Comparative Evaluation of Premedication with Ketorolac and Prednisolone on Postendodontic Pain: A Double-blind Randomized Controlled Trial

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Abstract

Introduction: The present clinical trial aimed to evaluate and compare the effect of a single pretreatment dose of ketorolac (20 mg), prednisolone (30 mg), and placebo on postendodontic pain in patients undergoing endodontic therapy for irreversible pulpitis or pulpal necrosis using a visual analog scale. **Methods:** Ninety-two subjects were included in the present trial; 46 subjects had a pulpal diagnosis of irreversible pulpitis, and the other 46 had pulpal necrosis. These subjects were randomly allocated into 1 of the 3 pretreatment medication groups: ketorolac (20 mg), prednisolone (30 mg), or a placebo. The drugs were administered 30 minutes before the procedure followed by a routine single-visit root canal treatment. Preoperative and postoperative pain was evaluated using a visual analog scale at 6 time intervals. A comparison between the different groups was performed using one-way analysis of variance followed by the Tukey post hoc test. A comparison of pain within each group at various time intervals was performed using repeated measures analysis of variance followed by the paired *t* test and Bonferroni correction. **Results:** At the end of 6 hours, in irreversible pulpitis cases, the ketorolac group showed an effective reduction in pain scores compared with the other drugs. At the end of 12 hours, the prednisolone group significantly reduced the pain scores compared with the other drugs. **Conclusions:** From this study, it could be concluded that a single pretreatment dose of prednisolone has a more sustained effect in reducing postendodontic pain compared with placebo or ketorolac. *(J Endod 2017;■:1–7)*

Key Words

Corticosteroids, intravenous, nonsteroidal anti-inflammatory agents, pretreatment analgesic, randomized controlled trial, root canal therapy, visual analog pain scale

Significance

Patients often judge the quality of endodontic care received by the presence and intensity of postoperative pain. This study shows that a preemptive dose of prednisolone promotes a greater reduction in postoperative pain than ketorolac or placebo.

Posttreatment endodontic pain has been reported in 25%–69% of all endodontic patients (1–3). Among various reasons, the most probable causes for pain during and after endodontic treatment are tissue injury caused by endodontic instrumentation, periapical contamination, caustic irrigants, intracanal medications, and occlusal discrepancies (4, 5). The tissue injury triggers a barrage of nociceptor activation and local inflammatory processes that are regulated by chemical mediators released from damaged tissues and agents of vascular or neural origin, such as prostaglandins, leukotrienes, bradykinin, serotonin, and cytokines. These inflammatory mediators may in turn activate and sensitize nociceptors, leading to peripheral sensitization (6, 7).

Pretreatment analgesia is providing analgesia to patients before endodontic treatment is started. This technique can decrease the establishment of central and peripheral sensitization, which has the potential to reduce postoperative pain and postoperative analgesic intake (8, 9).

In this context, drugs that modulate the inflammatory response such as steroidal (corticosteroids) and nonsteroidal anti-inflammatory drugs (NSAIDs) can be considered for the prevention and control of peripheral factors in postendodontic pain (10). Ketorolac and prednisolone are potent anti-inflammatory agents belonging to the NSAID and corticosteroid groups, respectively.

Ketorolac is an NSAID that inhibits prostaglandin synthesis in the periphery, which is a key component in sensitizing the nociceptors to other inflammatory mediators (11, 12). Prednisolone is a synthetic glucocorticoid, a derivative of cortisol. A steroid-induced protein, lipocortin, has antiphospholipase A_2 activity, preventing the synthesis of arachidonic acid and thereby reducing the biosynthesis of both cyclooxygenase and lipoxygenase products (13).

The effectiveness of preemptive analgesics is well established in surgical models; however, the literature is unclear regarding endodontic models. Many trials favor the use of preemptive anti-inflammatory drugs for endodontic pain (14–16), whereas some have shown no favorable outcomes (9, 17). Studies have evaluated the efficacy of 1 or more NSAIDs or a corticosteroid premedication against a

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placebo (9, 14–16). However, concrete evidence on which class of premedication is best suited for postendodontic pain control does not exist. Hence, this study was conducted to compare the severity of postoperative pain in patients undergoing single-visit endodontic therapy with irreversible pulpitis or necrotic pulp after a single dose of ketorolac (20 mg), prednisolone (30 mg), or placebo as a premedication.

Material and Methods

Selection of Subjects

Approval of the study protocol and ethical clearance were obtained from the Institutional Review Board, Bapuji Dental College and Hospital, Davangere, India. A patient information form was given to all enrolled participants, and their informed consent was obtained. The study subjects recruited in this triple-blind, parallel, randomized controlled trial were from the pool of patients selected in the Department of Conservative Dentistry and Endodontics, Bapuji Dental College and Hospital.

Sample Size

The sample size was calculated considering the mean expected difference and pooled standard deviation from previous literature (16). The minimum sample required to detect differences between 6 groups (with type I error at 5% and power at 80%) was found to be 9 subjects per group. The sample size was increased to 15 participants per group to account for the potential refusal to participate, procedural errors, or loss of patients during the trial.

Inclusion and Exclusion Criteria

Inclusion criteria included cases with a pulpal diagnosis of irreversible pulpitis or pulpal necrosis in single-rooted teeth. Exclusion criteria were cases with acute periapical conditions (acute apical periodontitis/acute apical abscess) or teeth with a periapical index score >3. The periapical index is a severity-based ordinal scale scoring system used in radiographic evaluations of apical periodontitis (18). Also, patients with a known allergy, sensitivity, or history of other adverse reactions to the medications administered and analgesics/anti-inflammatory drugs taken within the last 6 hours were excluded from the study.

Subject Allocation and Randomization Method

An examiner not involved in the trial assessed 121 patients for eligibility based on case history and clinical and radiographic examination (Table 1). Patients were diagnosed using a standard protocol and assigned to the pulpal necrosis or irreversible pulpitis groups (as shown in Table 2). The intraoral periapical radiographs were viewed on an x-ray viewer, and the areas other than the periapex were covered with 4 pieces of black photographic paper. The periapical region was then scored between 1 and 5 categories according to the periapical index using reference photographs (18). Among them, 13 patients did not meet the inclusion/exclusion criteria, and 16 patients refused to participate in the trial. Provisional diagnoses of irreversible pulpitis (46 subjects) and pulpal necrosis (46 subjects) were made for the included 92 subjects. A computer-generated random sequence of the chosen subjects was obtained. Allocation concealment to ensure proper randomization was performed using sealed numbered opaque envelopes; patients had to randomly pick up their envelope, which contained the group code. The drugs were placed in 3 identical opaque containers and were coded (code A, ketorolac; code B, prednisolone; or code C, placebo). All medications were orally administered 30 minutes before the initiation of conventional root canal therapy. The tablets were dispensed by a blinded investigator not involved in the study. The code details were not revealed to the principal operator until the end of the study. Similarly, the patient was also unaware of which 1 of the 3 medications he or she was taking.

Intervention

Thirty minutes before the endodontic procedure, ketorolac (20 mg, Ketorol; Dr. Reddy's Labs Limited, Princeton, NJ), prednisolone (30 mg, Wysolone; Pfizer Ltd [Wyeth Ltd], New York, NY), or a placebo was administered. Root canal therapy in all cases (vital and nonvital teeth) was completed by the principal investigator in a single visit. After explanation of the treatment procedures (according to individual needs), the tooth was anesthetized by a nerve block using 1 to 2 doses (1.8 mL each) of anesthetic solution (2% lidocaine with 1:100,000 epinephrine, Lignox; Indoco [Warren, Mumbai, India]). After this, the tooth was isolated with a rubber dam, and access preparation was performed. Apical patency was maintained with a number 10 K-file. Cleaning and shaping were performed with a hybrid technique using hand K-files (Kendo; VDW, München, Germany) and the ProTaper (Dentsply Maillefer, Ballaigues, Switzerland) rotary system for all teeth. Sodium hypochlorite (3%) and EDTA (17%) were used during canal preparation, whereas saline was used as the final irrigant. Apical preparation was performed with files at least 3 sizes greater than the initial apical file. After drying the canals with sterile paper points, they were coated with AH Plus (Dentsply Maillefer) sealer using lentulospirals and obturated with gutta-percha using the lateral condensation technique. The tooth was then temporized using Cavit (3M ESPE, St Paul, MN) and reduced from occlusion.

Patients were kept under observation for 3 hours from the time the drug was administered. A rescue medication (ibuprofen) was prescribed, and the patients were instructed to take it only if they experienced severe pain postoperatively. If rescue medication was taken within the 48 hours after the treatment, then the patient was excluded from the study.

Assessment of Pain after Root Canal Treatment

Patients' pain intensity experience was measured using the visual analog scale (VAS), which consists of a 10-cm line anchored by 2 extremes, "no pain" and "pain as bad as it could be." Patients were asked to make a mark on the line that represents their level of perceived pain. They were instructed to complete a pain diary at specific intervals (ie, before the commencement of any treatment [baseline score]; immediately after treatment completion; and 6, 12, 24, and 48 hours after the commencement of treatment). All subjects were recalled after 2 days to return the pain diary and for a clinical evaluation.

Statistical Analysis

Normality of the data was tested using the Kolmogorov-Smirnov test. Because the data showed normal distribution, parametric tests were used for comparing the means.

Pain experienced by subjects belonging to different drug groups was analyzed using one-way analysis of variance (ANOVA) followed by the Tukey post hoc test. A subgroup analysis between irreversible pulpitis cases and pulpal necrosis cases was performed using the unpaired *t* test. A comparison of pain (mean VAS scores) within each group at various time intervals was performed using repeated-measures ANOVA followed by the paired *t* test and Bonferroni correction.

Results

There were 42 women and 44 men included in this clinical trial. There were no significant differences between the groups with respect to