







## Effectiveness of Single Dose Premedication of Piroxicam and Prednisolone on Post Endodontic Pain in One Visit Root Canal Treatment: A Randomized Clinical Trial

 Anum TANWIR,  Shahbaz AHMED,  Hira AKHTAR,  Umair WAHID,  
 Maria Shakoor ABBASI,  Naseer AHMED

### ABSTRACT

**Objective:** The objective of this study was to compare the effectiveness of premedication drugs including single dose Piroxicam and Prednisolone in regard to post endodontic pain at different time intervals (24, 48, 72 and 96 hours) after single visit root canal treatment.

**Methods:** This randomized clinical trial (registration no. NCT04124822) was performed in operative dentistry department of a private clinical institute. One hundred twenty patients identified with symptomatic irreversible pulpitis were included in the study. The pain intensity levels were marked through the use of visual analog scale (VAS) before the commencement of treatment. The participants were randomly allocated in three groups, Group I (n=40) received no medication (control), Group II (n=40) received Piroxicam (20 mg) and Group III (n=40) received Prednisolone (20 mg). The drugs were administered thirty minutes before the endodontic procedure was initiated. Root canal treatment was carried out followed by placement of provisional restoration in a single appointment. The patients were instructed to continue marking their pain intensity levels after 24, 48, 72 and 96 hours using VAS. All patients were called for follow up after 4 days for clinical evaluation and the placement of permanent restoration. The effectiveness of each drug over different time interval was studied employing ANOVA test. The significance level was set at  $P \leq 0.05$ .

**Results:** The results of the present study revealed that a higher percentage of patients in all 3 groups, reported no post-operative pain at all evaluated time durations (24, 48, 72, and 96 hours). However, the long term effectiveness (96 hours) of both drugs to reduce post-endodontic pain was observed to be statistically insignificant. There was no significant difference in demographic data in terms of age ( $P=0.14$ ), gender ( $P=0.12$ ), whilst tooth type ( $P \leq 0.05$ ) showed statistically significant value.

**Conclusion:** Pre-medication with either single dose piroxicam or prednisolone was able to prevent post-endodontic pain in patients with symptomatic irreversible pulpitis.

**Keywords:** Endodontic treatment, piroxicam, prednisolone, post-endodontic pain, pre-medication

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From the Department of Pediatric Dentistry (A.T.  anum.tanwir@gmail.com), Baqai Medical University (BMU), Karachi, Pakistan; Department of Operative Dentistry & Endodontics (S.A., H.A., U.W.), Dr. Ishrat-ul-Ebad Khan Institute of Oral Health Sciences (DIKIOHS) at Dow University of Health Sciences (DUHS), Karachi, Pakistan; Department of Prosthodontics (M.S.A., N.A.), Altamash Institute of Dental Medicine (AIDM), Karachi, Pakistan

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### HIGHLIGHTS

- Single dose premedication simplifies conventional treatment strategy.
- Both drugs Piroxicam and Prednisolone have shown to be equally effective with no side effects reported.
- With immediate pain relief and anxiety reduction, reduced treatment time.

sibility of residual symptoms which can be attributed to the effects of inflammation regarded as PE. Roughly 25-69% patients reported moderate to severe post-operative pain. (2, 4, 5). Mild endodontic pain rarely lasts and is mostly handled with anti-inflammatory drug (non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen) (4, 5). Studies reported that a preoperative symptomatic patient will experience moderate to severe pain 47-60% in the first 24 hours and 16-24% of patients at 72 hours (6).

### INTRODUCTION

The management of post endodontic pain (PE) is still a problem and a topic of interest. Root canal treatment involves the removal of inflamed or necrotic pulp tissue and sealing the root canal system against the bacterial recontamination. However, at times pain relief is not instant and permanent (1-3). There is a pos-

Many approaches have been investigated for pain relief after root canal procedure. Pharmacological strategies such as narcotics, analgesics, intra-canal and systemic glucocorticosteroids (GCS), NSAIDs, long action anesthetics, antibiotics, trephination, occlusal reduction, and hypnosis (7, 8). Many drugs have been tested for the management of (PE). The most commonly preferred drugs are NSAIDs and steroids or a combination of these two (7-10).

Modern dentistry focuses on the newer models of pain control, one of which is the use preventive measures, to control pain before the procedure which ultimately helps in reducing the post-operative pain (11). In addition, studies have shown that preoperative and postoperative pain shows strong relationship (11). The rationale of administration of preemptive analgesia is to allow the clinician to extend the analgesic effect of the drug via prevention of peripheral sensitization (7, 8). Additionally, a single dose of anti-inflammatory drug administered before the procedure releases anti-inflammatory mediators to combat with acute inflammation and reduces side effect commonly noticed with repeated drug dose regime during post-operative period (9, 10).

Traditionally, in order to relief postoperative pain, administration of local anesthesia was the preferred technique. This pain relief therapy has limited efficacy in irreversible pulpitis, due to difficulty in achieving effective anesthesia in these clinical scenarios (11). Therefore, nowadays oral administration of drugs is a preferred clinical technique to manage patients' pain. The procedure holds the advantage of being convenient and effective which reduces patient anxiety and discomfort (12, 13). NSAIDs has the ability to inhibit PG synthesis and effectively lower pain threshold levels; making them the gold standard against which the efficacy of other analgesic drugs are evaluated (14).

A recent study conducted on pain control by Praveen et al. (15) have reported that ketorolac group (short acting NSAID) showed significant reduction in pain scores till 6 hours; achieving peak analgesia in 2 to 3 hours. However, the drug failed to provide pain relief for longer duration when compared to Prednisolone (corticosteroid); which provided pain relief up to 12 hours. Similar results were observed when the efficacy of single pretreatment dose of Prednisolone was compared with placebo or ketorolac. Prednisolone showed to be more effective in alleviating PE compared with the other drugs (10, 15, 16).

Furthermore, various studies have favoured the use of Prednisolone over other groups as it is able to provide longer therapeutic effect (17, 18). This advantageous property is due to its longer half-life of 12 to 36 hours and the ability of the drug to reach peak plasma level in 1-2 hours (17, 19). Piroxicam is a nonselective NSAID, its half-life is 50 hours and it reaches peak level 1.5 to 2 hours after oral administration. NSAIDs inhibits PG synthesis by slowing down the activity of the enzyme, Cyclooxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2) (19).

This study aimed to evaluate the effect of preemptive drug on pain control. The effectiveness of long acting corticosteroid

against long acting NSAIDs was evaluated up to 96 hours in order to determine the best pharmacological agent for the management of post-endodontic pain control.

## MATERIALS AND METHODS

This randomized clinical trial was conducted in the department of operative dentistry at a private clinical institution. For ethical consideration of the trial, approval was obtained on 10<sup>th</sup> May 2018 from Institutional Ethical Review Board (IRB-1142/DUHS/Approval/2018/54) and it is registered under clinical trial registry (registration no. NCT04124822). As for confidentiality and anonymity of patient's data, verbal and written consents were taken on the consent forms.

Patients belonging to age group of 20-40 years were included. Single rooted tooth diagnosed with symptomatic irreversible pulpitis with visual analog scale (VAS) score 5-10, and healthy periapical area, having negative history of painkillers administered with 7 days before procedure were included in the study. Patients with any systematic problem, allergic to NSAIDs and/or corticosteroids, pregnant or lactating and previously treated/initiated root canal treatment were excluded from the study.

The sample size was calculated using PASS version 11, paired sample t- test with 99% confidence interval, 99% power of the test, mean and standard deviation  $48.85 \pm 9.95$  (20), the calculated sample size was 15 per group, which was increased up to 40 patients per group. Non-probability (purposive) sampling technique was used for patient recruitment. Patients were divided into three groups: group 1 received no medication(-control), group 2 received Piroxicam and group 3 received prednisolone. Therefore, total sample size for this study was 120 patients.

The diagnosis of symptomatic irreversible pulpitis was made from the chief complaint and the clinical examination. Pre-operative pain was the main diagnostic sign of symptomatic irreversible pulpitis. Pulp sensitivity was confirmed by a positive response to a prolonged exaggerated response (>10 s) with moderate-to-severe pain to a cold test, using ethyl chloride spray. After obtaining informed consent (verbally and written), baseline pain score using VAS was recorded for the patient on the proforma.

Patients were randomly divided into following 3 groups; with an equal sample of 40 patients (n=40) in each group. Group I: Control, Group II: Piroxicam (20 mg), Group III: Prednisolone (20 mg). A random sequence of the participants was generated via computer software (MS Excel). A certified dental hygienist was responsible for administration of the pre-medication protocol for each patient before commencement of root canal therapy. Patients allocated in control group did not receive any medication before root canal therapy was initiated whereas patients allocated in groups II and III received Piroxicam and Prednisolone respectively, 30 minutes before the procedure. To ensure blinding protocol, grouping was not revealed to the principal investigator till the end of the study.

Root canal treatment (RCT) was initiated 30 minutes after the administration of pre-medication. A second reading of

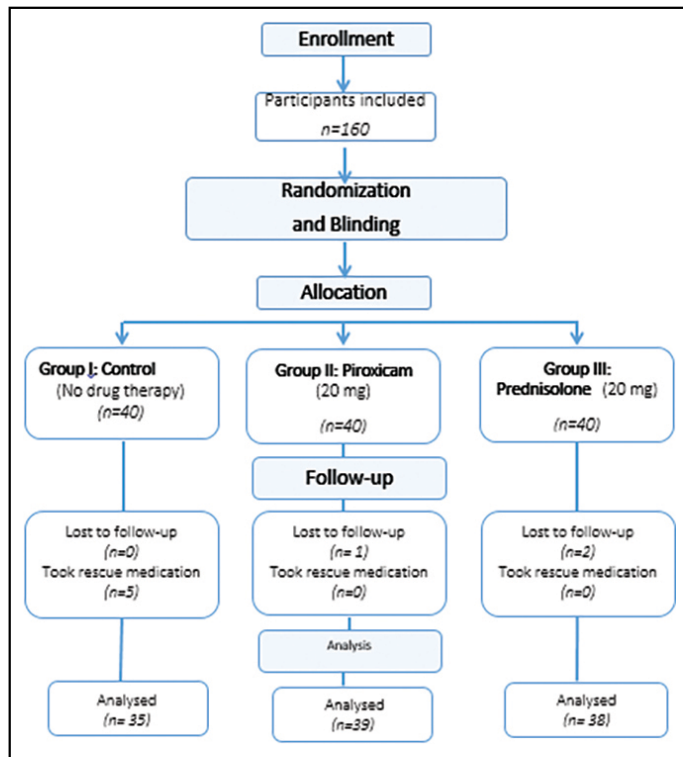


Figure 1. Consolidated standard of reporting trials (CONSORT) flow-chart of participants throughout the trial

pain score was recorded on the proforma before the RCT procedure was carried out.

An emergency drug (ibuprofen, 200mg) was prescribed to the patient at the end of the RCT procedure. The patients were instructed to take the drug only if they experience moderate-severe pain within 96 hours. The patients who took the rescue drug were excluded from the study.

For the assessment of pre-operative and post-endodontic pain (up to 96 hours) was measured using the visual analog scale (VAS). The scale consists of a 10-cm line fixed by 2 extreme ends, “no pain” and “severe pain.” The scale is divided into mild, moderate and severe categories as below (20):

- No pain : range of 0-1
- Mild pain: range of 2-4
- Moderate pain : range of 5-7
- Severe pain : range of 8-10

Patients were thoroughly informed about the details of the questionnaire and asked to mark their pain intensity level at 24, 48, 72 and 96 hours after the procedure. Follow up was taken on call or by message. All patients were re-called for follow up after 4 days for a clinical and radiographic evaluation and placement of core buildup by the principal investigator.

**Statistical analysis**

Data was entered and analyzed using SPSS version 23 (Chicago IL). Demographic and clinical variables (such as age, gender

**TABLE 1.** Distribution of demographic and clinical variables of study

Variables	Total n=112	Group I (Control) n=35	Group II (Piroxicam) n=39	Group III (Prednisolone) n=38
Age (years)				
20-27	31	8	8	15
28-34	29	7	12	10
35-40	52	20	18	14
Gender				
Female	71	22	28	21
Male	41	13	10	18
Tooth type				
Incisors	21	2	12	7
Canine	15	3	9	3
Premolar (single rooted)	76	30	17	29

and tooth type) were analyzed using descriptive statistics. Paired sample t-test was used for intra-group comparison between all study groups. For inter-group comparisons ANOVA was used followed by Duncan and LSD post-hoc tests. A p-value of ≤0.05 was considered statistically significant.

**RESULTS**

Out of 120 patients treated, 3 patients were excluded due to loss on follow-up and 5 patients took ibuprofen as a rescue drug before the 92 hour time interval; as they experienced severe post-operative pain. Therefore, the sample size after exclusion of the above mentioned 8 patients were as follows: n=35 patients in group I (control), n=39 patients in group II (Piroxicam) and n=38 patients in group III (Prednisolone) (Fig. 1).

The demographic and clinical data regarding the distribution of age range, gender and tooth type is shown in Table 1. There was no significant difference in demographic data in terms of age (P=0.14), gender (P=0.12), whilst tooth type (P≤0.001) showed statistically significant value.

The results of the present study revealed that a higher percentage of patients in all 3 groups, reported no post-operative pain at all evaluated time durations (24, 48, 72, and 96 hours).

At 24 hours interval, participants in group I(Control) showed 3.4% moderate pain while 13.8% patients with severe pain. In group II(piroxicam) showed no moderate to severe pain and in group III (prednisolone) only a small population of 7% showed postoperative severe pain.

At 48 hours interval, patients in group I (control) showed moderate pain in 3% and severe pain in 10.6% of the patients. While in group II(piroxicam) patients showed no pain and in group III(prednisolone) 7% of the patients experience mild pain only.

At 72 hours interval,group I (control) 10% patients showed severe pain post operatively. While in group II piroxicam) and III (prednisolone) patients showed no moderate to severe pain. At 96 hours interval, group I (control) 7.4% of the patient showed severe Post EP. In contrast, groups II (piroxicam) and III (prednisolone) showed no moderate to severe pain.

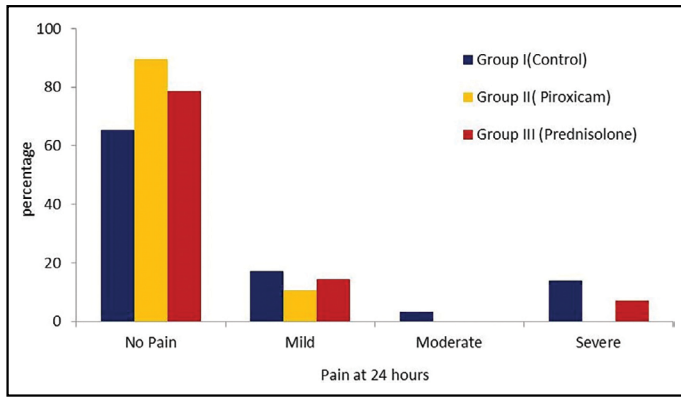


Figure 2. Distribution of pain intensity scores at 24 hours interval of participants in all study groups

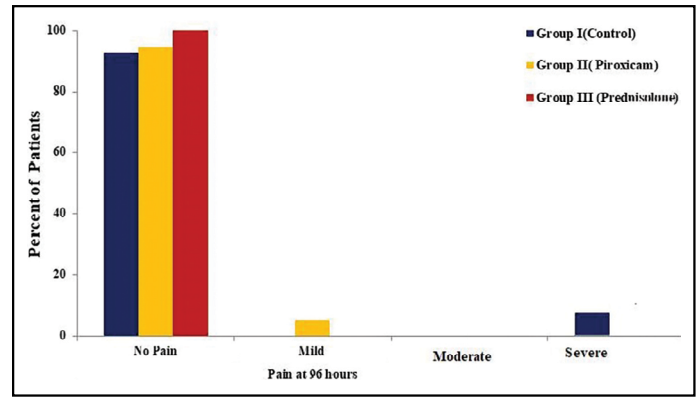


Figure 5. Distribution of pain intensity scores at 96 hours interval of participants in all study groups

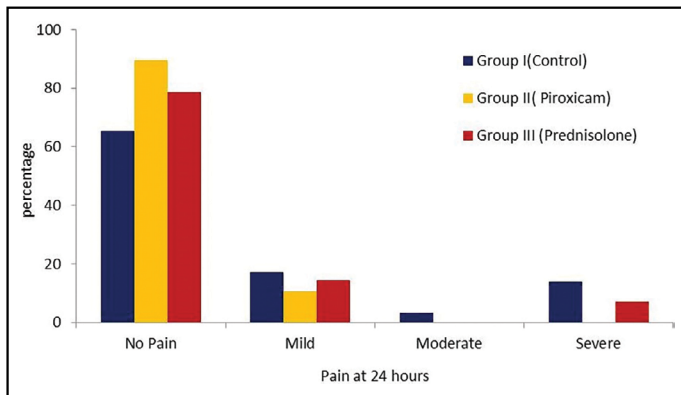


Figure 3. Distribution of pain intensity scores at 48 hours interval of participants in all study groups

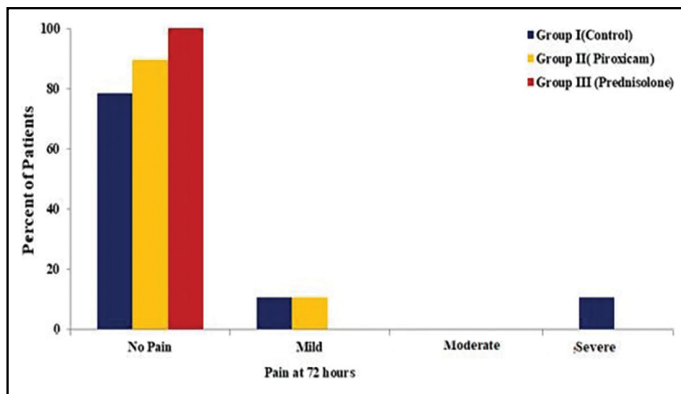


Figure 4. Distribution of pain intensity scores at 72 hours interval of participants in all study groups

Thus the bar charts representing pattern of pain intensity levels of patients at different time intervals are shown in Figures 2-5

The present study also compared pre and post-medication pain intensity scores within each group. The results of the study showed substantial decrease in the pain intensity level in patients administered Piroxicam and Prednisolone ( $P \leq 0.001$ ), whereas in group I, p-value could not be calculated as there is no difference in its mean and standard deviation (Table 2).

The pre and post-EP scores between control and experimental groups was also evaluated; statistically significant results were

noted between groups I and II at 24,48 and 72 hours, whereas significant differences were recorded between group I and III at 72 hours only as shown in Table 3.

**DISCUSSION**

Anticipation and experience of pain related to endodontic therapy (pretreatment, treatment, and post-treatment pain) is a major source of fear for patients and concern for dentists. Immediate pain relief increases patient confidence and reduces treatment anxiety and time (21). It is reported that premedication with single dose of of corticosteroid reduces the chances of adverse effects, as it can modulate the release of inflammatory mediators and reduce the occurrence of side effects compared with repeated drug doses during the endodontic procedure (22, 23). This study was conducted to compare the long term efficacy of single dose premedication of Piroxicam and Prednisolone on post EP in one visit root canal treatment using VAS scale.

It was observed in the present study that patients in groups II and III did not take any rescue medication but in group 1 few patients took rescue medication; this further validates the importance of preoperative drug administration. Similar findings were also reported in previous studies suggesting the administration of Single oral premedication was beneficial to control post EP (16, 24).

Previous studies on endodontic pain perception measured pain levels directly at 6 hours interval after single visit endodontic treatment, which can be influenced by residual anesthetic effect. (15, 17); hence the current study compared the VAS score of all three groups before the administration of anesthesia. Piroxicam and Prednisolone was able to significantly reduce pain levels pre-operatively (Table 2). Whereas in the control group, no comparison can be drawn to pre and post medication pain scores as pain level remained the same, due to administration of no interventional drug therapy (Table 2).

In the current study significant difference in pain intensity levels were observed between group I (control) and group II (piroxicam) at different time intervals (Table 3). Similar results were found in other studies which reduced post EP up to 48 hours as compared to placebo (19, 25). On contrary, a study by Nir et al. (26) showed preoperative administration of Oxicams resulted in an insignificant reduction in postoperative analgesic consumption.

**TABLE 2.** Intra group comparison of VAS score Pre and Post medication

Groups	Visual Analog Scale (VAS) scores		P*
	Pre-medication	Post-medication	
	Mean±SD	Mean±SD	
Group I (Control)	8.48±2.42	8.48±2.42	-
Group II (Piroxicam)	8.63±1.14	0.36±0.94	<0.001
Group III (Prednisolone)	8.51±1.44	0.10±0.44	<0.001

\*: Paired sample t-test; level of significance <0.05. SD: Standart deviation

In the present study, a significant difference in pain intensity levels was observed between group I (control) and group III (prednisolone) at 72 hours interval only (Table 3). During the entire 96 hour evaluation time period, patients who received Prednisolone only experienced moderate pain during the initial 48 hours only, after which pain levels reduced significantly to no pain level at 96 hours interval. Similar results were reported by previous authors, who showed effective reduction in post EP up to 48 hours interval using corticosteroid when used preoperatively (25, 26).

In the present study no significant difference was observed between group II (Piroxicam) and group III (Prednisolone) at all-time intervals (Table 3), therefore, the second null hypothesis of the study was accepted as both premedication drugs showed insignificant comparisons. This finding suggests that both drugs reduce post EP to similar levels and carry similar efficacy and potency with anti-inflammatory activity for long term intervals.

A randomized, blinded, single center study design was chosen for the present study to minimize bias and allow powered study comparisons between the groups. The adaptation of a single-center, randomized controlled trial with large sample size and a single operator not only reduces bias but also allows generalization of the study results (27).

Negative placebo was used as control group in the study following the conventional method of root canal treatment to exclude psychological bias from the study. Studies showed that placebo has some amount of psychological effect on pre and post EP (28).

A single centered study of pain assessment which was only performed on single rooted tooth presenting with irreversible pulpitis with subjective pain assessment were the noted findings as study limitations.

**CONCLUSION**

Premedication with single dose of 20 mg prednisolone or piroxicam was effective for the control of postoperative endodontic pain up to 96 hours after single-visit root canal treatment, in patients with symptomatic irreversible pulpitis.

**Disclosures**

**Conflict of interest:** The authors deny any conflict of interest.

**Ethics Committee Approval:** This study was approved by The DUHS Institutional Review Board (Date: 10/03/2018, Number: 2018/54).

**Peer-review:** Externally peer-reviewed.

**Financial Disclosure:** This study was self-funded.

**Authorship contributions:** Concept – A.T., S.A.; Design – A.T., S.A.; Supervision – A.T., S.A.; Funding - A.T.; Materials - U.W., H.A.; Data collection and/or processing – U.W., H.A.; Analysis and/or interpretation – M.S.A., N.A.; Literature search – M.S.A., N.A., A.T.; Writing – H.A., M.S.A., A.T.; Critical Review – U.W., H.A., N.A., A.T., S.A.

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**TABLE 3.** Inter-group comparison of Visual Analog Scale (VAS) score at different time intervals

Time intervals	Group I (Control)	Group II (Piroxicam)	Group III (Prednisolone)	P*	Significant differences at Post-hoc**
	Mean±SD	Mean±SD	Mean±SD		
Pre-medication (30 mins)	8.48±2.42	8.63±0.14	8.51±1.44	0.96	-
Post-medication (30 mins)	8.48±2.42	0.36±0.94	0.10±0.44	0.075	-
24 hours	1.79±0.40	0.26±0.13	0.79±0.40	0.007	I-II
48 hours	1.39±0.36	0.21±0.10	0.5±0.30	0.014	I-II
72 hours	1.07±0.35	0.16±0.08	0 (0)	0.013	I-II, I-III
96 hours	0.67±0.33	0.11±0.07	0 (0)	0.129	-

\*: ANOVA, level of significance <0.05, \*\*: Post-hoc Duncan and LSD test. SD: Standart deviation, LSD: Least significant difference

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