Post-tonsillectomy Hemorrhage in Patients Receiving Ketorolac Analgesic

Yadav D,[1] Dangol B,[1] Shrestha N,[1] Pandit S,[2] Nepal A[1]

[1]Department of ENT-HNS,

Patan Hospital,

Patan Academy of Health Sciences,

Lagankhel, Lalitpur, Nepal.

[2]Consultant Radiation Oncologist,

Kathmandu Cancer Center,

Tathali, Nala Road, Bhaktapur, Nepal.

Corresponding Author

Deepak Yadav

Department of ENT-HNS,

Patan Hospital,

Patan Academy of Health Sciences,

Lagankhel, Lalitpur, Nepal.

E-mail: dyd286@gmail.com

Citation

Yadav D, Dangol B, Shrestha N, Pandit S, Nepal A. Post-tonsillectomy Hemorrhage in Patients Receiving Ketorolac Analgesic. *Kathmandu Univ Med J.* 2023;81(1):3-6.

ABSTRACT

Background

Ketorolac, the non-steroidal anti-inflammatory drug, is thought to have less sedation as well as postoperative nausea and vomiting in comparison to opioids, but with higher risk of post-tonsillectomy hemorrhage as reported in some of the literatures. There is no consensus till date in the use of ketorolac in the management of pain following tonsil and adenoid related surgeries.

Objective

To find out the incidence of hemorrhage following tonsil and adenoid related surgeries in patients receiving ketorolac in postoperative period.

Method

This is a retrospective chart review of patients undergoing tonsil and adenoid related surgeries who had received ketorolac during April, 2013 to May, 2019 at department of ENT-HNS, Patan Academy of Health Sciences (PAHS), Lalitpur, Nepal. Post-tonsillectomy hemorrhage rate was calculated in pediatric and adult patients.

Result

During the study period, 103 patients (male – 50 and female – 53) received ketorolac in postoperative period. Tonsillectomy and adenotonsillectomy were performed in 71and 32 patients respectively. Forty-five patients were < 18 years whereas 58 were ≥ 18 years. Most common indication for surgery was recurrent tonsillitis (66/103) followed by adenotonsillar hypertrophy (31/103). Post-tonsillectomy hemorrhage was observed in 15 patients; among them, four out 45 were < 18 years and 11 out of 58 ≥ 18 years. All five patients out of 15, who required surgical intervention for post-tonsillectomy hemorrhage, were ≥ 18 years and were operated for recurrent tonsillitis. Rest of the patients (10/15) were managed conservatively. None of the patients required blood transfusion.

Conclusion

Ketorolac is not associated with increased risk of post-tonsillectomy hemorrhage in children and can safely be administered. Whereas in adults, recurrent tonsillitis being the most common indication for tonsillectomy, it should be used cautiously.

KEY WORDS

Adenoidectomy, Adenotonsillectomy, Ketorolac, Tonsillectomy, Non-steroidal anti-inflammatory drugs

INTRODUCTION

Pain and bleeding following tonsillectomy are major concerns in otolaryngologic practice. Nonsteroidal anti-inflammatory drugs (NSAIDs), used for pain control during postoperative period, are thought to inhibit platelet aggregation and prolong bleeding time and hence may increase the risk of perioperative bleeding. Whereas the use of opioids is associated with higher incidence of sedation as well as postoperative nausea and vomiting. A Cochrane review of 2013 did not find significant risk of postoperative hemorrhage with the use of NSAIDs in comparison to other analgesics or placebo in children undergoing tonsillectomy.[1] On the other hand, use of NSAIDs are found to have significantly reduced risk of vomiting.

Among NSAIDs, ketorolac, having analgesic efficacy equivalent to morphine, was thought to have higher incidence of post-tonsillectomy hemorrhage (PTH) ranging 4.4 to 18%, but Cochrane review of 2013 has not found increased risk of PTH in children in comparison to other NSAIDs.[1-3] In contrary, a systemic review by Chan and Parikh mentions that ketorolac is associated with five-fold increased risk of bleeding in adults but not in children.[4] Hence use of ketorolac remains controversial and depends on the preference of attending surgeon.[5]

As ketorolac is being used for postoperative pain management in patients undergoing adenoid and tonsil related surgeries, this study wanted to find out the incidence of hemorrhage postoperatively and compare it with published literature.

METHODS

It is a retrospective review of all patients undergoing adenotonsillectomy and tonsillectomy during April, 2013 to May, 2019 at department of ENT-HNS, PAHS, Lalitpur, Nepal. List of all patients undergoing aforementioned surgery were retrieved from the medical record section and the files were extracted. Details as per the proforma were documented. All patients who received ketorolac as analgesic were included in the study. Cases with missing records, postoperative drug order or progress note were excluded from the study.

All patients underwent adenoidectomy with adenoid curette and completeness of excision confirmed with appropriately sized rigid nasal endoscope or endoscopic assisted adenoidectomy with microdebrider. Tonsillectomy was performed with cold dissection technique and hemostasis secured with bipolar cautery. All surgeries were performed under general anesthesia. Perioperative medications were prescribed as per standard hospital protocol. Surgeries were performed by various surgeons working in the ENT-HNS department. All patients were kept admitted for 4 to 5 days and received intravenous ketorolac in postoperative period according to the body weight. Patients were discharged on oral analgesics (paracetamol and/or ibuprofen) once they had adequate oral intake and healthy slough in the tonsillar fossa was noticed. All patients received intravenous antibiotics postoperatively and changed to oral at the time of discharge which was continued for further 3 to 4 days. All patients were followed up routinely for two weeks postoperatively.

Type of hemorrhage was classified based on time of onset. Hemorrhage occurring within 24 hours of surgical procedure was defined as primary hemorrhage whereas hemorrhage occurring later than 24 hours of surgical procedure was defined as secondary hemorrhage. Severity of postoperative hemorrhage was stratified as Type 1 – bleeding observed at home, not requiring any intervention, Type 2 – bleeding that required readmission for observation, Type 3 – bleeding that required surgical intervention (return to theatre).[6] Type 3 hemorrhage was the main outcome measure. Data was analyzed in MS excel. Approval from institutional review board was obtained (drs1907051266).

RESULTS

During the study period, 226 patients underwent adenoid or tonsil related surgeries. Files were not found in 64 patients; drug order or progress note was missing in 16 patients whereas 38 patients received paracetamol in postoperative period. Five patients who underwent adenoidectomy alone for adenoid hypertrophy, thought they received ketorolac, were not included in the study. Hence, only 103 patients were included in the study, out of which 50 were male and 53 were female. The median age of the patients was 20 years with age range of 3 to 42 years. There were 45 patients with age < 18 years and 58 patients with age ≥ 18 years. The most common indication for surgery was recurrent tonsillitis (66), followed by adenotonsillar hypertrophy (31), suspected tonsillar malignancy (2), tonsillar keratosis (2), adenoid hypertrophy (1) and tonsillar hypertrophy (1). Seventy-one (68.9%) patients underwent tonsillectomy whereas 32 (31.1%) patients underwent adenotonsillectomy.

Hemorrhage was observed in 15 out of 103 (14.6%) patients, out of which primary hemorrhage was observed in two patients (1.9%) whereas secondary hemorrhage was observed in 13 patients (12.6%). PTH occurred in 13 out of 71 (18%) patients undergoing tonsillectomy and two out of 32 (6%) patients undergoing adenotonsillectomy. Out of 66 patients undergoing tonsillectomy for recurrent tonsillitis, 12 (18%) developed PTH whereas one out of two patients undergoing tonsillectomy for tonsillar keratosis developed PTH. Hemorrhage was observed in four out 45 (9%) patients < 18 years and 11 out of 58 (19%) patients ≥ 18 years. Type 1, 2 and 3 hemorrhage were observed

in two, eight and five patients respectively. All patients with type 3 hemorrhage had undergone tonsillectomy for recurrent tonsillitis. None of the patients experienced type 3 hemorrhage in < 18 years but five out of 58 (9%) patients ≥ 18 years experienced type 3 hemorrhage. Most of the patients (8/15) were managed conservatively with oral care, prolonged antibiotics and intravenous fluids, whereas in two out of eight patients, who had type 2 hemorrhage, chemical cautery was applied over bleeding point. In five patients, who had type 3 hemorrhage, electrocautery was required to control the ongoing bleed. Two out of five patients required general anesthesia for electrocautery to manage bleeding. None of the patients required blood transfusion.

DISCUSSION

The incidence of PTH reported in the literature varies widely (1 to 19%).[7] In this study, though overall incidence of PTH was 14.6% (15/103), type 3 hemorrhage, which is of concern as they had to be managed in operation theater, was observed in 4.8% (5/103). Most of the study only mentions about the PTH which requires to be seen by otolaryngologists or had to be managed in operation theater.[8,9] This leads to underreporting of PTH events managed nonsurgically and hence variation in incidence of PTH.[1]

According to the practice followed, patients were admitted for 4 to 5 days and kept under strict follow up for two weeks. At the time of discharge, every patient was instructed to visit the hospital and report even the minor events like blood tinged sputum which was documented in the file. At each visit, examination findings of tonsillar fossa were documented. This practice helped us to extract data of even the historical bleed without objective evidence. In this study, PTH was classified as Type 1 – bleeding observed at home, not requiring any intervention, Type 2 – bleeding that required readmission for observation, Type 3 – bleeding that required surgical intervention (return to theatre).[6] The studies which include PTH managed nonsurgically reports similar incidence of PTH (11%) as this study.[7,10] Ikoma et al. and Walner and Karas have categorized type 2 bleeding who were managed under local anesthesia and type 3 bleeding who required general anesthesia whereas in current study, return to operation theatre was categorized as type 3 even if electrocautery was done under local anesthesia.[10,11] So far only two out of eight patients with type 2 hemorrhage were managed with chemical cautery whereas rest of them were managed conservatively and only two out of five patients with type 3 hemorrhage, who were managed with electrocautery, required general anesthesia. None of the patients required external carotid artery ligation and no mortality was reported during the study period as described by Walner and Karas in the standardization of reporting PTH.[11]

Primary PTH is attributed to surgical technique and reopening of blood vessels whereas secondary PTH is attributed to sloughing of the primary eschar and infection. Primary PTH ranges from 0.1 to 5.8% and secondary PTH ranges from 0.2 to 7.5%.[5] In this study, primary and secondary PTH were 1.9% and 12.6% respectively. Most of the studies reports higher incidence of PTH among adults than pediatric population which is also reflected in current study.[5,7,12,13] The incidence of PTH in patients < 18 years versus ≥ 18 years were 8.9% and 19% respectively. None of the pediatric patients suffered from type 3 hemorrhage. Apart from older age, male sex, recurrent tonsillitis, smoking, excessive intraoperative blood loss, elevated postoperative mean arterial pressure, etc. has been found as risk factors for PTH.[9,14-16] Most common indication for tonsillectomy in < 18 years and ≥ 18 years were adenotonsillar hypertrophy and recurrent tonsillitis respectively. The National Prospective Tonsillectomy Audit demonstrated PTH of 1.4% for adenotonsillar hypertrophy and 3.7% for recurrent tonsillitis.[13] One of the reasons for higher PTH in adults in this study could be the difference in indication of surgery in both the age groups. The influence of surgical technique which has bearing on PTH can be neglected in this study, as all tonsillectomies were performed with cold dissection technique and hemostasis was obtained with bipolar cautery whereas the individual variation in surgical technique cannot be omitted.[5]

NSAIDs use, with concern over its role in inhibiting platelet aggregation, in perioperative period as an independent risk factor for PTH is controversial as recent literature do not show increased incidence of PTH particularly in children.[1,17] In the study by Mudd et al. which reviewed 6710 children undergoing tonsillectomy, out of 222 children requiring surgical control of PTH, 166 received ibuprofen.[17] The authors found that age ≥ 12 years and diagnosis of recurrent tonsillitis were independent risk factors rather than ibuprofen.[17] Pfaff et al. reviewed 6014 children and did not find difference in PTH, when age is controlled, among those who received ibuprofen (3.6%), and those who received acetaminophen and codeine (3.4%).[18] The studies conducted in the nineties by Bailey et al. and Judkins et al. found increased incidence of PTH with use of ketorolac and supported the manufacturer's warning against its administration in perioperative period of surgical procedure where hemostasis is a major concern.[2,19] The systemic review and meta-analysis of 10 studies by Chan and Parikh found five-fold increased risk of PTH with ketorolac in adults but not in children. But indication of tonsillectomy as a confounding factor could not be excluded by the authors as the diagnosis was not available for analysis at the individual patient level.[4] However, a 2013

review from Cochrane Collaboration did not find increased risk of PTH with ketorolac in comparison to other NSAIDs.[1] The incidence of PTH, in the current study, in pediatric patients is less than the adults but because of the various factors as discussed earlier it cannot be attributed to the use of ketorolac alone.

Records of many patients were missing and hence this may not reflect the true incidence of PTH at our institution. Earlier during the study period, we were using paracetamol and/or ibuprofen as analgesics. Most of the missing records belonged to early years of the study. Had it been available then comparison between various drugs could have produced better results.

CONCLUSION

Ketorolac use is not found to be associated with increased risk of PTH in pediatric patients where adenotonsillar hypertrophy is the common indication for surgery. Recurrent tonsillitis, which is the independent risk factor for increased PTH, being the most common indication for surgery in adults in this study, the influence of ketorolac in PTH in adults cannot be excluded.

REFERENCES

1. Lewis SR, Nicholson A, Cardwell ME, Siviter G, Smith AF. Nonsteroidal anti-inflammatory drugs and perioperative bleeding in paediatric tonsillectomy. 2013 Jul 18. In: Cochrane Database Syst Rev [Internet] John Wiley & Sons, Ltd. 2013. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7154573/. Record No.: CD003591.
2. Bailey R, Sinha C, Burgess LP. Ketorolac tromethamine and hemorrhage in tonsillectomy: a prospective, randomized, double-blind study. *Laryngoscope.* 1997 Feb;107(2):1660-9.
3. Baugh RF, Archer SM, Mitchell RB, Rosenfeld RM, Amin R, Burns JJ, et al. Clinical practice guideline: tonsillectomy in children. *Otolaryngol Head Neck Surg.* 2011 Jan;144(1 Suppl):S1-30.
4. Chan DK, Parikh SR. Perioperative ketorolac increases post-tonsillectomy hemorrhage in adults but not children. *Laryngoscope*. 2014 Aug;124(8):1789-93.
5. Mitchell RB, Archer SM, Ishman SL, Rosenfeld RM, Coles S, Finestone SA, et al. Clinical Practice Guideline: Tonsillectomy in Children (Update). *Otolaryngol Head Neck Surg*. 2019 Feb;160(1_suppl):S1–42.
6. Diercks GR, Comins J, Bennett K, Gallagher TQ, Brigger M, Boseley M, et al. Comparison of Ibuprofen vs Acetaminophen and Severe Bleeding Risk After Pediatric Tonsillectomy: A Noninferiority Randomized Clinical Trial. *JAMA Otolaryngol Head Neck Surg.* 2019 Jun 1;145(6):494-500.
7. McLean JE, Hill CJ, Riddick JB, Folsom CR. Investigation of Adult Post-Tonsillectomy Hemorrhage Rates and the Impact of NSAID Use. *Laryngoscope.* 2022;132(5):949-53.
8. Windfuhr JP, Chen YS. Incidence of post-tonsillectomy hemorrhage in children and adults: a study of 4,848 patients. *Ear Nose Throat J*. 2002 Sep;81(9):626-8.
9. Windfuhr JP, Chen YS, Remmert S. Hemorrhage following tonsillectomy and adenoidectomy in 15,218 patients. *Otolaryngol Head Neck Surg*. 2005 Feb;132(2):281-6.
10. Ikoma R, Sakane S, Niwa K, Kanetaka S, Kawano T, Oridate N. Risk factors for post-tonsillectomy hemorrhage. *Auris Nasus Larynx*. 2014 Aug;41(4):376-9.
11. Walner DL, Karas A. Standardization of reporting post-tonsillectomy bleeding. *Ann Otol Rhinol Laryngol*. 2013 Apr;122(4):277-82.
12. Gonçalves AI, Rato C, de Vilhena D, Duarte D, Lopes G, Trigueiros N. Evaluation of post-tonsillectomy hemorrhage and assessment of risk factors. *Eur Arch Otorhinolaryngol*. 2020 Nov 1;277(11):3095-102.
13. Royal College of Surgeons. National Prospective Tonsillectomy Audit Final Report [Internet]. 2005 [cited 2023 Feb 8]. Available from: https://www.rcseng.ac.uk/library-and-publications/rcs-publications/docs/tonsillectomy-audit/
14. Inuzuka Y, Mizutari K, Kamide D, Sato M, Shiotani A. Risk factors of post-tonsillectomy hemorrhage in adults. *Laryngoscope Investig Otolaryngol*. 2020 Dec;5(6):1056-62.
15. Myssiorek D, Alvi A. Post-tonsillectomy hemorrhage: an assessment of risk factors. *Int J Pediatr Otorhinolaryngol*. 1996 Sep 1;37(1):35–43.
16. Spektor Z, Saint-Victor S, Kay DJ, Mandell DL. Risk factors for pediatric post-tonsillectomy hemorrhage. *Int J Pediatr Otorhinolaryngol.* 2016 May;84:151-5. doi: 10.1016/j.ijporl.2016.03.005. Epub 2016 Mar 18. PMID: 27063772.
17. Mudd PA, Thottathil P, Giordano T, Wetmore RF, Elden L, Jawad AF, et al. Association Between Ibuprofen Use and Severity of Surgically Managed Posttonsillectomy Hemorrhage. *JAMA Otolaryngol Head Neck Surg.* 2017 Jul 1;143(7):712-7.
18. Pfaff JA, Hsu K, Chennupati SK. The Use of Ibuprofen in Posttonsillectomy Analgesia and Its Effect on Posttonsillectomy Hemorrhage Rate. *Otolaryngol Head Neck Surg.* 2016 Sep;155(3):508-13.
19. Judkins JH, Dray TG, Hubbell RN. Intraoperative ketorolac and posttonsillectomy bleeding. *Arch Otolaryngol Head Neck Surg*. 1996 Sep;122(9):937-40.