**Original Article**

# Efficacy of Premedication with Oral Dextromethorphan and Ibuprofen for Pain Relief After Root Canal Therapy in Patients with Irreversible Pulpitis

**M. Zare Jahromi [1], E. Ahmadpour [2]✉.**

[1] Assistant Professor, Department of Endodontics, School of Dentistry, Islamic Azad University, Isfahan-Khorasgan, Iran
[2] Postgraduate Student, Department of Endodontics, School of Dentistry, Islamic Azad University, Isfahan-Khorasgan, Iran

**Abstract**

**Background and Aim:** Researchers have been in search of medications with less side effects to relieve pain after root canal therapy. This study aimed to assess the efficacy of premedication with oral dextromethorphan and Ibuprofen to decrease pain after endodontic treatment.

**Materials and Methods:** This double blind clinical trial was conducted on 45 patients. The selected teeth had irreversible pulpitis and spontaneous pain with no periapical lesion. The patients were randomly divided into three groups of 15. One-session treatment was scheduled for them and after signing informed consent forms, the patients received a single dose of dextromethorphan, ibuprofen or placebo one hour preoperatively. The severity of pain was measured before and two, four, eight and 12 hours after endodontic treatment using a visual analog scale (VAS). Two endodontists performed the treatments. The data were analyzed using the Mann Whitney, Kruskal Wallis and Friedman test.

**Results:** The mean severity of pain in the dextromethorphan and ibuprofen groups was significantly different from that in the placebo group at the five assessment time points ($P<0.05$). The mean severity of pain was not significantly different between the dextromethorphan and ibuprofen groups at any time point ($P>0.05$).

**Conclusion:** The results showed that the analgesic efficacy of dextromethorphan and ibuprofen was equally greater than that of placebo.

**Key Words:** Premedication, Analgesics, Root Canal Therapy, Pain

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✉ Corresponding author:
E. Ahmadpour, Postgraduate Student, Department of Endodontics, School of Dentistry, Islamic Azad University, Isfahan-Khorasgan, Iran

*e.ahmadpour@khuisf.ac.ir*

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## Introduction

According to the definition by the International Association for the Study of Pain, pain is an unpleasant feeling and emotional experience, associated with an actual injury or possibility of tissue injury [1]. The most important issue in pain relief in endodontics is to accurately find the cause of pain. However, a wide range of analgesics may need to be prescribed in severe, intolerable pain to decrease signals transmitted by the peripheral pain receptors and prevent central hyperalgesia [2]. Pain control during and after endodontic treatment is an important part of root canal therapy [1] and is a serious challenge for clinicians [3,4]. Several strategies are used for endodontic pain control such as administration of long-acting analgesics [5] and premedication with analgesics [6]. The logic behind premedication is to prevent the progression of hyperalgesia by decreasing the input of pain signals to peripheral receptors [2].

Non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen are among pain relievers

commonly prescribed for endodontic pain control [2]. NSAIDs are among the most commonly used analgesics after endodontic treatment and include ibuprofen, ketorolac and piroxicam [2,6,7].

Premedication with NSAIDs before endodontic treatment has been shown to be effective [2] since NSAIDs inhibit the synthesis of prostaglandins by decreasing the activity of cyclooxygenase 1 (COX1) and 2 (COX2) enzymes [2,8]. COX2 synthesizes prostaglandins [9], which play key roles in progression of inflammation and generation of pain [10].

The analgesic effects of NSAIDs are mainly related to the inhibition of COX2. Inhibition of COX1 results in gastrointestinal ulcers and bleeding, renal disorders and inhibition of platelet aggregation [11]. Gastrointestinal problems occur following inhibition of COX1 and subsequent inhibition of synthesis of prostaglandins, which protect the gastric mucosa [9]. NSAIDs are contraindicated in patients with gastrointestinal ulcers and those allergic to aspirin [2,9].

Dextromethorphan is among the most effective anti-cough medications. It is the methylated dextrorotary analogue of levorphanol and has slight affinity for μ opioid receptors, causing sedation. In contrast to codeine, it does not cause dependence. Dextromethorphan increases the analgesic effect of morphine and other μ opioid receptors. It is the non-competitive antagonist of N-methyl-D-aspartate receptor and is effective for prevention of central hypersensitivity [12,13]. Clinical studies have shown antihyperalgesic effects of dextromethorphan [14,15]. Premedication with dextromethorphan has analgesic effects [16] and it has been suggested for pain control [16,17]. This study aimed to assess the efficacy of premedication with dextromethorphan compared to ibuprofen for pain relief following endodontic treatment.

## Materials and Methods

This double blind clinical trial was conducted on 45 patients between 20 to 50 years including 27 females and 18 males with irreversible pulpitis and spontaneous pain in mandibular first molars. The diagnosis of irreversible pulpitis was made based on vitality tests, clinical examinations and assessment of subjective and objective signs and symptoms of patients. The study protocol was approved in the ethics committee of our university (code:IR.IAU.NAJAFABAD.REC.1395.13) and registered in www.irct.ir (code:IRCT 2016070228732N1). The patients had not used any medication prior to treatment, were not pregnant or nursing, had no history of allergy, had not used NSAIDs for 12 hours prior to treatment and had only one painful tooth in the mandible. The teeth had vital pulp during access cavity preparation and had no radiolucency on radiographs. According to the Declaration of Helsinki in 2008, all patients signed informed consent forms prior to the study.

Considering the double blind design of the study, the capsules (A, B and C) were coded; 15 capsules contained 600 mg ibuprofen (Aria Pharmaceuticals, Tehran, Iran), 15 contained 30 mg dextromethorphan (Raha Pharmaceuticals, Tehran, Iran) and 15 contained 100 mg sugar. The severity of pain was determined at baseline using a visual analog scale (VAS) from 0 to 100. Data including age, sex, tooth number, pulp status, baseline pain severity according to the VAS and treatment plan were recorded in patient files. The patients were divided into three groups (n=15). Group 1 patients took one dextromethorphan tablet. Group 2 patients took one ibuprofen and group 3 took one placebo tablet one hour before the treatment. An assistant blinded to the group allocation of tablets gave tablets to patients. Patients' code and tablets' code were recorded in a datasheet. The patients and clinicians were blinded to the group allocation of tablets as well. Treatments were performed by two endodontists with five years of clinical experience. Patients received inferior alveolar nerve block injection with 1.8 mL of 2% lidocaine and 1/80,000 epinephrine (DarouPakhsh, Tehran, Iran). Injections were performed by an endodontist using a 27 gage needle after aspiration. After 15 minutes, anesthesia was ensured (lip corner anesthesia, not feeling the sharp tip of an explorer pressuring the gingiva and no response to vitality tests), access cavity was prepared in the occlusal surface and endodontic treatment of teeth was performed. Root canal treatment was performed using the crown-down technique. Irrigation with 5.2% sodium hypochlorite was performed using 27 gage needle. Working length was determined

radiographically and ensured with apex locator (Root ZX2, J Morita USA Inc., CA, USA). Root canals were filed with #30 file or larger (depending on the canal size). After completion of filing, canals were dried with paper points and filled with gutta-percha (Metabiomed, Chungbuk, Korea) and AH26 sealer (Dentsply Maillefer, Ballaigues, Switzerland) using lateral compaction technique. A cotton pellet was placed in the pulp chamber and access cavity was temporarily restored with Cavit (Golchai, Tehran, Iran). Occlusion was checked and adjusted. Analgesics were prescribed for patients to use if they felt severe intolerable pain. Patients were requested to record their pain severity at two, four, eight and 12 hours after treatment using VAS. In the next visit for permanent restoration of teeth, the questionnaires were collected from patients and those who reported taking analgesics at home were excluded from the study. Data were recorded and analyzed using the Mann Whitney test, Kruskal Wallis test and Friedman test.

## Results

Friedman test was used to compare the mean severity of pain in the three groups at five different time points (Table 1, Diagram 1). The mean severity of pain in the placebo group was not significantly different at the five time points (P=0.153). However, this difference was significant in dextromethorphan (P=0.001) and ibuprofen (P=0.001) groups. The Kruskal Wallis test compared the mean severity of pain in the three groups at different time points. The mean severity of pain before endodontic treatment (P=0.299) and at two hours after treatment (P=0.643) was not significantly different among the three groups. But, significant differences were noted among the groups in the mean severity of pain at four hours (P=0.032), eight hours (P=0.001) and 12 hours (P=0.001) after endodontic treatment. The Mann Whitney test was applied for pairwise comparisons and showed no significant difference in pain intensity of placebo and dextromethorphan groups before endodontic treatment (P=0.087) and two hours after treatment (P=0.713). But the difference between these two groups was significant at four hours (P=0.009), eight hours (P=0.001) and 12 hours (P=0.001). According to the Mann Whitney test, the mean severity of pain was not significantly different between the placebo and ibuprofen groups before (P=0.202) and at two (P=0.641) and four hours (P=0.067) after treatment but this difference was significant at eight (P=0.003) and 12 hours (P=0.001) post-treatment. According to the Mann Whitney test, the mean severity of pain was not significantly different between dextromethorphan and ibuprofen groups at any time point (P>0.05).

## Discussion

Several studies have assessed the efficacy of analgesics with minimal side effects for pain control in endodontics [1,2,7]. This double-blind clinical trial was designed to assess the efficacy of premedication with dextromethorphan and ibuprofen for pain control early after endodontic treatment. The results showed that patients who used placebo as premedication did not experience any reduction in pain severity in early hours after endodontic treatment. This was expected and shows that the psychological effect of placebo was not significant for pain control. Abu-Sarma et al, [18] in 2009 assessed post-surgical pain using VAS in 76 patients who underwent rhinoplasty after premedication with dextromethorphan and placebo and concluded that the dextromethorphan group experienced significantly less pain and used significantly fewer opioids compared to the control group. Ramezani et al, [19] in 2013 assessed postoperative pain after endodontic treatment of molar teeth with irreversible pulpitis and noticed that premedication with ibuprofen caused significantly greater pain reduction compared to Zintoma and placebo at all time points, which was in agreement with our findings. Our results showed that the mean severity of pain after using ibuprofen and dextromethorphan at different time points was not significantly different. However, reduction in pain severity in the first two hours was greater in patients taking ibuprofen compared to those taking dextromethorphan; this finding may be attributed to the half-life of these two medications. The results of this study showed that analgesic effect of ibuprofen was faster while analgesic effect of dextromethorphan was delayed. The reason is the fact that the effect of ibuprofen is mainly on the peripheral pain receptors while analgesic effect of

**Table 1.** Mean severity of pain according to VAS in the three groups at different time points

| Group | Pain at baseline | 2 hours | 4 hours | 8 hours | 12 hours |
|---|---|---|---|---|---|
| **Ibuprofen** | 4<br>Max:7<br>Min:2 | 4.2<br>Max:4.5<br>Min:1 | 2.2<br>Max:4.5<br>Min:1 | 4.1<br>Max:3<br>Min:0 | 9.0<br>Max:2.5<br>Min:0 |
| **Dextromethorphan** | 1.3<br>Max:6.5<br>Min:2 | 9.2<br>Max:4<br>Min:1.5 | 9.1<br>Max:4<br>Min:1 | 3.1<br>Max:2<br>Min:0.5 | 9.0<br>Max:2<br>Min:0 |
| **Placebo** | 1.3<br>Max:7<br>Min:2 | 9.2<br>Max:4.5<br>Min:1.5 | 3.1<br>Max:4.5<br>Min:2 | 1.3<br>Max:5<br>Min:2 | 4.2<br>Max:4<br>Min:1.5 |

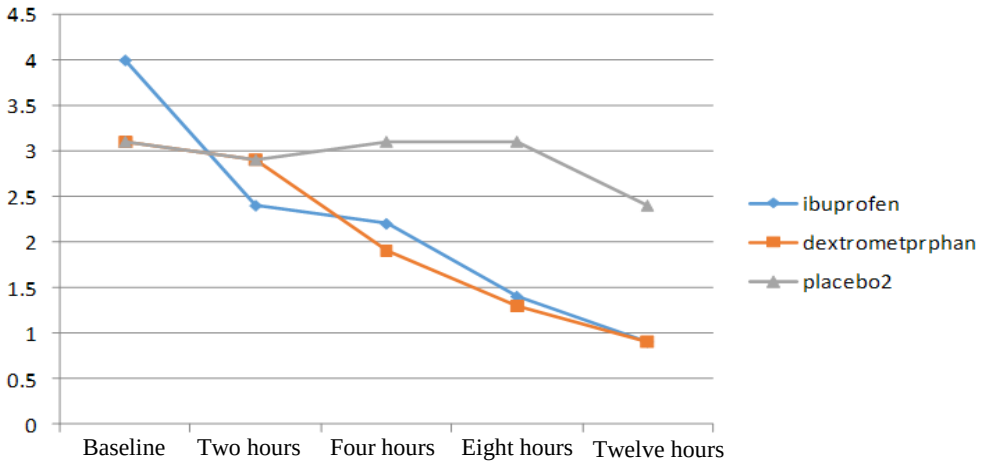


**Diagram 1.** Mean severity of pain in the three groups at different time points (pain according to VAS/Time)

dextromethorphan is exerted on NMDA receptors in the spine and the central nervous system [13]. This finding was in line with those of Gordon et al [20].

Considering the time to initiation of effect of ibuprofen and dextromethorphan which is 15-30 minutes and acceptable analgesic effects of dextromethorphan [18-20] with less side effects than other antagonists of NMDA receptors, as well as the possibly lower side effects of this drug than ibuprofen for pain relief especially endodontic pain, in patients with gastrointestinal problems, dextromethorphan can be suggested as premedication for post-endodontic pain relief. Studies on the same medications for pain relief reported similar results. For example, Talakoub and Molaeinasab [21] in 2005 evaluated the efficacy of premedication with dextromethorphan to decrease the need for morphine during surgery and concluded that oral dextromethorphan decreased pain and the need for morphine injection during surgery. Also, use of this medication caused maximum reduction in systolic blood pressure during the procedure. Aoki et al, [16] in 2006 compared the placebo, dextromethorphan and diclofenac as premedication and found that the need for additional analgesics after oral surgery was significantly less in the group using dextromethorphan compared to the placebo group but the difference between placebo and diclofenac group was not significant, which was in agreement with our results regarding the optimal analgesic efficacy of dextromethorphan.

Entezary et al, [22] in 2013 evaluated the analgesic effects of dextromethorphan after knee injury and concluded that post-surgical pain in the group

receiving dextromethorphan was significantly less than that in the placebo group. Mokhtari et al, [23] in 2016 evaluated the effect of premedication with ibuprofen and indomethacin on post-endodontic pain and concluded that both medications were effective for pain control but ibuprofen had greater analgesic efficacy.

## Conclusion

Based on the results of this study, analgesic efficacy of oral dextromethorphan was acceptable and comparable to that of ibuprofen; however, further studies are required before clinical administration of this drug.

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