

To Evaluate the Effect of Ketorolac Tromethamine, Tramadol and Placebo During Periodontal Surgery: A Double Blind Study

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ABSTRACT

Objectives: The efficacy of single oral dose Ketorolac Tromethamine, Tramadol and Placebo was evaluated in pain control after periodontal surgery.

Materials and Methods: The study design is a split mouth study involving three quadrants of the same patient. 20 patients requiring flap surgeries in at least three quadrants were recorded. Patients were randomly divided into three groups as per the medications given, either 10 mg ketorolac or 50 mg tramadol or placebo tablets at least 30 minutes before administration of local anesthesia (LA). The duration of surgery from the time of incision to the placement of the last suture is recorded. After the completion of the surgery, patients were asked to rate their subjective operative pain intensity using a visual analog scale.

Results: Differences were statistically significant in VAS score between ketorolac and placebo, and tramadol and placebo group. Comparison of sum of pain intensity showed significantly greater pain levels in the placebo than in the ketorolac group and tramadol group.

Conclusion: The results of this single-dose, parallel-group, and double blind placebo-controlled study showed that 10-mg

ketorolac and 50-mg tramadol administered immediately before periodontal surgery was effective for better response by the patient during the procedure. However, ketorolac and tramadol premedication neither affected delayed pain levels, nor postoperative analgesic consumption.

Key Words: Ketorolac, Tramadol, Anesthesia, Periodontal Surgery.

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INTRODUCTION

Pain is unpleasant sensory and emotional experience associated with tissue damage or during any surgical procedure. Pain after periodontal surgical procedures is a common occurrence. The perception of pain is highly subjective and therefore varies considerably among individuals. Injury to tissue during surgical procedure results in the release of chemical mediators of inflammation. Some of these mediators evoke pain (histamine, acetylcholine, and bradykinin), and others cause hyperalgesia, which is characterized by decreased pain threshold and increased sensitivity to supra-threshold stimuli.¹⁻³ Nonsteroidal anti-inflammatory analgesics drugs (NSAIDs) have become an important part of pain control in dental treatment. They inhibit the

formation and release of prostaglandins. It is proposed that when NSAIDs are given preoperatively, absorption and distribution of the medication may occur before the initiation of the tissue trauma, the ensuing synthesis of prostaglandins, and the subsequent inflammatory response. The NSAIDs have the advantage of being analgesic as well as anti-inflammatory and are therefore the rational choice for pain associated with inflammation. At the same time the NSAID's are liable to produce gastrointestinal adverse effects such as gastritis and peptic ulcer and thus should be used cautiously. Analgesics such as Tramadol, which are non-NSAIDs, can also be tried on dental patients.¹

Ketorolac Tromethamine

Ketorolac tromethamine is a nonsteroidal anti-inflammatory drug with an analgesic potency comparable with morphine, but without the opiate receptor-associated side effects.

The beneficial effects of ketorolac are probably due to its ability to block prostaglandin synthesis by preventing the conversion of arachidonic acid to the endoperoxides.

Tramadol

This centrally acting analgesic relieves pain by opioid as well as additional mechanisms. Its analgesic action is only partially reversed by opioid antagonist naloxene.

AIM AND OBJECTIVES

The purpose of the present study was to evaluate the analgesic effect of preoperative administration of ketorolac tromethamine 10 mg, Tramadol 50 mg and placebo on operative pain during periodontal surgery

MATERIALS AND METHODS

This was a randomized, single-dose, double-blind placebo controlled clinical trial of parallel design.

The study included 20 patients who were scheduled for flap surgery in atleast 3 quadrant.

In each patient, one quadrant was given ketorolac before the surgery and the other two quadrants were given tramadol and placebo before the surgery.

Exclusion Criteria

- Below 18 years of age,
- Pregnant patients, nursing mothers,
- Hypersensitive or allergic to NSAIDs and Opioids.
- Receiving treatment with systemic corticosteroids or anticoagulants, and
- Patients suffering from active peptic ulceration, gastrointestinal hemorrhage, liver or kidney disease, hemopoietic disorders, or any other significant medical problem.

Patients were randomized under double blind conditions to receive either 10 mg tablet of ketorolac tromethamine, 50 mg cap of tramadol or placebo tablet 30 minutes before administration of LA and divided into 3 GROUPS:

GROUP A (Ketorolac)

GROUP B (Tramadol)

GROUP C (Placebo)

All procedures were performed under LA, and the total volume of anesthetic used was recorded. Surgical procedure comprised of mucoperiosteal flap elevation, and root debridement was to be achieved. The duration of surgery from the time of incision to the placement of the last suture was recorded.

At the completion of the surgery, the patients were supplied with printed record forms and were asked to rate their subjective pain intensity during surgical procedure and post procedure using a Wong-baker faces pain rating visual analog scale (VAS).²

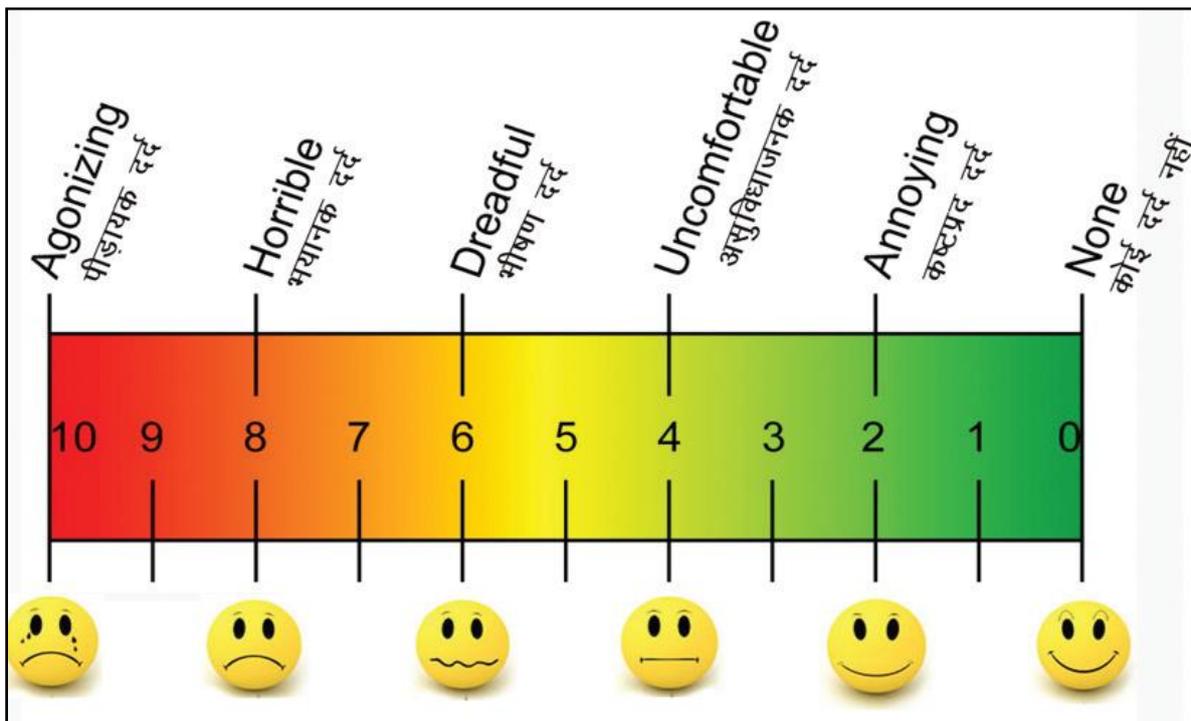


Fig 1: Wong-baker faces pain rating scale

RESULTS

Surgical factors that could have influenced the subject's analgesic responses to study medication included:

Duration of surgery,

Amount of LA administered

Patient's pain perception was noted on a scale of 0-10 using Visual analog scale (VAS)

Differences were statistically significant in VAS score between ketorolac and placebo, and tramadol and placebo group. Comparison of sum of pain intensity showed significantly greater pain levels in the placebo than in the ketorolac group and tramadol group. Results indicated that preoperative treatment with ketorolac significantly reduced initial pain intensity of operative pain as compared with tramadol and placebo.

Table 1: Ketorolac Group

Group A ketorolac	Amount of LA Given (ml)	Time Taken (min)	VAS Score
MEAN	2.57ML	98.60	0.90
SD	0.80	40.50	1.47

Table 2: Tramadol Group

Group B Tramadol	Amount of LA Given (ml)	Time Taken (min)	VAS Score
MEAN	2.87ml	90	1.90
SD	0.96	29.45	1.72

Table 3: Placebo Group

Group C placebo	Amount of LA Given (ml)	Time Taken (min)	VAS Score
MEAN	2.95ml	112.75	3.05
SD	0.66	41.24	1.80

Table 4: Comparison Between all three groups on the basis of amount of LA and time taken using T test.

GROUPS	Amount of LA Given (ml)	Time Taken (min)	VAS Score
A vs B	0.3	0.5	0.1
A vs C	0.2	0.3	<0.001**
B vs C	0.8	0.1	<0.05*

*Statistically significant (P < 0.05)

** Highly statistically significant.

DISCUSSION

Periodontal surgical cases cause severe pain and results inflammatory response. Use of analgesics NSAIDs can reduce the pain during operative procedure. The function of analgesic NSAIDs is primarily inactivation of cyclo-oxygenase, it is an enzyme that converts arachidonic acid into eicosanoids like prostaglandins and leukotrienes.⁴⁻⁶ There are two different pathway of cyclo-oxygenase have been identified: COX-1, exists in the stomach, intestines, kidneys, and platelets, and COX-2, expressed the part of inflammatory process.⁷ Ketorolac is a (NSAID) with potent analgesic effect with relatively less side effect. Numerous clinical trials of preoperative and postoperative pain treatment in patient have shown that ketorolac is very effective as the major opioid analgesics, like morphine, and more effective than codeine. Ketorolac can be administered intravenously, intramuscularly and orally. The recommended oral dosage is 0.25 mg/kg to a maximum of 1.0 mg/kg/day, with a maximum duration of 7 days.

Tramadol hydrochloride is used as another option rather than NSAIDs. This drug was first synthesized in 1962, and was commercially available in 1977. The course of action of tramadol are μ -opioid receptors (μ -OR) agonism and inhibition of the monoamine reuptake.⁸ Twenty-three metabolites of tramadol have been identified as a result of demethylation, oxidation and conjugation (sulphation and glucuronidation) in the liver.^{8,9} Analgesic action mechanism of tramadol is inhibition of the reuptake of monoamines, such as norepinephrine (NE) and serotonin [5-hydroxytryptamine (5-HT)] that are released from nerve endings. By inhibition of the reuptake of monoamines, it inhibits pain transmission in the central nervous system.¹⁰ Tramadol is primarily work as serotonin reuptake inhibitor,

tramadol for noradrenaline reuptake inhibition is primarily responsible for the agonist activity on the μ -opioid receptor.¹¹ NSAIDs produce side effects such as gastric irritation which leads to ulceration and bleeding disorders. Despite the inflammatory response, one drugs has been used in this study was a non-NSAID, so that we can compare analgesic efficacy of non-NSAIDs versus NSAID's to placebo which was evaluated in this study. In this study the results were significant with the analgesic efficacy of single oral doses of either tramadol or ketorolac for periodontal flap surgeries with an acceptable incidence and severity of side effect. We did not find significant difference between the analgesic efficacy of tramadol and ketorolac however the value of ketorolac was high than tramadol. We also looked at whether there is any need for analgesics for post-surgical pain as the patient is already receiving a local anesthetic prior to surgery and found that a significant proportion of patients do not experience pain severe enough to require analgesics. Single oral dose of either tramadol or ketorolac was very efficient than placebo in relieving pain, over the first 6 h. Other studies corroborate with results.^{2,3} We find preoperative administration of analgesics were more efficacious in relieving the pain than postoperative administration. Analgesic function of tramadol is due to higher affinity binding of the O-demethylated metabolite to opioid receptors. It has a quick onset of action. The analgesic effect of tramadol starts within an hr and reaches to peak within 2-3 hr.

The preoperative administration of ketorolac was found to be effective. Ketorolac inhibits the enzyme cyclo-oxygenase pathway results inhibiting the synthesis of prostaglandins, which is a mediator of inflammation and pain. Periodontal surgical produces a fair amount of injury to the surrounding tissue, which leads to

release of arachidonic acid that is converted into prostaglandin by cyclo-oxygenase. Inhibition of cyclo-oxygenase pathway even before releasing of arachidonic acid from injured tissue ensures the synthesis of prostaglandins is blocked and pain and inflammation is reduced. Sufficient residual pain remains despite adequate local anesthesia. Ketorolac has been reported in some patient to produce nausea, vomiting, dyspepsia, and prolongation of bleeding time, whereas tramadol effects on the gastrointestinal tract are fairly low and its CNS effects are more prominent likewise anxiety, confusion, visual disturbance, and dependence. Pain assessment using a VAS was appropriate for this study. The results indicated that the measure of pain intensity is adequately valid. In other studies.¹²⁻¹⁴

The pre- and postoperative administration of ketorolac was found to be equally effective in controlling dental pain. Tramadol was found to be more effective postoperatively than preoperatively. The present study demonstrated that ketorolac and tramadol treatment immediately before periodontal surgery significantly reduced operative pain as compared with placebo; however pain felt during procedure is less in ketorolac than tramadol.

Preoperative ketorolac treatment significantly reduced pain intensity on the day of surgery.

CONCLUSION

The results of this single-dose, parallel-group, and double blind placebo-controlled study showed that 10-mg ketorolac and 50-mg tramadol administered immediately before periodontal surgery was effective for better response by the patient during the procedure.

However, ketorolac and tramadol premedication neither affected delayed pain levels, nor postoperative analgesic consumption.

No disadvantages related to this method of administration were noted.

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