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Oral Preemptive Analgesic Efficacy in Post Operative Pain, Nausea and Vomiting in Third Molar Removal Surgery - A Randomised Control Trial

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KEYWORDS
Third Molar Surgery,
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ABSTRACT:

Objective: This randomized controlled clinical trial aimed to evaluate the efficacy of oral preemptive analgesia in reducing postoperative pain, nausea, and vomiting following third molar extraction.

Methods: A randomized, single-blind, placebo-controlled clinical trial was conducted with 129 patients requiring surgical removal of impacted mandibular third molars. Participants were divided into two groups: Group A (Test, n=69) received oral aceclofenac 100 mg, paracetamol 325 mg, and serratiopeptidase 15 mg as a combination 60 minutes before surgery. Group B (Control, n=60) received a Vitamin C tablet as placebo. Postoperative pain levels were assessed using a visual analog scale (VAS) at 1, 6, 12, 24, 48, and 72 hours post-surgery. Rescue analgesic consumption and time to first analgesic intake were also recorded.

Results: Patients in Group A reported significantly lower pain scores at all time points ($p < 0.05$). The need for rescue analgesics was lower in the test group, and the time to first analgesic intake was longer compared to the control group. The incidence of nausea and vomiting was also markedly reduced in Group A, with fewer participants requiring rescue antiemetics compared to Group B ($p<0.05$). Additionally, participants in Group A demonstrated a quicker return to normal activities.

Conclusion: Preemptive oral analgesia significantly reduced postoperative pain and the incidence of nausea and vomiting following third molar surgery. This strategy could improve patient comfort and recovery, suggesting its utility as part of routine perioperative management in the field of oral surgery.

1. Introduction

The concept of preemptive analgesia to reduce the magnitude and duration of postoperative pain was paved in 1983 by Woolf, who showed evidence for a central component of post injury pain hypersensitivity in experimental studies. Subsequently, an overwhelming

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amount of experimental data demonstrated that various antinociceptive techniques applied before injury were more effective in reducing the postinjury central sensitization phenomena as compared with administration after injury(1). The definition of preemptive analgesia has varied, thereby causing confusion and misunderstanding of the concept. Because the original observations in experimental studies suggested that timing of analgesic treatment was important to obtain efficient reduction of postoperative pain hypersensitivity phenomena, we performed a study to evaluate the efficacy of oral preemptive analgesia in reducing postoperative pain, nausea, and vomiting following third molar extraction(2)

The possibility of surgical extraction should be considered if the affected third molar is positioned abnormally. Only following clinical and radiological examinations which are also conducted following any potential complaints from the assessed patient can this be ascertained.(3) Many analgesic medications, which fall into three main categories, are typically used to treat pain. These include opioids, adjuvants (antidepressants, anticonvulsants, and local anesthetics), and non-opioid medications (nonsteroidal antiinflammatory drugs [NSAIDs])(4). Following surgical tooth extraction, NSAIDs are the most often prescribed analgesics, either by themselves or in conjunction with other medications(5). Both the COX-1 and COX-2 enzyme isoforms are inhibited by common NSAIDs. Conversely, selective COX-2 inhibitors prevent the severe gastrointestinal effects linked to COX-1 suppression by selectively inhibiting the COX-2 isoform(4,6). Pain, edema, and trismus are caused by prostaglandins, which are postsurgical mediators that are first released during the acute ammatory phase. A good clinical paradigm for assessing the postoperative impact of anti-inflammatory medications on these events is the surgical extraction of third molars(7). Preemptive analgesia is a pharmaceutical approach used in this context to manage, reduce, or possibly prevent postoperative pain associated with dental treatments. In recent decades, a lot of research has been done on this pain management technique(7,8).

The surgical removal of impacted third molars is one of the most common procedures in oral and maxillofacial surgery. Postoperative pain, inflammation, and swelling significantly affect patient recovery. Preemptive analgesia is an approach where pain management is initiated before the noxious stimulus, aiming to reduce central sensitization and improve postoperative pain control(9).Non-steroidal anti-inflammatory drugs (NSAIDs) like aceclofenac 100 mg, paracetamol 325 mg, and serratiopeptidase 15 mg as a combination are commonly used for pain management in third molar surgery. However, evidence regarding its preemptive efficacy in third molar surgery remains limited(10). This study evaluates the impact of preemptive oral aceclofenac 100 mg, paracetamol 325 mg, and serratiopeptidase 15 mg as a combination of postoperative pain and analgesic consumption following mandibular third molar extractions. Postoperative pain, nausea, and vomiting (PONV) are common complications following third molar (wisdom tooth) extraction, often necessitating effective pain management strategies(10,11). Oral preemptive analgesia, administered before surgery, is hypothesized to reduce these postoperative symptoms by mitigating the central sensitization associated with surgical trauma(12).

2. Materials and Methods

Study Design and Participants

This study was designed as a randomized, double-blind, placebo-controlled trial conducted at the Department of Oral & Maxillofacial Surgery, Saveetha Dental College and Hospital. Ethical approval was obtained on 30 th November 2023 by the Institutional Human Ethical Committee and the IHEC number is as follows - IHEC/SDC/OMFS - 2304/23/295 and the study was registered in Clinical Trial Registry of India (ICMR - NIMS) and CTRI number is CTRI/2024/11/077104 and all the participants provided informed consent.The Inclusion Criteria are patients aged between 18–35 years and with an indication for impacted mandibular third molar extraction and patients under American Society of Anesthesiologists (ASA) I or II status.A randomized, double-blind, placebo-controlled clinical trial was conducted with 129 patients requiring surgical removal of impacted mandibular third molars. Participants were divided into two groups: Group A (Test, n=69) received oral aceclofenac 100 mg, paracetamol 325 mg, and serratiopeptidase 15 mg as a combination 60 minutes before surgery. Group B (Control, n=60) received a Vitamin C tablet as placebo. Postoperative pain levels

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were assessed using a visual analog scale (VAS) at 1, 6, 12, 24, 48, and 72 hours post-surgery. Rescue analgesic consumption and time to first analgesic intake were also recorded.

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All patients underwent a standardized surgical procedure under local anesthesia (2% lidocaine with 1:100,000 epinephrine) and were prescribed 500 mg paracetamol every 8 hours postoperatively, with tramadol (50 mg) as a rescue analgesic.

Outcome Measures

Primary Outcome: Postoperative pain intensity assessed using the VAS scale at 1, 6, 12, 24, 48, and 72 hours and Secondary Outcomes include Total analgesic consumption (mg used per patient) and time to first analgesic intake.

Statistical Analysis

Data were analyzed using SPSS v.25. Continuous variables were expressed as mean ± standard deviation. Repeated measures ANOVA was used to compare pain scores over time, and the Kaplan-Meier method was used for time-to-first-analgesic analysis. A p-value <0.05 was considered statistically significant.

3. Results

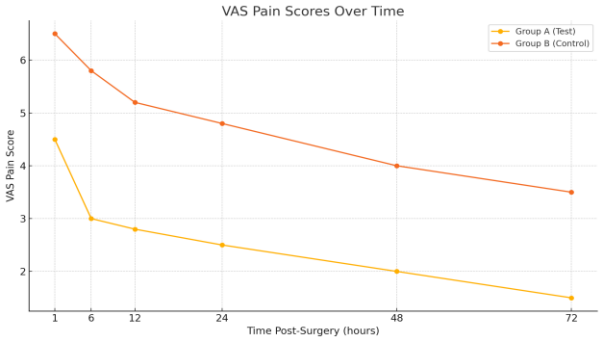
The final analysis included 129 patients (69 tests, 60 controls). No significant differences were observed between the groups in terms of age, gender, or surgical duration ($p > 0.05$).

Pain Scores (VAS)

Patients in Group A had significantly lower VAS scores at all time points compared to Group B ($p < 0.05$) (Figure 1). The greatest difference was observed at 6 and 12 hours postoperatively. No significant adverse effects (gastric discomfort, nausea, dizziness) were reported in either group.

Table 1: represents the comparison of average VAS score between Group A (Test) and Group B (Control) in relation to 1,6,12,24,48 and 72 hours after surgical removal of lower third molar.

Time Post surgery (hrs)	Group A (Test) VAS	Group B (Control) VAS
1	4.5	6.5
6	3.0	5.8
12	2.8	5.2
24	2.5	4.8
48	2.0	4.0
72	1.5	3.5



Graph 1: is the line graph comparing VAS pain scores post surgery in the given time interval.

Time to First Rescue Analgesic

- Group A: 5.2 ± 1.1 hours.
- Group B: 2.4 ± 0.9 hours ($p < 0.01$).

Analgesic Consumption

- Mean zerodol sp intake (mg):
- Group A: 320 mg ± 80
- Group B: 800 mg ± 120 ($p < 0.001$)

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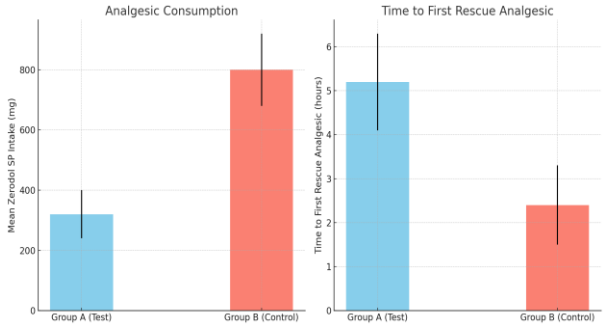
Group	Mean (hours)	Standard deviation (hours)
Group A (Test)	5.2	1.1
Group B (Control)	1.1	0.9

Group	Mean (mg)	Standard deviation (mg)
Group A (Test)	320	80
Group B (Control)	800	120

Table 2 and 3 represent the average time and dosage of the drug given to groups A and B respectively.



Graph 2: is the bar diagram representing average time and dosage of the drug given to two participant groups.

4. Discussion

This study demonstrates that preemptive oral analgesics significantly reduces postoperative pain and analgesic consumption after third molar extraction. These findings align with previous studies, which suggest that NSAIDs administered preoperatively reduce central sensitization and inflammatory mediator release(13).

From a therapeutic standpoint, they work by inhibiting cyclooxygenase (COX), which inhibits prostaglandin synthesis and the way these arachidonic acid metabolites work in concert with other mediators to support local ammatory reactions and hyperalgesia(14). This process involves two primary isoforms of COX: the constitutive form, COX-1, which is expressed in nearly all tissues and is in charge of the regular physiological functions of prostaglandin (like vascular homeostasis and gastric mucosal protection), and the inductive form, COX-2, which is expressed in a small number of tissues, including the kidney, prostate, and brain, and is primarily in charge of prostaglandin synthesis and the mediation of responses to pathological processes like inflammation, pain, and fever(1,15).

The degree of surgical difficulty in extracting third molars is correlated with the tooth's location, depth of impaction, angulation, and root architecture. Age, sex, body mass, surgical time, and tissue trauma, including odontosection and osteotomy, are all linked to the incidence of discomfort, trismus, and edema during the postoperative phase following third molar surgery. Furthermore, postoperative pain is significantly influenced by soft tissue(1). Patients are more receptive to the oral method, which also doesn't need expert training(16). Control of postoperative pain, edema, and trismus has been the subject of continuous research in the held of oral and maxillofacial surgery, since pain can significantly reduce the quality of life of the patient(17). The local anesthesia drug decreases the in ammatory response and hyperalgesia by modulating ectopic neuronal discharges, blocking sodium channels, and modulating G protein-coupled receptors and calcium and potassium channels.The rapid absorption and higher bioavailability of analgesics may explain its superior effectiveness in early postoperative pain control. Patients in the ibuprofen group had a longer time to first analgesic request, indicating better pain control in the immediate postoperative period(18).Limitations of this study include the short follow-up duration and the single-center design. And the difficulty of treatment and amount of bone removed may also alter the post operative outcomes which were not assessed in this study. Further multicenter trials with larger sample sizes are needed to confirm these findings(19).

5. Conclusion

Preemptive administration of oral analgesics significantly reduces postoperative pain, nausea and vomiting and the need for rescue analgesics following lower third molar extraction. These findings support the use of oral aceclofenac 100 mg, paracetamol 325 mg, and serratiopeptidase 15 mg as a combination 60 minutes before surgery. as a safe and effective strategy for preemptive analgesia in oral surgery.

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