia in Dental Practice. W.B. Saunders Co; Philadelphia, 1968.
- Carnow R. An analysis of the patient reaction under N2O + O2 analgesia. J Oregon Dent Assoc, 38: 13–16, 1969.
- Verwest TM, Primosch RE, Courts FJ: Variables influencing hemoglobin oxygen desaturation in children during routine restorative dentistry. Pediatr Dent, 15: 25–29, 1993.
- Rohlfing GK, Dilley DC, Lucas WJ, Vann WF: The effect of supplemental oxygen on apnea and oxygen saturation during pediatric conscious sedation. Pediatr Dent, 1: 8–16, 1998.
- Henry RJ, Vaikuntam J, Jones DJ: The influence of midazolam and nitrous oxide on respiratory depression in laboratory rats. Pediatr Dent, 18: 281–86, 1996.
- Anderson J, Vann WF: Respiratory monitoring during pediatric sedation: pulse oximetry and capnography. Pediatr Dent, 10: 94–101, 1988.
- Whitehead G, Durr D, Adair S, Proskin H: Monitoring sedated pediatric dental patients. J Dent Child, 55: 329–33, 1988.
- Hasty MF, Vann WF, Dilley DC, Anderson J: Conscious sedation of pediatric dental patients: an investigation of chloral hydrate, hydroxyzine pamoate, and meperidine vs. chloral hydrate and hydroxyzine pamoate. Pediatr Dent, 13: 10–19, 1991.

- Litman RS, Kottra JA, Berkowitz RJ, Ward DS: Upper air way obstruction during midazolam/nitrous oxide sedation in children with enlarged tonsils. Pediatr Dent, 20: 318–320, 1998.
- 32. Litman RS, Kotta JA, Verga KA, Berkowitz RJ, Ward DS: Chloral hydrate sedation: the additive sedative and respiratory depressant effects of nitrous oxide. Anesth Analg, 86: 724–728, 1998.
- Annequin D, Carbajal R, Chauvin P, Gall O, Tourniaire B, Murat I. Fixed 50% nitrous oxide oxygen mixture for painful procedures: a French survey. Pediatrics, 105: e47, 2000.
- 34. Faddy SC, Garlick SR. A systematic review of the safety of analgesia with 50% nitrous oxide: can lay responders use analgesic gases in the prehospital setting? Emerg Med J, 22: 901–906, 2005.
- Litman RS, Berkowitz RJ, Ward DS: Level of consciousness and ventilatory parameters in young children during sedation with oral midazolam and nitrous oxide. Arch Pediatr Adolesc Med, 150: 671–675, 1996