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ORIGINAL RESEARCH

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Comparison of celecoxib and acetaminophen for pain relief in pediatric day case tonsillectomy: A randomized double-blind study

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Abstract

Objective: Post-tonsillectomy pain is a common morbidity in children. The aim of this study was to compare the efficacy of celecoxib with acetaminophen on pain relief in pediatric day-case tonsillectomy.

Methods: We compared the analgesic effect of celecoxib (99 patients) with acetaminophen (100 patients) for the management of post-tonsillectomy pain. Post-tonsillectomy pain score was evaluated three times a day for 7 days. In addition, the incidence of post-tonsillectomy bleeding and the rate of patients who returned to regular diet were evaluated.

Results: In the first day, we observed lower mean pain score in the celecoxib group, than the acetaminophen group ($P = 0.013$). The overall pain score in other days was not significantly different between the two groups. In the celecoxib group, more patients resumed regular amount of oral intake within the first 3 days. Also, the rate of post-tonsillectomy bleeding in the two groups was not statistically different.

Conclusion: We recommend celecoxib as a more suitable choice than acetaminophen for post-tonsillectomy pain management in the first day and resuming regular diet within 3 days.

Level of Evidence: 1b.

KEYWORDS

acetaminophen, celecoxib, cyclooxygenase-2 inhibitors, post-tonsillectomy hemorrhage, post-tonsillectomy pain

1 | INTRODUCTION

Analgesic selection in tonsillectomy is a major and controversial issue in the field of pediatric otolaryngology. Pain is the most common post-tonsillectomy morbidity that persists until the first week, and then dramatically declines. In addition, the most potentially life-threatening complication is post-tonsillectomy bleeding. The incidence of postoperative bleeding has a wide range of 0.2% to 2.2% for

primary bleeding within 24 hours after tonsillectomy and 0.1% to 3% for secondary bleeding.[1] In a recent systematic review, Francis et al reported the 4.2% bleeding rate after tonsillectomy in children.[2]

Regarding postoperative pain management, acetaminophen (paracetamol) and nonsteroidal anti-inflammatory drugs (NSAIDs) are two common categories of drugs that are usually used. Nonselective NSAIDs inhibit both cyclooxygenase-1(COX-1) and COX-2. The adverse effects of blocking COX-1 are gastric mucosal injury, hematologic disorder, and kidney damage.

In addition, selective COX-2 inhibitors such as celecoxib, rofecoxib, and valdecoxib are as effective as nonselective COX-2 inhibitors and opioids with fewer side effects.[3] Recently, researchers have shown an increased interest in the usage of COX-2 inhibitors for postoperative pain management.[4]

In addition, comparative researches between NSAIDs and acetaminophen have identified that NSAIDs are more effective than acetaminophen in some procedures (eg, children with acute musculoskeletal injuries, chronic nonspecific low back pain, arthroscopic knee surgery, postoperative orthopedic pain).[5-7] But in other conditions (eg, after blunt limb injury, lateral ankle sprains, and musculoskeletal pain) similar analgesic effects were observed.[8-11]

It is interesting that just a few studies addressed the analgesic effect of selective COX-2 inhibitors in pediatric day case tonsillectomy. One of early study on this issue is that of Bean-Lijewski et al in 2007 that compared rofecoxib with acetaminophen plus hydrocodone in a period of 72 hours postoperatively in pediatric tonsillectomy. They reported substantial pain reductions just after swallowing in the rofecoxib group.[12] In 2015, Murto et al compared oral celecoxib with placebo and concluded that a three-day usage of celecoxib reduces early post-tonsillectomy pain in children.[13]

Since the character and level of postoperative pain are directly related to the type of surgical procedure, for better pain management, researchers should conduct more procedure-specific and age-specific studies. However, there has not been direct comparative research between celecoxib as a selective COX-2 inhibitor and just acetaminophen in pediatric ambulatory tonsillectomy. Therefore, we have decided to carry out a randomized double-blind study to assess the analgesic effect of these drugs. We hypothesized that the use of celecoxib would lead to more improved postoperative pain than acetaminophen without increasing the risk of postoperative complications.

2 | MATERIALS AND METHODS

This prospective randomized double-blind clinical trial was carried out on 240 children, who underwent (adeno)tonsillectomy from January 2019 to December 2020 in Dastghaib hospital, affiliated with Shiraz University of Medical Sciences and Dena private hospital. An informed consent form was obtained from parents and the research protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (Code: Ir.sums.rec.1394.s946) and was registered in the Iranian Registry of Clinical Trials, Primary Registry in the World Health Organization (WHO) Registry Network (IRCT code: IRCT2015080919470N29).

Inclusion criteria were: 3 to 15 year old children who had undergone day case tonsillectomy due to recurrent tonsillitis, standard body weight (BMI 5-85 percentile), normal growth and development, normal physical development, living nearby the hospitals (maximum 30 minutes by car). Moreover, at least one of the parents should have a high school education to support the child and follow the correct procedure. Since postoperative pain is significantly less important and shorter in tonsillectomy for obstruction, rather than infection.[14] It would be more relevant to include only one kind of indication in the study design. Therefore, no tonsillectomies for obstruction cases were included in the current study. The indication of recurrent tonsillitis was defined by Paradise criteria for tonsillectomy,[15] in this study. Exclusion criteria were: any contraindications to celecoxib or acetaminophen such as patients with a known allergy to celecoxib or other NSAIDs, and sulphonamide, asthma, any hematologic disorder, cardiovascular disease, gastrointestinal disease, kidney or liver dysfunction, and history of using any analgesic medication within 12 hours before surgery. In addition, we ruled out all specific diseases related to either abnormal growth or physical and mental development.

Based on Vallee et al's study,[16] a sample of at least 72 participants in control and intervention groups (144 totally) would be required to have 90% power at a significance level of 0.05 for detecting one score mean difference between groups in visual analogue scale (VAS) score. At first, 240 eligible participants were randomly assigned in two groups by blocked randomization method. Given a block size of two, there were two possible ways to assign participants to a block; AB, BA (A stands for celecoxib and B stands for acetaminophen). By Excel software, we generated 120 numbers between zero and nine. For even numbers (0, 2, ..., 8) we selected AB order and we considered BA order for odd numbers (1, 3, ..., 9). For AB, the first patient was assigned to celecoxib and the second to acetaminophen, while this order was reversed for BA. Finally 100 patients were analyzed in acetaminophen group and 99 patients in celecoxib group.

Children and parents did not know the difference between analgesics (blinding of the participants). Parents wrote down pain scores, and the statistician as the final assessor was blind to the selection group.

Technique of anesthesia was similar for the two groups. A 20-gauge IV catheter was inserted by a nurse. Premedication was with 0.01 mg/kg midazolam and 2 mg/kg fentanyl before induction of anesthesia. Then, anesthesia was induced with 5 to 7 mg/kg thiopental, and tracheal intubation was facilitated with 0.2 mg/kg atracurium. Anesthesia was maintained with isoflurane, 35% oxygen, and nitrous-oxide with intermittent positive pressure ventilation. On completion of the procedure with regular and adequate rate and depth of respiration, extubation was done. Day case tonsillectomy was performed by using cold dissection and hemostasis was done by ligation of bleeders with bipolar electrical cautery. Adenoidectomy was performed by

curettage. All procedures were performed by the senior author. Details of operation have been presented in another article.[17] All procedures were extracapsular tonsillectomy, which was performed by a single surgeon via cold steel technique, and ligation of bleeders by bipolar cautery. After tonsillectomy, patients were transferred to the recovery room. Then, in the post recovery room, anesthesiologist checked the patient's condition and patients were ready to transfer to the otolaryngology ward. All patients were observed for at least 8 hours in the ward and analgesics were ordered by an otolaryngologist.

The primary outcome parameter was the intensity of postoperative pain within the first week. The secondary outcome was the incidence of postoperative bleeding within 10 days. A patient was considered to have post-tonsillectomy bleeding when; (1) he/she developed simple oropharyngeal bleeding that required electrical or chemical cauterization requiring outpatient management; or (2) developed bleeding that required readmission to the hospital merely for observation or (3) required surgical intervention and ligation of bleeders in the operating room or blood transfusion requirement. Another secondary outcome was the rate of children who returned to regular diet each day.

Since literature evidence shows that VAS is significantly more within the first week and decreases rapidly after that,[18,19] and postoperative bleeding also might occur within 10 days,[20] we followed patients for 10 days after surgery. The first loading dose of oral acetaminophen after discharge consisted of 40 mg/kg oral suspension of 120 mg/5 mL, 4 hours after tonsillectomy and was then followed by 15 mg/kg four times a day (6, 12, 18, and 24 hours) for 7 days. While, the first dose of oral celecoxib 6 mg/kg was administered 1 hour preoperatively followed by 3 mg/kg twice a day after discharge for 7 days. Peak plasma of celecoxib (oral administration) concentration occurs after 2 to 4 hours and its half-life occurs about 11 hours.[21] Also, the onset of action of acetaminophen (oral administration) is 15 to 30 minutes, and its duration of action is 4 to 6 hours.[22] Oral celecoxib suspension 100 mg/5 mL was prepared in opaque bottles by the author who is pharmacologist in the local hospital pharmacy. Sodium diclofenac 50 mg suppository was given as a rescue painkiller to patients who suffered from pain and their VAS pain score was more than 4. Also, the usage and the time to the first usage of rescue analgesics were recorded up to 3 days after the operation. Since we did not expect severe pain in the second week, the analgesic prescription was taken as needed (PRN) and not according to the regular schedule.

Prior to discharge, patients were visited by an academic otolaryngologist and if the patients were awake and alert with normal vital signs, they were allowed to leave the hospital. A teaching booklet and a checklist were given to the parents by the anesthesiology resident at the time of discharge. The booklet included a set of recommendations for management of postoperative common signs and symptoms such as pain and those that require more medical attention such as bleeding. Also, the booklet contained the anesthesiology resident's telephone number for further communication in case of any adverse reactions to drugs such as skin rash, bloody or tarry stool, vomit that look like the coffee ground, itching, dark urine, swelling in ankles, feeling shortness of breath.

The checklist consisted of special charts to record daily pain score according to Wong and Baker Pain Rating Scale, which is a pain score according to facial expression from 1 (no pain) to 10 (worst, unbearable pain).[23] The first and second pain score was assessed by parents, albeit under supervision of an anesthesiology resident, at 4 and 8 hours after surgery. Then pain score was evaluated three times a day, after breakfast, after lunch, and after dinner within 7 days after surgery. In addition, parents wrote down the type and the amounts of foods their child ate at breakfast, lunch, and dinner. We defined "the return to regular diet" as resuming the regular amount of Iranian traditional diet as similar as the preoperative period, in two consecutive days. Regarding temperature and texture, the Iranian regular diet is comparable to other regular diets in all of the world.[24]

The same anesthesiology resident called the parents every three days, until the tenth day to check the condition of the patients, answered their concerns and encouraged them to fill the pain scale. Furthermore, an appointment was arranged in the third day and 10th day after surgery, when patients were visited by the otolaryngologist.

Statistical analysis was done using repeated measures analysis of variance, Cox regression, chi-square test, and *t*-test. All statistical analyses were carried out using SPSS software (IBM SPSS Statistics for Windows, Version 21.0. Armonk, New York: IBM Corp.).

3 | RESULTS

A total of 268 patients enrolled in the study at first. Then, 28 children were excluded due to not meeting inclusion criteria or declined to participate. The remaining participants were randomly divided into two groups of 120 patients. At the end of study, 99 patients in celecoxib group and 100 patients in acetaminophen group were analyzed (Figure 1). There were no significant differences between the two groups considering the age ($P = 0.088$) and gender ($P = 0.110$; Table 1).

Mean pain score at 4 and 8 hours post-tonsillectomy were 7.2 ± 1.6 and 6.7 ± 1.7, respectively, in acetaminophen group and in celecoxib group 6.9 ± 2.2, 6 ± 1.9. The difference between groups at 4 hours post-tonsillectomy was not statically significant ($P = 0.272$) but it was significant at 8 hours post-tonsillectomy ($P = 0.007$). Also, means of pain scores after breakfast (4.9 ± 2.0 vs 6.6 ± 1.8), lunch (4.6 ± 1.9 vs 6.3 ± 1.4), and dinner (4.8 ± 2.1 vs 6.2 ± 1.5) in celecoxib group were less than acetaminophen in first day post-tonsillectomy ($P < 0.001$). But in other days there were no significant differences between the means of pain scores between the two groups in all measurements; after breakfast, lunch, and dinner ($P > 0.05$). Pain scores within one week after operation in both groups are shown in Figure 2.

As shown in (Table 2), the rate of additional rescue analgesic use within 7 days after the operation was not significantly different between the celecoxib and acetaminophen groups ($P > 0.05$). Moreover, the time of the first use was not significant between the acetaminophen and celecoxib groups (17.9 vs 18.2 hours, $P = 0.072$; Table 2).

Regarding post-tonsillectomy bleeding, one patient in celecoxib group (1%) was admitted to the hospital in 3 days after surgery. She was a 6 year old girl who required controlled bleeding in the operating

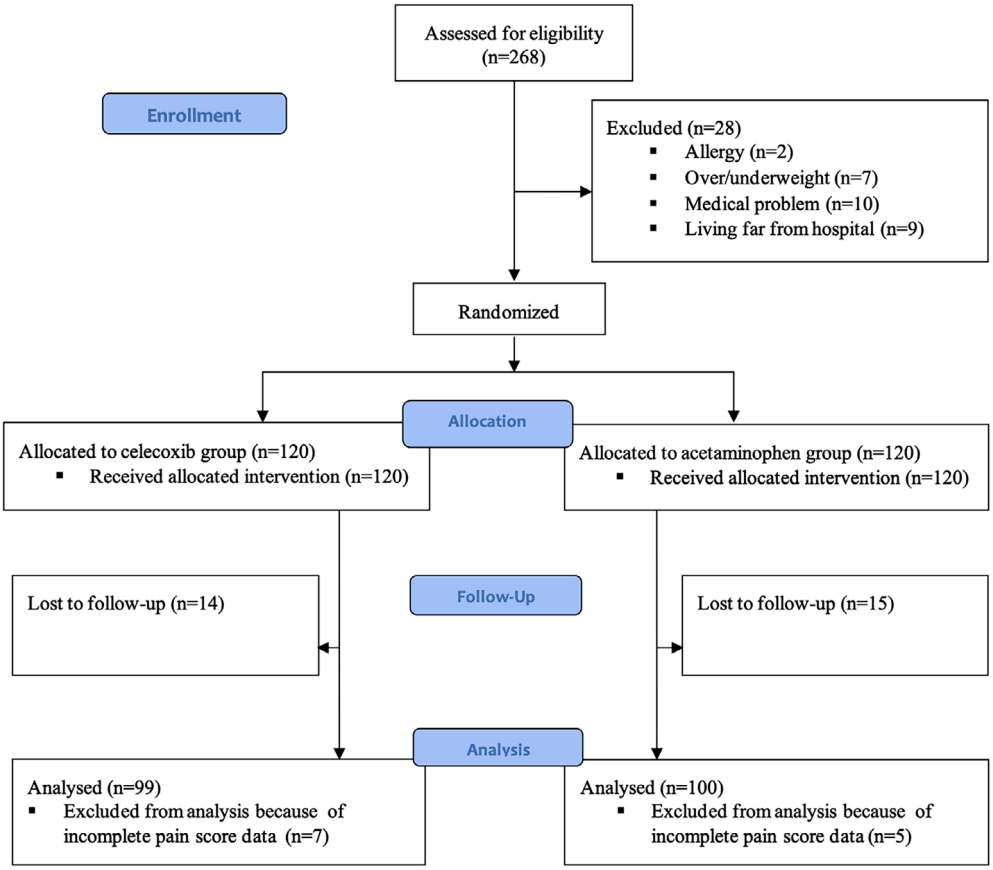

FIGURE 1 CONSORT trial flow diagram

TABLE 1 Baseline characteristics and post-tonsillectomy bleeding of patients

	Acetaminophen group (n = 100)	Celecoxib group (n = 99)	*P*-value
Sex, male	67(67.0)[a]	55(55.5)	0.110
Age, y	7.3 ± 1.9(4-13)[b]	7.8 ± 2.2(3-14)	0.088
Post-tonsillectomy bleeding	0(0)	1(1)	0.497

[a]N (%).
[b]Mean ± SD (range).

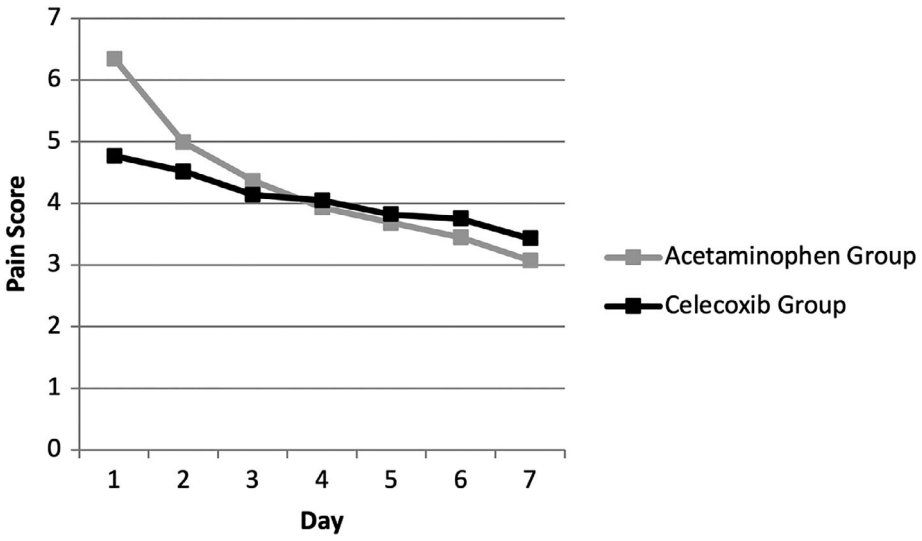

FIGURE 2 Mean pain scores post-tonsillectomy within one week in acetaminophen and celecoxib groups

TABLE 2 Use of additional rescue analgesic in acetaminophen vs celecoxib groups

		Acetaminophen group (n = 100)	Celecoxib group (n = 99)	*P*-value
Additional rescue analgesic use				
	Day 1	10(10.0)[a]	8(8.1)	0.637
	Day 2	10(10.0)	8(8.1)	0.637
	Day 3	8(8.0)	7(7.1)	0.804
	Day 4	7(7.0)	7(7.1)	0.984
	Day 5	7(7.0)	6(6.1)	0.789
	Day 6	4(4.0)	4(4.0)	1.000
	Day 7	3(3.0)	4(4.0)	0.721
Giving additional rescue analgesic for the first time	Hour	17.9 ± 0.7[b]	18.2 ± 1.5	0.072

[a]N (%).
[b]Mean ± SD.

room, but there was no need for blood transfusion. Also, there was no post-tonsillectomy bleeding within 10 days after operation in the acetaminophen group. The difference between the two groups was not significant ($P = 0.497$). No serious side effects such as renal failure, gastrointestinal bleeding, and drug reaction were detected.

Number of patients who resumed a regular diet within the first 3 days post-tonsillectomy between acetaminophen and celecoxib groups was significantly different ($P < 0.05$). More patients in celecoxib group used regular diet (Table 3).

There were no significant differences in the time to return to regular diet in three measured stages between the acetaminophen and celecoxib groups. The median time to return to regular diet after breakfast was 6 days for the acetaminophen group and 5 days for the celecoxib group ($P = 0.253$, Table 4, Figure 3A). The median time to return to regular diet after lunch was 5 days for the acetaminophen group and 4 days for the celecoxib group ($P = 0.430$, Table 4, Figure 3B). The median time to return to regular diet after dinner was 5 days for both the acetaminophen and celecoxib groups ($P = 0.148$, Table 4, Figure 3C).

TABLE 3 Number of patients who resuming regular diet within one week in acetaminophen and celecoxib groups

	Group	Day1	Day2	Day3	Day4	Day5	Day6	Day7
After breakfast	Acetaminophen	3(3)[a]	4(4)	14(14)	27(27)	37(37)	41(41)	71(71)
	Celecoxib	17(17.2)	20(20.2)	31(31.3)	33(33.3)	32(32.3)	39(39.4)	58(58.6)
	P-value	0.001[b]	0.000[b]	0.004[b]	0.330	0.488	0.817	0.076
After lunch	Acetaminophen	1(1)	11(11)	16(16)	33(33)	50(50)	67(67)	81(81)
	Celecoxib	21(21.2)	22(22.2)	29(29.3)	40(40.4)	42(42.4)	54(54.5)	70(70.7)
	P-value	0.000[b]	0.033[b]	0.025[b]	0.279	0.284	0.082	0.099
After dinner	Acetaminophen	2(2)	10(10)	9(9)	28(28)	43(43)	54(54)	76(76)
	Celecoxib	20(20.2)	28(28.3)	32(32.3)	34(34.3)	44(44.4)	50(50.5)	63(63.6)
	P-value	0.000[b]	0.001[b]	0.000[b]	0.334	0.837	0.622	0.065

[a]N(%).
[b]Significant at $P < .05$.

TABLE 4 - Median times to return to regular diet (day) and Cox regression outputs

	Group			Median		95% CI for Median		
After breakfast	Celecoxib			5.000		(4.170, 5.830)		
	Acetaminophen			6.000		(5.353, 6.647)		
		Beta	**SE**	**Wald**	**df**	**P-value**	**HR**	**95% CI for HR**
	Group	-0.200	0.175	1.309	1	0.253	0.818	(0.580, 1.154)
	Group			**Median**		**95% CI for Median**		
After lunch	Celecoxib			4.000		(3.399, 4.601)		
	Acetaminophen			5.000		(4.554, 5.446)		
		Beta	**SE**	**Wald**	**df**	**P-value**	**HR**	**95% CI for HR**
	Group	-0.128	0.163	0.622	1	0.430	0.880	(0.640, 1.210)
	Group			**Median**		**95% CI for Median**		
After dinner	Celecoxib			5.000		(4.526, 5.474)		
	Acetaminophen			5.000		(4.545, 5.455)		
		Beta	**SE**	**Wald**	**df**	**P-value**	**HR**	**95% CI for HR**
	Group	-0.239	0.165	2.098	1	0.148	0.787	(0.569, 1.088)

Abbreviation: HR, hazard ratio.

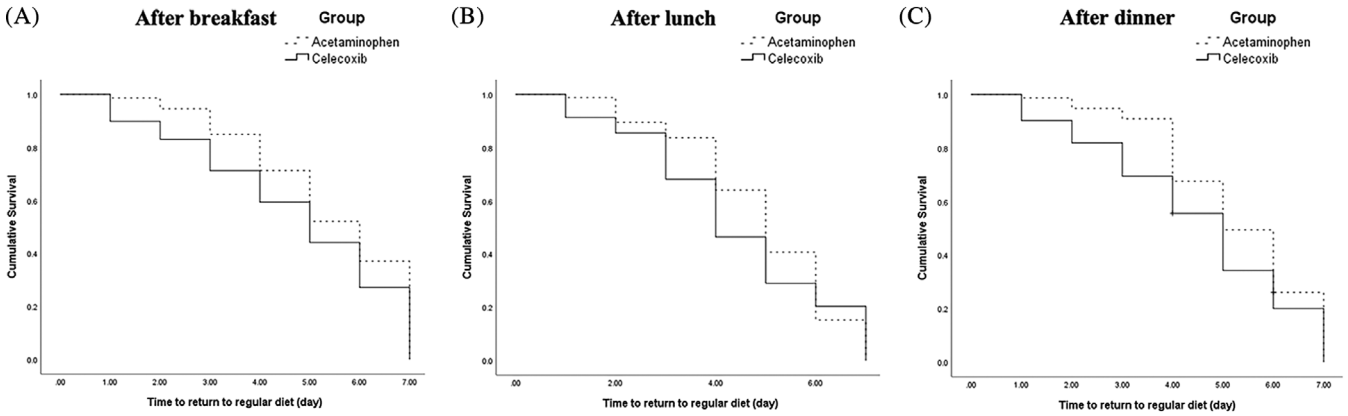

FIGURE 3 Survival functions of the time to return to regular diet for the celecoxib and acetaminophen groups in three stages: after breakfast (A), after lunch (B), and after dinner (C)

TABLE 5 Summary of researches regarding the effect of COX-2 inhibitors on post-tonsillectomy pain

Author (y)	Type of analgesia (number of patients)	Age of patients (y)	Conclusion
Pickering et al (2002)[33]	Combining paracetamol with: • Rofecoxib (40) • Ibuprofen (40) • Placebo (40)	7	The combination of ibuprofen (but not rofecoxib) with paracetamol was beneficial.
Joshi et al (2003)[34]	• Rofecoxib (34) • Placebo (32)	6	A single preoperative dose of rofecoxib reduced postoperative pain.
Sheeran et al (2004)[35]	• Rofecoxib (23) • Placebo (22)	7-7.5	There was no significant difference between the groups.
Naesh et al (2005)[36]	• Paracetamol with rofecoxib (20) • Paracetamol with placebo (20)	15-43	Three was not a significant difference in analgesic effect between the groups.
Nikanne et al (2005)[37]	• Ketoprofen (39) • Celecoxib (37) • Placebo (39)	16-47	Ketoprofen was better in the first 4 h postoperatively but in the next 20 h, it was similar to celecoxib. After discharge celecoxib was better and the recovery was faster.
Bean-Lijewski et al (2007)[12]	• Rofecoxib (20) • Hydrocodone with acetaminophen (20)	8-10	Rofecoxib was better than hydrocodone with acetaminophen.
Valee et al (2007)[16]	• Acetaminophen with morphine (40) • Rofecoxib with morphine (40)	7-8	The combination of rofecoxib and morphine was better than acetaminophen and morphine.
Murto et al (2015)[13]	• Celecoxib (141) • Placebo (141)	2-18	A 3-day course of celecoxib was better than placebo.
Li et al (2016)[38]	• Parecoxib (30) • Placebo (40)	3-7	A single intravenous injection of parecoxib was beneficial.
Tan et al (2016)[39]	Three Parecoxib groups: • 0.25 mg/kg (18) • 1 mg/kg (18) • 2 mg/kg (18)	9	There were no differences in analgesic effect between different doses of parecoxib.
Van Daele et al (2016)[40]	• Celecoxib (9) • Placebo (6)	19-32	Analgesic effect and recovery were better in celecoxib group.
Ng et al (2017)[41]	• Celecoxib (40) • Placebo (40)	18-55	There was no significant difference between the groups.
Current study	• Celecoxib (99) • Acetaminophen (100)	3-15	Celecoxib was better than acetaminophen in the first day.

4 | DISCUSSION

One of the more significant findings to emerge from this prospective randomized clinical trial study is that celecoxib administration can lead to less pain in comparison with acetaminophen in the first post-operation day. Studies show that the most severe post-tonsillectomy pain develops within the first 3 days, chiefly in the first 24 hours.[25-27] Additionally, we found that more patients who used celecoxib returned to regular diet in comparison with acetaminophen. However, the rate of post-tonsillectomy bleeding was similar in both groups, with a relatively small sample groups of approximately 100 patients enrolled per arm, the power would not be sufficient to detect a difference between the groups. So the authors do not claim that celecoxib does not increase the bleeding risk compared to acetaminophen. Regarding the side effects COX-2 inhibitors, it seems that short term usage of them may be safe in healthy children.

Four studies were carried out on the effect of COX-2 inhibitors in adult outpatient otolaryngology surgery. In two of them by Issioui et al, they found that quality of recovery was considerably improved in the celecoxib or rofecoxib group alone or in combination with acetaminophen.[28,29] In a similar setting, Watcha et al found that while celecoxib was effective, rofecoxib was better regarding postoperative pain and postoperative recovery.[30] Recart et al revealed that 400 mg oral celecoxib was a more potent analgesic than 200 mg as a premedication.[31] In the above mentioned researches, there were small sample size of the studies, and a wide range of surgeries in different anatomic areas; while, the type and site of surgeries were not considered as a confounding factor in postoperative pain scoring. This view is supported by Sommers et al who reported that difference exists between the prevalence of intolerable postoperative pain in various otolaryngology surgeries. They stated that oropharyngeal surgery had more severe pain in comparison to nose, ear, neck, and salivary gland surgeries.[32]

Over the past decade, there have only been a few published studies that describe the effect of COX-2 inhibitors on pediatric post-tonsillectomy pain[33-41] (Table 5). As shown in (Table 5), some researchers investigated the effect of COX-2 inhibitors in combination with acetaminophen or other analgesics, and some other studies selected a single-drug comparison method. No ideal post-tonsillectomy analgesic has been identified, nor has the frequency of its administration been detailed.[15] Since, evidence for combination regimens is sparsely documented and no well-documented gold standard exists,[42] combination regimens of acetaminophen with NSAIDs are not common in our practice setting. Also, because of ethical issues, comparison to a placebo is not appropriate at this point. Therefore, we compared celecoxib with acetaminophen, according to the routine of our center. In this regard, assessing the effect of COX-2 inhibitors combining with acetaminophen is recommended for further studies.

Surveys such as those conducted by Naesh et al[36] and Ng et al,[41] question the usefulness of COX-2 inhibitors in post-tonsillectomy pain. In contrast, others highlight the need for COX-2 inhibitors. Regarding pediatric post-tonsillectomy pain, two studies indicate that COX-2 inhibitors are effective analgesics. Bean-Lijewski et al,[12] compared rofecoxib with combination of hydrocodone and acetaminophen. They concluded that rofecoxib was better than hydrocodone with acetaminophen. However, the sample size was small and they observe the patients for only 72 hours, but it is one well-known experiment in children. Building on the work of Bean-Lijewski et al[12] and Murto et al[13] compared celecoxib with placebo only for a 3-day course. Children received celecoxib 6 mg/kg preoperatively, and then 3 mg/kg twice daily for five doses. They found that patients who received celecoxib had a modest pain reduction in the first and second postoperative days. Also, they observed no difference in pain score and functional recovery improvement in celecoxib group at seventh day postoperatively.

We draw on the work of Murto et al,[13] who emphasized the importance of a study with a higher dose of celecoxib and longer duration of treatment of at least 1 week. Similarly, we hold the view that celecoxib is effective in early post-tonsillectomy pain. Mean of pain in the first day was 6.35 in the acetaminophen group and 4.77 in the celecoxib group. The pain score was statistically significant lower (1.58 VAS) in the celecoxib group. This difference was also clinically relevant. 10% to 20% of the range of the pain scale was regarded as the minimum range of clinically significant pain score after tonsillectomy in previous studies (equivalent to 1-2 VAS in our study).[13]

Current data remains scarce and poor surrounding the efficacy of COX-2 inhibitors in postoperative pediatric (adeno)tonsillectomy analgesia. Recently Stokes et al conducted a systematic review on the analgesic efficacy of COX-2 inhibitors in pediatric (adeno)tonsillectomy. However they have concluded these medications have some usefulness in postoperative pain. But they confirm insufficiency and heterogeneity of researches.[43]

Acetaminophen syrup and celecoxib suspension are approximately the same price about 30 cents per 60 mL bottle, in our region. However, celecoxib suspension has better organoleptic characteristics, such as improved taste. On the other hand, celecoxib suspension is administered once or twice a day instead of acetaminophen syrup that should be administered at 4 to 6 hours intervals. In regard to celecoxib administration, the suspension has more compliance and acceptability than acetaminophen syrup, especially in children.

Actually, due to heterogeneity in methodologies, types and doses of analgesics, patients' age, method of surgery, and variety of pain scoring, comparison of our result with other studies is somewhat difficult. For example, different types of tonsillectomy procedures such as "hot" or "cold steel" techniques and ligation or diathermy for hemostasis. In the present study, the rate of bleeding was within the range of literature. However, in the both groups similar bleeding rate was detected which has not precisely presented the effect of celecoxib on post-tonsillectomy bleeding rate because of relatively small sample size, as a drawback.

The strength of our study was its nature, which was randomized clinical trial. Also, there was no difference in parents' compliance between the two groups, and their compliance was satisfactory. In addition, all the operations were performed by a single surgeon and anesthesiologist. Hence, level of expertise was not a confounding

factor. As tonsillectomy has been associated with increased sensitivity to the respiratory side effects of opioid medications,[44,45] we did not prescribe opioids to reduce the risk of respiratory complications. On the other hand, since there have been conflicting conclusions in the literature concerning the association between ibuprofen and increased post-tonsillectomy bleeding,[46-48] its administration in this type of procedure is not routine in our center. Therefore, we recommend future studies with a larger sample size based on procedure-specific research. It could be helpful to find evidence for optimizing multimodal pain management or combination therapy with other COX-2 inhibitors and compression between the effectiveness and safety of ibuprofen and COX-2 inhibitors such as celecoxib. In addition, we suggest further studies on comparing the combination of acetaminophen/COX-2 inhibitors with acetaminophen/placebo.

5 | CONCLUSION

The clinical lesson learned from this trial was that celecoxib may be more effective than acetaminophen at the first day of post-tonsillectomy surgery and also resuming regular diet during the first 3 days. Despite these promising results, questions remain regarding satisfactory management of post-tonsillectomy pain.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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