

Comparison Between Preoperative Use of Sublingual Piroxicam with that of Oral Ketorolac on Postoperative Pain Following Single Visit Root Canal Therapy –A Double Blind Randomized Control Study

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Abstract: The purpose of this study was to determine if preoperative use of single dose of 20mg sublingual piroxicam and 20mg dispersible ketorolac would significantly reduce postendodontic pain, when compared with 600mg ibuprofen following single visit root canal treatment. An additional objective was to compare the efficacy of sublingual piroxicam and dispersible ketorolac on post endodontic pain following single visit root canal treatment. A total of 70 adult patients consented to a double-blind, single-dose oral administration of 20mg of ketorolac, 20mg of piroxicam, 600 mg of ibuprofen, before single visit root canal therapy. Each Patient-reported visual analog scale ratings of pain intensity were conducted upon initial clinical presentation and at 6, 12, 24 and 48 hours and 72 h after completion of single visit root canal treatment.

The results showed that at 6hrs period after single visit root canal treatment, all the three drugs Ketorolac, Piroxicam, Ibuprofen are equally effective in reducing post operative pain. Observation at 12th and 24th hours post operative period showed that ketorolac and Piroxicam demonstrated significantly better pain relief than ibuprofen. At 24th and 48th hours post operative period Piroxicam was statistically significant in reducing post endodontic pain when compared with ketorolac and ibuprofen.

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I. Introduction

Endodontics deals with the diagnosis and treatment of pulpal and periradicular diseases. The main indications for root canal therapy are irreversible pulpitis and pulpal necrosis caused by carious process, tooth fracture, or dental trauma. The root canal therapy can be performed in either multiple visits or in single visit. Single visit root canal treatment is attractive to the patient because it saves time, reduce the cost of the procedure and is expected to be less stressful.

Although endodontic treatment eliminates pain, postoperative pain following root canal treatment has been reported to be 3–58% (1,2). Postoperative pain is thought to be related, to a periapical inflammatory response produced by the endodontic instrumentation. If the periapical inflammatory reaction is a major contributor to post endodontic pain, then it is possible that administration of a nonsteroidal anti-inflammatory drug (NSAID) before root canal therapy will interfere with the inflammatory process before it begins; therefore, presumably decreasing post endodontic pain. Preemptive analgesia has been defined as an antinociceptive treatment that prevents altered processing of afferent input amplifying postoperative pain.

Ibuprofen generally is considered the prototype of contemporary NSAIDs and has a well documented efficacy and safety profile. Clinical studies indicate ketorolac single-dose efficacy greater than that of morphine, pethidine (meperidine) and pentazocine in moderate to severe postoperative pain. Piroxicam 20 mg and 40 mg, produced significantly longer durations of analgesia than aspirin 648 mg, and it appears that the analgesic effect of piroxicam may extend for up to 24 hours in a substantial proportion of patients. Apart from common oral route of drug administration, novel oral drug delivery systems that dissolve or disperse quickly in a few seconds after placement in the mouth such as sublingual, dispersible systems are introduced. Efficacies of these systems have been evaluated in randomized clinical trials conducted in acute postsurgical pain patients. In spite of advantages such as drugs given in these route bypasses the GI tract and hepatic portal systems, increased bioavailability, rapid onset of action (3,4). Endodontic literature is replete with investigations on efficacy of these delivery systems in reducing post endodontic pain.

The purpose of this study was to determine if preoperative use of single dose of sublingual piroxicam and dispersible ketorolac would significantly reduce postendodontic pain, when compared with ibuprofen following single visit root canal treatment. An additional objective was to compare the efficacy of sublingual piroxicam and dispersible ketorolac on post endodontic pain following single visit root canal treatment.

II. Materials And Methods

This study was conducted as a double blind randomized control trial. Patients who presented to the Government Dental College, Kozhikode, Kerala postgraduate endodontic clinic were evaluated for this study. A clinical examination was conducted that included thermal and electric pulp testing, percussion and palpation evaluation, periodontal probing, mobility assessment, and a periapical radiograph. All past and present symptoms were noted. A diagnosis was determined on the basis of the history, clinical, and radiographic features.

Inclusion criteria:

1. Patients in whom 2 posterior teeth are diagnosed as having irreversible pulpitis (with similar root canal morphology in same arch on contralateral side).
2. Patients reporting with spontaneous pain of at least 3 (0-10) in visual analog scale before root canal therapy.
3. Both genders, between 20-50 years of age.
4. Patient reads and understands questionnaires.
5. Patient provides informed consent.

Exclusion Criteria:

1. History of allergy to NSAIDs or local anesthetics.
2. Younger than 18 yr or older than 65 yr. Analgesic intake within last 12 h.
3. History of ulcers, active asthma, decreased renal function, decreased hepatic function, hemorrhagic disorders, or poorly controlled diabetes mellitus.
4. Current use of drugs contraindicated with NSAIDs.
5. Pregnant or nursing.
6. Teeth with advanced periodontal diseases.
7. Teeth that were tested as non vital.

Procedure Methodology:

If a patient met all the above criteria, he/she was informed of the nature of study and invited to participate. 70 patients signed a consent form outlining the procedure and its possible risks. The patients were divided randomly into 2 groups; each group has 35 patients. Each patient had two teeth to be treated for root canal treatment. Teeth were randomly divided into test teeth and control teeth. One hour before the treatment patients in the first group received preoperative single dose of 20mg dispersible ketorolac for the test teeth following which single visit root canal treatment was completed. During the next appointment which was scheduled one week after the first one, same patient received preoperative single dose of ibuprofen before the single visit root canal treatment for the control teeth. Similarly patient in the second group received preoperative single dose of 20mg sublingual piroxicam for the test teeth and ibuprofen for the control teeth following which single visit root canal treatment was completed. The teeth were distributed equally among the groups relative to tooth type, root length, apparent canal size. One operator treated all the patients in this study.

One hour after oral administration of the test medication. Local anesthetic was administered and endodontic access was achieved under rubber dam isolation. Working lengths were determined by using electronic apex locators (Propex- Dentsply, Maillefer). Canal preparation was performed using a crown-down technique. Cleaning and shaping were performed in the presence of EDTA gel. Sodium hypochlorite (5.25%) and saline were used as irrigants. According to the size of the final preparation the master gutta percha cone was selected and verified with radiograph. Canals were dried thoroughly using paper points. Finally complete obturation of canals was performed using gutta percha and seal apex sealer (Kerr, Bioggio) using lateral compaction technique. A cotton pellet was placed in the pulp chamber space and Cavit (ESPE Dental) was used as a temporary filling material. The occlusion was evaluated and reduced when necessary. Final radiographs were taken.

The patients were dismissed with a VAS form to fill out at 6,12,24,48, and 72 h after initiation of therapy. Postoperative instructions and an extra dosage of the test medication were given to the patient. The patients were instructed to indicate in the pain survey if this additional medication was required and record the time it was taken.

Statistical Analysis

On completion of the study data from VAS scores are analyzed using SPSS version 19 and statistically analyzed using paired t test.

III. Result

Out of the 70 subjects, 35 subjects in each group. Group 1(Dispersible Ketorolac and Ibuprofen), 3 subjects did not return the VAS form and 3 subjects did not have their tooth obturated, and in group 2(Sublingual Piroxicam and Ibuprofen), 3 subjects did not return the VAS form 2 subjects did not have their tooth obturated, and were excluded from study and only 59 subjects were analyzed.

Out of 59 subjects, 24 males (40.7%) and 35 (59.3%) females participated in this study. Group: 1 of the 29 subjects included in this group 10 (34.5%) were males and 19 were females (65.5 %). Group: 2 of the subjects included in this group 14 (46.7%) were males and 16 were females (53.3 %). Out of 59 subjects participated in the study, 59.3% and 40.3% are in age group of 18-30, 31-40 respectively. Group: 1 of the 29 subjects included in this group, the minimum age included in this group was 19 and the maximum age was 40 years with mean age of 28.79. Group: 2 Of the 30 subjects included in this group, the minimum age included in this group was 19 and the maximum age was 42 years with mean age of 29.10.

At 6hrs after single visit root canal treatment, all the three drugs Dispersible Ketorolac, Sublingual Piroxicam, Ibuprofen are equally effective in reducing post operative pain. Observation at 12th and 24th hour showed that Dispersible Ketorolac and Sublingual Piroxicam are significantly effective in reducing postoperative pain when compared with ibuprofen. Which was statistically significant (12hr p value = 0.00, 0.00; 24hr p value = 0.03, 0.00 respectively). After 48 hours, all the patients showed pain reduction. When comparing the effectiveness of Dispersible Ketorolac and Sublingual Piroxicam, there was no significant difference between Dispersible Ketorolac and Sublingual Piroxicam at 6th, 12th, and 72nd hour after root canal treatment. However at 24th and 48th hour after completion of root canal treatment Sublingual Piroxicam was statistically significant in reducing pain (24hr p value = 0.00; 48hr p value = 0.02).

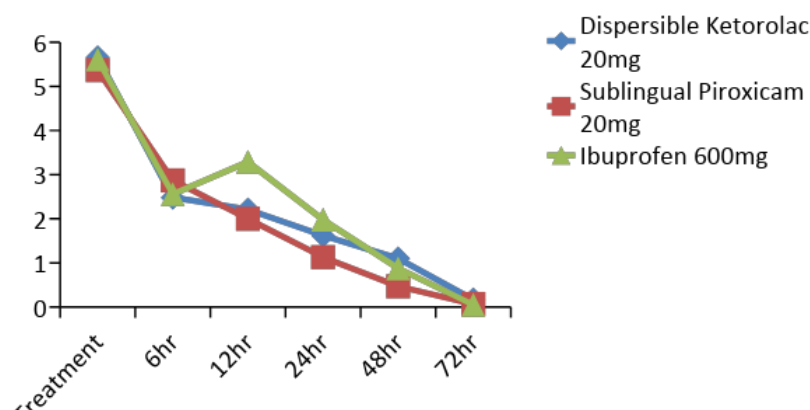
Table no 1: post endodontic pain assessment - comparison between Dispersible Ketorolac and Ibuprofen at various time intervals by paired t test.

Group	Paired Samples	Sig(2-tailed)
1	Pair 1 At 6thhr Dispersible Ketorolac - Ibuprofen	0.466
1	Pair 2 At 12thhr Dispersible Ketorolac - Ibuprofen	0.000
1	Pair 3 At 24thhr Dispersible Ketorolac - Ibuprofen	0.003
1	Pair 4 At 48thhr Dispersible Ketorolac - Ibuprofen	0.356
1	Pair 5 At 72ndhr Dispersible Ketorolac - Ibuprofen	0.640

Table no 2: post endodontic pain assessment - comparison between Sublingual Piroxicam and Ibuprofen at various time intervals by paired t test.

Group	Paired Samples	Sig(2-tailed)
2	Pair 1 At 6thhr Sublingual Piroxicam - Ibuprofen	0.286
2	Pair 2 At 12thhr Sublingual Piroxicam - Ibuprofen	0.000
2	Pair 3 At 24thhr Sublingual Piroxicam - Ibuprofen	0.000
2	Pair 4 At 48thhr Sublingual Piroxicam - Ibuprofen	0.156
2	Pair 5 At 72ndhr Sublingual Piroxicam - Ibuprofen	0.662

FIG 1: Line graph - representing the effect of prophylactic administration of various drugs on postoperative pain following endodontic treatment at various time intervals.



IV. Discussion

Post operative pain is more likely to arise within few hours following RCT. The prevalence of postoperative pain following root canal treatment has been reported to be 3–58% (1, 2). Patients who have postoperative pain need analgesics that have fewer side effects for relieving the pain. Reduction in postoperative pain after prophylactic administration of NSAIDs has been proved both in oral surgery models (5) and endodontic models (6). Preemptive administration of NSAIDs before conventional root canal therapy can block the COX pathway and might block the pain sensation before it even begins. COX (also known as PG endoperoxide H synthase) catalyzes the conversion of arachidonic acid to PGH₂. This is the key and rate limiting step in the biosynthesis of prostanoid. Of the two isoforms (COX-1 and COX-2), COX-1 are constitutively expressed in cells and are responsible for the production of cytoprotective prostanoids. In contrast COX-2 are regulated by extracellular stimuli such as cytokines and are considered to be associated with the production of inflammatory prostanoids (7).

Apart from common oral route of drug administration, novel oral drug delivery systems that dissolve or disperse quickly in a few seconds after placement in the mouth such as sublingual, dispersible systems are introduced. Efficacies of these systems have been evaluated in randomized clinical trials conducted in acute postsurgical pain patients (3, 4). In spite of advantages such as drugs given in these route bypasses the GI tract and hepatic portal systems, increased bioavailability, rapid onset of action. Endodontic literature is replete with investigations on efficacy of these delivery systems in reducing post endodontic pain.

This study was conducted as a double blind randomized control trial. The operator and the patients were both unaware of capsule contents (double-blind randomized clinical trial). Double-blind drug administration and the elimination or matching of other variables can lead to increased internal validity and more precise results. In this study, only patients in whom 2 posterior teeth are diagnosed as having irreversible pulpitis (with similar root canal morphology in same arch on contralateral side) are included. One of the disadvantages of studies measuring post endodontic pain is that pain is subjective and is different for each individual. So it is inappropriate to evaluate effectiveness of drug by comparing the pain perception between different individuals. To avoid this in our study patients with two teeth diagnosed as having irreversible pulpitis are selected and post endodontic pain perception is measured after administration of two different drugs in the same individual. VAS was chosen to measure pain in this study as it is valid, reliable, easily understood by patients and widely used in endodontic literature (10).

Ibuprofen blocks both the COX-1 and COX-2 enzymes, but it is a safe, cost-effective with highly effective analgesic and anti-inflammatory action for postendodontic pain (8). Some authors found that prophylactic dose of 600mg ibuprofen reduced post endodontic pain. Ketorolac is a member of the pyrrolo-pyrrole group of NSAIDs structurally and pharmacologically related to zomepirac and indomethacin. The drug is strongly (99%) protein bound, with the degree of binding apparently independent of the plasma concentration of the drug (9). For this reason, an initial loading dose of approximately twice the maintenance dose is recommended.

Piroxicam is one of the oxamic derivatives, a class of eno-lic acids that have antiinflammatory, analgesic, and antipyretic activity. Piroxicam is completely absorbed after oral administration; peak concentrations in plasma occur within 2 to 4 hours. Neither food nor antacids alter the rate or extent of absorption. There is enterohepatic cycling of piroxicam, and estimates of the half-life in plasma have been variable; a mean value appears to be about 50 hours. After absorption, piroxicam is extensively (99%) bound to plasma proteins. At steady state (e.g., after 7 to 12 days). This might attribute to our result that prophylactic

administration of 20 mg of sublingual piroxicam before root canal therapy was more effective at reducing post endodontic pain at 12 and 24 h after initiation of treatment, when compared with 600 mg of ibuprofen. There was no significant difference between efficacy of sublingual piroxicam, dispersible ketorolac and ibuprofen at 48th hour and 72nd hour after root canal treatment. This was expected, because the endodontic procedure should have reduced the pain by this time.

V. Conclusion

In summary prophylactic single dose administration of Dispersible Ketorolac, Sublingual Piroxicam, and Ibuprofen are equally effective in reducing postoperative pain at 6 hour after single visit root canal treatment. The results of this study also showed that prophylactic single dose administration of Sublingual Piroxicam relieved post endodontic pain more effectively than Dispersible Ketorolac at 24 – 48 hrs duration after single visit root canal treatment. Sublingual piroxicam's analgesic efficacy, longer duration of action, lower gastrointestinal toxicity, suggest that it may be useful as a preemptive analgesic when post endodontic pain is anticipated.

References

- [1]. Ng YL, Glennon JP, Setchell DJ, Gulabivala K. Prevalence of and factors affecting post-obturation pain in patients undergoing root canal treatment. *Int Endod J* 2004 Jun;37(6):381-91.
- [2]. Sathorn C, Parashos P, Messer H. The prevalence of postoperative pain and flare-up in single- and multiple-visit endodontic treatment: a systematic review. *Int Endod J* 2008 Feb;41(2):91-9 Epub 2007 Oct 23.
- [3]. Trindade PA, Giglio FP, Colombini-Ishikiriama BL, et al. Comparison of oral versus sublingual piroxicam during postoperative pain management after lower third molar extraction. *Int J Oral Maxillofac Surg.* Mar;40(3):292-7.
- [4]. Nappi G, Micieli G, Tassorelli C, Viotti E, Altavilla T. Effectiveness of a piroxicam fast dissolving formulation sublingually administered in the symptomatic treatment of migraine without aura. *Headache* 1993 Jun;33(6):296-300.
- [5]. Dionne RA, Campbell RA, Cooper SA, Hall DL, Buckingham B. Suppression of postoperative pain by the preoperative administration of ibuprofen in comparison to placebo, acetaminophen, and acetaminophen plus codeine. *J Clin Pharmacol* 1983;23:37-43.
- [6]. Flath RK, Hicks ML, Dionne RA, Pelleu GB. Pain suppression after pulpectomy with preoperative flurbiprofen. *J Endodon* 1987;13:339-47.
- [7]. Yucel-Lindberg T, Ahola H, Nillson S, Carlstedt-Duke J, Modeer T. Interleukin 1-_α induces expression of cyclooxygenase-2 mRNA in human gingival fibroblasts. *Inflammation* 1995;19:549-60.
- [8]. Habib S, Matthews RW, Scully C, Shepherd JP. A study of the comparative efficacy of four common analgesics in the control of postsurgical dental pain. *Oral Surg Oral Med Oral Pathol* 1990;70:559-63.
- [9]. Rooks WH, 2nd, Maloney PJ, Shott LD, et al. The analgesic and anti-inflammatory profile of ketorolac and its tromethamine salt. *Drugs Exp Clin Res* 1985;11(8):479-92.
- [10]. Battrum D, Gutmann J (1996) Efficacy of Ketorolac in management of pain associated root canal treatment. *J Can Dent Assoc* 62, 36-42.

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