Nonsteroidal Anti-inflammatory Drugs and Postoperative Bleeding Following Adenotonsillectomy in Pediatric Patients

Anita Jeyakumar, MD; Todd M. Brickman, MD; Mary E. Williamson, MD; Keiko Hirose, MD; Paul Krakovitz, MD; Kenneth Whittemore, MD; Christopher Discolo, MD

Objective: To assess the effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on bleeding for pediatric adenotonsillectomy in a retrospective study, based on the common practices at 2 different tertiary care facilities.

Design: A retrospective study.

Setting: Two different tertiary care facilities.

Patients: Children up to 16 years of age, who underwent elective adenotonsillectomy or tonsillectomy, were included in the study. All indications for adenotonsillectomy, and all surgical techniques were included. Children with a bleeding tendency, and those with contraindications to the use of NSAIDs (eg, because of allergy), were excluded from the study.

Interventions: Nonsteroidal anti-inflammatory drugs.

Main Outcome Measure: Postoperative bleeding in patients.

Results: A total of 1160 patients were selected who met the criteria: 673 patients underwent an adenotonsillectomy or tonsillectomy and did not receive any preoperative and postoperative ibuprofen, and 487 patients underwent routine adenotonsillectomy or tonsillectomy and were given postoperative ibuprofen. We noted a 0.7% postoperative bleeding rate in patients who were not allowed to take ibuprofen perioperatively. There was a 1.0% postoperative bleeding rate in patients who were allowed to take ibuprofen perioperatively (P=.75).

Conclusion: Ibuprofen is not a contraindication to adenotonsillectomy or tonsillectomy and should be used in the control of postoperative pain if it is indicated in the patient.

METHODS

A retrospective study was designed to measure the effect of ibuprofen, based on the common practices at 2 academic tertiary referral centers. Institutional review board approval was obtained from both institutions. On review with a statistician, it was determined that 373 patients would be needed in each study arm to attain sufficient power for the study.

At one major academic institution, patients were given ibuprofen (5 mg/kg) without reservation in the postoperative recovery area and were instructed to alternate ibuprofen (5 mg/kg) with acetaminophen (15 mg/kg) without reservation in the postoperative recovery area and were instructed to alternate ibuprofen (5 mg/kg) with acetaminophen codeine every 3 hours. Also, patients are not limited from ibuprofen use preoperatively. At the second academic institution, patients were told not to take ibuprofen up to 5 days before surgery and for 2 weeks after surgery. The patients were given acetaminophen (15 mg/kg) or acetaminophen codeine only for postoperative pain relief.

A total of 1160 patients were reviewed. All patients were 16 years or younger at the time of surgery. The patients were all candidates for elective tonsillectomy and adenotonsillectomy. The patients were followed for 1 month after surgery, as was the standard of care at both institutions. Patients who were lost to follow-up were not included in the study. Also excluded from the study were patients with any documented history of bleeding disorders. There were 673 patients who did not use any ibuprofen in preoperative and postoperative periods, and 487 patients had weight-appropriate use of ibuprofen in the preoperative and postoperative periods. Of the 673 patients who did not use any ibuprofen, 385 were based at one institution and the remaining 288 were from the second institution, based on the practices of a single health care provider at the institution. The end point for each patient was determined at the 1-month postoperative follow-up examination or if there was noted to be a postoperative bleeding episode that required any intervention.

The NSAID and no NSAID groups were compared on bleeding rates using the Fisher exact test. The associations between other factors, and postoperative bleeding and institution were assessed using $\chi^2$ tests, Fisher exact tests, or 2-sample $t$ tests as appropriate.

RESULTS

This study is a retrospective medical chart review of tonsillectomy patients at 2 institutions (The Cleveland Clinic Foundation, Cleveland, Ohio [institution A] and the University of Rochester, Rochester, New York [institution B]). Some patients in institution B were given NSAIDs and some were not. At institution A, of 385 patients, none were given NSAIDs. Institution B had 775 patients, of whom 487 received NSAIDs and 288 did not.

The Table compares the NSAID and no NSAID groups on bleeding rates and other factors. Patients from both institutions (A and B) are included. Of the 673 patients not given NSAIDs, 5 (0.7%) had postoperative bleeding, while 5 of 485 subjects (1.0%) given NSAIDs had bleeding. The difference between groups was not statistically significant ($P = .16$). Patients with bleeding were significantly younger than those without bleeding (mean [SD] age, 4.5 [2.3] years vs 6.7 [3.4] years; $P = .02$).

Bleeding rates at institution B were analyzed to eliminate institution effects (Table). Although there were no bleeding episodes among the 288 patients not given NSAIDs and 5 episodes among the 485 given NSAIDs, this difference was not statistically significant ($P = .16$).

In comparing institutions A and B, they did not differ significantly on bleeding rates, although patients from institution A were significantly younger (Table).

COMMENT

Although a long-practiced procedure, tonsillectomy is still an extremely common operation and considered the most common major surgical procedure performed in children. Hemorrhage is the most common complication. An estimated 2% to 3% of patients have hemorrhage, and 1 of 40 000 patients die from bleeding.⁴ Bleeding may be classified as intraoperative, primary (occurring within the first 24 hours), or secondary (occurring between 24 hours and 10 days). Most cases of intraoperative and primary bleeding are attributed to surgical technique. However, cases of secondary bleeding can be due to multiple causes, most commonly, the loss of surface eschar. The role of NSAIDs in bleeding is not clear in the literature, and we chose to study the effect of ibuprofen, specifically.

Nonsteroidal anti-inflammatory drugs are effective in the management of mild to moderate postoperative pain in children. They can decrease or even eliminate the need for opioid analgesics, thus reducing or eliminating opioid-induced adverse effects.⁵ Nonsteroidal anti-inflammatory drugs, acetaminophen, and opioids are active analgesics and can have additive effects when combined. Because opioids and NSAIDs produce analgesia by different mechanisms, the simple additive effect of administering an opioid in combination with an NSAID is often substantially greater than the analgesia achieved by doubling the dose of either drug administered alone.⁶,⁷ The increasing perioperative use of NSAIDs in children has, however, raised concerns about complications secondary to impaired hemostasis.

Acetaminophen and ibuprofen produce analgesic and antipyretic effects by inhibiting the synthesis of prostaglandins. Specifically, acetaminophen and ibuprofen interfere with cyclooxygenase enzyme activity, thereby preventing the conversion of arachidonic acid to prostaglandins and thromboxanes. Acetaminophen acts predominantly in the central nervous system and therefore lacks anti-inflammatory properties. Ibuprofen acts both peripherally and centrally.⁸

The commonly used NSAIDs, such as ketorolac tromethamine, diclofenac, ibuprofen, and ketoprofen, have reversible antiplatelet effects, which are attributable to the inhibition of thromboxane synthesis.⁹ This adverse effect is of concern during the perioperative period. Bleeding time is usually slightly increased, but in most patients it remains within normal limits in children with normal coagulation systems.⁹,¹¹

Our study has the following limitations. (1) Bleeding from postoperative days 2 to 10 could be attributed either to the continued use of the NSAIDs or to the loss of eschar at 3 to 10 days. (2) Institution A did not administer NSAIDs, so we cannot adjust for institution in the analysis. Differences or the lack of differences between the NSAID and no NSAID groups could be due to differ-
The significant effects of NSAIDs on platelet function are reversible and related in part to blood concentration. Virtually no antiplatelet effect would be present after 5 to 6 drug half-lives.\textsuperscript{12,13} Therefore, any bleeding attributable to single doses of these medications would have to occur in the immediate postoperative period and certainly within the first 24 hours. We did not have any immediate postoperative bleeding (defined as occurring within 24 hours of surgery) in any of the study arms. During the 1-month follow-up period, we did not observe a statistical difference in bleeding rates between the patients who received NSAIDs and those who did not ($P=.75$). We conclude that ibuprofen can be given at a dose of 5 mg/kg, every 6 hours, safely in the perioperative period for a tonsillectomy patient. Ibuprofen is not a contraindication to adenotonsillectomy or tonsillectomy and should be used in the control of postoperative pain if it is indicated in the patient.

Submitted for Publication: January 5, 2007; final revision received March 9, 2007; accepted March 29, 2007. 
Correspondence: Anita Jeyakumar, MD, Department of Otolaryngology, Washington University School of Medicine, St Louis, MO 63110 (jeyakumara@ent.wustl.edu).

Author Contributions: Dr Jeyakumar had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Jeyakumar, Brickman, Hirose, Krakovitz, and Whittemore. Acquisition of data: Jeyakumar, Brickman, Williamson, and Krakovitz. Analysis and interpretation of data: Jeyakumar, Hirose, and Discolo. Drafting of the manuscript: Jeyakumar, Brickman, and Hirose.
REFERENCES