Original Article

Post-tonsillectomy pain management in University of Port Harcourt Teaching Hospital: a comparison between suppository diclofenac sodium and suppository acetaminophen

Okechi Chibuzo Mbalaso [1], Olubusola Temitope Alagbe-Briggs [2], Opubo Benedict da Lilly-Tariah [3]

[1]Formerly Senior Registrar in Otorhinolaryngology Department, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.
Trust Doctor in ENT, Surrey & Sussex Healthcare NHS Trust, United Kingdom
[2]Consultant Anaesthetist, Department of Anaesthesia, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.
[3]Consultant Otorhinolaryngologist, Department of Otorhinolaryngology, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.

Abstract

Background: Post-tonsillectomy pain management poses a challenge due to limited treatment options. With opioid analgesics largely contraindicated, non-opioid analgesics are mainstay of treatment.
Aim: This study compared effects of diclofenac and acetaminophen suppository on post-tonsillectomy analgesia and oral intake among paediatric patients at the institution of study.
Methods: This was a single blind randomized controlled study involving 60 paediatric patients undergoing tonsillectomy under GA, randomized into Groups A (diclofenac sodium suppository) and B (acetaminophen suppository) of 30 patients each for post-operative analgesia. Pain scores in both groups using the FLACC Scale 24 hours post-operatively, time to first oral intake and frequency, rescue analgesia and duration of hospital stay were monitored.
Results: Patients mean age was 3.71±1.30 years. Group A had lower pain scores across all time intervals (p = 0.01). Rescue analgesia was 19(63.4%) and 27(90.0%) in Groups A and B respectively (p = 0.05). Although the difference in time to first oral intake was shorter in Group A (388.7min vs 488.7min; p = 0.33), frequency of oral intake (p = 0.01) and duration of hospital stay (p = 0.05) were better in Group A.
Conclusion: Diclofenac suppository was more effective for post-tonsillectomy pain than acetaminophen suppository. Rescue analgesia requirement was high in both groups but significantly lesser in Group A. No significant difference occurred in time to first oral intake, but there was significantly better oral intake and lesser duration of hospital stay in Group A.

Keywords: Post-tonsillectomy pain, diclofenac suppository, acetaminophen suppository

Address for correspondence: Dr. Olubusola Temitope Alagbe-Briggs, Department of Anaesthesia, University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.
Email: busolabriggs@yahoo.co.uk
Phone: +2347035712687
Received: 08-12-2024, **Accepted:** 28-12-2024

Access this article online	
Quick Response Code:	**Website:** www.phmj.org.ng
	DOI: https://doi.org/10.60787/phmj.v18i3.182

How to cite this article: Mbalaso OC, Alagbe-Briggs OT, da Lilly-Tariah OB. Post-tonsillectomy pain management in University of Port Harcourt Teaching Hospital: a comparison between suppository diclofenac sodium and suppository acetaminophen. Port Harcourt Med J 2024;18(3):122-130.

INTRODUCTION

Tonsillectomy, with or without adenoidectomy, is the commonest surgical procedure carried out by Otorhinolaryngologists worldwide and the most frequent in-patient surgical procedure performed on children below 15 years of age.[1] Though the tonsils and adenoids provide immunologic response to air or food-borne pathogens, their removal becomes indicated when they become enlarged causing obstructive symptoms, (commonest indication), are a seat of recurrent infections or as part of other surgical procedures.[2,3]

Adenotosillectomy was found to be the commonest otorhinolaryngological surgery performed in Port Harcourt by da Lilly-Tariah and Peterside in 2008 with a prevalence rate of 22.1%,[4] while Somefun et al[5] in the year 2000 recorded 115 cases in Lagos over a 3-year period. Over 500,000 tonsillectomies with or without adenoidectomy are performed in the USA annually.[1] Onotai and da Lilly-Tariah in 2013 found the highest incidence of adenotonsillectomies among the age group of 3-5 years,[2] this being the peak age group, as reported in other studies.[1,6,7]

All surgical techniques for tonsillectomy result in tissue damage and inflammation with resultant post tonsillectomy pain. The resultant odynophagia and reduced oral intake contribute to delayed patient recovery and discharge.[8] This increases the economic burden on the care givers especially in the LMIC's where most patients make direct out-of-pocket payment of hospital bills due to poor health insurance coverage.[9] Adequate analgesia is therefore essential to enhance early patient discharge after sugery and overall quality care.[10,11]

The World Health Organization Analgesic Ladder recommends the use of non-opioids for mild pain, weak opioids for moderate pain and strong opioids for severe pain.[12] Opioid analgesics are however unsuitable for post-tonsillectomy analgesia due to the associated and unwanted risks of nausea, vomiting, sedation and respiratory depression.[13] This limits the choice of analgesia to non-opioids. Acetaminophens are commonly used and safe at normal doses but may not provide adequate analgesia alone.[14] It also has a narrow therapeutic index and can cause hepatic toxicity at high doses.[15] Non-steroidal anti-inflammatory drugs (NSAIDS) have been shown to be effective analgesics in the paediatric population and can be used alone or in combination with acetaminophen but have the risk of causing platelet inhibition and post tonsillectomy haemorrhage.[16] The latter is a greatly undesirable complication, therefore medications that can increase its risk are traditionally avoided. Both ibuprofen and diclofenac are traditional NSAID's, however diclofenac has been found to show a degree of COX 2 selectivity compared to ibuprofen, thereby reducing the risk of platelet inhibition and post-tonsillectomy bleed. Diclofenac is also readily available as a suppository formulation compared to ibuprofen.

The rectal route however is commonly utilized for post tonsillectomy analgesia in the early postoperative period because oropharyngeal pain can limit oral drug ingestion. The intravenous route of administration though an option for acetaminophen, is not for diclofenac and this study was designed for both agents to be administered via the same route in the study groups.

Assessment of pain in children is also challenging as crying, which is the commonest symptom of pain in the paediatric age group is also seen in a lot of other non-painful conditions such as hunger or fear. Secondly, little children are unable to express themselves with appropriate words, but various pain assessment tools developed for different paediatric age groups have been classified as observational or self-assessment pain scales.[17]

There is no single unified post tonsillectomy analgesic plan at the study institution but preferences for either suppository diclofenac or suppository acetaminophen are individualised. This study therefore compared the effects of suppository acetaminophen and suppository diclofenac on post-tonsillectomy (with or without adenoidectomy) pain relief, using an appropriate age specific pain scoring system and the oral intake.

METHODOLOGY

Following institutional approval and informed consent from the eligible patients' parents/guardian, a prospective single blind randomized controlled study was conducted

among 60 consecutive paediatric patients aged between 1-7 years scheduled for tonsillectomy with or without adenoidectomy over a six (6) month period.

Patients with history of asthma, sickle cell, kidney and liver diseases, allergy to NSAIDS or acetaminophen, personal or family history of bleeding disorders, abnormal clotting profile, those booked for adenoidectomy alone, and nonconsenting parents/guardians were excluded. Those who met the inclusion criteria were then randomized by an independent observer (who picked a labelled piece of paper bearing A or B from an opaque envelop), into two treatment groups (A and B): Group A (diclofenac sodium suppositories at a dose of 3mg/kg/day in 2 divided doses) and Group B (acetaminophen suppository at 60mg/kg/day in 3 divided doses). Patient/care giver was blind to the treatment received. General anaesthesia was induced using halothane as volatile agent (1 - 3%) in 100% oxygen, the airway was secured with appropriate sized, non-kinkable cuffed tracheal tubes following use of short acting depolarising muscle relaxant (suxamethonium 1.5mg/kg), and all patients received fentanyl at 1.5µg/kg as the only intra-operative analgesic at induction. Pharyngeal packs were further inserted, and patients were manually ventilated. Adenotonsillectomy was performed in all patients by cold-steel dissection with ties**.** Following recovery from anaesthesia, pain scores and oral intake were assessed over a period of 24 hours. The first dose of suppository analgesia was administered by the researcher on the operating table immediately after extubation and subsequent doses were administered by the ward nurses according to the study protocol at 12 hourly intervals for Group A (diclofenac suppository), and 8 hourly intervals for Group B (acetaminophen suppository) over the next 24 hours using a calibrated meter rule to measure corresponding and calculated suppository length. Rescue analgesia was given using intramuscular diclofenac at half the suppository dose when child experienced moderate to severe pain (Face, Leg, Activity, Cry, and Consolabilty - FLACC Pain Score ≥ 5), before the next scheduled suppository dose of analgesia.

Post-tonsillectomy pain assessed by the researcher, using the FLACC scale over 24 hours at 2 hourly intervals for the first 12 post-operative hours, then 6 hourly for the next 12 hours, was the primary outcome. Secondary outcomes assessed were time to first oral intake, frequency of oral intake, need for rescue analgesia, presence of side effects and duration of hospital stay.

Data was analyzed with the Software for Statistical Product and Service Solutions (SPSS) version 20 (IBM SPSS, New York, USA) and presented as tables and charts. Qualitative variables were expressed as frequencies and proportions, while quantitative variables were assessed for normality using Shapiro-Wilks's statistics. Means and standard deviation (for normally distributed variables), medians and interquartile range (non-normally distributed variables), Chi square tests (differences in proportions between groups), independent t test (differences in means between the groups) and Mann-Whitney U test (differences in medians) were utilized. Statistically significant level was set at $p<0.05$.

RESULTS

A total of 60 patients (30 in each group) who had adenotonsillectomy participated in the study. Demographic distribution of study participants shown in Table 1 shows no statistically significant difference among groups. There was however a strong positive correlation between the weight and analgesic dose received in both groups (Figure 1).

Table 2 shows the distribution of the FLACC pain scores using the Shapiro-Wilks test of normality, and this showed a non-parametric distribution. A comparison of the mean ranks and median FLACC pain scores across groups (Table 3), shows that group A patients (diclofenac) had significantly lower pain scores across all time intervals than group B patients (acetaminophen).

The mean pain scores in both groups were highest within the first 4 postoperative hours and subsequently declined (Figure 2).

There was no rescue analgesia in 11(36.7%) patients in group A, while 3(10.0%) had no rescue analgesia in group B. ($p = 0.05$). The mean time to first post-tonsillectomy oral food intake was lesser in Group A than in Group B ($p = 0.33$). Frequency of oral intake was more

in Group A (p = 0.01) and duration of hospital stay was also shorter in Group A (46.4 hours vs 49.6 hours; p = 0.05). There were also no observed side effects in both groups (Table 1).

Table 1: Demographic and clinical characteristics of study participants

Variable	Group A(n-30)	Group B(n-30)	Total (n-60)	P-value
Age (mean±SD)	3.73 ± 1.33	3.70 ± 1.29	3.71 ± 1.30	*0.92*
Sex (n/%)				
Male	17 (56.7)	16 (53.3)	33 (55.0)	*0.80*
Female	13 (43.3)	14 (46.7)	27 (45.0)	
Total	30	30	60	
Rescue analgesia (n/%)				
None	11 (36.7)	3 (10.0)	14 (23.3)	
I dose	11(36.7)	14(46.7)	25(41.7)	*0.05**
2doses	8(26.7)	13(43.3)	21(35.0)	
Oral Intake				
First oral intake (mins)				
	388.7	488.7	-	*0.33*
Frequency of oral intake (n)				
2	2(6.7)	2(6.7)	4(6.7)	
3	8(26.7)	14(46.7)	22(36.7)	*0.01**
4	6(20.0)	12(40.0)	18 (30.0)	
≥5	14(46.7)	2(6.7)	16(26.7)	
Side Effects				
PONV	0(0)	0(0)	0(0)	
Excess Bleeding	0(0)	0(0)	0(0)	
Duration of hospital stay (hours)				
	46.4	49.6	-	*0.05**

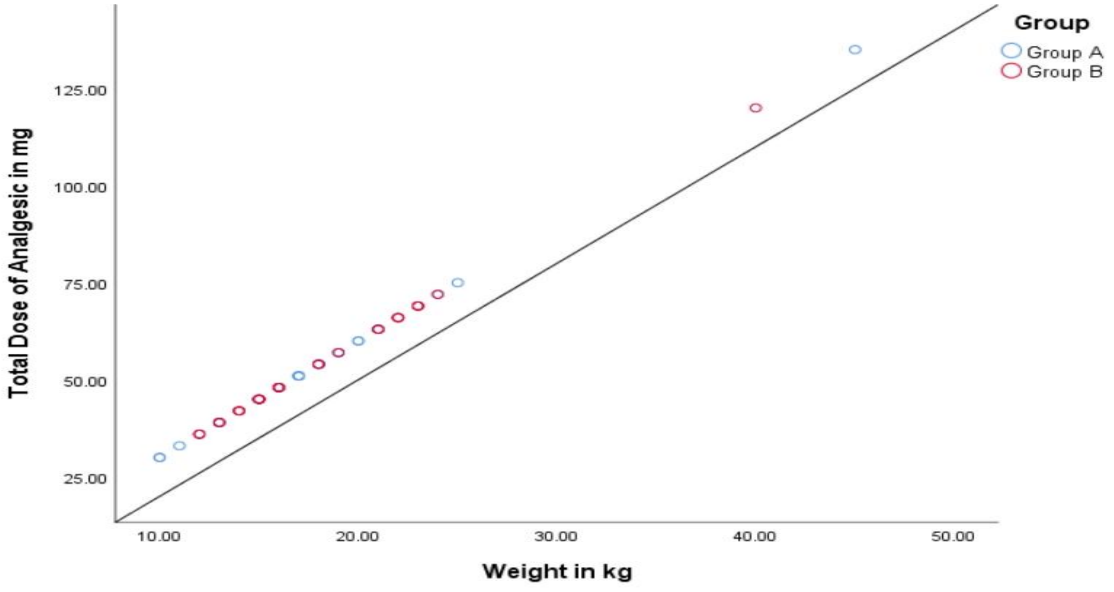

Figure 1: Relationship between weight and analgesic dose in Group A and Group B

Table 2: Distribution of FLACC pain scores using Shapiro Wilk's test of normality

FLACC score		Statistics	N	P-value
Pain Score At 2hrs	Group A	0.914	30	*0.02**
	Group B	0.904	30	*0.01**
Pain Score At 4hrs	Group A	0.885	30	*0.01**
	Group B	0.779	30	*0.00**
Pain Score At 6hrs	Group A	0.929	30	*0.05**
	Group B	0.851	30	*0.00**
Pain Score At 8hrs	Group A	0.891	30	*0.01**
	Group B	0.731	30	*0.00**
Pain Score At 10hrs	Group A	0.879	30	*0.00**
	Group B	0.883	30	*0.00**
Pain Score At 12hrs	Group A	0.848	30	*0.00**
	Group B	0.778	30	*0.00**
Pain Score At 18hrs	Group A	0.903	30	*0.01**
	Group B	0.857	30	*0.00**
Pain Score At 24hrs	Group A	0.845	30	*0.00**
	Group B	0.842	30	*0.00**

**Statistically significant*

Table 3: Mean ranks and Median FLACC scores across Groups (Mann-Whitney U test)

FLACC pain score	Group A(N=30)		Group B(N=30)		U test statistics	Z score	P-value
	Mean Rank	Median	Mean Rank	Median			
2 hours	24.33	3.00	36.67	4.00	265.00	-2.78	*0.01**
4 hours	24.42	3.00	36.58	4.00	267.50	-2.83	*0.00**
6 hours	24.22	3.00	36.78	4.00	261.50	-2.87	*0.00**
8 hours	23.27	2.00	37.73	3.00	233.00	-3.35	*0.00**
10 hours	24.87	2.00	36.13	3.00	281.00	-2.57	*0.01**
12 hours	25.33	2.00	35.67	3.00	295.00	-2.43	*0.01**
18 hours	24.38	2.00	36.62	3.00	266.50	-2.82	*0.00**
24 hours	24.25	2.00	36.75	3.00	262.50	-2.88	*0.00**

**Statistically significant*

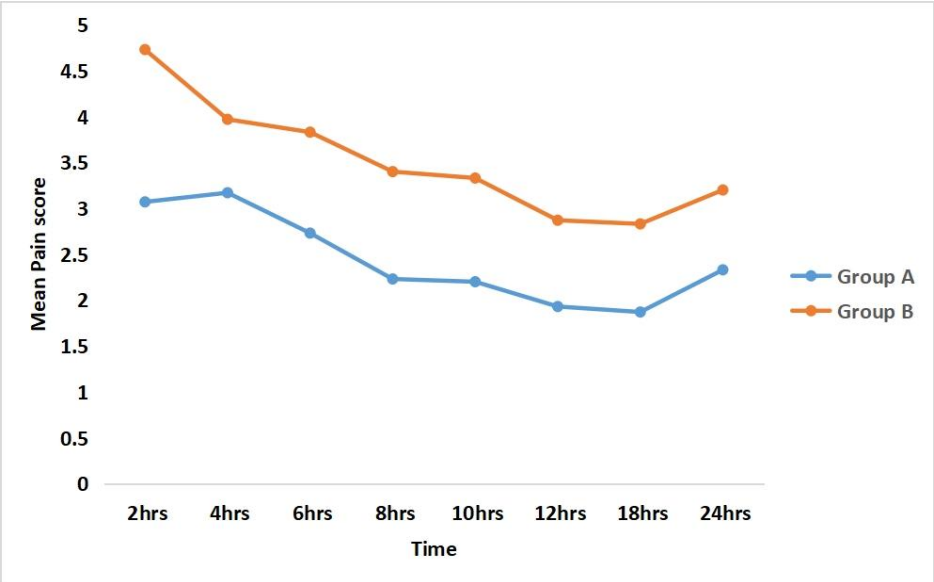

Figure 2: Mean pain scores among Groups

DISCUSSION

This study has shown that following adenotonsillectomy, more patients experienced analgesia and had more oral intake with use of diclofenac sodium suppository than with paracetamol suppository. However, the difference in time to first oral intake was insignificant. The demographic characteristics were not statistically significant with male preponderance being a known finding by previous researchers.[3,6,8] Both adenoids and tonsils removal between ages 2 to 5 years in keeping with the peak age of lymphoid tissue and tonsillar enlargement, inflammation and infection is also well documented.[2,6,7]

A strong positive correlation between the weight and analgesic dose received in both groups was also found. Other studies have utilized suppository analgesic doses within the same range. Ubale and Trasy[18] administered single doses of suppository diclofenac and suppository acetaminophen at 2mg/kg and 20mg/kg, respectively. Tawalbeh et al[19] administered diclofenac and acetaminophen at 3mg/kg/day (in 2 divided doses) and 60mg/kg/day in 4 divided doses respectively. Romsing et al[20] on the other hand administered diclofenac at 3mg/kg/day but gave acetaminophen at a high dose of 90mg/kg/day. Pharmacokinetically, oral drug administration is preferred but is not ideal in the immediate post tonsillectomy period due to the likely side effects of anaesthestics such as drowsiness, nausea and vomiting with risk of aspiration, and pain at the operation site. The rectal route as utilized in this study is therefore a reliable alternative route of drug administration in the early post-tonsillectomy period. Various researchers have employed the rectal, oral and a combination of both routes in the administration of post-tonsillectomy analgesia. Ubale and Trasy[18] and Ibekwe and Oghenekaro,[7] have used the rectal route to compare the analgesic efficacy of diclofenac sodium and acetaminophen, and to study the place of NSAIDS in post-tonsillectomy analgesia in children respectively. Merry et al[21] on the other hand administered analgesics via the oral route. In their study, the first analgesic dose was given prior to induction of anaesthesia and subsequent doses administered at six hourly intervals postoperatively. While the oral route remains a valid means of drug administration, it can increase risk of intraoperative aspiration. Romsing et al[20] also utilized the oral route to compare the analgesic efficacy of diclofenac and high dose acetaminophen on pain after tonsillectomy. Tawalbeh et al[19] employed both the oral and rectal routes to study the effect of diclofenac sodium and acetaminophen on post adenotonsillectomy pain in children. In their study, diclofenac was administered rectally in the immediate postoperative period before awakening, while acetaminophen was given orally. With this methodology, there may be likelihood of some delay in the oral administration of acetaminophen postoperatively in an awake child, compared to diclofenac which was inserted rectally while child was still asleep. This discrepancy in timing could have influenced outcomes in favour of diclofenac in their study.

Assessment of pain in children can be challenging as previously highlighted, as other conditions may mimic pain and younger children cannot express pain appropriately. Several pain assessment tools have therefore been developed to overcome these challenges. The Face Legs Activity Cry and Consolability (FLACC) scale was used in the present study. Other workers[18,21] have utilized the Visual Analogue Scale (VAS) in children aged 5 to 15 years, while Yallapragda and Shenoy[22] used a combination of FLACC scale (for children less than 7years) and the Visual Analogue Scale for children older than 7 years. Tawalbeh et al[19] used the time to first solid intake as a crude parameter for assessment, while Ibekwe and Oghenekaro[7] assessed post-tonsillectomy pain using the ability to swallow and time of commencement of oral intake. However, considering the mean age of the subjects in the present study, self-reporting of pain was not feasible, hence the use of the FLACC scale as a choice**.** Postoperatively, the mean pain scores were highest within the first 2 hours (group A) and the first 4hours (group B), followed by a gradual decline afterwards in both groups (Figure 2), but pain scores were lower at all time intervals in group A compared to group B. Ubale and Trasy[18] used the VAS to monitor post-tonsillectomy pain in their study groups following the administration of single doses of suppository acetaminophen and suppository diclofenac respectively at induction of anaesthesia. They also noted a

significant increase in post-tonsillectomy pain scores among the acetaminophen group, compared to the diclofenac group from the sixth postoperative hour, while our study observed a significant difference in pain scores in both groups earlier. This could be due to the higher dose of diclofenac suppository in the present study (3mg/kg/day) compared to the dose of 2mg/kg used by Ubale and Trasy[18] Similarly, Tawalbeh et al[19] in their comparative study of diclofenac sodium and acetaminophen for treatment of pain after adenotonsillectomy in children aged 3 to 14 years, also observed that children who received diclofenac sodium had less pain compared to those who received paracetamol.

In contrast however, Romsing et al[20] in a randomized, double-blinded study of 48 children between the ages of 5 to 15 years found that diclofenac was not more effective than high-dose acetaminophen for post-tonsillectomy analgesia. Higher dose of acetaminophen (90mg/kg/24h) was however utilized, compared to our study. Also, Merry et al[21] found no significant difference in pain scores among three groups of children randomized to receive either acetaminophen alone, ibuprofen alone or a combination of both, post-tonsillectomy. Their study was however done in older children aged 6 to 14 years, who may tolerate pain better than younger children recruited in the present study. Besides, other causes may mimic pain in younger children thereby tending to increase their pain scores.

Rescue analgesia requirements were significantly different in the two groups with much increased requirements in the acetaminophen group. Similar findings were also made by Ubale and Trasy[18] but not with Merry et al[21] who found the rescue analgesia requirement to be similar among children who received ibuprofen or acetaminophen alone, but significantly less in children who received a combination of the two medications. This may be explained by the greater analgesic effectiveness of multimodal analgesia than single drug use. Since more than 60% of patients in both groups in our study required rescue analgesia, it could be deduced that diclofenac or acetaminophen suppositories alone did not adequately control pain in both groups. Further studies that compare the efficacy of a combination of diclofenac and acetaminophen suppositories to each drug used alone for treating post-tonsillectomy pain, may shed more light on this.

There was no statistically significant difference in the meantime to first post-tonsillectomy oral food intake between both drug groups, though it was shorter in the diclofenac group. The difference in the frequency of oral food intake was however significant, with the diclofenac group having more frequent oral intake. Similar findings were also documented by Tawalbeh et al.[19] Ibekwe and Oghenekaro[7] reported that approximately fifty percent of children who received rectal diclofenac, commenced oral intake within six hours of full recovery - a comparable timing in the diclofenac group of the index study. Romsing et al[20] noted less nausea and vomiting in the diclofenac group compared to the paracetamol group. This may also correlate to better oral intake in the diclofenac group.

One of the documented side effects of NSAIDS is their inhibition of platelet activation with increased risk of bleeding.[23] This is a major concern for Otolaryngologists globally and many are reluctant to use NSAIDS for post-tonsillectomy analgesia. A systematic review of 25 randomized trials by Moiniche et al[24] on NSAIDS and the risk of operative site bleeding after tonsillectomy showed that NSAIDS significantly correlated with increased rate of reoperation due to bleeding. Similarly, a meta-analysis of 7 randomized trials by Krishna et al[25] found an increased risk of post-tonsillectomy haemorrhage with the use of aspirin but not with non-aspirin NSAIDS. Conversely, a systematic review and meta-analysis of 36 randomized controlled trials by Riggin et al[26] concluded that NSAIDS are not associated with increased risk of post-tonsillectomy bleeding, readmission or need of reoperation due to bleeding in both adults and children. Also, Cardwell et al[27] in a Cochrane review of 13 trials involving 955 children in which NSAIDS were compared with other analgesics or placebo reported that NSAIDS did not increase bleeding requiring return to the operating room.

Acetaminophen has the risk of severe hepatotoxicity following overdose,[28] but the

present study recorded no side effects with analgesic drugs used and in keeping with reports from previous workers.[7,18,19,21] Safe doses were employed and patients with abnormal coagulation profiles known to be prone to post-tonsillectomy bleeding[29] were excluded, Our sample size was however not representative and the monitoring period of 48 hours was short.

The significantly shorter mean duration of hospital admission in the diclofenac group compared to the acetaminophen group can be explained by the fact that better post tonsillectomy analgesia in the diclofenac group translated to better oral intake which resulted in earlier discharge. Tawalbeh et al[19] also observed earlier hospital discharge in the diclofenac group compared to the acetaminophen group.

CONCLUSION

Suppository diclofenac was more effective in controlling post-tonsillectomy pain than suppository acetaminophen, but neither of the two drugs was able to adequately control post tonsillectomy pain. There was no significant difference in the time to first post-tonsillectomy oral food intake in both groups, but suppository diclofenac significantly enhanced more frequent oral intake and shorter hospital stay. The FLACC scale appears to be a fair objective tool and is recommended for assessment of post-tonsillectomy pain in paediatric patients, provided other non-painful conditions of discomfort are excluded. As both agents were not wholly effective as monotherapy for post-tonsillectomy pain, further studies are suggested to compare the effect of combination therapies.

Financial support and sponsorship
Nil

Conflicts of interest
There are no conflicts of interest

REFERENCES

1. Derkay CS. Pediatric otolaryngology procedures in the United States: 1977–1987. Int J Pediatr Otorhinolaryngol 1993; 25:1-12.
2. Onotai L, da Lilly-Tariah OB. Adenoid and tonsil surgeries in children: How relevant is pre-operative blood grouping and cross-matching? Afr J Paediatr Surg 2013; 10(3):231-234.
3. Okafor BC. Tonsillectomy: an appraisal of indications in developing countries. Acta Otolaryngol 1983; 96(5-6):517-522.
4. da Lilly-Tariah OB, Peterside OA. The Scope of ear, nose and throat surgeries in the theatre in University of Port Harcourt Teaching Hospital. J Med Trop 2008; 10(1):15-22.
5. Somefun AO, Nwawolo CC, Mazai AE, Okeowo PA. Adenoid and tonsil operations: An appraisal of indications and complications. Niger J Surg 2000; 7(1):16-19.
6. Ameye SA, Owojuyigbe AM, Adeyemo A, Adenekan AT, Ouche S. Pediatric adenotonsillectomy in a low resource setting: Lessons and implications. Niger J Surg 2016; 22(2):77-80.
7. Ibekwe UM, Oghenekaro E. Post-adenotonsillectomy analgesia in children: the place of non-steroidal anti-inflammatory drugs. Port Harcourt Med J 2019; 13(1):41-45.
8. Onotai LO, Ebong EJ. Day-case adenoid and tonsil surgeries in children: a private clinic experience in a resource poor country. J Med Res Pract 2013; 2:144-147.
9. Onotai LO, Nwankwo NC. A review of the Nigerian healthcare funding system and how it compares to that of South Africa, Europe and America. J Med Med Sci 2012; 3(4):226-231.
10. 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; 144(1 Suppl): S1-30.
11. Abou-Jaoude PM, Manoukian JJ, Daniel SJ, Balys R, Abou-Chacra Z, Nader ME, et al. Complications of adenotonsillectomy revisited in a large pediatric case series. J Otolaryngol 2006; 35(3):180-185.
12. Jadad AR, Browman GP. The WHO Analgesic Ladder. JAMA 1995; 274(23):1870-1873.

13. Sutters KA, Isaacson G. Post tonsillectomy pain in children. Am J Nurs 2014; 114(2):36-42.

14. Lavonas EJ, Reynolds KM, Dart RC. Therapeutic acetaminophen is not associated with liver injury in children: a systematic review. Pediatrics 2010; 126(6): e1430-1444.

15. Li C, Martin BC. Trends in emergency department visits attributable to acetaminophen overdoses in the United States: 1993-2007. Pharmacoepidemiol Drug Saf 2011; 20(8):810-818.

16. Kokki H. Nonsteroidal anti-inflammatory drugs for postoperative pain: a focus on children. Pediatr Drugs 2003; 5:103-123.

17. Redmann AJ, Wang Y, Furstein J, Myer CM 3rd, de Alarcon A. The use of the FLACC pain scale in pediatric patients undergoing adenotonsillectomy. Int J Pediatr Otorhinolaryngol 2017; 92:115-118.

18. Ubale P, Trasy V. Comparison of analgesic efficacy of diclofenac sodium suppository over acetaminophen suppository for post tonsillectomy pain relief in pediatric age group: randomized study. Anaesth Pain Intensive Care 2016; 20(2):137-142.

19. Tawalbeh MI, Nawasreh OO, Husban AM. Comparative study of diclofenac sodium and paracetamol for treatment of pain after adenotonsillectomy in children. Saudi Med J 2001; 22(2):121-123.

20. Romsing J, Ostergaard D, Drozdziewicz D, Schultz P, Ravn G. Diclofenac or acetaminophen for analgesia in paediatric tonsillectomy outpatients. Acta Anaesthesiol Scand 2000; 44(3):291-295.

21. Merry AF, Edward KE, Ahmad Z, Barber C, Mahadevan M, Frampton C. Randomized comparison between the combination of acetaminophen and ibuprofen and each constituent alone for analgesia following tonsillectomy in children. Can J Anesth 2013; 60(12):1180-1189.

22. Yallapragada SV, Shenoy T. Comparison of preoperative rectal paracetamol with paracetamol-diclofenac combination for postoperative analgesia in pediatric surgeries under general anaesthesia. Anesth Essays Res 2016; 10(2):301-304.

23. Furst DE, Ulrich RW, Varkey-Altamirano C. Nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, nonopioid analgesics, and drugs used in gout. In: Katzung BG, Masters SB, Trevor AJ (eds). Basic and clinical pharmacology, 11th edn. Singapore: McGraw-Hill, 2009; 622-624.

24. Møiniche S, Rømsing J, Dahl JB, Tramèr MR. Nonsteroidal anti-inflammatory drugs and the risk of operative site bleeding after tonsillectomy: a quantitative systematic review. Anesth Analg 2003; 96(1):68-77.

25. Krishna S, Hughes LF, Lin SY. Postoperative hemorrhage with nonsteroidal anti-inflammatory drug use after tonsillectomy: a meta-analysis. Arch Otolaryngol Head Neck Surg 2003; 129(10):1086-1089.

26. Riggin L, Ramakrishna J, Sommer DD, Koren G. A 2013 updated systematic review and meta-analysis of 36 randomized controlled trials; no apparent effects of non-steroidal anti-inflammatory agents on the risk of bleeding after tonsillectomy. Clin Otolaryngol 2013; 38(2):115-129.

27. Cardwell ME, Siviter G, Smith AF. Non-steroidal anti-inflammatory drugs and perioperative bleeding in paediatric tonsillectomy. Cochrane Database Syst Rev 2005;(2):CD003591. Update in: Cochrane Database Syst Rev 2013;(7):CD003591.

28. Grosser T, Smyth E, FitzGerald GA. Anti-inflammatory, antipyretic, and analgesic agents; Pharmacotherapy of gout. In: Brunton LL, Chabner BA, Knollmann BC (eds). Goodman and Gilman's The pharmacological basis of therapeutics, 12th edn. China: McGraw-Hill, 2011; 962-977.

29. Sun GH, Auger KA, Aliu O, Patrick SW, DeMonner S, Davis MM. Posttonsillectomy hemorrhage in children with von Willebrand disease or hemophilia. JAMA Otolaryngol Head Neck Surg 2013; 139(3):245-249.