

Effect of Preemptive Acetaminophen Administered Within 1 Hour of General Anesthesia on Gastric Residual Volume and pH in Children

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Purpose: Determine whether preoperative oral acetaminophen increases gastric residual volume and lowers gastric pH.

Design: Prospective, randomized.

Methods: Healthy children, 1 to 14 years, having elective magnetic resonance imaging (MRI) were randomized to oral acetaminophen within 1 hour of induction versus fasting. Gastric volume and pH were measured immediately after intubation. Adverse events were documented from induction through 72 hours post MRI.

Findings: Thirty-seven children completed the study (16 treatment, 21 control). Gastric residual volume between groups was not significantly different. The acetaminophen group had significantly higher pH than control group (1.86 ± 0.42 vs 1.56 ± 0.34 ; $P \leq .044$). Three children in the control and 6 in the treatment group experienced minor adverse events.

Conclusions: Findings suggest administering oral acetaminophen prior to induction of anesthesia is not associated with increased gastric residual volume and increases the gastric pH. Further study is needed to examine outcomes such as aspiration pneumonitis risk.

Keywords: gastric volume, gastric pH, aspiration, acetaminophen.

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Conflict of interest: none to report.

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THE USE OF PREEMPTIVE nonopioid analgesics has been found to reduce surgical pain while decreasing opioid consumption and associated adverse effects.¹⁻⁷ Children who undergo surgery, however, often do not have intravenous lines in place before anesthesia, and thus, preemptive analgesia with the nonopioid acetaminophen is often administered either orally or rectally.⁷ Given the increased bioavailability of the oral route, this is the preferred method. Yet, oral administration of acetaminophen immediately before surgery has raised concerns regarding the potential risk for pulmonary aspiration. Pulmonary aspiration of gastric contents and subsequent pneumonia or pneumonitis during the perioperative period can be devastating and is one of the most dreaded

complications of general anesthesia, albeit rare with reported incidences ranging from 0.02 to 0.2%.⁸⁻¹² Importantly, the risk of aspiration is linked not only to the presence of gastric contents, but also to the volume and acidity (ie, pH level) of the contents. It has been demonstrated that a gastric content pH less than 2.5 increases risk of chemical pneumonitis because of caustic actions of acids on epithelial cells in the airway followed by an acute inflammatory response.^{13,14} Preoperative guidelines specify fasting times for both solids and clear liquids to minimize gastric volume, but typically are not clear on whether administration of oral medications is permissible and safe.

Previous studies evaluating the effects of oral premedication on the volume and pH of gastric contents after induction of anesthesia have yielded mixed results depending on the medications administered.^{7,15,16} For instance, administration of paracetamol was found to have minimal effects on the volume of gastric contents whereas anticholinergics such as glycopyrrolate and atropine were in fact associated with decrease in volume and increased pH of gastric contents.^{7,15} Anderson et al⁷ also note with few exceptions (monoamine oxidase inhibitors and tricyclic antidepressants) that anesthesia providers allow children to have routine medications up until surgery with no reported complications as a consequence of this practice.⁷ However, it remains unclear whether large volumes of medications such as those sometimes required with liquid acetaminophen add risk. This prospective randomized controlled investigation was undertaken to determine whether there is a difference in gastric residual volume and gastric content pH between children who receive oral acetaminophen in the immediate preoperative period compared with those who are not given this premedication.

Hypothesis

We tested the hypothesis that children who received oral acetaminophen within 1 hour of induction of general anesthesia would have a higher gastric volume and lower pH of their gastric contents when measured just after induction compared with children who did not receive oral acetaminophen.

Methods

After the approval of the Institutional Review Board and informed consent from parents and assent from children as appropriate, healthy children (ie, ASA physical status I and II) aged 1 to 14 years scheduled for an elective magnetic resonance imaging with general anesthesia were recruited. Patients with known disorders of gastric motility, absorption, gastrointestinal reflux, those with metabolic or liver dysfunction, obesity (greater than 20% over ideal body weight), or acetaminophen allergy were excluded. In addition, we excluded those whose anesthetic plan did not include endotracheal intubation. All children met standard Anesthesia Guidelines for nil per os of solids (6 hours) and clear fluids (2 hours) before inclusion.

Patients were randomized to one of two groups, treatment versus control. The treatment group received liquid oral acetaminophen 15 mg/kg approximately 30 to 60 minutes before the scheduled procedure per our institution's general preoperative practice. The control group received no preemptive acetaminophen. Research observers, postoperative care providers, and anesthesia providers were blinded to whether the subjects received preoperative oral acetaminophen. Neither group was given any other oral medication before induction.

A trained research observer recorded the exact time and nature of anesthesia induction and intubation and recorded any adverse event including coughing, gagging, or vomiting during that period. After induction and endotracheal intubation, the anesthetist advanced a multiperforated gastric tube (Salem sump) and suctioned the gastric contents from the stomach. The patient was turned side to side during suctioning to promote complete evacuation of stomach contents.¹⁷ In our study, gastric contents were measured for volume and pH by the trained observer. Previous studies measuring pH utilized pH paper or compared pH paper to a radiometer and reported good correlation.¹⁸⁻²⁰ In this study, gastric pH was measured using a Mettler Toledo Seven pH meter with a Mettler Toledo InLab Micro Pro electrode. The meter was calibrated before each measurement by trained research staff. Calibration was recorded. The electrode was

stored as per manufacturer's specifications between measurements.

The remainder of the magnetic resonance imaging proceeded as per standard anesthesia routine and at the discretion of the anesthesia provider. Observation continued after the procedure and the following events were documented: new onset coughing, wheezing, oxygen desaturation, respiratory distress, and vomiting. Patients' records were reviewed for adverse events that may have occurred up to 3 days after the procedure.

Statistical Analysis

All analyses were conducted using SPSS (version 22; IBM, Armonk, NY). The 2-tailed *t* test was used to compare residual gastric volume and pH between groups. χ^2 tests were used to compare induction events and adverse outcomes. Statistical significance was accepted at *P* values of $< .05$.

Results

Thirty-seven children mean aged 5.1 ± 2.8 years were enrolled. Sixteen (43%) of these children were randomized to receive preoperative acetaminophen and 21 (57%) were randomized to the control group. There were significantly more females in the control group, but otherwise there

were no differences in demographic characteristics or fasting times between groups (Table 1). Children in the treatment group received oral acetaminophen, 14.77 ± 0.95 mg/kg in volumes ranging from 4.6 to 15 mL (mean 8.55 ± 2.8 mL), 27.06 \pm 12.6 minutes before induction of general anesthesia (range 8 to 51 minutes).

A description of the gastric content volume and pH of the groups is shown in Table 2. Note there was a significant difference in the measured acidity of the control and treatment groups, with the treatment group significantly higher than the control group ($P \leq .044$). There was no correlation between time from acetaminophen to induction and gastric residual volume per kilogram ($\rho = 0.21$, $P = .444$).

Three children in the control group (19%) and six (29%) in the treatment group experienced a nonsignificant adverse event ($P = .702$) (Table 3). One child in the treatment group vomited during extubation and experienced coughing during the postanesthesia care unit stay with no additional events during follow-up. This child was fasted for 2.37 hours preoperatively and had received 10 mL (320 mg) of acetaminophen 33 minutes before induction. There were no reported adverse events in the 72-hour postdischarge period (Table 3).

Table 1. Description of Study Groups

	Acetaminophen Group (n = 16)	Control Group (n = 21)
Age (y)	5.4 \pm 3.1	4.9 \pm 2.5
Gender		
Male	11 (69%)	5 (24%)
Female	5 (31%)	16 (76%); $P = .006$
Weight (kg)	20.9 \pm 10.2	20.9 \pm 10.5
Body mass index	16.8 \pm 3.1	17.3 \pm 2.8
Race		
Caucasian	15 (94%)	19 (91%)
African American	1 (6%)	2 (9%)
ASA		
I	5 (31%)	2 (10%)
II	11 (69%)	19 (90%)
Fasting duration (h)		
Clear liquids	6.05 \pm 3.97	5.68 \pm 4.92

ASA, American Society of Anesthesiologists.

Table 2. Gastric Content Characteristics of the Groups

	Acetaminophen Group (n = 16)	Control Group (n = 21)
Total volume (mL)	13 ± 9.8	8.2 ± 8.6
Volume (mL/kg)	0.67 ± 0.5	0.41 ± 0.62
Gastric pH	1.86 ± 0.42	1.56 ± 0.34; <i>P</i> ≤ .044

Discussion

The purpose of this study was to determine whether administration of oral acetaminophen was associated with changes in gastric contents that could potentially pose increased risk for pulmonary aspiration. Findings demonstrated that compared with children who had fasted for a mean of 5.68 hours, those who received oral acetaminophen within 1 hour of general anesthesia had a similar gastric residual volume that was significantly less acidic. Although six children who received oral acetaminophen experienced adverse symptoms during the perioperative period compared with three in the control group, these were minor (eg, mostly coughing) and were not associated with adverse sequelae. Findings suggest that oral liquid acetaminophen may not be associated with changes in gastric contents that would be indicative of increased risk for pulmonary aspiration.

Oral acetaminophen had been routinely administered to children in our preoperative setting for a

number of years. However, recent Food and Drug Administration safety concerns led to the removal of the more concentrated acetaminophen formula (80 mg/0.8 mL), leaving only the 160 mg/5 mL formula for use in all children.²¹ This change meant that a considerably larger volume of medication was needed to provide an effective preemptive analgesic dose of 15 mg/kg. Not surprisingly, this change raised concerns about patient safety. Our results regarding the nature of gastric contents suggest that liquid acetaminophen given in volumes ranging from 5 to 15 mL may not raise the aspiration risk posed to children about to undergo general anesthesia. In a similar study of 81 children, gastric volume and pH were not significantly different between those given acetaminophen orally versus rectally.⁷ In contrast, our data suggest that oral acetaminophen was associated with slightly higher pH (1.86) compared with findings from this previous study (pH 1.83). Importantly, the gastric pH of both groups is likely not clinically significant and indeed fell into a category deemed to be high risk for pneumonitis.²² Gastric residual volumes were greater in our study but were not significantly

Table 3. Adverse Events During and After the Procedure

Acetaminophen	Acetaminophen Group (n = 16)	Control Group (n = 21)
During induction		
Laryngospasm	1 (6%)	0
Coughing	1 (6%)*	3 (14%)
Gagging	0	2 (9.5%)
After the procedure		
Vomiting during extubation	1 (6%)*	0
Vomiting in recovery room	2 (13%)	1 (5%)
Coughing	1 (6%)*	0
Within 3-day follow-up		
Pneumonia	0	0
Fever	0	0
Readmission	0	0

*Same patient.

different between our groups. It is possible that the time from administration to gastric suction may have contributed to the slight difference in these findings given that our mean time from administering acetaminophen (pH 4.68) to suction was 27 minutes compared with 90 minutes in the previous study. Importantly, several children in our study group experienced minor adverse events during the perioperative period. The most concerning, raising alarm for increased aspiration risk was a child who vomited during extubation and who experienced additional coughing during the recovery stay. Although such adverse events are relatively uncommon during the perioperative period and indeed were not significantly different from the control group, we cannot readily dismiss these as clinically unimportant. Given that the intravenous formulation of acetaminophen is now more widely available for use in children and has a rapid onset of analgesic action, its use for children who have intravenous lines in place may provide the safest non-opioid analgesic option.

Limitations

Findings from this study are limited first by the small sample size. We had determined, a priori,

that 41 subjects per group would be needed to demonstrate a significant difference in gastric residual volume (2-tailed *t* test, 80% power). However, given changes in research personnel and practice with more patients undergoing sedation without a secure airway in our setting, the study was ended early. A post hoc analysis of our results suggests that to demonstrate a significant difference in the gastric volumes found here, we would need 74 patients per group. Another factor limiting the ability to generalize findings is that children in our study had their gastric contents aspirated immediately after induction. This study procedure could have reduced the risk of later adverse effects thus biasing our adverse outcome findings. Finally, restricting our sample to healthy children without underlying risk for aspiration limits broader generalizability.

Conclusions

Our study suggests that administering preemptive oral acetaminophen to children before induction of anesthesia may not be associated with added aspiration risk based on the residual volume or nature of gastric contents. Further study in a larger sample would be needed to confirm findings.

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