Level of Sedation with Nitrous Oxide for Pediatric Medical Procedures

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BACKGROUND: Nitrous oxide (N_2O) delivered at a concentration <50% is accepted as a minimal sedation drug by both the American Society of Anesthesiologists and the American Academy of Pediatrics. The expected level of sedation at an N_2O concentration >50% is less clear.
METHODS: We conducted a retrospective chart review for all children receiving N_2O for procedural sedation at Children's Hospitals and Clinics of Minnesota. Patient age, maximal N_2O concentration, duration of N_2O administration, completion of procedure, and adverse events were recorded. Level of sedation was assessed on a 0 to 6 scale.
RESULTS: N_2O was administered on 1858 occasions to 1585 patients younger than 18 years. Most administrations (91.3%) were N_2O concentration >50%. Level of sedation scores were as follows: 6 (inadequate) = 1.3%; 5 (minimal) = 94.3%; and 4 (drowsy) = 4.3%; no patient reached a sedation score <4. Fifty-nine patients (3.3%) had adverse events of which 6 (0.3%) were atypical. There was no difference between N_2O ≤50% and N_2O >50% in the level of sedation or number of adverse events. More children ≤2 years (7.4%) achieved a sedation level of 4 than those older than 2 years (4%), but they experienced a similar rate of adverse events. There was no difference in the level of sedation by duration of N_2O administration. Inadequately sedated patients were younger than the remainder of the group. Most procedures (94.1%) were completed with the patient calm and still.
CONCLUSIONS: A significant number of children remain minimally sedated while receiving N_2O at concentrations >50% via nasal hood using a system designed to titrate N_2O concentration from 0% to 70%. Adverse event rates of patients receiving >50% N_2O in this manner are similar to rates reported in large studies of 50% N_2O administration. (Anesth Analg 2010;110:1399–405)

Although classified as an anesthetic gas, the potency of nitrous oxide (N_2O) is significantly less than other inhaled drugs frequently used to provide general anesthesia. The minimal alveolar concentration (that produces immobility in 50% of subjects exposed to a noxious stimulus) for N_2O is 104%, a level not achievable outside of a hyperbaric environment. N_2O delivered at a concentration <50% is accepted as a minimal sedation drug by the American Society of Anesthesiologists (ASA)[1] and at a concentration ≤50% by the American Academy of Pediatrics (AAP).[2] In concentrations >50%, however, the AAP cautions that "the likelihood for moderate or deep sedation increases."[2] According to the most recent guidelines, children intended to remain in a minimally sedated state require no more than observation and intermittent assessment of their level of sedation. Children intended to reach a level of moderate sedation require continuous monitoring of oxygen saturation and heart rate and intermittent recording of respiratory rate and arterial blood pressure.

Several studies, including one with >35,000 patients, have addressed the issue of safety of N_2O delivered at a fixed concentration of 50% N_2O:50% oxygen; however, these studies do not address the level of sedation achieved at this concentration.[3–6] Other studies have demonstrated safe delivery of N_2O in concentrations up to 70%.[7–9] One of these, in a pediatric emergency department setting, showed that "N_2O 70% provides similar sedation depth to N_2O 50% with no increase in adverse events."[9] The current investigation evaluated the level of sedation in children receiving N_2O for procedural sedation throughout our children's hospital system. We hypothesized that children administered N_2O at a concentration >50% would reach an equal level of sedation as those administered ≤50%.

METHODS

After approval by the IRB of Children's Hospitals and Clinics of Minnesota, a retrospective chart review was conducted for all children aged 18 years and younger receiving N_2O for procedural sedation from September 2006 through January 2008. Because the study involved only data collected routinely for patient care documentation, the need for specific written informed consent was waived.

N_2O Sedation Process

All children receiving N_2O sedation at Children's Hospitals and Clinics of Minnesota undergo a standardized presedation assessment to identify potential contraindications to sedation and/or N_2O. N_2O is administered by a registered nurse who has had institutional training in N_2O administration as described elsewhere.[10,11] N_2O sedation occurs in various departments throughout our hospital system, including the emergency department, radiology department, hematology/oncology clinic, special diagnostics unit, and short-stay areas. N_2O is administered via a continuous flow device (Porter Instrument Company, Hatfield, PA), which allows titration of N_2O from 0% to 70% with oxygen as the remaining gas. This standard "dental" N_2O flowmeter

Table 1. Level of Sedation Score	
6	Inadequate = anxious, agitated, or in pain
5	Minimal = spontaneous awake without stimulus
4	Drowsy = eyes open or closed, but easily arouses to consciousness with verbal stimulus
3	Moderate-deep = arouses to consciousness with moderate tactile or loud verbal stimulus
2	Deep = arouses slowly to consciousness with sustained painful stimulus
1	Deeper = arouses, but not to consciousness, with painful stimulus
0	Anesthesia = unresponsive to painful stimulus

includes a fail-safe device that terminates N_2O flow in the event of cessation of oxygen flow. A scavenging apparatus designed to eliminate exhaled N_2O is an integral part of the equipment and minimizes occupational exposure to N_2O. A standard dental nasal hood is used to administer the N_2O. The starting concentration and titration of N_2O are at the discretion of the sedation nurse. Although not protocolized, usual practice is to begin administration at 50% to 60% N_2O with titration to higher or lower concentration within 2 to 3 minutes based on patient response to the procedure. Sedation depth is recorded using the Children's Hospital of Wisconsin Sedation Scale (Table 1), which is a validated modification of the Ramsay scale.[12] N_2O concentration, patient oxygen saturation, and sedation level are documented in the medical record at 3- to 5-minute intervals or sooner if a change is made in N_2O concentration. Verbal distraction (e.g., storytelling and soothing discourse) is provided throughout the procedure. Our protocol dictates that all children receive 100% oxygen for 3 to 5 minutes after N_2O administration. Postprocedure documentation includes an electronic medical record prompt for description of the completeness of the procedure with limited options (completed, patient calm and still during procedure; completed, patient unable to stay still or calm; not completed, inadequate sedation; not completed, complications with sedation; not completed, problems not related to sedation; or other). This descriptive set corresponds to standardized study data collected by the Pediatric Sedation Research Consortium (PSRC) for analysis of multiinstitutional sedation practices.[13] Postprocedure documentation also includes adverse event choices corresponding to the PSRC study dataset and an area to enter additional information.

Children receiving N_2O as a single drug for procedural sedation are monitored with pulse oximetry and direct nursing observation until return to their baseline level of alertness. Patients receiving sedative medication in addition to N_2O receive more intensive monitoring (e.g., heart rate, respiratory rate, and arterial blood pressure every 5–10 minutes) per hospital policy for moderate sedation. Per hospital policy, all patients receiving N_2O as a single drug who reach a level of moderate sedation also require more frequent vital sign documentation.

Data Collection
The patient age and procedure performed at the time of N_2O administration were recorded. The total duration of N_2O administration and maximal concentration of N_2O

delivered at any time during the sedation event were recorded. The lowest sedation score (corresponding to deepest level of sedation) reached at any time during the sedation event was noted. A description of completion of procedure and adverse event information was recorded.

Statistical Analysis
Descriptive statistics including median and range were used to describe the continuous variables such as age and duration of procedure. Frequency distribution was performed to describe categorical variables including the minimal level of sedation and the maximal N_2O concentration. Nonparametric Mann-Whitney test was used to compare age and procedure duration between N_2O low and high groups. χ^2 test was conducted to compare the level of sedation between groups ≤2 years and >2 years of age. $P < 0.05$ was considered to indicate a statistically significant difference. All statistical analyses were completed using SPSS 15.0 (SPSS, Chicago, IL).

RESULTS
A total of 2045 N_2O administrations were recorded in patients younger than 18 years during the study period. Level of sedation score data were missing for 187 administrations leaving 1858 sedation events available for analysis. These 1858 administrations were performed in 1585 patients because several patients received N_2O sedation on more than one occasion.

The median patient age was 5.2 years (range, 0.2–17.9 years). The median duration of administration was 6 minutes, with a range of 1 to 73 minutes. Characteristics including maximal N_2O concentration administered and procedures performed with N_2O sedation are shown in Table 2. Most administrations (91.3%) used a maximal N_2O concentration >50%.

Most patients were assessed at a sedation level of 5 (94.3%) or 6 (1.3%) with 4.3% reaching a sedation level of 4. No patient reached a sedation level <4. There was no difference in the number of patients reaching a sedation level of 4 between those receiving N_2O ≤50% (4 of 161 patients; 2.5%) and those receiving N_2O >50% (76 of 1697 patients; 4.5%) ($P = 0.234$). There was no difference in duration of N_2O administration between the groups reaching a level of sedation score of 4 and those remaining at level 5 or 6 (Table 3). Although there was no difference in median patient age between groups with a sedation score of 4 versus those at 5 or 6 (Table 3), when patients ≤2 years were compared with those >2 years, more of the younger patients (7.4%) achieved a sedation level of 4 than those older than 2 years (4%) ($P = 0.044$). Patients judged to be inadequately sedated (sedation level 6) were younger (median, 3.2 years; range, 0.8–16.8 years) than the remainder of the group (median, 5.2 years; range, 0.2–18.9 years) ($P = 0.017$).

Of the 80 patients reaching a sedation level of 4, 3 received a sedative or potentially sedating medication before N_2O sedation. One child received 0.5 mg/kg oral midazolam 24 minutes before N_2O administration. This child had a presedation history and physical examination per protocol for moderate sedation in anticipation of using the combination of midazolam and N_2O. Another patient received 0.3 mg/kg oral midazolam for a prior attempt at

Table 2. Characteristics of Nitrous Oxide (N$_2$O) Sedation Events

Maximum nitrous oxide concentration	n	%
30	16	0.9
40	14	0.8
50	131	7.1
60	511	27.5
65	240	13.0
70	946	50.9

	Overall n (% of total) (n = 1858)	Successfully completed n (% per procedure)	Unable to complete n (% per procedure)	Completion unknown n (% per procedure)
Procedures performed with nitrous oxide sedation				
Urinary catheterization (urologic imaging, urodynamics)	1095 (58.9)	1012 (92.4)	5 (0.5)	78 (7.1)
Botulinum toxin or other intramuscular injection	174 (9.4)	168 (96.6)	0	6 (3.4)
Vascular access or venipuncture	154 (8.3)	122 (79.2)	4 (2.6)	28 (18.2)
Computed tomography scan	100 (5.4)	91 (91.0)	1 (1.0)	8 (8.0)
Enteral tube placement (nasogastric tube) or replacement (gastrostomy/gastrojejunal tube)	67 (3.6)	59 (88.1)	1 (1.5)	7 (10.4)
Minor surgical (e.g., laceration repair, joint injection, incision, and drainage of abscess)	39 (2.1)	37 (94.9)	0	2 (5.1)
Lumbar puncture	36 (1.9)	29 (80.5)	1 (2.8)	6 (16.7)
Other				
Electromyelography/nerve conduction	17 (0.9)	17 (100)	0	0
Gastrograffin enema	8 (0.4)	8 (100)	0	0
Foreign body removal	7 (0.4)	7 (100)	0	0
Cast/splint placement	4 (0.2)	4 (100)	0	0
Other	10 (0.5)	9 (90.0)	0	1 (10.0)
Associated with other completed procedure (specific N$_2$O procedure information unavailable)	109 (5.9)	0	0	109 (100)
No information	38 (2.0)	13 (34.2)	2 (5.3)	23 (60.5)

Table 3. Level of Sedation Compared with Age and Duration of Procedure

	Sedation score = 4 (n = 80)	Sedation score = 5 or 6 (n = 1778[a])	P[b]
Age (y)			
Median	5.5	5.2	0.639
Range	0.7–16.6	0.2–17.9	
Duration (min)			
Median	7	6	0.062
Range	3–55	1–73	

[a] Seven patients missing duration data excluded from duration analysis.
[b] Mann-Whitney test.

Table 4. Complications with Nitrous Oxide (N$_2$O) Sedation

	≤50% N$_2$O		>50% N$_2$O	
	n	%	n	%
Complications				
No complications	152	98.1	1551	96.5
Vomiting	0	0	29	1.8
Nausea	1	0.6	6	0.4
Inadequate sedation	0	0	8	0.5
Agitation/delirium	0	0	2	0.1
Other	2	1.3	11	0.7
Description of other complications				
Apnea >15 s[a]	1			
Oxygen saturation 89%[a]			1	
Unresponsive episode with oxygen saturation 83%[a]			1	
Stridor[a]			1	
Seizure[a]			2	
Diaphoresis			1	
Burpy/hiccupy			1	
Gaggy	1		2	
Expectorated large amount of clear phlegm			1	
Screaming			1	

[a] Patients described in detail in text.

nasogastric placement 90 minutes before N$_2$O administration. One child received acetaminophen-hydrocodone (0.09 mg/kg hydrocodone) 81 minutes before N$_2$O administration. The remainder of the 80 patients received either nonsedating medication (2 acetaminophen, 3 ondansetron, and 1 valproic acid) or no medication before the N$_2$O administration.

Adverse event data were available for 1762 sedation encounters (Table 4). Fifty-nine patients experienced ad-

verse events, 3 of 155 patients (1.9%) in the ≤50% N_2O group and 56 of 1607 (3.5%) in the high-concentration group ($P = 0.343$). There was no difference in adverse events between patients ≤2 years and >2 years of age ($P = 0.067$).

Six patients experienced atypical adverse events. A 2-year-old girl with trisomy 21 hospitalized with pansinusitis, adenotonsillar hypertrophy, herpes stomatitis, and intermittent oxygen desaturation received 50% N_2O and then 100% oxygen for 3 minutes to facilitate peripheral venous cannulation. Her oxygen saturation remained at 100%. On return to room air, she was noted to have "apnea >15 seconds" with no associated color change or oxygen desaturation. She returned to her baseline state with no specific intervention. A 16-month-old boy was administered 65% to 70% N_2O and then 100% oxygen for 2 minutes to facilitate peripheral venous cannulation and urethral catheterization for radionuclide renogram. On return to room air, he developed oxygen desaturation to 89%. Additional supplemental oxygen was given and he returned to baseline status shortly thereafter. A 3-year-old boy hospitalized with acute encephalopathy was administered 60% to 70% N_2O, then 100% oxygen for 3 minutes for an unsuccessful attempt at lumbar puncture. On return to room air, the child "became unresponsive" with oxygen saturation decreasing to 83%. He recovered with stimulation and supplemental oxygen and returned to baseline status within 10 minutes. N_2O was then used for a subsequent successful lumbar puncture during which the patient was noted to "respond normally." No adverse events were noted during the second N_2O administration. A 2-month-old infant diagnosed in utero with a left neck mass was scheduled for computed tomographic (CT) scan of the head and neck when the mass, which had not been previously clinically apparent, became visible to caregivers. He received 70% N_2O followed by 100% oxygen during CT imaging with oxygen saturation remaining at 100% throughout. The presence of stridor was noted in the postprocedure assessment form. No airway intervention was required. The child was discharged shortly after the scan at baseline status. Two patients (aged 12 months and 17 months) developed generalized tonic-clonic seizure activity lasting 2 to 3 minutes, one during N_2O administration and one while receiving 100% oxygen after discontinuation of N_2O. Both patients developed oxygen desaturation of 78% to 79% during clinical seizure activity, promptly returning to 100% saturation with application of 100% oxygen by facemask. Neither patient required any specific airway intervention, although one received oral suctioning for a small amount of thin secretions. Both returned to baseline clinical status and were discharged to home later the same day.

Procedure completion information was available for 1590 sedation events. Most procedures (94.1%) were completed with the patient calm and still. For 5.0%, the procedure was completed with the patient unable to remain still or calm. Only 14 of 1590 events (0.9%) were unable to be completed because of either inadequate sedation or problems unrelated to sedation. All of the incomplete procedures used N_2O >50%. Procedure completion information was unavailable for 268 sedation events. Of these, 109 were

Table 5. Patient Responsiveness at American Society of Anesthesiologists[1] and American Academy of Pediatrics[2] Recognized Levels of Sedation	
Minimal	A drug-induced state during which patients respond normally to verbal commands, cognitive function, and coordination may be impaired
Moderate	A drug-induced depression of consciousness during which patients respond purposefully to verbal commands either alone or accompanied by light tactile stimulation
Deep	A drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after repeated verbal or painful stimulation
General anesthesia	A drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation

coupled to an additional sedated procedure (e.g., deep sedation for magnetic resonance imaging) that was completed; however, because the completion descriptor could not be ascribed directly to the N_2O sedation, completion data from these events were excluded from analysis. Twenty-three events had no postsedation notation of completion or procedure performed. Breakdown of procedures by completion status is shown in Table 2.

DISCUSSION

In the interest of patient safety, the AAP originally published "Guidelines for the Elective Use of Conscious Sedation, Deep Sedation, and General Anesthesia in Pediatric Patients" in 1985 to aid practitioners in providing sedation to pediatric patients with appropriate assessment, monitoring, documentation, and equipment.[14] This document has been regularly updated, most recently in 2006.[2] While acknowledging that sedation occurs along an unbroken continuum from anxiolysis to general anesthesia, the process of breaking the continuum into definable levels (Table 5) allows for prescription of elements such as provider skill level, patient monitoring, and equipment that are appropriate to the potentially increased risks that accompany each deeper level of sedation.[1,2] However, because sedation occurs along a continuum, the distinction between each level may be difficult to discern. Placing the child who requires "light tactile stimulation" to "respond purposefully to verbal commands" into a moderate sedation category may be straightforward; however, deciding whether the child with eyes open responds "normally to verbal commands" versus "purposefully to verbal commands" or whether that child is in a "drug-induced state" in which "cognitive function and coordination may be impaired" versus a "drug-induced depression of consciousness" may be more problematic, allowing for some subjectivity in the categorization of the level of sedation between minimal and moderate.

This distinction, however, is more than just a matter of semantics. As stipulated in the ASA and AAP sedation guidelines, a child receiving a drug expected to result in

moderate sedation requires more intensive monitoring than a child receiving a drug expected to result in minimal sedation. In addition, presedation requirements may be more onerous for children receiving moderate sedation than for those receiving minimal sedation. At our institution, children scheduled for moderate sedation are required to undergo a separate presedation history and physical examination by their primary practitioner within 7 days of their scheduled procedure. Therefore, the expectation of level of sedation to be achieved by a given sedation medication has an effect not only on the institutional policies and procedures required for its use but also on the potential cost and time burden for patients, families, and the overall health care system.

In turn, these burdens may limit children's access to N_2O, a drug that has not only demonstrated to be useful for pediatric procedures by virtue of its analgesic and amnesic properties but has also been suggested to be a cost-effective alternative to other sedatives.[15–17] As our study shows, children receiving N_2O via a nasal mask, even in high concentrations, can remain in a minimally sedated state. The fact that a small percentage of patients achieve a deeper level of sedation than minimal highlights the ASA and AAP admonishment that "practitioners of sedation must have the skills to rescue the patient from a deeper level than that intended for the procedure."[2] Because of the pharmacokinetic properties of N_2O, patients who inadvertently reach a level of moderate sedation when minimal sedation is intended would be expected to return rapidly to a baseline level of alertness upon discontinuation of inhalation.

Although N_2O has been used for decades by dentists to provide sedation and anxiolysis for their patients, there are few data in the dental literature regarding the level of sedation with which to compare this study. In 1 prospective study of the psychomotor effect of N_2O, all 59 children, aged 4 to 13 years, were able to participate in a drawing activity while inhaling 50% N_2O.[18] In another study, all 25 children, aged 4 to 10 years, receiving N_2O titrated to achieve "relative analgesia" with a concentration 40% to 60% (mean 51%) were interactive enough to choose a color representing their level of pain.[19] The paucity of data regarding level of sedation, particularly at N_2O concentrations >50% and as a single drug sedative, likely reflects current dental practice. Although 89% of respondents to a survey of pediatric dentists reported the use of N_2O in their practice, only 1.8% reported using it at a concentration >50%.[20] In addition, only 29% of pediatric dentists reported using only N_2O for sedation[21]; the remainder used other sedative drugs in addition to N_2O. Dental practice also requires that N_2O be administered via a nasal mask while the mouth remains open for treatment. When delivered in this manner, the concentration of N_2O measured in the nasopharynx of cooperative volunteers was significantly lower than the flowmeter setting.[22] Although considerable interindividual differences were noted, inspired N_2O measured in the nasal mask averaged 31% lower than the flowmeter setting with a further decrease of 19% to the nasopharynx.[22]

We found no difference in the level of sedation or number of adverse events between children administered N_2O at a concentration >50% and those administered ≤50% in this study. In the medical literature, the most comparable study is that by Babl et al.,[9] who reported their experience with high-concentration N_2O in a pediatric emergency department. They found that 52 of 484 patients (10.7%) receiving 70% N_2O and 3 of 90 patients (3.3%) receiving 50% N_2O reached moderate or deep sedation, choosing to define moderate sedation as a sedation score of 3 and deep sedation as a score of ≤2. None of our patients reached a sedation score ≤3. Although Babl et al. excluded patients receiving additional sedative drugs for analysis, patients receiving analgesics, including opioids, were included but not quantified. In addition, the type of mask used for N_2O delivery in that study was not specified. For our study, a dental nasal mask, not a full facemask, was used for gas delivery. Although our patients are instructed to breathe through the nose while keeping the mouth closed, room air may be entrained, resulting in decreased inspired N_2O concentration. This may also account for the increased level of sedation in children ≤2 years in our study, whose mouths may be partially covered by our single-sized nasal mask. Our minimal sedation rate of 94.3% is consistent with the observation of Kanagasundaram et al.[7] that 93.3% of children were "awake" during administration of 50% to 70% N_2O in an emergency department setting. A future prospective evaluation of level of sedation using an independent observer would be useful in addressing differences in study findings. Similar to Babl et al., who relied on nurses and physicians participating in the procedural sedation to record the level of sedation for their report, we relied on the assessment and documentation of level of sedation by nurses responsible for N_2O administration. This nursing group is diverse, with staff working in the emergency department, radiology department, hematology/oncology clinic, special diagnostics unit, and short-stay areas of the institution. All of these nurses, however, receive training in institutional sedation policies and procedures, including use of the sedation scoring system, and are also responsible for monitoring and scoring children undergoing moderate and deep sedation for other procedures.

The overall adverse event rate of 3.3% (3.5% for the >50% group) seen in this study is less than the 8.3% reported by Babl et al.[9] in their report of high-concentration N_2O, but similar to rates found in larger studies of 50% N_2O administration.[3,4] Two of our patients, both of whom received high-concentration N_2O, developed unexplained oxygen desaturation. This rate of 11.4 per 10,000 is similar to the rate of 13.1 per 10,000 reported by Babl et al. As in that study, none of our patients required specific airway intervention other than administration of increased concentration of oxygen or had any clinical evidence of aspiration or laryngospasm. It is unclear whether some of the adverse events in this study were attributable to the administration of N_2O or to the underlying condition of the patient. For example, oxygen desaturation in the child with encephalopathy and an unresponsive episode may have been attributable to seizure or breath-holding rather than a specific response to N_2O.

We did observe an uncommon adverse event, with 2 patients developing seizures temporally associated with

N₂O administration. Although 1 case report in the literature clearly demonstrated the onset of electroencephalographic and clinical seizure activity with N₂O inhalation in an otherwise healthy 9-month-old infant,[23] the cause/effect relationship between N₂O administration and the clinical seizure activity demonstrated by the patients in this study remains speculative and is the subject of an ongoing review.

There are limitations of this study. Only the maximal concentration of N₂O administered was recorded. Our system allows rapid titration of N₂O concentration based on patient response, and titration to a lower concentration during the procedure may have occurred for some of the patients. Only the total time N₂O was administered, not the total time spent at the maximal concentration of N₂O, was used for analysis. In addition, procedures performed during the study period had various degrees of stimulation from noninvasive procedures (e.g., CT scans) to more painful procedures such as botulinum toxin A injections. It could be surmised that a child may reach a deeper level of sedation with less stimulation; however, no attempt was made to quantify the degree of stimulation or correlate with level of sedation for this study.

Conclusions regarding quality of sedation cannot be drawn from this study. Although the majority of procedures were noted as "completed, patient calm and still," the scale used is rather subjective. Although developed by the PSRC as a tool to ascertain whether sedation was not completed because of problems with the sedation itself or because of technical issues not related to the procedural sedation (equipment breakdown, etc.), this scale has not been validated. No information on mask acceptance was collected. One could speculate that poor mask tolerance may have played a role in the inadequately sedated group, whose median age was significantly younger than the whole.

No attempt was made to determine an optimal N₂O concentration for pediatric procedural sedation. Because the anesthetic and analgesic mechanisms of action occur by separate (although perhaps overlapping) pathways,[24] adequacy of analgesia and amnesia may not directly correlate with the level of sedation achieved. N₂O at 70% delivered by full facemask has been shown to be more effective than 50% for venipuncture.[25,26] Whether there is any added advantage to high-concentration N₂O compared with 50% for other procedures and with other delivery devices remains an area for future investigation.

Because a nasal mask was used to deliver N₂O for this study, conclusions cannot be generalized to the delivery of high concentration of N₂O via a full facemask system. Caution must also be observed if N₂O is administered in combination with other sedating medications because the combination increases the likelihood for moderate or deep sedation.[2] Even 30% N₂O may produce deep sedation when administered via a full facemask after premedication with oral midazolam, and a higher concentration (60%) administered after midazolam premedication may result in no response to painful stimulation.[27]

In conclusion, this study suggests that a significant number of children, particularly those older than 2 years, remain minimally sedated while receiving N₂O at concentrations >50% via nasal hood using a system designed to titrate N₂O concentration from 0% to 70%. There was no difference in the level of sedation or adverse events between children administered N₂O at a concentration >50% and those administered ≤50% when delivered in this fashion. The adverse event rate noted with N₂O >50% in this study is similar to rates reported in large studies of N₂O administered at 50% concentration.

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