Comparison of Effect of Oral Premedication with Ibuprofen or Dexamethasone on Anesthetic Efficacy of Inferior Alveolar Nerve Block in Patients with Irreversible Pulpitis: A Prospective, Randomized, Controlled, Double-blind Study

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Abstract

The purpose of this prospective, randomized, double-blind, placebo-controlled study was to determine the effect of preoperative oral administration of ibuprofen or dexamethasone on the success rate of inferior alveolar nerve block (IANB) in patients with symptomatic irreversible pulpitis. Seventy-eight patients with irreversible pulpitis were randomly divided into 3 groups (26 per group) and given one of the following at 1 hr prior to performing local anesthesia: a placebo; 400 mg ibuprofen; or 4 mg dexamethasone. Each patient recorded their pain level on a visual analog scale before taking the medication or placebo, at 15 min after completion of IANB, and during treatment if pain occurred. The success of the anesthesia was defined as no or mild pain at any stage during the endodontic procedure. The success rate of the IANB was 38.5, 73.1, and 80.8% with the placebo, ibuprofen, and dexamethasone, respectively. Both ibuprofen and dexamethasone were significantly more effective than the placebo. No significant difference was observed, however, between the two experimental medications in terms of effectiveness. The results of the present study suggest that premedication with ibuprofen or dexamethasone increases the success rate of an IANB in patients with symptomatic irreversible pulpitis in the mandibular molars.

Key words: Dexamethasone — Ibuprofen — Inferior alveolar nerve block — Irreversible pulpitis
**Introduction**

Pain control is an important factor in reducing fear and anxiety in patients undergoing endodontic procedures. Inferior alveolar nerve block (IANB) is an effective anesthetic technique for management of pain during such procedures in the mandible. The success rate of IANB drastically decreases, however, in patients with irreversible pulpitis. Activation of nociceptors by inflammatory mediators such as prostaglandins (PGs) is considered a major cause of this phenomenon. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the chemical inflammatory mediators that activate or sensitize peripheral nociceptors. Investigations into the effect of premedication with NSAIDs on the success rate of IANB have been conducted, but have yielded contradictory results.

Glucocorticoids are another class of drugs that prevent the production or release of inflammatory mediators. Previous studies have shown that dexamethasone can help reduce or prevent postoperative endodontic pain, regardless of the route of administration (single oral dose, periapical infiltration, or intraligamentary injection). Dexamethasone is well absorbed after oral administration and has a bioavailability of 61 to 86%. Plasma concentrations of dexamethasone reach a maximum level at 1 to 2 hr after administration. The terminal plasma half-life of dexamethasone is 4.0 ± 0.9 hr. It has been reported that a single oral dose of dexamethasone is safe and that it has no side effects or contraindications. Shahi et al. has reported that premedication with dexamethasone resulted in a success rate of 38.2% in patients with asymptomatic irreversible pulpitis, which was significant in comparison with the control IANB, at only 12.7%.

The purpose of this prospective, randomized, double-blind, placebo-controlled study was to compare the efficacy of two different types of anti-inflammatory medication (ibuprofen and dexamethasone) against a placebo in terms of the success rate of IANB during endodontic procedures for irreversible pulpitis in the mandibular molars.

**Materials and Methods**

The protocol of this study was approved by the Ethics Committee of Mashhad University of Medical Sciences (approval no. 931223). The sample size was calculated with a type I error of 0.05 and statistical power of 80% on the basis of a previous report. Seventy-eight adult patients participated in the study. All had been referred to the Endodontics Department of this institute and were otherwise in good health. The exclusion criteria were as follows: under 18 year of age; a history of allergies or hyper-sensitivity to ibuprofen, dexamethasone, or local anesthetics; pregnant or nursing women; evidence of any form of peri-apical pathosis (other than a widened periodontal ligament) on preoperative radiograms; and an absence of a vital coronal pulp on access opening. No analgesics were permitted for at least 8 hr before the endodontic procedure. A vital mandibular first or second molar showing prolonged moderate or severe pain lasting more than 10 sec in response to a cold test with 1,1,1,2-tetrafluoroethan (Green Endo-Ice; Hygienic corp., Akron, OH, USA) was required. Informed consent was obtained from all patients.

The patients were then divided into 3 groups of 26 patients each. Simple random sampling was performed by balanced (permuted) block randomization. A pharmacist prepared identical-appearing capsules of ibuprofen, dexamethasone, and placebo. Group 1 received the placebo (cellulose); group 2, 400 mg ibuprofen; and group 3, 4 mg dexamethasone. The same pharmacist was also responsible for encoding the capsules to ensure that both the clinician and the patient were blinded to the medication. Before taking the capsules, the patients rated their pain on the Heft-Parker visual analog scale (VAS). The VAS is divided into the following 4 categories: 1, no pain, defined as 0 mm; 2, mild pain, defined as >0 mm and ≤54 mm; 3,
moderate pain, defined as >54 mm and <114 mm; and 4, severe pain (worst possible pain), defined as ≥114 mm.

At 1 hr after capsule administration, the patients were required to rate their pain level again in response to a cold test and then receive a standard IANB comprising 1.8 ml of 2% lidocaine and 1:80,000 epinephrine (Darupaksh, Tehran, Iran). Following completion of the IANB procedure, the patients were questioned regarding lip numbness every 5 min over the next 15 min. If complete lip numbness was not achieved within 15 min, the block was considered unsuccessful and the patient excluded from the study. If the IANB was successful, the patient was asked to rate their pain level again during a similar cold pulp sensitivity test. Access cavity preparation was conducted only in patients showing no response to the cold test. The teeth involved were isolated with a rubber dam and endodontic access performed. The patients were instructed to inform the clinician if they felt any pain during access preparation or initial instrumentation. If the patient felt pain, the procedure was interrupted while the patient rated their pain level using the VAS. If the patient recorded mild pain (0 mm to 54 mm on the VAS), the IANB was considered successful and treatment continued. Any pain level greater than mild pain was considered a failure. In these cases, the treatment was continued after administration of a supplementary injection. To ensure comparability of results, all the patients were treated by the same clinician. Upon completion of the endodontic treatment (pulpectomy), the patients were monitored for 48 hr to assess any side effects or flare-up.

An χ² test was used to determine the distribution of the study population in terms of sex, age group, and tooth type. A one-way ANOVA was used to compare pain scores among the three groups. Logistic regression was performed to determine the relationship between type of premedication and success rate. Premedication was defined as the independent variable and the result in each patient (success or failure) as the dependent variable. In this analysis, the placebo group was considered as the reference category. The odds ratio (OR), 95% confidence interval (CI), and p value were determined. The significance level was set at α = 5% (p < 0.05).

Results

None of the patients reported any side effects or flare-up after the procedure. The sex, age, tooth type, and initial pain ratings are presented in Table 1. No significant differences (p > 0.05) were observed among the groups. The overall success rates for the placebo, ibuprofen, and dexamethasone groups were 38.5, 73.1, and 80.8%, respectively (Table 2). The logistic regression analysis revealed a statistically significant difference in the success rate among the three groups (p = 0.005). A significant difference was observed in the success rate between the dexamethasone and placebo groups (OR = 6.72, 95% CI: 1.91 to 23.57; p = 0.003), and between the ibuprofen and placebo groups (OR = 4.34, 95% CI: 1.34 to 14.03; p = 0.014). No statistically significant difference was observed in the success rate between the dexamethasone and ibuprofen groups (OR = 1.55, 95% CI: 0.42 to 5.70; p > 0.05).

Discussion

The results of the present study demonstrated that premedication with dexamethasone or ibuprofen significantly increased the success rate of IANB in the treatment of mandibular molars with symptomatic irreversible pulpitis. No significant difference was observed in age, sex, initial pain rating, or tooth type among the three groups. Therefore, it is unlikely that these variables influenced the results.

Difficulty in achieving profound pulpal anesthesia in patients with irreversible pulpitis is a common clinical problem. Breakdown of damaged cell membrane in inflamed pulp triggers release of arachidonic acid (AA)9,27. This is then acted on by cyclooxygenase or
prostaglandin H synthase enzymes, which transform it into eicosanoids, which in turn produce PGs\textsuperscript{16,23}. Voltage-gated sodium channels are the target of local anesthetics, and PGs increase the expression, depolarization, and activity of these channels\textsuperscript{25}. Drugs which inhibit PGs tend to increase the effect of local anesthesia in patients with irreversible pulpitis. One recent meta-analysis revealed moderate evidence that oral NSAIDs before administration of IANB provided better analgesia in patients with irreversible pulpitis\textsuperscript{8}. In the current investigation, the overall success rates for the placebo, ibuprofen, and dexamethasone groups were 38.5, 73.1, and 80.8\%, respectively. The contributory effect of premedication with ibuprofen on IANB success rates in treatment of teeth with irreversible pulpitis has been evaluated in several previous studies\textsuperscript{1,13-15,21}. The primary function of ibuprofen is blocking the ongoing production of PGs\textsuperscript{7}. Parirokh \textit{et al.}\textsuperscript{15} and Noguera-Gonzalez \textit{et al.}\textsuperscript{13} reported that premedication with ibuprofen significantly improved the success rates of IANB. The present results are in agreement with those of these earlier reports. Three other investigations, however, have reported that ibuprofen had no significant effect on IANB success rates\textsuperscript{1,14,21}. The different inclusion criteria applied in the studies by Aggarwal \textit{et al.}\textsuperscript{1} and Oleson \textit{et al.}\textsuperscript{14} may account for the discrepancy with the present results. In the latter two studies, patients had been referred for endodontic treatment due to spontaneous pain. However, in the current study, as well as in those by Parirokh \textit{et al.}\textsuperscript{15} and Noguera-Gonzalez \textit{et al.}\textsuperscript{13}, patients were selected based on the presence or absence of prolonged pain in response to a cold pulp test. Parirokh \textit{et al.}\textsuperscript{15} has mentioned that premedication with PG inhibitors in patients with spontaneous pain is less effective because of the high level of previously released PGs.

In the present study, both dexamethasone and ibuprofen were found to increase the suc-

| Table 1 Distribution of baseline variables for control, ibuprofen, and dexamethasone groups |
|----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Characteristics                 | Group 1 (placebo) (n = 26) | Group 2 (ibuprofen) (n = 26) | Group 3 (dexamethasone) (n = 26) | p value         |
| Age                             | 20–45            | 76.9 (20)       | 80.8 (21)       | 76.9 (20)       | 0.928           |
|                                | 45–60            | 23.1 (6)        | 19.2 (5)        | 23.1 (6)        |                 |
| Sex                             | male             | 38.5 (10)       | 38.5 (10)       | 38.5 (10)       | 1               |
|                                | female           | 61.5 (16)       | 61.5 (16)       | 61.5 (16)       |                 |
| Tooth type                      | first molar      | 53.8 (14)       | 61.5 (16)       | 57.7 (15)       | 0.854           |
|                                | second molar     | 46.2 (12)       | 38.5 (10)       | 42.3 (11)       |                 |
| Before-anesthesia pain score    | 120.8 (± 13.8)   | 116.3 (± 23.3)  | 121.7 (± 21.1)  | 0.577           |

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cess rates of IANB. Glucocorticoids inhibit the breakdown of AA, resulting in inhibition of the formation of inflammatory mediators. In a study by Shahi et al., premedication with 0.5 mg dexamethasone significantly increased the success rate of IANB; moreover, no significant difference was observed between the dexamethasone and ibuprofen groups. Although their statistical results showed that dexamethasone improved the efficacy of IANB in mandibular molars with asymptomatic irreversible pulpitis, the success rate was still very low (38.2%).

To our knowledge, the optimal moment for oral administration of corticosteroids and their impact on increasing the success rate of IANB remain to be evaluated in clinical trials. According to the literature, a single oral dose of 4 mg dexamethasone is recommended to reduce post endodontic pain. Therefore, in the present study, 4 mg dexamethasone was administered and no side effects subsequently observed.

No statistically significant difference was observed between the ibuprofen and dexamethasone groups in terms of the success rates of IANB (p=0.51). Stronger recommendations can be made, however, after further in vivo studies with higher sample sizes have been conducted.

Although premedication with ibuprofen or dexamethasone resulted in more effective anesthesia, neither drug provided complete anesthesia during the endodontic procedure. This may have been due to the presence of already activated nociceptors in the inflamed pulp.

**Conclusion**

In conclusion, the results of the present study support the effectiveness of preoperative administration of ibuprofen or dexamethasone before IANB in the treatment of patients with irreversible pulpitis.

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