

A Potent Pre-Medication in Periodontal Surgical Procedures - Ketorolac Tromethamine 10mg: A Randomized Controlled Trial.

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Short Communication

Received: 12/02/2014
Revised: 21/02/2014
Accepted: 07/03/2014

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Keywords: Ketorolac, periodontal surgery, pain, analgesia, pre-medication.

ABSTRACT

Oral ketorolac tromethamine (KT) in 10 and 20mg postoperative doses in an oral surgery pain model have proven to be equally analgesic as 400mg ibuprofen, and significantly better than acetaminophen and acetaminophen-codeine combinations. It prevents pain by blocking arachidonic-acid pathway. To evaluate the analgesic effect of preoperative KT-10mg, on pain during and after open flap debridement (OFD) surgery. 42-patients were randomized (21-controls, 21-tests). Oral KT-10mg was given to test-group 10 minutes before administration of the local-anesthesia (L.A), prior to OFD. Visual analogue scale (VAS) was used to assess pain, immediately after OFD, and every hour after that until, first onset of pain, & time of onset of pain. The mean values of time of onset of pain in test-group was 3.57 hours, while it was 2.33 hours in the control-group ($p=0.005$). KT-10mg pre-medication was effective in pain reduction during surgery. However, it neither affected delayed pain levels, nor postoperative analgesic consumption.

INTRODUCTION

Postoperative pain following oral surgical procedures is a matter of considerable consequence to most patients, and clinical strategies aimed to reduce its incidence and severity is greatly appreciated.

Factors contributing to the occurrence of postoperative dental pain are complex, but many are related to the inflammatory process that is initiated by surgical trauma [1]. 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. The prostaglandins have been demonstrated to act, at least in part, by the latter mechanism [2].

Pain after periodontal surgical procedures is a common occurrence. Many factors may influence pain intensity, such as the nature, duration, and extent of the surgery, and psychological aspects, such as stress and anxiety [3]. Postoperative pain has been reported to peak in the first 24 hours after periodontal surgery. The intensity of this pain is related to the surgical procedure itself [4].

Ketorolac tromethamine (KT) is a nonsteroidal anti-inflammatory drug(NSAID) with an analgesic potency comparable to morphine, but without the opiate-receptor-associated side effects [5]. The beneficial effects of ketorolac are probably due to the drug's ability to block prostaglandin synthesis by preventing the conversion of arachidonic acid to the endoperoxides.

Previous studies have shown that the oral formulation in 10 and 20 mg postoperative doses in an oral surgery model provided the same analgesia as 400 mg ibuprofen, and significantly better analgesia than acetaminophen and acetaminophen codeine combinations [6]. However, limited research exists comparing the effect of such drugs, when given pre-operatively & their effect on patient's pain perception, during & after periodontal surgery.

The primary purpose of the present study was to evaluate the analgesic effect of preoperative

administration of KT 10 mg, on pain during and after open flap debridement surgery. Its secondary objectives were: 1) To evaluate the effect of 10 mg single dose of KT on pain control during and after open flap debridement. 2) To evaluate the analgesic efficacy of KT on pain control till the first onset of pain. 3) To evaluate the efficacy of KT on patient's perception of pain based on VAS scale.

MATERIALS AND METHOD

This was a randomized control trial. Prior to commencement of the study, institutional ethical committee approval was obtained. 42 patients indicated and scheduled for periodontal surgery underwent periodontal surgery of a particular quadrant, selected with flip coin method to either receive no medication (Control n=21) or KT 10 mg (test n=21).

Patients were selected from the OPD of Dept. of Periodontics, KMSDCH. Patients fulfilling following criterias were excluded from the study, < 18 years of age, pregnant patients, nursing mothers, patients receiving treatment with systemic corticosteroids or anticoagulants, patients suffering from active peptic ulceration & gastrointestinal hemorrhage, patients who were hypersensitive or allergic to NSAIDs. All the patients taking part in this study were informed regarding the study and informed consent was obtained. Principal investigator evaluated all the patients. The dose of oral KT 10 mg was given 10 minutes before the administration of the local anesthesia prior to beginning of the surgical procedure.

Patients were explained about the visual analogue scale (VAS) and asked to assess pain according to it. VAS commonly consists of a vertical or horizontal line, 10 cm in length, with words that convey "no pain" at one end, and "worst pain" at the opposite end. It was modified using numerical rating scales and Wong-Baker Faces Pain Rating Scale. The patients were asked to place a mark on the line that corresponded to the intensity of the pain he or she experienced. Assessments were made at the following times:

- At the end of surgical procedure and every hour after that, until;
- First onset of pain.
- The time when patient started taking prescribed analgesics (time of onset of pain.)

The principal investigator dispensed medications. Patients in test group did not take any medication after the surgical procedure nor did the patients in the control group. Patients were given conventional NSAID's after the surgery for three days, only after the first onset of pain, and then on, as per the prescription provided by the surgeon. Recordings were marked by the patient, and had informed the principal investigator regarding the hour of first onset of pain and had handed over the VAS score recorded sheet to the principal investigator during the next visit. The examiner examining the pain score was kept blinded. Patients were given a telephonic reminder on the number provided by the patient at 1,2,3,4,5 and 6 hours.

RESULTS

As shown in table 1, the initial pain episodes for patients in both the groups are shown. For test group, 0 patient had pain at 1st hr, 1 patient (4.76) had pain at 2nd hr, 4 patients (19.04) had pain at 3rd hour, 13 patients (61.9) had pain at 4th hr, 19 patients (90.47) had pain at 5th hr & by 6th hr, all 21 patients (100%) in this group experienced pain.

Table 1: Initial pain episode

Hour of experiencing pain	Test		Control	
	No.	%	No.	%
0	0	0	0	0
1	0	0	4	19.04
2	1	4.76	13 (+9)	61.9
3	4 (+1)	19.04	18 (+5)	85.71
4	13 (+9)	61.9	21 (+3)	100
5	19 (+6)	90.47	21 (+0)	100
6	21 (+2)	100	21 (+0)	100
Total	21	100	21	100

Similarly, the initial pain episodes for patients in the control group are shown. 4 patients (19.04%) had pain at 1st hr, 13 patients (61.9%) had pain at 2nd hr, 18 patients (85.71%) had pain at 3rd hour & all 21 patients (100%) had pain by the 4th hr. Graph 1 shows the pictorial representation of the same data.

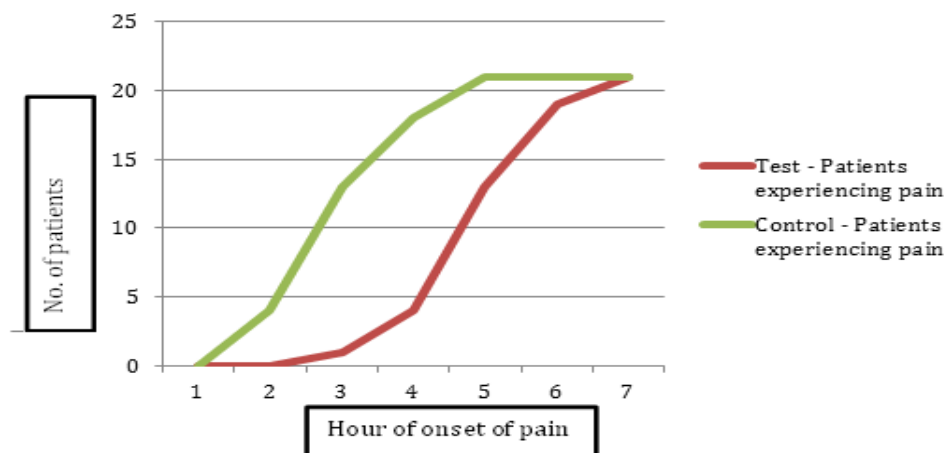
Table 2 shows intensity of pain experienced by both the groups, as expressed in VAS. The mean score for test group was 0.29±0.46, 0.38±0.50, 0.48±0.60, 0.90±0.31, 1.55±1.0, 1.36±0.67 & 1.33±1.98 respectively at baseline, 1st, 2nd, 3rd, 4th, 5th & 6th hour. Similarly for control group, it was 1.10±1.26, 2.22±2.07, 3.56±2.92,

1.00±0.00 & 2.00±0.00 respectively for baseline, 1st, 2nd, 3rd & 4th hour respectively. The difference between the 2 groups was statistically significant for baseline, 1st & 2nd hour (p value = 0.004, 0.00, 0.001 respectively.).

Table 2: Intensity of pain

	VAS (Mean±SD)						
	0	1	2	3	4	5	6
KT (test)	0.29±0.46	0.38±0.50	0.48±0.60	0.90±0.31	1.55±1.0	1.36±0.67	1.33±1.98
No drug (control)	1.10±1.26	2.22±2.07	3.56±2.92	1.00±0.00	2.00±0.00	-	-
P value	0.004	0.000	0.001	0.58	0.13	-	-

Graph 1: Initial pain episode for both the groups



DISCUSSION

The present study demonstrated that KT treatment immediately before periodontal surgery significantly reduced operative pain as compared to no medication group. Patients receiving the preoperative dose of KT had a significant increase in the amount of time between the presurgical drug administration and the need for postoperative analgesics. The rationale for prophylactic NSAIDs administration is that the presence of the drug in the tissues at the time of surgery results in blocking of both the synthesis and direct effects of prostaglandins, and thereby limits operative pain and other components of surgically induced inflammation. Studies on clinical efficacy of NSAID premedication, however, seem to suggest that surgical pain control is strictly related to many factors, such as patient selection, nature of medication, and drug regimen [7]. Furthermore, although NSAIDs may produce adequate analgesia and anti-inflammatory effects, the unwanted side effects may limit their practicality.

Oral KT is completely absorbed, with a mean peak plasma concentration occurring at an average of 44 minutes after a single 10-mg dose [8]. It is strongly (99%) protein bound, with the degree of binding apparently independent of the plasma concentration of the drug [9]. Plasma half-life is 4 to 6 hours in the normal adult, and analgesia may be maintained for 6 to 8 hours [10]. Although preoperative KT treatment significantly reduced pain intensity on the day of surgery, delayed pain levels were not affected by presurgical treatment [11]. It is possible to admit that this pain model may have masked the delayed analgesic efficacy of preoperatively administered ketorolac.

This study also confirmed the results of other studies regarding post-operative pain control, as no pain for first few hours or mild pain then on was noticed by patients taking ketorolac medication as compared to no medication group.

CONCLUSION

The results of this single-dose, parallel-group, and single blind study showed that 10-mg KT administered immediately before periodontal surgery was effective for better response by the patient during the procedure in terms of pain reduction. However, ketorolac premedication neither affects delayed pain levels, nor postoperative analgesic consumption. No disadvantages related to this method of administration were noted.

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