EFFECT OF NITROUS OXIDE/INTRANASAL KETOROLAC COMBINATION ON THE SUCCESS OF THE INFERIOR ALVEOLAR NERVE BLOCK IN PATIENTS WITH SYMPTOMATIC IRREVERSIBLE PULPITIS

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Abstract

Introduction: Previous studies have reported increased success of the inferior alveolar nerve block using premedication with ketorolac. One study reported having an increased success rate of the IANB with the addition of nitrous oxide. Recently, ketorolac has been made available with intranasal delivery. Therefore, the purpose of this prospective, randomized, double-blind study is to determine the effect of the combination of nitrous oxide/intranasal ketorolac on the anesthetic success of the inferior alveolar nerve block in patients experiencing symptomatic irreversible pulpitis.

Methods: One hundred and two patients experiencing moderate to severe pain with symptomatic irreversible pulpitis in a mandibular posterior tooth were recruited. Patients were randomly divided into two groups and received either 31.5 mg intranasal ketorolac or placebo thirty minutes prior to administration of nitrous oxide/oxygen. Ten minutes after administration of nitrous oxide/oxygen, the IANB was given. Following profound lip numbness, endodontic treatment was performed. Success was defined as the ability to perform endodontic access and instrumentation with no to mild pain.

Results: The success rate of the IANB was 46% (24/52) in the placebo group and 54% (27/50) in the ketorolac group with no significant difference between the groups ($p=0.428$).

Conclusions: Premedication with intranasal ketorolac did not significantly increase the success of the inferior alveolar nerve block. The 46% and 54% success rates support previous findings that administration of nitrous oxide/oxygen increases the success of IANB in patients diagnosed with symptomatic irreversible pulpitis. Supplemental anesthesia will still be needed to achieve adequate anesthesia.

DEDICATION

To Hayley and my family, thank you for all of your love and support over the past two years.

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Chapter 1: Introduction

The inferior alveolar nerve block (IANB) does not always result in successful pulpal anesthesia. Achieving profound anesthesia is paramount for any dental procedure, especially endodontic therapy. High failure rates have been found for the inferior alveolar nerve block, especially in patients diagnosed with symptomatic irreversible pulpitis (1-8). The success rate for an IANB in patients presenting with symptomatic irreversible pulpitis, (defined as mild to no pain upon endodontic access), ranges from 15%-57% (1-5,7,9-12). There are multiple theories explaining the failure to achieve pulpal anesthesia: central core theory, tetrodotoxin resistant sodium channels, increased number of voltage gated sodium channels, altered resting potentials, lower pH of inflamed tissues, accessory nerve innervation, decreased pain thresholds, and diffusion of anesthetic following the path of least resistance (13-18). With the low success rate of the IANB in patients diagnosed with symptomatic irreversible pulpitis, it is necessary to employ other measures to provide endodontic treatment with no to mild pain.

Traditionally, when failure of an inferior alveolar nerve block occurs, supplemental anesthetic techniques are used to gain adequate pulpal anesthesia. Examples include: buccal infiltration, intraosseous, intraligamentary and intrapulpal injections. Research has been conducted to improve the success of the inferior alveolar nerve block so that the clinician does not have to rely solely on supplemental injections.

Many studies have attempted to increase the success of the IANB through buffering, varying anesthetics and dosing, and preoperative medications to no avail (8, 19-24).

A study by Oleson and coauthors (12) investigated the effect of premedication with 800 mg of ibuprofen on the success of an IANB in patients diagnosed with symptomatic irreversible pulpitis. One hundred patients were given 800 mg of ibuprofen or placebo 45 minutes prior to IANB. Success was defined as no or mild pain upon access or instrumentation. The results showed a success rate of 41% for 800 mg ibuprofen and 35% for placebo with no statistically significant difference between the groups ($p=0.57$).

Simpson and coauthors (22) studied the effect of a preoperative combination of 800mg ibuprofen/1000 mg acetaminophen on the success of the IANB in patients diagnosed with symptomatic irreversible pulpitis. One hundred patients were randomly divided and given 800 mg ibuprofen/1000 mg acetaminophen or placebo 45 minutes prior to IANB. The results of the study showed no statistically significant difference between the two groups ($p=0.37$), with a 32% success rate for the combination ibuprofen/acetaminophen and 24% success rate for placebo.

Fullmer and coauthors (23) investigated the effect of premedication with a combination of 1000 mg acetaminophen/10 mg hydrocodone on the success of IANB in patients with symptomatic irreversible pulpitis. One hundred patients were included in the study. The success rate for the acetaminophen/hydrocodone group was 32% and for

the placebo group the rate was 28% with no statistically significant difference between the groups (p=0.662).

Shahi and coauthors (24) compared the effect of premedication with 400 mg ibuprofen, 0.5 mg dexamethasone or placebo on the success of an IANB in patients diagnosed with asymptomatic irreversible pulpitis. One hundred sixty five patients were randomly divided into three groups and administered the assigned drug one hour prior to IANB. The results showed no statistically significant difference when comparing ibuprofen and placebo (p=0.055) or ibuprofen and dexamethasone (p=0.34). However, a statistically significant difference was found when comparing dexamethasone and placebo (0.001).

One method that has shown increased success is administration of nitrous oxide. A recent study by Stanley and coauthors found increased success of the inferior alveolar nerve block in patients diagnosed with symptomatic irreversible pulpitis when nitrous oxide was administered (25). However, the increase was not enough to overcome the clinical problems associated with the treatment of irreversibly inflamed teeth.
More recent studies in dentistry have focused on attempting to increase the success rate of the inferior alveolar nerve block through premedication with ketorolac (26-29). One investigation found an increase in pulpal success rate when ketorolac was injected intraorally (30). The results of this study showed that the success rate was not high enough for clinical significance. A recent review (31) called for more studies evaluating preemptive NSAIDs.

Ketorolac is indicated for the management of moderate to severe pain and has traditionally been administered via intramuscular or intravenous routes. Recently, ketorolac has been made available in an intranasal spray (Sprix®, Regency Therapeutics, Shirley, New York). Sprix® has shown decreased postoperative pain in oral surgery and medical models (32,33).

Although increased success has been shown for both nitrous oxide and ketorolac individually, neither has shown significant success rates. Perhaps the combination of two effective medications with varying mechanisms of action would improve overall success rates and reduce pain for patients. No study has investigated the efficacy of a combination of nitrous oxide/oxygen and intranasal ketorolac for increasing the success of the inferior alveolar nerve block in patients diagnosed with symptomatic irreversible pulpitis. Therefore, the purpose of this prospective, randomized, double-blind study was to determine the effect of the combination of nitrous oxide/intranasal ketorolac on the anesthetic success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis.

Chapter 2: Materials and Methods

One hundred and two adult patients participated in this study. All were emergency patients of The Ohio State University College of Dentistry and in good health as determined by a health history and oral questioning.

Inclusion criteria were: 18 to 64 years of age; over 110 pounds in weight; in good health (ASA classification I or II); informed consent granted. Exclusion criteria were: under 18 or over 64 years of age; less than 110 pounds in weight; allergy to nitrous oxide or ketorolac; history of significant medical problem (ASA classification III or greater); angioedema or bronchospastic reactivity to aspirin or other NSAIDS; gastrointestinal problems; depression, schizophrenia or bipolar disorder; inability to use a nasal mask (nasopharyngeal obstructions, respiratory infection, or sinusitis); recently taken CNS depressants (including alcohol or any analgesic medications); pregnancy; lactating; or inability to give informed consent. The Ohio State University Human Subjects Review Committee approved the study on April 6, 2015 (2014H0427). Written informed consent and HIPAA research authorization were obtained from each patient (Appendix A, B). After completion of the medical history and consent form, the subjects completed the Corah's Dental Anxiety Scale questionnaire (34-36).

Each patient had a vital mandibular posterior tooth (molar or premolar with a clinical diagnosis of symptomatic irreversible pulpitis), had been actively experiencing

pain, and had a prolonged response to cold testing with Endo-ice® (1,1,1,2 tetrafluoroethane; Hygenic Corp., Akron Ohio). 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.

Each patient rated his or her initial pain on a Heft Parker visual analogue scale (VAS) (37). The VAS was divided into four categories: no pain was 0 mm; mild pain was greater than 0 mm and less than or equal to 54 mm (faint, weak, mild); moderate pain was greater than 54 mm and less than 114 mm; and severe pain was equal to or greater than 114 mm (strong, intense, maximum possible).

The two treatments were assigned random, six-digit numbers using the website random.org. Each patient was randomly assigned a six-digit random number to determine which treatment regimen would be administered. Only the random numbers were recorded on the data collection sheets to blind the experiment to both the operator and patient. The patients randomly received either 31.5 mg of intranasal ketorolac (Sprix®, Regency Therapeutics, Shirley, New York) or intranasal bacteriostatic 0.9% sodium chloride (Central Ohio Compounding, Columbus, Ohio) 30 minutes prior to the inferior alveolar nerve block.

An assistant not involved in the inferior alveolar nerve block injections or endodontic access instructed the patient in the administration of the blinded treatment regimen. The operator (DS) did not see either bottle and was not involved with any distribution or administration of the medication or placebo. The patients were informed that intranasal ketorolac or saline were to be administered by dispensing one spray of

medicine in each nostril. This followed the regimen according to the Sprix® manufacturer's instruction. The patients were instructed to gently blow their nose prior to 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 one spray into each nostril with the tip of the bottle facing away from the center of their nose. The patients noted any sensations/side effects (burning, tingling, drainage, sneezing) during administration of the medication or placebo.

The nitrous oxide/oxygen was given 10 minutes prior to the inferior alveolar nerve block (20 minutes following intranasal ketorolac or placebo) with a scented nasal mask (Accutron, Inc., Phoenix, AZ) and nitrous oxide machine (McKesson Equipment Company, Chesterfield, UK). Oxygen was given 15 minutes after intranasal drug delivery for a period of 5 minutes prior to administration of the nitrous oxide/oxygen. Oxygen was also given for 5 minutes after the administration of nitrous oxide at the end of the appointment. The nitrous oxide/oxygen was titrated over a five-minute period until a 30% to 50% concentration of nitrous oxide was achieved. Stanley and coauthors (25) found a 50% success rate for IANB when given in conjunction with nitrous oxide compared with 28% for placebo. Stanley and coauthors (25) used a nitrous oxide/oxygen concentration of 30-50%. Therefore, we used a range of 30-50% in the current study. However, a few patients reached the desired sedation level at dosage below 30% and a few patients required more than 50% to achieve the required level of sedation. Even so, most patients fell into the 30-50% range reported by Stanley et al (25). The practitioner administering the nitrous oxide (DS) monitored the patient for sedation, and then the

patient was maintained at this level for 5 minutes prior to the injection of local anesthetic. The patient was instructed to rate their perceived level of sedation prior to injection of local anesthetic.

Before the injection, each subject was informed of the pain ratings for needle insertion, needle placement, and deposition of solution and was shown the visual analogue scale (VAS). During each phase of the injection, the operator informed the subject when each phase of the injection was complete. Immediately after the inferior alveolar nerve block, subjects rated the pain for each injection phase on the VAS as outlined previously.

An inferior alveolar nerve block was administered 15 minutes prior to endodontic access (10 minutes after nitrous oxide/oxygen administration and 30 minutes after intranasal ketorolac/placebo) with 1.8 ml 2% lidocaine with 1:100,000 epinephrine (Xylocaine, AstraZeneca LP, Dentsply, York, PA) using a conventional inferior alveolar nerve block with a 27-gauge 1½-inch needle (Monoject; Tyco Healthcare Group LP, Mansfield, MA).

Topical anesthetic gel (20% benzocaine, Patterson Dental Supply, Inc., St. Paul, MN) was passively placed at the inferior alveolar nerve block injection site for 60 seconds using a cotton tip applicator. The needle was inserted (needle insertion) with landmarks described by Jorgensen and Hayden (38). The needle was then advanced to the target site (needle placement). After gentle contact with bone, the needle was withdrawn 1 mm, aspiration was performed and the anesthetic solution was deposited over a 1-minute time period (solution deposition). Patients were then asked to rate the

pain of the three phases of the injection on the 170 mm VAS. The patients then received a second inferior alveolar nerve block using 1.8 ml 2% lidocaine with 1:100,000 epinephrine. The pain of the second block was not recorded due to numbness already achieved with the first injection.

The patient was questioned every minute for 15 minutes following the second IANB if his/her lip was numb. If profound lip numbness was not recorded at 15 minutes, the block was considered missed and another block was given, and the patient was excluded from the study. Once profound lip numbness was achieved, the patients were then given a buccal nerve block using 0.4 ml 2% lidocaine with 1:100,000 epinephrine. The buccal nerve block was not given for pulpal anesthesia but was administered solely for soft tissue comfort in the placement of the rubber dam.

At 15 minutes post-injection, the tooth was 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 using the Heft-Parker visual analogue scale. The extent of access achieved when the patient felt pain was recorded as within dentin (1), entering the pulp chamber (2), or file placement (3). The numbers 1, 2 and 3 were used to convey to the patient the extent of access achieved. The success of the inferior alveolar nerve block was defined as the ability to access and instrument the tooth without pain (VAS score of zero) or mild pain (VAS rating less than or equal to 54 mm).

If the patient experienced moderate or severe pain during endodontic access, a buccal infiltration of 1.8 ml of 4% articaine with 1:100,000 epinephrine (Septocaine,

Septodont, New Castle, DE) was given at the apex of the tooth being treated. If the buccal infiltration was not successful and the patient felt moderate to severe pain during continued access, then an intraosseous injection was given. The intraosseous injection was administered distal to the tooth having treatment using either the Stabident system (Stabident, Fairfax Dental Inc,, Miami, FL) or X-Tip intraosseous anesthetic delivery system (Dentsply Maillefer, Ballaigues, Switzerland) and 1.8 ml 2% lidocaine with 1:100,000 epinephrine. If the patient continued to experience moderate to severe pain during treatment, a second intraosseous injection was given mesial to the tooth. In five patients, an intrapulpal injection was also necessary to complete treatment.

After receiving emergency endodontic treatment, patients rated the degree of satisfaction with the treatment using an analogue scale for assessing satisfaction (Appendix L). The patients also recorded their treatment pain as greatest pain felt during the procedure using the visual analogue scale (VAS). The ratings were completed at the end of the appointment when the operator left the room. The satisfaction survey and treatment pain rating were given to the front desk when checking out. It was emphasized that the satisfaction survey would not affect the operator's grades or standing in the residency so that patients were encouraged to be honest in their assessment.

Comparisons between the intranasal ketorolac and intranasal saline groups for gender and anesthetic success were analyzed using the chi-square test, whereas differences in age, initial pain scores, sedation rating, injection pain, treatment pain and degree of satisfaction were analyzed using the Bonferroni-Randomized test. Anxiety level between the groups was analyzed using the Raw Wilcoxon Signed-Ranks test. With

100 subjects (50 in each group) and a non-directional alpha risk of 0.05, the power of the Chi-square test to detect a difference of ±30 percentage points in anesthetic success was 91%. However, because of potential withdrawal by subjects, the number was set to 110. Comparisons were considered significant if $p<0.05$.

Chapter 3: Results

Table 1 illustrates the subject profile for both the ketorolac/N_2O-O_2 (treatment) and N_2O-O_2 (control) groups. In both the treatment and control groups there were more female than male subjects. In the control group, the distribution was 65% female and 35% male. For the treatment group it was 64% female and 36% male with no significant difference between the control and treatment groups (p=0.883). Mandibular first and second molars comprised a majority of the teeth treated for both treatment and control groups with no significant difference between the two (p=0.772).

Table 2 describes the average age of the subjects along with their anxiety level and initial pain prior to treatment. The average age of the subjects in the control and treatment groups was 35 and 34 years, respectively, with no statistical difference between groups (p=1.000). Anxiety level was measured using Corah's Anxiety and is scored from 4-20. The median Corah anxiety level for control group was 9. The treatment group had a median Corah anxiety level of 11 with no significant difference (p=0.058) between the two groups when analyzed using the Wilcoxon Signed-Ranks test. A score between 9 and 12 indicates moderate anxiety when using Corah's Dental anxiety scale. Initial pain level for subjects to be included in the study had to be moderate, which corresponds to greater than 84 mm based on a 170 mm Heft-Parker VAS. The mean initial pain ratings for the control and treatment groups were 130 mm and 129 mm, respectively, with no significant

difference between the groups (p=1.000). There was no significant difference in sedation ratings between the two groups (p=1.000) as seen in Table 3. Table 4 shows sedation ratings by category. The control groups had a mean sedation rating of 60 mm on a 100 mm VAS while the treatment group had a mean of 61 mm.

Table 5 describes the anesthetic success of the IAN block, articaine infiltration and intraosseous injection for both the treatment and control groups. There was no statistical difference between the groups for any of the three injections; IAN block (p=0.428), articaine infiltration (p=0.357) or intraosseous injection (p=0.121). The success of the IAN block for both the control and treatment groups was 46% and 54%, respectively.

Table 6 compares the pain of the three phases of the IANB injections (needle insertion, needle placement and solution deposition) between the two groups. All injection pain values were based on a 170 mm Heft-Parker VAS. For the IAN block, the control group had mean pain scores of 57 mm on insertion, 58 mm on placement and 54 mm on deposition, all falling within the mild to moderate pain category with clustering closer to the mild pain category and with larger standard deviations for all injection pain ratings. The treatment group had mean pain scores of 49 mm on insertion, 46 mm on placement and 48 mm on deposition, all falling within the mild pain category. For articaine infiltration both the control group and treatment group reported only mild pain for all phases of the injection. The values for intraosseous injection (I/O) were similar to those of the articaine infiltration in that all values fell within the mild pain range. There

was no statistical difference (p=1.000) between the groups for any of the injections or phases of injection.

Table 7 illustrates the amount of pain felt (none, mild, moderate or severe) for both groups on needle insertion, needle placement and solution deposition of the IAN block. During the needle insertion phase, 50% of the control group noted moderate pain while 56% of the treatment group marked mild pain. During the needle placement phase, 46% of the control group noted moderate pain while 42% of the treatment group marked mild pain. During the anesthetic deposition phase, 46% of the control group noted moderate pain while 42% of the treatment group marked mild pain.

Table 8 illustrates the amount of pain felt (none, mild, moderate or severe) for both groups during needle insertion, needle placement and solution deposition of the articaine infiltration. A majority of the subjects for both the control and treatment group noted mild pain for all phases of the injection.

Table 9 illustrates the amount of pain felt, none, mild, moderate or severe for both groups on needle insertion, needle placement and solution deposition of the I/O injection. For both groups and all phases of the injection a majority of the subjects noted mild pain.

Table 10 illustrates the failure point (dentin, chamber or canal) for all three injections for both groups. For the IAN block, both the control group and treatment groups had a majority of their failures in dentin, 61% and 65%, respectively. The same was true for the articaine infiltration with 47% failure in dentin for the control group and 64% for the treatment group. The I/O injection for the control group failed one time in

the dentin and one time in the chamber. The I/O injection for the treatment group failed twice in the dentin and twice in the chamber.

Both the control and treatment groups had the same mean satisfaction rating of 96 mm based on a 100 mm VAS as shown in Table 11. Table 12 describes satisfaction ratings by category.

Table 13 shows the treatment pain rating for both groups with no statistically significant difference between groups (p=1.000). The average treatment pain rating for the control group was 42 mm and for the treatment group it was 33 mm, both based on the 170 mm Heft-Parker VAS.

Chapter 4: Discussion

The purpose of this prospective, randomized, double-blind study was to determine the effect of the combination of nitrous oxide/intranasal ketorolac on the anesthetic success of the inferior alveolar nerve block in patients experiencing symptomatic irreversible pulpitis. The results of this study are summarized in the proceeding Tables 1-13. Table 1 illustrates the subject profile for both the control group (N_20-O_2) and treatment group (ketorolac/ N_20-O_2). The total number of subjects treated in the current study was 102. There were 34 (65%) females and 18 (35%) males in the control group. The treatment group consisted of 32 (64%) female and 18 (36%) males. Statistically, there was no significant difference between the groups when comparing gender ($p=0.883$). We did not control for the number of females and males in each group because the patients were randomly divided into treatment and control groups as they presented to the clinic for emergency treatment. While there was a higher percentage of females to males in both groups, the results were similar to those found in an American Dental Association survey of endodontists (39). The results of the survey showed that of the patients presenting for endodontic treatment, 59% were female and 41% were male, which is a similar distribution to the current study (39). The percent of female patients in the current study was also similar to that found in previous symptomatic irreversible pulpitis studies performed at The Ohio State University College of Dentistry Division of

Endodontics which ranged from 41% to 68% (7,8,12, 21,22,23,25,40). A study by Liddel and Locker (41) was conducted by sending a questionnaire to randomly selected voters about "their thoughts, feelings, and behavior regarding dental treatment." The results of this study found that women were significantly more affected by pain than men ($p \leq 0.001$). It is important to note that there was no statistically significant difference between the groups ($p=0.883$) with regard to gender. Had there been a significantly higher percentage of females patients in either group, there would have been potential for the results to show an increase in success for the opposing group.

Of the teeth treated throughout this study, 83% in the control group and 82% in the treatment group were mandibular first or second molars. There was no significant difference in tooth type between the two groups ($p=0.722$) (Table 1). The percent of first and second molars treated in this study was similar to that which was found in previous symptomatic irreversible pulpitis studies performed at The Ohio State University College of Dentistry Division of Endodontics that ranged from 70% to 97% (7,8,12,21,22,23,25,40). A retrospective study by Fowler and coauthors (42) investigated the anesthetic success of an IANB in molars and premolars in patients diagnosed with symptomatic irreversible pulpitis. The results of that study showed an anesthetic success rate of 39% for premolars, 28% for first molars and 25% for second molars. Although there was no statistically significant difference in tooth type treated, the anesthetic success rates were not the same for each tooth. With an unequal distribution of premolars to molars between the groups there would be potential for skewing of results. Since there

was no significant difference between the groups in tooth type treated (p=0.722) (Table 1), it was not likely a confounding variable in the current study.

The mean age of the subjects in this study was 35 (±12) years for the control group and 34 (±12) years for the treatment group (Table 2). The subject age ranged from 18 to 64 years for the control group and 18 to 65 years for the treatment group. There was no statistical difference in age between the groups (p=1.000). Patients under the age of 18 were not included because they were unable to give consent. Patients over the age of 65 were not included because the adverse effects of using intranasal ketorolac may be significantly increased (43). Additionally, some studies have shown that there may be changes in pain perception in aging adults due to physiologic changes (44). Gibson suggests that as a person ages, their threshold for pain appears to increase (44). Nordenram and coauthors (45) studied local anesthesia in elderly patients and found that elderly patients had significantly shorter onset time compared to younger patients. Because there was no significant difference in age between the groups, pain perception as related to age should not have been a significant factor.

Table 2 shows the results of the Corah Dental Anxiety Scale (DAS). Corah's DAS was used in this study because it provides a fast and easy way to assess a patient's anxiety (46). Using the Corah Dental Anxiety Scale, it is possible to have scores ranging from 4 to 20. A score less than 9 is considered low anxiety, between 9 and 12 moderate anxiety, 13 to 14 high anxiety and 15 to 20 severe anxiety. The median Corah DAS score for the control group was 9 and the score for the treatment group was 11. There was no statistical difference between the groups (p=0.058) and the median scores for both the

treatment and control groups fell within the moderate category. Eli and co-authors (47) have reported that between 10-30% of patients experience anxiety toward dental treatment. It is important to assess a patient's anxiety level prior to treatment because an increased anxiety level may lead to an increased perception of pain (47). Eli and co-authors (47) examined the relationship between anxiety and pain perception during dental implant placement. They evaluated patients at three different time periods: preoperatively, post-operatively, and four weeks post-operatively. They found that at each time point the greatest predictor of perceived pain was the patient's state of anxiety (47). A longitudinal population-based study by Maggirias and Locker (48) attempted to look at psychological factors and perceptions of pain associated with anxiety. They found a significant association between dental anxiety scores and reports of pain. Their results showed that patients with anxiety scores between 12 and 20 were more likely to report having a painful experience than those with a lower score between 4 and 7. Patients with a higher dental anxiety score were also more likely to report pain that was moderate to severe in nature. Since there was no significant difference in anxiety level between the groups and both fell within the moderate category, anxiety as a factor influencing pain perception throughout the study should be reduced.

Prior to inclusion in the current study, patients were asked to record their level of presenting pain on a 170 mm Heft-Parker visual analogue scale. The VAS was divided into four categories: no pain was 0 mm; mild pain was greater than 0 mm and less than or equal to 54 mm (faint, weak, mild); moderate pain was greater than 54 mm and less than 114 mm; and severe pain was equal to or greater than 114 mm (strong, intense, maximum

possible)(37). In order to be included in the study, patients had to be experiencing moderate to severe pain and have a diagnosis of symptomatic irreversible pulpitis. It is important to note that the patients had a diagnosis of symptomatic irreversible pulpitis and not asymptomatic irreversible pulpitis. A study by Argueta-Figueroa and coauthors (49) investigated the efficacy of 4% articaine on the success of IANB in patients diagnosed with asymptomatic irreversible pulpitis versus symptomatic irreversible pulpitis. They found the success rate of an IANB to be 64% for symptomatic patients and 87% for asymptomatic patients. Their results show that patients presenting with symptomatic irreversible pulpitis will have a lower success rate in achieving adequate anesthesia from an IANB than patients diagnosed with asymptomatic irreversible pulpitis. Table 2 displays the mean initial pain scores for patients in both the control and treatment groups. Patients in the control group had a mean pain score of 130 mm ±24 mm which was similar to that of the treatment group with a mean of 129 mm ±22 mm. There was no statistically significant difference ($p=1.000$) in initial pain when comparing the control and treatment groups. Due to the high IANB anesthetic failure rate in patients with symptomatic irreversible pulpitis, a significant difference in initial pain between the groups could have skewed the results. Since there was no difference between the groups with regard to initial pain, it should be limited as a confounding factor.

In the current study, nitrous oxide was used to increase the success of the inferior alveolar nerve block. Nitrous oxide is the most commonly used inhalation anesthetic in dentistry (50). It has an impressive safety record and is excellent for providing conscious sedation for apprehensive dental patients. Nitrous oxide also provides a mild analgesic

effect (50). The most common estimate of analgesic efficacy suggests 30% nitrous oxide is equivalent to 10 to 15 mg morphine (51).

Nitrous oxide has very low blood solubility, giving it the fastest onset and recovery among commonly used inhalation anesthetics (50). Nitrous oxide is not a potent anesthetic, but it is incredibly safe because it has a minimum alveolar concentration of approximately 105% (52). Minimum alveolar concentration refers to "percent of concentration of the gas at 1 atmosphere that renders 50% of patients unresponsive to a surgical stimulus" (50). The mechanism of action for the inhalation anesthetics, nitrous oxide in particular, is not completely understood. The analgesic effects of nitrous oxide are currently believed to be related to the release of endogenous opioid peptides. The proposed mechanism is that nitrous oxide causes the release of endogenous opioid peptides, which bind opioid receptors in the gamma-aminobutyric acid (GABA) pathway, inhibiting the inhibitory tone of GABA (53). This sequence leads to the inhibition of ascending nociceptive signals. The anxiolytic properties of nitrous oxide are similar to those of benzodiazepines. It is believed that nitrous oxide binds to the benzodiazepine binding site activating $GABA_A$, causing the activation of three enzymes: nitric oxide synthase, soluble guanylyl cyclase, and cyclic GMP-dependent protein kinase (53). The anesthetic effects of nitrous oxide are related to the inhibition of N-methyl-D-aspartate (NMDA) glutamate receptors. Inhibition of the NMDA glutamate receptors by nitrous oxide decreases the excitatory effect on the nervous system (53).

Malamed states "The first sign of clinical evidence of the effect of nitrous oxide is usually the feeling of light-headedness" (54). He also states that this is typically followed

by a tingling sensation in the arms or legs or a "feeling of warmth, floating, or heaviness" (54). This relative analgesic state is typically achieved with nitrous oxide concentrations of 30% to 50% (54).

In 1967, Parbrook (55) was able to summarize the dose-related effects of nitrous oxide and associated clinical characteristics that were observed. He divided the dose-related effects into different classifications representing the four zones of analgesia. Zone I represents patients experiencing some analgesia but are able to maintain full verbal contact (51). Zone I is usually seen at nitrous oxide concentrations ranging from 6% to 25% (55). Zone II occurs at concentrations ranging from 26-45% and represents patients that are slightly sedated and are experiencing some slight dissociative analgesia. Zone III consists of patients presenting with substantial inebriation but are usually able to maintain slight verbal contact. Zone III is usually seen at concentration from 46% to 65%. Zone IV is found at a concentration from 66% to 85% and represents light general anesthesia.

A recent study found increased pulpal anesthesia success of the inferior alveolar nerve block with the use of nitrous oxide (25). Stanley and coauthors (25) studied the effect of nitrous oxide on the efficacy of the inferior alveolar nerve block in patients diagnosed with symptomatic irreversible pulpitis. One hundred patients were randomly divided and received nitrous oxide/oxygen at a concentration of 30%-50% or 100% oxygen (placebo). The IANB success rate for the nitrous oxide group was 50% and for the placebo group the success rate was 28% with a statistically significant difference between the groups ($p=0.0241$). This study showed that administration of 30%-50% nitrous oxide increased the success of the inferior alveolar nerve block in patients

diagnosed with symptomatic irreversible pulpitis. Although increased success was found, supplemental anesthesia was still required. However, this increase was not enough to overcome the clinical problems of painless treatment of irreversibly inflamed teeth. One of the aims of this study was to confirm or deny the increased success of the inferior alveolar nerve block using nitrous oxide. The administration of nitrous oxide/oxygen to every patient in the current study allowed for comparison of the anesthetic success rate to that of Stanley and coauthors (50%)(25). Since the success rate reported by Stanley and coauthors (25) was 50%, there was still room to increase the success of the IANB through the use of premedication with intranasal ketorolac. If premedication with intranasal ketorolac were successful, we would have expected to see a statistically significant increase in the success rate of the IANB over the control group. If this result was observed, the study could be repeated with intranasal ketorolac alone to confirm the results, thus removing nitrous oxide/oxygen as a variable. Analyzing the recorded data (displayed in Table 3) shows that of the 102 subjects in the study, the range of nitrous oxide/oxygen used was between 15% and 65%. The median concentration of nitrous oxide/oxygen use was 35%. Our target range of nitrous oxide/oxygen was 30%-50%. Although the planned range for nitrous oxide/oxygen use was between 30%-50%, clinically some patients required a higher or lower concentration to achieve the desired effect. In the current study one patient was at 15% nitrous oxide/oxygen, 6 at 20%, 2 at 25%, 3 at 60% and 1 at 65%. Of the 13 patients outside the target range, 7 were in the ketorolac group, which included all three patients at the 60% nitrous oxide/oxygen level. These patients were outside the target range but reflect the variability between patients

and that the desired effects described by Malamed are subjective and do not always occur between 30% and 50% concentration. Even though there was a range of 15% to 65% nitrous oxide/oxygen used, there was no statistically significant difference between the groups when comparing sedation rating (p=1.000). This shows that percent of nitrous oxide/oxygen used was not likely a differentiating factor between the groups.

The results in Table 5 describe the success rates of the inferior alveolar nerve block, buccal infiltration of articaine and intraosseous injection of lidocaine. Thirty minutes prior to inferior alveolar nerve block, patients randomly received either 31.5 mg of intranasal ketorolac (Sprix®, Regency Therapeutics, Shirley, New York) or bacterial static sodium chloride 0.9% (placebo) (Central Ohio Compounding, Columbus, Ohio). Preliminary studies by McAleer and coauthors (56) compared the pharmacokinetic actions of intramuscular versus intranasal delivery of 15 mg and 30 mg of ketorolac. In pharmacology, T_{max} is the time it takes a drug to reach maximum plasma concentration after administration (57). McAleer and coauthors (56) showed intranasal ketorolac was rapidly absorbed and exhibited a T_{max} of 30-45 minutes with a half-life of 5-6 hours. One difference between the 30 mg intranasal (IN) and intramuscular (IM) administraion was that in the IM group there was a higher maximum observed plasma concentration (56). They concluded that 30 mg IN ketorolac was equivalent to about 20 mg IM ketorolac, which was still within the therapeutic range of 15-30 mg (56). In the current study, intranasal ketorolac was administered 30 minutes prior to the IANB to ensure peak plasma concentration had been reached when access preparation was initiated. Twenty minutes following administration of either intranasal ketorolac or placebo, nitrous-

oxide/oxygen was titrated over a period of ten minutes to the previously described level of sedation. Administration of two cartridges of 2% lidocaine with 1:100,000 epinephrine was given by IANB and then patients were monitored for 15 minutes until profound lip numbness was achieved. The total time elapsed from the administration of intranasal ketorolac or placebo to the start of endodontic access was 45 minutes.

If profound lip numbness was not achieved, the patients were dismissed from the study. In the current study, no patients were dismissed due to a missed block. A retrospective study by Fowler et al (58) looked at the incidence of missed blocks using 1 versus 2 cartridges of 2% lidocaine with 1:100,000 epinephrine in vital asymptomatic patients and patients experiencing symptomatic irreversible pulpitis. Their results showed that the incidence of a missed block following two cartridges of 2% lidocaine with 1:100,000 epinephrine was 3.8 % for vital asymptomatic teeth and 2.3% for symptomatic irreversible pulpitis. Another retrospective study by Fowler and coauthors (42) looked at the success of the inferior alveolar nerve block and buccal infiltration in patients with symptomatic irreversible pulpitis. Of the 375 patients included in the study, 274 were administered 1 cartridge of 2% lidocaine with 1:100,000 epinephrine and 101 were administered 2 cartridges of 2% lidocaine with 1:100,000 epinephrine. Their results showed a success rate of 25-39% for molar and premolars. In the current study, the success rate for the inferior alveolar nerve block was 46% in the control group and 54% for the treatment group. There was no statistically significant difference between the two groups ($p=0.428$). The results of the current study showed a higher success rate for the IANB than the previously mentioned retrospective study by Fowler et al (42). From these

results we can deduce that the intranasal ketorolac likely did not increase the efficacy of the inferior alveolar nerve block. Comparing the results, 46% and 54% are similar to those found by Stanley and coauthors (25) (50%) when evaluating the effect of nitrous oxide/oxygen on the efficacy of the inferior alveolar nerve block in patients experiencing irreversible pulpitis without ketorolac. Therefore, the increase in success rate (although not high enough without supplemental anesthesia) was likely due to the effects of the nitrous oxide rather than of ketorolac.

We were hoping to see an increase in the success rate of the IANB due to ketorolac and its pain relieving effects, but unfortunately this was not seen. Historically, opioids have been the mainstay for pain management, but with their many adverse side effects newer pain medications have been developed. One such medication is ketorolac, a non-selective nonsteroidal anti-inflammatory drug (NSAID) that inhibits both cyclooxygenase enzymes, cyclooxygenase-1 (COX1) and cyclooxygenase-2 (COX2). In contrast to ibuprofen, ketorolac has almost 400 times more selectivity for COX1 than COX2 (59). The selectivity of ibuprofen is more evenly distributed with respect to COX1 and COX2 enzymes. Ketorolac and other non-selective NSAIDs exert their analgesic, anti-inflammatory and antipyretic effects thorough the inhibition of cyclooxygenase. After cell injury, arachidonic acid is released from the damaged cell membranes which is then converted through a series of enzymatic processes to thromboxane, prostaglandins and prostacyclin. (59). Both COX1 and COX2 are involved in the formation of prostaglandins. COX1 is found mostly in healthy tissues, including gastric mucosa, CNS and platelets (59). COX2 differs from COX1 in that it is primarily

inducible and can be upregulated by the actions of cytokines, macrophages or growth factors (59). COX2 is seen in higher concentrations when prostaglandins are elevated. (59). One of the effects of prostaglandins is their ability to influence pain perception by sensitizing afferent nerve endings (43). Some animal models have shown that NSAIDs may exert some central analgesic effect through the inhibition of COX (59). Oleson and coauthors (12) and Simpson and coauthors (22) previously showed that premedication with ibuprofen does not increase the success of an IANB. Since ketorolac is more selective for COX1, which is found in the CNS, it may be possible that ketorolac has central analgesic activity that ibuprofen does not possess (59).

Ketorolac is indicated for the management of moderate to severe pain and has traditionally been administered via intramuscular or intravenous routes. Recently, ketorolac has been made available in an intranasal spray (Sprix®, Regency Therapeutics, Shirley, New York). Sprix® has been show to decrease postoperative pain in oral surgery and medical models (32,33). In dentistry, most drugs are administered orally, which has disadvantages of decreased absorption rates and delayed onset. Intranasal administration is advantageous over oral administration because it allows for fast absorption. Ketorolac tromethamine is commercially available as a salt which lends to its highly water soluble characteristics and ease of use intranasally (43). The bioavilability of ketorolac, when given orally, IM or IV can range from 80% to 100% compared to the intranasal route of 65% to 75% (43). Similar to other NSAIDs, ketorolac is highly protein bound in the plasma, approximately 99% (59). As stated earlier, following administration of intranasal ketorolac, it is rapidly absorbed within 30 to 45 minutes with a half-life of 5-6 hours

(56,60). The drug is eliminated in the urine (90%) following metabolic break down via glucoronidation and parahydroxylation in the liver (43).

Intranasal drug delivery is an attractive option because of the nasal mucosa's high permeability and rich vascularity (61). "The main advantages of intranasal delivery are ease of administration, a rapid onset of action and the avoidance of gastrointestinal and hepatic first-pass effects; accordingly, the nose constitutes a very valuable route for the administration of active principals with low oral bioavailability" (61). Absorption, distribution, metabolism and elimination are the pharmacokinetic steps affecting a drug in the body. Of these steps, absorption is the most important factor when considering intranasal delivery (61). The nasal cavity is divided into three areas: vestibule, atrium and the turbinates, of which there are superior, middle and inferior turbinates. (61). Intranasal drugs are primarily absorbed in the inferior turbinate because of its rich vascularity and a high surface area (61). The nose receives its arterial blood supply from the internal and external carotid, which terminate into a dense capillary bed near the inferior turbinate (61). The venous supply "involves the sphenopalatine, facial and ophthalmic veins and then the internal jugular vein, which in turn drains (via the subclavian vein and the superior vena cava) into the right heart chambers; this explains the absence of a hepatic first-pass effect (61)." A drug's physiochemical properties and volume administered greatly affect the absorption (61). Due to 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 (61). This volume correlates to the manufactures recommended dosing of the intranasal ketorolac that was administered during the current study with one spray in each

nostril (100 μL) with each containing 15.75 mg ketorolac tromethamine. One study showed that giving a single dose of 100 μL results in greater distribution compared to a 50 μL dose (62). The size of the particle in the nasal spray must be larger than 10 μM to avoid passing directly into the lower airway on inhalation, thus bypassing the nasal mucosa (61). If the solution to be administered is too viscous, then the area of deposition will be decreased which then may decrease the amount of drug absorbed (62). The ideal molecule intended for intranasal administration would have: "a low molecular weight, high lipophilicity and zero net charge at physiologic pH (61)." In the current study, ketorolac was an attractive option for premedication not because it is more effective than ibuprofen, but that the intranasal route of administration may be more effective than traditional oral delivery.

A study by O'Hara and coauthors compared postoperative pain in patients receiving 10, 30, or 90 mg ketorolac IM to 6 or 12 mg morphine (63). There were 155 patients who participated in the study. They were instructed to rate their pain at 30 minutes postoperatively and then every hour for 6 hours. The results showed that patients receiving 30 or 90 mg ketorolac reported less pain than 6 mg morphine after 1 hour. There was no statistically significant difference when comparing 30 or 90 mg ketorolac to 12 mg of morphine at 3 hours but at hour 4, 30 or 90 mg ketorolac provided better pain relief. Based on this study, a single dose of 30 or 90 mg ketorolac appears to provide similar analgesic efficacy as 12 mg morphine.

Sadeghein and coauthors (64) compared the analgesic effects of 10 mg oral ketorolac tromethamine to oral acetaminophen/codeine (325 mg/10 mg) in patients

experiencing acute apical periodontitis. Sixty-six patients were randomly assigned to a treatment group and asked to rate their pain every 10 minutes for 90 minutes after receiving the medication. The results showed that 10 mg ketorolac provided a statistically greater analgesic effect ($p=0.005$) when compared to acetaminophen/codeine (325 mg/10 mg). These findings are not surprising considering that multiple studies have shown NSAIDs to be as, if not more, effective than opioids at managing postoperative pain without the adverse side effects associated with opioid use (65-67).

Forbes and coauthors (68) compared the analgesic efficacy of 10 mg ketorolac tromethamine, 650 mg aspirin and 600 mg/60 mg acetaminophen/codeine following extraction of third molars. One hundred twenty-eight patients participated in the study and rated their pain hourly for 6 hours. Their results showed that ketorolac was statistically better than aspirin ($p<0.05$) for both peak and total analgesia, and significantly better than acetaminophen/codeine ($p<0.05$) except for peak pain intensity and peak pain relief. Ketorolac's analgesic efficacy lasted for six hours compared to aspirin and acetaminophen/codeine, which lasted only four hours. The results show that the day of surgery ketorolac provided better pain relief than aspirin and acetaminophen/codeine but no statistically significant difference was seen after the first day extending out to day six (68).

Singla and coauthors (69) evaluated the efficacy of 31.5 mg intranasal ketorolac to placebo for postop pain in patients undergoing abdominal surgery. Patients received either ketorolac or placebo every 6 hours for 48 hours and then up to 4 times a day for up to 5 days. All participants had morphine as an escape drug if needed. The results showed

that the pain intensity difference scores for the ketorolac group were significantly higher than the placebo group indicating that ketorolac has a greater analgesic efficacy (69). Morphine use in the ketorolac group decreased 26% over the 48 hour period compared to placebo.

Brown et al. (33) compared the analgesic efficacy of 30 mg intranasal ketorolac compared to placebo postoperatively for patients undergoing hysterectomies or hip replacements. Patients received either intranasal ketorolac or placebo three times a day for up to five days and rated their pain. The results of this study showed that the pain intensity difference score for ketorolac was higher than placebo indicating that intranasal ketorolac provides better analgesia than placebo. As in the previous study, morphine use as a rescue drug was 34% lower in the ketorolac group than placebo.

Grant and coauthors (32) studied the effectiveness of intranasal ketorolac at managing postoperative pain in patients undergoing third molar extraction. Eighty patients were randomly divided into two groups with one group receiving 31.5 mg intranasal ketorolac and the other placebo. The results of this study revealed that intranasal ketorolac provided more rapid pain relief for up to 8 hours when compared to placebo.

More recent studies in dentistry have focused on attempting to increase the success rate of the inferior alveolar nerve block through premedication with ketorolac. Akhlaghi et al. (70) studied the efficacy of buccal infiltrations of ketorolac on improving the success rate of IANB in patients with irreversible pulpitis. In this study, 40 volunteers with a diagnosis of asymptomatic irreversible pulpitis were divided into two groups. All

patients were given an IANB with 1.8 ml 4% articaine 1:100,000 epinephrine and buccal infiltration 0.9 ml 4% articaine 1:100,000 epinephrine. Half (20 patients) of the patients were randomly selected to receive a buccal infiltration of 30 mg/ml ketorolac tromethamine while the other half received saline. Endodontic treatment was initiated 15 minutes after the IANB. Success was defined as no to mild pain throughout treatment. Based on this definition, the results showed a success rate of 15% for the control group and 40% for the ketorolac group. The results were statistically significant between the two groups (p=0.043) (REF). The results of the current study do not indicate that ketorolac had any effect on the success of the IANB. The study by Akhlaghi and coauthors (70) included only 40 subjects, 20 in each group giving 80% power. By including 20 subjects in each group the statistically significant difference could have been due to a biased sample. All patients were given buccal infiltration of articaine, which is known to increase the success of an IANB in symptomatic irreversible pulpitis. Studies have shown success rates for supplemental buccal infiltration of articaine in patients diagnosed with symptomatic irreversible pulpitis to be 38% to 54% (7,10,12,22,42). The success rates in the previously mentioned studies are comparable with the 40% success rate found by Akhlaghi (70) indicating that the success may likely be due to the supplemental articaine and not the infiltration of ketorolac. It is surprising to note that the control group only had a success rate of 15% considering all patients in the study were administered a buccal infiltration of 4% articaine. It is possible that the success seen may have more to do with a small sample size than the infiltration of ketorolac.

A study conducted by Yadav and coauthors (26) evaluated the efficacy of 10 mg of preoperative oral ketorolac on the success of the IANB when given with or without buccal and lingual infiltrations. One hundred and fifty patients were divided into two groups, one received 1.8 ml 4% articaine with 1:100,000 epinephrine for the IANB while the other received 1.8 ml 2% lidocaine with 1:80,000 epinephrine. Each major group of 75 was then further subdivided into 3 groups (25 in each), one received 0.9 ml buccal infiltration and 0.9 ml lingual infiltration with articaine or lidocaine, a second was given a preoperative oral dose of 10 mg ketorolac and the third subgroup received preoperative oral medication of 10 mg ketorolac plus 0.9 ml buccal infiltration and 0.9 ml lingual infiltration with either articaine or lidocaine. Fifteen minutes following the IANB, endodontic treatment was initiated. Success was defined as no to mild pain upon access or instrumentation. The results showed a statistically significant increase in the success of the IANB when comparing 2% lidocaine for an IANB with 10 mg oral ketorolac premedication (40% success) to the 4% articaine IANB plus ketorolac premedication and buccal and lingual infiltration with articaine (76% success) ($p=0.003$)(26). One way to explain these results is that we know giving a supplemental buccal infiltration will increase the success of the IANB in irreversible pulpitis. Matthews and coauthors found a success rate of 58% when giving supplemental buccal infiltration of articaine after a failed IANB in patients with symptomatic irreversible pulpitis (7). When comparing the articaine IANB/buccal and lingual infiltrations/ketorolac group (76% success) to the lidocaine IANB/buccal and lingual infiltration (32% success) in Yadev et al's. (26) study there was a statistically significant difference ($p=0.00025$). A statistically significant

difference was also found when comparing lidocaine IANB/buccal and lingual infiltrations (32% success) to articaine IANB/buccal and lingual infiltrations (64% success) ($p=0.014$). One explanation is that from previous studies we know that giving buccal plus lingual infiltrations with the IANB will increase the success of the IANB in symptomatic irreversible pulpitis (10). Aggarwal and coauthors (10) found a success rate of 67% for buccal and lingual infiltrations of articaine following a failed IANB and 47% for lidocaine. The final statistically significant difference in Yadev et al's. (26) study was between the articaine IANB/buccal and lingual infiltrations/ketorolac group (76% success) and articaine/ketorolac group (48% success) ($p=0.007$). Their results show that adding a buccal and lingual infiltration of articaine will increase the success of the IANB in irreversible pulpitis and that it is likely not the ketorolac premedication that was given that increased success. In order to truly investigate whether ketorolac significantly increases success of the IANB, one should compare an IANB to IANB plus ketorolac. Adding multiple variables decreases the power and muddies the overall impact of the study.

A study by Saha and coauthors (27) studied the effect of oral premedication with ketorolac, diclofenac potassium or placebo on the efficacy of the IANB in patients with symptomatic irreversible pulpitis. The study consisted of 126 patients, 42 in each group. The patients were randomly assigned to one of three groups: 10 mg ketorolac, 50 mg diclofenac potassium or placebo, and were given the corresponding premedication one hour prior to the IANB. One cartridge of 2% lidocaine with 1:200,000 epinephrine was given via IANB fifteen minutes prior to endodontic access. Success was defined as

no pain upon access or instrumentation. The results showed a statistically significant difference when comparing ketorolac to diclofenac potassium (p=0.034). The success rate for the IANB with ketorolac was 76% and diclofenac potassium was 55%. When comparing diclofenac potassium to placebo there was also a statistically significant difference (p=0.012) with success rates of 55% and 29%, respectively. The results of this study are different than those found in the current study with an IANB success rate of 54% compared to 76%. When looking at the data, Saha and coauthors (27) report mean pre-injection VAS (170 mm) scores of 85.74 mm for the ketorolac group, 81.62 mm for the diclofenac potassium group and 84.55 mm for the placebo group. The mean VAS values are considerably lower than those of the current study, 130 mm for the control group and 129 mm for the treatment group. To be included in the current study, the initial pain rating had to be ≥85 mm, corresponding to moderate/severe pain. The initial presenting diagnosis is an important factor when considering anesthetic success rates of the IANB. Patients diagnosed with asymptomatic irreversible pulpitis in a mandibular posterior tooth have a higher anesthetic success rate than those diagnosed with symptomatic irreversible pulpitis (49). With such a non-distinct preoperative diagnosis, it is difficult to conclude that premedication with ketorolac was successful. It is possible that the patients who actually had a diagnosis of symptomatic irreversible pulpits were not randomly divided between the groups leading to biased results.

Aggarwal and coauthors (28) studied the efficacy of premedication with NSAIDs on the success of the IANB in patients diagnosed with irreversible pulpitis. Sixty-nine adult patients were randomly divided into three treatment groups and given

premedication of 600 mg ibuprofen, 20 mg ketorolac or placebo. Inferior alveolar nerve blocks with 1.8 ml 2% lidocaine and 1:200,000 epinephrine were given 1 hour after premedication. Fifteen minutes after the IANB and confirmation of lip numbness, endodontic access was initiated. Success was defined as none to mild pain upon access and instrumentation. The results showed a success rate of 29% (7/24) for placebo, 27% (6/22) for ibuprofen and 39% (9/23) for ketorolac with no significant difference between the groups ($p>0.05$) (28). The success rate for the ketorolac group (39%) was lower than what was found in the current study (46%). The conclusion found by Aggarwal et al. (28) was similar to the current study with ketorolac not increasing the success rate of the IANB in patients diagnosed with symptomatic irreversible pulpitis.

Another study by Aggarwal et al (30) compared the effects of buccal infiltration with 4% articaine with 1:100,000 epinephrine, 0.9 ml 4% articaine with 1:100,000 epinephrine plus 1 ml/30 mg ketorolac, 1 ml/4 mg dexamethasone or no buccal infiltration on the success of the IANB in patients diagnosed with irreversible pulpitis. Ninety-four adult volunteers were included in this study and were randomly divided into 4 groups of 23 or 24 patients per group. All patients were instructed to fill out an initial pain rating scale and were only included if they were experiencing moderate to severe pain. Initially, 1 ml/30 mg ketorolac was to be given alone, but because of extreme pain on injection in the first two patients, the protocol was changed and 0.9 ml 4% articaine was given 10 minutes prior to infiltration with ketorolac. The results of this study showed a 39% (9/23) success rate for the IANB alone, 45% (11/23) for dexamethasone, 54% (13/24) for articaine and 62% (15/24) for articaine plus ketorolac (30). Both the articaine

infiltration group and articaine plus ketorolac groups had a statistically significant increase in the IANB success when compared to the control group ($p<0.05$). Aggarwal and coauthors (30) concluded that the combination of 0.9 ml 4% articaine plus 1 ml/30 mg ketorolac increased the success of the IANB in patients experiencing irreversible pulpitis. This study failed to show a significant difference between the articaine group and articaine plus ketorolac group. Because there was no statistically significant difference between the groups, we cannot conclude that the addition of ketorolac will increase the success of the IANB in irreversible pulpitis.

Jena and coauthors (29) studied the effect of preoperative medications on the success of the IANB in patients diagnosed with irreversible pulpitis. One hundred patients were randomly divided into five groups (20 each) based on the premedication they received: 600 mg ibuprofen, 10 mg ketorolac, combination of 400 mg etodolac with 500 mg paracetamol, combination of 100 mg aceclofenac with 500 mg paracetamol or placebo. Patients were given the premedication 30 minutes prior to the IANB. The patients initial pain was recorded by stimulating the tooth using Green Endo-ice® spray and then asking them to rate their level of pain on a 170 mm Heft-Parker VAS. Thirty minutes following premedication, an IANB was given using 2% lignocaine with 1:100,000 epinephrine. Fifteen minutes after the IANB, endodontic access and instrumentation was begun and patients were asked to report any pain during treatment which was recorded on the VAS. The results of the study revealed that ketorolac had a 70% success rate ($p=0.229$), ibuprofen 55% ($p=0.866$), combination of aceclofenac with paracetamol 55% ($p=0.650$), combination etodolac with paracetamol 50% ($p=0.871$) and

placebo 40% (29). Based on the results in their tables, none of the treatment groups were significantly different when compared to placebo. One problem with this study, which may explain the improved success rates, was the patient's initial presenting diagnosis. Stimulating the tooth with cold prior to evaluating the initial pain rating may have lead to an incorrect diagnosis of symptomatic irreversible pulpitis when the true diagnosis was asymptomatic irreversible pulpitis. Previous studies have shown that patients experiencing asymptomatic irreversible pulpitis have a higher success rate with regard to the IANB than those with symptomatic irreversible pulpitis (49). The small sample size of 20 patients per group creates difficulty when attempting to detect a statistically significant difference. This could have been improved by increasing the number of patients per group.

Four of the six studies reviewed indicated that ketorolac improved the success rate of the IANB. Yadev and coauthors (26), and Saha and coauthors(27) used an oral administration of ketorolac while Akhlaghi and coauthors(70) and Aggarwal and coauthors (30) used an infiltration of ketorolac. Jena and coauthors (29) reported a 70% success rate following preoperative oral administration of ketorolac, but their results were not significantly different from placebo. Although these studies attempted to show increased success, it is evident that there are flaws in the study designs. It is difficult to show increased success when the initial diagnosis is questionable. Also, the small sample sizes used open up for the possibility of having biased results. Neglecting the aforementioned problems, the success rates obtained in these studies ranged from 40% to 76%. These success rates are still not high enough to achieve pulpal anesthesia without

the use of supplemental injections. A study by Aggarwal and coauthors (28) giving oral premedication of 20 mg ketorolac compared to 600 mg ibuprofen or placebo showed no statistically significant increases in the success of the IANB. These results are in agreement with those of the current study suggesting that premedication with ketorolac does not appear to increase the success of the IANB in patients diagnosed with symptomatic irreversible pulpitis. The intranasal ketorolac seemed to be well tolerated by the patients with only few minor side effects. The most common complaints were of a burning, tingling or itching sensation after administration. These symptoms were reported by approximately 50% of patients but were transient, lasting only a few minutes. According to the manufacture's website, these adverse effects occur in ≥2% of patients and at a rate twice that of placebo. In the placebo group, 32% (17/52) of patients reported a weird smell, bad taste, burning or itching sensation upon administration. As in the treatment group, these side effects lasted only a few minutes. Had increased success been observed at the rates of the previous studies (40%-76%), it would be difficult to justify the use of intranasal ketorolac due to its high cost (~$190 per bottle) and mediocre results. The ease of use, low cost, analgesic and anxiolytic properties of nitrous oxide make it a much better alternative than intranasal ketorolac.

When the inferior alveolar nerve block fails to provide adequate anesthesia, a supplemental anesthetic injection may be used. Supplemental injections include: infiltration, intraosseous, intraligamentary and intrapulpal. As is seen in Table 5, 51 patients (28 from the control group and 23 from the treatment group) required supplemental anesthesia. During the current study, if patients experienced moderate to

severe pain, treatment was stopped and supplemental anesthesia was administered. The first supplemental injection given was a buccal infiltration of 1.8 ml 4% articaine with 1:100,000 epinephrine. The success rate of the supplemental buccal infiltration of articaine was 39% (11/28) for the control group and 52% (12/23) for the treatment groups. There was no significant difference between the groups regarding success of the supplemental buccal infiltration when analyzed using the chi-square test ($p=0.357$).

Articaine was used as the local anesthetic agent for the buccal infiltration because it has been shown to have a higher success rate than lidocaine (71). Haase and coauthors (71) studied the efficacy of articaine versus lidocaine for buccal infiltration following an inferior alveolar nerve block of first molars in asymptomatic patients. Seventy-three patients randomly received one cartridge of 2% lidocaine with 1:100,000 epinephrine or 4% articaine with 1:100,000 epinephrine following the IANB (71). An electric pulp tester was used to assess pulpal anesthesia, with success defined as two consecutive 80 readings within 10 minutes of the IANB. The results showed a success rate of 75% for 2% lidocaine and 88% for 4% articaine with a statistically significant difference between the groups ($p<0.05$).

Matthews and coauthors (7) studied the success of supplemental buccal infiltration of 4% articaine with 1:100,000 epinephrine following a failed IANB in patients diagnosed with symptomatic irreversible pulpitis. Similar to the current study, patients were only given the supplemental buccal infiltration if they experienced moderate to severe pain upon access or instrumentation. Of the 82 patients that participated in their study, 55 required supplemental anesthesia. The results showed that

the success rate of buccal infiltration of articaine after a failed IANB in patients experiencing symptomatic irreversible pulpitis was 58% (32/55). Studies by Oleson and coauthors (12) and Simpson and coauthors (22) found success rates of buccal infiltration with articaine to be 41% and 38%, respectively. Fowler and coauthors (42) performed a retrospective study on the success rate of the inferior alveolar nerve block and supplemental buccal infiltration of articaine in patients diagnosed with symptomatic irreversible pulpitis. Three hundred seventy-five patients participated in the study and received 2% lidocaine with 1:100,000 epinephrine for the inferior alveolar nerve block. Of those patients, 221 failed to achieve adequate anesthesia and required supplemental buccal infiltration of 4% articaine with 1:100,000 epinephrine. The results showed success rates ranging from 42% to 48% for first and second molars. The success rates of buccal infiltration found in these studies were similar to the results in the current study of 39% in the control group (11/28) and 52% in the treatment group (12/23) with no significant difference between the groups ($p=0.357$).

When supplemental buccal infiltration of articaine fails to provide adequate anesthesia, an intraosseous injection may be given. In the current study, 28 patients, 17 from the control group, and 11 from the treatment group, required a supplemental intraosseous injection to achieve adequate pulpal anesthesia. The intraosseous injection allows for delivery of the anesthetic directly into the cancellous bone adjacent to the tooth resulting in immediate anesthesia (2,72-80). Following a failed inferior alveolar never block and supplemental buccal infiltration, the Stabident perforation system was used to deliver 1.8 ml 2% lidocaine 1:100,000 epinephrine distal to the tooth requiring treatment.

The results of the current study showed a supplemental intraosseous success rate of 88% (15/17) for the control group and 64% (7/11) for the treatment group.

A study by Nusstein and coauthors (1) investigated the success rate of a supplemental intraosseous injection of 1.8 ml 2% lidocaine with 1:100,000 epinephrine following an IANB in patients diagnosed with symptomatic irreversible pulpitis. The success rate of pulpal anesthesia, defined as no to mild pain upon access or instrumentation, was 90%(ch6 ref 1). These results were duplicated by Oleson and coauthors (12) in a study that looked at the effect of premedication with ibuprofen on the anesthetic efficacy of 2% lidocaine used for an intraosseous injection. The study included 100 patients diagnosed with symptomatic irreversible pulpitis in a mandibular posterior tooth. Of the 100 patients, 33 required a supplemental intraosseous (IO) injection. Their results showed a success rate for the IO injection of 88% (15/17) in the ibuprofen group and 94% (15/16) in the placebo group with no statistically significant difference between the two ($p>0.05$)(12). Simpson and coauthors (22) studied the effect of premedication with a combination 800 mg ibuprofen/1000 mg acetaminophen on the success of the inferior alveolar nerve block in patients diagnosed with symptomatic irreversible pulpitis. Of the 100 patients who participated in the study, 50 required a supplemental intraosseous injection. The results showed a success rate of 86% (18/21) for the ibuprofen/acetaminophen group and 79% (23/29) for the placebo group.

A study by Parente and coauthors (82) using 0.45 ml to 0.90 ml of 2% lidocaine with 1:100,000 epinephrine intraosseously following failed pulpal anesthesia with the IANB, resulted in a success rate of 79%. When the injection was repeated, increasing the

total anesthetic dosage to a range of 0.9 ml to 1.9 ml, the success rate increased to 91% (82). Dunbar and coauthors (76) showed that an intraosseous injection of 2% lidocaine with 1:100,000 epinephrine following an IANB resulted in quick onset and approximately 60 minutes of pulpal anesthesia. Gallatin and coauthors (80) studied the duration of pulpal anesthesia using intraosseous 3% mepivacaine following an IANB and found a duration of only 30 minutes. A study by Reisman and coauthors (2) investigated the success rate of supplemental intraosseous 1.8 ml 3% mepivacaine compared to the IANB alone and found that 3% mepivacaine resulted in an 80% success rate in symptomatic irreversible pulpitis. This rate is lower than when 2% lidocaine is used, but when a second cartridge of 3% mepivacaine was administered intraosseously, the success rate increased to 98% (2). A study by Bigby and coauthors (81) found that a supplemental intraosseous injection of 1.8 ml 4% articaine 1:100,000 epinephrine in patients with irreversible pulpitis had an 86% success rate, which is comparable to 2% lidocaine. These studies showed that when a vasoconstrictor cannot be used, profound pulpal anesthesia can still be achieved using mepivacaine and that articaine does not need to be used for intraosseous injections. The success rates in the intraosseous studies are similar to those found in the current study, 88% (15/17) for the control group and 64% (7/11) for the treatment group. Although there appears to be a large percent difference between the two groups, there was no statistically significant difference ($p=0.121$) when analyzed using the Chi-Square test. If the sample size had been larger, it is unknown whether a significant difference would be seen. However, because the control group had

a higher percent success rate it can be deduced that ketorolac would not likely have an impact on the anesthetic success.

Table 6 illustrates the pain of injection for the inferior alveolar nerve block, buccal infiltration of articaine and intraosseous injection. Perceived pain was recorded by the patient at each phase of the injection: needle insertion, needle placement, solution deposition using a 170 mm Heft-Parker VAS. Any values less than or equal to 54 mm were considered mild pain. Pain scores of the IANB for the control group, ranged from 54 mm – 58 mm during all phases of the injection. For the treatment group, pain ranged from 49 mm – 60 mm. There was no statistically significant difference between the groups during any phase of the IANB. When comparing the pain on needle insertion for the treatment group with a mean pain score of 49 mm (mild) to that of the control group, 57 mm (moderate) there was no statistically significant difference ($p=1.000$). The same is true when comparing pain on deposition for the treatment group (60 mm, moderate) verses the control group (54 mm, mild) ($p=1.000$). Although the pain scores correlated to different categories on the 170 mm VAS, the values were all clustered around the mild/moderate split. No significant difference and clustering lead to no likely difference of clinical value. When looking at Table 7 we see that of the patients in the treatment group, 56% reported mild pain and 40% moderate pain on insertion while in the control group 40% reported mild pain and 50% moderate pain on insertion. During the placement phase of the IANB, 44% of the control group reported mild pain and 46% reported moderate pain. For the treatment group, 42% reported mild pain and 38% reported moderate pain. With regard to the deposition phase, in the control group 38%

reported mild pain and 46% moderate pain. In the treatment group, 42% reported mild and 40% reported moderate pain on deposition. During all phases of the IANB injection, for both groups, a majority of patients experienced only mild to moderate pain. A study by McCartney and coauthors (83) studied the pain at each phase of the injection for the inferior alveolar nerve block in patients diagnosed with irreversible pulpitis. The results showed that 55% to 59% of patients rated pain on insertion as moderate, which is similar to the results obtained in the current study. In addition, they found that 35% to 70% of patients rated the pain on placement as moderate and 52% reported moderate pain on deposition. Stanley and coauthors (25) reported that 64% of patients noted no to mild pain with the IANB needle insertion, 55% felt no to mild pain on placement and 55% reported no to mild pain on solution deposition. Again, the results shown by McCartney and coauthors (82) and Stanley and coauthors (25) (also used nitrous oxide) are similar to those obtained in the current study with the majority of patients reporting only mild pain. Since the results are similar to McCartney et al (81), a study with a larger sample size, any variation in mild to moderate injection pain is likely representative of this population's reaction to the injections versus any difference due to ketorolac. Since we consistently find that the pain of an injection is only mild, it would be hard to detect a significant difference with the ketorolac unless it was painless.

Table 6 shows that both groups had mean pain ratings within the mild pain category for all phases of the supplemental articaine deposition. Table 8 breaks down the pain ratings into categories and shows that for both groups, during all phases of the injection, over 80% of patients reported feeling no to mild pain on injection. The IANB

may provide adequate soft tissue anesthesia leading to a decrease in pain reported during articaine deposition. Matthews and coauthors (7) studied the efficacy of supplemental buccal articaine after a failed IANB in patients with symptomatic irreversible pulpitis. They found the mean pain scores to be 13 mm ±11 mm on insertion, 11 mm ±17 mm on placement and 16 mm ±27 mm on deposition when using the a 170 mm Heft-Parker VAS. These values all fell within the mild pain category (0 mm to ≤54 mm). A study by Haase and coauthors (71) compared the anesthetic efficacy of 4% articaine versus 2% lidocaine after the IANB. They reported mean pain ratings for insertion, placement and deposition during articaine buccal infiltration to be 20 mm ±25mm, 17 mm ±24 mm and 23 mm ±27 mm, respectively. For lidocaine they obtained similar result with 17 mm ±20 mm on insertion, 20 mm ±27mm on placement and 22 mm ±26 mm on deposition. For both groups, articaine and lidocaine, all values for each phase of the injection fell within the mild pain category. The results of these studies parallel the results found in the current study with the majority of patients reporting mild pain for all phases of the supplemental buccal infiltration.

As shown in Table 9, a majority of patients rated their pain as none to mild on the 170 mm VAS for the supplemental intraosseous injection. These results are similar to the pain ratings for supplemental buccal infiltration. For the control group, the mean pain scores for insertion placement and deposition were 15 mm, 17 mm and 30 mm, respectively. For the treatment group, the mean pain scores were 14 mm for insertion, 13 mm on placement and 23 mm for deposition. A study by Nusstein and coauthors (1) looked at the anesthetic efficacy of 2% lidocaine as a supplemental intraosseous injection

using the Stabident system in patients diagnosed with symptomatic irreversible pulpitis. The results showed that a majority of patients (76%) reported no pain and 19% experienced mild pain on solution deposition. Bigby and coauthors (81) studied the efficacy of articaine for intraosseous anesthesia in patients diagnosed with symptomatic irreversible pulpitis using the Stabident system (81). The results showed that 51% of patients reported mild pain on perforation and 62% reported mild pain on deposition. These results are similar to those found in the current study with a majority of patients in both groups reporting mild pain during all phases of the intraosseous injection. There was no significant difference between groups regarding injection pain for either the buccal infiltration or intraosseous injection. Due to the small sample size for the supplemental buccal infiltration and intraosseous injections, we would not expect to see a significant difference between the groups.

Table 10 illustrates the anesthetic failure point for all three injections and the depth (dentin, chamber, canal) at which the anesthetic failure occurred. With regard to the inferior alveolar nerve block, both groups had a majority of the failures within dentin. For the control group 61% failed in the dentin and 65% failed for the treatment group. Similar results were found for the articaine buccal infiltration with most of the failures occurring within dentin; 47% in the control group and 64% in the treatment group. A study by Kennedy and coauthors (4) studied the effects of needle deflection on the success of IANB in patients diagnosed with symptomatic irreversible pulpits. They found that when the inferior alveolar nerve block failed, which corresponded to moderate to severe pain, it would fail 44%-57% of the time within dentin. In a study by Claffey and

coauthors (5) comparing the efficacy of articaine to lidocaine for use in the inferior alveolar nerve block, when looking at the failure points for both anesthetics, both failed within dentin. Of the failures, 50% from the articaine group and 44% from the lidocaine group failed within dentin. More recent studies that investigated methods to increase the success of the IANB found similar results to the current study with 32% to 71% of the anesthetic failures after IANB occurring in dentin (8,12,23,25). Because the pulp was not reached, an intrapulpal injection cannot be given, leaving us with the current regimen of buccal infiltration, intraosseous and intraligamentary injections.

The satisfaction ratings of the patients involved with the study, shown in Table 11, were based on a 100 mm visual analogue scale. After treatment was completed, the operator would leave the room and patients recorded their level of satisfaction with the treatment rendered. The scale had 4 descriptors to help the patients rate their level of satisfaction: not satisfied, somewhat satisfied, moderately satisfied and completely satisfied. Both groups had a mean satisfaction rating of 96 mm, the control group had a standard deviation of ±7 mm and the treatment group had a standard deviation of ±9 mm. The satisfaction ratings in the current study are in the same range 88-96 mm as those recorded in previous studies (8,21,23,25,40). Patients also recorded the maximum amount of pain that they remembered feeling during treatment. This was recorded on the same 170 mm Heft-Parker VAS that was used throughout the study. The mean treatment pain rating for the control group was 42 mm ±41 mm and for the treatment group it was 33 mm ±43 mm with no significant difference between the groups (p=1.000). The mean treatment pain rating for both groups fell within the mild pain category on the 170 mm

VAS. Similar values, 54-79 mm, corresponding to mild/moderate pain were found in previous studies (21,40). Despite positive patient satisfaction, roughly 50% of patients experienced moderate to severe pain due to inadequate anesthesia from the IANB alone, 46% for the control group and 54% for treatment group.

Chapter 5: Summary and Conclusion

The inferior alveolar nerve block does not predictably provide adequate pulpal anesthesia in mandibular posterior teeth diagnosed with symptomatic irreversible pulpitis. Recent studies have shown the success rate of the inferior alveolar nerve block to range from 15% to 57% in patients with symptomatic irreversible pulpitis (Ch 6 ref 1-10). Traditionally, supplemental anesthetic techniques such as buccal infiltration, intraosseous, intraligamentary and intrapulpal have been used to increases the anesthetic success rate. A recent study found an increased success of the inferior alveolar nerve block when nitrous oxide/oxygen was administered (Stanley REF). The increased success rate observed was still not adequate enough to provide predictable profound pulpal anesthesia in patients diagnosed with symptomatic irreversible pulpitis. A recent review has called for more studies evaluating premedication with NSAIDs (ref 13 from IRB proposal). One NSAID in particular, ketorolac, has recently been formulated for intranasal use. The intranasal route of administration was attractive because of its fast absorption and ease of use. Some recent studies using ketorolac have shown increased success of the inferior alveolar nerve block in irreversible pulpitis, though none of them used an intranasal route of administration (Aggarwal, Jena, Akhlaghi, Yadev, Saha). Although increased success has been shown for both nitrous oxide and ketorolac

individually, neither has shown complete pulpal aneathesia. Perhaps, the combination of two effective medications with different mechanisms of action would improve overall success rates and reduce pain for patients. No study has investigated the efficacy of a combination of nitrous oxide/oxygen and intranasal ketorolac in increasing the success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis. It was hypothesized that the combination of nitrous oxide/intranasal ketorolac would increase the anesthetic success of the inferior alveolar nerve block in patients experiencing symptomatic irreversible pulpitis.

We found there to be no statistically significant difference between the combination of nitrous oxide/oxygen and ketorolac (treatment group) compared to nitrous oxide/oxygen and placebo (control group). The success rate of the inferior alveolar nerve block was 54% for the treatment group and 46% for the control group ($p=0.428$). Within the parameters of the current study, the combination of nitrous oxide/oxygen and intranasal ketorolac did not significantly increase the success rate of the inferior alveolar nerve block in patients diagnosed with symptomatic irreversible pulpitis compared to nitrous oxide/oxygen and placebo. However, these results further confirm those found by Stanley and coauthors (REF) that the administration of nitrous oxide/oxygen with an IANB will increase the success of an IANB in patients diagnosed with symptomatic irreversible pulpitis.

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APPENDIX A

TABLES

Table 1. Subject Profile

		N_2O-O_2 (Number/Percent)	Ketorolac/N_2O-O_2 (Number/Percent)	P-values*
Gender	Female	34 (65)	32 (64)	0.883
	Male	18 (35)	18 (36)	
Tooth Type	First Molar	25 (48)	20 (40)	0.722
	Second Molar	18 (35)	21 (42)	
	Third Molar	1 (2)	2 (4)	
	First Premolar	3 (6)	1 (2)	
	Second Premolar	5 (10)	6 (12)	

* Values Analyzed using the Chi-Square Test

Table 2. Subject Age, Anxiety Level and Initial Pain

Group	Number	Variable	Mean	Std Dev	Median	Min.	Max.	Between Group P-values
N_2O-O_2	52	Age	35	12	31	18	64	1.000***
		Corah Anxiety (4-20)*	-	-	9	4	19	0.058****
		Initial Pain (mm)**	130	24	132	85	170	1.000***
Ketorolac/N_2O-O_2	50	Age	34	12	30	18	65	1.000***
		Corah Anxiety (4-20)*	-	-	11	4	19	0.058****
		Initial Pain (mm)**	129	22	127	84	170	1.000***

* Based on Corah's Dental Anxiety Scale. Possible Values 4-20
** Based on 170 mm Heft-Parker VAS
*** Values analyzed using the Bonferroni-Randomized test
****Values analyzed using the Raw Wilcoxon Signed-Ranks test

Table 3. Sedation Ratings

Group	Number	Mean (mm)*	Std Dev	Minimum	Maximum	P-value**
N_2O-O_2	52	60	22	8	100	1.000
Ketorolac/N_2O-O_2	50	61	21	18	100	

* Based on 100 mm VAS
** Values analyzed using the Bonferroni-Randomized test

Table 4. Sedation Ratings by Category

Group	Not Sedated	Somewhat Sedated	Moderately Sedated	Completely Sedated
N_2O-O_2	-	10% (5/52)	44% (23/52)	46% (24/52)
Ketorolac/N_2O-O_2	-	10% (5/50)	46% (23/50)	44% (22/50)

Table 5. Distribution of the Experimental Groups by Type of Anesthetic Success

Group	Number	N_2O-O_2	Ketorolac/N_2O-O_2	P-Value*
IAN Block Success	102	24/52 (46%)	27/50 (54%)	0.428
Articaine Success	51	11/28 (39%)	12/23 (52%)	0.357
I/O Success	28	15/17 (88%)	7/11 (64%)	0.121

*Values Analyzed using the Chi-Square Test

Table 6. Injection Pain

		N_2O-O_2			Ketorolac/N_2O-O_2			P-values**
		N	Mean*	Std Dev	N	Mean*	Std Dev	
IAN Block								
	Insertion	52	57	36	50	49	31	1.000
	Placement	52	58	37	50	59	46	1.000
	Deposition	52	54	43	50	60	48	1.000
Articaine								
	Insertion	28	16	30	23	13	24	1.000
	Placement	28	16	31	23	9	13	1.000
	Deposition	28	19	27	23	20	22	1.000
I/O								
	Insertion	17	15	19	11	14	23	1.000
	Placement	17	17	23	11	13	22	1.000
	Deposition	17	30	32	11	23	32	1.000

* Based on 170 mm Heft-Parker VAS

** Values analyzed using the Bonferroni-Randomized test

Table 7. IAN Injection Pain

	Group	None	Mild	Moderate	Severe
Insertion	N_2O-O_2	2 (4%)	21 (40%)	26 (50%)	3 (6%)
	Ketorolac/N_2O-O_2	2 (4%)	28 (56%)	20 (40%)	-
Placement	N_2O-O_2	1 (2%)	23(44%)	24 (46%)	4 (8%)
	Ketorolac/N_2O-O_2	3 (6%)	21 (42%)	19 (38%)	7 (14%)
Deposition	N_2O-O_2	3 (6%)	20 (38%)	24 (46%)	5 (10%)
	Ketorolac/N_2O-O_2	2 (4%)	21 (42%)	20 (40%)	7 (14%)

Table 8. Articaine Injection Pain

	Group	None	Mild	Moderate	Severe
Insertion	N_2O-O_2	6 (21%)	19 (68%)	2 (7%)	1 (4%)
	Ketorolac/N_2O-O_2	5 (22%)	16 (69%)	2 (9%)	-
Placement	N_2O-O_2	8 (29%)	17 (61%)	2 (7%)	1 (3%)
	Ketorolac/N_2O-O_2	4 (17%)	18 (78%)	1 (4%)	-
Deposition	N_2O-O_2	7 (25%)	17 (61%)	4 (14%)	-
	Ketorolac/N_2O-O_2	2 (9%)	18 (78%)	3 (13%)	-

Table 9. I/O Injection Pain

	Group	None	Mild	Moderate	Severe
Insertion	N_2O-O_2	4 (23%)	12 (71%)	1 (6%)	-
	Ketorolac/N_2O-O_2	3 (27%)	7 (64%)	1 (9%)	-
Placement	N_2O-O_2	5 (29%)	9 (53%)	3 (18%)	-
	Ketorolac/N_2O-O_2	3 (27%)	7 (64%)	1 (9%)	-
Deposition	N_2O-O_2	3 (18%)	9 (53%)	5 (29%)	-
	Ketorolac/N_2O-O_2	2 (18%)	7 (64%)	2 (18%)	-

Table 10. Anesthetic Failure Point

	Group	IAN		Articaine		I/O	
		Number	Percent Failure (%)	Number	Percent Failure	Number	Percent Failure (%)
Dentin	N_2O-O_2	28	17/28 (61%)	17	8/17 (47%)	2	1/2 (50%)
	Ketorolac/N_2O-O_2	23	15/23 (65%)	11	7/11 (64%)	4	2/4 (50%)
Chamber	N_2O-O_2	28	10/28 (36%)	17	7/17 (41%)	2	1/2 (50%)
	Ketorolac/N_2O-O_2	23	5/23 (22%)	11	2/11 (18%)	4	2/4 (50%)
Canal	N_2O-O_2	28	1/28 (3%)	17	2/17 (12%)	-	-
	Ketorolac/N_2O-O_2	23	3/23 (13%)	11	2/11 (18%)	-	-

Table 11. Satisfaction Ratings

Group	Number	Mean (mm)*	Std Dev	Minimum	Maximum	P-value**
N_2O-O_2	52	96	7	69	100	
Ketorolac/N_2O-O_2	50	96	9	59	100	1.000

* Based on 100 mm VAS

** Values analyzed using the Bonferroni-Randomized test

Table 12. Satisfaction Ratings by Category

Group	Not Satisfied	Somewhat Satisfied	Moderately Satisfied	Completely Satisfied
N_2O-O_2	-	-	-	100% (52/52)
Ketorolac/N_2O-O_2	-	-	4% (2/50)	96% (48/50)

Table 13. Treatment Pain Ratings

Group	Number	Mean (mm)*	Std Dev	Minimum	Maximum	P-value**
N_2O-O_2	52	42	41	0	162	
Ketorolac/N_2O-O_2	50	33	43	0	148	1.000

* Based on 170 mm Heft-Parker VAS

** Values analyzed using the Bonferroni-Randomized test

APPENDIX B

CONSENT FORM

The Ohio State University Consent to Participate in Research

Study Title: Effect of nitrous oxide/intranasal ketorolac combination on the success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis.

Principal Investigator: Dr. Melissa Drum

Sponsor: Not Applicable

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. Why is this study being done?

The purpose of this study is to see if the combination of nitrous oxide/intranasal ketorolac (gas and drug nose spray) improves the success of numbing during treatment.

2. How many people will take part in this study?

One Hundred and ten people (110) will take part in this study.

3. What will happen if I take part in this study?

You have a tooth, which is hurting (painful), and you are aware that it needs a root canal. If you decide to participate in this study, you will be required to complete a medical history questionnaire, a HIPAA authorization and consent form. If you are a woman able to have children, you will be required to take a urine pregnancy test before participation. The study requires one appointment but you will need at least one additional appointment to finish the root canal if you elect to save your tooth.

The tooth causing you pain will first be tested to make an accurate diagnosis. It will first be tested with a cold cotton pellet chilled with an ice spray. Your tooth may hurt for a few moments after being tested with the cold. The cold pellet will be removed immediately after you feel the sensation in your tooth. The cold test is used routinely before root canal treatment.

You will be asked to rate the pain you are having prior to any treatment. You will also fill out a form to rate how anxious you are. You will then randomly receive either intranasal ketorolac (pain drug) or intranasal placebo (saline). Neither your doctor nor you will know which one you will receive. Ketorolac is an NSAID (like advil or motrin) and is indicated for use of moderate to severe pain especially in oral surgery and medical models. After 20 minutes, you will then receive a gas mixture of nitrous oxide and oxygen. Nitrous oxide is sometimes referred to as "laughing gas," and is a gas that is used to reduce anxiety. After breathing the nitrous oxide/oxygen gas mixture, you will fill out a form to rate how relaxed you feel.

After receiving nitrous oxide for 10 minutes, one injection (shot) will be given in the back of your jaw to numb your lower teeth (inferior alveolar injection) using 2% lidocaine with 1:100,000 epinephrine which is an anesthetic (numbing solution) similar to novocaine. You will be asked to rate the amount of pain you feel when the injection is being given. You will do this by marking your pain with a pen on a line graph. You will then be given a second injection (shot) in the back of your jaw using the same 2% lidocaine with 1:100,000 epinephrine.

Following the numbing injections, the doctor will begin asking you every minute for 15 minutes whether you are experiencing lip numbness. At 15 minutes if your lip is not numb, you will be given extra numbing. Next, a small opening will be made in the top of your tooth to begin the root canal. If you feel pain, you will raise your hand and will be asked to rate the pain. If you have moderate or severe pain, more

numbing will be done. Routine emergency root canal treatment will then be completed. You will then be asked to rate your satisfaction with the treatment you received.

4. How long will I be in the study?

You are aware that you will have one appointment, which will last approximately 120 minutes.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

As you may know, nitrous oxide (laughing gas) may cause: a feeling of nausea, which is rare; light-headedness, a tingling sensation in your arms or legs; feeling of warmth, floating, or heaviness. The effects of nitrous oxide (laughing gas) are short term. You will be placed on oxygen after treatment to ensure that the nitrous oxide is removed from your body.

Intranasal ketorolac (nose drug) may cause some nasal discomfort and irritation. The irritation is generally mild and transient, lasting less than 5 minutes.

You may have pain associated with the local anesthetic (numbing solution) or soreness at the site of the injections (shots) for approximately two days. Where you receive the injection, you may have swelling (hematoma-a collection of blood in your mouth) or a bruise may develop. You may experience a feeling of anxiety, lightheadedness or fainting, and or a temporary increase in your heart rate. Your toothache may stay the same or worsen during the study. The tingling sensation and/or slight discomfort (pain) produced by the cold ice spray may be uncomfortable to you. You may have an allergic reaction to the local anesthetic (itching or hives, very rare), or have an unexpected infection (rare) which could result in permanent nerve damage. You may have soreness of your gum tissue for a few days or a possible altered sensation of your lip or tongue that may last up to a few weeks. Your tooth may feel sore to bite on for a few days. All of the complications listed in this paragraph can occur after normal (non-study) treatment because these same injections must be done whether or not you participate in the study.

If you are a woman able to have children, you will be questioned regarding pregnancy or suspected pregnancy and will not be allowed to participate if pregnant, suspect a pregnancy, trying to become pregnant, or nursing. Additionally, you will be required to take a urine pregnancy test before you can start this study. The reason for excluding pregnant or potentially pregnant women is because of the laughing gas (nitrous oxide) and the nose drug (intranasal ketorolac).

7. What benefits can I expect from being in the study?

You will not directly benefit from this study.

8. What other choices do I have if I do not take part in the study?

You may have the emergency endodontic procedure completed without having nitrous oxide/intranasal ketorolac or nitrous oxide/placebo administered.

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify

you. At most, the website will include a summary of the results. You can search the website at any time.

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

10. What are the costs of taking part in this study?

The cost of the study drugs (nitrous oxide/intranasal ketorolac) will be covered. Because routine endodontic treatment will be performed, other costs (parking, cost of treatment) will not be reimbursed in this study. The study will pay for the cost of the urine pregnancy test when indicated.

11. Will I be paid for taking part in this study?

Yes, you will be paid $75.00 for your participation. By law, payments to subjects are considered taxable income.

12. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

13. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Dr. Melissa Drum or Dr. Daniel Stentz at 614-292-3596.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact Dr. Melissa Drum or Dr. Daniel Stentz at 614-292-3596.

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form**.**

Printed name of subject	**Signature of subject**
	AM/PM
	Date and time
Printed name of person authorized to consent for subject (when applicable)	**Signature of person authorized to consent for subject (when applicable)**

Relationship to the subject	Date and time AM/PM

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	Signature of person obtaining consent AM/PM Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	Signature of witness AM/PM Date and time
Printed name of witness	Signature of witness AM/PM Date and time

APPENDIX C

PRIVACY FORM

THE OHIO STATE UNIVERSITY

AUTHORIZATION TO USE
PERSONAL HEALTH INFORMATION IN RESEARCH

Title of the Study: Effect of nitrous oxide/intranasal ketorolac combination on the success of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis.

Protocol Number: 2014H0427

Principal Investigator: Dr. Melissa Drum

Subject Name_____

Before researchers use or share any health information about you as part of this study, The Ohio State University is required to obtain your authorization. This helps explain to you how this information will be used or shared with others involved in the study.

- The Ohio State University and its hospitals, clinics, health-care providers, and researchers are required to protect the privacy of your health information.
- You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you. Please carefully review this information. Ask if you have any questions or do not understand any parts of this notice.
- If you agree to take part in this study your health information will be used and shared with others involved in this study. Also, any new health information about you that comes from tests or other parts of this study will be shared with those involved in this study.
- Health information about you that will be used or shared with others involved in this study may include your research record and any health care records at The Ohio State University. For example, this may include your medical records, x-rays, or laboratory results. Psychotherapy notes in your health records (if any) will not, however, be shared or used. Use of these notes requires a separate, signed authorization.

Please read the information carefully before signing this form. Please ask if you have any questions about this authorization, the university's Notice of Privacy Practices or the study before signing this form.

Those Who May Use, Share, and Receive Your Information as Part of This Study

- Researchers and staff at The Ohio State University will use, share, and receive your personal health information for this research study. Authorized Ohio State staff not involved in the study may be aware that you are participating in a research study and have access to your information. If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office records.

Initials/Date: _____

- Those who oversee the study will have access to your information, including the following:
    - Members and staff of The Ohio State University's Institutional Review Boards, including the Western Institutional Review Board
    - The Ohio State University Office of Responsible Research Practices
    - University data safety monitoring committees
    - The Ohio State University Office of Research.

- Your health information may also be shared with federal and state agencies that have oversight of the study or to whom access is required under the law. These may include the following:
    - Food and Drug Administration
    - Office for Human Research Protections
    - National Institutes of Health
    - Ohio Department of Job and Family Services.

- These researchers, companies and/or organization(s) outside of The Ohio State University may also use, share and receive your health information in connection with this study:
    - None

The information that is shared with those listed above may no longer be protected by federal privacy rules.

Authorization Period

This authorization will not expire unless you change your mind and revoke it in writing. There is no set date at which your information will be destroyed or no longer used. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be completed.

Initials/Date_____

Signing the Authorization

- You have the right to refuse to sign this authorization. Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form.
- You will not be able to take part in this study and will not receive any study treatments if you do not sign this form.

  If you sign this authorization, you may change your mind at any time. Researchers may continue to use information collected up until the time that you formally changed your mind. If you change your mind, your authorization must be revoked in writing. To revoke your authorization, please write to: *Dr. Melissa Drum at the College of Dentistry, 305 w 12th avenue, the Ohio State University, Columbus, Ohio 43210 or Dr. Fonda Robinson at the College of Dentistry, 305 w 12th avenue, the Ohio State University, Columbus, Ohio 43210.*

- Signing this authorization also means that you will not be able to see or copy your study-related information until the study is completed. This includes any portion of your medical records that describes study treatment.

Contacts for Questions

- If you have any questions relating to your privacy rights, please contact: *Matthew Stalsworth at the College of Dentistry, 1130F Postle Hall, 305 w 12th avenue, the Ohio State University, Columbus, Ohio 43210. 614-292-3016*
- If you have any questions relating to the research, please contact: *Dr. Melissa Drum at the College of Dentistry, 305 W. 12th Ave., The Ohio State University, Columbus, OH 43210, 614-292-3596*

Signature

I have read (or someone has read to me) this form and have been able to ask questions. All of my questions about this form have been answered to my satisfaction. By signing below, I permit *Dr. Melissa Drum* and the others listed on this form to use and share my personal health information for this study. I will be given a copy of this signed form.

Signature_____
_____

(Subject or Legally Authorized Representative)

Print Name _____ Date_____ Time _____
AM/PM

_____

(If legal representative, also print relationship to subject)

APPENDIX D

HEALTH HISTORY QUESTIONNAIRE

THE OHIO STATE UNIVERSITY
COLLEGE OF DENTISTRY

Subject # _____
Date _____
Date of Birth _____

Medical History

1. Do you have or have you had any of the following?

a. rheumatic fever or rheumatic heart disease……	NO	YES
b. heart murmur or mitral valve prolapse……	NO	YES
c. heart disease or heart attack……	NO	YES
d. artificial heart valve……	NO	YES
e. irregular heart beat……..	NO	YES
f. pacemaker……	NO	YES
g. high blood pressure……	NO	YES
h. chest pains or angina……	NO	YES
i. stroke……	NO	YES
j. artificial joint……	NO	YES
k. hepatitis/liver disease……..	NO	YES
l. tuberculosis……..	NO	YES
m. thyroid problem……	NO	YES
n. kidney disease……	NO	YES
o. diabetes (sugar)……	NO	YES
p. asthma……	NO	YES
q. HIV or other immunosuppressive disease……..	NO	YES
r. radiation or cancer therapy……..	NO	YES

2. Do you or have you had any disease, condition, or problem not listed here? NO YES

3. Have you ever been hospitalized? NO YES

4. Have you had excessive or prolonged bleeding requiring special treatment? NO YES

5. Have you had an allergic reaction to any drugs or medications?
   (Circle all that apply: penicillin; codeine; aspirin; anesthetics; other) NO YES

6. Are you currently under the care of a physician (M.D., D.O.)? NO YES
   When were you last seen by a physician?_____
   Name of Physician_____
   Street address_____
   City, State, and Zip Code_____
   Phone_____

7. Are you pregnant or nursing? Estimated date of delivery_____ NO YES

8. Have you had any trouble associated with previous dental treatment? NO YES

9. How often do you have dental check ups? _____ Date of last Exam_____

10. Do you have any lumps or sores in your mouth now? NO YES

11. Do you smoke or use smokeless tobacco? NO YES

12. Are you currently taking any drugs or medications (such as antibiotics, heart medicine, birth control pills?) NO YES

Current Medications

Trade Name	Generic Name	Dose/Frequency	Reason

Summary of Patient's Medical Status:_____

_____

_____

Medical Risk Assessment

☐ ASA I (healthy individual)
☐ ASA II (mild systemic disease)
☐ ASA III (severe disease but not incapacitating)
☐ ASA IV (incapacitating systemic disease)

Medical Consultation Required

☐ No (healthy and/or stabilized disease)

☐ Yes (ASA III or IV; cardiac murmur; vague hx; recent major disease; recent diagnosis/operation; uncontrolled disease; blood pressure; etc.)

To the best of my knowledge, the above information is correct and complete.

_____ _____

Patient's Signature Date

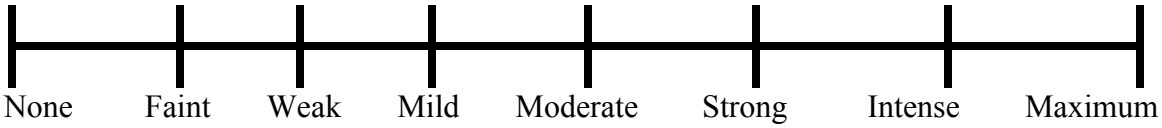
APPENDIX E

INITIAL PAIN RATING VISUAL ANALOG SCALE

Initial Pain Rating

Date: _____
Code #: _____

1. Please mark a vertical line " | " on the line below to rank the level of pain you are feeling today.



APPENDIX F

CORAH'S DENTAL ANXIETY SCALE

CORAH'S DENTAL ANXIETY SCALE

Code_____
Pre-Injection Questionnaire

PLEASE ANSWER THE FOLLOWING QUESTIONS BY CIRCLING THE ANSWER THAT BEST DESCRIBES HOW YOU FEEL.

1. If you had to go to the dentist tomorrow, how would you feel about it?
a) I would look forward to it as a reasonably enjoyable experience.
b) I wouldn't care one way or the other.
c) I would be a little uneasy about it.
d) I would be afraid that it would be unpleasant and painful.
e) I would be very afraid of what the dentist might do.

2. When you are waiting in the dentist's office for you turn in the chair, how do you feel?
a) Relaxed.
b) A little uneasy.
c) Tense.
d) Anxious.
e) So anxious that I sometimes break in a sweat or almost feel physically sick.

3. When you are in the dentist's chair waiting while she/he gets her/his drill ready to begin working on your teeth, how do you feel?
a) Relaxed.
b) A little uneasy.
c) Tense.
d) Anxious.
e) So anxious that I sometimes break in a sweat or almost feel physically sick.

4. You are in the dentist's chair to have your teeth cleaned. While you are waiting and the dentist is getting out the instruments, which she/he will use to scrape your teeth around your gums, how do you feel?
a) Relaxed.
b) A little uneasy.
c) Tense.
d) Anxious.
e) So anxious that I sometimes break in a sweat or almost feel physically sick.

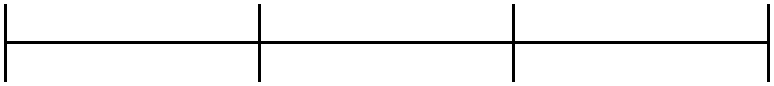
APPENDIX G

SEDATION RATING VISUAL ANALOG SCALE

Code Number:_____
Name:_____

Sedation Rating

Mark a vertical line " | " on the point on the scale line that best describes your sedation.



Not Sedated	**Somewhat Sedated**	**Moderately Sedated**	**Completely Sedated**

APPENDIX H

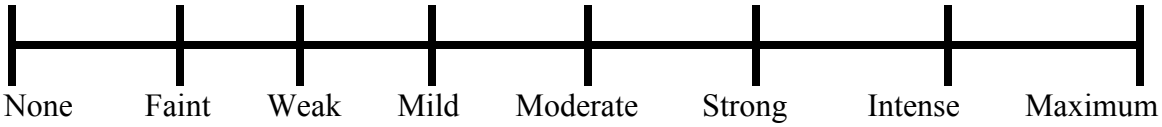
IANB INJECTION PAIN RATING VISUAL ANALOG SCALE

Inferior Alveolar Nerve Block Pain Rating

Date: _____
Code #: _____

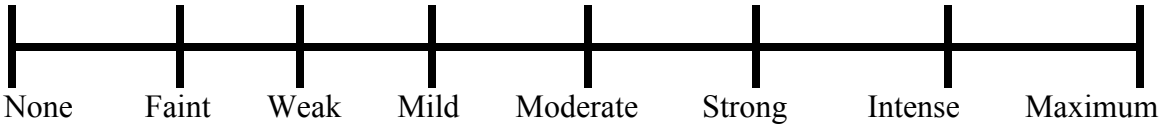
Needle Insertion

1. Please place an "X" on the line below to rank the level of pain felt during needle insertion



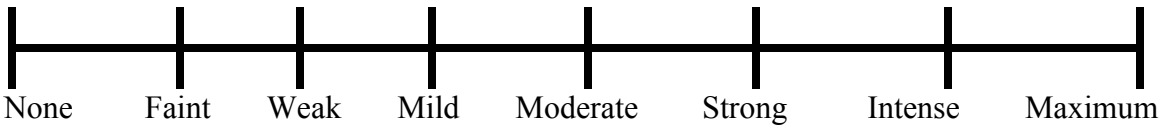
Needle Placement

2. Please place an "X" on the line below to rank the level of pain felt during needle placement.



Solution Deposition

3. Please place an "X" on the line below to rank the level of pain felt during solution deposition.



APPENDIX I

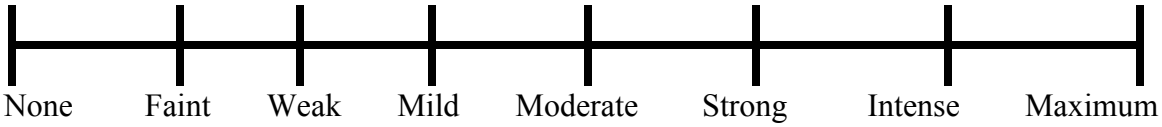
IANB ACCESS PAIN RATING VISUAL ANALOG SCALE

Inferior Alveolar Nerve Block Access Pain Rating

Date: _____
Code #: _____

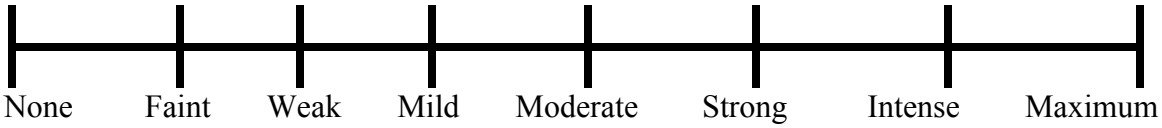
Dentin

1. Please place an "X" on the line below to rank the level of pain.



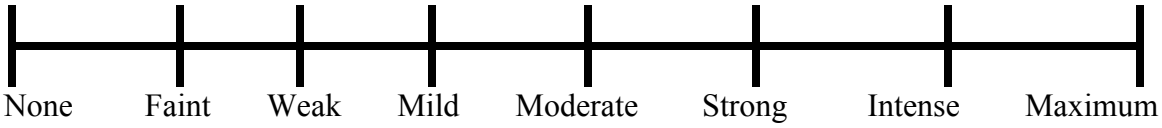
Pulp Chamber

2. Please place an "X" on the line below to rank the level of pain.



Instrument Canals

3. Please place an "X" on the line below to rank the level of pain.



APPENDIX J

SUPPLEMENTAL INJECTION PAIN RATING

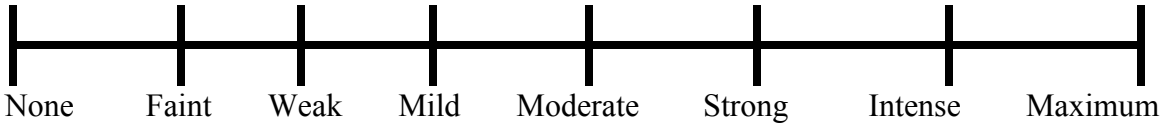
VISUAL ANALOG SCALE

Supplemental Injection Pain Rating

Date: _____
Code #: _____

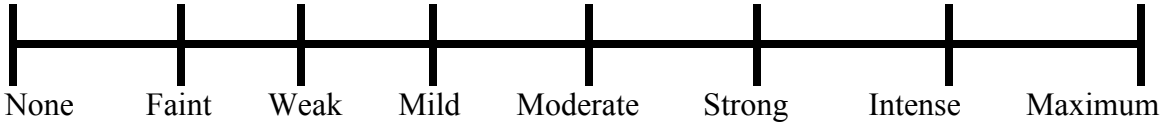
Needle Insertion

1. Please place an "X" on the line below to rank the level of pain felt during needle insertion



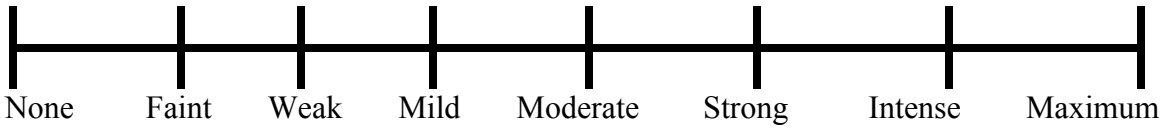
Needle Placement

2. Please place an "X" on the line below to rank the level of pain felt during needle placement.



Solution Deposition

3. Please place an "X" on the line below to rank the level of pain felt during solution deposition.



APPENDIX K

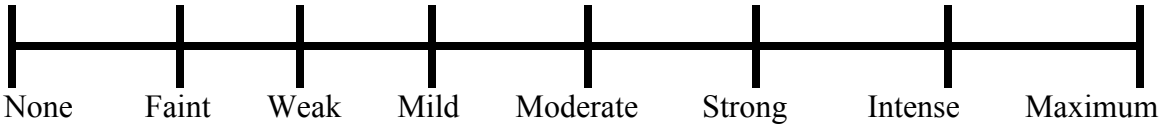
SUPPLEMENTAL ACCESS PAIN RATING VISUAL ANALOG SCALE

Supplemental Access Pain Rating

Date: _____
Code #: _____

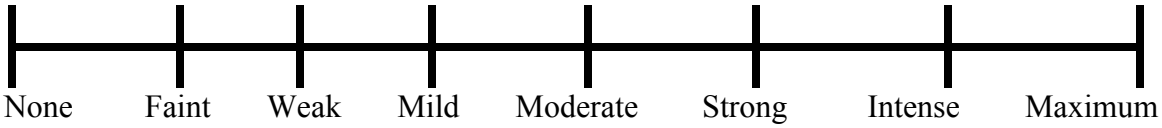
Dentin

1. Please place an "X" on the line below to rank the level of pain.



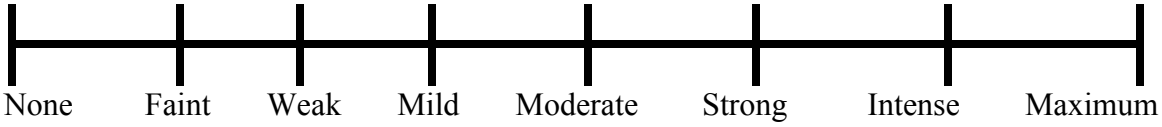
Pulp Chamber

2. Please place an "X" on the line below to rank the level of pain.



Instrument Canals

3. Please place an "X" on the line below to rank the level of pain.



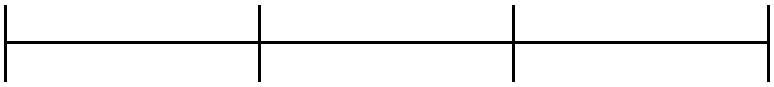
APPENDIX L

SATISFACTION RATING AND TREATMENT PAIN RATING VISUAL ANALOG SCALE

Pt. Number:_____

Satisfaction Rating

Mark a vertical line " | " on the point on the scale line that best describes your satisfaction.

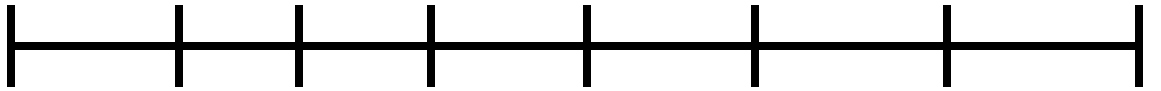


Not Satisfied **Somewhat Satisfied** **Moderately Satisfied** **Completely Satisfied**

Treatment Pain Rating

Do you remember feeling pain during the treatment, if yes, what was the greatest amount of pain you felt?

Please place an "X" on the line below to rank the level of pain.



None Faint Weak Mild Moderate Strong Intense Maximum