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# Postoperative Non-steroidal Anti-inflammatory Drugs and Risk of Bleeding in Pediatric Intracapsular Tonsillectomy

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## ABSTRACT

Tonsillectomy with or without adenoidectomy is one of the most frequently performed surgeries in the United States, with over 500,000 performed annually. Post-tonsillectomy hemorrhage is one of the most feared complications; thus, medications that could increase the risk of postoperative bleeding traditionally have been avoided. With recent FDA guidelines encouraging a departure from codeine-based medications in pediatric patients undergoing tonsillectomy, we examined the use of ibuprofen for post-tonsillectomy pain control. The records of 449 children who underwent tonsillectomy and received ibuprofen for postoperative pain control were reviewed and compared to a cohort of 1731 children who received codeine for pain postoperatively. Outcomes measured included rates of secondary post-tonsillectomy hemorrhage (PTH), secondary PTH requiring operative control, and emergency room evaluation for dehydration. Use of ibuprofen after pediatric intracapsular tonsillectomy was found to be associated with a statistically significant increase in secondary PTH and secondary PTH requiring operative control; however, ibuprofen was found to provide pain control that is at least equivalent to narcotic. Rates of secondary PTH with postoperative ibuprofen use remain within the national average. We propose that, despite the increased risk of bleeding, the use of ibuprofen is appropriate for use postoperatively in pediatric tonsillectomy patients, given its ability to control pain and lack of respiratory depression effects.

## INTRODUCTION

Post-tonsillectomy pain traditionally has been controlled with acetaminophen in combination with a narcotic, such as codeine, hydrocodone, or oxycodone. Deaths due to respiratory depression have been reported in children given codeine post-tonsillectomy.<sup>1</sup> Many of the deaths have been in children who possess forms of the liver microenzyme CYP2D6 that make them extensive or ultrarapid metabolizers of codeine.<sup>2</sup>

The current concerns regarding rapid metabolism of codeine products in children following tonsillectomy<sup>3</sup> have led to widespread reconsideration of post-tonsillectomy pain management regimens for the pediatric population. Non-steroidal anti-inflammatory drugs (NSAID), specifically ibuprofen, have gained favor as an alternative to narcotics for postoperative pain control. While NSAIDs provide adequate post-tonsillectomy analgesia,<sup>4</sup> their routine use remains controversial as NSAIDs also cause platelet dysfunction that may lead to increased risk of post-tonsillectomy hemorrhage (PTH). The clinical impact of this potentially increased bleeding risk with NSAID use remains unclear.

This study examines whether the use of ibuprofen in children post-intracapsular tonsillectomy affects the likelihood of clinically significant bleeding. The incidence of PTH requiring either non-surgical or surgical intervention is compared in children who received ibuprofen and acetaminophen versus those who received acetaminophen with narcotic for post-tonsillectomy pain. Secondly, the incidence of emergency department (ED) evaluation for pain or poor oral intake is examined.

## METHODS

A sample of children who underwent tonsillectomy or adenotonsillectomy for infections or sleep-disordered breathing at Nemours/Alfred I. duPont Hospital for Children (N/AIDHC) between 2011 and 2013 was reviewed. Intracapsular tonsillectomy was performed on all children. Postoperatively, families received verbal and written instruction to use alternating acetaminophen and ibuprofen as needed for their child's pain. This cohort of children was then compared to a cohort of children who underwent intracapsular tonsillectomy or adenotonsillectomy at N/AIDHC between 2002 and 2005 who used acetaminophen with codeine or hydrocodone as needed for pain.<sup>5</sup> Data collected included patient age and gender; indication for surgery; use of postoperative ketorolac; occurrence of primary or secondary PTH; evaluation in the ED for PTH, pain, or poor oral intake; and need for reoperation due to secondary PTH. Children with known coagulopathies were excluded. The association between categorical variables was expressed as odds ratios (OR) with 95% confidence intervals. Differences in the relative proportions between categorical variables were analyzed using Fisher exact test and chi-square analysis, as appropriate.

## RESULTS

**Table 1.** Comparison of Outcome Measures for Narcotic and NSAID Groups

	Narcotic (n = 1731)	NSAIDs (n = 449)	P value
Secondary PTH	19 (1.1%)	17 (3.8%)	< 0.0001
Secondary PTH requiring operative control	8 (0.5%)	7 (1.6%)	0.01
Dehydration	52 (3%)	19 (4.2%)	0.23

**Table 2.** Postoperative Ketorolac Use and Post-Tonsillectomy Hemorrhage

	Ketorolac Used (n = 161)	No Ketorolac Used (n = 288)	P value
Primary PTH	4 (4.3%)	5 (1.7%)	0.73
Secondary PTH	5 (3.1%)	12 (4.2%)	0.80

There were 449 patients studied who underwent tonsillectomy or adenotonsillectomy at N/AIDHC between 2011 and 2013 (NSAID group). Of these, 244 (54.3%) were female, and 205 (45.7%) were male; the mean age at time of surgery was 9.5 years (SD, 3.2 years). The secondary data set examined 1731 patients who underwent intracapsular tonsillectomy or adenotonsillectomy at N/AIDHC between 2002 and 2005 (Narcotic group). Forty-eight percent were female, and 52% were male; the mean age at time of surgery was 6 years.

There were 7 (3.8%) episodes of secondary PTHs in the NSAID group and 19 (1.1%) episodes of secondary PTHs in the Narcotic group, a difference that was statistically significant ( $P < 0.0001$ , OR 3.5, 95% CI 1.7–7.2). In the NSAID group, seven (1.6%) required control of their PTH in the operating room, as compared to eight (0.5%) in the Narcotic group. The increased rate of PTH requiring control in the operating room was significantly higher in the NSAID group ( $P = 0.01$ , OR 3.4, 95% CI 1.1–10.1). In the NSAID group, 161 patients received ketorolac postoperatively for pain control, and 288 did not. In those who received ketorolac, there were four (4.3%) episodes of primary PTH and five (3.1%) episodes of secondary PTH. Of those not receiving ketorolac, there were five (3.1%) with primary PTH and 12 (4.2%) with secondary PTH. Administration of ketorolac was found to have no statistically significant effect on rates of primary ( $P = 0.73$ ) or secondary ( $P = 0.80$ ) PTH.

In the NSAID group, 19 of 512 (3.71%) patients were evaluated in the ED for pain or poor oral intake. In the narcotic group, 52 of 1731 (3.79%) were admitted for dehydration. The incidence of ED evaluation for pain or poor oral intake was not statistically significant between groups ( $P = 0.23$ ).

## DISCUSSION

Several studies have been undertaken in recent years to evaluate the increased risk of PTH in children using NSAIDs, and suggest that there is evidence that NSAIDs increase this risk.<sup>6-10</sup> In a 2003 study by Marrett, the preoperative use of NSAIDs was associated with increased risk of reoperation for hemostasis versus those who received placebo or narcotic.<sup>6</sup> A study by Moiniche that same year found that postoperative NSAID use leads to increased likelihood of having a PTH requiring reoperation.<sup>7</sup> A more recent systematic review and meta-analysis by Riggan<sup>10</sup> again found that patients receiving NSAIDs in the postoperative period have an increased risk for PTH. Limitations of these studies include the use of several different NSAID agents and inclusion of both pediatric and adult patients.

The current study examines differences in a pediatric population who underwent intracapsular tonsillectomy and for whom parents received standard verbal and written instruction regarding the recommended postoperative pain regimen. In our population, patients receiving postoperative ketorolac and ibuprofen had a statistically significant higher rate of secondary PTH with no increased bleeding attributed to use of ketorolac. Despite the observed increase in PTH, the overall rate of PTH and PTH requiring operative control remain within the national average. The relative increase in PTH must be weighed against the risks of respiratory depression associated with postoperative codeine use, especially in the pediatric sleep-disordered breathing population.

A limitation of our study involves variation in the dosage of ibuprofen administered; with some surgeons prescribing 5 mg/kg/dose and others 10 mg/kg/dose. As a retrospective study, the number of NSAID doses actually taken also remains unknown. Both limitations will be addressed in a future prospective study. Finally, it is noteworthy that in the narcotic group, children evaluated in the ED for hyperemesis thought to be due to codeine were not considered in the dataset. As such, it is possible that the difference in the number of children in the NSAID group and narcotic group presenting to the ED for nausea and vomiting, noted to be not significantly different, is underestimated.

## CONCLUSION

The debate on the ideal pain control regimen for children post-tonsillectomy persists. Our review suggests that NSAIDs increase the likelihood of clinically significant, secondary PTH; the rate of secondary PTH observed, however, still falls within national averages. Conversely, NSAIDs appear to provide adequate pain relief, resulting in at least an equivalent incidence of ED evaluation for poor oral intake as compared to narcotic, and not conferring an increased risk for suppression of respiratory drive. Future studies aim to evaluate whether the number of doses and the amount of ibuprofen given per dose affects risk for PTH and to continue to examine the effects of ketorolac on primary and secondary PTH.

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