Efficacy of Ketorolac Buccal Infiltrations and Inferior Alveolar Nerve Blocks in Patients with Irreversible Pulpitis: A Prospective, Double-blind, Randomized Clinical Trial

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Abstract

Introduction: The purpose of this prospective, randomized, double-blind, placebo-controlled study was to determine whether ketorolac buccal infiltrations (BIs) helped to improve the success of inferior alveolar nerve blocks (IANBs) in patients with acute irreversible pulpitis (AIP). **Methods:** Forty adult volunteers with AIP in a mandibular molar were included in this study. Patients were instructed to evaluate their pain by using a Heft-Parker visual analog scale. They were randomly divided into 2 groups ($n = 20$). All patients received standard IANB injection and after that a BI of 4% articaine with 1:100,000 epinephrine. After 5 minutes, 20 patients received a BI of 30 mg/mL ketorolac, and the other received a BI of normal saline (control group). Endodontic access cavity preparation (ACP) was initiated 15 minutes after the IANB when the patient reported lip numbness and had 2 electric pulp tests with no responses. The patient's pain during caries and dentin removal, ACP, and canal length measurements (CLM) was recorded by using Heft-Parker visual analog scale. Successful anesthesia was defined as no or mild pain during any of these steps, without the need for additional injection. Data were statistically analyzed by using Mann-Whitney U and χ^2 tests. **Results:** Successful anesthesia after an IANB plus BI of articaine was obtained in 15% of patients in the control group at the end of CLM. Adding BI of ketorolac significantly increased the success rate to 40% ($P < .05$). Patient's pain during ACP and CLM was significantly lower in the ketorolac group ($P < .05$). **Conclusions:** Ketorolac BI can increase the success rate of anesthesia after IANB and BI with articaine in patients with AIP. *(J Endod 2016;42:691–695)*

Key Words

Anesthesia, inferior alveolar nerve block, irreversible pulpitis, ketorolac

Local anesthesia is an essential requirement for endodontic procedures (1–3). Although the inferior alveolar nerve block (IANB) is the most common technique for pulp anesthesia in mandibular teeth (1, 4–10), it is not always completely successful (4–6). In these situations, total removal of the dental pulp without pain is not always possible (11).

Clinical studies have reported the IANB failure rate to be between 44% and 81% (4, 6). Malamed (12) found that obtaining pulp anesthesia in lower molar teeth was difficult in 91% of cases. Many plausible factors have been suggested for this high failure rate such as inaccurate injection technique, needle deflection, the central core theory, and unpredictable spread of anesthetic solution. There are also patient factors including anatomic variations, accessory innervations, and psychological issues (4, 13, 14). Unfortunately, achieving successful local anesthesia can be more difficult in patients with inflamed pulp tissues (1, 4).

Failure of anesthesia occurs almost 8 times more often in inflamed pulps (9, 14, 15). It can be attributed to the altered response of peripheral nociceptors in the presence of inflammatory mediators such as prostaglandins (PGs) (4, 6, 13, 16). It has been shown that the tissue level of PGs is associated with patient's pain (17). The PGs reduce the threshold of nociceptors by sensitizing them to bradykinins and histamines, hence facilitating the excitability of the voltage-gated sodium channels and increasing depolarization (1, 5, 18). In addition, increased Nav1.8 and Nav1.9 subtypes of tetrodotoxin-resistant sodium channels on C nerve fibers in inflamed pulps can prevent anesthesia with certain anesthetic solutions (such as lidocaine) because of the poor ability to block these 2 subtypes (14, 18). Vasodilation caused by inflammatory mediators increase the systemic uptake of anesthetic solutions (3, 16).

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ketorolac may have sufficient inhibitory effect on PG synthesis by inactivating the cyclooxygenase (COX) pathway, the enzyme that produces PGs and thromboxane A_2 from arachidonic acid (19). A high level of arachidonic acid and their metabolites has been reported in inflamed pulps (1). Also according to another theory, NSAIDs have an effect on the central pathway of the hypothalamic PG system (serotoninergic, beta-endorphin, and monoaminergic) involved in nociception (19). It has been hypothesized that premedication with NSAIDs will influence the success of local anesthesia in patients with irreversible pulpitis.

Ketorolac or ketorolac tromethamine is a racemic mixture of S- and R-enantiomeric forms in the family of heterocyclic acetic acid derivatives (19). According to Jamali et al (20) and Mroszczak (21), the analgesic efficacy of ketorolac depends on the

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racemic mixture concentrations of S and R enantiomers. For short-term management of moderate to moderately severe pain, analgesia at the opioid level is required (19). Ketorolac is as effective as morphine or meperidine for pain relief (1, 5, 22, 23). It is a nonselective COX inhibitor that acts by inhibiting the bodily synthesis of PGs (1). Various preparations are available, including tablets, injections, intranasal sprays, and ophthalmic solutions (19). Parenteral administration increases the drug's absorption and onset of action (24). It is available as a tromethamine salt, which augments its water solubility (25, 26), which improves its absorption (26). Its bioavailability is 80%–100% after oral, intramuscular, and intravenous administration (27). The effects begin rapidly within 10 minutes after intramuscular and intravenous injection, and peak analgesia is achieved after 75–150 minutes (19).

Penniston and Hargreaves (28) concluded that periapical infiltration of ketorolac could affect the anesthetic efficacy of an IANB. Another study (11) was discontinued because of severe transient pain after ketorolac injection. Although Aggarwal et al (1) have shown that an articaine infiltration plus ketorolac provides significant increase in IANB success rate, more evidence is required to determine the effects of a ketorolac intraoral injection when severe pain is present.

Therefore this prospective, double-blind, randomized study was designed to determine the effect of a buccal infiltration of ketorolac on the anesthetic efficacy of IANB combined with a buccal infiltration when using articaine with 1:100,000 epinephrine in patients with acute irreversible pulpitis.

Materials and Methods

Forty healthy adult volunteers from Endodontic Department of Dental Branch, Azad University of Medical Sciences, Tehran, Iran were included in this prospective, randomized, double-blind study. This study was approved by the ethics committee of the institution, and power calculation after a pilot study dictated that a sample size of 40 subjects would give 80% power in the success rate of the 2 test groups. Hence, forty patients aged between 18 and 65 years who met the inclusion criteria were invited to participate in this study. Oral questioning and a written questionnaire determined the patients' information, health condition, and preoperative pain. Informed written consent was obtained from each patient. To be included in the study, the patients had to have pain in a mandibular molar (visual analog scale >54) with prolonged response to cold testing (Aeronova GmbH & Co, Cologne, Germany) (lingering pain for more than 45 seconds), absence of any periapical radiolucency on a periapical radiograph (except for a widened periodontal ligament of not more than 0.75–1 mm), a class I or II medical history (American Society of Anesthesiologists), and ability to understand the consent forms and the pain record scales. The exclusion criteria included a known allergy, sensitivity, or contraindications to any NSAIDs or local anesthetics, history of active peptic ulcer, bleeding problems or anticoagulant use, active asthma, decreased renal or liver function, pregnancy or breastfeeding, history of known or suspected drug abuse, patients who had taken NSAIDs, antidepressants, or sedatives within 24 hours before the root canal treatment (RCT), patients experiencing pain in more than 1 mandibular molar (1, 4), and patients where the first injection of IANB did not produce lip numbness.

Before initiating the treatment, the patients were asked to rate their pain on a 170-mm Heft-Parker visual analog scale (HP-VAS 1984) marked with no pain on one side and maximum pain on the other side without millimeter marks. The scale was divided into 4 categories (1):

1. 0 = no pain
2. 1–54 mm = mild pain
3. 55–114 mm = moderate pain
4. >114 mm = severe pain

Patients were provided with an explanation of the treatment procedure, and they were instructed about how to use the pain scales.

Forty packages including questionnaires, consent forms, 2 sterile packs including 2 articaine carpules (Artinibsa; INIBSA Dental S.L.U, Barcelona, Spain) and a self-aspirating syringe (JUYA Co, Tehran, Iran), an insulin syringe (Soha Co, Tehran, Iran), and two 27-gauge long and short needles (Nik Rahnama Kar Co, Tehran, Iran) were provided. A trained final year dental student who was blinded regarding the treatment procedures loaded the ketorolac (Exir Pharmaceutical Company, Boroojerd, Iran) and normal saline into disposable insulin syringes and coded (numeric) the packages according to random number tables. According to the manufacturer's recommendations regarding the photosensitivity of ketorolac, the packages were retained in dark boxes. To ensure blinding, neither the operator nor the assistant had any knowledge about the chosen solutions. All patients received a standard IANB injection that used 1.8 mL 4% articaine containing 1:100,000 epinephrine after negative aspiration. They also received a buccal infiltration of 0.9 mL articaine immediately after the block injection. An injection rate of 1 mL/min was used for each injection. After 5 minutes, 20 patients received a supplemental buccal infiltration of 30 mg/mL ketorolac tromethamine adjacent to the periapical region of the tooth to be treated. The other 20 patients received a buccal infiltration of normal saline. The pulp anesthesia was evaluated every 5 minutes by using an analog electric pulp tester (EPT) (Parkell Inc, Edgewood, NY). The endodontic procedure was commenced 15 minutes after the initial IANB if the patient had lip numbness and 2 consecutive negative responses to the EPT. Otherwise, the patient was excluded from the study. The second author who was not aware of the solutions carried out all the injections.

The patients' age, gender, pain on percussion, and initial pain before starting the treatment were evaluated and compared between the groups. If the patient felt pain during the caries and dentin removal (CDR), access cavity preparation (ACP), and canal length measurements (CLM) stages, then the level of pain was recorded by using the HP-VAS. Whenever an extra injection was applied because of severe pain, the patient's pain score was recorded, and that patient was excluded from the remainder of the study. Successful anesthesia was defined as the absence of pain or only mild pain present during any of the stages of treatment.

The findings were evaluated by using SPSS 22 (IBM Corp, Somers, NY). In this study the role of related factors (gender, pain on percussion, initial pain score, and age [age ranges, 18–27, 28–36, 37–45, and 46–54 years]) were evaluated between 2 groups. The data were statistically analyzed by using Mann-Whitney U and χ^2 tests. The significance level was set at $P < .05$.

Results

For each group 20 patients were assigned, received the treatment, and were analytically assessed. There were not any patient losses.

TABLE 1. Comparison of Age, Gender, Percussion Pain, and Initial Pain

	Control (placebo) (N = 20)	Ketorolac (N = 20)	P value
Age (y)	34.4 ± 10.5 (18–54)	35.7 ± 9 (21–53)	.67
Gender	7 men, 13 women	9 men, 11 women	.37
PP	9 positive, 11 negative	8 positive, 12 negative	.50
IPS	111.5 ± 29.2	106.5 ± 29.0	.64

IPS, initial pain score (HP-VAS); PP, percussion pain.