RESEARCH ARTICLE

Ketamine Sedation After Administration of Oral Contrast: A Retrospective Cohort Study

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ABSTRACT

BACKGROUND: The American Academy of Pediatrics and American Society of Anesthesiologists have published consensus-based fasting guidelines intended to reduce the risk of pulmonary aspiration. The purpose of our study was to compare the rate of adverse events in patients sedated with ketamine within 2 hours of oral contrast intake to those who were nil per os (NPO).

METHODS: A retrospective cohort review of a database of children between July 2008 and May 2011. The rate of adverse events in children sedated with ketamine after intake of oral contrast for an abdominal computed tomography were compared with those sedated without taking oral contrast.

RESULTS: One hundred and four patients sedated for a computed tomography scan; 22 patients were sedated within 2 hours of taking oral contrast, and 82 were NPO. The 2 groups were comparable with regard to gender, race, and American Society of Anesthesiologists status. The mean (SD) time between the second dose of oral contrast and induction of sedation was 58 (24) minutes. Vomiting occurred in 4 of 22 patients in the oral contrast group (18%; 95% confidence interval 2%–34%) and 1 of 82 patients in the NPO group (1%; 95% confidence interval, 0%, 4%; $P < .001$). There was no difference in oxygen desaturation between the groups ($P = .6$).

CONCLUSIONS: Children who received oral contrast up to 58 minutes before ketamine sedation had a higher rate of vomiting than those who did not receive oral contrast. We did not identify cases of clinical aspiration, and the incidence of hypoxia between the 2 groups was not statistically significant.

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The American Academy of Pediatrics and the American Society of Anesthesiologists (ASA) have published consensus-based preprocedural fasting guidelines for diagnostic and therapeutic procedural sedation. They recommend patients fast from intake of clear liquids at least 2 hours before elective procedures requiring general anesthesia, regional anesthesia, or sedation/analgesia. This guideline is intended to reduce the risk of pulmonary aspiration of gastric contents and facilitate the safe and efficient conduct of sedation.[1,2]

Previous studies have indicated that there is no association between preprocedural fasting and adverse events in emergency department settings.[3] The safety of administering enteric contrast for computerized tomography (CT) <2 hours before sedation has been studied. Ziegler et al showed that 367 patients who received sedation (337 with pentobarbital and 30 with chloral hydrate) had no associated complications to oral contrast administration.[4] The practice of administering oral contrast material within 2 hours of propofol sedation for abdominal CT in children has also been shown to be relatively safe compared with those kept traditional nil per os (NPO) for similar procedures.[5] Unlike propofol and other sedative agents, ketamine sedation is independently associated with a higher incidence of vomiting.[6] Vomiting during such sedation could theoretically increase risk of pulmonary aspiration.[7] However, patients undergoing sedation after oral contrast intake within 2 hours of ketamine sedation has not been adequately characterized.

The purpose of our study was to compare the rate of adverse events in patients sedated with ketamine within 2 hours of oral contrast intake to those who were kept NPO.

METHODS

For the purpose of continuous quality improvement, we established a patient sedation database. Demographics and sedation-related variables are entered into the database daily. We conducted a retrospective cohort study in which we evaluated the database of children sedated in an inner-city tertiary care children's hospital sedation program between July 2008 and May 2011. The study was approved by the institutional human research review board.

Children sedated with ketamine within 2 hours of taking oral contrast for an abdominal CT were designated as the "oral contrast group." All ketamine sedations performed during the same time period who were NPO (subjects not allowed to ingest clear fluids ≥2 hours, 4 hours for breast milk, and 8 hours for solids before sedation) were designated as the NPO group.

The following data were extracted: age, gender, physical status classification as defined by the ASA,[8] time between oral contrast and induction of sedation, volume of oral contrast with diluents for oral contrast group, ketamine dose, midazolam dose, and adverse events including failed sedation (the inability to achieve adequate level of sedation to perform the procedure and premature arousal/movement before completion of study); abnormal oxygen saturation level (oxygen saturation ≤95%); apnea (cessation of breathing for >20 seconds); vomiting, suctioning, use of oxygen or any other event of risk deemed to be caused by the sedative. Patients with any missing data element in the database were excluded from the study.

All participants, from both the outpatient and inpatient units, were electively scheduled for sedation. All were kept NPO based on recommendation from the American Academy of Pediatrics and the ASA[1,2] except for oral contrast in the oral contrast group who underwent an abdominal CT. In accordance with hospital policy for sedation; respiratory rate, heart rate, blood pressure, and pulse oximetry were monitored continuously from the time of induction to discharge. The sedation area was equipped with airway management devices (including oxygen, masks, laryngoscopes, endotracheal tubes of various sizes, and suction devices) and staffed with personnel competent in pediatric sedation and airway management.

Sedation level was measured using the Ramsay Sedation Scale. This scale assigns a score of 1 to 6 based on clinical assessment of the level of sedation. A score of 4 was accepted as an adequate level of sedation for the procedure.[9] Patients were determined to be eligible for discharge when they achieved a score of 10 according to the Aldrete criteria.[10]

On the basis of institutional guidelines, ketamine was administered intravenously at an initial dose of 1 to 2 mg/kg with intravenous midazolam administered as a 0.5 to 1 mg/dose (maximum of 2 does) until sufficient sedation was achieved to perform the CT.

At our institution, abdominal CT scan with oral contrast was preferred during the study period. These patients were administered age-based volumes of oral contrast with diluents separated into 2 doses: one 4 hours before scan and one 30 minutes before scan (Table 1).

The primary outcome variable was rate of vomiting in cases and controls. Secondary outcome variables include rate of oxygen desaturation, apnea, and failure to sedate.

We described children who took oral contrast and children in the control group in terms of mean age and frequencies for gender, race, and ASA status. Two-sample independent t test was used to compare differences in the mean age and ketamine dose. Differences between gender, race, ASA status, and rate of adverse events between cases and controls were compared using the Pearson χ^2 test. Exact 95% confidence intervals (CI) are reported when appropriate. Statistical significance was accepted for $P < .05$. All statistical tests were performed using the Statistical Package for the Social Sciences software (SPSS Inc, version 20.0; Chicago, IL).

RESULTS

We identified 104 children sedated with ketamine during the study period. Twenty-two patients were sedated within 2 hours of taking oral contrast, and 82 were NPO. No patients were excluded. There was no overlap between the 2 groups. Descriptive characteristics of the groups are presented in Table 2. Patients in the oral contrast group were younger than those NPO (mean age (SD): 1.9 (0.6) years versus 2.3 (1.2) years ($P = .001$). There was no difference in

TABLE 1 Oral Contrast Protocol for Abdominal CT by Age (Gastrografin)

Age	Protocol
Newborn–6 mo	2–4 mL mixed in clear fluids ×2
6 mo–1 y	6 mL mixed in 180 mL clear fluid ×2
2 y	8 mL mixed in 240 mL clear fluid ×2
3 y	9 mL mixed in 270 mL clear fluid ×2
6 y	12 mL mixed in 360 mL clear fluid ×2
10 y	16 mL mixed in 540 mL clear fluid ×2

One dose to be given 4 h before and 1 dose 30 minutes before scan.

gender, race, ASA status, or ketamine dose between the groups. Seven (32%) and 6 (27%) of patients in the oral contrast group, had a primary diagnosis of neuroblastoma and Wilm's tumor, respectively (Table 3). Patients in the NPO group did not have an abdominal mass as a primary diagnosis.

The mean (SD) volume of the second dose of oral contrast ingested before the study was 228 (46) mL, the mean (SD) time between the second dose of oral contrast and induction of sedation was 58 (24) minutes, and the mean (SD) dose of ketamine was 1.9 (0.35) mg/kg in oral contrast group and 1.9 (0.44) mg/kg in NPO group ($P = 0.9$).

Five (23%; 95% CI: 5%–40%) oral contrast and 3 (4%; 95% CI: 0%–8%) in the NPO group experienced a respiratory adverse event or vomiting ($P = .002$). The most common adverse event was emesis in 4 oral contrast patients (18%; 95% CI: 2%–34%) and 1 NPO group patient (1%; 95% CI, 0%–4%; $P < .001$). Of these, 3 cases vomited while sedated; 1 vomited after the procedure was completed and before discharge. There was no statistically significant difference in the rate of hypoxia between oral contrast 1 (5%; 95% CI: 0%–14%) and NPO group 2 (2%; 95% CI: 0%–5%; $P = 0.6$) (Table 4). The hypoxia was transient in both groups, both responded to head positioning and supplemental oxygen.

DISCUSSION

Our results demonstrate a statistically significant increase in vomiting in patients who received oral contrast before ketamine sedation compared with those who were kept NPO in our patient population. NPO guidelines have been examined with regard to safety with other sedative agents. Ziegler et al examined the safety records in 367 patients who received oral contrast material before sedation for abdominal CT with chloral hydrate in 30 patients and pentobarbital in 337. The results showed that vomiting occurred in 4 cases (1%).[4] Babl et al studied adverse events in nitrous oxide sedation and found that there was no statistically significant difference in emesis rate in patients who met and did not meet fasting guidelines.[11] Also, Kharazmi et al in a cohort of 85 patients showed that the practice of administering oral contrast material within 2 hours of propofol sedation for abdominal CT in children seems to be relatively safe compared with those kept traditional NPO for similar procedures.[5] Its use for induction and maintenance of anesthesia has been associated with a lower incidence of postoperative nausea and vomiting[12]; this finding could be because of propofol's inherent antiemetic effect. In contrast, ketamine sedation has been shown to be associated with higher rates of vomiting compared with other agents, with rates ranging from 4% to 8% irrespective of fasting status.[3,13,14] This can explain why ketamine when used in a setting of full stomach was associated with a higher rate of vomiting.

Fasting is intended to reduce the risk of pulmonary aspiration of gastric contents and facilitate the safe and efficient conduct of sedation and anesthesia.[15] The emptying of clear liquids follows first-order kinetics; that is, the rate of emptying is proportional to the volume present.[16] Raidoo et al found that in a primate model, the maximum acid aspirate volume that will not cause damage to the lungs is 0.8 mL/kg.[17] Although increased gastric contents theoretically increase the risk of aspiration pneumonia, there is no known gastric fluid volume (GFV) that places a particular patient at clinically relevant risk or eliminates all the risk. GFV has been used as a surrogate marker for pulmonary aspiration risk in studies evaluating fasting protocol safety.[18,19] In our study population, the mean volume of oral contrast ingested less than 1 hour before induction was 228 ± 46 mL. Even though it is not possible to objectively predict GFV from the amount ingested,[20] it would be reasonable to assume that the amount of fluid ingested within 57 minutes of induction of sedation can leave a significant amount of contrast in the stomach depending on the rate of gastric emptying.

Ketamine is a unique agent in procedural sedation and analgesia in that it is a "dissociative" anesthetic that functions by blocking communication between the thalamic and limbic regions of the brain,

TABLE 2 Demographic Characteristics of Children Sedated With Oral Contrast and Kept NPO

Characteristics	Oral Contrast ($n = 22$)	NPO ($n = 82$)	P
Median age (y) (SD)	1.9 (0.6)	2.3 (1.2)	.001
Male gender (%)	14 (64)	41 (50)	.3
Race (%)			
Caucasian	13 (59)	35 (43)	.2
African American	7 (32)	32 (39)	.5
Other	2 (9)	15 (18)	.3
ASA status (%)			
I	13 (59)	37 (45)	.2
II	8 (36)	45 (55)	.1
III	1 (5)	0 (0)	.05
Ketamine dose (mg/kg) (SD)	1.9 (0.35)	1.9 (0.44)	.9

TABLE 3 Primary Diagnosis of Children Sedated With Oral Contrast

Primary Diagnosis	Frequency *n* (%)
Neuroblastoma	7 (32)
Wilms tumor	6 (27)
Teratoma	3 (14)
Rhabdomyosarcoma	1 (5)
Splenomegaly	1 (5)
Lymphadenopathy	1 (5)
Renal cyst	1 (4)
Abdominal mass	1 (4)
Germ cell tumor	1 (4)

thereby preventing the brain from processing external stimuli.[21] It provides excellent sedation, amnesia, and analgesia and preserves muscle tone, maintaining protective airway reflexes and spontaneous respiration.[22,23] Although a short-acting sedative is an ideal agent for elective CT scans, during our study period, ketamine was chosen because of previous experience with successful sedations and limited choices for the sedation team.

Although effective for procedural sedation, vomiting with ketamine is frequently encountered. In the largest 2 emergency department (ED) ketamine series, the incidence of predischarge vomiting was 7% and 8%. Green et al analyzed a meta-analysis of a database that included 8282 ketamine sedations from 32 reports. They concluded that the most important independent predictors of emesis were high intravenous dose (initial dose of 2.5 mg/kg or a total dose of 5.0 mg/kg), intramuscular route, and increasing age (peak at 12 years).[24] Our cases were sedated with less than 2 mg/kg of ketamine intravenously and mean age of <2 years.

Despite its increased use in ED procedural sedation, clinically apparent pulmonary aspiration has never been reported during procedural sedation in children but vomiting during such sedation could theoretically increase its risk.[7,25] Our study showed no difference in the rate of oxygen desaturation between the oral contrast and NPO groups despite higher rate of vomiting in the oral contrast group sedated with ketamine. Ketamine's ability to preserve muscle tone, maintaining protective airway reflexes can be a theoretical reason why pulmonary aspiration was not seen even in the presence of higher incidence of vomiting with this agent, although our study was not powered to conclusively prove this.

Patients sedated in clinical departments such as the ED may have rates of gastric emptying that vary from those of healthy patients on whom NPO guidelines are based. Trauma is a frequent and clinically significant cause of gastroparesis or significantly delayed gastric emptying. A death related to the aspiration of contrast material has been reported in an adult who had abdominal CT evaluation for trauma. Several cases of aspiration of contrast material in children who underwent CT as part of a trauma evaluation have also been reported. These cases have spurred much debate concerning the safety of administering enteric contrast material for CT examination of trauma patients.[26–28] Also, Hoffman et al in a study population of 960 patients identified adverse events or complications in 40 (4.2%) sedations. Nine patients became hypoxic, and 2 pediatric cases of aspiration occurred during sedation, both of whom met NPO criteria.[29]

Multiple patient variables should be considered when sedating pediatric patients. In addition to NPO status, one should be cognizant of the fact that variables, including gastric volume at the time of sedation, agents used for sedation, associated comorbidities that might delay gastric emptying or predispose to emesis, and compromised ability to protect the airway play a role in assessing risk for aspiration.

TABLE 4 Complication Rates of Children Sedated With Oral Contrast ($n = 22$) and Those Kept NPO ($n = 82$)

Complications	Oral Contrast, *n* (%; 95% CI)	NPO, *n* (%, 95% CI)	*P*
Hypoxia	1 (5; 0%–14%)	2 (2; 0%–5%)	.6
Vomiting	4 (18; 2%–34%)	1 (1; 0%–4%)	.001

There are several limitations to this study. The retrospective study design limited the data to what was documented by the sedation service providers. Some adverse events may not have been captured by the current study design because we did not follow up patients once they were discharged from the sedation unit. Adverse events, including emesis, could have occurred on the way home or at home. Patients may have been admitted with complications such as aspiration without our knowledge. Given that all patients were required by our protocol to be at baseline (awake and alert) before discharge, we would not expect any significant adverse events to have occurred after discharge.

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 rare event. A recent review of aspiration during procedural sedation and analgesia pooled the data on aspiration risk during general anesthesia and found the overall incidence of aspiration to be 1:3, 420.[25] Projecting data from the anesthesiology literature, one would need an extremely large denominator for adequate power to ascertain risk factors for aspiration during sedation and analgesia. However, these data are based on patients who fasted in accordance to the national guideline. The results of our study indicate a difference in the rate of vomiting between fasted patients and those who ingested contrast as prescribed before their examination. The absence of aspiration in our study could be due to either a small sample size or ketamine's ability to preserve muscle tone maintaining protective airway reflexes.

The higher rate of vomiting in the oral contrast group is not easily explained and may be secondary to factors that we did not systematically collect, such as ancillary medications or primary diagnosis. It is interesting that those in the oral contrast group had abdominal masses, which certainly may be a contributor to increased vomiting and may have shown statistical significance if our numbers were larger.

Considering the rare practice of sedating children with a full stomach, it would not be feasible to collect a large sample size sufficiently powered to detect the risk of aspiration. Our data add to the sedation literature and provide numerical data for future meta-analysis.

In conclusion, children who received oral contrast up to 57 minutes before ketamine sedation had a higher rate of vomiting than those who did not receive oral contrast. However, there was no evidence of aspiration, or higher incidence of adverse events such as apnea or oxygen desaturation. We advise consideration of ketamine associated vomiting for patients who require oral contrast within 2 hours before an abdominal CT.

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