

EFFICACY OF CELECOXIB AND ACECLOFENAC ON POSTOPERATIVE PAIN, SWELLING, MOUTH OPENING AND INFECTION AFTER SURGICAL REMOVAL OF IMPACTED THIRD MOLAR

Dentistry

Reshu Rastogi	Post graduate trainee III Year, Department of Oral and maxillofacial surgery, Kothiwal dental college, Moradabad.
Pratik	Tutor, Department of orthodontics & Dentofacial orthopaedics, RIMS, Ranchi.
Sourav Kumar	Private Practitioner, Rosera, Samastipur, Bihar, India.
Abhijeet Singh	Post graduate trainee III Year, Department of Oral and maxillofacial surgery, Kothiwal dental college, Moradabad.
Nagesh Upreti	Post graduate trainee II Year, Department of Oral and maxillofacial surgery, Kothiwal dental college, Moradabad.
Shailesh V Swami	Post graduate trainee I Year, Department of Oral and maxillofacial surgery, Kothiwal dental college, Moradabad.

ABSTRACT

The use of NSAIDs is widespread, but due to their mechanism of action they could affect the mucosa of the upper gastrointestinal tract. It is well recognised that using selective cyclooxygenase 2 (COX-2) inhibitors reduces the risk for such harm. NSAIDs or other types of medication were typically used to compare the effectiveness of selective COX-2 inhibitors in the treatment of postoperative pain. Studies from the past also utilised COX-2 inhibitors given postoperatively as a single dose, or in conjunction with other treatments. In this comparative study, the efficacy and safety of the selective COX-2 inhibitor celecoxib and Aceclofenac on postoperative pain, swelling and mouth opening after surgical removal of impacted third molar. This was a parallel-group comparison study 12 third mandibular molar extraction patients received celecoxib and 12 received aceclofenac. There was no significant difference in the patients' perception of effectiveness in relation to the two groups, with scores of for 74.5% in the celecoxib group and 77.4% in the Aceclofenac group, respectively. These findings show that celecoxib has comparable clinical benefits to Aceclofenac for severe pain following extraction of the third mandibular molar.

KEYWORDS

Celecoxib, Aceclofenac, pain, NSAIDS

INTRODUCTION:

Surgical extraction of the Impacted third molar, is one of the most commonly performed oral and maxillofacial surgery procedures and is associated with a range of symptoms such as pain, swelling and transient loss of normal jaw function are usually associated with it¹. Various inflammatory mediators produced in response to it are leukotrienes, prostaglandins (PGs), and platelet activating factors resulting in increase in vasodilatation and vascular permeability of the surgical site, leading to peripheral oedema and local tissue alterations. NSAIDs mainly exert their anti-inflammatory action by inhibiting COX-1 and COX-2. However, as the inhibition of COX-1 is associated with a lack of gastric protection. A new class of NSAIDs, selectively inhibiting the COX-2 enzyme provides excellent anti-inflammatory efficacy with almost no influence on the gastrointestinal tract in recent decades².

There is currently no robust evidence indicating the same efficacy of COX-2 inhibitors for the treatment of the acute phase postoperative discomfort after surgical extraction of impacted third molars. PGE2 is a measurable marker of post-traumatic pain, fever, and inflammation, and has been isolated in many body systems, including saliva in the oral cavity⁴. Decreasing local and systemic PGs levels with the use of drugs is a well-known method for reducing clinical inflammation.

Some previous studies have evaluated the effects of a non-steroidal anti-inflammatory drug (NSAID) on tissue prostaglandin levels in gingival crevicular fluid. A comparative difference in preoperative and postoperative PGE2 levels serves as a useful tool in gauging quantitatively the efficacy of the administration of pharmacological agents, and a corresponding reduction of pain and inflammation.

MATERIALS AND METHODS:

Current Research was conducted in the department of Oral and Maxillofacial Surgery, Kothiwal Dental College and Research Centre, Moradabad. The participants were patients having their third mandibular molars extracted during September 2020 to march 2021. Patients between the ages of 18 and 32 who needed extraction of their third mandibular molar for the first time were chosen as patients. The institutional review board gave their approval to the study's informed consent form and patient recruitment documentation. Prior to taking part in this trial, every patient gave written informed consent.

The following was the eligibility criteria:

Inclusion criteria:

- a.) Age between 18 and 32 years;
- b.) good general health;
- c.) The presence of one impacted third molar in the mandible with a class II position, type B impaction;
- d.) absence of pericoronitis or signs of inflammation during the last 30 days.

Exclusion criteria:

- a.) The presence of any systemic disease;
- b.) consumption of oral contraceptives or 2 other medications;
- c.) consumption of any immunosuppressive or anti-inflammatory drugs during the 3 months prior to the study;
- d.) status of pregnancy or lactation; previous history of excessive drinking;
- e.) allergy to local anaesthetic;
- f.) smoking habit.

The aim of our study was to assess the efficacy of celecoxib and Aceclofenac on postoperative pain, swelling and mouth opening after surgical removal of impacted third molar. The objectives of our study was to compare the two NSAIDS of different groups using various clinical parameters:

- 1.pain (VAS Score)
- 2.swelling
- 3.interincisal distance
- 4.infection

STUDY DESIGN:

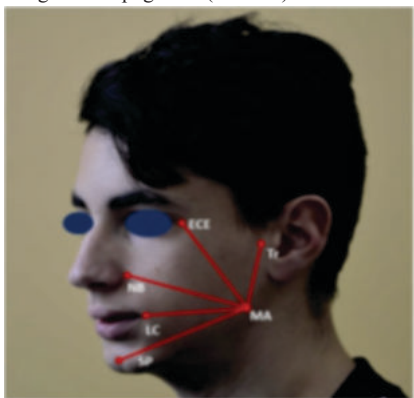
This is a comparative study of parallel groups. Celecoxib 200 mg was the study medication, while subjects were randomly assigned to receive either Aceclofenac 100 mg or celecoxib 200 mg. The present study was conducted in department of Oral and Maxillofacial Surgery, Kothiwal Dental College and Research centre, Moradabad, Uttar Pradesh. This in-vivo prospective study includes 24 subjects, 12 in each group i.e. group 1 (celecoxib- 200mg) and group 2 (Aceclofenac 100 mg). Relevant information was recorded, including sex, age, weight, outpatient/inpatient, medical history, and systemic illnesses. In all the cases medical history is to be recorded to rule out any

significant systemic condition. Written informed consent was taken from each patient of both the groups. Routine investigations were done prior to the procedure. OPG of the patient was done to assess the position of the tooth, the degree of tooth impaction, and the degree of tooth/root formation of each third molar. Each enrolled candidate was randomly allocated to any group. All surgeries were performed by the same clinician in order to avoid any possible bias with regard to surgeon variability. The same mucoperiosteal flap with subsequent osteotomy had been performed in all patients. The bone had to be removed with a round bur in a straight hand-piece under continuous saline solution irrigation. In all the subjects removal of the third molar was done by sectioning the tooth followed by suturing.

Immediately after surgery, postoperative therapy was carefully explained to each patient. They must be instructed to follow a liquid and cold diet for the first 24 hours. Patients were also encouraged to maintain good oral hygiene and informed of the possible symptoms resulting from the surgical intervention. Possible surgical complications such as pain, swelling, drug intolerance, was explained to all patients. The patients received 2% lidocaine and 1:100,000 epinephrine and underwent third mandibular molar extraction because of impaction or pain. Patients were prescribed analgesic (celecoxib 200mg BD for 3 days) and antibiotics to prevent infection.

OUTCOMES:

The parameters of each procedure were recorded immediately post surgery, along with the overall surgery time. The primary outcome variable assessed was the degree of postoperative pain. The patient was able to express their distress in a more unbiased manner as a result. The intensity of the pain was recorded using a 10-cm VAS, ranging from 0 (no pain) to 10 (maximum pain). Following surgery, each patient was asked to rate how much pain they felt at 1st post op day, 15th post op day and 1st month post operatively. The appearance of postoperative swelling was examined as the secondary outcome. Pre- and postoperative values of the following facial measurements, were obtained at each follow up sessions as described in below picture: mandibular angle to tragus (MA-Tr), mandibular angle to external corner of the eye (MA-ECE), mandibular angle to nasal border (MA-NB), mandibular angle to labial commissure (MA-LC), and mandibular angle to soft pogonion (MA-SP).



The maximum mouth opening was measured in order to do a clinical investigation of potential trismus. Using a calibrated sliding calliper (Thera Bite range of motion scales), this was done at baseline, at 1st post op day, 15th post op day & 1st month after surgery. Each follow-up session included an evaluation of the variations in the metrics from baseline. Last secondary outcome i.e infection was assessed by presence of foul smell and pus discharge at all follow up sessions.

STATISTICAL ANALYSIS:

Data was analysed using Statistical Package for Social Sciences (SPSS) version 21, IBM Inc. Descriptive data was reported for each variable. Summarized data was presented using Tables and Graphs. Data was not normally distributed as tested using the Shapiro-Wilk W test (p-value was less than 0.05). Chi square was used for categorical variables. For Mouth opening using Mann whitney U test. A level of $p < 0.05$ was considered statistically significant.

RESULTS:

Of the total 24 patients enrolled, 12 were randomly allocated to receive Aceclofenac 100 mg and 12 to receive celecoxib 200mg. The mean age of the 24 patients (10 male, 14 female) found to be eligible for the study

was 25.9+3.9 years. Twelve patients (7 male, 5 female) were randomly allocated to the Aceclofenac group, and 12 patients (4 male, 8 female) to the celecoxib group.

The peak postoperative pain score was seen in 9 patients on 1st post op day in celecoxib group and in 6 patients in the Aceclofenac group. Further comparison between the groups showed that the mean VAS score was significantly lower in the Aceclofenac group at 1st post op day following surgery compared to the other group, while it did not differ significantly at the other time point (graph 1). At the last follow up, measurements of the facial distances taken pre- and postoperatively to gauge the degree of swelling in the study groups did not differ between the two groups ($P > 0.05$), while at 1st post op day it was present in all patients in celecoxib group and in 6 patients in Aceclofenac group at 1st post op day. Chi square test was used and level of significance set at $p < 0.05$ on 1st post operative day (graph 2). However, the comparison of maximum mouth opening between time points in each of the study groups highlighted statistically significant differences when the baseline values were compared to postoperatively. Moreover, in the celecoxib group, a significant difference in mean maximum mouth opening was demonstrated postoperatively when the value at 1st post operative day was compared to the value at 1st month postoperatively (graph 4). Infection was found to be absent at all time periods among all the 12 patients in both the groups. The Chi Square test was used to compare for infection among two groups. The Difference failed to reach the level of significance at all intervals of time.

DISCUSSION:

This study's objective was to assess the efficiency of Aceclofenac and celecoxib in reducing perioperative discomfort following procedures for third molar surgery. An effective COX-2 inhibitor with anti-inflammatory and analgesic effects is aceclofenac. Additionally, aceclofenac targets glycosaminoglycan production and mediates chondroprotective actions. It manifests with additional gastrointestinal (GI) side symptoms include dyspepsia, nausea, and abdominal pain¹. Celecoxib is a COX-2 selective inhibitor with potential anti-neoplastic effects as well as anti-inflammatory and analgesic qualities¹³. It has a lower frequency of GI side effects but more cardiovascular adverse events. Aceclofenac is linked to more GI harm, whereas celecoxib is linked to more cardiovascular harm and less GI harm⁵.

For the postoperative management of pain following the extraction of impacted third molars, NSAIDs have recently been shown to be an effective anti-inflammatory drug⁶. However, a number of studies have shown that NSAID-using people experience negative pharmacological effects after using the medication. According to Olmedo et al.²¹, 37.3% of patients who needed supplementary therapy with ketorolac or ketoprofen after having their third molars extracted experienced negative side effects such as drowsiness (10.7%), pyrosis (10.3%), and stomach lesions (8%)⁹. When used as a preventive anti-inflammatory medication in third molar surgery, 120 mg of etoricoxib showed promising results, according to Costa et al. Based on these preliminary findings, the current study was conducted to examine the effects of celecoxib and aceclofenac as postsurgical treatments following extraction of impacted third molars¹². According to the present study's findings, Aceclofenac had a much greater pain-reduction effect following surgery than celecoxib on 1st post operative day and it was further managed by ketorolac or ketoprofen after third molar surgery. Nonetheless, celecoxib significantly reduced pain on the 2nd post-operative day compared to aceclofenac, and by day 15th there was no pain in both the groups. This conjecture is supported by a study done by Morse et al. evaluated the preventive analgesic effectiveness of ibuprofen compared to rofecoxib and a placebo. Ibuprofen and rofecoxib produced similar outcomes at 1, 3, and 4 hours following third molar surgery, the authors of that study found¹¹. Furthermore, Yamashita et al.¹³ reported that loxoprofen and celecoxib were equally effective at treating early-stage acute pain when used to treat postoperative discomfort following third molar surgery³. Following the intervention, postoperative pain in the group of patients receiving celecoxib medication exhibited a peak at 1st post op day; pain levels then steadily dropped over the course of the subsequent follow-up sessions. In contrast, the peak pain level in group came at 2nd post operative day respectively, after surgery.

The results for swelling values were similar across all groups. The inflammatory and oedema reactions that happen as a result of surgical

trauma can be used to explain the swelling. Prostaglandins and cyclooxygenases, which are produced after arachidonic acid is released from the cell membrane of cells at the surgical site, are the major products of this mechanism⁷. Contrary to the findings of the current study, recent research has demonstrated that the COX-2 inhibitor celecoxib is one of the most effective mediators, comparable to other NSAIDs, for reducing the production of arachidonic acid, which results in a clinical reduction in edema.

The assessment of trismus revealed a substantial increase in maximal mouth opening in the celecoxib group at the 15th post-operative day and the 1st month postop day values obtained at baseline to those obtained at each follow-up session after surgery¹⁰. These findings are in line with those of De Menezes and Cury, who conducted a study using nimesulide, and Björnsson et al. who conducted a study using ketoprofen, both of which showed that the use of NSAIDs led to a significant improvement in swelling and a decrease in trismus following third molar surgery. When compared to other NSAIDs like diclofenac, celecoxib has the advantage of being associated with fewer occurrences of pyrosis and upper and lower gastrointestinal lesions⁸. All 12 patients in both groups were determined to be free of infection at all times. Two groups were compared for infection using the CHI Square test. At all points in time, The Difference was unable to achieve the threshold of significance.

CONCLUSION:

The current investigation demonstrated that the selective COX-2 inhibitor celecoxib had an analgesic effect comparable to that of currently available NSAIDs like aceclofenac. The selective COX-2 inhibitor celecoxib may be helpful for the management of acute pain given that even short-term usage of traditional NSAIDs results in subclinical gastrointestinal abnormalities. Persons who have a history of gastrointestinal problems and elderly patients may find its use to be particularly advantageous. Celecoxib has no impact on platelet function. Platelet aggregation inhibition is one of the negative effects of COX-1 inhibitors. In addition to patients with chronic pain, the use of selective COX-2 inhibitors, such as celecoxib, may be preferable in conditions requiring the long-term use of anti-inflammatory analgesics, such as temporomandibular joint problems and cancer pain. The short comings of the study are more sample size and longer follow up is required. Compared to , aceclofenac, celecoxib has a longer half-life, making it more persistent and lasting for over 24 hours. But because it takes 28 min longer than aceclofenac for its effects to take action, this drawback must be made up for by increasing the first dose. It should be encouraged to search for pain relief alternatives to NSAIDs and corticosteroids by finding even more efficient medications or pharmacological combinations after third molar surgery.

REFERENCES:

1. G. Isola1, M. Matarese, L. Ramaglia, M. Cicciu', G. Matarese.2019.Evaluation of the efficacy of celecoxib and ibuprofen on postoperative pain, swelling, and mouth opening after surgical removal of impacted third molars: a randomized, controlled clinical trial. *Int. J. Oral Maxillofac.Surg.* February 2019.
2. Francis K L Chan et al.2011 Celecoxib versus omeprazole and diclofenac in patients with osteoarthritis and rheumatoid arthritis (CONDOR): a randomised trial. *thelancet.com* on July 15, 2011.
3. Y. Yamashita, N. Sano, D. Shimohira, A. Danjo, M. Goto.2014.A parallel-group comparison study of celecoxib with loxoprofen sodium in third mandibular molar extraction patients. *Int. J. Oral Maxillofac. Surg.* 2014; 43: 1509–1513.
4. P. Mehra, U. Reebye, M. Nadershah, D. Cottrell.2013. Efficacy of anti-inflammatory drugs in third molar surgery: a randomized clinical trial. *Int. J. Oral Maxillofac. Surg.* 2013; 42: 835–84.
5. Jehad Al-Sukhun, Sana Al-Sukhun ,b Heikki Penttilä ,b Nureddin Ashammakhi, and Raja Al-Sukhun.2012. *J Craniofac Surg* 2012;23: 526Y529.
6. Tanarat Boonriong, Boonsin Tangtrakulwanich, Prapakorn Glabglay, Sasikaan Nimmaanrat.2010. *BMC Musculoskeletal Disorders* 2010, 11:246.
7. Cheung R, Krishnaswami S, Kowalski K.2007.Analgesic efficacy of celecoxib in postoperative oral surgery pain: a single-dose, twocenter, randomized, double-blind, active-and placebo-controlled study. *Clin Ther* 2007;29:2498–510.
8. Leese PT, Hubbard RC, Karim A, Isakson PC, Yu SS, Geis S.2004.Effects of celecoxib, a novel cyclooxygenase-2 inhibitor, on platelet function in healthy adults: a randomized, controlled trial. *J Clin Pharmacol* 2000;40:124–32.
9. Olmedo MV, Galvez R, Vallecillo M. Double-blind parallel comparison of multiple doses of ketorolac, ketoprofen and placebo administered orally to patients with postoperative dental pain. *Pain* 2001;90:135–41.
10. Shi S, Klotz U.2008. Clinical use and pharmacological properties of selective COX-2 inhibitors. *Eur J Clin Pharmacol* 2008;64:233–52.
11. Morse Z, Tump A, Kevelham E.2006. Ibuprofen as a pre-emptive analgesic is as effective as rofecoxib for mandibular third molar surgery. *Odontology* 2006;94:59–63.
12. Costa FW, Soares EC, Esses DF, Silva PG,Bezerra TP, Scarparo HC et al.2015. 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;44:1166–74.
13. Shiota T, Ohno KS, Michi KI, Kamijo R,Nagumo N et al.2001.A study of the dose-response of YM177 for treatment of postsurgical dental pain. *Oral Ther Pharmacol* 2001;20:154–72.

