



## Postoperative nonsteroidal anti-inflammatory drugs and risk of bleeding in pediatric intracapsular tonsillectomy



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### ABSTRACT

**Objectives:** In light of current FDA guidelines on opioid use in children, we sought to determine the risk of post-tonsillectomy hemorrhage (PTH) in children who received ibuprofen with acetaminophen versus those who received narcotic with acetaminophen for postoperative pain control.

**Methods:** This was an IRB-approved retrospective chart review of patients at a tertiary-care pediatric center. The medical records of 449 children who received acetaminophen and ibuprofen following intracapsular tonsillectomy with or without adenoidectomy were reviewed (NSAID group) and compared with medical records of 1731 children who underwent intracapsular tonsillectomy and received acetaminophen with codeine or hydrocodone with acetaminophen postoperatively (narcotic group). Main outcome measure was the incidence of PTH requiring return to the operating room. Secondary outcome measures included incidence of primary PTH, secondary PTH, and postoperative evaluation in the emergency department or readmission for pain and/or dehydration.

**Results:** Incidence of PTH requiring return to the operating room was higher in the NSAID group (1.6%) compared with the narcotic group (0.5%),  $P = 0.01$ . Incidence of primary PTH was significantly higher in the NSAID group (2%) versus the narcotic group (0.12%),  $P < 0.0001$ . Incidence of secondary PTH was 3.8% in the NSAID group and 1.1% in the narcotic group ( $P < 0.0001$ ).

**Conclusion:** Use of ibuprofen after intracapsular tonsillectomy in children is associated with statistically significant increase in PTH requiring return to the operating room, as well as an increase in overall rates of both primary and secondary PTH. Ibuprofen provides pain control that is at least equivalent to narcotic and is not associated with respiratory depression. Further study of ibuprofen use in the post-tonsillectomy patient is warranted.

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## 1. Introduction

Tonsillectomy is one of the most common surgical procedures performed on pediatric patients in the United States; more than 500,000 surgeries are performed annually [1]. Complications after surgery can include pain, dehydration, and bleeding. Post-tonsillectomy hemorrhage (PTH) is one of the most serious complications of tonsillectomy; though rare, PTH can be life

threatening. Post-tonsillectomy hemorrhage is separated into primary bleeds, which occur within 24 h of surgery, and secondary bleeds, occurring more than 24 h after surgery. The incidence of primary PTH is estimated at 0.2–2.2% and secondary PTH at 0.1–3% [2].

Post-tonsillectomy pain has traditionally been controlled with acetaminophen in combination with a narcotic, such as codeine, hydrocodone, or oxycodone. Deaths from respiratory depression have been reported in children given codeine post tonsillectomy [3]. Many of the deaths have been in children who possess forms of the liver microenzyme CYP2D6, which make them extensive or ultrarapid metabolizers of codeine. For a given dose of codeine, extensive and ultrarapid metabolizers produce relatively high amounts of morphine, the active opioid metabolite, placing them at increased risk for respiratory depression. The FDA has released drug safety warnings regarding pediatric deaths secondary to

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codeine use after tonsillectomy because of this genetic variation in the CYP2D6 enzyme [4].

The current concerns regarding rapid metabolism of codeine products in children following tonsillectomy [5] have led to widespread reconsideration of post-tonsillectomy pain management regimens for the pediatric population. Nonsteroidal anti-inflammatory drugs (NSAIDs), specifically ibuprofen, have gained favor as an alternative to narcotics for postoperative pain control. While NSAIDs provide adequate post-tonsillectomy analgesia [6], their routine use remains controversial as NSAIDs also cause platelet dysfunction that may lead to increased risk of PTH. The clinical impact of this potentially increased bleeding risk with NSAID use remains unclear. Meta-analyses have noted that the postoperative use of NSAIDs may increase the risk of PTH requiring reoperation [7,8]. Given this, one meta-analysis suggests cautious NSAID use [7] while another recommends avoiding NSAID use [8] until further data are available.

This study examines whether the use of ibuprofen over a one to two week postoperative period in children following intracapsular tonsillectomy affects the likelihood of clinically significant bleeding requiring return to the operating room. Post-tonsillectomy hemorrhage requiring return to the operating room was selected as primary outcome as we consider it to be the most clinically meaningful complication in children undergoing intracapsular tonsillectomy. Secondly, the overall incidence of primary and secondary PTH, as well as the incidence of emergency department (ED) evaluation or readmission for pain with or without dehydration is examined.

## 2. Methods

This retrospective study was approved by the Institutional Review Board at Nemours/Alfred I. duPont Hospital for Children (AIDHC). A sample of children who underwent tonsillectomy or adenotonsillectomy for infections or sleep-disordered breathing at AIDHC between 2011 and 2013 was reviewed. Intracapsular tonsillectomy was performed on all children. Intracapsular tonsillectomy technique involves removing approximately 90% of the tonsillar tissue via microdebrider, leaving the capsule intact. Suction electrocautery is then used to ablate the remaining tissue and to obtain hemostasis. Postoperatively, families received verbal and written instruction to use weight-based alternating acetaminophen and ibuprofen as needed for their child's pain (NSAID group). Data collected included patient age; sex; indication for surgery; use of postoperative ketorolac; occurrence of primary or secondary PTH; evaluation in the ED with or without hospital admission for PTH, pain, or poor oral intake; and need for reoperation because of secondary PTH. Children with known coagulopathies were excluded.

The cohort of children who underwent surgery between 2011 and 2013 and used ibuprofen and acetaminophen postoperatively was then compared with a cohort of patients who underwent intracapsular tonsillectomy or adenotonsillectomy at AIDHC between 2002 and 2005. Families in this group were

instructed to use acetaminophen with codeine or hydrocodone as needed for pain (narcotic group). Information on this cohort has been published previously [9].

Technique and equipment for intracapsular tonsillectomy remained consistent among surgeons and over the time periods evaluated. Surgeries in the narcotic group were performed by five attending surgeons, while surgeries in the NSAID group were performed by eight attending surgeons. Of the latter eight surgeons, four were involved in surgeries for both the NSAID and narcotic group.

Return to the operating room was dictated by surgeon preference after evaluation of child; generally, medical observation was preferred in the absence of active bleeding and clean tonsillar fossae. If clot or active bleeding was identified, the child was rapidly returned to the operating room.

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-squared analysis, as appropriate. The significance level for all hypothesis tests was set at 0.05.

## 3. Results

There were 449 patients in the NSAID group. Indications included chronic adenotonsillitis in 186 (41.4%), sleep-disordered breathing in 221 (49.2%), or both in 42 (9.4%). Of these, 244 (54.3%) were female, and 205 (45.7%) were male, with a mean age at time of surgery of 9.5 years (SD, 3.2 years). Of 449 patients, 177 (39.4%) received intravenous ketorolac in the immediate postoperative period. There were 1731 patients in the narcotic group. Surgical indications included chronic adenotonsillitis (22.3%), sleep-disordered breathing (69.5%), or both (8.2%). Forty-eight percent were female, and 52% were male, with a mean age at time of surgery of 6 years (SD, 3.4 years).

Though the mean patient ages differ between narcotic and NSAID groups, no statistically significant association was found between age at surgery and primary and secondary bleeding ( $P = 0.18$  and  $P = 0.45$ , respectively) for the NSAID group. For the narcotic group, no statistically significant association between age and secondary bleeding was found ( $P = 0.31$ ). Given only two primary bleeding events in the narcotic group, a meaningful statistical analysis regarding primary bleeding and age could not be performed.

In the NSAID group, 7 (1.6%) required control of their PTH in the operating room, compared with 8 (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). There were nine episodes (2%) of primary PTH in the NSAID group and two episodes (0.12%) of primary PTH in the narcotic group. The incidence of primary PTH was significantly different between groups ( $P < 0.0001$ ). There were 17 (3.8%) secondary PTHs in the NSAID group and 19 (1.1%) secondary PTHs in the narcotic group, a difference that was statistically significant ( $P < 0.0001$ ; OR, 3.5; 95% CI, 1.7–7.2) (Table 1).

**Table 1**

Comparison of outcome measures for narcotic and NSAID groups.

	Narcotic (n = 1731)	NSAIDs (n = 449)	Odds ratio	95% Confidence interval	P value
Primary PTH	3 (0.2%)	9 (2%)	11.78	2.9–55.0	<0.0001
Secondary PTH	19 (1.1%)	17 (3.8%)	3.5	1.7–7.2	<0.0001
Secondary PTH requiring postoperative control	8 (0.5%)	7 (1.6%)	3.4	1.1–10.1	0.01
Evaluation in ED and/or readmission for pain with or without dehydration	57 (3.3%)	19 (4.2%)	1.3	0.7–2.3	0.41

ED, emergency department; NSAID, nonsteroidal anti-inflammatory drug; PTH, post-tonsillectomy hemorrhage.

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