Does Montelukast Have an Effect on Post-tonsillectomy Pain Control in Children? A Randomized Trial Study

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Abstract

Objective. Tonsillectomy surgery is associated with severe postoperative pain that usually requires analgesics including opioids. Pain control is still a big problem after tonsillectomy surgery. We aimed to evaluate the efficacy of preemptive analgesia using montelukast for pediatric post-tonsillectomy pain management. This is the first-time use of montelukast in post-tonsillectomy pain.


Settings. University teaching and research hospital.

Subjects and Methods. A total of 60 children, aged 5 to 15 years, American Society of Anesthesiologist class I-II, scheduled for elective tonsillectomy were enrolled in this clinical trial study. The patients were randomized into 2 groups: the montelukast group (group M, n = 30) and control group (group C, n = 30). Group M received an oral montelukast tablet and group C received placebo at 2400 PM on the morning before surgery. Post-tonsillectomy pain was evaluated with the Wong-Baker FACES Scale during the 24 hours after surgery. Patients’ intraoperative hemodynamic parameters and intraoperative and postoperative complications were recorded.

Results. There were statistically significant differences between group C and group M for Wong-Baker FACES pain rating scale scores (P < .05). In the 24 hours after surgery, the total number of patients using rescue analgesics was higher in group C than in group M, and the difference was statistically significant (P < .001). There was no significant difference in demographic parameters (P > .05). There were no significant differences in postoperative nausea and vomiting, otalgia, trismus, fever, or halitosis between the groups (P > .05).

Conclusion. Preemptive montelukast can be used safely to reduce the serious pain caused by tonsillectomy in children.

Keywords
post-tonsillectomy analgesia, tonsillectomy, montelukast, pediatrics
Noxious interventions such as surgery can cause prolonged changes in central neural function and extreme response to pain associated with a lowered pain threshold.9 Preemptive analgesia reduces the central sensitization due to noxious interventions all throughout the perioperative period.10

The purpose of this study was to assess the efficacy of a preemptive single dose of montelukast for post-tonsillectomy analgesia.

**Materials and Method**

This prospective, randomized, double-blinded study was begun after receiving the approval of the Ataturk University Local Ethics Committee and informed consent of the patients. This study was conducted from December 2013 to February 2014. The study included 60 patients with chronic tonsillitis, defined as chronic infection of the palatine tonsils on the basis of recurrent tonsillitis (a frequency of at least 7 episodes in the past year or at least 5 episodes per year for 2 years according to the American Academy of Otolaryngology—Head and Neck Surgery), who were aged 5 to 15 years and with American Society of Anesthesiologists (ASA) class I-II planned for tonsillectomy. The study flow diagram can be seen in Figure 1. On the preanesthesia examination, the patients had normal body temperature and no active upper or lower respiratory tract infection. The criteria for exclusion from the study were known allergy to the drugs to be used in the study; renal, hepatic, pulmonary, or cardiac disease; ASA III-IV; younger than 5 years or older than 15 years, active upper or lower respiratory tract infection, and no permission from families for participation in the study.

The patients were preemptively divided into 2 groups by the computerized randomization: montelukast group (group M) and placebo or control group (group C). The placebo was produced by a pharmacist to be the same size, taste, and color as the original drug. Children aged 5 years received montelukast 4 mg (Singulair 4-mg chewable tablet), and children aged 6 years and older received 5 mg montelukast (Singulair 5-mg chewable tablet) in group M. Group C received the placebo. For both groups, the drug was taken at 12:00 AM the night before the operation in the hospital. The patients were taken into the operation room at 8:00 AM the next day. All tonsillectomies were performed by the same surgeon, who had not been informed about which drug the child received, using the cold dissection tonsillectomy technique.

The electrocardiography, noninvasive blood pressure, oxygen saturation, and end-tidal carbon dioxide level of all patients were monitored continuously. All patients were monitored intraoperatively. All patients received induction with standard thiopental intravenously (IV) 3 to 5 mg/kg and fentanyl IV 1 μg/kg. Rocuronium bromide 0.6 mg/kg was used as muscle relaxant. For maintenance of the anesthesia, 2% sevoflurane was given in a mixture of 45%:55% O2:N2O. The patients’ preinduction

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**Figure 1.** Study flow diagram.
basal values of systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation, and pulse were determined, and after induction, they were recorded intraoperatively every 5 minutes. After the operation, the patients were decurarized with neostigmine IV 0.04 mg/kg and atropine 0.02 mg/kg and extubated. Following surgery, the patients were taken into the postoperative recovery room. After entering the recovery room, each patient’s pain status was measured with the Wong-Baker FACES Scale (Figure 2) at 15, 30, and 45 minutes and at 1, 2, 4, 8, 12, and 24 hours. An anesthesiologist who had not been informed about the drug to be given to the patients scored the patients according to the Wong-Baker FACES Scale. Paracetamol (Calpol suspension 120 mg/5 mL; GlaxoSmithKline, Istanbul, Turkey) 10 mg/kg was received every 6 hours routinely in all patients. Patients with a Wong-Baker score of 3 points and greater received meperidin HCl (Aldolan ampul, 100 mg/2 mL, Liba, Turkey) IV 0.3 mg/kg as postoperative rescue analgesic. Patients were continued in their assigned group and continued to be evaluated after they were given rescue medication. The number of patients needing additional analgesia was recorded.

**Statistical Analysis**

The difference in mean pain scores of the 2 groups in the study by Aysenur et al in our clinic was 10%. Accordingly, we determined that the number of patients required in each group was 27, based on a power of 95% and alpha error of .05 by using Russ Lenth’s Piface Java module. The Statistical Package for Social Sciences (SPSS Inc, Chicago, IL) 20.0 Program was used for the statistical evaluation of the obtained data. In the descriptive statistics, the numerical data were presented as mean and standard deviation, and the categorical data were represented as numbers and percentages. The χ² test was used for the comparison of the categorical data, and the Student t test and its variant, the Mann-Whitney U test, were used for the comparison of numerical data. P < .05 was accepted as statistically significant.

**Results**

The postoperative pain scores at 15, 30, and 45 minutes and at 1, 2, 4, 8, 12, and 24 hours postoperatively for the 2 groups are reported in Table 1. The Wong-Baker FACES scores of group M and group C patients showed normal distribution according to the histogram graphics. The data were analyzed using the Student t test. There was a statistically significant difference between the 2 groups in terms of the Wong-Baker FACES scores at all times. Pain scores of group M were less than those of group C (P < .001 at 2, 4, 8, 12, and 24 hours; P = .001 at 15 minutes and 1 hour; P = .014 and P = .005 at 30 and 45 minutes, respectively). The changes in postoperative pain scores are shown in Figure 3.

The total number of patients using rescue analgesic (25 patients in group C and 9 patients in group M required rescue analgesics) was higher in group C than in group M, and the difference between the groups was statistically significant (P < .001).

![Wong-Baker FACES Pain Rating Scale](image_url)
The demographic and operative data are shown in Table 2. There was no statistically significant difference in the parameters (age, weight, gender, duration of anesthesia, and duration of surgery) among the groups ($P > .05$).

There was no statistically significant difference between the 2 groups in terms of intraoperative systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and oxygen saturation ($\text{SpO}_2$; $P > .05$).

The postoperative parameters related to morbidity are shown in Table 3. There was no significant difference between the 2 groups in terms of morbidity (fever, bleeding, etc; $P > .05$).

**Discussion and Conclusion**

The results of this study showed that the Wong-Baker FACES scores and the number of patients needing rescue analgesics in the early postoperative period were significantly lower in group M compared with group C.

Although tonsillectomy has been accepted as a minor surgery, post-tonsillectomy pain is a frequent problem. Almost all patients undergoing tonsillectomy experience serious pain in the postoperative period and need analgesics. There have been many studies on post-tonsillectomy pain. Some of the measures against pain are topical ketamine and tramadol administration, peritonsillar infiltration of local anesthetics, and preemptive multimodal analgesia. One of the most frequent causes of pain is postoperative trauma, and the etiopathogenesis of pain is the underlying inflammation. For this reason, pain due to postoperative trauma has been described as an acute pain accompanied by the inflammatory process.

Montelukast is a leukotriene receptor antagonist. It is used particularly for the treatment of asthma in children. Montelukast has been shown to improve life quality and respiratory functions in children, with side effects similar to those of placebo. Leukotrienes are derived from arachidonic acid and are one of the mediators that play a role in the occurrence of pain. Montelukast can inhibit pain by acting as a leukotriene receptor antagonist. As far as we know, there has been no study in the literature on the use of montelukast in post-tonsillectomy pain control. Therefore, this study is the first study on the use of montelukast to relieve pain in tonsillectomy. However, there have been some studies on the use of montelukast against dysmenorrhea with successful results. These studies have reported that montelukast reduces menstrual pain with its anti-inflammatory effect, which decreases the vascular permeability and inhibits cytokines.

In general, pain can be successfully relieved by knowing the mechanisms of pain. Leukotrienes, which are among the products of arachidonic acid metabolism, may play a role in the occurrence of pain. They can cause pain by increasing vascular permeability and causing migration, aggregation, and degranulation of neutrophils. In our study, we wanted to determine whether pain would be relieved or not by inhibiting the leukotriene receptor, which plays a role in the mechanism of pain. For this purpose, we preferred to use a preemptive single dose of montelukast, which has been used with safety for many years. The aim of analgesia is to inhibit painful stimulants from reaching the central nervous system and to provide a lower need for analgesics in the postoperative period.
In our study, we recorded the patients needing rescue analgesics in the postoperative period. As a result, we found that 25 patients in group C but only 9 patients in group M required rescue analgesics, and the difference between the groups was significant, as shown by the \( \chi^2 \) test (\( P < .001 \)). However, nausea and vomiting were determined to be insignificantly different between the 2 groups.

Many drugs are available for pain control in the posttonsillectomy period, administered in different dosages and through different routes. Among these, opioids are widely used for analgesia. Pediatric anesthetists in the United Kingdom have reported that in the post-tonsillectomy period, 68% of their patients required morphine and meperidine for analgesia. However, the use of these drugs is associated with a high incidence of postoperative nausea and vomiting. The other important side effects of the drugs are sedation and respiratory depression. Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective in reducing post-tonsillectomy pain, but because of their antiplatelet effect, they may increase the probability of bleeding. In the study by Lewis et al., NSAIDs were associated with an increased risk of surgical intervention. However, there was no statistically significant difference. Also, NSAIDs did not change the frequency of perioperative bleeding requiring nonsurgical intervention. Therefore, there is no sufficient evidence to exclude an increased risk of bleeding. However, nausea and vomiting were determined to be insignificantly different between the 2 groups.

To relieve post-tonsillectomy pain, peritonsillar infiltration of local anesthetics has also been applied, but this has resulted in complications such as serious upper respiratory tract obstruction. In our study, we used an oral drug to avoid such complications.

Our study has some limitations. For correction of these limitations, new studies are required. In our study, we used montelukast as a single dose. Montelukast, which has rare side effects, can be used for a certain period of time in the postoperative period to better evaluate its analgesic effect. Furthermore, leukotrienes are not the only mediators in pain mechanism. Some other mediators such as prostaglandins also play a role in the pain mechanism. Along with inhibition of leukotriene receptors, NSAIDs, which control pain by reducing prostaglandin production through inhibition of cyclooxygenase, may also be used. Thus, the co-effect of these 2 different mechanisms can be assessed. One should not forget the risk of postoperative bleeding. Montelukast can be used together with topical agents such as tramadol and ketamine or with peritonsillar infiltration of local anesthetics, and the effect of these treatment modalities can be assessed.

In conclusion, we are of the opinion that in pediatric patients, montelukast usage is more effective than the placebo, and montelukast can be safely used to reduce pain caused by tonsillectomy in the 24 hours postoperatively.

**Author Contributions**

Ilker Ince, data analysis, drafting, final approval, accountability for all aspects of the work; Ozgur Yoruk, data analysis, drafting, final approval, accountability for all aspects of the work; Ali Ahiskaliloglu, data analysis, drafting, final approval, accountability for all aspects of the work; Mehmet Aksoy, data analysis, drafting, final approval, accountability for all aspects of the work; Aysenur Dostbil, data analysis, drafting, final approval, accountability for all aspects of the work; Mine Celik, data analysis, drafting, final approval, accountability for all aspects of the work.

**Disclosures**

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**References**


