

Comparison of Efficacy of Two Different Combination of Analgesics and Anti-Inflammatory Drugs in Post-Operative Pain Management Following Surgical Removal of Impacted Mandibular Third Molars

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ABSTRACT

Aim: The aim of the study was to evaluate the analgesic and anti-inflammatory efficacy of ketorolac plus tramadol as one group and ketorolac plus placebo as one group after surgical removal of mandibular third molar

Materials And Methods: A prospective randomized study conducted with 100 patients that required removal of mesioangularly impacted mandibular third molar. The systematic statistical analysis was performed after the data collection was done. Patients were categorized into two groups (Group 1: ketorolac and tramadol, Group 2: ketorolac and placebo) in a crossover manner. Subjective and objective observations recorded that include age, gender, and pain score using visual analog scale. Each patient was evaluated using a visual analogue scale.

Results: Pain intensity at the postoperative 1st, 6th, 12th, 24th hourly postoperative pain was measured. Mesioangular (75%) impacted teeth, 15% Horizontal (15%) impacted teeth, and 10% Distoangular (10%) impacted teeth were studied. Group A had a difficulty level of 7.4 and group B had a difficulty index of 7.8. Mean duration of surgery in Group A was 45 ± 6 minutes and in Group B was 48 ± 8 minutes. Acute pain relief was observed in the Ketorolac group within half an hour (min VAS was 2.68) but for a shorter duration of 4-5 hrs. The tramadol and ketorolac groups, however, had greater depth (min VAS score 1.65) and duration of analgesia (8-10 hrs). Complications such as nausea/vomiting (8%), drowsiness/sedation (6%), and upper gastric pain/acidity (8%), were more common in the tramadol group, while upper gastric pain/acidity was more common in the Ketorolac group.

Conclusion: Tramadol induces delayed analgesia around 1 hour and reaches its maximum effect in 3 to 4 hours. Its analgesic effect lasts a longer duration for about 8 to 10 hours. In our study we concluded that an analgesic effect of ketorolac alone was lost for only 4 hours but the combination of ketorol and a tramadol was lost for 6 to 8 hours.

Key words: Non-steroidal anti-inflammatory drugs (NSAIDs), Ketorolac, Tramadol, Visual analogue scale (VSA), Impacted teeth

HOW TO CITE THIS ARTICLE: Yandeti Srinivasulu, Abdul Wahab, Dinesh Prabu, Comparison of Efficacy of Two Different Combination of Analgesics and Anti-Inflammatory Drugs in Post-Operative Pain Management Following Surgical Removal of Impacted Mandibular Third Molars, J Res Med Dent Sci, 2021, 9(9): 136-139

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Received: 10/08/2021
Accepted: 13/09/2021

INTRODUCTION

Impacted third molar extraction causes soft and bone tissue trauma, which can lead to an acute inflammation that causes severe discomfort and suffering. Pain is a subjective symptom that is influenced by a variety of factors such as age, sex, anxiety, pain threshold, and surgical difficulty. Pain after impacted third molar surgery under local anaesthesia has been shown to be of short duration and peaks in intensity in the early post-operative period, necessitating the use of analgesics for relief. Postoperative pain can be distressing for the patient and have an impact on their quality of life. As a result, several

research studies for better pain control following impacted third molar surgery have been conducted, and various types of drugs have been offered [1]. After third molar surgery, pain management is even more important, and it should be addressed before the pain becomes unbearable. The longer uncontrolled pain persists, the more sensitive the patient may become to painful stimuli. Within the first 5-8 hours after third molar surgery, pain reaches a strong intensity or a peak [2]. Many clinicians have attempted to reduce the post-operative pain by using anti-inflammatory drugs.

The anti-inflammatory drugs are broadly categorized into steroidal (Narcotic analgesics) and non-steroidal (NSAIDs). Drug dependence, respiratory depression, constipation, nausea, vomiting, and drowsiness are all possible side effects of narcotic analgesics, which act

directly on opiate receptors in the central nervous system. Non-steroidal anti-inflammatory drugs (NSAIDs), which act by prostaglandin synthesis to achieve analgesic and anti-inflammatory actions but are associated with poor gastrointestinal and renal tolerance and risk of interference with coagulation systems. The best postoperative medication is one that provides long analgesic cover, easy administrable, should be safe and cost economical [3].

Among the nonsteroidal anti-inflammatory drugs investigated, ketorolac is one of the pharmacological options available, it is reported to have a potent analgesic effect like opioids as well as a moderate anti-inflammatory activity, which seems adequate for the treatment of moderate-to-severe acute pain [4–6]. This medication has been studied for pain reduction after third molar operations due to these properties.

Despite these promising findings, rescue medication for pain relief was still necessary, even with the administration of ketorolac, which suggests that preoperative administration is not enough to eliminate postoperative pain [7,8].

Combining analgesics may provide greater analgesia than the individual agents through the synergistic action of the individual drugs and allowing the use of lower doses for each medication may improve the patients' tolerability [9].

However, among the several possible drug combinations, there is a lack of knowledge regarding which combination and the respective drug dosages have a better analgesic efficacy [10].

Combining a nonsteroidal anti-inflammatory medicine (NSAID) like ketorolac with an opioid analgesic like tramadol could potentially reduce postoperative discomfort. Clinical studies have reported that the combination of tramadol 37.5 mg was effective and well tolerated in patients with dental pain [11].

MATERIALS AND METHODS

Study setting and data collection: A prospective randomized study conducted with 100 patients that required removal of mesio angularly impacted mandibular third molar.

The systematic statistical analysis was performed after the data collection was done. Patients were categorized into two groups (Group 1: Ketorolac and tramadol, Group 2: Ketorolac and placebo) in a crossover manner. Subjective and objective observations recorded that include age, gender, and pain score using visual analog scale. Each patient was evaluated using a visual analogue scale (Figure 1).

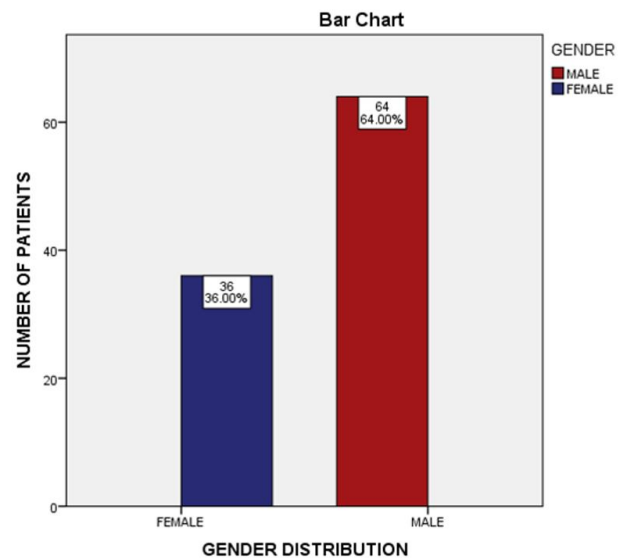


Figure 1: Bar diagram depicting the gender distribution of patients in two age groups where blue bar represents female and red bar indicates males. X axis indicates the gender and Y axis indicates the no of patients. In this study, incidence of females was more compared to males in both the groups in surgical removal of impacted teeth.

Patients were reported to Saveetha Dental College for pain treatments. The Patients were reported to the Department of Oral and Maxillofacial Surgery for surgical removal of third molar impaction.

Ethical committee approval for this study was obtained from the Institutional Ethics Committee with the following ethical approval number. SDC/SIHEC/2020/DIASDATA/0619-0320.

Sampling

Patients who underwent pericoronitis treatment at Saveetha Dental College were included in the study population by Systematic Sampling.

Inclusion criteria: Patients of all age groups and gender with impacted mandibular third molars with diagnosis of pericoronitis were included.

Exclusion criteria: Patients with impacted teeth other than third molars, and common dental problems were excluded from the study.

Duplicate patient records and incomplete data were excluded. Datas were reviewed by an external reviewer. Totally, n=100 patients were included. Demographic data such as the patient's age, gender and pericoronitis, pericoronal abscess were also recorded.

Data analysis

The data was tabulated in Microsoft Excel 2016 (Office 10) before being exported to SPSS (Statistical Package for Social Sciences) for Windows version 20.0, SPSS Inc, Chicago IU, USA) for statistical analysis. Chi-square test was employed with a level of significance set at $p < 0.05$.

RESULTS

A total of 100 patients were enrolled in the study to compare the analgesic efficacy of Ketorolac versus Tramadol were equally divided into Group A and Group B. Mean age was 31 ± 8.1 years in Group A and 33 ± 10.4 in Group B. Group A included 34 males (68%), 16 females (32%) whereas Group B included 30 males (60%), 20 females (40%)

Study includes Mesioangular (75%), 15% Horizontal (15%) and 10% Distoangular (10%) type of impacted teeth. Mean difficulty index for group A was 7.4 and for group B was 7.8. Mean duration of surgery in Group A was 45 ± 6 minutes and in Group B was 48 ± 8 minutes. Acute pain relief was observed in the Ketorolac group within half an hour (min VAS was 2.68) but for a shorter

duration of 4-5 hrs. However, depth (min VAS score 1.65) and duration of analgesia (8-10 hrs) was more in the tramadol and ketorolac group. Complications like nausea/vomiting (8%) and drowsiness/sedation (6%) were observed more in the tramadol group whereas upper gastric pain/acidity (8%) was more in the Ketorolac group.

The level of pain increased after surgery, reaching a peak after 3 h for both groups. In the following hours, pain intensity started to decrease, but few patients reported pain 12 h after the surgery (Table 1). The comparison of both groups in each time assessment only revealed significant differences in the 6th hour period, with the Ketorolac+tramadol group having a lower degree of pain intensity than the Ketorolac group.

Table 1: Pain measurement.

| Day | Group | Mean \pm Standard deviation | Mean difference | P Value |
|----------|---------|-------------------------------|-----------------|---------|
| 1st hour | Group 1 | 10.3 \pm 11.6 | -3.8 | 0.5 |
| | Group 2 | 14.2 \pm 15 | | |
| 6th hour | Group 1 | 3.7 \pm 6.4 | -7.1 | 0.004 |
| | Group 2 | 9.8 \pm 14 | | |
| 12 hours | Group 1 | 3.3 \pm 6.2 | -3.1 | 0.06 |
| | Group 2 | 5.3 \pm 8.3 | | |
| 24 hours | Group 1 | 2.6 \pm 7 | -2.8 | 0.09 |
| | Group 2 | 5.4 \pm 9.8 | | |

DISCUSSION

Tramadol is a synthetic opioid of the benzenoid class used to treat moderate to severe pain both acute and chronic. Its potency is comparable to morphine, and its analgesic effects continue for around 6 hours. It acts by two different mechanisms. First, it works by binding to the μ -opioid receptor. Secondly, it acts as a serotonin-norepinephrine reuptake inhibitor [12,13]. Ketorolac is a first-generation non-steroidal anti-inflammatory drug (NSAID) of family heterocyclic acetic acid derivatives, used for short-term management of moderate to severe pain and usually not prescribed for longer than five days. Ketorolac is a non-selective COX inhibitor. Its mode of action is by inhibiting the bodily synthesis of prostaglandins by competitive blocking of the enzyme cyclooxygenase (COX). Its onset of action is approx. 30 minutes, reaches its peak effects in 45-60 minutes, and has a half-life of 4-6 hours [14].

It is said that "the pain of the mind is worse than the pain in the body" and its management would require alleviating both the mental and physical pain, making the patient comfortable. Ketorol causes an early analgesic effect within half an hour and exhibits its highest impact after that. Ketorol induces an early analgesic effect within half an hour and shows its maximum effect after that. Its analgesic effect lasts for about 4-5 hrs. Tramadol induces delayed analgesia around 1 hour and reaches its maximum effect in 3-4 hours. Its analgesic effect lasts a longer duration for about 8-10 hrs. Both the medications

provide good analgesic effects [15,16]. Intravenous ketorolac 30 mg provides better pain control postoperatively as compared to 50 mg of tramadol after third molar surgery [17]. In the treatment of postoperative pain, 100 mg tramadol is as effective as 20 mg ketorolac. If given prior to an oral surgical operation, intramuscular 30 mg ketorolac provides superior pain relief than intravenous 50 mg tramadol. In comparison to tramadol, ketorolac had better pain scores and overall postoperative analgesic intake [18].

Ketorolac should be avoided in patients with kidney and coagulation disorders as it interferes in renal and platelet functions. No bleeding episodes were observed in the tramadol group. Post-operative nausea, vomiting and sedation are the most common side effects of tramadol. Our study shows 8% patients' complaints about nausea/vomiting and 6% for drowsiness and sedation [19,20]. Gastric pain with acidity was observed in 8% cases in the ketorolac group. This is since ketorolac inhibits the prostaglandin synthesis which reduces the protective mechanism of prostaglandins on the gastric mucosa leading to dyspepsia and upper gastric pain. Only 2% cases presented with acidity in the tramadol group. One of the biggest issues in the healthcare business is providing effective and safe analgesia. Tramadol is a relatively new opioid medication with improved analgesic properties and no risk of tolerance or physical dependence. It is known to be one of the safest postoperative analgesic medicines used for chronic pain

management. In oral surgery, however, a comprehensive review and meta-analysis revealed that tramadol has poorer analgesic efficacy and safety than NSAIDs [21]. Ketorolac is a commonly used NSAID for the short-term management of acute postoperative pain in dentistry.

CONCLUSION

Tramadol induces delayed analgesia around 1 hour and reaches its maximum effect in 3 to 4 hours. Its analgesic effect lasts a longer duration for about 8 to 10 hours. In our study we concluded that an analgesic effect of ketorolac alone was lost for only 4 hours but the combination of ketorolac and a tramadol was lost for 6 to 8 hours.

CONFLICT OF INTEREST

No conflict of interest.

FUNDING FOR STUDY

Nil.

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