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Original Article

Dentistry Section

Efficacy of Celecoxib and Diclofenac Sodium in the Management of Postoperative Pain, Swelling and Mouth Opening after Surgical Removal of Impacted Third Molars: A Split-mouth Randomised Clinical Study

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ABSTRACT

Introduction: The surgical removal of mandibular third molars is generally followed by complaints of pain, trismus, and swelling. The duration of surgery and the reflection of a mucoperiosteal flap have been shown to affect the intensity and frequency of postoperative complaints. Pain from third molar surgery typically begins within one to three hours after surgery and ranges in intensity from moderate to severe. Numerous analgesics have been used to minimise pain and discomfort following the surgical removal of impacted third molars. Commonly used agents include ibuprofen, diclofenac sodium, paracetamol, or their combinations. Newer drugs, such as selective COX inhibitors, have not been extensively used for minor oral surgical procedures.

Aim: To compare the clinical efficacy of celecoxib and diclofenac sodium on pain, swelling, and mouth opening after the surgical removal of impacted mandibular third molars.

Materials and Methods: A split-mouth randomised controlled clinical trial was conducted in the Department of Oral and Maxillofacial Surgery at BharatiVidyapeeth DU Dental College and Hospital, Pune, Maharashtra, India. The study duration was six months, from August 2022 to January 2023. A total of 21 subjects (11 males and 10 females) who required surgical extraction of an impacted mandibular third molar were selected. All subjects were randomly allocated to receive one of the following treatments twice a day for five days after surgery: celecoxib 200 mg (n=11) or diclofenac sodium 75 mg (n=10). Pain scores were evaluated using the Visual Analogue Scale (VAS) on postoperative day one, two, and three. Swelling and mouth opening were evaluated on Postoperative Day (POD) two and seven. Intergroup comparison was done using Student's t-test.

Results: The mean age of the study participants was 28±1.5 years, and the mean VAS score for pain evaluation with celecoxib was 6.61, 5.38, and 5.00 on day 1 (p=0.027), 2 (p=0.972), and 3 (p=0.809), respectively. The difference in swelling values for the celecoxib group was significant, while there were no significant differences in the values of mouth opening.

Conclusion: It was concluded that celecoxib 200 mg is a better analgesic and anti-inflammatory compared to diclofenac sodium 75 mg. Celecoxib was easily tolerable and comfortable for the patients. There was no significant difference in the values of mouth opening.

Keywords: Non-steroidal anti-inflammatory drugs, Postoperative sequalae, Wisdom tooth surgery

INTRODUCTION

A significant portion of cases in modern oral surgery involves the surgical removal of third molars, which requires surgical competence and planning during preoperative diagnosis, as well as aftercare [1]. Few attempts have been made to examine patients' expectations regarding the surgical intervention's results. Following third molar surgery, patients' perceptions of their recovery have been documented [2]. Third molar surgical extractions are frequently followed by complaints of discomfort, trismus, and edema. It has been demonstrated that the length of surgery and the reflection of a mucoperiosteal flap influence the severity and frequency of postoperative symptoms [3].

After third molar surgery, patients often experience moderate to severe pain that starts between one and three hours following the procedure [4]. Treating a patient before they experience severe pain is more humane and aligns with current tendencies towards more aggressive, preventive, and systematic methods of pain management. Furthermore, it is now understood that the longer pain is left untreated, the more susceptible the patient may become to painful stimuli. Hyperalgesia can develop after nociception is increased through both central and peripheral processes. Prompt analgesic intervention can help avoid this upregulation of the nociceptive system within the central nervous system [5].

Third molar surgical experiences are desirable pain models to evaluate the efficacy of oral analgesics due to the following characteristics: the surgeries are elective, patients are healthy with few confounding disease states, the procedures are consistent and generally completed within the one-hour timeframe, and the procedure is associated with intense pain and inflammation. Third molar extraction patients are standardised models for the assessment of acute surgical pain, particularly those who present with bilaterally impacted mandibular third molars, as they offer the opportunity to perform two identical surgical procedures at different times. In crossover experiments, these patients serve as their own controls. An estimated 63.5% of patients report significant pain at least once on day one. Consequently, oral analgesics are offered as standard medical treatment for five days following surgery. Non-Steroidal Anti-inflammatory Drugs (NSAIDs) are effective at reducing mild to moderately acute pain that develops after third molar surgery [6].

Numerous analgesics have been used to minimise pain and discomfort following the surgical removal of impacted third molars. Commonly used agents include ibuprofen, diclofenac sodium, paracetamol, or their combinations. Newer drugs, such as selective COX inhibitors, have not been extensively used for minor oral surgical procedures. The authors proposed to investigate celecoxib, a selective Cyclooxygenase-2 (COX-2) inhibitor.

Diclofenac sodium is a popular non-selective NSAID that is commonly used by the majority of doctors after third molar removal. However, despite its effectiveness, it is associated with several Gastrointestinal (GI) side effects, which can be unpleasant for patients recovering from wisdom tooth removal surgery [7]. In the present study, celecoxib, a selective COX-2 inhibitor, was investigated as it has been shown to minimise the side effects that are more common with popular non-selective NSAIDs. Historically, medications with proprietary names ending in "coxib," such as celecoxib or etoricoxib, have been considered to have the most selective effects on COX-2 enzymes and were created to reduce the GI toxicity associated with the use of conventional NSAIDs. However, some have claimed that they have less favorable Cardiovascular (CV) profiles than non-selective drugs [8].

Celecoxib, a COX-2 inhibitor with dosages ranging from 25 mg to 400 mg, was recently the subject of a randomised controlled trial that examined its effectiveness in treating postoperative pain in individuals undergoing third molar surgery [9]. According to the findings of that pilot trial, celecoxib doses of 200 mg and 400 mg were more effective than a placebo for treating immediate postoperative pain [9]. Additionally, a similar clinical trial that examined the efficacy of celecoxib and loxoprofen in treating postoperative pain discomfort following the surgical extraction of impacted mandibular third molars revealed that celecoxib and loxoprofen were similarly beneficial [10]. These preliminary results were validated by a Cochrane review that assessed the pain-relieving activity of another COX-2 inhibitor, etoricoxib [11].

Despite being on the market for a long time, the use of celecoxib among dental practitioners is very limited after minor oral surgical procedures. The present study aimed to compare the clinical efficacy of celecoxib and diclofenac sodium on pain, swelling, and mouth opening after surgical removal of impacted mandibular third molars and shed some light on the advantages of celecoxib over other NSAIDs.

MATERIALS AND METHODS

A randomised controlled clinical trial was conducted in the Department of Oral and Maxillofacial Surgery, BharatiVidyapeeth DU Dental College and Hospital, Maharashtra, India. The study duration was six months, from August 2022 to January 2023. The study received approval from the Institutional Ethics Committee (Registration number-EC/NEW/INST/2019/329). Informed consent was obtained from all patients before the procedure commenced.

Inclusion criteria: The study included patients aged between 18-45 years, with a weight within 50-80 kg, who were willing to participate. Patients with a surgical site free of active infection and any significant systemic diseases were included. Patients free of drug reactions (allergies) and those with a clinical and radiographic diagnosis of impacted 3rd molars with bilateral similar angulation and the same difficulty index were included in the study.

Exclusion criteria: The study excluded medically compromised patients, known mentally challenged patients, and those who were unable to communicate. Pregnant and lactating women, as well as patients unwilling to be part of the study or unable to come for follow-up, were also excluded.

Sample size calculation: The sample size was determined to be 21 patients. The calculation considered two groups, with an effect size of 0.40, alpha=0.050, and a power level of 0.80 for pain, which was the selected primary variable for analysis [12].

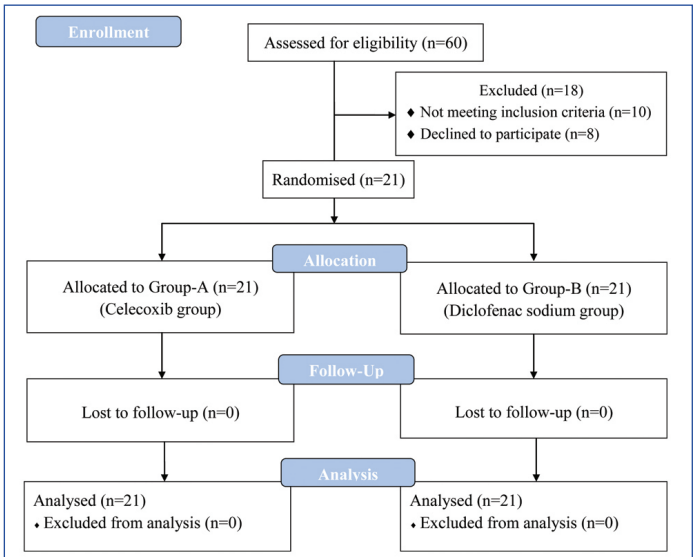
The primary variable, "pain," showed a difference of 0.60 (mean) between the groups and a Standard Deviation (SD) of 0.75. After evaluating these values, it was determined that a minimum of 21 patients in each group was necessary.

Study Procedure

Patients with bilaterally symmetrical impacted mandibular third molars were included in the study. The study employed a split-mouth technique, wherein the removal of impacted mandibular third molars was performed with a time interval of at least 21 days. The researcher (operating surgeon) was blinded to the choice of drugs given to the patients in both groups. Another person was instructed to prescribe the medications in a random sequence for all patients without the operating surgeon's knowledge. Prior to the procedure, a detailed medical and dental history was obtained.

Group A received cap celecoxib (200 mg) and tab augmentin 625 mg (amoxicillin 500 mg+potassium clavulanate 125 mg) two hours before the surgery as preoperative medication. Following the surgical removal of the third molar, tab augmentin 625 mg, cap celecoxib (200 mg), and Pan 40 (pantoprazole 40 mg) were prescribed. All medications were prescribed for five days.

Group B received tab diclofenac sodium (75 mg) and tab augmentin 625 mg (amoxicillin 500 mg+potassium clavulanate 125 mg) two hours before the surgery as preoperative medication. Following the surgical removal of the third molar, tab augmentin 625 mg, tab diclofenac sodium (75 mg), and Pan 40 (pantoprazole 40 mg) were prescribed. All medications were prescribed for five days [Table/Fig-1].



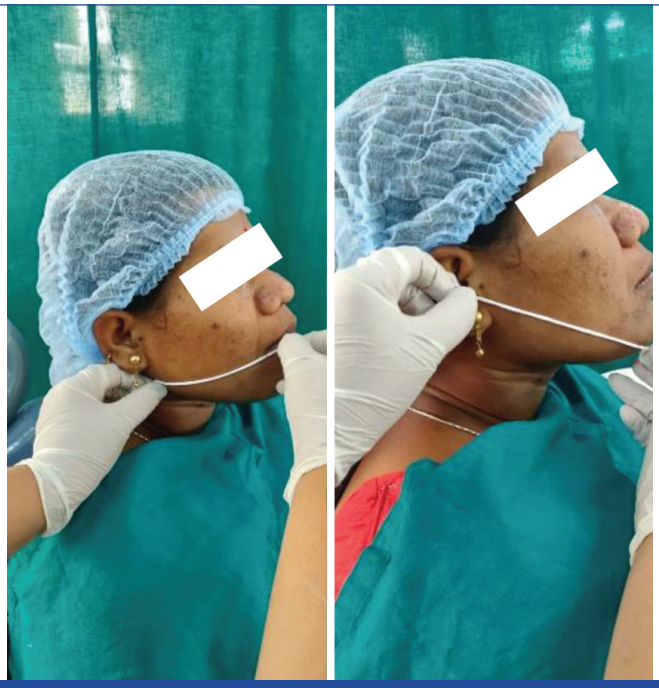
[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) 2010 flowchart.

Local anesthesia with adrenaline in a 1:200,000 ratio was administered, and inferior alveolar, lingual, and long buccal nerve blocks were given. An appropriate incision was made, and the flap was reflected. The impacted tooth was surgically removed, and the flap was sutured with non-resorbable (3-0) silk sutures. Each patient underwent two surgical extractions separated by at least 21 days. During the first surgical removal of the impacted lower third molar, the patient received the appropriate dosage of oral celecoxib. During the contralateral surgical removal of the impacted lower third molar after 21 days, the patient received the appropriate dosage of oral diclofenac sodium, following the same protocol as the previous surgery.

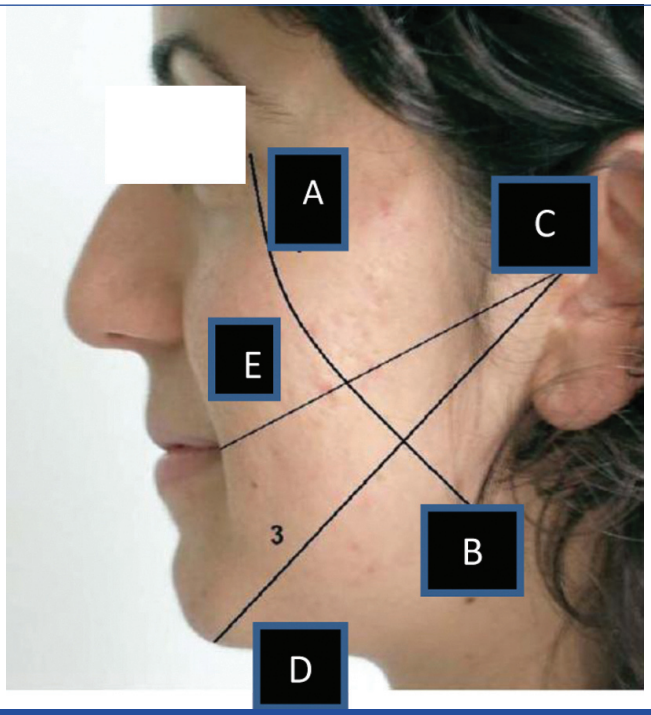
The parameters studied in the present study were as follows:

- **Pain:** Postoperative pain was evaluated using a 10-point VAS, with a score of "0" indicating "no pain" and "10" indicating "very severe pain." Pain was evaluated on the 1st, 2nd, and 3rd postoperative days.

- **Swelling:** Measured using the Gabka J and Matsumura T technique on the 2nd and 7th postoperative days [Table/Fig-2a,b,3] [13]:
  - This required measuring the distances from the tragus to the soft tissue pogonion on the operated side (line CD).
  - Measuring the distance from the tragus to the corner of the mouth on the operated side (line CE).
  - Measuring the distance from the lateral canthus of the eye to the angle of the mandible on the operated side (line AB).
  - The measurements were done using a flexible rubber scale. To eliminate observer bias, only one observer measured the swelling in all patients.
- **Trismus:** It was evaluated by measuring the interincisal distance at Maximum Mouth Opening (MMO) (cm) with a ruler between the maxillary and mandibular incisal edges. It was measured on the 2nd and 7th postoperative days [Table/Fig-4].



[Table/Fig-2a,b]: Measurement of swelling values at Postoperative Day (POD) 2 for a patient (celecoxib group).



[Table/Fig-3]: Lines depicting the measurement of swelling.

[Table/Fig-4]: Measurement of mouth opening at Postoperative Day (POD) 2 (celecoxib group).

STATISTICAL ANALYSIS

The software used was the Statistical Package for Social Sciences (SPSS), version 21.0 (IBM Corp., Released 2012, IBM SPSS Statistics for Windows, version 21.0, Armonk, NY, USA: IBM Corp.). The comparison of facial swelling, mouth opening, and mean VAS score between diclofenac and celecoxib at different time points was conducted using an independent t-test. The comparison of the pain score between different time points for diclofenac and celecoxib individually was done using a repeated measures Analysis of Variance (ANOVA) test.

RESULTS

All enrolled patients completed the study without any postoperative complications. The mean age of the 21 patients (11 males and 10 females) who were found eligible for the study was 28±1.5 years. Postoperative healing was good in all patients, and no adverse events such as infections or abscesses were observed during the follow-up period. The mean duration of surgery was similar in the two groups: 22.43 minutes for the celecoxib group and 24.58 minutes for the diclofenac sodium group.

The mean value of the VAS score for pain evaluation in the celecoxib group was 6.61, 5.38, and 5.00 on day one (p=0.027), day two (p=0.972), and day three (p=0.809), respectively. The difference was statistically significant on day two and three. Post-hoc analysis of the celecoxib group showed that the difference between day one and two, as well as between day one and three, was statistically significant. However, the difference between day two and three was not statistically significant [Table/Fig-5-7].

Postoperative evaluation times (in days)	Diclofenac sodium 75 mg	Celecoxib 200 mg	p-value
	Mean±Std. Deviation	Mean±Std. Deviation	
1st	7.23±0.54	6.61±0.80	0.027*
2nd	6.14±0.73	5.38±0.59	0.972
3rd	5.86±0.65	5.00±0.71	0.809

[Table/Fig-5]: Comparison of pain using mean VAS score between diclofenac and celecoxib on day one, two and three, postoperatively using Student's t-test.
*p<0.05=statistically significant

Comparison of pain (in days)	Wilk's lambda value		p-value
One vs two vs three	47.481		0.001*
	Mean difference	Standard error	p-value
One vs two	1.095	0.153	0.001*
One vs two	0.286	0.156	0.249
One vs three	1.381	0.146	0.001*

[Table/Fig-6]: Comparison of pain using mean VAS scores at three different time points (day one, two and three) for diclofenac sodium using repeated measures ANOVA test.
*p<0.05=statistically significant

Comparison of pain (in days)	Wilk's lambda value		p-value
One vs two vs three	40.845		0.001*
	Mean difference	Standard error	p-value
One vs two	1.238	0.194	0.001*
Two vs three	0.381	0.129	0.023*
One vs three	1.619	0.176	0.001*

[Table/Fig-7]: Comparison of pain using mean VAS scores at three different time points (day one, two and three) for celecoxib using repeated measures ANOVA test.
*p<0.05=statistically significant

For the celecoxib group, the mean values of facial swelling for lines AB, CD, and CE on day two were 9.65 mm, 11.83 mm, and 11.51 mm, respectively. Similarly, on day seven, the values were 9.20 mm, 11.23 mm, and 11.13 mm, respectively. The difference, as determined by Student's t-test, was found to be statistically significant [Table/Fig-8-10].

Postoperative evaluation times (in days)	Diclofenac sodium 75 mg	Celecoxib 200 mg	p-value
	Mean±SD	Mean±SD	
2nd	11.88±1.65	9.65±0.95	0.004*
7th	11.46±1.63	9.20±0.96	0.005*

[Table/Fig-8]: Comparison of facial swelling (in mm) for AB between diclofenac and celecoxib on 2nd and 7th day postoperatively using Student's t-test.
*p<0.05=statistically significant

Postoperative evaluation times (in days)	Diclofenac sodium 75 mg	Celecoxib 200 mg	p-value
	Mean±SD	Mean±SD	
2nd	11.89±1.50	11.83±0.65	0.005*
7th	11.55±1.48	11.23±0.83	0.026*

[Table/Fig-9]: Comparison of facial swelling (in mm) for CD between Diclofenac and Celecoxib on 2nd day and 7th day postoperatively using Student's t-test.
*p<0.05=statistically significant

Postoperative evaluation times (in days)	Diclofenac sodium 75 mg	Celecoxib 200 mg	p-value
	Mean±SD	Mean±SD	
2nd	13.67±2.35	11.51±1.24	0.001*
7th	13.18±2.38	11.13±1.31	0.001*

[Table/Fig-10]: Comparison of facial swelling (in mm) for CE between diclofenac and celecoxib on 2nd day and 7th day postoperatively using Student's t-test.
*p<0.05=statistically significant

The mean value of mouth opening for the celecoxib 200 mg group on day two and day seven was 29.24 mm and 40.71 mm, respectively. However, the difference between them was not found to be statistically significant [Table/Fig-11].

Postoperative evaluation times (in days)	Diclofenac sodium 75 mg	Celecoxib 200 mg	p-value
	Mean±SD	Mean±SD	
2nd	27.33±3.86	29.24±4.49	0.434
7th	37.52±2.40	40.71±2.05	0.130

[Table/Fig-11]: Comparison of mouth opening (in mm) between diclofenac and celecoxib on 2nd day and 7th day postoperatively using Student's t-test.

DISCUSSION

The purpose of the present study was to assess the efficacy of celecoxib and diclofenac sodium in preventing perioperative discomfort following third molar surgery, specifically focusing on the effectiveness of celecoxib in treating postoperative pain, facial edema, and mouth opening. Treatment with celecoxib was found to significantly reduce the onset and persistence of postoperative pain compared to diclofenac sodium.

Observing pain is a highly subjective and varied experience influenced by various physical and emotional factors. Therefore, estimating pain accurately is challenging. In this study, a Visual Analog Scale (VAS) was used as a reliable tool to measure postoperative pain. VAS is easily understood by patients, reproducible, and commonly used in the literature. Recent studies have shown that NSAIDs are effective in relieving pain after surgical removal of impacted third molars [14]. However, there have been reports of adverse effects in patients using NSAIDs postoperatively [14-16]. Olmedo et al., found that 37.3% of patients required additional therapy with ketorolac or ketoprofen after third molar surgery, and these patients experienced adverse events such as lethargy, heartburn, and stomach lesions [17]. Potent and selective COX-2 inhibitors, which are a type of NSAID, have been shown to be effective in treating dental pain [18,19]. Costa et al., reported favorable effects using 120 mg etoricoxib as a preventive anti-inflammatory therapy in third molar surgery [20]. Celecoxib and ibuprofen were evaluated by Isola et al., in 2019 for their ability to reduce postoperative complications following surgical removal of impacted mandibular third molars [12]. Treatment with celecoxib and ibuprofen improved the primary outcome compared to the placebo group. Moreover, participants in the celecoxib group demonstrated a significant decrease in postoperative pain levels at six hours (p=0.001), 12 hours (p=0.011), and 24 hours (p=0.041) after surgery, compared to the other groups.

The present study demonstrated that treatment with celecoxib reduced the incidence and severity of postoperative pain following third molar surgery compared to diclofenac sodium. Morse et al., assessed the effectiveness of ibuprofen as a preventive analgesic and compared it to rofecoxib and a placebo [21]. According to the authors, ibuprofen and rofecoxib showed similar outcomes at one, three, and four hours following third molar surgery. Yamashita et al., found that loxoprofen and celecoxib were equally effective in treating early-stage acute pain when administered for postoperative discomfort after third molar surgery [10].

In the present study, the mean value of the VAS score for pain evaluation on day one was 7.23 for diclofenac sodium 75 mg and 6.61 for celecoxib 200 mg, with a statistically significant difference between them. These pain score data indicated that celecoxib had superior analgesic efficacy in the early stages of recovery compared to diclofenac sodium. These findings are consistent with other studies that have shown the effectiveness of celecoxib, at doses ranging from 120 mg to 200 mg, in reducing postoperative pain in dental procedures or third molar surgery in the short term (at two hours) [9,22].

Swelling is one of the most common sequelae after surgical removal of impacted mandibular third molars. Prostaglandins and cyclooxygenases produced after the release of arachidonic acid from the cell membrane of surgical site cells are primarily responsible for swelling [23]. Celecoxib, a COX-2 inhibitor, has been found to be effective in reducing the release of arachidonic acid, leading to a clinical decrease in edema, similar to other NSAIDs [23,24]. Isola et al., in the same study conducted in 2019, found no significant differences in swelling values between the groups receiving celecoxib and ibuprofen [12]. However, in contrast to their findings, the present study showed significantly lower swelling values in the celecoxib group compared to the diclofenac sodium group.

After third molar extraction, Mubarak and Al-Adily in 2021 examined the anti-inflammatory effects of prednisolone and etoricoxib. Prednisolone 10 mg significantly reduced facial swelling after extraction of an impacted third molar compared to the other two groups, while etoricoxib 120 mg showed no significant change in the results [25]. Trismus, which makes it difficult for patients to eat and speak, negatively affects their quality of life. Therefore, reducing trismus leads to less discomfort and a higher quality of life. Trismus was assessed by comparing the MMO at each follow-up session.

After surgically extracting mandibular third molars from 60 individuals, Moghaddamnia et al., (2012) examined the effects of prednisolone and celecoxib on pain and MMO [26]. Each patient received one tablet of either 100 mg celecoxib or 5 mg prednisolone before surgery, and one tablet was given every eight hours following surgery. Analysing the data revealed no significant difference in MMO between the groups. In the present study, the mean value of mouth opening for celecoxib on day two and day seven was 29.24 and 40.71, respectively, with p-values of 0.434 and 0.130. The data analysis showed that there was no significant difference in MMO.

In the study by Isola et al., (2019), the assessment of trismus, determined by comparing the MMO values obtained at baseline to those obtained at each follow-up session, revealed a substantial reduction in the celecoxib group at 24, 72, and seven days following surgery [12]. Similarly, Sotto-Maior et al., concluded that there was no significant difference between the groups in mouth opening reduction scores at 24 and 48 hours postoperatively [27]. Moore et al., (2005) conducted a preliminary randomised prospective clinical trial comparing the analgesic efficacy and reduction in trismus of preoperative rofecoxib, intraoperative dexamethasone, and combined rofecoxib and dexamethasone following third molar extraction surgery among 35 subjects [28]. The results of this small, randomised controlled clinical trial demonstrated that the most efficient therapeutic approach for reducing trismus after surgical extraction of third molar teeth is intraoperative dexamethasone. The best pain alleviation was experienced during the first several days following surgery when dexamethasone and rofecoxib were combined.

The present study suggests that celecoxib, used as postoperative therapy after surgical removal of third molars, proved to be a better drug in its analgesic effect on the first postoperative day. Celecoxib was found to be both safe and easy to use in the postoperative management of discomfort following third molar surgery. There was a significant reduction in swelling among the groups receiving celecoxib compared to diclofenac sodium. However, neither of the drugs had an effect on mouth opening.

Limitation(s)

The duration of analgesic administration was only five days, which is insufficient to fully understand the side effects associated with the drugs. The broader effects of the drugs can be better analysed in conditions such as osteoarthritis and other chronic conditions, where analgesics are given for a longer period of time.

CONCLUSION(S)

According to the present study, celecoxib, when administered as postoperative therapy following third molar surgery, performs better than diclofenac sodium in managing perioperative and postoperative pain. Celecoxib was found to be safe and easy to use for managing discomfort after third molar surgery. The findings of this pilot study are promising, but further investigation is needed to better understand the potential advantages of celecoxib for postoperative therapy after the removal of an impacted third molar.

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