



ORAL SURGERY

ORAL MEDICINE

ORAL PATHOLOGY

ORAL AND MAXILLOFACIAL SURGERY

Editor: Larry J. Peterson

## Nitrous oxide–oxygen or oral midazolam for pediatric outpatient sedation

Sarah A. Hulland, DDS, MSc, FRCD(C),<sup>a</sup> Marshall M. Freilich, DDS, MSc, FRCD(C),<sup>b</sup> and George K. B. Sándor, MD, DDS, FRCD(C), FRCS(C), FACS,<sup>c</sup> Toronto, Ontario, Canada  
THE HOSPITAL FOR SICK CHILDREN, BLOORVIEW MACMILLAN CHILDREN'S CENTER, AND THE UNIVERSITY OF TORONTO

**Objective.** A total of 1112 pediatric outpatient sedations, by either nitrous oxide–oxygen inhalation (N<sub>2</sub>O) or oral midazolam, administered over a 10-year period were reviewed. Patient responses and outcomes were evaluated to ascertain the safety of these sedation techniques.

**Study design.** A total of 819 patients were included in this study. Patient health status, age, weight, behavior, treatment rendered, and length of treatment were recorded. Vital signs (heart rate, blood pressure, oxygen saturation) were recorded for the N<sub>2</sub>O group. Complications and successful completion of treatment were also noted.

**Results.** Both the N<sub>2</sub>O and midazolam groups demonstrated a low complication rate with a high rate of successful completion of treatment. Patients receiving N<sub>2</sub>O were somewhat older on average and underwent a greater number of surgical procedures than patients in the midazolam group. Vital signs recorded in the N<sub>2</sub>O group were observed to remain stable throughout treatment.

**Conclusions.** The use of either oral midazolam or nitrous oxide–oxygen as single agents provides safe and effective conscious sedation in the pediatric outpatient population.

(*Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;93:643-6)

The adage that “children are not simply small adults” has particular relevance to the selection of a conscious sedation technique for the pediatric patient population. Differences in cardiovascular and respiratory physiology between children and adults must be considered in

the selection of an ideal sedation technique for young patients. It is imperative that the technique selected be safe, be readily accepted by the patient, should not compromise the airway, and should prevent hypoventilation and bradycardia. Psychosocial interactions among child, parent, and clinician will affect the selection process, as well as the success of the technique.

Decreasing access to hospital operating rooms in some jurisdictions demands that many practitioners reconsider the use of sedation in the outpatient setting. Management difficulties can often be encountered in children between 18 months and 6 years of age because of fear and anxiety resulting from a lack of experience, immature reasoning development, and limitation of coping skills.<sup>1</sup> The judicious use of sedatives can be very beneficial to the child, dentist, and parent in allaying apprehension and minimizing the child's attempts to resist treatment.<sup>2-4</sup> These agents can be combined with psychological management techniques to expand the range of patients who can be treated in the office environment.<sup>5</sup> When combined with psychological management techniques, this “psychopharmacologic

Presented in abstract form at the meeting of the American Association of Oral and Maxillofacial Surgeons, Boston, Mass, Sep 29-Oct 2, 1999, and at the Scandinavian Federation of Oral and Maxillofacial Surgeons Conference in Oulu, Finland, June 2000.

<sup>a</sup>Associate Staff, Pediatric Dentistry, The Hospital for Sick Children, Toronto, Ontario, Canada; Staff Pediatric Dentist, Bloorview MacMillan Children's Center, Toronto.

<sup>b</sup>Former Fellow, Division of Oral and Maxillofacial Surgery, The Hospital for Sick Children; Staff Oral and Maxillofacial Surgeon, Bloorview MacMillan Children's Center.

<sup>c</sup>Director, Oral and Maxillofacial Surgical Services, Department of Dentistry, The Hospital for Sick Children and Bloorview MacMillan Children's Center; Associate Professor, University of Toronto.

Received for publication Apr 19, 2001; returned for revision May 17, 2001; accepted for publication Feb 28, 2002.

Copyright © 2002 by Mosby, Inc.

1079-2104/2002/\$35.00 + 0 7/12/124763

doi:10.1067/moe.2002.124763

logic" approach can help create an environment of mutual cooperation.<sup>6</sup> Several different types of sedation agents are available, but the ideal agent should be efficacious at the level of dosage that minimally alters vital signs, ensures rapid recovery, and is associated with a low incidence of adverse reactions. The most commonly used techniques include the administration of inhalation or oral sedative agents.

Inhalation sedation with nitrous oxide–oxygen is the most common sedation technique used in dentistry.<sup>7</sup> This technique has several advantages, including rapid onset, ability to titrate to effect, analgesia, and rapid recovery from sedation. Its successful application depends on the patient's willingness to accept placement of the nasal mask, as well as their allowance for the procedure to be performed. However, inhalation sedation use may prove difficult or impossible in the treatment of recalcitrant or hysterical children.<sup>2</sup>

Orally administered sedatives are well accepted by children and are usually perceived as nonthreatening. Oral sedation is complicated by variable absorption and the inability to titrate the dose to the desired effect, characteristics that may produce unpredictable levels of sedation.<sup>2</sup> Benzodiazepines are a commonly used class of sedative agents. Midazolam, a newer-generation benzodiazepine, has a wide toxic/therapeutic ratio and margin of safety and does not produce the prolonged sedation associated with other benzodiazepines such as diazepam. When taken orally, midazolam is rapidly absorbed in the gastrointestinal tract, produces its peak effect in 30 minutes, and has a short half-life of 1.75 hours. This makes it a desirable drug for short procedures.<sup>3</sup> When given in amounts between 0.5 and 0.75 mg/kg of body weight, oral midazolam has been found to be an effective sedative agent for pediatric outpatients.<sup>8,9</sup> Midazolam has been shown to enhance anterograde amnesia when used preoperatively in pediatric patients.<sup>10,11</sup>

The purpose of this study was to judge the relative safety and efficacy of oral midazolam or nitrous oxide–oxygen for the provision of outpatient conscious sedation in the pediatric dental population.

## MATERIAL AND METHODS

Records were reviewed of patients who underwent either nitrous oxide–oxygen (N<sub>2</sub>O) or oral midazolam as single-agent sedatives for procedures performed at the Hospital for Sick Children, Department of Dentistry (Toronto, Ontario, Canada), between 1988 and 1998. Patients were excluded if records were incomplete or if multiple sedatives were administered at 1 visit. Health histories were reviewed, and an American Society of Anesthesiologists (ASA) status was assigned. Midazolam (Versed, Hoffman-La Roche, Mississauga, On-

**Table I.** Treatment rendered by sedation type

Treatment	Nitrous oxide–oxygen: # of patients (%)	Midazolam: # of patients (%)
Restorative	99 (30.4%)	322 (41%)
Simple extraction	46 (14%)	361 (46%)
Restorative + extraction	11 (3.4%)	24 (3%)
Surgical extraction	118 (36.2%)	23 (2.9%)
Pathology/biopsy	14 (4.3%)	0
Endodontics	8 (2.5%)	0
Implants	0	0
Other	23 (7.1%)	19 (2.4%)
Treatment aborted	7 (2.1%)	37 (4.7%)

tario, Canada) was administered orally, dosed at 0.5 mg/kg to a maximum of 10 mg per appointment. N<sub>2</sub>O was administered by means of a nasal hood and titrated to the level that would allow completion of treatment and child cooperation. The N<sub>2</sub>O gas mixer was set up to limit a gas flow to no higher than a maximum N<sub>2</sub>O concentration of 70%. In this group, recorded vital signs included heart rate, blood pressure, and oxygen saturation as determined by noninvasive blood pressure monitoring and pulse oximetry. All the N<sub>2</sub>O records were reviewed by one investigator (M.M.F.), and the midazolam records were all reviewed by another investigator (S.A.H.).

## RESULTS

The N<sub>2</sub>O group consisted of 240 patients (126 males and 114 females) who underwent a total of 326 sedations. Patients were provided with a range of dental and surgical treatment as summarized in Table I. Patients in this group ranged in age from 3 to 14 years (mean age, 10.8 years). Approximately 189 patients were classified as ASA I; 47, ASA II; and 4, ASA III. Mean recorded treatment length was 45.2 minutes, with a range of 9 to 100 minutes. Vital sign recordings are presented in Table II.

Treatment was discontinued in 7 of the 326 sedations (2.2%), and marked resistance was noted in 3 cases (0.9%), but this did not prevent treatment from proceeding. No restraint use was recorded for this group. Reported complications were low for the N<sub>2</sub>O group, with nausea noted in 5 cases (1.5%) and vomiting in 5 cases (1.5%).

In the midazolam group there was a total of 579 patients (310 males and 269 females). These patients underwent a total of 786 sedations. In this group, 522 were classified as ASA I and 57 as ASA II. Patient weights ranged from 11 kg to 44 kg (mean, 16.9 kg). Patient ages at initial visit ranged from 0.5 years to 8.1 years (mean, 3.6 years); age at treatment ranged from 0.9 to 10.5 years (mean, 5.4 years). Length of treatment

**Table II.** N<sub>2</sub>O/O<sub>2</sub> group—vital sign recordings

Vital sign	Initial	Midtreatment	Final
Oxygen saturation	98.6% (94%-100%)	98.5% (96%-100%)	98.4% (94%-100%)
Heart rate (bpm)	88.3.0 bpm (55-155 bpm)	89.1 bpm (53-151 bpm)	89.4 bpm (52-142 bpm)
Systolic pressure	116.3 mm Hg (90-146 mm Hg)	113.9 mm Hg (90-149 mm Hg)	114.2 mm Hg (92-153 mm Hg)
Diastolic pressure	60.2 mm Hg (37-91 mm Hg)	59.1 mm Hg (37-95 mm Hg)	58.5 mm Hg (37-83 mm Hg)

bpm, beats per minute.

ranged from 40 minutes to 138 minutes (mean, 76.7 minutes). Patients received a midazolam dose range of 5.4 to 10 mg for a mean dose of 8.6 mg. Patients receiving midazolam underwent a wide variety of procedures (Table I). A total of 239 patients (30%) were restrained by using a papoose board and Pedi-Wrap, and 46 patients (5.9%) were recorded as having been restrained by people or had their hands held during procedures. In 37 patients, treatment was aborted because of lack of cooperation (4.7%), whereas marked resistance was noted in 98 patients (12.5%), but this did not interfere with the completion of treatment. There were few reported complications in the midazolam group. Two patients experienced hallucinations (0.25%) and 9 patients vomited during their procedures (1.1%). There were no recorded cases of nausea without vomiting.

## DISCUSSION

It has been suggested that the number of children who require some form of sedation to enable the provision of necessary dental care is increasing. This has been linked to a smaller proportion of children requiring an increase in dental care.<sup>12,13</sup> There is also an increased awareness of the true incidence of dental caries in a younger population.<sup>14</sup> Parental schedules are restricted with respect to the amount of time available away from work. It is often perceived that there is pressure from several directions for the dental clinician to provide the maximum amount of care during the minimum number of visits to the dental office. This approach is not unrealistic in the management of the psychological and physiological well-being of these children.

Despite the widespread acceptance of N<sub>2</sub>O and the increasing usage of oral midazolam in pediatric dentistry and surgery, little has been reported on the overall safety of these agents in the pediatric dental patient population. N<sub>2</sub>O is widely used because of its provision of a significant analgesic effect with minimal respiratory depression at concentrations less than 50%.<sup>7-10,15-21</sup> N<sub>2</sub>O achieves a rapid peak clinical effect and is rapidly eliminated from the system when administration is stopped. Apprehensive children who are potentially

cooperative are ideal candidates for this technique, but the technique is contraindicated in children who are recalcitrant or hysterical.<sup>1</sup>

Caution should be used when administering nitrous oxide to children with chronic otitis media because of the ready diffusion of the agent into air-filled spaces, including the middle ear.<sup>22</sup> Acute upper respiratory tract infections decrease the efficacy of nitrous oxide because of the decreased ability to breathe nasally. Recognized adverse reactions such as nausea and vomiting have been reported,<sup>8,21</sup> but Houck and Ripa<sup>23</sup> suggest that children have a natural tendency to vomit easily that is unrelated to eating before treatment, concentration of nitrous oxide, or duration of the sedative procedure. This suggests that the incidence of vomiting can be predicted by a history of hyperemesis, which should be noted in the medical history.<sup>23,24</sup> In the current study, we observed a very low reported incidence of nausea or vomiting in patients receiving either form of sedation.

N<sub>2</sub>O has been reported to cause a decrease in both systolic and diastolic blood pressure.<sup>3</sup> In this study, both systolic and diastolic blood pressures were observed to remain stable throughout procedures performed under the conditions described. It has been reported that more than 20% of patients will demonstrate at least one occurrence of oxygen desaturation during N<sub>2</sub>O administration.<sup>7</sup> In this study, the oxygen saturation remained stable throughout the sedations, but the authors reaffirm the recommendation that oxygen saturation monitoring by means of pulse oximetry be provided for patients receiving N<sub>2</sub>O inhalation sedation.

Oral sedation has been reported to have several advantages, including ease of administration, relative safety, convenience, and economic expedience.<sup>7</sup> Its use may be complicated by refusal of the child patient or their inability to swallow tablets or capsules. The level of sedation and the onset of action can be unpredictable at times because of the variability in absorption and metabolism.<sup>10,21,25</sup> The timing of administration should be monitored by the clinician to ensure consistency for the onset of the desired effect, as well as patient safety. Midazolam has some noted potential side effects, in-

cluding hypercarbia, hypoxia, and dysphoria in some children, thus monitoring during the recovery period has been recommended—although not recorded—in this study.<sup>10,25</sup> Although there is a potential for respiratory depression, this effect is more commonly produced in the elderly than in children.<sup>26</sup> The reported incidence of postoperative nausea and vomiting after local anesthesia and sedation is less than that after general anesthesia (6% versus 14%).<sup>8</sup> This paralleled the effect that the time to discharge home was less for patients receiving sedation.<sup>8</sup> This study observed a very low complication rate with the use of oral midazolam in the pediatric dental outpatient setting.

In our review of the administration of single-agent sedation techniques in the provision of dental care in the pediatric population, we found that the profile of patients managed under each modality was moderately different in that the patients managed with N<sub>2</sub>O were from an older age group. This is consistent with the requirement that there be a level of cooperation and understanding before the application of the nasal mask. In addition, this increase in age is consistent with the types of dental treatments rendered for an older population. Despite these obvious differences in the patient populations, the treatments that were provided were successful in the majority of the cases and the side effects experienced were minimal. This indicates that both these single-agent sedation techniques are appropriate and safe in the pediatric dental population. The choice of which technique to use should be predominantly made on the basis of the child's age, developmental status, and experiences.

## CONCLUSIONS

On the basis of a 10-year retrospective study, the use of nitrous oxide–oxygen or oral midazolam as single agents provides safe and effective conscious sedation in the pediatric outpatient population. This study provides a basis for a prospective study to further investigate the use of these agents in the provision of conscious sedation.

## REFERENCES

- Henry RJ, Jerrell RG. Ambient nitrous oxide levels during pediatric sedations. *Pediatr Dent* 1990;12:87-91
- Lanza V, Mercadante S, Pignataro A. Effects of halothane, enflurane, and nitrous oxide on oxyhemoglobin affinity. *Anesthesiology* 1988;68:591-4.
- Field LM, Dorrance DE, Krzeminska EK, Barsoum LZ. Effect of nitrous oxide on cerebral blood flow in normal humans. *Br J Anesth* 1993;70:154-9.
- Apses T. The effect of nitrous oxide sedation on the blood pressure of pediatric dental patients. *ASDC J Dent Child* 1975;42:364-6.
- Rohlfing GK, Dilley DC, Lucas WJ, Vann WF. The effect of supplemental oxygen on apnea and oxygen saturation during pediatric conscious sedation. *Pediatr Dent* 1998;20:8-16.
- Verwest TM, Primosch RE, Courts FJ. Variables influencing hemoglobin oxygen desaturation in children during routine restorative dentistry. *Pediatr Dent* 1993;15:25-9.
- Braham RL, Bogetz MS, Kimura M. Pharmacologic patient management in pediatric dentistry: an update. *ASDC J Dent Child* 1993;60(4-5):270-80.
- Brandt SK, Bugg JL. Problems of medication with the pediatric patient. *Dent Clin North Am* 1984;28:563-79.
- Silver T, Wilson C, Webb M. Evaluation of two dosages of oral midazolam as a conscious sedation for physically and neurologically compromised pediatric dental patients. *Pediatr Dent* 1994;16:350-9.
- Smith BM, Cutilli BJ, Saunders W. Oral midazolam: pediatric conscious sedation. *Compendium* 1998;19:586-92.
- Kain ZN, Hofstadter MB, Mayes LC, Krivutza DM, Alexander G, Wang SM, et al. Midazolam. Effects on amnesia and anxiety in children. *Anesthesiology* 2000;93:676-84.
- Murray J. Prevalence of dental caries: retrospect and prospect. *Dent Update* 1998;25:374-8.
- Waldman HB, Perlman SP. Are we reaching very young children with needed dental services? *ASDC J Dent Child* 1999;66:390-4.
- Moynihan P. The British nutrition foundation oral task force report: Issues relevant to dental health professionals. *Br Dent J* 2000;188:308-12.
- Henry RJ, Vaikuntam J, Jones DJ. The influence of midazolam and nitrous oxide on respiratory depression in laboratory rats. *Pediatr Dent* 1996;18:281-6.
- Twersky RS, Hartung J, Berger BJ, McClain J, Beaton C. Midazolam enhances anterograde but not retrograde amnesia in pediatric patients. *Anesthesiology* 1993;78:51-5.
- Feld LH, Negus JB, White PF. Oral midazolam preanesthetic medication in pediatric outpatients. *Anesthesiology* 1990;73:831-4.
- Giovannitti JA. Regimens for pediatric sedation. *Compend Contin Educ Dent* 1992;8:1008-12.
- Brandt SK and Bugg, JL. Problems of medication with the pediatric patient. *Dent Clin North Am* 1984;28:563-79.
- Sorenson HW, Roth GI. A case for nitrous oxide–oxygen inhalation sedation: as aid in the elimination of the child's fear of the 'needle.' *Dent Clin North Am* 1973;17:51-66.
- Sacchetti A, Schafermeyer R, Gerardi M, Granet J, Fuerst RS, Cantor R, et al. Pediatric analgesia and sedation. *Ann Emerg Med* 1994;23:237-50.
- Sándor GKB, Tolas AG. Spontaneous tension pneumothorax following out-patient general anaesthesia. *J Oral Maxillofac Surg* 1982;40:596-600.
- Houck WR, Ripa LW. Vomiting frequency in children administered nitrous oxide–oxygen in analgesic doses. *ASDC J Dent Child* 1971;38:404-6.
- Chye EPY, Young IG, Osbourne GA, Rudkin GE. Outcomes after same-day oral surgery. A review of 1,180 cases at a major teaching hospital. *J Oral Maxillofac Surg* 1993;51:846-9.
- Phero JC. Pharmacologic management of pain, anxiety and behavior: conscious sedation, deep sedation and general anesthesia. Keynote address 8th Annual Symposium College of Diplomates of the American Board of Pediatric Dentistry. *Pediatr Dent* 1993;15:429-34.
- Cote CJ. Sedation for the pediatric patient. *Pediatr Clin North Am* 1994;41:31-58.

### Reprint requests:

George K. B. Sándor, MD, DDS, FRCD(C), FRCS(C), FACS  
The Hospital for Sick Children  
S-527, 555 University Ave  
Toronto, Ontario  
Canada M5G 1X8  
gsandor@sickkids.ca