Efficacy of Celecoxib in reducing the postoperative pain caused by third molar surgery: A systematic review

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Introduction

Third mandibular molar surgery is the most prevalent oral surgical procedure. The removal of impacted third molars has various postoperative complications including pain. Side effects in this procedure have an unfavorable effect on the quality of life of patients and disrupt patients' socioeconomic activities after third molar extraction. Also, studies have shown that age and gender do not affect pain caused by third molar surgery. Inflammatory mediators including prostaglandins, leukotrienes, and platelet-activating factors, are released in response to the surgical extraction of the third molar. The production of these inflammatory mediators leads to a raise in vasodilatation of the surgical area, results in some tissue alternations, pain, and edema. Several strategies including pharmacological methods have been demonstrated to reduce complications following third molar surgery. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for pain relief in third molar surgery. NSAIDs inhibit cyclooxygenase (COX) activity, thus suppressing the production of inflammatory mediators such as prostaglandin E2. COX is divided into Cyclooxygenases COX-1 and COX-2 enzymes. Inhibition of COX-1 causes harms to the gastrointestinal mucosa such as perforation, ulcer, and bleeding. Nowadays, cyclooxygenase-2 inhibitors are gaining popularity due to the lack of damage to the gastrointestinal mucosa. However, they may lead to cardiovascular effects is certain doses.

Celecoxib is an anti inflammatory drug (NSAID) that inhibits cyclooxygenase (COX) selectively and only inhibits COX 2, unlike the ordinary NSAIDs. Celecoxib suppresses the production of prostaglandins responsible for pain and does not lead to the aforementioned adverse effects in the gastrointestinal mucosa. Celecoxib appears hazardous in doses of 400 mg or greater based on randomized results. There is no strong evidence to show an increased risk of cardiovascular events at doses of 200 mg or less.

This selective NSAID is used to relieve pain caused by rheumatoid arthritis and osteoarthritis. This study is aimed to assess the efficacy of Celecoxib in reducing the postoperative pain caused by third molar surgery.

Methods and Materials

Protocol: Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines followed for reporting. Search strategy: Literature search was carried out on the PubMed, Scopus, and Science Direct databases, dated up to April 2020. Searches were limited to published and peer-reviewed articles in the English language. The following keywords: "third molar", "pain", and "celecoxib" were used and checked with the Mesh (Medical Subject Headings) database. The reference lists of all primary studies were searched manually for additional relevant publications. Eligibility criteria: The study question was assessed by the PICOS components: Population (Patients who have had third molar surgery), Intervention (Celecoxib as a pain reliefer), Comparison (Placebo, Ibuprofen, or Tramadol as pain reliefers), Outcome (reducing in terms of postoperative pain), and Study (Randomized Controlled Trials). Studies were included if they (I) had available full-text in the English language (II) measured pain via reliable scales (III) were Randomized Controlled Trials (RCTs). Studies were excluded if they (I) were unpublished articles (II) were non-peer-reviewed articles (III) had other study designs instead of RCTs (IV) had incomplete data.

Quality Assessment

For quality assessment Consolidated Standards of Reporting Trials (CONSORT) checklist was used. The checklist contains 25 primary items and we allocated one score to each item. Finally, the scores of each article were summed, and based on the final score; they were divided into high quality (19–25), average quality (10–18), and low quality (0 9).

Risk of bias:

The risk of bias in this research assessed using the Cochrane Collaboration's assessment tool [26]. Seven domains of bias were evaluated; (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) others [26].

Results

Title, abstract, full-text of Fourteen randomized controlled trials screened and after quality assessment ten studies included based on predetermined inclusion and exclusion criteria. The oldest and the latest included studies were in 2002, 2019, respectively. The studies included in the review all had a follow-up period of over 6 months. The most dominant scale used for measuring the intensity of the postoperative pain was the visual analogue scale (VAS) among the studies. This scale is ranged from 0 (no pain) to 10 (maximum pain). The maximum pain intensity was observed in all the groups (Placebo, Ibuprofen, Tramadol, and Celecoxib) at 4 hours and 8 hours after the extraction. Seven studies (70% of the papers) indicated that Celecoxib (Dose:200 – 400 mg) compared with Placebo, Ibuprofen (Dose: 400-600 mg), or Tramadol has more analgesic effects after third molar surgery ($P<0.001$). Moreover, Tramadol appeared to be less effective in reducing postoperative pain than Ibuprofen. Subjects using Celecoxib showed a significant reduction in post operation pain scores at 6 h ($P < 0.001$), 12 h ($P = 0.011$), and 24 h ($P = 0.041$) after third molar

surgical removal. Therefore, more passed time after surgery leads to less analgesic efficacy of Celecoxib. However, Celecoxib has not shown any effects on facial swelling. On the other hand, three studies showed null results (30% of the papers) and demonstrated that analgesic efficacy of Celecoxib is equal with traditional NSAIDs including Ibuprofen. No gastrointestinal side effects were reported for Celecoxib compared with Ibuprofen, Tramadol, or placebo. The quality of evidence was assessed as high. Low risk of bias was observed among studies.

Conclusion

Based on the available literature and evidence, the analgesic efficacy of selective COX-2 inhibitor Celecoxib is significant and compared with Ibuprofen and Tramadol may lead to more pain relief after third molar surgical extraction. Also, common gastrointestinal side effects that are observed in conventional NSAIDs, are not reported for Celecoxib. Therefore, Celecoxib may be advantageous for old individuals and children with a history of gastrointestinal illnesses. Also, it could be desirable for diseases that require the long-term use of anti-inflammatory analgesics, such as cancer pain and temporomandibular joint disorders. Finally, mentioned cardiovascular side effects of this drug at a dose of 400 mg, physicians should consider doses 200 mg or less for patients.