Effect of a Combination of Intranasal Ketorolac and Nitrous Oxide on the Success of the Inferior Alveolar Nerve Block in Patients with Symptomatic Irreversible Pulpitis: A Prospective, Randomized, Double-blind Study

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Abstract

Introduction: Previous studies in patients with irreversible pulpitis have reported increased success of the inferior alveolar nerve block (IANB) using premedication with ketorolac. Preemptive nitrous oxide administration has also shown an increase in the success of the IANB. Recently, ketorolac has been made available for intranasal delivery. Perhaps combining ketorolac and nitrous oxide would increase success. Therefore, the purpose of this prospective, randomized, double-blind study was to determine the effect of a combination of intranasal ketorolac and nitrous oxide/oxygen on the anesthetic success of the IANB in patients presenting with symptomatic irreversible pulpitis. **Methods:** One hundred two patients experiencing spontaneous moderate to severe pain with symptomatic irreversible pulpitis in a mandibular posterior tooth participated. Patients were randomly divided into 2 groups and received either 31.5 mg intranasal ketorolac or intranasal saline placebo 20 minutes before the administration of nitrous oxide/oxygen. Ten minutes after the administration of nitrous oxide/oxygen, the IANB was given. After profound lip numbness, endodontic treatment was performed. Success was defined as the ability to perform endodontic access and instrumentation with no pain or mild pain. **Results:** The odds of success for the IANB was 1.631 in the intranasal saline/nitrous oxide group versus the intranasal ketorolac/nitrous oxide group with no significant difference between the groups (P = .2523). **Conclusions:** Premedication with intranasal ketorolac did not significantly increase the odds of success for the IANB over the use of nitrous oxide/oxygen alone. Supplemental anesthesia will still be needed to achieve adequate anesthesia. *(J Endod 2017;■:1–5)*

Key Words

Endodontic pain, intranasal ketorolac, ketorolac, symptomatic irreversible pulpitis

Significance

Premedication with intranasal ketorolac did not significantly increase the odds of success for the inferior alveolar nerve block over the use of nitrous oxide/oxygen alone.

The inferior alveolar nerve block (IANB) does not always result in successful pulpal anesthesia (1). The overall success rate (defined as no or mild pain upon endodontic access) for an IANB in patients presenting with symptomatic irreversible pulpitis ranges from 15%-57% (1). Fowler et al (2) evaluated success in molars and premolars in patients with symptomatic irreversible pulpitis. They found the IANB success rate was 28% for first molars, 25% for second molars, and 39% for premolars, with no significant differences when comparing molars with premolars.

Studies have attempted to increase the success of the IANB through buffering, varying anesthetics and dosing, the use of the Gow-Gates and Vazirani-Akinosi techniques, and preoperative medications (1). Generally, the results have not proven to be completely effective (1). One method that has shown increased success is the administration of nitrous oxide. Stanley et al (3), in mandibular teeth diagnosed with symptomatic irreversible pulpitis, found the administration of 30%–50% nitrous oxide resulted in a statistically significant increase in the success (50%) of the IANB versus 28% without nitrous oxide. However, the increase was not high enough to ensure clinical success without the use of supplemental anesthesia.

Studies in endodontics have focused on the use of ketorolac for pain reduction (4), using it as an oral premedication (5–8) or as a buccal infiltration (9, 10) to increase the success of the IANB. Although some studies have shown an improved effect (6–10), Aggarwal et al (5) did not. A review by Li et al (11) called for more studies to evaluate preemptive nonsteroidal anti-inflammatory drugs (NSAIDs) and their impact on IANB success.

Ketorolac is indicated for the management of moderate to severe pain (12). Ketorolac and other nonselective NSAIDs exert their analgesic, anti-inflammatory, and antipyretic effects through the inhibition of cyclooxygenase (12). Because ketorolac is more selective for cyclooxygenase 1, which is found in the central nervous system,

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it may be possible that ketorolac has central analgesic activity that ibuprofen does not possess (12). Ketorolac has a good safety profile (13, 14). Ketorolac has traditionally been administered via intramuscular or intravenous routes.

Recently, ketorolac has been made available as an intranasal spray (Sprix; Regency Therapeutics, Shirley, NY). Sprix has been shown to decrease postoperative pain in oral surgery (15, 16) and medical models (17–20).

In dentistry, most drugs are administered orally, which has the disadvantages of decreased absorption rates and delayed onset. The intranasal administration of ketorolac was rapidly absorbed, exhibited a maximum plasma concentration within 30 to 45 minutes of administration, and had a half-life of 5 to 6 hours (13, 14). McAleer et al (13) concluded that 30 mg intranasal ketorolac was equivalent to approximately 20 mg intramuscular ketorolac. Intranasal drug delivery is an attractive option because of the ease of administration, rapid onset of action, avoidance of gastrointestinal and hepatic first-pass effects, and the nasal mucosa's high permeability and rich vascularity (21). Intranasal drugs are primarily absorbed in the inferior turbinate because of its vascularity and large surface area (21). However, because of the limited space in the nasal cavity, the volume of drug administered should be less than 200 μL total or, in other words, 100 μL in each nostril (21). This volume correlates to the manufacturer's recommended dose of 1 spray in each nostril (100 μL), with each containing 15.75 mg ketorolac tromethamine. The intranasal route of administration may be more effective than traditional oral delivery.

Although increased success of the IANB has been shown for both nitrous oxide and ketorolac individually, neither has shown success rates that would ensure clinical success without the use of supplemental anesthesia. Perhaps the combination of the 2 medications with varying mechanisms of action would improve overall success and reduce intraoperative pain for patients. No study has investigated the efficacy of a combination of intranasal ketorolac and nitrous oxide/oxygen for increasing the success of the IANB in patients diagnosed with symptomatic irreversible pulpitis. Therefore, the purpose of this prospective, randomized, double-blind study was to determine the effect of a combination of intranasal ketorolac and nitrous oxide/oxygen on the anesthetic success of the IANB in patients presenting with symptomatic irreversible pulpitis.

Materials and Methods

One hundred two adult patients participated in this study. All were emergency patients and in good health as determined by a health history and oral questioning. Exclusion criteria were as follows: under 18 or over 64 years of age; less than 110 lb in weight; allergy to nitrous oxide or ketorolac; history of significant medical problem (American Society of Anesthesiologists classification III or greater); taking pentoxifylline or probenecid, kidney disease, bleeding disorder, stomach ulcer, heart disease, angioedema, or bronchospastic reactivity to aspirin or other NSAIDS; depression, schizophrenia, or bipolar disorder; nasopharyngeal obstructions, respiratory infection, or sinusitis; recently took central nervous system depressants (including alcohol or any analgesic medications); pregnancy; lactating; or the inability to give informed consent. The Ohio State University Human Subjects Review Committee approved the study, and written informed consent was obtained from each patient.

Each patient had a vital mandibular posterior tooth (molar or premolar) with a clinical diagnosis of symptomatic irreversible pulpitis, was actively experiencing pain, and had a prolonged response to cold testing with Endo-Ice (1,1,1,2 tetrafluoroethane; Hygenic Corp, Akron, OH). Patients with no response to cold testing, periradicular pathosis (other than a widened periodontal ligament), or no vital coronal pulp tissue upon access were excluded from the study.

We included posterior teeth to evaluate the teeth that would commonly require endodontic treatment and that have the most difficulty achieving profound anesthesia (1). A study by Fowler et al (2) showed that the success rates of the IANB in patients with symptomatic irreversible pulpitis for first molars, second molars, and premolars were not significantly different. Therefore, based on this evidence-based research, using posterior teeth is acceptable when evaluating the IANB.

Each patient rated his or her initial pain on a Heft-Parker 170-mm visual analog scale (VAS) (22). The VAS was divided into 4 categories. No pain corresponded to 0 mm. Mild pain was defined as greater than 0 mm and less than or equal to 54 mm. Mild pain included the descriptors of faint, weak, and mild pain. Moderate pain was defined as greater than 54 mm and less than 114 mm. Severe pain was defined as equal to or greater than 114 mm. Severe pain included the descriptors of strong, intense, and maximum possible. Patients had to present with spontaneous moderate to severe initial pain to be included in the study.

The 2 treatments (intranasal ketorolac or intranasal saline placebo) were assigned random 6-digit numbers. Each patient was assigned a 6-digit random number to determine which treatment regimen would be administered. Only the random numbers were recorded on the data collection sheets to maintain blinding of the experiment.

The patients randomly received either 31.5 mg intranasal ketorolac (Sprix) (1 spray of 15.75 mg ketorolac tromethamine per nostril) or intranasal bacteriostatic 0.9% sodium chloride (1 spray per nostril using a similar-sized spray bottle as Sprix made by Central Ohio Compounding, Columbus, OH) 30 minutes before the IANB.

A trained research assistant not involved in the IANB injections or endodontic access administered either intranasal ketorolac or intranasal saline. The principal investigator (D.S.) was not present in the operatory, did not see either spray bottle, and was not involved with the administration of the medication or the saline placebo. The patients were informed that intranasal ketorolac or saline was to be administered by dispensing 1 spray in each nostril. This followed the instructions provided by the Sprix manufacturer (23). The patients were instructed to gently blow their nose before the administration of the nasal spray and advised that during administration they were not to inhale. The patients were then instructed to tilt their head slightly forward and deposit 1 spray into each nostril with the tip of the bottle facing away from the center of their nose. The patients reported any sensations/side effects (eg, burning or tingling) during administration of the medication or placebo.

The nitrous oxide/oxygen was administered 10 minutes before the IANB (20 minutes after intranasal ketorolac or intranasal saline) with a scented nasal mask (Accutron, Inc, Phoenix, AZ) and a nitrous oxide machine (McKesson Equipment Company, Chesterfield, UK). A 6-L/min flow rate of 100% oxygen was established, and the patient adjusted the nasal hood for comfort. Patients were instructed to breathe through their nose. After 5 minutes of 100% oxygen, the nitrous oxide/oxygen was titrated until an ideal sedation level was reached at a 30%–50% concentration. The patient was maintained at this level for 5 minutes before the injection of local anesthetic.

An IANB was administered 15 minutes before endodontic access (10 minutes after nitrous oxide/oxygen administration and 30 minutes after intranasal ketorolac or saline) with 3.6 mL 2% lidocaine with 1:100,000 epinephrine (Xylocaine; AstraZeneca LP, Dentsply, York, PA) using a conventional IANB (24) with a 27-G 11/2-inch needle (Monoject; Tyco Healthcare Group LP, Mansfield, MA). Before the IANB, topical anesthetic gel (20% benzocaine; Patterson Dental Supply,