Comparison of Analgesic Efficacy of Etoricoxib and Aceclofenac in Post Operative Pain Management after Periodontal Flap Surgery

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Abstract

Background: The purpose of the study was to compare the analgesic efficacy of Etoricoxib (90 mg once a day) and Aceclofenac (100 mg twice a day) in post-operative pain management after periodontal flap surgery for three days.

Material & Methods: 15 subjects underwent, periodontal flap surgical procedures in at least two quadrants were randomly divided for administration of 90 mg tablet Etoricoxib orally once daily after surgery in one quadrant & administration of 100 mg tablet Aceclofenac orally twice daily for 3 days postoperatively after surgery in another quadrant. The postoperative pain was evaluated using Visual analogue scale.

Results: Study demonstrated that both Etoricoxib and Aceclofenac had significant post-operative pain control within 24 hours. In the present study Aceclofenac showed significant difference in post-operative pain control in first 4 hours than Etoricoxib.

Conclusion: Aceclofenac showed better overall results in controlling post-operative pain compared to Etoricoxib up to 24 hours.

Keywords: Analgesia, Etoricoxib, Aceclofenac, Post-operative pain, Periodontal Flap surgery.

INTRODUCTION

Periodontal disease is a chronic inflammatory infection having a high prevalence worldwide.[1] Periodontal treatment is experienced as painful by a substantial number of patients, during & after which there is an expectation of discomfort, postoperative pain, and dentin hypersensitivity .[2] Scaling and root planning, one of the most common procedures in

periodontal practice, can promote pain of significant duration and magnitude.[3] Periodontal surgical therapies, when necessary, also generates pain and discomfort with greater intensity than that caused only by scaling and root planning.[4-6]

Pain is an unpleasant, sensory and emotional experience associated with tissue injury or infection, resulting in cellular damage.[7] Post-operative pain after periodontal surgical procedures is a matter of considerable consequence to most patients. Many factors contribute towards occurrence of post-operative dental pain like duration, extent & complications which may relate to the inflammatory process that is initiated by surgical trauma.

There is no universally accepted method for measuring pain. Patient-reported outcomes are of most importance in pain measurement, as pain is a subjective phenomenon and varies person to person. Visual analogue scales have proved to be satisfactory in the subjective measurement of pain. It is a 10-point scale where pain experienced is marked as no pain to severe unbearable pain .[8]

Cyclooxygenase (COX) pathways have long been targeted for the treatment of inflammatory pain, through the use of NSAIDs. With the demonstration of two major COX isoforms, COX-1 and COX-2, involved in the production of prostaglandins, but with different distribution and regulation, preferential and selective COX-2 inhibitors have been developed.[9]

Acetaminophen, Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids analgesics are prescribed to subside pain. NSAIDs are commonly the first options in pain management after surgical procedures, especially due to the less severe side effects compared to others. The role of preoperative and postoperative medications in reducing postoperative complications has been extensively evaluated.[10]

Aceclofenac is a phenyl acetic acid derivative NSAID with preferential COX-2 inhibitory activity.[11] It exhibits anti-inflammatory and analgesic properties and thus used for pain management after many dental procedures.[12] The new class of NSAIDs with selective inhibition of the COX-2 anti-inflammatory activity has been developed, the *-coxibs* NSAIDs. The *-coxibs* exhibit minimal damage to gastric mucosal & peptic ulceration with ulcer bleeds at a lower rate than with traditional NSAIDs. Etoricoxib is a newer COX-2 inhibitor has the highest COX-2 selectivity. As the half-life of Etoricoxib is 24 hours, it is suitable for once-a-day treatment.[13]

Thus this study was undertaken to compare the analgesic efficacy of Etoricoxib & Aceclofenac in reduction of pain after periodontal flap surgical procedures.

MATERIAL AND METHODS

Study Design and Ethical Consideration

The study was single-center, single-blind, split mouth, cross over randomized controlled clinical trial. Ethical approval was obtained at the beginning of the study from the Institutional Ethical Committee. The participants were informed about the study protocol & written informed consent was obtained.

Sample Selection and Inclusion Criteria

The study recruited 15 patients (18-65 years) with generalized chronic periodontitis who were who were scheduled for flap surgery in at least two quadrants. The study took place in Department of Periodontology, RUHS College of Dental Sciences, Jaipur from January 2023 and March 2023.

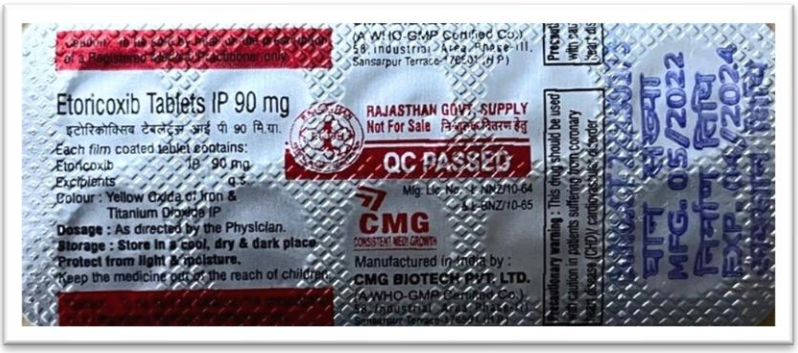
Patients who fulfilled the following criteria were included in the study :1) having generalized chronic periodontitis & planned for Periodontal flap surgery; 2) in good systemic health 3.) Had no history of drug allergy and non-consumption of analgesics two weeks prior to surgery. Patients were excluded if they met any of the following criteria: 1.) Patients who had infectious diseases, history of asthma, peptic ulceration, or other disorders of the upper gastrointestinal tract; 2.) With history of ischemic heart disease / hypertension / cardiac failure / cerebrovascular disease or pre-disposed to cardiovascular events 3.) Consumption of any immunosuppressive or anti-inflammatory drugs 1 month prior to the study; 4.) Pregnant women and lactating mothers. 5.) Smokers, alcohol abusers & tobacco chewers.

After completion of phase I therapy i.e. scaling & root planning, all the patients who were participating in the study were scheduled for periodontal flap surgical procedure, under local Anesthesia (2% lidocaine with 1: 100,000 epinephrine) by an experienced periodontist. Mucoperiosteal flap was

elevated & after completion of open flap debridement sutures were place. In each patient, after completion of periodontal flap procedure of first quadrant, Tab Etoricoxib 90 mg OD[14] & for second quadrant, Tab Aceclofenac 100mg BD[15] was prescribed. At least a 4-week interval between the appointments was set for adequate healing.

Test Drug Protocols

Patients underwent Periodontal flap surgery in which least two quadrants were randomly allocated for administration of either of the test drugs orally within 1 hour after completion of surgery. Tab Etoricoxib 90 mg once a day was administered after surgery in either of the quadrant. After 1 month of healing, Surgical procedure was performed for another quadrant and Tab Aceclofenac 100 mg was administered twice a day for post-operative pain management. The test drug of the respective group was randomly assigned for each surgical intervention (either of the surgical quadrant). The appearance of drug packaging was identical.



Picture 1. Tab Etoricoxib 90 mg

Picture 2. Tab Aceclofenac 100 mg

Data Collection

At the completion of the surgery, the patients were given post-operative instruction and supplied with a printed record forms and were asked to rate their subjective postoperative pain intensity using a visual analog scale (VAS) at 2 hours, 4 hours, 6 hours, 12 hours, 18 hours, 24 hours, 48 hours & 72 hours on a scale of 0 to 10; where 0 is for no pain and 10 is for worst pain. Each patient is provided with an additional rescue analgesic; Tab paracetamol 500mg, every 4 to 6 hours if the pain scale crosses moderate to severe pain.[16,17] The quantity and frequency of use were documented whenever the administration of medications (rescue and other medicines) were necessary.

Statistical Analysis

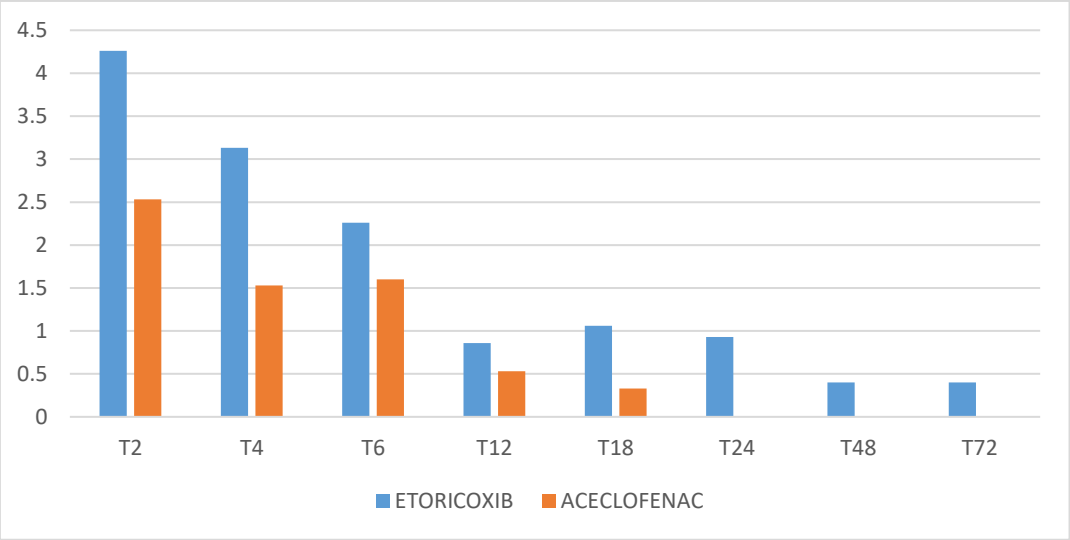
Statistical analysis was performed to characterize both the test drugs using statistical software SPSS version 22 (India).[18] Pain scores after administration of Etoricoxib and Aceclofenac were tabulated for the same individual. Differences between the effects of test drugs at different examination times (intergroup comparisons) were performed using student paired t test. These variations served as response variables for the conclusion of investigation. P value less than 0.05 was taken as significant.

Table 1. Post-operative pain scores of Etoricoxib and Aceclofenac group at various evaluation times and no. of rescue medicine.

Pain Score Study Group	T2	T4	T6	T12	T18	T24	T48	T72	No. of Rescue Analgesics
Etoricoxib	4.26 ± 2.46	3.13 ± 2.44	2.26 ± 3.29	0.86 ± 1.08	1.06 ± 1.98	0.93 ± 1.65	0.4 ± 0.48	0.4 ± 0.48	2
Aceclofenac	2.53 ± 1.54	1.53 ± 1.45	1.6 ± 1.62	0.53 ± 0.71	0.33 ± 0.47	0	0	0	1
P Value	**0.02**	**0.037**	0.49	0.33	0.17	0	0	0	-

Significant p values are shown in bold.

Figure 1. VAS pain score of Etoricoxib group and Aceclofenac group recorded at specific postoperative time intervals. Data are expressed as the mean ± standard deviation.



RESULTS

The study recruited a total of 15 subjects, 6 males (40%) and 9 females (60%) whose ages ranged from 18 to 65 years with a mean ± SD of 39 ± 7.6 years. Pain scores assessed through the VAS scale at different evaluation time are shown in Table 1 & 2 and the dynamic changes between the test drugs in each group is shown in Figure 1. At all the time points, administration of Aceclofenac was having less pain score compared to Etoricoxib. The peak postoperative pain score was seen at 2 hours for both with more pain score reduction observed in Aceclofenac use ($P < 0.001$) compared to the use of Etoricoxib. Further statistically significant reduction in mean VAS score were observed in both Etoricoxib use & Aceclofenac use at 4 hours which was higher for Aceclofenac. On Intragroup comparison, statistically significant reduction in mean VAS score was observed with Etoricoxib use at 12 hours. Intergroup comparison revealed mean pain score values at 2 h ($P = 0.02$), 4 h ($P = 0.038$), 6 h ($P = 0.049$), 12 h ($P = 0.33$), 18 h ($P = 0.17$) and 24 h ($P = 0.0$) after surgery, which were significantly lower for Aceclofenac than Etoricoxib (Figure 1). There was a steady deterioration in pain scores in both during successive evaluation intervals, with differences almost equal to zero after 24 hours.

Surgical characteristics did not differ for either of the quadrant. Local anesthetic was injected at all appropriate sites, not more than recommended quantity before surgery. Postoperative healing was uneventful in all patients, without adverse events being present during the follow-up. One subject after Aceclofenac use & two subjects after Etoricoxib use took the rescue analgesic in first 24 hours.

DISCUSSION

The current study looked at the efficacy of an oral NSAID, which is a type of medication that is routinely administered after oral surgical procedures. It is vital to note that the time and extent of the surgery may have an impact on pain perception.[2] Postoperative pain after periodontal surgeries is predicted to be milder and of shorter duration than other more complex oral surgeries.[5] Postoperative pain has been found to be more in intensity in the first 24 hours following periodontal surgery, then decreases gradually.[19] The mechanism of action of NSAIDs for pain relief is traditionally attributed to decreased prostaglandin synthesis due to cyclooxygenase inhibition, hence avoiding peripheral and central sensitization.[20,21] Other pathways, such as contact with the endocannabinoid system or ionic channels, could be related to their analgesic effects.[22,23] According to the literature, NSAIDs may produce adequate analgesic effect to alleviate most postoperative dental pain.[24]

Aceclofenac, a highly selective cox-2 inhibitor and NSAID of the phenyl acetic acid group, was authorized for medical use in 1992. Aceclofenac is water-insoluble, although it is conjugated in human hepatocytes and metabolized to the main metabolite 4-hydroxy aceclofenac. Aceclofenac has a plasma half-life of 4-4.3 hours. Aceclofenac is a powerful anti-inflammatory agent that works by reducing the expression or production of inflammatory mediators.[25] Etoricoxib is a novel COX-2-selective inhibitor with analgesic efficacy in the treatment of acute pain and primary dysmenorrhea, with rapid onset and long-lasting pain alleviation. Etoricoxib deliver pain alleviation that was both immediate and sustained over a 24-hour period.[26]

Pain is subjective, and its experience varies person to person. As a result, only patients are capable of assessing their own suffering. For this purpose, A Visual Analogue Scale use is recommended by Berge[27], Caporossi & Studzinski[28].

The objective of this study was to evaluate the efficacy of Etoricoxib and Aceclofenac in the postoperative pain management after Periodontal Flap Surgery. The Study demonstrated that both Etoricoxib and Aceclofenac had significant post-operative pain control within 24 hours after surgery. No statistically significant difference was discovered after 24 hours following surgical procedure, validating these findings. Results found with the Visual Analogue Scale showed that the Aceclofenac use had a lower pain score at all time points in the study compared with Etoricoxib use. While **Isola G et al** study compared effectiveness of Etoricoxib and Diclofenac on pain and perioperative sequelae after surgical avulsion of mandibular third molars found that compared to diclofenac and placebo, Etoricoxib had a significant analgesic effect throughout the first postoperative week.[28] While in a study by **Caporossi & Studzinski** found that there were no statistically significant differences in pain alleviation between NSAIDs and dexamethasone, at any post-operative time.[29]

This is the first kind of study comparing analgesic efficacy of Etoricoxib and Aceclofenac for post-operative pain management after Periodontal Flap Surgery. In the present study, both Etoricoxib and Aceclofenac had significant post-operative pain control within 24 hours. Aceclofenac showed significant difference in post-operative pain control in first 4 hours than Etoricoxib. **Lima et al** in a study comparing analgesic efficacy of two tablets of 100 mg Aceclofenac taken orally either 1 h before surgery or in the early postoperative period in controlling pain after surgical extraction of impacted mandibular third molars found that 200 mg Aceclofenac dose was efficient in controlling pain.[30] Etoricoxib took 12 hours to show significant difference in pain reduction. A study by Costa et al demonstrated statistically significant difference in pain reduction following removal of unerupted mandibular third molars over a 48-h period.[31] Both Etoricoxib and Aceclofenac required the use of a rescue analgesic in a few patients.

There were no reported adverse effects with the usage of Etoricoxib in the current investigation. According to the published Cochrane reviews,[32,33] Etoricoxib 120 mg use has been shown to be relatively safe. **Lima et al** in a study recommended maximum daily dose of 200 mg Aceclofenac in a day.[30]

The limitations of the present study are significant heterogeneity of included studies, implying differences between them, such as follow-up length, small sample size, risk of bias, different analgesics,

and pain metrics. Additionally, the findings of this study should be interpreted with caution, as unique characteristics of the sample, the precise evaluation intervals, the pain measurement scale and some potential carryover impact may influence the results. Additionally, Pain threshold levels are very subjective and must be taken into account in the current investigation.

CONCLUSION

Aceclofenac showed better overall results in controlling post-operative pain compared to Etoricoxib in first 24 hours of post-surgery. Nevertheless, there were no significant difference in the use of rescue medications. However, more research is needed to determine the possible benefits of Etoricoxib and Aceclofenac in postoperative therapy following periodontal flap surgery.

BIBLIOGRAPHY

1. Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJL, Marcenes W.Global burden of severe periodontitis in 1990- 2010: A systematic review and meta-regression. J Dent Res 2014; 93: 1045–1053.
2. Canakci CF, Canakci V. Pain experienced by patients undergoing different periodontal therapies. Journal of the American Dental Association. 2007;138:1563-1573.
3. Aslund M, Suvan J, Moles DR, D'Aiuto F, Tonetti MS. Effects of two different methods of non-surgical periodontal therapy on patient perception of pain and quality of life: a randomized controlled clinical trial. Journal of Periodontology.2008;79(6):1031-1040. https://doi.org/10.1902/jop.2008.070394. Jun.
4. Curtis JW Jr, McLain JB, Hutchinson RA. The incidence and severity of complications and pain following periodontal surgery. Journal of Periodontology. 1985;56:597-601.
5. Mei CC, Lee FY, Yeh HC. Assessment of perception following periodontal and implant surgeries. Journal of Clinical Periodontology. 2016;43:1151-1159.
6. Bahammam MA, Kayal RA, Alasmari DS, et al. Comparison between dexamethasone and ibuprofen for postoperative pain prevention and control after surgical implant placement: a double-masked, parallel-group, placebo-controlled randomized clinical trial. Journal of Periodontology. 2017;88:69-77.
7. Melzack R, Wall P, editors. Textbook of pain. 4th ed. New York, NY: Churchill. Livingstone; 1999.
8. Scott J, Huskisson E. Graphic representation of pain. Pain 1976;2(2):175-84
9. González-Barnadas A, Camps-Font O, Martín-Fatás P, Figueiredo R, Gay-Escoda C, Valmaseda-Castellón E. Efficacy and safety of selective COX-2 inhibitors for pain management after third molar removal: a meta-analysis of randomized clinical trials. Clin Oral Investig. 2020 Jan;24(1):79-96. doi: 10.1007/s00784-019-02910-3. Epub 2019 Apr 23. PMID: 31016540.
10. Edmund B. Prevention and Management of Post-Operative Pain in Oral Surgery. Prim Dent J. 2018;7(3):57-63.
11. Brogden RN, Wiseman LR. Aceclofenac. A review of its pharmacodynamic properties and therapeutic potential in the treatment of rheumatic disorders and in pain management. Drugs 1996: 52: 113– 124.
12. Legrand E. Aceclofenac in the management of inflammatory pain. Expert Opin Pharmacother 2004: 5: 1347–1357.
13. Daniels et al. Evaluation of the Dose Range of Etoricoxib in an Acute Pain Setting Using the Postoperative Dental Pain Model. Clin J Pain 2011;27:1–8.
14. Malmstrom K, Sapre A, Couglin H, Agrawal NG, Mazenko RS, Fricke JR Jr. Etoricoxib in acute pain associated with dental surgery: a randomized, double-blind, placebo- and active comparator-controlled dose-ranging study. Clin Ther. 2004;26(5):667-79. doi: 10.1016/s0149-2918(04)90067-7. PMID: 15220011.
15. Asmawi, M.Z., O.M. Arafat, S. Amirin and I.M. Eldeen. In vivo antinociceptive activity of leaf extract of Crinum asiaticum and phytochemical analysis of the bioactive fractions. Int. J. Pharmacol. 2011; 7: 125-129.
16. Cetira Filho EL, Carvalho FSR, de Barros Silva PG, et al. Preemptive use of oral nonsteroidal anti-inflammatory drugs for the relief of inflammatory events after surgical removal of lower third molars: a systematic review with meta-analysis of placebo controlled randomized clinical trials. Journal of Cranio-MaxilloFacial Surgery. 2020;48:293-307.
17. Santos BFE, Costa FO, Pinto-Júnior AAC, Araújo AVA, Cyrino RM, Cota LOM. Postoperative pain and edema control following different protocols of preemptive analgesia in the surgical removal of impacted third molars: a triple-blind parallel randomized placebo-controlled clinical trial. Journal

of CranioMaxillo-Facial Surgery. [published online ahead of print January 11, 2021].
18. Priyanka Gogoi. Application of SPSS Programme in the Field of Social Science Research. International Journal of Recent Technology and Engineering (IJRTE). 2020 ;8(5): 2277-3878.
19. Seymour RA, Blair GS, Wyatt FAR.Post-operative dental pain and analgesic efficacy. Part I. Br J Oral Surg. 1983;21:290–297. https://doi.org/10.1016/0007-117X(83)90017-3
20. Burian M, Geisslinger G.COX-dependent mechanisms involved in the antinociceptive action of NSAIDs at central and peripheral sites. Pharmacol Ther .2005;107:139–154. https://doi.org/10. 1016/j.pharmthera.2005.02.004
21. Cashman JN. The mechanisms of action of NSAIDs in analgesia. Drugs.1996; 52(Suppl):5–23. https://doi.org/10.2165/00003495- 199600525-00004.
22. Guindon J, LoVerme J, De Léan A et al Synergistic antinociceptive effects of anandamide, an endocannabinoid, and nonsteroidal anti-inflammatory drugs in peripheral tissue: a role for endogenous fatty-acid ethanolamides? Eur J Pharmacol .2006;550: 68–77. https://doi.org/10.1016/j.ejphar.2006.08.045.
23. Arslan R, Bektas N.The role of TRP and K+ ion channels in analgesic effect of NSAIDs. Clin Exp Heal Sci.2018; 8:301–307. https:// doi.org/10.5152/clinexphealthsci.2018.832.
24. Wong YJ, Keenan J, Hudson K et al. Opioid, NSAID, and OTC analgesic medications for dental procedures: PEARL network findings. Compend Contin Educ Dent 2016;37:710–718
25. González-Alvaro I, Carmona L, Díaz-González F, et al. Aceclofenac, a new nonsteroidal antiinflammatory drug, decreases the expression and function of some adhesion molecules on human neutrophils. J Rheumatol 1996;23(4):723–729.
26. Malmstrom, K., Sapre, A., Couglin, H., Agrawal, N. G., Mazenko, R. S., & Fricke, J. R. Etoricoxib in acute pain associated with dental surgery: A randomized, double-blind, placebo- and active comparator-controlled dose-ranging study. Clinical Therapeutics.2004; 26(5), 667–679. doi:10.1016/s0149-2918(04)90067-7.
27. Berge TI. The use of a visual analogue scale in observer assessment of postoperative swelling subsequent to thirdmolar surgery. Acta Odontol Scand 1989: 47: 167–174.
28. Isola G, Matarese G, Alibrandi A, Dalessandri D, Migliorati M, Pedullà E, Rapisarda E. Comparison of Effectiveness of Etoricoxib and Diclofenac on Pain and Perioperative Sequelae After Surgical Avulsion of Mandibular Third Molars: A Randomized, Controlled, Clinical Trial. Clin J Pain. 2019;35(11):908-915. doi: 10.1097/AJP.0000000000000748. PMID: 31368908.
29. Caporossi LS, Dos Santos CS, Calcia TBB, Cenci MS, Muniz FWMG, da Silveira Lima G. Pharmacological management of pain after periodontal surgery: a systematic review with meta-analysis. Clin Oral Investig. 2020 ;24(8):2559-2578. doi: 10.1007/s00784-020-03401-6. Epub 2020 Jun 22. PMID: 32572640.
30. Presser Lima PV, Fontanella V. Analgesic efficacy of aceclofenac after surgical extraction of impacted lower third molars. Int J Oral Maxillofac Surg. 2006;35(6):518-21. doi: 10.1016/j.ijom.2005.09.001. Epub 2005; 8. PMID: 16278069.
31. Costa FW, Soares EC, Esses DF, Silva PG, Bezerra TP, Scarparo HC, Ribeiro TR, Fonteles CS. A split-mouth, randomized, triple-blind, placebo-controlled study to analyze the pre-emptive effect of etoricoxib 120 mg on inflammatory events following removal of unerupted mandibular third molars. Int J Oral Maxillofac Surg. 2015;44(9):1166-74. doi: 10.1016/j.ijom.2015.06.012. Epub 2015 Jul 3. PMID: 26144571.
32. Clarke R, Derry S, Moore RA. Single dose oral etoricoxib for acute postoperative pain in adults. Cochrane Database Syst Rev. 2014 8;2014(5):CD004309. doi: 10.1002/14651858.CD004309.