Research Article

Effectiveness of cyclooxygenase-2 inhibitors in the management of post-extraction pain

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ABSTRACT

Aim: The aim of this study is to evaluate the effectiveness of cyclooxygenase-2 (COX-2) inhibitors in the management of post-extraction pain. **Background:** Dental pain is associated with fear and avoidance of dental treatment by many people. Extractions being one of the most common procedures in dentistry are associated with varying degrees of pre-operative and post-operative pain. Analgesics are medications that are used to alleviate pain. The analgesics are basically nonsteroidal anti-inflammatory drugs (NSAIDs) which have many subclasses such as salicylates, mefenamic acid, COX-1 and 2 inhibitors, preferential COX-2 inhibitors, and selective COX-2 inhibitors. Their mechanism of action varies and also the adverse effects. **Results:** The Mann–Whitney U-test revealed that there existed no significant difference in the effectiveness between non-selective NSAIDs and selective COX-2 inhibitors in the management of post-extraction pain as $P = 0.556$ which is greater than 0.05. **Conclusion:** This study inferred equal effectiveness between COX-2 inhibitors and NSAIDs. However, COX-2 inhibitors induce lesser side effects and hence can be preferred in suitable clinical conditions.

KEY WORDS: Conventional nonsteroidal anti-inflammatory drugs, Extraction, Pain, Selective cyclooxygenase-2 inhibitors

INTRODUCTION

Dental extractions are one of the most commonly performed treatment procedures in oral surgery. Extractions can also be termed as one of the most feared dental procedures. The main reason for people avoiding dental treatment, in particular extractions, is the fear of pain. With the use of local anesthetics, the pain inflicted on the patient during extraction is totally zero. However, the patient experiences pain after the effect of local anesthesia wanes off. The degree of pain may range from mild to severe based on the complexity of extraction performed. The management of post-extraction pain involves primarily the use of analgesics. Analgesics are drugs designed to abolish pain without any loss of consciousness. The drug group of analgesics includes simple analgesics, opioid analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs). Among these NSAIDs are the most commonly used analgesics. These NSAIDs act by inhibiting the enzyme cyclooxygenase (COX) nonselectively, i.e., it inhibits both COX-1 and COX-2 simultaneously. The inhibition of COX-1 is known to cause a range of side effects including damage to gastrointestinal mucosa and platelet aggregation.[1,2] Hence, selective COX-2 inhibitors were introduced which selectively inhibit the enzyme COX-2.

In literature, there are several studies discussing the effectiveness of NSAIDs in controlling post-extraction pain. However, there are very few studies discussing the effects of selective COX-2 inhibitors in specific. Further, there are not much number of studies to compare the effectiveness of COX-2 inhibitors and non-selective NSAIDs in controlling post-operative pain or post-extraction pain.

Hence, this study aims to evaluate the effectiveness of COX-2 inhibitors in the management of post-extraction pain.

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MATERIALS AND METHODS

Nature of the Study

This was an experimental *in vivo* randomized controlled trial involving human subjects.

Study Design

The study design was a randomized controlled trial with the split-mouth design.

Study Setting

This study was conducted at Saveetha Dental College and Hospitals, Chennai, India.

Selection of Subjects

A total of 60 human subjects satisfying the following inclusion and exclusion criteria were selected.

Inclusion Criteria

The following criteria were included in the study:

- Age group between 15 and 25 years
- Both genders
- Patients undergoing bilateral orthodontic extractions in the same arch
- Patients undergoing bilateral impaction surgeries on the same arch.

Exclusion Criteria

The following criteria were excluded from the study:

- Patients allergic to local anesthetics
- Patients allergic to NSAIDs
- Pregnant women
- Teeth with dental caries and periodontitis.

Informed Consent

This study was approved by the Institutional Ethical Committee and informed consent was obtained.

METHODOLOGY

The 60 selected subjects were categorized into two Groups A and B, respectively.

Group A involves extraction in the right side first followed by the left and Group B the vice versa.

Using a coin flip method the patients were allocated into Group A and Group B.

Allocation concealment was done using the sequentially numbered, opaque, sealed envelopes method and post-operative analgesic aceclofenac was denoted as X and COX-2 inhibitor celecoxib was denoted as Y.

Following extractions by different operators, subjects in Group A received the allocated post-operative analgesic and the cumulative analgesic effect after 3 h was evaluated. Aceclofenac is a NSAID. 100 mg tablet of aceclofenac (Zerodol by Ipca Laboratories) was administered through oral route. Group B drug was celecoxib which is a selective COX-2 inhibitor. 200 mg capsule of celecoxib (Zycel by Zydus Synovia) was administered orally.

Blinding

This design constitutes a triple blinded study as the patient, operator, and evaluator were blinded of the therapeutic intervention.

Sample Size Estimation

A pilot study was initiated with 10 subjects first and based on the results sample size was reworked to 60 subjects.

Dropouts

All the patients completed the treatment and there were no dropouts in the study.

Evaluation of Outcome Measure

Pain relief or analgesic effect was the desired outcome measure. This was evaluated using a numerical visual analog scale (VAS) ranging from 0 to 100 with 0 denoting no pain and 100 denoting extreme pain.

- 0–25 Mild pain
- 26–50 Moderate pain
- 51–75 Severe pain
- 76–100 Extreme pain.

No side effects or adverse reactions observed in the patients following administration of post-operative analgesics.

A Mann–Whitney U-test was done for statistical analysis of the observed data.

RESULTS

The statistical analysis revealed the following results:

The Mann–Whitney U-test revealed that there existed no significant difference in the effectiveness between non-selective NSAIDs and selective COX-2 inhibitors in the management of post-extraction pain as $P = 0.556$ which is greater than 0.05.

DISCUSSION

NSAIDs have an intense anti-inflammatory and analgesic action. They are of different subclasses as follows: Salicylates, indoles, oxicams, propionic acid derivatives, pyrazole derivatives, fenamates, and selective COX-2 inhibitors.

The mechanism of action of NSAIDs is the inhibition of the enzyme COX, interfering with the production of prostaglandins, which accounts for their efficacy

Table 1: Pain responses of participants

Group A		Group B		Mann–Whitney U-test *P* value
Aceclofenac	Celecoxib	Celecoxib	Aceclofenac	
7.84±3.41	7.76±3.82	7.81±3.26	7.78±3.61	0.556>0.05

and also their adverse effects.[3] The importance of COX and prostaglandins is that they are associated with many biological activities and body functions. Prostaglandins are potent mediators of inflammation, whose actions result in edema, pain, and vasodilation. Hence, inhibiting these compounds can produce analgesia and anti-inflammatory actions. The spectrum of action of NSAIDs does not only stop with COX and prostaglandins but also extend to include other mediators of inflammation such as thromboxanes and leukotrienes. Thromboxanes are chemical mediators involved primarily in platelet aggregation. Therapeutic doses of nonselective NSAIDs lead to gastrointestinal bleeding and inhibition of mucoprotective prostaglandins. All the NSAIDs except COX-2 inhibitors possess this action.

Elaborating on the enzyme COX, there are two forms namely, COX-1 and COX-2. These enzymes differ in their availability and action. COX-1 is present in all the tissues and is associated with the production of prostanoids. The actions of COX-1 are cytoprotective in nature and deal with the normal cytological functions in cells, platelets, and kidney.[4] On the other hand, COX-2 is not present in all the tissues and is released during tissue injury and inflammation, most importantly without any action on platelets. Hence, there is a delay in their activation and release when compared to COX-1 enzyme. Nonselective group of NSAIDs includes drugs such as aspirin, acetaminophen, naproxen, ibuprofen, and ketoprofen, which have the actions of both COX-1 and COX-2 enzymes. The inhibition of COX-1 leads to inhibition of platelet aggregation which has both useful effects (prevents myocardial infarction and stroke) and adverse effects (increased risk of bleeding). Possibly this also contributes to the adverse effects such as gastric irritation, nausea, and vomiting experienced on prolonged use of nonselective NSAIDs.[4,5]

The drug class of selective COX-2 inhibitors includes celecoxib, rofecoxib, parecoxib, and etoricoxib. These drugs have only the actions of COX-2 enzymes, sparing the COX-1 actions, thus lesser incidence of gastric irritations and erosions, and other actions on platelets and other tissues. However, as they do not inhibit platelet aggregation, they increase the risk of myocardial infarction and stroke in susceptible patients.[6-8]

Pain can be defined as a sensory or subjective symptom due to actual or potential damage or described in such terms. Post-operative pain sets in once the effect of anesthesia wanes off. In dentistry, one of the most common situations encountered is the post-operative dental pain following extractions. This is also one of the common fears in patients visiting the dentist and also a reason for avoidance of dental treatment.

Dental extractions involve the following classes of drugs, namely local anesthetics, analgesics, and antibiotics.

Analgesics are usually given as a course for 3–5 days. According to Ravinthar *et al*., paracetamol (78%), followed by diclofenac (17%) and ibuprofen (5%), is the most commonly prescribed analgesics by the dentists in the region of current study.[9] Further, the use of COX-2 selective inhibitors has been considered to be safer than that of conventional NSAIDs in a perioperative dental setting as they lack the inhibition of platelet aggregation, reducing the risk of operative bleeding.[9-18]

In the current study, the mean VAS score obtained for both drug groups was similar, i.e., Group A aceclofenac and celecoxib have mean VAS scores of 7.84 ± 3.41 and 7.76 ± 3.82, respectively. Group B celecoxib and aceclofenac have mean VAS scores of 7.81 ± 3.26 and 7.78 ± 3.61, respectively, indicating a very minimal difference between the two groups. On Mann–Whitney U-test statistical analysis of the scores, $P = 0.556$ was obtained which is greater than 0.05. This indicates that the difference in the effectiveness of controlling post-operative dental pain between the drug groups of conventional NSAIDs and selective COX-2 inhibitors is insignificant. However, based on the difference in the adverse effects impacted by these two groups, a more targeted drug choice can be made, i.e., in patients with increased risk of gastric irritation and ulcers, selective COX-2 inhibitors can be prescribed, while in those with an increased risk of cardiovascular diseases, conventional NSAIDs can be prescribed.

CONCLUSION

This study inferred equal effectiveness between COX-2 inhibitors and NSAIDs. However, COX-2 inhibitors induce lesser side effects and hence can be preferred in suitable clinical conditions.

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