Duration-Related Efficacy of Postoperative Antibiotics Following Pediatric Tonsillectomy

A Prospective, Randomized, Placebo-Controlled Trial

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Objective: To determine whether a 3-day course of postoperative antibiotics is as effective as a 7-day course in reducing pain and reducing time to resumption of a normal diet and level of activity following pediatric tonsillectomy.

Design: A prospective, randomized, placebo-controlled trial.

Setting: Academic medical center.

Patients: Forty-nine patients were enrolled in the study. Preoperative demographic information was obtained.

Interventions: Tonsillectomy with or without adenoidectomy was performed by the senior author (J.J.) using electrocautery. Patients were randomized to receive either a 3- or 7-day course of amoxicillin.

Main Outcome Measures: Parents were asked to record the following information: analgesic use for the first 7 postoperative days, postoperative days the child initiated his or her usual diet and level of activity, and medical treatment for oral hemorrhage or dehydration.

Results: Of the 49 patients, 26 were randomized to receive 7 days of postoperative antibiotics (group A) and 23 to receive 3 days of antibiotics, followed by 4 days of placebo (group B). Results were obtained for 47 of the enrolled patients (96%). No statistically significant difference was noted between the 2 groups with regard to postoperative pain or time to resumption of a normal diet and level of activity.

Conclusion: A 3-day course of antibiotics following pediatric tonsillectomy is as effective as a 7-day course with regard to postoperative analgesic use and resumption of normal diet and level of activity.

Trial Registration: clinicaltrials.gov Identifier: NCT00662987


The first recorded tonsillectomy was performed more than 2000 years ago. Today, tonsillectomy is one of the most commonly performed procedures in pediatric otolaryngology. The tonsillectomy rate for those younger than 15 is estimated to be 45.6 per 10,000 children. The leading indications for tonsillectomy in this age group are sleep-related breathing disorders and recurrent tonsillitis.

Tonsillectomy is a relatively safe procedure, with a reported mortality rate between 1 in 16,000 and 1 in 35,000. However, tonsillectomy is associated with significant morbidity, particularly during the first week after the procedure. Associated morbid conditions include postoperative hemorrhage, lethargy, halitosis, and pain. Pain can lead to decreased oral intake and ultimately dehydration.

The use of postoperative antibiotics to relieve pain following pediatric tonsillectomy was first reported more than 50 years ago. It is thought that the normal oral bacterial flora colonize the denuded tonsillar fossae and release inflammatory mediators that cause pain. Antibiotic use after tonsillectomy may quantitatively lessen the bacterial content and thus reduce pain.

The majority of otolaryngologists choose to prescribe antibiotics following tonsillectomy. However, there is conflicting evidence in the literature regarding this practice in the pediatric population. One prospective randomized controlled trial failed to detect a significant difference in analgesic use or resumption of normal diet. To the contrary, 3 prospective, randomized controlled trials describe reduced use of analgesics and decreased time to resuming a normal diet and level of activity. In these studies, a 7-day course...
of antibiotic was used. The benefits were statistically significant early in the antibiotic course. Therefore, we sought to demonstrate that a shorter course of antibiotics was equally efficacious following pediatric tonsillectomy.

METHODS

All pediatric patients scheduled for tonsillectomy with or without adenoidectomy from an outpatient otolaryngology practice were recruited for the study. Exclusion criteria included an allergy to penicillin, preexisting medical condition requiring perioperative antibiotics (ie, endocarditis), and history of antibiotic use in the week prior to tonsillectomy. Institutional review board approval was obtained.

Preoperative demographic information was obtained, including the patients’ age, sex, indications and planned procedure. All subjects received perioperative dose of cefazolin sodium and dexamethasone sodium phosphate. Tonsillectomy with or without adenoidectomy was performed by the senior author (J.J.) using electrocautery. The majority of patients were discharged home the same day.

Patients were randomized to receive either a 3- or 7-day course of amoxicillin using a random table of numbers. Group A received a 3-day course of amoxicillin (bottle 1), followed immediately by a 4-day course of amoxicillin (bottle 2). Group B received a 3-day course of amoxicillin (bottle 1), followed immediately by a 4-day course of placebo (bottle 2). The dose of amoxicillin was 40 mg/kg (up to a maximum of 800 mg) divided twice daily. The placebo was created by an affiliated children’s pharmacy as a bubblegum flavored syrup to mimic the color, taste, and consistency of the antibiotic suspension. The cost of the antibiotic and placebo was covered by an institutional grant. Patients were also prescribed acetaminophen with codeine for analgesia. The dose of codeine phosphate was 0.5 to 1 mg/kg.

Each family was given a standardized form to record the following information: number of doses of analgesic used for the first 7 postoperative days, postoperative days the child initiated his or her usual diet and level of activity, and medical treatment for oral hemorrhage or dehydration. A postoperative appointment was scheduled for 3 weeks following tonsillectomy. At this time, the patient was evaluated and data sheets were collected. Those patients without data forms were contacted by telephone by a blinded physician to obtain the available data. The 2 groups were first compared regarding the amount of pain medication used during the recovery period. The results are summarized in Table 2.

We were able to obtain results on 47 of the enrolled patients (96%). Both patients lost to follow-up were in group B. One patient in group A had an early postoperative fever and was removed from the study drug and given cefalexin. Another patient in group A had a fever after completing the study medication and was given an additional course of antibiotics. One patient in group A and one in group B discontinued the medication at days 4 and 3, respectively, secondary to diarrhea. One patient in group A did not use the study medication at all.

An intention-to-treat analysis was performed on the available data. The 2 groups were first compared regarding the amount of pain medication used during the recovery period. The results are summarized in Table 2. There was no statistically significant difference detected between the 2 groups for any of the first 7 postoperative days. However, there was a trend of less pain medication used in group B patients during days 1 to 4. For these days, the difference in the number of doses of pain medication use between group A and group B per day was 0.21 and the 95% confidence interval (CI) around the difference was −0.28 to 0.72. The range of the 95% confidence interval includes the clinically significant difference of 0.5 doses or greater in favor of the 3-day course.

Next, the groups were compared with regard to return to normal diet and level activity. The results are summarized in Table 3. There was no statistically significant difference detected between the 2 groups for either measure. The difference in the number of days to return to normal diet between group A and group B was 0.26 days in favor of 3-day antibiotic course and the 95% CI around this difference was −1.57 to 2.09. The range of the CI includes the 1-day difference in return to normal diet that was deemed clinically meaningful. The wide range suggests that the data are compatible with either the 7-day or 3-day course being superior.

The difference in the number of days to return to normal level of activity between group A and group B was 0.84 and the range of the 95% CI was −1.39 to 3.07, which includes the 1-day difference in return to normal level of activity that was deemed clinically meaningful. Again, the wide range of the 95% CI suggests that either the 7-day or 3-day course is superior.

RESULTS

Forty-nine patients were enrolled in the study. Twenty-six patients were randomized to receive 7 days of postoperative antibiotics (group A). Twenty-three patients were randomized to receive 3 days of antibiotics, followed by 4 days of placebo (group B). The mean age of the patients was 4.9 years (range, 1–13 years). The majority of the patients were male (n=35). Obstructive sleep symptoms were the indication for surgery in the majority of cases (n=46). Most patients also had an adenoidectomy performed at the same time (n=47). Otherwise, the demographics of the patient populations were similar among the 2 groups (Table 1).

<p>| Table 1. Demographics of Patients Randomized to Receive Either a 3- or 7-Day Course of Amoxicillin |
|---------------------------------|-----------------|-------------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Demographic</th>
<th>Group A</th>
<th>Group B</th>
<th>Total</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>20</td>
<td>15</td>
<td>35</td>
<td>.53</td>
</tr>
<tr>
<td>Female</td>
<td>8</td>
<td>7</td>
<td>15</td>
<td>.84</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>5.0</td>
<td>4.7</td>
<td>4.9</td>
<td>.49</td>
</tr>
<tr>
<td>T&amp;A</td>
<td>24</td>
<td>23</td>
<td>47</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>T alone</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>OSA</td>
<td>24</td>
<td>22</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; OSA, obstructive sleep apnea; T, tonsillectomy; T&A, tonsillectomy and adenoidectomy.

a Randomized to receive 7 days of postoperative antibiotics.
b Randomized to receive 3 days of antibiotics, followed by 4 days of placebo.
The available prospective literature regarding postoperative antibiotic use in pediatric patients following tonsillectomy is conflicting. Telian et al conducted the first study in the 1980s that showed a significant reduction in postoperative fever, pain, lassitude, mouth odor, and poor oral intake with antibiotic use after tonsillectomy. In this prospective, randomized, double-blind study, perioperative ampicillin followed by a 7-day course of amoxicillin was compared with placebo. A 7-day course of antibiotics was chosen because of the clinical observation that the presence of eschar and symptoms approximated this period. The authors acknowledged the possibility of a shorter or longer course being of equal or greater efficacy. Of note, those patients who received antibiotics experienced benefit primarily during their early postoperative course. Those in the antibiotic group had subjective pain for an average of 3.3 days and halitosis for 2.6 days, tolerated soft diet at 1.3 days, and resumed normal activity level at 4.2 days.

Jones et al randomized patients to cefaclor or amoxicillin and found no statistically significant difference using the same outcome measures as Telian et al. Two subsequent prospective trials confirmed the benefit of postoperative antibiotics in the pediatric tonsillectomy patient. Linden et al compared postoperative amoxicillin use with no treatment using various methods of tonsillectomy. Patients were randomized to receive antibiotics as well as undergo tonsillectomy using electrocautery, laser, and blunt dissection methods. Postoperative antibiotics were associated with a significant reduction in pain medication use in the electrocautery and laser groups. There was not a significant difference in the blunt dissection group. Colreauv et al randomized patients to receive amoxicillin–clavulanate potassium or no treatment and found a significant reduction in days to resumption of normal diet, pain, and amount of pain medicine consumed in the antibiotic group.

One prospective trial did not detect a difference between children treated with postoperative antibiotics following tonsillectomy. Lee et al performed a prospective trial comparing a 5-day course of amoxicillin with no treatment. They did not detect a statistically significant reduction in any of their morbidity measures, including pain, diet, and activity. Patients were not randomized and were assigned to a treatment group according to surgeon preference.

Based on our results, a 3-day course of antibiotics is as effective as a 7-day course. A shorter course of antibiotics carries other potential advantages, including decreased cost, increased patient compliance with medications, and a decrease in antibiotic-associated complications and bacterial resistance. The incidence of adverse effects (diarrhea) from the antibiotics, while rare, was equal between the 2 groups. A potential disadvantage, outside of the study measures, would be increased postoperative fever and infection. Interestingly, both pa-

### Table 2. Pain Medication Use (Number of Weight-Based Doses of Acetaminophen With Codeine Liquid Used Daily)

<table>
<thead>
<tr>
<th>Day</th>
<th>Group A</th>
<th>Group B</th>
<th>P Value</th>
<th>Difference of Means</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.42</td>
<td>2.26</td>
<td>.77</td>
<td>0.16</td>
<td>-.06 to +1.18</td>
</tr>
<tr>
<td>2</td>
<td>2.32</td>
<td>2.05</td>
<td>.62</td>
<td>0.27</td>
<td>-.76 to +1.31</td>
</tr>
<tr>
<td>3</td>
<td>1.60</td>
<td>1.42</td>
<td>.70</td>
<td>0.18</td>
<td>-.73 to +1.09</td>
</tr>
<tr>
<td>4</td>
<td>1.36</td>
<td>1.05</td>
<td>.53</td>
<td>0.21</td>
<td>-.63 to +1.25</td>
</tr>
<tr>
<td>5</td>
<td>1.16</td>
<td>1.05</td>
<td>.81</td>
<td>0.09</td>
<td>-.74 to +0.96</td>
</tr>
<tr>
<td>6</td>
<td>0.68</td>
<td>0.89</td>
<td>0.58</td>
<td>-0.19</td>
<td>-0.96 to +0.54</td>
</tr>
<tr>
<td>7</td>
<td>0.40</td>
<td>0.89</td>
<td>.11</td>
<td>-0.49</td>
<td>-1.12 to +0.14</td>
</tr>
<tr>
<td>1-4</td>
<td>1.91</td>
<td>1.70</td>
<td>NA</td>
<td>NA</td>
<td>-0.28 to +0.72</td>
</tr>
<tr>
<td>5-7</td>
<td>0.75</td>
<td>0.95</td>
<td>NA</td>
<td>NA</td>
<td>-0.63 to +0.23</td>
</tr>
</tbody>
</table>

Abbreviation: NA, not applicable.

a Randomized to receive 7 days of postoperative antibiotics.
b Randomized to receive 3 days of antibiotics, followed by 4 days of placebo.
tients with this problem were in group A. The one patient with postoperative hemorrhage was in group A, but this is hardly sufficient for a conclusion. The readmission rate for hemorrhage in our study (2.1%) lies within the reported range.

The prospective, randomized, blinded and placebo-controlled nature of our study confirms its robustness. Nevertheless, we acknowledge limitations of the study. Our study does not rule out the possibility of clinically meaningful differences in pain medication use and return to normal diet and activity level between the 2 groups. Additional studies with larger sample sizes are required to clarify the true impact of duration of antibiotic use. As in most pediatric literature, parents were used as surrogates to report patient symptoms. Also, analgesic use was used as an indicator of pain, rather than measuring pain directly. Lastly, various methods exist to perform a tonsillectomy, including cold knife, electrodessication, and coblation, in addition to various partial techniques. The study by Linden et al8 suggested that there may be a difference in the postoperative course among these groups. Therefore, it may be that our data are not generalizable to children undergoing tonsillectomies with alternate techniques.

In conclusion, a 7-day course of antibiotics following pediatric tonsillectomy has no clear benefit over a 3-day course with regard to postoperative analgesic use and resumption of normal diet and level of activity.

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Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Johnson and Jones. Acquisition of data: Johnson, Rickert, and Jones. Analysis and interpretation of data: Rickert and Jones. Drafting of the manuscript: Johnson and Rickert. Critical revision of the manuscript for important intellectual content: Johnson, Rickert, and Jones. Statistical analysis: Rickert. Obtained funding: Johnson. Study supervision: Jones.

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REFERENCES