

# Comparing the Effect of Acetaminophen Suppository before and after Tonsillectomy on Pain Severity in Children

Gholamali Dashti Khavidaki<sup>1</sup>, Aliakbar Keykha<sup>2</sup>, Alireza Rahat Dahmardeh<sup>3\*</sup>, Atefe Nikjo<sup>4</sup>

**Background:** Pediatric tonsillectomy is associated with major complications such as severe postoperative pain. Hence, this study aimed to compare the effect of acetaminophen suppository administered before and after surgery on the pain severity of tonsillectomy.

**Methods:** The present double-blind clinical trial was performed on 100 children undergoing tonsillectomy, who were randomly divided into two groups of 50 receiving respectively rectal acetaminophen 40 mg/kg preoperatively (Group 1) and postoperatively (Group 2).

**Results:** The first group consisted of 28 boys and 22 girls, and the second group had 26 boys and 24 girls. According to Chi-square test, there was no significant difference in terms of gender in the two groups ( $p=0.668$ ). Comparison of pain scores with repeated measures ANOVA showed lower pain severity in the first group at all hours compared with the second group.

**Conclusion:** The preoperative use of acetaminophen suppository significantly controls the pain after tonsillectomy.

**Keywords:** acetaminophen; tonsillectomy; children; pain

Tonsillectomy with or without adenoidectomy based on clinical evidence is one of the best strategies for treatment of chronic tonsillitis and obstructive sleep apnea syndrome [1-2]. Both of these surgeries are associated with considerable pain [3]. The pain control is one of the most important postoperative problems for the patient. The pain relief plays a key role in quality of life and recovery period among children [4]. There are several approaches to manage postoperative pain. The use of non-steroidal drugs and opioids are two of the main ways in this regard [5-6]. The opioids show the best effect to control pain, but opioid-induced respiratory depression (OIRD) is one of the major concerns and can even be caused in children because of taking codeine [7]. The use of opioids and codeine to relieve pain after tonsillectomy has been associated with mortality in patients undergoing surgery due to obstructive sleep apnea [8-9]. For this reason, the US Food and Drug Administration has banned the use of codeine for children undergoing tonsillectomy and adenoidectomy [10]. The use of analgesics to relieve pain without respiratory depression effect is ideal. It has become clear that different types of

non-steroidal painkillers can relieve post-tonsillectomy pain and meet the need for taking opioids [11-12]. Concerns on the risk of increased bleeding caused a reluctance to use them. It has recently been reported that acetaminophen plus ibuprofen is safe for postoperative use and has a better effect than acetaminophen with codeine [13-14]. Previous studies have reported the impact of intraoperative intravenous acetaminophen in reducing postoperative pain and opioid consumption in pediatric tonsillectomy [15]. As well, the use of oral acetaminophen in combination with ibuprofen can greatly reduce postoperative pain, but does not increase the risk of bleeding [6]. Another study compared the effect of acetaminophen suppository with diclofenac and showed that the pain relief effect of diclofenac was better than acetaminophen though acetaminophen can also control pain in patients [16]. Nevertheless, no study was found on the effect of rectal medication use before and after surgery. The aim of this study was to compare the effect of prescribing acetaminophen suppository before and after surgery on the severity of pain caused by pediatric tonsillectomy.

## Methods

The present double blind clinical trial was performed on children undergoing elective tonsillectomy after obtaining approval by the Research and Technology Deputy of Zahedan University of Medical Sciences, Iran, acquiring the code of IR.ZAUMS.REC.1394.147 from the Ethics Committee of the University and receiving informed consent from the patients' legal guardian. The sample size was considered to be 100 according to previous studies and the formula for calculating the sample size [16]. The patients were selected by convenience sampling method and divided into two groups using random number tables.

From the <sup>1</sup>Department of Otolaryngology, Zahedan University of Medical Science, Zahedan, Iran.

<sup>2</sup>Community Nursing Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.

<sup>3</sup>Department of Anesthesiology and Intensive Care Medicine Zahedan University of Medical Sciences, Zahedan, Iran.

<sup>4</sup>Zahedan University of Medical Sciences, Zahedan, Iran.

Received: 12 November 2017, Revised: 3 December 2017, Accepted: 18 December 2017

The authors declare no conflicts of interest.

\*Corresponding author: Alireza Rahat Dahmardeh, MD. Department of Anesthesiology and Intensive Care Medicine Zahedan University of Medical Sciences, Zahedan, Iran. E-mail: dr.dahmardeh@gmail.com

Copyright © 2018 Tehran University of Medical Sciences

Inclusion criteria were age range of 5 to 15 years, ASA class I, candidates for elective tonsillectomy, no history of endocrine disorders (diabetes, thyroid disorders, adrenal insufficiency), cerebral palsy, psychiatric disorders, congenital heart disorders, bleeding disorders, liver failure, no history of known hypersensitivity to acetaminophen.

Exclusion criteria included dissatisfaction with participation in the study, bleeding at the site of surgery and the need for re-manipulation to control bleeding, and airway impairment requiring intubation.

Firstly, all patients were pre-oxygenated with 100% oxygen for 3 minutes. Then, midazolam 0.05 mg/kg was injected. The induction of anesthesia was continued by injecting fentanyl 2 µg/kg and thiopental 5 mg/kg. All patients received cisatracurium 0.15 mg/kg to facilitate intubation. After intubation, the anesthesia was maintained with 60% nitrous oxide in combination with oxygen and propofol 100-150 µg/kg/min. Remifentanyl 0.1-0.2 µg/kg/min was applied to maintain heart rate and blood pressure in the range of 20% baseline. The patients received a total of 10 ml/kg crystalloid solution during surgery. After induction of anesthesia and before surgery, the patients in the first group received acetaminophen suppository 40mg/kg. The second group was administered with the same amount of medication after surgery and prior to extubation. Same surgical team performed all surgical procedures for the patients. Electrocauter was used for homeostasis. Dexamethasone 0.2 mg/kg was injected intravenously to reduce postoperative nausea and vomiting. The effects of anesthetic drugs were then reversed using intravenous neostigmine 0.05 mg/kg and atropine 0.2 mg/kg. After complete consciousness, the patients were transferred to the recovery department. A trained nurse who was unaware of the positions of patients in the studied groups measured the patients' pain severity using a visual analog scale at 1, 2, 6, 12 and 24 after surgery. On this scale, the patients scored for

their pain severity ranging from zero to 10 (0= minimum pain and 10= maximum pain). At each stage, the patients were injected with oral ibuprofen 10 mg/kg for the VAS score over three and intravenous pethidine 0.5 mg/kg for the VAS score over seven. The amount of consumed drugs was recorded in both groups. At last, the data regarding pain severity, the amount of consumed drugs and the demographic profile were analyzed in both groups by SPSS version 19 software using chi-square test, independent t-test and repeated measures ANOVA.

## Results

In the present study, the participants (n=100) included 54 boys and 46 girls. The group receiving acetaminophen before surgery (Group 1) consisted of 28 (56%) boys and 22 (44%) girls, and the group receiving acetaminophen suppository after surgery (Group 2) had 26 (52%) boys and 24 (48%) girls.

According to Chi-square test, there was no significant difference in terms of gender in the two groups (p=0.668). The mean age of the patients was 9.34 ± 2.69 years, 9.17 ± 2.90 years in the first group and 9.5 ± 2.42 years in the second group, but no significant difference was found between the two groups based on the independent t-test (p = 0.543). The repeated measures ANOVA test was used to compare the pain scores of patients in the AVS. The test results showed that the mean score of pain in both groups was on the rise up to 6 hours after surgery, followed by declining. However, the pain severity was lower in the first group at all hours compared with the second group (Table 1).

The results of comparing the amount of consumed analgesic drugs in the two groups showed that the intake of oral and intravenous analgesics in the first group was lower than the second group (Table 2).

**Table 1- Comparing the mean scores of pain in two groups**

Group	Pain assessment hours									
	1	P	3	P	6	P	12	P	24	P
A	3.84±2.17	0.002	3.66±1.89	0.004	3.82±2.03	0.001	3.44±1.96	0.001	3±2	0.001
B	4.36±2.16		4.80±1.93		5.20±2.5		4.82±2.08		4.36±2.08	

**Table 2- Comparing the frequency of consumed analgesic drugs in two groups**

Type of analgesic	Group receiving rectal acetaminophen preoperatively, n (percentage)	Group receiving rectal acetaminophen postoperatively, n (percentage)	P
Oral ibuprofen	15 (30%)	25 (50%)	0.041
Intravenous pethidine	8 (16%)	20 (40%)	0.008

## Discussion

The results obtained from the current study demonstrated that the use of acetaminophen suppository immediately prior to the onset of tonsillectomy compared to after surgery could significantly attenuate the pain in the first 24 hours and significantly reduce the consumption of analgesics. In line with the present study, Haddadi et al. compared the duration of analgesic effects of intravenous and rectal acetaminophen after tonsillectomy in children. Their results indicated that only 10.4% of patients had no pain in the intravenous acetaminophen group while 43.8% of patients had no pain complaint in the rectal acetaminophen group [17]. Dashti et

al investigated the prophylactic effect of acetaminophen suppository on postoperative pain and opioid requirements after adenotonsillectomy in 104 children. They showed that the patients who received acetaminophen suppository before surgery had less pain at various hours in comparison with the control group and had a significant reduction in the need for analgesics [18]. The postoperative pain can be investigated in three phases. The first phase involves electrical transmission of pain impulses to the relevant centers and gets a sense of pain. In the second phase, the necessary chemicals and neurotransmitters are produced from nerve terminals. In the third phase, invasion of phagocytes and fibroblasts occurs; this phase attenuates with

the formation of scars. If the first phase can even be controlled before starting the mechanism of induced pain, the pain will be significantly reduced [19]. It seems that the analgesic effect of preoperative rectal acetaminophen is due to the control of first phase in the mentioned mechanism. Liu et al. reported that an alternating ibuprofen and acetaminophen regimen provided an effective treatment for severe pain after pediatric tonsillectomy and did not increase rate of bleeding [6]. Kelly et al. compared the effects of oral morphine, acetaminophen and ibuprofen on the pain severity of the first day after tonsillectomy and reported that there were no differences seen in analgesic effectiveness, tonsillar bleeding, or adverse drug reactions. On the first postoperative night, the level of oxygen desaturation in the morphine group was more than the other two groups, so it may be unsafe in certain children to control the pain caused by tonsillectomy [20]. There is no comparative evaluation between acetaminophen and other drugs in the present study. Nevertheless, the results revealed that the use of acetaminophen could well control pain in children, consistent with the results of the mentioned study. According to the results, if this drug is administered prior to stimulation of pain receptors upon initiation of surgery, it could be more effective. Neda et al. examined the effect of diclofenac and acetaminophen suppositories alone and combination of both drugs in controlling pain after tonsillectomy in children and reported the maximum pain control effect in the group taking diclofenac suppository alone [21]. The main difference between the two studies was that the drug was prescribed in all three groups in the mentioned study after surgery and actually after stimulating the pain receptors. As well, the prescriptive dose of acetaminophen in the group receiving acetaminophen suppository alone was lower than the current study (35 mg/kg) and in the combined group (17.5 mg/kg), these two variations can be a good justification for the difference between the results. Bedwell et al. in the two groups of patients after tonsillectomy utilized the combination of acetaminophen with codeine and acetaminophen with ibuprofen; they reported less pain, fewer side effects and more safety in the second group [13].

## Conclusion

Administration of acetaminophen suppository prior to the onset of the surgery compared to postoperatively prescription attenuates appropriately the pain for 24 hours after surgery, and it is recommended to be used before tonsillectomy.

## Acknowledgement

This article has been adopted from the Thesis for Doctor of Medicine approved and funded by Research and Technology Deputy of Zahedan University of Medical Sciences, Iran, with the code of IR.ZAUMS.REC.1394.147. The researcher would like to express own gratitude to the Research and Technology Deputy of the University and the staff as well as personnel of operating room at the Khatamol-Anbia Hospital of Zahedan.

## References

1. Baugh RF, Archer SM, Mitchell RB, Rosenfeld RM, Amin R, Bums JJ, et al. Clinical practice guideline: tonsillectomy in

- children. *Otolaryngol Head Neck Surg.* 2011; 144(1 suppl):S1-30.
2. Mitchell RB, Kelly J. Outcomes and quality of life following adenotonsillectomy for sleep-disordered breathing in children. *ORL J Otorhinolaryngol Relat Spec.* 2007; 69(6):345-8.
3. Subramanyam R, Varughese A, Willging JP, Sadhasivam S. Future of pediatric tonsillectomy and perioperative outcomes. *Int J Pediatr Otorhinolaryngol.* 2013; 77(2):194-9.
4. Bean-Lijewski JD, Kruitbosch SH, Hutchinson L, Browne B. Post-tonsillectomy pain management in children: Can we do better? *Otolaryngol Head Neck Surg.* 2007; 137(4):545-51.
5. El-Fattah A, Ramzy E. Pre-emptive triple analgesia protocol for tonsillectomy pain control in children: double-blind, randomised, controlled, clinical trial. *J Laryngol Otol.* 2013; 127(4):383-91.
6. Liu C, Ulualp SO. Outcomes of an alternating ibuprofen and acetaminophen regimen for pain relief after tonsillectomy in children. *Ann Otol Rhinol Laryngol.* 2015; 124(10):777-81.
7. Prows CA, Zhang X, Huth MM, Zhang K, Saldana SN, Daraiseh NM, et al. Codeine-related adverse drug reactions in children following tonsillectomy: A prospective study. *Laryngoscope.* 2014; 124(5):1242-50.
8. Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. Codeine, ultrarapid-metabolism genotype, and postoperative death. *N Engl J Med.* 2009; 361(8):827-8.
9. Kelly LE, Rieder M, van den Anker J, Malkin B, Ross C, Neely MN, et al. More codeine fatalities after tonsillectomy in North American children. *Pediatrics.* 2012; 129(5): e1343-7.
10. Kuehn BM. FDA: no codeine after tonsillectomy for children. *JAMA.* 2013; 309(11): 1100.
11. Rusy LM, Houck CS, Sullivan LJ, Ohlms LA, Jones DT, McGill TJ, et al. A double-blind evaluation of ketorolac tromethamine versus acetaminophen in pediatric tonsillectomy: analgesia and bleeding. *Anesth Analg.* 1995; 80(2):226-9.
12. St. Charles CS, Matt BH, Hamilton MM, Katz BP. A comparison of ibuprofen versus acetaminophen with codeine in the young tonsillectomy patient. *Otolaryngol Head Neck Surg.* 1997; 117(1):76-82.
13. Bedwell JR, Pierce M, Levy M, Shah RK. Ibuprofen with acetaminophen for postoperative pain control following tonsillectomy does not increase emergency department utilization. *Otolaryngol Head Neck Surg.* 2014; 151(6):963-6.
14. Mattos JL, Robison JG, Greenberg J, Yellon RF. Acetaminophen plus ibuprofen versus opioids for treatment of post-tonsillectomy pain in children. *Int J Pediatr Otorhinolaryngol.* 2014; 78(10):1671-6.
15. Subramanyam R, Varughese A, Kurth CD, Eckman MH. Cost-effectiveness of intravenous acetaminophen for pediatric tonsillectomy. *Paediatr Anaesth.* 2014; 24(5):467-75.
16. Jabbari moghaddam Y KL, Radfar R, Ragifar R. Comparisinal Results of Paracetamol and Diclofenac Suppository on Post Tonsillectomy Pain Control in Children . *Medical Journal of Tabriz University Medical Sciences and Health Services.* 2009; 31(1):31-4.
17. Haddadi S, Marzban S, Karami MS, Heidarzadeh A, Parvizi A, Nabi BN. Comparing the duration of the analgesic effects of intravenous and rectal acetaminophen following tonsillectomy in children. *Anesth Pain Med.* 2014; 4(1): e13175.
18. Dashti G, Amini S, Zanguee E. The prophylactic effect of rectal acetaminophen on postoperative pain and opioid requirements after adenotonsillectomy in children. *Middle East J Anaesthesiol.* 2009; 20(2):245-9.
19. Nazem M, Sajedi P, Goharian V, Shirvani M. Comparing the effects of preincisional infiltration of Bopivacaine with postoperative rectal Acetaminophen on reducing postoperative pain after pediatric surgery. *arak medical university journal* 2006; 9(3):99-105.
20. Kelly LE, Sommer DD, Ramakrishna J, Hoffbauer S, Arbab-tafti S, Reid D, et al. Morphine or ibuprofen for post-tonsillectomy analgesia: a randomized trial. *Pediatrics.* 2015; 135(2):307-13.
21. Neda SJ, Farzad Z, Hamidreza J, sede Bahman S, Hamidreza Z. Comparative efficacy of diclofenac suppository and acetaminophen suppository alone And simultaneous prescription in controlling pain after tonsillectomy surgery in children. *Arak Medical University Journal.* 2016; 19(112):46-55.