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Efficacy of Piroxicam and Tramadol as a Pre-Emptive Analgesic Agent for Mandibular Third Molar Surgery

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Objectives: The purpose of this clinical trial is to examine the effectiveness of 20 mg piroxicam with 50 mg tramadol as a pre-emptive analgesic for mandibular third molar surgery.
Methods: In this prospective study, 30 patients were referred to the Department of Oral and Maxillofacial Surgery in Chennai for surgical removal of impacted mandibular third molars with similar difficulty indexes under local anesthetic. Patients were randomly distributed to one of two groups: Group A received 20 mg piroxicam intramuscularly (IM) 50 minutes before surgery, while Group B received 50 mg tramadol IM 50 minutes before surgery. The time to analgesic re-medication, Pain intensity (VAS Scores) at 1st, 2nd, 12th, 24th hour, total analgesic consumption was evaluated.
Results: When compared to the group getting 50 mg of tramadol IM, the group receiving 20 mg of piroxicam IM demonstrated differences in pain intensity as measured by the visual analog scale and total analgesic consumption [lesser values], and the results were statistically significant($p<0.05$). However, there were no statistically significant differences between the two groups in terms of time to first rescue analgesic medication, number of patients requiring the rescue analgesic procedure (10 mg of oral ketorolac), and number of patients without the need for

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analgesic during the evaluation period. (P >0 .05).
Conclusion: Within the limits of the study, patients who received 20 mg of piroxicam before surgery had less pain intensity and total analgesic consumption than those who received 50 mg of tramadol before surgery. In comparison to pre-emptively administered tramadol, piroxicam showed superior analgesic effects for intermediate surgical operations when given preoperatively.

Keywords: Third molar; pre-emptive analgesia; impacted, mandibular molar; postsurgical pain; piroxicam; tramadol.

1. INTRODUCTION

The extraction of impacted third molar teeth is one of the most common oral surgical procedures performed in dentistry, and it inevitably results in a number of postoperative complications, the most common of which is pain [1]. As the effects of the local anaesthetic drug wear off, pain normally sets in. Pre-emptive analgesia refers to the administration of an analgesic before the onset of a painful stimulus. It entails antinociceptive therapy to avoid central neural sensitization, which exacerbates postoperative pain [2]. Analgesics given before to surgical trauma are thought to have a pre-emptive effect, indicating that analgesia will begin prior to the surgical stimulus, lowering CNS input and, thus, pain [2].

Tramadol is a low-addiction opioid analgesic that is clinically useful in treating moderate to moderately severe pain. It induces analgesia against a variety of pain situations in acute therapeutic use, including postsurgical pain, obstetric pain, terminal cancer pain, and pain of cardiac origin. By decreasing monoamine reuptake, the analgesic appears to affect the transmission of pain signals at opioid receptors [3]. After mandibular third molar surgery, several nonsteroidal anti-inflammatory medications (NSAIDs) have been used to manage pain, swelling, and trismus.[4]. These drugs work by inhibiting the enzyme cyclooxygenase (COX), which controls the inhibition of prostaglandin (PG) generation [5].

Piroxicam is an acidic enolic NSAID that inhibits the inducible Cox-2 enzyme preferentially and has a lower effect on the constitutive Cox-1 enzyme [6,7]. As a result, it is commonly used to treat acute and chronic pain, as well as inflammatory and degenerative diseases [7]. Intraperitoneal piroxicam and morphine have also been demonstrated to have an antinociceptive synergism [8]. Nonsteroidal anti-inflammatory medicines have been shown to provide postoperative analgesia comparable to that of opioids (NSAIDS) [9,10]. NSAIDs have also been shown to have an opioid-sparing impact, as well as a reduction in opioid-induced nausea, vomiting, and respiratory depression. This decrease in opioid use and negative effects may benefit the patient by increasing postoperative analgesia and possibly shortening hospital stays [11].

Previously, our team has extensive expertise working on a variety of research projects in a variety of areas [12–26]. We decided to explore this project because of the growing trend in this field. We hope to examine the pre-emptive analgesic effectiveness of 20 mg piroxicam and 50 mg tramadol for mandibular third molar surgery based on this motivation.

2. MATERIALS AND METHODS

2.1 Study Setup

This randomised prospective controlled clinical study was done among patients who visited the oral surgery clinic's outpatient dental department between June 2020 and March 2021. The study comprised 30 adult patients who were randomly selected and allocated to the department of oral and maxillofacial surgery for surgical removal of an impacted mandibular molar using a simple lottery approachThe patients were separated into two groups, each with 15 patients, with Group A receiving 20 mg of piroxicam intramuscularly 50 minutes before surgery and Group B receiving 50 mg of tramadol intramuscularly 50 minutes before surgery.

2.2 Inclusion Criteria

- Patients between 18 years-50 years of age
- Both genders
- A partially bony impacted mandibular third molar based on clinical and radiographic diagnosis
- Up to the day of surgery, no pain associated with the subject third molar

2.3 Exclusion Criteria

- Patients with incomplete clinical and radiological records.
- Patients with severe systemic conditions like diabetes and hypertension.
- Analgesics usage 3 days prior to the procedure, previous history of seizure disorder, lactation or pregnancy , oral contraceptive usage, and known hypersensitivity to the study drugs.

2.4 Procedure

All surgical treatments were performed by the same surgeon at the Department of Oral and Maxillofacial Surgery, and evaluations were performed by a single independent investigator. Two 1.8-mL capsules of 2 percent lidocaine–containing 1:100,000 epinephrine were used to block the lingual, buccal, and inferior alveolar nerves, resulting in anaesthesia. Surgery began once anaesthetic was administered. An incision was made along the anterior border of the ascending ramus of the jaw, distal to the mandibular second molar, to prepare a mucoperiosteal flap. The surgical incision was closed using this flap. No. 3-0 silk was used for suturing.A partial bony impacted mandibular third molar was removed in each patient. The length of time between analgesic re-medication was recorded. The patients were given four 10-mg oral ketorolac pills and told to take one of them as a rescue drug at least six hours apart, depending on their needs. The patients returned the unused ketorolac at the end of the evaluation period (24 hours). The pills were counted to ascertain the quantity of pills ingested and the number of individuals in each group who didn't require any medication. The total amount of analgesics consumed was also calculated.

2.5 Diagnostic Criteria

2.5.1 Post Operative Pain Evaluation by Visual Analogue Scale

The pain was measured using a 100-mm visual analog scale (VAS). The VAS was a numerical scale ranging from 0 to 100, with 0 signifying no pain or discomfort and 100 representing the most severe pain or discomfort. The VAS report was completed at the 1st, 2nd, and 12-hour mark after the procedure, with the final evaluation taking place at 24 hours.

2.6 Study Parameters

For the purposes of the study, the following information was gathered:

- The patient's age
- The patient's gender
- Postoperative VAS pain Scores
- It's time to re-medicate with analgesics (ie, the time from the end of the surgery until the intake of the first rescue analgesic medication became necessary for the patient)
- The number of patients in each group who did not require any medication.
- The number of patients who require a rescue analgesic technique (10 mg of oral ketorolac)
- Total analgesic consumption

The study subjects were distributed into four age groups- Group 1 was 11-20 years old, Group 2 was 21-30 years old, Group 3 was 31-40 years old, and Group 4 was 41-50 years old.

2.7 Data Collection

Patients who reported to the Outpatient Department between June 2020 and March 2021 were used to collect data for the research parameters. A single examiner completed all of the assessments, and two investigators examined and recorded the results.

2.8 Statistical Analysis

IBM SPSS version 23.0 software was used to tabulate and analyze the data. Frequency and percentage were used to express descriptive statistics. The Student's t-test was used to compare variables between the Piroxicam and Tramadol groups (time to analgesic re-medication, number of patients in each group who did not need any pill, number of patients requiring the rescue analgesic process, total analgesic intake). The effects over time of the pre-emptive analgesics on pain intensity were evaluated by Mann-Whitney U-Test. The significance level was set at $P<0.05$ with a confidence interval of 95%.

3. RESULTS

This study enrolled a total of 30 patients, with a 100 percent participation rate.

3.1 Age Distribution

The patients who were the youngest and oldest were 18 and 50 years old, respectively. The age distribution of study participants revealed that the majority of patients were between the ages of 31 and 40. (67.50%).

3.2 Gender Distribution

Over the course of a ten-month period, the gender distribution of study subjects revealed that 20 patients (75%) were women and 10 patients (25%) were men.

3.3 Post Operative Pain Evaluation by Visual Analogue Scale

Pain score at 1st and 2nd hours after surgery were different between the two analgesic groups; the mean VAS scores recorded after injection of piroxicam at 1 and 2 hours respectively were significantly lower than after tramadol at 1st and 2 hours, respectively. The pain intensity was also highest at the end of 2nd hour for the tramadol group (Fig. 1). No significant differences in pain scores were observed between the two analgesics at 12 and 24 hours post-surgery (P>0.05) [Mann-Whitney U test].

3.3.1 Time to first rescue analgesic medication, number of patients requiring rescue analgesia, number of patients without the need of analgesia, total analgesic consumption

The parameters: There were no significant statistical differences (P >.05) in the time to first rescue analgesic medication, the number of patients requiring the rescue analgesic treatment (10 mg of oral ketorolac), or the number of patients without the need for analgesic during the evaluation period. However, there was a statistically significant difference in overall analgesic usage between the two groups.(p=0.019) [Table 1].

There was no statistically significant difference on comparison of the parameters between the two groups, in time to usage of first rescue analgesic medication (p=0.42), the number of patients who require the rescue analgesic treatment (10 mg of oral ketorolac) (p=0.12), number of patients without the need for analgesic during the evaluation period (0.15). However, the difference between total analgesic consumption between the 2 groups was statistically significant (p=0.019).

4. DISCUSSION

"Pre-emptive analgesia" refers to the administration of analgesia before the onset of surgical stimulation. It prevents or lowers central hyperexcitability, resulting in better postoperative analgesia and a lower need for analgesics [27]. Pre-emptive analgesia is a contentious topic in oral surgery, with reports both in favor and against it [28]. As a result, several criteria and processes for evaluating the quality of randomised clinical trial reports in pain research have been developed. Blind assessments are said to yield much lower and more consistent scores than open assessments [29].

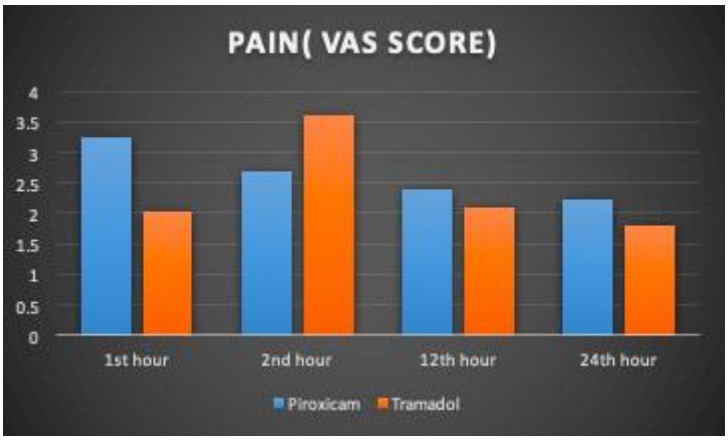

Fig. 1. Bar diagram depicting VAS scores of the piroxicam group (blue) and the tramadol group (orange) at the 1st, 2nd, 12th, and 24th-hour post-surgery. The X-Axis depicts the Post extraction hour and Y-Axis represents the VAS Scores

The VAS scores of the tramadol group were higher than the piroxicam group at the 2nd-hour post-surgery

Table 1. Depicts the distribution of variables (the time to first rescue analgesic medication, number of patients who require the rescue analgesic treatment (10 mg of oral ketorolac), number of patients who do not require the usage of analgesic during the evaluation period , and total analgesic consumption) between Piroxicam Group and Tramadol Group

Parameters	Piroxicam Group (Mean)	Tramadol Group (Mean)	Test Value	P-Value
Time to first rescue analgesic (hr)	1.05	0.95	1.23	0.42
No. of patients (%) requiring rescue analgesic during the period of evaluation (24hr)	6	3	5	0.12
No. of patients (%) who do not require analgesic during the evaluation period (24 hr)	1	6	-4	0.15
Total analgesic usage (mg)	12.6	24.2	-34.3	0.019*

**Statistically significant; Independent sample t-test*

Ong et al. [30] conducted a meta-analysis to assess the ability of pre-emptive analgesia interventions to reduce postoperative analgesic requirements, prolong the time to first rescue analgesia, and attenuate and alleviate postoperative pain scores. They found an overall beneficial effect in selected analgesic regimens, which was most pronounced after epidural analgesia, local wound infiltrations, and systemic NSAID administration. Preoperative morphine lowered pain scores and postoperative analgesic doses in patients undergoing abdominal hysterectomy, according to recent research by Richmond et al. [31]. Another study found that giving 30 mg of ketorolac IV instead of 50 mg of tramadol IV preoperatively improves pre-emptive analgesic efficacy in third molar surgery [32].

Isiordia et al. [28] performed a study which showed that patients receiving 15 mg of preoperative meloxicam had less pain intensity and total analgesic consumption than those receiving 50 mg of preoperative tramadol. All of these results were in accordance with the results of our study. However, a study by Nekoofar et al. [7] found no significant differences in the analgesic efficacy of meloxicam, piroxicam, or placebo, but did find that the time factor had a significant influence on lowering postoperative pain after endodontic treatment.

The dose of 50 mg tramadol employed in this study was chosen since it has been found to be effective and safe in the management of postoperative pain after third molar surgery.

According to [32–34], Tramadol is a safe and effective postoperative analgesic that lasts much longer than morphine. Tramadol's extensive use is hampered by the drug's significant side effects of nausea and vomiting [35]. Because this was a single-dose research, the major side effects were not visible.

Piroxicam's principal mode of action is the inhibition of COX, which determines PG inhibition. The PGs are released from injured tissues and directly sensitise peripheral nociceptors. They also play a role in primary and secondary hyperalgesia, both of which are crucial in pain regulation [36]. In comparison to other NSAIDs, piroxicam's suppression of the peroxidase enzyme gives a superior gastrointestinal tolerance. Furthermore, because of its long half-life, piroxicam may have a longer clinically significant effect when administered preoperatively [37].

This is the first study to compare piroxicam to an opioid analgesic as pre-emptive analgesics for pain control after third molar surgery, and few studies have compared its analgesic performance to other NSAIDs in this acute pain clinical paradigm [38–40]. These trials have demonstrated that piroxicam can be an effective pain reliever following the extraction of a mandibular third molar. In comparison to meloxicam, greater doses of tramadol (100 or 200 mg) might have a better analgesic effect. However, adverse symptoms, particularly nausea and vomiting, are likely to be common. Dental pain is primarily inflammatory, and evidence-based medicine has determined that nonsteroidal anti-inflammatory drugs (NSAIDs) are the best analgesic for dental pain [41,42]. Our university is dedicated to high-quality evidence-based research and has achieved success in a number of areas [16,43–62].

5. CONCLUSION

Within the confines of this study, it may be inferred that patients who received 20 mg of piroxicam preoperatively had reduced pain intensity and total analgesic intake than those who received 50 mg of tramadol preoperatively.Therefore, piroxicam given preoperatively showed superior analgesic properties for intermediate surgical procedures in comparison to pre-emptively administered tramadol.

6. LIMITATIONS

As the VAS Scores were based on patients' perception, a subjective opinion regarding the results was obtained, hence it would be a limitation of our study. Also, the pain threshold for different patients would not be similar.

7. FUTURE SCOPE

Although the literature provides a number of studies on the pre-emptive analgesic efficacy of piroxicam and tramadol, there are limited studies related to comparing piroxicam with an opioid analgesic both as pre-emptive analgesics for pain relief following third molar surgery.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

CONSENT

All of the participants were informed about the potential hazards of oral surgery and experimental therapies, and they signed a written consent form that had been approved by the institution.

ETHICAL APPROVAL

The Institutional Ethical Committee mentioned their approval to the project (SDC/SIHEC/2020/ DIASDATA/0619-0320).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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