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COMPARISON OF LOW DOSE ETORICOXIB AND ACECLOFENAC-PARACETAMOL COMBINATION AS PRE-EMPTIVE ANALGESIC IN THIRD MOLAR SURGERY – A RANDOMISED CLINICAL TRIAL.

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ABSTRACT:

Introduction : The extraction of third molars is one of the most common procedures performed by oral surgeons. Painful stimuli during surgical intervention or in the perioperative period may cause changes in the nervous system and affect postoperative pain levels. Pre-emptive analgesia in the preoperative period is a strategy used in the management of postoperative pain that may greatly impact the patient's perception of pain.

Materials and methods: This study was designed as a randomised, parallel, double blinded trial. 100 Healthy patients if they were older than 18 years old, had horizontal impacted teeth, did not take analgesics or anti-inflammatory drugs a week prior were included in the study and divided randomly into 2 groups. Post operative pain assessment was done using VAS Scale at immediate post op, 1 hour post op and post operative day 1. Both the drugs were given 30 minutes before the surgery. Rescue medication was analysed by Pearson linear correlation ($P<0.05$).

Results: There is statistically significant difference between two pre-emptive analgesia (low dose etoricoxib and a combination of aceclofenac and paracetamol) with a significant lower value of VAS in etoricoxib group at immediate, 1 hour and 24 hour duration (P Value = 0.00)

Conclusion: This study revealed that a low dose of etoricoxib has pre-emptive analgesic effect, resulting in the reduced use of analgesics after third molar removal compared to Aceclofenac - paracetamol combination.

Keywords: Pre-emptive analgesia, Etoricoxib, Third molar, Extraction, Post-operative pain, Aceclofenac, paracetamol.

INTRODUCTION:

Under local anaesthesia, the removal of impacted mandibular third molars causes damage to bone and muscle tissue, which leads to inflammatory problems in the immediate postoperative

period which includes discomfort, edema, trismus, and alveolitis[1]. A mandibular third molar extraction is a crucial clinical tool for assessing the analgesic potency of novel medications. Moderate to severe pain that begins after the anaesthetic activity and lasts for several days results from surgical injuries to the soft tissue, notably trauma to the mandibular bone[2]. NSAIDs and other analgesics like opioids are used for post operative pain management[10]. Preemptive strategies concentrate on reducing or stopping the occurrence of hyperalgesic states and preventing postoperative analgesic flare-ups. In order to manage or prevent central sensitization, preventive analgesic measures are performed[1]. Pre-emptive analgesia can be achieved pharmacologically in a number of ways, including localised blocks using local anaesthetics, intravenous opioid delivery, and the use of N-methyl-D-aspartate receptor antagonists, corticosteroids, and non-steroidal anti-inflammatory medications (NSAIDs) . Most common being NSAIDS.

Two cyclooxygenase isoforms, cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX- 2), are present in NSAIDs [3]. COX-1 is constitutively expressed in tissues and encourages prostaglandin production (PG). The NSAIDs' indirect effects on PGE2, which has a cytoprotective effect on the gastrointestinal system, as well as on PGE2 and PGI2, which control renal blood flow, may be the cause of the NSAIDs' adverse effects on the stomach and kidneys [4]. Systematic reviews and meta-analyses of randomised controlled trials have demonstrated that selective COX-2 medicines selectively inhibit the COX-2 isoform, avoiding the unpleasant gastrointestinal effects linked to COX-1 inhibition[5].

A promising medication for pre-emptive analgesia, etoricoxib is a strong and selective cyclo-oxygenase 2 (COX-2) inhibitor with limited gastrointestinal adverse effects and favourable pharmacological characteristics[6]. Large dosages of the pre-emptive analgesic etoricoxib (120 mg) have been shown to lessen discomfort following tooth extraction surgery. Few studies have been done on the use of low-dose etoricoxib (60 mg) after extraction of an impacted tooth, therefore the findings cannot be used as a foundation for clinical practice. Our research trial was conducted to determine if a pre emptive low dose of etoricoxib (60 mg) could effectively reduce pain following third molar surgery.

Also in previous studies, Etoricoxib was not compared with any other NSAIDS. So the trial was conducted to compare low dose etoricoxib (60mg) with Aceclofenac-paracetamol combination as a pre emptive drug to reduce postoperative pain following third molar surgery.

MATERIALS AND METHODS:

Study Design: : Randomised clinical trial

Study setting : The study was conducted in the outpatient department of Oral and Maxillofacial surgery in a private dental college in Chennai during March 2022 to October 2022.

Study population:

The study population included patients with horizontally impacted mandibular 3rd molars. The patients were randomly divided and assigned to two groups using random sequence allocation

in 1:1 ratio as follows: GROUP 1: Low dose etoricoxib 60 mg (n=50), GROUP 2: Aceclofenac - Paracetamol combination (n=50). The operator and the patients were blinded to the type of drugs administered. To prevent postoperative infection, 500 mg dose of amoxicillin and 400 mg dose of metronidazole tablets were taken orally, 3 times a day, for 5 days.

Inclusion criteria:
Patients were included if they were older than 18 years old, had horizontally impacted teeth, did not take analgesics or anti-inflammatory drugs a week prior to the study.

Exclusion criteria:
Patients were excluded if they took NSAIDs and COX-2 inhibitors; were pregnant or nursing; had other serious diseases, such as liver, kidney and cardiovascular diseases; had ulcers or bleeding in the digestive tract; had the history of GI bleeding and gastritis; had inability to express subjective discomfort symptoms.

Ethical clearance:
- Prior to the start of the study, ethical clearance was obtained from the Scientific review board, Saveetha University.
- Written informed consent was obtained from the study participants.
- The anonymity of the participants was maintained.

Scheduling:
Details of individual cases were maintained in the pro forma. Panoramic radiographs were taken for all patients. Patients were explained in their native language regarding the treatment procedures.

Method:
The patients were given the randomly allocated drug and the procedure for surgical removal of the impacted tooth was started 30 minutes after the drug was given. Post operative pain was measured immediate post operatively, 1hr post operatively and 24 hours post operatively.

Sampling:
Simple random sampling was done by block randomization to select the study participants. Allocation ratio was kept at 1:1 into two groups. Blinding and allocation concealment was maintained using a sealed opaque envelope.

Surgical Procedure:
All operations were performed by the same attending doctor to minimise differences between operators. The same local anaesthesia technique was performed on the patients. The anaesthesia of inferior alveolar, lingual and buccal nerves block was performed with 2% lidocaine with 1:200,000 epinephrine. Both groups received the same surgical procedure to reduce surgery related bias. The buccal mucoperiosteal flap was elevated, the bone was removed and the tooth was sectioned. After the tooth was extracted, the alveolar tissue was scraped and rinsed with sterile saline solution. The wound was sutured with a 4–0 silk, and the

suture was removed 1 week after the surgery. The operative time was calculated from flap dissection and suture after tooth extraction.

Pain assessment:
An 11-point (0 to 10) visual analogue score (VAS) was used to evaluate pain (0, no pain; 1–3, mild pain; 4–6, moderate pain; 7–9, severe pain; and 10, miserable pain.

Post operative pain was assessed and scored at immediate post op, 1 hour and 24 hours after the operation. Ibuprofen was prescribed as a rescue analgesic only in the case of VAS >4. The patients were asked to record their total consumption of ibuprofen within the first 24 hours and the time of the first rescue analgesic medication after the procedure was completed.

Statistical analysis:
Data were analysed with SPSS software (SPSS, Inc., USA). Independent t-test and Chi-square were used to determine significant differences between the two groups. The parametric outcomes were expressed as mean±standard deviation (SD).

RESULTS:

Table 1: Intergroup Comparison of postoperative pain with VAS

Post-Op Duration	Pre-emptive Analgesia Used	Mean ± SD	P value*
Immediate	Low dose etoricoxib	0.84 ± 0.71	0.00
	Aceclofenac + Paracetamol	2.88 ± 1.04	
1 hour	Low dose etoricoxib	2.06 ± 0.87	0.00
	Aceclofenac + Paracetamol	3.76 ± 1.15	
24 hour	Low dose etoricoxib	0.82 ± 0.69	0.00

	Aceclofenac + Paracetamol	1.50 ± 0.91	

*Independent sample t-test

Table 1 shows comparison between two pre-emptive analgesia (low dose etoricoxib and a combination of aceclofenac and paracetamol) of postoperative pain using VAS at immediate, 1hour, 24 hour duration.

The above table shows statistical significant difference between two pre-emptive analgesia (low dose etoricoxib and a combination of aceclofenac and paracetamol) with a significant lower value of VAS in etoricoxib group at immediate, 1 hour and 24 hour duration (P Value = 0.00)

Table 2: Need for Postoperative Rescue Analgesia

Group	Rescue Analgesia		P Value*
	Yes	No	
Low dose etoricoxib	31.4%	60%	0.006
Aceclofenac + Paracetamol combination	68.6%	40.0%	

*Pearson Chi-Square

Table 2 shows that 31.4% of patients had rescue analgesia for postoperative pain in low dose etoricoxib group while 68.6% patients had rescue analgesia for postoperative pain in Aceclofenac + Paracetamol combination group. Thus the difference found was statistically significant between the two groups (P Value = 0.006)

Discussion:

NSAIDs, corticosteroids, and long-acting local anaesthetics are the most frequently prescribed medications for postoperative pain prophylaxis prior to oral surgical interventions. By lowering peripheral sensitization, which is associated with a drop in the amounts of histamine, kinins, and prostaglandins in the blood at the site of the inflammatory process, these medications

change the level of nociception and encourage various COX-related gene expression patterns.[5]

This process involves two main COX isoforms: COX-1 (the constitutive form), which is expressed in almost all tissues and is in charge of the normal physiological functions of prostanoids (such as protecting the gastric mucosa and maintaining vascular homeostasis), and COX-2 (the inductive form), which is mainly in charge of prostanoid synthesis and mediating responses to pathological prostanoids and responses to pathological processes including inflammation, pain, and fever.[7]

Etoricoxib is a second-generation selective class of non- steroidal anti-inflammatory drug approved for the treatment of patients with rheumatism and osteoarthritis. Etoricoxib is chemically written as [5-chloro-2-(6-methylpyridin-3-yl)-3- (4- methylsulfonyl phenyl) pyridine]. This compound is a dipyridinyl derivative that has a (4-methylsulfonyl) phenyl group attached to the central ring. In many cell and whole-blood experiments, etoricoxib displays more than 100-fold selectivity for COX-2 vs COX-1. The main benefit of this medication is that it has lower gastrointestinal effects and is less active against COX-1 than other selective COX-2 inhibitors.[8]

The analgesic efficacy of aceclofenac 100 mg is more prolonged than that of paracetamol. Addition of paracetamol to NSAIDS will increase its effects and decrease dose-dependent side effects. Combination of aceclofenac (with its peripheral effect) and paracetamol (with its central effect) will give better analgesic efficacy than individual drugs.[9]

In the present clinical research, the pre-emptive administration of etoricoxib showed a superior postoperative analgesic effect in comparison to Aceclofenac-paracetamol at 0, 1 and 24 h after third molar removal. There was a statistically significant difference in peak pain between the two groups. The etoricoxib group displayed a pain peak at 6 h after surgery, while the placebo group showed a pain peak at 4 h postoperatively. This delay in the onset of the pain peak reinforces the importance of pre-emptive analgesia.

The apparent analgesic efficacy of etoricoxib is also reflected in the reduced number of rescue medications consumed during the evaluation period. As expected, day 0 was the period with the highest rescue medication consumption for both groups, and during the overall postoperative period, the etoricoxib group ingested the lower number of rescue medications when compared to the Aceclofenac-paracetamol group.

Several literatures done from our institution also provides knowledge in terms of third molar extraction and pre emptive analgesic effect. [11-20]

CONCLUSION:

This study revealed that a low dose of etoricoxib has preemptive analgesic efect, resulting in the reduced use of analgesics after third molar removal. In conclusion, the number of patients requiring rescue analgesics was lower for etoricoxib when compared to NSAIDs after third

molar surgery.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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