Preprocedural Fasting State and Adverse Events in Children Receiving Nitrous Oxide for Procedural Sedation and Analgesia

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Study Objective: Established fasting guidelines for analgesia and sedation are difficult to follow in the emergency department (ED), and the association between preprocedural fasting and adverse events has been questioned. We characterize the fasting status of patients receiving procedural sedation and analgesia with nitrous oxide (N_2O) in a pediatric ED and assess the relationship between fasting status and adverse events.

Methods: A prospective case series was conducted in a children's hospital ED over an 8-month period. Patients receiving N_2O for procedural sedation and analgesia were enrolled and followed up by telephone call. Preprocedural fasting state and adverse events, as well as N_2O concentration, adjunctive drugs, and deepest level of sedation, were recorded. Adverse events were analyzed in relation to fasting status.

Results: Two hundred twenty children who underwent procedural sedation and analgesia with N_2O were enrolled. Fasting status was obtained in 218 patients (99.1%). Of these, 155 (71.1%; 95% confidence interval [CI], 64.5%–77.0%) did not meet fasting guidelines for solids There were no serious adverse events and no episodes of aspiration (1-sided 97.5% CI, 0%–1.7%). While in the ED, 46 minor adverse events occurred in 37 patients (16.8%; 95% CI, 12.1%–22.4%). Emesis occurred in 15 patients (7%), including 4 (6.3%; 95% CI, 1.8%–15.5%) of 63 patients who met and in 11 (7.1%; 95% CI, 3.6%–12.3%) of 155 patients who did not meet fasting guidelines for solids. There was no significant difference in median fasting duration between patients with and without emesis.

Conclusion: Seventy-one percent of patients undergoing ED procedural sedation and analgesia with N_2O did not meet established fasting guidelines. In this series, there was no association between preprocedural fasting and emesis. There were no serious adverse events.

Key Words: nitrous oxide, procedural sedation and analgesia

The American Academy of Pediatrics (AAP)[1,2] and the American Society of Anesthesiologists (ASA)[3,4] have published consensus-based preprocedural fasting guidelines for diagnostic and therapeutic procedural sedation. These guidelines are difficult to follow for nonelective emergency department (ED) procedures requiring sedation and analgesia, in particular, in children who are often not fasted and require urgent or emergent procedures.

Data on fasting state and ED procedural sedation and analgesia are limited, but recent studies[5–10] have indicated that there is no association between preprocedural fasting and adverse events. The relationship between fasting status and adverse events during procedural sedation and analgesia with nitrous oxide (N_2O) has not been studied.

The primary objective of our study was to characterize the fasting status of patients receiving procedural sedation and analgesia with N_2O in a pediatric ED. Secondary objectives included assessing the relationship of preprocedural fasting state, N_2O concentration, and depth of sedation with observed adverse events.

METHODS

We conducted a prospective observational study in the ED of a large urban children's hospital with an annual ED census of 60,000 patients.

All children presenting to the ED from August 2003 to March 2004 who underwent procedural sedation and analgesia with N_2O were eligible for enrollment. There were no formal exclusion criteria. This study was approved by the hospital institutional review board.

When a child required procedural sedation and analgesia with N_2O, the examining doctor informed one of the researchers or trained research assistants. Informed verbal consent was obtained and recorded together with arrangements for a follow-up phone call. N_2O sedations were performed by ED medical and nursing staff based on published departmental guidelines[11] which do not specify a defined fasting time for N_2O. N_2O was administered by inhalation of a gas mixture with O_2. The administration was available in 2 forms, demand valve fixed 50% N_2O/50% O_2, marketed as Entonox (BOC Ltd, North Ryde, NSW, Australia), and the continuous-flow system via the Quantiflex (BOC Ltd) MDM machine, which delivers 0% to 70% N_2O and includes a scavenging system to decrease environmental contamination. Procedural sedation and analgesia with any agent in the ED are performed using standardized presedation assessment, monitoring during the procedure, and postsedation discharge criteria.

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A clinical report form was developed to record data before, during, and after procedural sedation and analgesia with N_2O. This included age, past medical problems, ASA class, time of injury (if applicable), procedure, drugs used in addition to N_2O, fasting times for solids and liquids, highest concentration of N_2O used, and deepest level of sedation.

The dietary history section of the questionnaire included date, time, and type and amount of last solid and clear liquid intake. In keeping with established AAP/ASA guidelines,[1–4] solids were defined to include nonclear liquids such as infant formula, breast milk, and nonhuman milk. Clear liquids included but were not limited to water, fruit juices, carbonated beverages, clear tea, and black coffee. Preprocedural fasting duration of the patients for solids and clear liquids was compared with the established ASA guidelines to determine the extent of compliance with these guidelines. ASA guidelines recommend a fasting time of 6 hours for solids and 2 hours for liquids in children older than 6 months.[3,4]

Patients were classified according to ASA physical status classification (class 1, normal healthy patient; class 2, patient with mild systemic disease with no functional limitation; class 3, patient with severe systemic disease with definite functional limitation; 4, patient with severe systemic disease that is a constant threat to life; and 5, moribund patient who is not expected to survive without the operation).

To measure the level of sedation, a sedation scale developed and validated at the Children's Hospital of Wisconsin[9] was used. The scale has 7 levels of sedation ranging from 6 to 0 (6, anxious, agitated or in pain; 5, spontaneously awake without stimulus (talking); 4, drowsy, eyes open or closed, but easily arouses to consciousness with verbal stimulus; 3, arouses to consciousness with moderate tactile or loud verbal stimulus; 2, arouses slowly to consciousness with sustained painful stimulus; 1, arouses, but not to consciousness, with painful stimulus; and 0, unresponsive to painful stimulus). Depth of sedation was assessed on an ongoing basis during the procedure; the deepest level of sedation was recorded on the clinical report form.

Adverse events were defined a priori as serious or mild. Serious adverse events included oxygen desaturation less than 95%, apnea, stridor, airway misalignment requiring repositioning, laryngospasm, bronchospasm, cardiovascular instability, pulmonary aspiration, unplanned hospital admission, endotracheal intubation, permanent neurological injury, or death. Inadequate sedation was not regarded as an adverse event.

Patients were followed up by telephone within 72 hours by one of the researchers to examine the incidence of adverse events after discharge from the ED.

The electronic ED log was reviewed daily for patients who received procedural sedation and analgesia with N_2O who were not included in the study.

All data were entered into SPSS software version 11.5 for Windows (SPSS, Inc, Chicago, Ill) for statistical analysis. Data were analyzed by using descriptive statistics, χ^2 analysis (with Fisher exact test for dichotomous variables), independent-samples *t* test (for continuous parametric data), and Mann-Whitney *U* test (for continuous non parametric data). Fasting status was considered a dichotomous variable (compliant vs noncompliant), and fasting duration (in hours) and age (in months) were considered a continuous variable. Fasting status was analyzed regarding association with emesis in the ED as the time of greatest risk for the patient. Median values are reported as median with interquartile range (IQR). For all tests, values of *P* less than 0.05 were considered statistically significant. Confidence intervals (CIs), power, and sample size calculations were performed on Stata software (version 6.0 Stata Corp, College Station, Tex).

RESULTS

Two hundred twenty patients (age range, 14 months to 17 years; with a median age of 8 years and 3 months) undergoing procedural sedation and analgesia with N_2O were enrolled during the 8-month data collection period. One hundred thirty-two patients (60.0%) were boys. Two hundred seven patients could be contacted for a follow-up call. According to the ASA physical status classification system, 209 patients (95.0%) were classes 1 and 2, and 11 patients (5.0%) were class 3. There were no class 4 or 5 patients.

The proportion of patients receiving various N_2O concentrations is listed in Table 1, with most (82.3%) receiving 70% N_2O. Eleven patients received N_2O via demand valve fixed 50% N_2O/50% O_2 and the remainder via variable concentration continuous-flow N_2O. The 220 patients underwent 235 procedures during the 220 episodes of procedural sedation and analgesia with the main indications listed in Table 2. The most frequent indications were orthopedic procedures (44.6%), laceration repair (21.4%), and vascular access procedures (18.2%). Of the 15 patients who underwent more than one procedure, 12 had additionally an intravenous (IV) line placed, and 3 had a plaster or backslab applied.

Some patients received other drugs in addition to N_2O. Adjunctive drugs are listed in Table 3. Lignocaine infiltration (20.0%) was the most frequent local agent, and morphine (12.3%) was the most frequent systemic agent.

Depth of sedation was observed during procedural sedation, and the deepest level of sedation was recorded in 218 patients (99.1%; Table 4). The majority of patients had scores in a range equivalent to moderate sedation (depth of sedation scores 4 and 5). Fifteen patients (6.9%) were deeply sedated (depth of sedation scores, 0–3); 2 of which had

TABLE 1. N_2O Concentration Used for Procedural Sedation and Analgesia and Adverse Events in the ED

% N_2O	Total (%)	AE (%)	Vomiting (%)
50	28 (12.7)	4 (14.3)	1 (3.6)
60	11 (5.0)	1 (9.1)	0 (0.0)
70	181 (82.3)	32 (17.7)	14 (7.7)
Total	220 (100.0)	37 (16.8)	15 (6.8)

AE indicates adverse event.

TABLE 2. Main Indications for Procedural Sedation and Analgesia With N_2O and Adverse Events in the ED

Procedure	Subtotal (%)	Total (%)	AE (Rate)	Vomiting (Rate)
Orthopedic procedures		98 (44.6)	14 (14.3)	5 (5.1)
Fracture reduction	59 (26.8)			
Application of plaster or backslab, etc	28 (12.7)			
Joint dislocation reduction	11 (5.0)			
Laceration repair		47 (21.4)	9 (19.2)	5 (10.6)
Nonfacial laceration repair	25 (11.4)			
Facial laceration repair	22 (10.0)			
Vascular access procedures		40 (18.2)	9 (22.5)	2 (5.0)
Peripheral IV line placement	39 (17.7)			
Central venous line placement	1 (0.5)			
Foreign body removal		15 (6.8)	1 (6.7)	1 (6.7)
Other		20 (9.1)	4 (20.0)	2 (10.0)
Abscess drainage, incision	5 (2.3)			
Removal of dressing	4 (1.8)			
Wound debridement	2 (0.9)			
Temporary pain relief	2 (0.9)			
Paraphimosis reduction	1 (0.5)			
Application of enema	1 (0.5)			
Pelvic examination	1 (0.5)			
Nasogastric tube placement	1 (0.5)			
Lumbar puncture	1 (0.5)			
Arthrocentesis	1 (0.5)			
Moved patient	1 (0.5)			
Total	220 (100.0)		37 (16.8)	15 (6.8)

received 60% N_2O, and 13 had received 70% N_2O. Fifteen patients (6.9%) were anxious, agitated, or in pain (depth of sedation score, 6).

Fasting Status

Of the 220 patients who underwent procedural analgesia and sedation with N_2O, accurate fasting status was obtained in 218 patients (99.1%; Fig. 1). Of these 218 patients, 63 (28.9%; 95% CI, 23.0%–35.4%) met, and 155 (71.1%; 95% CI, 64.5%–77.0%) did not meet fasting guidelines for solids. Of 218 patients, 39 patients had milk recorded as last drink which was categorized under solids/nonclear liquids. Of the remaining 179 patients, 142 (79.3%; 95% CI, 72.6%–85.0%) patients met, and 37 (20.6%; 95% CI 15.0%–27.3%) did not meet fasting guidelines for clear liquids. Median fasting duration was 4.4 hours (IQR, 3–6.5) for solids and 4.0 hours (IQR, 2.2–6.3) for liquids.

Adverse Events

None of the 220 patients in this study had a serious adverse events, and no airway manipulations, intubations, or unplanned admissions were required. There were no cases of desaturation or clinically apparent pulmonary aspiration (1-sided 97.5% CI, 0%–1.7%). Thirty-seven patients (16.8%; 95% CI, 12.1%–22.4%) experienced 46 mild adverse events in the ED (Table 5). Nine patients experienced more than one mild adverse event. All adverse events were mild and temporary. The most common adverse event was emesis in 15 (6.8%). Of these, 12 patients (80%)

TABLE 3. Adjunctive Drugs in Procedural Sedation and Analgesia With N_2O and Adverse Events in the ED

Adjunctive Drugs	Total (%)	AE (%)	Vomiting (%)
Systemic agents			
Morphine	27 (12.3)	5 (18.5)	2 (7.4)
Paracetamol + codeine	25 (11.4)	4 (16.0)	2 (8.0)
Paracetamol/ibuprofen	14 (6.4)	5 (35.7)	1 (7.1)
Codeine	5 (2.8)	2 (40.0)	0 (0.0)
Midazolam	3 (1.4)	0 (0.0)	0 (0.0)
Local agents			
Lignocaine infiltrate	44 (20.0)	6 (13.6)	3 (6.8)
ALA	16 (7.3)	4 (25.0)	2 (12.5)
AnGel	11 (5.0)	2 (18.2)	2 (18.2)
No adjunctive agents	102 (46.4)	17 (16.7)	6 (5.9)

Some patients had more than one adjunctive drug. ALA indicates amethocaine, lignocaine, and adrenaline (topical); AnGel, amethocaine 4% (topical).

TABLE 4. Deepest Level of Sedation During Procedural Sedation and Analgesia With N_2O and Adverse Events in the ED (n = 218)

Depth of Sedation	Total (%)	AE (%)	Vomiting (%)
0	1 (0.5)	0 (0.0)	0 (0.0)
1	0 (0.0)	0 (0.0)	0 (0.0)
2	1 (0.5)	1 (100.0)	1 (100.0)
3	13 (6.0)	2 (15.4)	1 (7.7)
4	88 (40.3)	19 (21.6)	10 (11.4)
5	100 (45.9)	10 (10.0)	1 (1.0)
6	15 (6.9)	5 (33.3)	2 (13.3)
Total	218 (100.0)	37 (17.0)	15 (6.9)

Deepest level of sedation was not recorded in 2 patients.

vomited during N_2O administration itself; the rest vomited after the procedure was completed and before discharge.

Median age for patients with adverse events in the ED was 106 months (IQR, 73–142), and for patients without adverse events, 94 months (IQR, 62–131; $P = 0.20$). Median age for patients with emesis was 93 months (IQR, 63–134), and for patients without emesis, 100 months (IQR, 63–133 months; $P = 0.98$).

Patients who received 70% N_2O vomited twice as often (7.7%) as patients receiving 50% N_2O (3.6%; Table 1). However, when comparing 70% N_2O versus either 50% or 60% N_2O, the difference in the rate of adverse events ($P = 0.71$) or vomiting ($P = 0.47$) was not statistically significant.

A summary of the patients who vomited is listed in Table 6. Of the 15 patients who vomited in the ED, 12 vomited during the procedure, and 8 had received more than 10 minutes of N_2O administration before vomiting. However, patients vomited as early as 1 minute after commencing N_2O administration. Fourteen patients received 70% N_2O. Four received additional codeine or morphine.

There was no clear pattern in the relationship between adverse events and the type of procedure as shown in Table 2.

The adverse events rate for each drug regimen is listed in Table 3. There was no association between the addition of other drugs to N_2O and adverse events ($P = 0.55$) or vomiting ($P = 0.91$).

When comparing patients who achieved a sedation score of 3 or less (deep sedation) with patients with a depth of sedation score more than 3, there was no association between depth of sedation and adverse events ($P = 0.75$) or vomiting ($P = 0.31$; Table 4).

Adverse Events and Fasting Status

There was no statistically significant difference in emesis rate in patients who met and did not meet fasting guidelines. Emesis in the ED occurred in 4 (6.3%; 95% CI, 1.8%–15.5%) of 63 patients who met and in 11 (7.1%; 95% CI, 3.6%–12.3%) of 155 patients who did not meet fasting guidelines for solids ($P = 0.84$). Likewise, there was no significant difference in the fasting duration of patients with and without emesis. For solids, median fasting duration for patients with emesis was 4.2 hours (IQR, 2.92–6.2), and without emesis, 4.4 hours (IQR, 3.0–6.6; $P = 0.63$). For liquids, median fasting duration for patients with emesis was 3.8 hours (IQR, 2.5–6.2), and without emesis, 4.0 hours (IQR, 2.2–6.4; $P = 0.77$).

A visual breakdown of fasting duration (for both solids and clear liquids) in 2-hour increments with associated numbers of cases of adverse events and emesis is depicted in Figure 1. Between 0 and 8 hours, cases of adverse events and emesis are distributed evenly throughout the different fasting durations, highlighting the observed lack of association between preprocedural fasting state and adverse events.

Follow-up

Of the 207 patients (94.1%) with follow-up phone call, 37 patients (17.9%) experienced 44 mild adverse events after discharge. The most frequent adverse events experienced were nausea (12; 5.8%), emesis (8; 3.6%), and nightmares (7; 3.4%; Table 5). Table 5 also shows the distribution of patients who experienced side effects at any time whether in the ED or after discharge. It shows that overall emesis (9.5%), nausea (7.3%), and dizziness (7.3%) were the most frequent adverse events experienced by patients. Of the 15

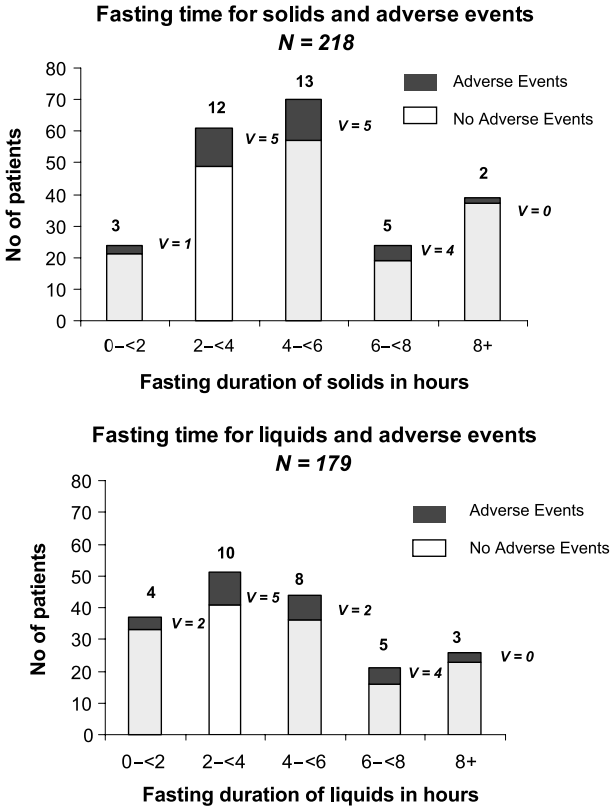

FIGURE 1. Breakdown of fasting duration for solids (n = 218) and clear liquids (n = 179) in 2 hour increments (see text). Associated numbers of cases of adverse events in the ED (located above the dark sections of the bars) and emesis (V; located to the right side of the bars).

TABLE 5. Adverse Events Associated With Procedural Sedation and Analgesia With N_2O

Adverse Events	Total (%)	ED (%)	After Discharge (%)
Vomiting	21 (9.5)	15 (6.8)	8 (3.9)
Nausea	16 (7.3)	4 (1.8)	12 (5.8)
Dizziness	16 (7.3)	10 (4.5)	6 (2.7)
Agitation	8 (3.6)	8 (3.6)	0 (0.0)
Nightmares	7 (3.2)	0 (0.0)	7 (3.4)
Restlessness	5 (2.3)	0 (0.0)	5 (2.3)
Hallucinations	4 (1.8)	4 (1.8)	0 (0.0)
Impaired coordination	3 (1.4)	0 (0.0)	3 (1.4)
Other*	8 (3.6)	5 (2.3)	3 (1.4)

Total indicates number of patients who encountered an adverse event either in the ED or after discharge.

*Other—in ED: tingling feeling (2), excitement (1), vibrating feeling (1), fainted (1); after discharge: headache (1), increased urination (1), numbness (1).

patients who vomited in the ED, 2 patients also experienced emesis after discharge from the ED.

LIMITATIONS

This study has several limitations. Despite being the largest series of ED use of N_2O, one of the main limitations is the small number of patients enrolled relative to the frequency of serious adverse events. In our study, there were no serious adverse events and, in particular, no pulmonary aspirations. Pulmonary aspiration is a very rare event, and in general anesthesia, a recent study[12] calculated the pooled incidence of aspiration to be 1:3420. In a review of pediatric sedations in various settings over 27 years, Cote et al[13] found no cases of pulmonary aspiration. Hoffman et al,[9] in a hospitalwide study of 960 pediatric sedations, described 2 cases of aspiration, although outside the ED, in fasted patients. In 1014 procedural sedations in a pediatric ED using various agents, 68 patients (6.7%) experienced adverse events, but there were no aspirations.[5] At this time, there are no data to indicate the frequency of pulmonary aspiration in procedural sedation and analgesia with N_2O. Although emesis is a limited proxy for pulmonary aspiration, we undertook a sample size calculation of the patients needed to show a difference in emesis rates for patients who met and who did not meet fasting guidelines. The calculations were limited by the lack of available data on fasting status and N_2O use and emesis rate and variable concentration N_2O use (50%–70%). However, assuming an emesis rate of 5% for fasted and 10% for unfasted patients and a distribution of 30% patients in the fasted and 70% in the unfasted group, 1080 patients would have been required to detect a difference at 80% power with an α level of 0.05. This would have required several years of data collection and would not have been feasible. In addition, the results of our study indicate an even smaller difference in the emesis rate between fasted and unfasted patients. Therefore, an even larger number of patients would be necessary for this study to be sufficiently powered to detect a difference between the fasted and unfasted patients.

Another limitation of this study is that a number of procedures under N_2O during the study period were missed. This was mainly due to a limited availability of research assistants and researchers in the ED and the dependence on ED clinicians to complete the data collection tools in their absence. Based on a review of the electronic ED log, 60 eligible patients were not enrolled during the study period. The age distribution and diagnosis of unenrolled patients were similar to the study group, although data on fasting times and adverse events could not be ascertained in the missed patients. However, there were no serious adverse events, endotracheal intubations, or unexpected admissions of unenrolled patients.

We did not explore why clinicians fasted some patients longer than others beyond availability of staff and equipment. Although current departmental guidelines[11] do not specify a defined fasting time for N_2O, it is possible that clinicians deliberately fasted some patients longer than others for a variety of reasons introducing a potential source of bias.

Furthermore, not all patients were followed up mainly because parents were unavailable for telephone follow-up or rarely because they did not give their permission to call.

DISCUSSION

Consensus-based AAP/ASA guidelines for procedural sedation and analgesia have been widely disseminated,[1–4] but the guidelines are difficult to follow in the ED setting, and data in the medical literature to support their use in the ED are lacking.[12,14] The high percentage of ED patients undergoing procedural sedation and analgesia not conforming to sedation guidelines has recently been documented in a large series.[5] We studied the fasting status of children receiving ED procedural sedation and analgesia with N_2O, which has not been studied before.

We found that 66% of the 218 patients with documented dietary history who underwent procedural sedation and analgesia with N_2O did not meet AAP/ASA preprocedural fasting guidelines. Many studies of N_2O use as a procedural agent do not include fasting information.[15–22] In 2 studies that used 50% N_2O, patients were not fasted[23,24]; in 3 studies using 30% to 50% N_2O, patients were fasted for 2 hours,[25–27] and in 1 study of 50% to 70% N_2O, patients were fasted for 4 hours for solids and 2 hours for clear liquids.[28] None of these studies have investigated the relationship between fasting status and adverse events. In our study, fasting status was not related to adverse events.

This adds to a small but growing body of literature, indicating a lack of association between fasting status and adverse events in procedural sedation and analgesia. Agrawal et al[5] found that, in 905 pediatric ED patients, 56% were not fasted according to AAP/ASA guidelines and that there was no significant difference in median fasting duration between patients with and without adverse events and between patients with and without emesis. Only 14 of these patients had received N_2O. In a study of 2085

TABLE 6. Description of Patients Who Experienced Emesis While Receiving N_2O in the ED (n = 15)

Age (y)	Sex	ASA Class	Sedation Indication	N_2O %	Max DOS	Adjunctive Drugs	Fasting Duration (h)		Length of N_2O (min)	Vomiting Time* (min)	Vomiting After Discharge	Other AEs
							Solids	Liquids				
2.9	M	II	Facial laceration repair	70	4	Lignocaine infiltrate	4.58	3.63	14	14	No	None
3.1	M	I	Removal of foreign body	70	4	Lignocaine infiltrate	0.78	N/A	20	20	No	None
5.1	M	I	Facial laceration repair	70	2	ALA	6.25	5.25	22	30	No	None
5.3	F	II	Nasogastric tube insertion	70	6	None	3.00	6.00	10	8	Yes	Agitation
5.1	F	I	Joint dislocation reduction	70	4	Morphine	2.92	2.92	7	25	No	None
5.1	M	I	Fracture reduction	70	4	AnGel, paracetamol + codeine	4.22	4.22	13	13	No	None
6.2	M	III	Peripheral IV line placement	50	5	AnGel	7.63	N/A	16	22	No	None
7.9	M	I	Removal of dressing	70	4	None	4.83	6.33	14	1	No	Dizziness
7.1	M	I	Other laceration repair	70	4	None	2.37	2.62	9	9	No	None
8.6	M	I	Fracture reduction	70	3	Paracetamol + codeine	3.83	3.83	25	25	No	None
8.7	F	I	Other laceration repair	70	4	Paracetamol, ALA, lignocaine infiltrate	4.00	7.50	15	8	No	None
11.2	M	I	Other laceration repair	70	6	None	2.47	2.47	6	4	No	Agitation, hallucination
14.1	F	I	Joint dislocation reduction	70	4	None	6.45	0.70	10	10	Yes	None
15.1	M	I	Application of plaster/ backslab	70	4	Morphine	6.92	6.92	35	35	No	None
17.4	F	III	Peripheral IV line placement	70	4	None	5.83	0.83	10	6	N/R	None

Max DOS indicates deepest level of sedation; N/A, not applicable; N/R, not recorded.
*Vomiting time was measured from the time N_2O was commenced.

pediatric ED patients receiving parenteral sedation, Roback et al[10] found that the incidence of adverse events was unrelated to fasting duration. In a study of 260 pediatric ED patients undergoing orthopedic procedures with fentanyl/midazolam or ketamine/midazolam, mean fasting duration for patients with emesis was 4.4 ± 2.5 hours compared with 5.0 ± 2.4 hours for those without emesis ($P = 0.40$).[8] In a study of 257 children undergoing ED procedural sedation with IV ketamine, 30 children had fasted for less than 1 hour; 100, 1 to 2 hours; and 127, longer than 3 hours. There was no emesis during the procedures, but emesis rates after the procedure increased with increased fasting duration from 6.6% to 14% to 15.7%, respectively, although this was not statistically significant.[6] In a retrospective study of 324 children undergoing sedation with chloral hydrate for echocardiography fasting for less or longer than 120 minutes did not lead to a statistically significant difference in the rate of emesis ($P = 0.74$).[7] In a hospitalwide study of 960 pediatric patients undergoing procedural sedation with a range of agents (not including N_2O),[9] adherence to preprocedural fasting guidelines did not affect the overall risk of complications.

Our study, the largest series of ED use of N_2O to date, indicates that this is a safe agent for procedural analgesia and sedation without serious adverse events and with a low rate of temporary mild adverse events. In a number of pediatric studies with N_2O concentrations ranging from 30% to 70%, no serious adverse have been reported.[15–18,20–30] In a large French survey series of 7571 children receiving demand valve 50% N_2O, a major adverse events rate of 0.3% is reported without specific details, although all adverse events resolved within minutes, and no patient needed airway intervention.[19] Minor adverse events are reported at variable rates. The French study mentioned reported a minor adverse events rate of 5%,[19] and the same group reported a minor adverse events rate of 37% and an emesis and nausea rate of 3.7% in 1019 children in a further study of demand valve 50% N_2O.[18] Henderson et al[21] reported a mild adverse events rate of 0% for 50% N_2O and 28% for 70% N_2O with no emesis in 39 and 43 children, respectively. The emesis rate of 7% in the ED in our study is similar to other reports.[17,25,28]

We found that a not negligible number of our patients had mild adverse events after discharge. In particular, 5% of patients vomited after discharge. This needs to be communicated with parents. Most studies of N_2O as an agent for procedural sedation and analgesia do not include follow-up information.[16–24,26–29] One study provides follow-up data after N_2O use as an agent for ED procedural sedation and analgesia. Luhmann et al[25] found no emesis after discharge in 103 patients who received continuous-flow 50% N_2O with or without midazolam.

We also found that N_2O caused deep sedation in 7% of patients undergoing procedural sedation and analgesia, a higher rate than previously reported. A limited number of studies of N_2O assess and report depth of sedation using a variety of assessment tools.[15,16,18,19,25,26,28,29] In 46 patients receiving 30% N_2O, none were sleepy or oversedated.[26] In 170 patients receiving continuous-flow 40% N_2O, all patients were conscious and responsive to verbal contact on a 6-point sedation scale.[15] In the 2 large French series of demand valve 50% N_2O, 25 (0.33%) of 7511 children were described as having a major adverse event including oversedation (defined as a loss of verbal contact),[19] and in the series of 1019 sedations, 2.1% were deeply sedated.[18] This was categorized as a minor adverse event, and depth of sedation was not further defined.[18] In 51 patients receiving continuous-flow 50% N_2O, 14 were found to be awake, 34 responsive to voice, 3 responded to pain, and none were unresponsive based on AVPU scores (alert, responsive to voice, responsive to pain, and unresponsive).[25] In 40 patients receiving continuous-flow 50% N_2O, no patients were unrousable (0) or asleep but rousable[1] based on a 0- to 3-point sedation scale.[16] Kanagasundaram et al[28] using continuous-flow 50% to 70% N_2O in 90 children, using the same scoring system, found 1% of patients to be asleep but rousable (1) and none to be unrousable (0). In a study of 82 patients either receiving 50% or 70% N_2O, none lost consciousness.[21]

Clinicians using N_2O in the ED setting at concentration greater than 50% need to be aware of and prepare for the potential to cause deep sedation. There were no serious adverse events in more deeply sedated patients in our study, but deeper sedation in general has been found to be associated with an increased risk of adverse events.[5,9] In a study of 25 children receiving 20% to 65% N_2O, Roberts and Wignall[31] found that the laryngeal reflex was maintained when radiopaque material was placed on the tongue during dental procedures. However, the combination of deep sedation and intraprocedural emesis theoretically conveys a high risk of aspiration.

In summary, we characterized fasting state and adverse events in procedural sedation and analgesia in the ED setting. We found that the majority of patients who were sedated were not fasted according to AAP/ASA fasting guidelines for procedural sedation and analgesia, and noncompliance with these guidelines did not affect the rate of adverse events, including emesis. Procedural sedation and analgesia with N_2O when embedded in comprehensive presedation and postsedation management by trained ED staff result in a low adverse events rate.

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