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Effectiveness of tenoxicam and ibuprofen for pain prevention following endodontic therapy in comparison to placebo: a randomized double-blind clinical trial

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Abstract: Tenoxicam is an effective analgesic and anti-inflammatory agent for symptomatic treatment of various conditions. The purpose of this study was to evaluate clinically the effectiveness of prophylactic tenoxicam and prophylactic ibuprofen in reducing post-endodontic pain compared with placebo. A total of 48 patients consented to a double-blind, single dose, prophylactic oral administration of 20 mg of tenoxicam, 200 mg of ibuprofen, or a placebo before root canal treatment. The root canal treatment was performed in one visit. The patients registered their degree of discomfort on a 100-mm visual analog scale, immediately postoperative, and 6, 12, 24, 48 and 72 h after initiation of root canal treatment. The two-way ANOVA test and Tukey HSD post hoc test showed that in the 6-h period, both 20 mg of tenoxicam and 200 mg of ibuprofen provided significantly better pain relief than the placebo. Prophylactic administration of a single dose of 20 mg tenoxicam or 200 mg ibuprofen before RCT provides an effective reduction at 6 h ($P < 0.05$). Because of the advantages of tenoxicam, it may be useful as a prophylactic analgesic when post-endodontic pain is anticipated. (J Oral Sci 53, 157-161, 2011)

Keywords: tenoxicam; ibuprofen; post-endodontic pain.

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Introduction

Postoperative pain following root canal treatment (RCT) can be a considerable problem for patients and endodontists. In spite of advances in RCT and better knowledge of pulpal and periapical inflammation, up to 40% of endodontic patients report postoperative pain of different degrees (1,2). Postoperative endodontic pain is often linked to inflammatory mediators (such as prostaglandins, leukotrienes, bradykinin, and serotonin) that activate sensitive nociceptors, leading to both peripheral and central mechanisms of hyperalgesia (3). Among inflammatory mediators, prostaglandins play a critical role in the pathogenesis of pulpal and periradicular disease (4).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed analgesics in enzootics (5). They inhibit prostaglandin synthesis by decreasing the activity of cyclo-oxygenase enzyme (COX). COX exists in at least two isoforms: COX-1 and COX-2. COX-1 enzymes are present in most tissues and regulate normal cell activities in the stomach, kidneys, endothelial cells, platelets, and other tissues. In contrast, COX-2 is an inducible enzyme. Release of COX-2 in normal tissue is rare, but comes into play when tissue injury and inflammation occur. This isoform is induced rapidly (in 1 to 3 h), and it can be detected in high concentrations in macrophages, monocytes, leukocytes, synovial cells, and fibroblasts in response to mediators of inflammation (6).

Previous studies have shown that preoperative administration of the NSAIDs ibuprofen, flurbiprofen, or rofecoxib suppress post-operative pain more effectively than a placebo (7, 8). Administration of NSAIDs before RCT will reduce the inflammatory process before it begins (9).

Tenoxicam is rather frequently prescribed because it specifically inhibits COX-2, which could imply a lower incidence of undesirable side effects such as gastric intolerance (10-12). A few studies in oral surgery models (13-15) and orthodontics (16) have compared tenoxicam and other NSAIDs. Additionally, the ability of prophylactic tenoxicam to control post-endodontic pain has not been analyzed. The purpose of this study was to evaluate clinically the effectiveness of either prophylactic tenoxicam or ibuprofen in reducing post-endodontic pain compared with placebo.

Materials and Methods

Subjects were selected from emergency patients attending the Dental School of Ataturk University. Patients were examined at entry for the etiology of their pain. If pain originated from a tooth, patients were screened according to the degree of their baseline pain, which was determined with the use of a 100-mm horizontal visual analog scale (VAS) (Fig. 1). Patients were asked to place a mark along the line to indicate the most severe pain they had experienced in the past 24 h. Patients who placed a mark at the 50 mm level or above were included in the study. Upon approval by the Institutional Review Board of Ataturk University, a consent form was signed by all patients before treatment. Patients' age ranged from 18 to 52 years. A complete medical history of all patients was taken. Only those patients who had no significant medical problems were considered for the study. Also, the presence of any of the following conditions contraindicated the inclusion of the patient in this study: currently taking anti-inflammatory agents, antibiotics, anti-depressants or other drugs; history of any allergic reaction to NSAIDs; analgesic ingestion within the last 12 h; previous endodontic treatment; or acute apical abscess. Vitality of the pulp was determined by an electric pulp-testing device (Digitest Pulp Vitality Tester, Farmingdale, NY, USA). Patients were only treated by one graduate endodontic resident.

Patients consented to double-blinded oral administration of either 200 mg of ibuprofen (17) (Advil liquid-gels, Wyeth, Aprilia, Italy), 20 mg of tenoxicam (15) (Tenox, Biofarma, Istanbul, Turkey), or a sugar placebo before RCT. Each medication was disguised so that the patient was not aware of the medication he or she was taking. The medications were encapsulated in similar capsules. The three test medications were randomized by a block randomization method using a spreadsheet program (Microsoft Excel, Santa Rosa, California, USA) into a group of 48 by the second author (H.S.T.). A power analysis established by G*POWER Ver. 3.0.10. (Franz Faul, Universität Kiel, Germany) software indicated that a sample size of 48 patients would give more than 80% power to detect significant differences with 0.415 effect size at a 0.05 significance level. Soon after oral administration of the test medication, local anesthetic solution (Ultracaine D-S forte: Aventis Pharma, Istanbul, Turkey) was administered, the rubber dam was placed and endodontic access was achieved. Working lengths were determined by an electronic apex locator (Propex, Dentsply-Maillefer, Ballaigues, Switzerland). Canal preparation was performed using a crown down technique. 5.25% sodium hypochlorite was used as an irrigant, and cleaning and shaping were performed in the presence of EDTA gel (File-Eze, Ultradent, South Jordan, UT, USA). One milliliter of 15% liquid EDTA (Rehber Kimya, Istanbul, Turkey) for 1 min, followed by 3 ml of 5.25% NaOCl, were used as final irrigants. The canals were rinsed thoroughly and dried with paper points. Finally, complete obturation of the canals was performed with gutta-percha and sealapex sealer (Kerr, Bioggio, Switzerland) using the lateral-compaction technique.

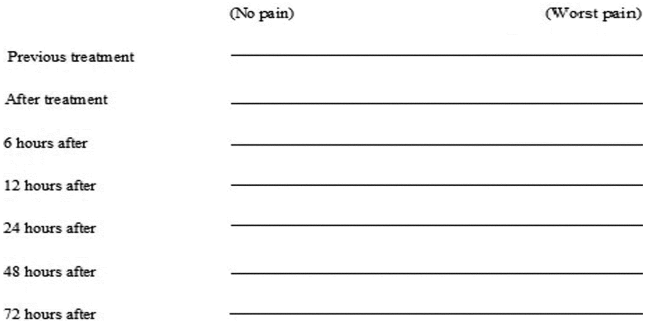

Fig. 1 VAS scale used to assess pain levels.

A cotton pellet was placed in the pulp chamber space and Cavit (ESPE Dental AG, Seefeld, Germany) was used as a temporary filling material. Final radiographs were taken. The patient immediately recorded his/her pain perception on the VAS after completion of the root canal therapy. He/she also recorded his/her pain perception 6, 12, 24, 48 and 72 h after initiation of the root canal therapy. Postoperative instructions and an extra dosage of the test medication were given to the patient. The patient was instructed to take the extra medication only if needed and to record the time it was taken on the pain survey. The subjects were asked to return their VAS on the third day. When they returned, they were also evaluated for possible side effects.

On completion of the study, data from VAS scores were statistically analyzed by the two-way ANOVA test and Tukey HSD post hoc test.

Results

Pain scores from 48 patients were recorded with the use of 100-mm VAS. The age of the patients ranged from 18 to 52 years, with a mean age of 36 years. Thirty-two females and 16 males participated in the study. Eleven incisors, 16 premolars and 21 molars were treated in this study.

There were 16 patients in each group. Median pain VAS scores were plotted in relation to time after administration of the drugs (Fig. 2). In the 6-h period, both tenoxicam and ibuprofen provided significantly better pain relief than the placebo ($P = 0.000$). There was no significant difference between tenoxicam and ibuprofen at 6 h ($P = 0.723$). In addition, there was no significant difference between tenoxicam, ibuprofen and the placebo at 12, 24, 48, and 72 h ($P > 0.05$). No side effects were reported by patients in any experimental group. Additionally, no patients took extra medication, which was provided in case of inadequate pain control.

Discussion

Postoperative pain is more likely to arise within a few hours following RCT (18). Patients who have postoperative pain need analgesics that have fewer side effects for relieving the pain. Consequently, the clinicians should minimize or prevent pain after RCT. Preoperative administration of NSAIDs has been demonstrated to reduce postoperative pain in oral surgery models and in RCT models (7-9, 19, 20). Prophylactic administration of NSAIDs before RCT can block the COX pathway and by this application, the pain sensation can be blocked even before it begins (9). In parallel with this opinion, researchers have showed that preoperative administration of NSAIDs decreased pain level at the initial hours after RCT (7-9). In contrast with these findings, Attar et al. declared that preoperative administration of NSAIDs treatment did not significantly reduce postoperative pain after RCT (21). However, in the present study, administration of preoperative NSAIDs reduced postoperative pain after RCT at 6 h. Additionally, all the drugs including placebo showed similar pain rating at the other time intervals except 6 h. In our study, pain level reduction by RCT began at 12 h.

Tenoxicam administered orally, rectally or parenterally is an effective analgesic and anti-inflammatory agent for the symptomatic treatment of various conditions, including rheumatoid arthritis and osteoarthritis. Compared with many other NSAIDs, it presents certain advantages in elderly patients with renal or hepatic impairment (22). Also, it is characterized by lower penetration into tissues, which explains reduced incidence of adverse reactions owing to this drug (23). This study demonstrated that prophylactic administration of 20 mg of tenoxicam before RCT was more effective in reducing postoperative pain 6 h after initiation of treatment when compared with the placebo.

Ibuprofen blocks COX-1 and COX-2 enzymes. It is safe, widely prescribed, inexpensive and has effective analgesic and anti-inflammatory action for post-operative pain (24). A prophylactic dose of 600 mg ibuprofen was used for evaluation of post-endodontic pain in previous studies. Some authors found that 600 mg ibuprofen reduced post-endodontic pain (8,9), while some did not (21). Also, doses of 50 to 800 mg ibuprofen were used for reduction of pain. Derry et al. suggested that 200 mg and 400 mg of ibuprofen had better efficacy in dental studies (17). Additionally, no study has evaluated the effect of a prophylactic single dose of 200 mg ibuprofen before RCT. In our study, prophylactic 200 mg ibuprofen was more effective in reducing postoperative pain at 6 h when

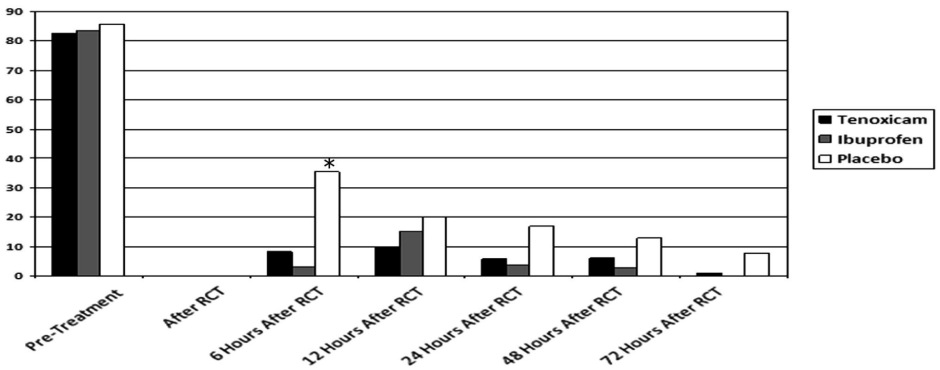

Fig. 2 Effect of prophylactic drug administration on post-endodontic pain.
*Significant difference exists for tenoxicam versus placebo ($P = 0.000$) and for ibuprofen versus placebo ($P = 0.000$).

compared with the placebo. In latter studies, researchers should compare different doses of ibuprofen to determine the optimum dose of prophylactic ibuprofen.

It is known that pain perception is a substantially subjective and variable experience regulated by multiple physical and psychological factors. Therefore, the measurement of pain is difficult (25). In the present study, VAS was chosen to measure pain, because this scale is a valid and reliable method, easily understood by patients, reproducible (26), and widely used in the endodontic literature (27, 28).

A prophylactic single dose of 20 mg tenoxicam or 200 mg ibuprofen administration before RCT provides effective reduction of post-operative pain at 6 h. Because of the advantages of tenoxicam, it may be useful as a prophylactic analgesic when post-endodontic pain is anticipated.

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