Effect of Nitrous Oxide on the Efficacy of the Inferior Alveolar Nerve Block in Patients with Symptomatic Irreversible Pulpitis

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Abstract

Introduction: The inferior alveolar nerve (IAN) block does not always result in successful pulpal anesthesia. Anesthetic success rates might be affected by increased anxiety. Nitrous oxide has been shown to have both anxiolytic and analgesic properties. Therefore, the purpose of this prospective, randomized, double-blind, placebo-controlled study was to determine the effect of nitrous oxide on the anesthetic success of the IAN block in patients experiencing symptomatic irreversible pulpitis. **Methods:** One hundred emergency patients diagnosed with symptomatic irreversible pulpitis of a mandibular posterior tooth were enrolled in this study. Each patient was randomly assigned to receive an inhalation regimen of nitrous oxide/oxygen mix or room air/oxygen mix (placebo) 5 minutes before the administration of the IAN block. Endodontic access was begun 15 minutes after completion of the IAN block, and all patients had profound lip numbness. Success was defined as no or mild pain (visual analog scale recordings) on access or instrumentation. **Results:** The success rate for the IAN block was 50% for the nitrous oxide group and 28% for the placebo group. There was a statistically significant difference between the 2 groups ($P = .024$). **Conclusions:** For mandibular teeth diagnosed with symptomatic irreversible pulpitis, administration of 30%–50% nitrous oxide resulted in a statistically significant increase in the success of the IAN block compared with room air/oxygen. *(J Endod 2012;38:565–569)*

Key Words

Inferior alveolar nerve block, irreversible pulpitis, nitrous oxide, pulpal anesthesia

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The inferior alveolar nerve (IAN) block is the most frequently used mandibular injection technique for achieving local anesthesia for endodontic treatment. However, the IAN block does not always result in successful pulpal anesthesia, especially in patients with symptomatic irreversible pulpitis. Failure has been reported 44%–81% of the time (1–13).

Recently, Matthews et al (9), Oleson et al (11), and Simpson et al (13) evaluated the anesthetic success rate of an IAN block in mandibular posterior teeth diagnosed with symptomatic irreversible pulpitis. Success (no or mild pain on endodontic access or initial instrumentation) was only 33%, 35%, and 24%, respectively. They found that a supplemental buccal infiltration with 4% articaine with 1:100,000 epinephrine resulted in successful pulpal anesthesia in 58%, 41%, and 38% of the posterior teeth, respectively. Unfortunately, these modest success rate improvements would not provide predictable pulpal anesthesia for all patients.

Many dental patients are anxious about dental treatment (14), and patients with pain reporting for emergency treatment might be even more anxious. Because of the nature of emergency treatment and the failure rate of the IAN block, patients might benefit from sedation.

Lindemann et al (7) conducted a study by using the anxiolytic triazolam (Halcion) for patients with mandibular posterior teeth diagnosed with symptomatic irreversible pulpitis in an attempt to reduce anxiety and increase successful anesthesia. There was no significant difference in successful pulpal anesthesia (no or mild pain on endodontic access or initial instrumentation) between the sublingual triazolam or placebo groups.

Nitrous oxide is the most commonly used inhalation anesthetic in dentistry (15). It has an impressive safety record and is excellent for providing conscious sedation for apprehensive dental patients. Moreover, nitrous oxide provides a mild analgesic effect (15). The most common estimate of analgesic efficacy suggests 30% nitrous oxide is equivalent to 10–15 mg morphine (16). Nitrous oxide might have potential benefits because of its sedation and analgesic effects.

No study has investigated the efficacy of nitrous oxide in increasing the success of the IAN block in patients with irreversible pulpitis. Therefore, the purpose of this prospective, randomized, double-blind study was to determine the effect of nitrous oxide/oxygen on the anesthetic success of the IAN block in patients experiencing symptomatic irreversible pulpitis.

Materials and Methods

One hundred adult patients participated in this study. All were emergency patients of the College of Dentistry and were in good health as determined by a health history and oral questioning. Exclusion criteria was as follows: subjects who were younger than 18 years; allergy to nitrous oxide; history of significant medical problem (American Society of Anesthesiologists III or greater); schizophrenia or bipolar disorder; inability to use a nasal mask (nasopharyngeal obstructions, respiratory infection, or sinusitis); taken central nervous system depressants or any analgesic medication within 8 hours before treatment; pregnancy; or were unable to give

informed consent. The Ohio State University Human Subjects Review Committee approved the study, and written informed consent was obtained from each patient.

To qualify for the study, each patient had a vital mandibular posterior tooth (molar or premolar), was actively experiencing moderate-to-severe pain, and had a prolonged response to cold testing with Green 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 on access were excluded from the study. Therefore, each patient had a tooth that fulfilled the criteria for a clinical diagnosis of symptomatic irreversible pulpitis.

Patients completed a Corah dental anxiety scale (17, 18) to rate their level of anxiety. Corah (17) developed a 4-item questionnaire that asks patients about 4 dentally related situations. The scale yields a score ranging from 4–20.

Each patient rated his or her initial pain on a Heft–Parker visual analogue scale (VAS) (19). The VAS ranged from 0–170 mm and was divided into 4 categories. No pain corresponded to 0 mm. Mild pain was defined as >0 mm and ≤54 mm. Mild pain included the descriptors of faint, weak, and mild pain. Moderate pain was defined as >54 mm and <114 mm. Severe pain was defined as ≥114 mm. Severe pain included the descriptors of strong, intense, and maximum possible. Patients had to present with moderate-to-severe initial pain to be included in the study.

The 100 patients randomly received either nitrous oxide/oxygen or room air/oxygen (placebo) by nasal mask 10 minutes before the administration of local anesthesia. Each patient was randomly assigned a 6-digit number to determine which inhalation regimen was administered. A trained doctor not involved in the administration of local anesthesia or endodontic treatment was responsible for administering either the nitrous oxide/oxygen or room air/oxygen.

The nitrous oxide/oxygen was administered with a scented nasal mask (Accutron, Inc, Phoenix, AZ) and nitrous oxide machine (McKesson Equipment Company, Chesterfield, UK). The scented mask helped to blind the subject to whether they were receiving the treatment or placebo. A 1-cm-diameter hole was drilled in 1 air intake hub of the nitrous oxide unit. This hub was used for those patients receiving the placebo. The hole allowed oxygen to flow past the intake opening, while also allowing room air to be breathed in and mixed with flowing oxygen. No hole was drilled in the hub for the treatment group. The hub, whether experimental or placebo, was covered during each procedure with a round molded dental mask (Mydent International, Hauppauge, NY), trimmed to a size similar to the intake hub, to keep the operator and patient blinded to the treatment received. The nitrous oxide monitor was directed away from the operator and patient. It was only visible to the doctor administering the inhalation regimen.

For the nitrous oxide/oxygen patients, 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 during a 5-minute period until an ideal sedation level was reached. Malamed (20) states that ideal sedation has been achieved when the patient experiences some or all of the following: feeling of lightheadedness, feeling of warmth throughout the body, numbness of the hands and/or feet, a feeling of euphoria, and a feeling of lightness or heaviness of the extremities. The doctor administering the nitrous oxide questioned the patient for these changes every 30 seconds. The operator performing the endodontic treatment was not present in the operatory. The range of nitrous oxide concentration was 30%–50%, which, according to Malamed, is the concentration typically required for analgesia. Once this level was achieved, the patient was maintained at this level for 5 minutes before the injection of local anesthetic.

The room air/oxygen treatment mimicked the nitrous oxide treatment except the setup included the altered gas exchange hub, previously described. 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 doctor mimicked the adjustment of the nitrous oxide flow rate and questioned the patient regarding sedation as described above. The mimicked adjustment and questions continued every 30 seconds for a 5-minute period. The operator performing the endodontic treatment was not present in the operatory. The patient was maintained on the room air/oxygen for 5 minutes before the injection of local anesthesia.

After the administration of either the nitrous oxide/oxygen or room air/oxygen mixture, the operator passively placed anesthetic gel (20% benzocaine; Patterson Dental Supply, Inc, St Paul, MN) at the IAN block injection site for 60 seconds by using a cotton-tip applicator. Patients then received a standard IAN block that was given in the manner described by Jorgensen and Hayden (21) by using a standard aspirating syringe and a 27-gauge 1¼-inch needle. The solution given was 3.6 mL of 2% lidocaine with 1:100,000 epinephrine (Xylocaine; Astra Zeneca LP, York, PA). A single operator (endodontic resident) administered all injections (W.S.).

After the IAN block, the patient was questioned for lip numbness every 5 minutes for 15 minutes. If profound lip numbness was not recorded by 15 minutes, the block was considered missed, and the patient was eliminated from the study. No subjects were eliminated as a result of lack of lip numbness.

Fifteen minutes after the injection (20 minutes after administration of the nitrous oxide/oxygen or room air/oxygen), the teeth were isolated with a rubber dam, and endodontic access was performed. Patients were instructed to definitively rate any pain felt during the endodontic procedure. If the patient felt pain, the treatment was immediately stopped, and the patient rated their discomfort by using the Heft–Parker VAS (19). The level of access achieved when the patient felt pain was recorded as within dentin, entering the pulp chamber, or initial file placement. The success of the IAN block was defined as the ability to access and clean and shape the canals without pain (VAS score of 0) or mild pain (VAS rating ≤54 mm).

The patients who reported moderate or severe pain (VAS rating >54 mm) during access into dentin or when entering the pulp chamber received supplemental anesthetic injections to complete treatment.

The patients were maintained on their original nitrous oxide/oxygen or room air/oxygen levels throughout the appointment. After endodontic treatment, the doctor administering the inhalation anesthesia treatment regimen placed the patient on 100% oxygen for at least 5 minutes. The patient was dismissed unescorted when it was determined that he/she was completely recovered from sedation.

Patients rated the degree of satisfaction they experienced during endodontic treatment on a 100-mm VAS. This VAS was divided into 4 categories. Not satisfied corresponded to 0 mm. Somewhat satisfied was defined as >0 mm and ≤33 mm. Moderately satisfied was defined as >33 mm but <66 mm. Completely satisfied was defined as ≥66 mm. The principal investigator explained the use of the VAS and then left the operatory as the patient completed the VAS.

With 100 subjects (50 in each group) and a nondirectional alpha risk of 0.05, the power of the χ^2 test to detect a difference of ±30 percentage points in anesthetic success was 86%. The data from this study were collected and statistically analyzed. Comparisons between the nitrous oxide/oxygen and room air/oxygen (placebo) groups for anesthetic success, gender, and tooth type were analyzed by using the χ^2 test or, if expected frequencies were <5, the Fisher exact test. The

TABLE 1. Initial Statistics for Nitrous Oxide and Placebo Groups

	Nitrous oxide group	Placebo group	*P* value
Total subjects	50	50	
Total analyzed	50	50	
Gender	Female: 30/50 (60%) Male: 20/50 (40%)	Female: 27/50 (54%) Male: 23/50 (46%)	.54*
Age (mean ± SD), y	33 ± 11	35 ± 13	.50†
Initial pain (mean ± SD), mm	128 ± 25	130 ± 23	.68†
Corah dental anxiety (mean ± SD)	11 ± 4	11 ± 4	1.00†
Tooth type	30 first molars (60%) 11 second molars (22%) 0 third molars (0%) 2 first premolars (4%) 7 second premolars (14%)	23 first molars (46%) 17 second molars (34%) 1 third molar (2%) 1 first premolar (2%) 8 second premolars (16%)	.48‡

SD, standard deviation.

*Values analyzed by using χ^2 test.

†Values analyzed by using the randomization test.

‡Values analyzed by using the Fisher exact test.

Corah dental anxiety scale, age, and initial pain were analyzed by using the randomization test. Comparisons were considered significant if $P < .05$.

Results

The gender, age, initial pain, Corah dental anxiety ratings, and tooth type of the patients are presented in Table 1. There were no significant differences between the nitrous oxide/oxygen and room air/oxygen groups. All subjects in both groups reported initial moderate-to-severe pain. One hundred percent of the patients had subjective lip anesthesia with the IAN blocks.

Anesthetic success is presented in Table 2. IAN block success was 50% for the nitrous oxide/oxygen group and 28% for the room air/oxygen group. There was a significantly higher anesthetic success rate in the nitrous oxide/oxygen group ($P = .024$).

The nitrous oxide dosing was titrated between 30% and 50% for the patients receiving the nitrous oxide regimen. The mean dose of nitrous oxide administered was 43% (±5%).

The mean satisfaction ratings of the nitrous oxide/oxygen group was 95 ± 7 mm, and the mean rating of the room air/oxygen group was 96 ± 10 mm (Table 3). There was no significant difference between the 2 groups.

Discussion

There were no statistically significant differences for the effect of gender, age, initial pain, anxiety rating, and tooth type, so these variables would be minimized between the 2 groups (Table 1). The mean initial pain ratings of 128 mm for the nitrous oxide/oxygen group and 130 mm for the room air/oxygen group correlated to severe pain on the VAS. This pain is representative of patients with symptomatic irreversible pulpitis (4–7, 9, 11, 13, 22–24) who present for emergency endodontic treatment.

The Corah Dental Anxiety Scale is a commonly used dental anxiety scale and is easy to administer (18). The rating in both groups averaged 11, which indicates moderate anxiety (Table 1) (18). Because the current study evaluated emergency patients in pain, the occurrence of moderate anxiety would be expected.

In previous studies of endodontic patients with irreversible pulpitis, success rates for the IAN block have ranged from 19%–57% (1–13). All of the patients in these studies had lip numbness with the IAN block. Our success rate with the IAN block in the room air/oxygen group (28%) was similar to the 19%–26% success rates recorded by Nusstein et al (1), Reisman et al (2), Claffey et al (5), Bigby et al (6), and Simpson et al (13) but lower than the 33% and 35% success rates recorded by Matthews et al (9) and Oleson et al, respectively (11). Differences in patient populations might account for the varied success rates among the studies. None of the reported success rates would be adequate to complete endodontic therapy.

The success of the IAN block in the nitrous oxide group (50%) was significantly better than that of the placebo group (28%). It was also higher than IAN block success rates found in recent studies by Matthews et al (7), Oleson et al (10), and Simpson et al (11). However, even with a success rate of 50%, half of the patients in this group still required the administration of supplemental anesthesia to complete endodontic treatment.

One of the reasons for using the nitrous oxide regimen was for sedation. However, Lindemann et al (7) found that sedation with sublingual triazolam did not statistically increase anesthetic success in patients with symptomatic irreversible pulpitis. Therefore, sedation does not appear to be sufficient to reduce pain during dental treatment. Profound local anesthesia is still required. If sedation were the only benefit of nitrous oxide, we would not expect a significant effect. Fortunately, in addition to sedation, nitrous oxide also has an analgesic effect (15). This is the effect that we hypothesized might increase the success of the IAN block.

Although the exact mechanism of action of nitrous oxide is not known, it is known that nitrous oxide does not work through a single mechanism. Research indicates that nitrous oxide activates its analgesic effect by causing the release of endogenous opiate peptides with subsequent activation of opioid receptors (25) and by the inhibition of N-methyl-D-aspartate (NMDA) glutamate receptors (25). NMDA typically incites an excitatory response in the nervous system; therefore, by blocking this effect, nitrous oxide creates the desired analgesic effect (25). An advantage of nitrous oxide in the current study is that it targets both opiate receptors and NMDA receptors to provide analgesia. The anxiolytic effect involves the activation of the gamma-aminobutyric acid A receptor through the binding site for benzodiazepines (25). The anxiolytic effect of nitrous oxide involves 3 key enzymes: nitric oxide

TABLE 2. Anesthetic Success

	Nitrous oxide group	Placebo group	*P* value
IAN block success	25/50 (50%)	14/50 (28%)	.024*

n = 100

*Values analyzed by using χ^2 test.

TABLE 3. Percentages and Satisfaction Ratings for Nitrous Oxide/Oxygen and Room Air/Oxygen Groups

Group	Not satisfied	Somewhat satisfied	Moderately satisfied	Completely satisfied	Mean*	*P* value†
N_2O/O_2	0% (0/49)	0% (0/49)	63% (31/49)	37% (18/49)	95 ± 7	.78
Air/O_2	0% (0/50)	2% (1/50)	58% (29/50)	40% (20/50)	96 ± 10	

n = 49 N_2O/O_2 group (1 patient did not fill out the form). n = 50 Air/O_2 group.

*Mean values on VAS ± standard deviation.

†There was no significant difference ($P > .05$) between the 2 groups.

synthase, soluble guanylyl cyclase, and cyclic guanosine monophosphate–dependent protein kinase (25). The inhibition of any of these enzymes blocks the anxiolytic effect of nitrous oxide.

The concentration of 30%–50% nitrous oxide was chosen for this study for 2 reasons. Jastak and Donaldson (16) theorized that a 30% dose of nitrous oxide is equivalent to a 10- to 15-mg dose of morphine. Second, a dose range of 25%–50% nitrous oxide has been commonly used in previous studies evaluating nitrous oxide sedation and analgesia during painful procedures (20, 26–28). Meskine et al (28) showed that 50% nitrous oxide use during liver biopsy resulted in significantly better analgesia versus Darvocet-N. Paris et al (26) found nitrous oxide sedation to be significantly better than morphine chlorhydrate in managing analgesia during the treatment of painful bedsores. Maslekar et al (27) conducted a randomized trial comparing sedation and pain control with 50% nitrous oxide with intravenous midazolam and fentanyl. They found that patients in the N_2O group reported significantly less pain and higher satisfaction than patients receiving midazolam-fentanyl. These studies show that the dose of nitrous oxide administered in the current study has been shown to provide improved analgesia in previous research designs.

Other studies in the literature have shown that higher doses of nitrous oxide are also effective in producing analgesia (29–31). Some have reported that 70% nitrous oxide showed a statistically significant improvement in pain scores. However, 70% nitrous oxide also resulted in significantly more side effects (nausea and vomiting), negating the advantages of improved analgesia.

Patient satisfaction ratings for both groups resulted in moderate-to-complete satisfaction 98%–100% of the time (Table 3). Gale et al (32), Davidhizar and Shearer (33), Schouten et al (34), and Fletcher et al (35) found patient satisfaction is related to maintaining a positive and professional attitude, practicing encouragement, avoiding defensiveness, and a caring manner. Communicative behavior of the dentist (bedside manner) being positively related to patient satisfaction might help explain why patients are satisfied with endodontic treatment even though pain might be involved with treatment. Patients might also be rating satisfaction in relation to their satisfaction of the emergency procedure completion in the hope that their discomfort will be abated.

Although the increase in success was statistically significant, the modest gain alone would not be deemed satisfactory for the completion of treatment (ie, without supplemental anesthesia). Nonetheless, the results showed that nitrous oxide sedation did increase the success of an IAN block and therefore might be a useful technique to add to the armamentarium used in the treatment of teeth with symptomatic irreversible pulpitis (ie, in addition to using supplemental anesthesia). Furthermore, if a patient were to present with irreversible pulpitis of a mandibular tooth and severe anxiety and requesting sedation, this study points to the possibility that nitrous oxide sedation might be preferable to oral sedation with triazolam. With nitrous oxide sedation the dose is titratable, the patient would not require a driver to accompany them, and they would not be sedated beyond the length of the treatment appointment.

In conclusion, for mandibular posterior teeth diagnosed with symptomatic irreversible pulpitis, administration of 30%–50% nitrous oxide/oxygen resulted in a statistically significant increase in the success of the IAN block compared with room air/oxygen.

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