Effect of preemptive acetaminophen on postoperative pain scores and oral fluid intake in pediatric tonsillectomy patients

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Postoperative pain is a significant problem that continues to be undertreated in the pediatric population. Preemptive administration of analgesics has recently emerged as a method to enhance pain management associated with surgery. The purpose of this study was to compare postoperative pain scores, rescue analgesic use, and oral fluid intake in children who received acetaminophen preoperatively to children who received postoperative acetaminophen.

The sample consisted of 28 children, 2-8 years of age, scheduled for elective tonsillectomy. Children were randomized into the control or the experimental groups. Anesthesia induction and maintenance were standardized. The experimental group received 15 mg/kg of oral acetaminophen preoperatively, and the control group received 20 mg/kg of rectal acetaminophen postoperatively.

Pain was scored with the FLACC (faces, legs, activity, cry, consolability) behavioral assessment tool. Scores were significantly lower for the experimental group at 30 minutes after awakening and significantly lower for the control group at 240 minutes (P<.05). Eight patients (57%) in the control group and only 4 (28%) in the experimental group required rescue morphine postoperatively. Total postoperative morphine was not significantly different between groups. There were no differences in time to initial oral fluid intake and total oral fluid intake postoperatively. Incidence of nausea and vomiting was high in both groups (64-78%).

These results provide evidence that preemptive acetaminophen may enhance analgesia in pediatric tonsillectomy patients. Preoperative acetaminophen is a safe, quick, and inexpensive intervention that can readily be incorporated into anesthesia practice.

Key words: Acetaminophen, pediatric, postoperative outcomes, preemptive analgesia, tonsillectomy.

Introduction

More than three million children in the United States undergo surgery every year, many of whom will experience significant pain. Researchers have found, however, that children receive less analgesia than adults for similar surgical procedures and emphasized the need for improved pain management. The use of preemptive analgesics has recently emerged as a potential method to improve pain management. Current literature suggests that sensory signals arising from tissue injury during
surgery can lead to increased excitability in the central nervous system that may contribute to hyperalgesia postoperatively. The theoretical basis of preemptive analgesia is to prevent the development of this hyperexcitability by diminishing the barrage of nociceptive inputs during surgery. Recent trials of preemptive analgesia have demonstrated lower postoperative pain scores and lower use of postoperative analgesics, which lend support to this theory.

Tonsillectomy is a procedure that is known to cause significant pain. Poor pain management in this population may contribute to the patient's inability to drink, leading to other problems such as volume depletion, fever, and prolonged recovery. Preemptive analgesia may help to improve patient outcomes and recovery in this population.

The purpose of this study was to examine differences in outcomes of children who receive acetaminophen prior to tonsillectomy and children who receive this drug postoperatively. Specific questions were:

1. Is there a difference in postoperative pain scores between groups?
2. Is there a difference in postoperative analgesia requirements between groups?
3. Is there a difference in time to oral fluid intake and amount of oral fluid intake between groups?

Materials and methods

Sample. Approval for this study was granted from the Institutional Review Board and written informed consent was obtained from parents. The 28 children included in this study were male and female, aged 2 to 8 years, and were scheduled for uncomplicated tonsillectomy. Children were excluded if they were known to have developmental delay, complicating health factors precluding the use of opioids or acetaminophen or any other factors which would interfere with pain assessment and management.

Design. Children were randomly assigned to either the control or experimental groups. Each child received an inhalational induction with halothane and was maintained with oxygen, nitrous oxide, and halothane titrated to depth of anesthesia. All subjects received 0.1 mg/kg morphine sulfate after intravenous catheter insertion and were endotracheally intubated. Neuromuscular blockade was accomplished at the discretion of the anesthetist, and ventilation was assisted or spontaneous. Tonsillectomy was performed using electrocautery excision without wound infiltration.

Subjects in the experimental group received 15 mg/kg oral acetaminophen 1 hour preoperatively. Subjects in the control group received 20 mg/kg rectal acetaminophen immediately postoperatively. These dosages of acetaminophen were not altered from the standard dosages used at this facility at the time of this study. These standards were based on dosage recommendations in the literature. The bioavailability of rectal acetaminophen is 30-40% compared with 60-70% for oral, and therefore dosage recommendations for the rectal route are higher.

Instrument. The FLACC (faces, legs, activity, cry, consolability) behavioral pain assessment tool was used to assess children's postoperative pain in this study (Figure 1). The FLACC tool incorporates five categories of behavior. Each category is scored from 0 to 2 which provides a total score between 0 and 10. This tool was developed to assess pain in young children who have difficulty in self-reporting their pain. The FLACC tool has good interrater reliability (r = .94; P < .001), and validity as demonstrated by significant correlations between FLACC and global ratings of pain (r = .41; P < .001) and between FLACC and the Observation Pain Scale (r = .81; P < .001).

The FLACC scores were assigned by nurses in the postanesthesia care unit (PACU) upon patient awakening and at the following time periods: 30, 60, 90, 120, 180, and 240 minutes. Morphine sulfate was used as the rescue analgesic for all patients. Time to administration and total dosage of rescue agent and time to and total amount of oral fluid intake were also recorded.

End analysis. The student’s t test was used to analyze the differences between group characteristics, FLACC scores, analgesics, and oral fluid intake. Chi-square was used to examine differences in incidence of nausea and vomiting between groups.

Results

The two groups were similar with regard to age and surgery duration (Table I). Average postoperative FLACC scores for each group were relatively low (Figure 2). Four patients in the control group and two in the experimental group had awakening FLACC scores of greater than 5, indicating significant pain. Although pain scores generally decreased throughout the recovery period, there was a small increase in scores at 180 and 240 minutes for the experimental group. The FLACC scores were statistically significantly lower for the experimental group at 30 minutes and for the control group at 4 hours postoperatively (P < .05).

Eight (57%) of the patients in the control group and four (28%) in the experimental group received...
Figure 1
FLACC scale

<table>
<thead>
<tr>
<th>Activity</th>
<th>Face</th>
<th>Legs</th>
<th>Consolability</th>
</tr>
</thead>
<tbody>
<tr>
<td>No particular</td>
<td>No particular</td>
<td>Normal position</td>
<td>Content, relaxed</td>
</tr>
<tr>
<td>expression or smile</td>
<td>expression or smile</td>
<td>or relaxed</td>
<td></td>
</tr>
<tr>
<td>Normal position</td>
<td>Normal position</td>
<td>Lying quietly,</td>
<td></td>
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<tr>
<td>or relaxed</td>
<td>or relaxed</td>
<td>normal position, moves easily</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lying quietly,</td>
<td>Occasional grimace or frown, withdrawn, disinterested</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>normal position, moves easily</td>
<td>Uneasy, restless, tense</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Moans or whimpers; occasional complaint</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Reassured by occasional touching, hugging or &quot;Talking to&quot; Distractible</td>
<td>2</td>
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Table I
Group characteristics

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<thead>
<tr>
<th></th>
<th>Control group (n=14)</th>
<th>Experimental group (n=14)</th>
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<tr>
<td>Mean age (years)</td>
<td>5.4 (±1.3)</td>
<td>6.1 (±1.7)</td>
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<tr>
<td>Surgery duration (minutes)</td>
<td>46.4 (±24.0)</td>
<td>39.4 (±13.9)</td>
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Figure 2
Postoperative FLACC scores

Table II
Postoperative outcomes

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Experimental group</th>
<th>P Values</th>
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</thead>
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<tr>
<td>Postoperative morphine (mg/kg)</td>
<td>0.039±0.044</td>
<td>0.013±0.024</td>
<td>.06</td>
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<tr>
<td>Average time to initial analgesic (minutes)</td>
<td>12.5±7.07</td>
<td>12.5±14.14</td>
<td>1.00</td>
</tr>
<tr>
<td>Postoperative oral fluids (mL)</td>
<td>55±78</td>
<td>67±73</td>
<td>.76</td>
</tr>
<tr>
<td>Minutes to initial oral intake</td>
<td>102±89</td>
<td>93.64±62</td>
<td>.45</td>
</tr>
</tbody>
</table>

rescue analgesics. The individual dosage requirements ranged from .02-.07 mg/kg for experimental patients and .03-1 mg/kg for the control group. The average morphine requirements were low for both groups, but the average requirement for the experimental group was less and approached significance (P=.06) (Table II). The average time from awakening to analgesic administration was identical for both groups (12.5 minutes).

The time to oral intake and total oral fluid intake was not significantly different between groups (Table II). Sixty-four percent of the control group and 78% of the experimental group experienced nausea and vomiting. This difference was not significant.

Discussion
Nonsteroidal anti-inflammatory agents and acetaminophen are frequently used in the pediatric
population to treat mild to moderate pain. These agents presumably mediate analgesia by blocking prostaglandin synthesis, thereby decreasing peripheral sensitization and the activation of nociceptors. These is recent evidence that these agents block prostaglandin synthesis in the central nervous system as well. Theoretically, these agents may act in the spinal cord to block mechanisms that would otherwise enhance central sensitization. Findings from several studies in adults and children have demonstrated decreased pain scores and less narcotic use postoperatively in patients who received preprocedural analgesia with nonsteroidal anti-inflammatory drugs or acetaminophen.

In this study, we found low postoperative FLACC scores overall, indicating relatively good analgesia for both groups. This was expected since all patients received morphine before incision. The group which received acetaminophen preoperatively had significantly lower FLACC scores in the early postoperative period, and fewer of these patients required rescue analgesics postoperatively, lending support for the concept that preemptive acetaminophen enhances pain relief in this population.

The FLACC scores gradually dropped during recovery for both groups, but the experimental group’s scores went up slightly toward the end of their stay. These trends in pain scores were expected based on the kinetics of acetaminophen described in the literature. Oral administration of acetaminophen in awake patients produces a peak plasma level in 30 to 60 minutes and has an average half-life of about 2 hours. Experimental patients in our study were therefore expected to have a preemptive analgesic effect that would produce lower pain scores in the early postoperative period. The late rise in pain scores of these patients at 240 minutes may relate to the fall in plasma levels of acetaminophen around this time.

Rectal acetaminophen achieves peak plasma levels between 100 and 170 minutes after administration, and the half-life is around 3.5 hours. The FLACC scores in the control group similarly follow the expected kinetics of the drug. Rectal suppositories were administered on arrival to the PACU while patients were still asleep, and therapeutic levels would be expected around 60 to 120 minutes after awakening. Pain scores dropped throughout the PACU stay, reaching “0” at 240 minutes, which may relate to the prolonged elimination of rectal drug.

The recommended dosages of rectal acetaminophen remain conservative (15-20 mg/kg) despite evidence that therapeutic levels may be difficult to achieve with this dose range. In our study we did not alter dosages from the standards utilized at this institution. However, recent studies that compare rectal acetaminophen to other analgesics have used higher dosages up to 35 mg/kg. In our study, patients who received 20 mg/kg rectal acetaminophen demonstrated good clinical analgesia in combination with the morphine dosages administered.

The overall requirements for rescue analgesia were low for both groups, again demonstrating good overall analgesia. Only four of the patients in the experimental group required rescue morphine postoperatively compared with eight in the control group. Interestingly, there was no difference between groups with regard to time to rescue analgesia. All patients who required rescue drug needed it early in the postoperative period. The difference in total amount of rescue analgesia required by each group approached significance, with the experimental group requiring less overall morphine. A larger sample may demonstrate a significant difference between groups.

There was no difference in the time to oral intake and the amount of oral intake between groups. Eighty percent of subjects in this study drank during the first 4 hours postoperatively. There were only six patients who did not drink at all during this time, and of these, five experienced postoperative nausea and vomiting. There were no differences in pain scores between children who drank and those who did not, thus, postoperative drinking was unrelated to pain in this study.

The incidence of nausea and vomiting was very high in both groups. The reported incidence of nausea and vomiting in the tonsillectomy population ranges from 30% to 80% and has been related to many factors including pharyngeal stimulation, swallowing of blood, and opioid administration. In studies where nausea was relatively low (30%), patients had received droperidol or phenergan preoperatively. The Splinter et al report found that tonsillectomy patients who underwent balanced anesthesia with sufentanil experienced significantly greater vomiting postoperatively than did those receiving halothane, nitrous oxide, and either morphine or meperidine. In our study, patients did not receive antiemetics unless they experienced significant nausea and emesis postoperatively. Adding an antiemetic intraoperatively would likely drop the incidence of this complication significantly.

There were several methodological limitations in this study design that confounded these interpretations. Rescue analgesics were titrated by PACU nurses to analgesia effect as measured by patient behaviors and FLACC scores. However, we did not standardize FLACC scores for which analgesia
should be administered, nor did we standardize the dosage increments for titration. Therefore, variations in nursing practice may have influenced this outcome measure for both groups. Nurses were not blinded to the timing and route of acetaminophen administration. Therefore, the possibility of observer bias cannot be overlooked. Lastly, the FLACC tool may not have been the assessment tool of choice for some of the patients under study. Careful review of data found that two of the four patients in the experimental group who received rescue morphine had FLACC scores of 0 or 1 at all data points postoperatively. It may be that these patients self-reported their pain but did not behaviorally display discomfort. These particular patients were 7 and 8 years old and would likely have been capable of self-report. Studies of behavioral pain scales suggest that children begin to mask behavioral distress at around age 7. Utilizing a self-report measure for children who are able to do so would strengthen pain assessment in this study.

Preoperative administration of oral acetaminophen provided greater pain relief than postoperative rectal administration in this study and reduced the requirement of postoperative rescue opiates in tonsillectomy patients. The literature as well as governmental guidelines (U.S. Agency for Health Care Policy and Research) highlight the undertreatment of children's pain and emphasize the need for improved assessment and management. Preemptive administration of analgesics may have implications toward enhancing pain management in the surgical population. Acetaminophen administered preoperatively is a safe, convenient, and inexpensive intervention that may be readily incorporated into anesthesia practice. Further study of this topic, perhaps with a double-blinded design and a larger sample size, is warranted.

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References:

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DIPRIVAN (propofol) Injectable Emulsion

**INDICATIONS**

- Intravenous sedation in infants and children in the intensive care unit to facilitate or facilitate endotracheal intubation or to facilitate or facilitate removal of intubation tubes.
- Analgesia in patients with pain and severe mobility limitations due to disease or surgery.
- Intravenous sedation in adult patients during mechanical ventilation or in the intensive care unit to facilitate or facilitate endotracheal intubation or to facilitate or facilitate removal of intubation tubes.
- Intravenous sedation in adult patients undergoing diagnostic procedures.
- Intravenous sedation in adult patients undergoing therapeutic procedures.
- Intravenous sedation in adult patients undergoing transplantation of organs.
- Intravenous sedation in adult patients undergoing procedures in the operating room or in the intensive care unit.
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