Efficacy of articaine versus mepivacaine administered as different supplementary local anesthetic techniques after a failed inferior alveolar nerve block with lidocaine in patients with irreversible pulpitis: An in vivo study

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Abstract
Aim: The aim of the present study was to assess the efficacy of articaine versus mepivacaine administered as different supplementary local anesthetic techniques after a failed inferior alveolar nerve block (IANB) with lidocaine in patients with irreversible pulpitis.

Materials and Methods: A total of 120 patients were included in the study. Patients were given IANB with 2 ml of 2% lidocaine hydrochloride with 1:80,000 epinephrine. Patients who showed subjective symptoms of IANB but did not secure pulpal anesthesia were randomly allocated to one of the following four groups by random sampling for supplementary local anesthesia – Group 1: buccal infiltration (BI) with 4% articaine with 1:100,000 epinephrine, Group 2: four-site intraligamentary (IL) injection with 4% articaine with 1:100,000 epinephrine, Group 3: BI with 2% mepivacaine with 1:100,000 epinephrine, and Group 4: four-site IL injection with 2% mepivacaine with 1:100,000 epinephrine.

Results: Group 1 – BI with articaine provided anesthesia success in 27 cases (90%, n = 30). Group 2 – IL injection with articaine provided anesthesia success in 20 cases (66.67%, n = 30). Group 3 – BI with mepivacaine provided anesthesia success in 21 cases (70%, n = 30). Group 4 – IL injection with mepivacaine provided anesthesia success in 15 cases (50%, n = 30). A significant difference between the four groups was found.

Conclusion: In patients with a mandibular first molar exhibiting symptomatic irreversible pulpitis, block injection with lidocaine along with supplemental BI with articaine allowed more pain-free treatments. Articaine showed better results when compared with mepivacaine.

Keywords: Articaine; inferior alveolar nerve block; mepivacaine

INTRODUCTION
Pain is an unpleasant, varying-intensity sensation associated with a present or potential tissue breakdown process. Acute pulp inflammation is the cause of pain in irreversible pulpitis, and certain alterations such as vasodilation, increased vascular permeability, and leukocyte leakage can be seen. Inflammation causes a large increase in internal tissue pressure because the pulp is unable to expand.[1]

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The correct administration of local anesthetic lays the groundwork for a successful dental procedure.\cite{2} When performing endodontic operations on patients, dentists must first get appropriate anesthetic.\cite{3} The most popular approach for anesthetizing posterior mandibular teeth during endodontic treatments is inferior alveolar nerve block (IANB). A local anesthetic solution is deposited in the pterygomandibular region, soaking the inferior alveolar nerve right before it enters the mandibular foramen. The failure rate for IANB is substantial, ranging from 7% to 77%.\cite{4} Patients with inflamed pulpal tissues have considerably lower success rates. Anatomic variations such as cross innervations and accessory innervations, decreased local pH, tachyphylaxis of anesthetic solutions, and activation of nociceptors such as tetrodotoxin and capsaicin-sensitive transient receptor potential vanilloid Type 1 have all been proposed as explanations for the failure of local anesthetics.\cite{4}

Anesthetic success rates have been evaluated using other approaches such as intraosseous, intraligamentary (IL), and infiltration injections.\cite{5} A mandibular buccal infiltration (BI) injection, which has been found to be successful for mandibular molar anesthesia in asymptomatic individuals despite the bigger cortical plate, is a very easy, safe, and comfortable adjunct anesthetic to traditional IANB.\cite{6} It is also less damaging to the periodontal ligament (PDL) and prevents bacteremia. IL injection is a procedure that can be utilized as a backup injection if IANB fails. A local anesthetic solution is injected into the cancellous bone close to the tooth to be anesthetized using the IL injection. According to previous research, supplemental IL injections achieve pulpal anesthetic in endodontic therapy with a success rate of 50%–96%.

Frequently used local anesthetic formulations in clinical dentistry are articaine, lidocaine, and mepivacaine.\cite{7} Articaine differs from other amide local anesthetics in that it is made from thiophene instead of benzene. Articaine structure has a thiophene ring, which makes it more lipid soluble. This increases the efficacy of the anesthetic agent by allowing more of it to diffuse through the nerve membrane. Because it has a lower ionization constant (pKa) than lidocaine, mepivacaine is commonly utilized in uncomfortable clinical conditions because it is more compatible with inflamed tissues and has a faster onset and longer duration of analgesia.\cite{11}

The purpose of this in vivo study was to compare the efficacy of articaine versus mepivacaine in patients with irreversible pulpitis after a failed IANB with lidocaine using different supplementary local anesthetic techniques, such as BI and IL injection.

**MATERIALS AND METHODS**

The patients in this prospective, randomized clinical trial ranged in age from 18 to 50 years old and presented to the department of conservative dentistry and endodontics, with the chief complaint of tooth discomfort owing to carious exposure. There were 120 mandibular first molars in total. All patients were told about the potential complications, and those who agreed to participate in the trial gave their informed consent and were confirmed by the ethical committee.

The inclusion criteria comprised patients of age 18–50 years old, good health, no facial paresthesia, a cariously exposed symptomatic mandibular molar, pain prior to treatment, a positive and lasting reaction to electric pulp testing, and not taking any drug that could impact pain perception. The exclusion criteria included teeth with full crowns and large restorations with overhanging margins, patients with known allergies or contraindications to any component of local anesthetic solution, and teeth with full crowns and large restorations with overhanging margins. Patients who were pregnant and history of significant medical conditions (American Society of Anesthesiologists Class II or higher) were also excluded from the trial.

An electric pulp tester (EPT) was used to record the baseline pulp sensitivity of the tooth with irreversible pulpitis (Coxo, Foshan, Guangdong, China). The function and validity of the pulp tester were first tested using a unanesthetized control tooth on the opposite side of the lower jaw. By employing the direct/Halstead technique, all the patients were administered IANB with 2 ml of 2% lidocaine with 1:80,000 epinephrine at a rate of 2 ml/min (Lignospan Special, Septodont). All local anesthetic injections were delivered using dental aspirating syringe (Waldent) and 27G long needles (Septoject; Septodont). All local anesthetic injections were given by a single operator. The effectiveness of IANB was evaluated 15 min after injection by asking the patient about all of the lip numbness and subjective IANB symptoms. When the patient did not exhibit these symptoms, the block was deemed missing, and the patient was removed from the research.

On a Heft-Parker Visual Analog Scale (HP VAS), all individuals were asked to rate their pain. Each subject was told of their HP VAS pain ratings and was asked to complete a baseline HP VAS to determine their level of pain prior to surgery. A 170-mm line with numerous descriptive names was used by HP VAS. The participants marked the scale where it best described their level of pain. The VAS was divided into four categories to interpret the data: no pain was defined as 0 mm on the scale; mild pain was defined as >0 mm and 54 mm, which included descriptors such as faint, weak, and mild pain; moderate pain was defined as >54 mm and 114 mm; and severe pain was defined as 114 mm and included...
descriptors such as strong, intense, and maximum possible pain.

Following IANB, pulp testing was performed on the test tooth every 2 min for 10 min, or until a maximum reading of 80 without sensation was achieved, whichever happened first. Patients who were able to obtain pulp anesthesia with IANB were given additional dental treatment. Patients with subjective IANB symptoms but no pulpal anesthesia were included in the research for supplemental local anesthetic.

Anesthetic test was carried out for lidocaine, articaine, and mepivacaine. One blinded assistant enrolled all participants and assigned them to intervention. There were an equal number of articaine and mepivacaine cartridges available that had been covered and given a code. Another assistant in the department was aware of the codes and gave out the cartridges randomly and in equal numbers according to the subgroups.

Group 1: BI with 4% articaine with 1:100,000 epinephrine (Septanest, Septodont). Group 2: four-site IL injection with 4% articaine with 1:100,000 epinephrine. Group 3: BI with 2% mepivacaine with 1:100,000 epinephrine (Scandonest, Septodont). Group 4: four-site IL injection with 2% mepivacaine with 1:100,000 epinephrine using dental aspirating syringe (Waldent) and needles (Septoject, Septodont). The sites of injection were cleaned with an antiseptic solution [Illustration 1].

The supplemental techniques were as follows:

- **BI**: entails placing a local anesthetic solution next to the tooth apex on the buccal side. With an aspirating dental cartridge syringe, injections were delivered gently over 30 s
- **IL injection (PDL)**: The needle was angled at 30° from the tooth’s long axis. The needle was firmly placed between the alveolar bone and the tooth in the mesial gingival sulcus at the mesiobuccal line angle of the tooth until resistance was felt. After injecting the local anesthetic solution, the needle and pressure were kept in place for another 20 s. The distal root underwent the same procedure. The gingival sulcus at the distobuccal line angle was the site of the distal injection. At the same time, the procedure was carried out at mesiolingual and distolingual aspects.

The test tooth’s pulp sensitivity was measured 5 min after each supplemental injection. The HP VAS was used to record the subject’s self-reported pain evaluation.

A successful outcome was defined as a negative reaction to electric pulp testing within 5 min after additional local anesthetic. After that, the patient’s endodontic treatment was completed, with no discomfort or weak/mild pain during endodontic access preparation and pulp extirpation.

During the access preparation or pulp extirpation, if the study subject’s self-reported pain on the HP VAS was >54 mm, the procedure was stopped, the anesthetic was deemed failed, and those participants were eliminated from further analysis in the study.

### RESULTS

Out of the 120 samples recorded, 30 subjects were distributed among the four groups each. Statistical analyses were performed using SPSS (Version 20.0, SPSS Inc., Chicago, Illinois, USA). Success and failure rates for all four supplemental local anesthetic techniques were recorded for all subjects and described in terms of number of patients and percentage. *t*-test was applied.

Group 1 – BI with articaine provided anesthesia success in 27 cases (90%, *n* = 30). Group 2 – IL injection with articaine provided anesthesia success in 20 cases (66.67%, *n* = 30). Group 3 – BI with mepivacaine provided anesthesia success in 21 cases (70%, *n* = 30). Group 4 – IL injection with mepivacaine provided anesthesia success in 15 cases (50%, *n* = 30). A significant difference between the four groups was found [Graph 1]. The overall success rate of articaine was 78.33% and that of mepivacaine was 60% [Graph 2].

Table 1 compares the success and failure rates of different groups.

Table 2 compares the overall success of articaine versus mepivacaine as a supplemental anesthetic.

### DISCUSSION

It is difficult to provide adequate anesthetic during caries removal, access cavity preparation, and initial canal instrumentation in mandibular molars with symptomatic irreversible pulpitis. The IANB is the most common...
technique for anesthesia in mandibular posterior teeth, and the most common drug is lidocaine solution. It is important to keep in mind that even the best injection technique and soft tissue numbness do not always guarantee analgesia during treatment. In patients with irreversible pulpitis, local anesthesia with an IANB may produce effective anesthesia in 70% of uninflamed pulp but only in 30% of patients with irreversible pulpitis. Individuals with irreversible pulpitis have eight times the risk of local anesthetic failure than normal patients, according to one study. The increased density of the buccal alveolar plate (which limits supraperiosteal infiltration in the case of intraligamentary injection), limited access to the inferior alveolar nerve, and a wide diversity in neuroanatomy could all contribute to lower success rates in the mandible in case of IANB.

Different injection methods and anesthetic drugs have been researched to tackle the difficulty of giving successful anesthesia other than IANB. As a result, more injection techniques and other anesthetic solutions should be researched, and their benefits utilized to treat patients more efficiently and comfortably. BI, IL, and intraosseous anesthetic procedures are often utilized supplementary anesthetic treatments. BI and IL injections were used as additional anesthetic treatments in the current investigation. BI has been employed as a supplementary anesthetic approach to the IANB for mandibular molar teeth, either for the first or second molars. When BI was used, Meechan et al. observed a greater success rate of anesthetic in the mandibular first molar. One of the disadvantages of using BI as the primary anesthetic approach in addition to IANB anesthesia is that lip
numbness cannot be utilized as an indicator of the latter’s success. Despite this disadvantage, Parirokh et al. [3] found that using both IANB and BI in mandibular molar teeth with irreversible pulpitis resulted in a greater success rate than using only IANB anesthesia. The IL injection approach was also used in the study since it is a generally available, simple-to-use procedure that does not require special equipment, is less expensive than intraosseous injection, and has a faster onset. The term “IL” is misleading since the anesthetic solution distributes over the cribriform plate’s outer surface, diffusing into crestal marrow spaces rather than the periodontal space. It has a relatively short action time (20 min) and a high rate of postoperative discomfort [4,9-11].

Only mandibular first molars were used in this study because several studies have only used mandibular first molars because the thicker cortical plate over the second molar may prevent adequate penetration of the anesthetic solution around the apical foramen of the tooth, resulting in ineffective anesthesia.

In dentistry, a variety of local anesthetics are now employed. Apart from lidocaine, which has been used in dentistry for decades, articaine and mepivacaine are also extensively utilized. The researchers utilized 4% articaine and 2% mepivacaine in this experiment.

Human permanent first mandibular molars with irreversible pulpitis and normal periapical radiography appearance were all chosen. The study’s effect was confirmed using strict inclusion criteria. [12]

In clinical research, a variety of approaches are utilized to assess the efficacy of pulpal anesthetics. Numbness of the soft tissues, lips, and tongue tips is one of them. The subject’s interpretation of pain, which is extremely varied and dependent on their emotional and psychological status as well as previous experiences, further complicates these indications (Certosimo and Archer, 1996). The EPT is a valuable tool for determining the depth of local anesthesia. EPT has also been shown to be a reliable method of assessing local anesthesia in teeth with noninflamed and inflamed pulps in studies. [13]

After each injection, all the subjects in this study had lip numbness. It should be mentioned that, even though all of the patients reported subjective symptoms of lip numbness, the anesthetic did not work in every case. A literature search indicated that this phenomenon can also be seen in uninflamed pulps, where the physician failed to get no response to the maximum stimulus on electric pulp testing despite successful lip numbness [6,7,14-18]. As a result, we chose to apply a lip numbness and electric pulp testing method before preparing the access cavity.

In addition, the Visual Analog Scale (VAS), a psychometric response scale, was employed as a measurement instrument for subjective features such as dental pain, and it has been successfully used in dentistry, mainly for patients who are symptomatic preoperatively.

All the participants in this study were given IANB utilizing the direct/Halstead method. The effectiveness of IANB was evaluated 15 min after injection by asking the patient about all the lip numbness and subjective IANB symptoms. When the patient did not exhibit these symptoms, the block was deemed missing, and the patient was removed from the research. Patients with subjective IANB symptoms but no pulpal anesthesia were included in the research for supplemental local anesthetic. They were assigned to one of the four groups below at random. Patients in Group 1 received BI with 4% articaine hydrochloride (HCL) with 1:100,000 epinephrine, whereas patients in Group 2 received four-site IL injection with 4% articaine HCL with 1:100,000 epinephrine. Patients in Group 3 received BI with 2% mepivacaine HCL with 1:100,000 epinephrine and patients in Group 4 received four-site IL injection with 2% mepivacaine HCL with 1:100,000 epinephrine.

The test tooth’s pulp sensitivity was measured 5 min after each supplemental injection or when a maximum value of 80 was reached without sensation. Patients who acquired pulp anesthesia after using supplemental anesthetic techniques were judged successful, whereas those who did not achieve
pulp anesthesia were termed failures. The results were then subjected to statistical analysis, with the t-test being used. In our study, the success rate of articaine for BI (Group 1) was 90% followed by mepivacaine with BI (Group 3) (70%) followed by articaine with IL (Group 2) (66.67%) followed by mepivacaine with IL (Group 4) (50%). Since $P < 0.05$, hence there is a significant difference between the four groups.

A significant difference was found when comparing IL technique using different local anesthetics, i.e., 66.67% for articaine and 50% for mepivacaine.

Hence, according to our study, BIs using articaine offer superior supplemental anesthesia.

When compared to a standard IANB, the infiltration technique is uncomplicated, causes less injection pain, is more comfortable for the patient, avoids tongue numbness, and has a reduced morbidity or risk of nerve injury.[19]

The greater infiltration success rate in the adult mandibular incisor region is assumed to be owing to the thin cortical plate of bone, both buccal and lingual, providing less barrier to infiltration. The PDL injection’s main potential benefit is that it produces pulpal and soft tissue analgesia in a localized area (one tooth) of the mandible without causing broad soft tissue anesthesia (e.g., tongue and lower lip). According to a study, injection (given with a standard syringe) causes only minor tissue damage in needle penetration. Mild-to-severe postoperative soreness, swelling and discoloration of soft tissues at the injection site, and extended ischemia of the interdental papilla, followed by sloughing and exposing of crestal bone, have all been reported as consequences. Mild soreness and sensitivity to bite and percussion for 2 or 3 days are the most reported postinjection effects. The most prevalent causes of postinjection discomfort are excessively quick injection (resulting in edema and minor protrusion of the tooth, resulting in sensitivity when biting) and[1,2] excessively large amounts of local anesthetic injected into the location.

The unusual molecular structure of articaine explains its rapid onset time. It is the only amide local anesthetic with a thiophene ring as well as an extra ester ring. Articaine’s thiophene ring boosts its liposolubility, making it more effective at penetrating lipid barriers than mepivacaine. Increased potency may be achieved by using local anesthetics with a high liposolubility. This property allows the anesthetic to penetrate the lipid neuron membrane and adjacent tissues more easily. The duration of the anesthetic effect is thought to be determined by the degree of anesthetic molecules binding to the nerve membrane.

The more secure a bond is, the slower the anesthetic is released from sodium channel receptor sites, and the longer the anesthetic action lasts. Courtney et al. discovered that a local anesthetic’s lipid solubility had no bearing on its activity on ionic channels.[20] Instead, Uhlein[21] discovered that the local anesthetic agent’s binding characteristics to plasma proteins have a stronger link to ionic channel action than lipid solubility.

In pulpal anesthesia, the 4% articaine with 1:100 000 epinephrine resulted in a faster onset time. The rate of epineural diffusion relates to the percentage of drug in the base form, which is proportional to the pKa of that agent, and the onset time of anesthesia is directly tied to that rate. The articaine group had a pKa of 7.8. In terms of safety, combining 4% articaine with 1:100 000 epinephrine reduces the number of patients who have adverse effects such as edema, hematoma, dizziness, nausea, allergy, and shock. Toxicity events following the administration of articaine for dental anesthesia are relatively infrequent. Because articaine has the shortest metabolic half-life among the anesthetics used in dentistry, its quick inactivation by plasma esterases may explain the apparent lack of overdose effects recorded following its administration.[6,13,22]

Articaine infiltration in the mandibular teeth should be investigated after the success of articaine infiltrations in both pulpal anesthesia and onset in the posterior mandibular (Kanaa et al., 2006; Robertson et al., 2007; and Matthews et al., 2009).[23-25]

In patients with irreversible pulps in mandibular posterior teeth, supplemental articaine BI offered a higher anesthetic success rate than mepivacaine BI following lidocaine IANB injections, according to a study.[7] Suplemental PDL injections have been found to aid achieve anesthesia for endodontic treatments with an 83%–86% success rate.[12] Mepivacaine is an effective, potent, and helpful intermediate-acting local anesthetic that can be used without a vasoconstrictor in dentistry. It is a highly effective topical anesthetic. The inclusion of a vasoconstrictor prolongs the activity but has no effect on systemic blood levels. The drop in pH seen in inflamed pulp may interfere with anesthetic dissociation; if this is the case, the fact that mepivacaine has an ionization constant (pKa) of 7.6 may mean that a greater quantity of the free base is able to cross the nerve sheath, resulting in a more complete interruption of the nerve stimulus. This could help to explain why mepivacaine performs better. To better knowledge and explain anesthetic failure in irreversible pulps, more research that correlates the neurophysiology of inflamed pulp with the performance of mepivacaine should be done.[1] 

Despite this disadvantage, the current study found that an additional buccal injection offers more predictable anesthesia than a traditional IAN block used alone. However, it is crucial to keep in mind that the worry,
Singhal, et al.: Articaine versus mepivacaine

anxiety, and stress that practically all patients with dental pain experience can have an impact on the outcomes.[26]

Currently, dentists start treating their patients 10–15 min after administering anesthesia. A supplementary approach should be employed if a patient experiences pain. The improved success rate reported in the current study by using a supplemental buccal injection can assist dentists to provide more predictable anesthesia for their patients while reducing the necessity for additional supplementary anesthetic treatments.

As a result, giving the patient, a buccal injection right after the IAN block injection can save time while also improving pain control.

Although BI has depicted superior results as compared to II, further studies need to be conducted with other kinds of supplemental anesthetic techniques so that the patient can be provided with a pain-free endodontic treatment.

CONCLUSION

Supplemental injections increased anesthetic success rates, and therefore, a combination of techniques should be considered prior to the root canal treatment of symptomatic irreversible pulps in mandibular molars. In patients with a mandibular first molar exhibiting symptomatic irreversible pulps, block injection with lidocaine along with supplemental BI with articaine allowed more pain-free treatments. Articaine showed better results when compared with mepivacaine.

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Conflicts of interest
There are no conflicts of interest.

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