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Original Article

Comparison of the success of inferior alveolar nerve anesthesia in the mandibular first molars with symptomatic irreversible pulpitis using two anesthetic solutions of prilocaine and mepivacaine: A randomized controlled clinical trial

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ABSTRACT

Background: This study aimed to compare the success rate of inferior alveolar nerve (IAN) anesthesia in the mandibular first molars with symptomatic irreversible pulpitis using two anesthetic solutions of prilocaine and mepivacaine.

Materials and Methods: The current randomized controlled clinical trial was conducted on 100 patients in two groups (n = 50). Standard injection of IAN block (IANB) was performed using two cartridges of 3% mepivacaine plain in the first group and using two cartridges of 3% prilocaine with 0.03 IU felypressin in the second group. Fifteen minutes after injection, the patients were asked about lip anesthesia. In case of a positive answer, the tooth was isolated with a rubber dam. Success was defined as no or mild pain on the basis of the visual analog scale recording upon access cavity preparation, entry into the pulp chamber, and initial instrumentation. Data were analyzed with SPSS 17 using the Chi-square test, and $P < 0.05$ was set as statistically significant.

Results: The patients' pain severities during the three stages were significantly different ($P = 0.001$, 0.0001, and 0.001, respectively). The success rate of IANB during access cavity preparation was 88% with prilocaine and 68% with mepivacaine. This rate during entry into the pulp chamber was 78% and 24%, respectively, which was 3.25 times higher with prilocaine than mepivacaine. The success rates during instrumentation were 32% and 10%, respectively, which was 3.2 times higher with prilocaine than mepivacaine.

Conclusion: The success rate of IANB in the teeth with symptomatic irreversible pulpitis was higher using 3% prilocaine with felypressin than using 3% mepivacaine.

Key Words: Anesthesia, inferior alveolar nerve, mepivacaine, prilocaine

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INTRODUCTION

Root canal treatment of the teeth affected by irreversible pulpitis and symptomatic apical periodontitis is more painful than treating teeth with necrotized pulp or asymptomatic apical periodontitis.[1] The pain in teeth with irreversible

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pulpitis is due to acute inflammation of the pulp,[2] and since pulp cannot expand, this inflammation increases intrapulpal pressure.[3] In such cases, if sufficient pulp anesthesia is not established, the patients experience pain, especially during the preparation of the access cavity or during instrumentation procedure.[1] The inferior alveolar nerve block (IANB) is the most common anesthetic technique used for mandibular posterior teeth during root canal treatment.[4] Few studies have shown that the IANB cannot establish successful pulp anesthesia,[5,6] and the range of this failure is from 7% to 77%.[7-9] Some other studies also have estimated this failure to range from 30% to 80% in the teeth with symptomatic irreversible pulpitis.[10-12] Supplementary techniques, such as buccal infiltration,[4] injection into the periodontal ligament (PDL),[13] intraosseous injection,[14] intrapulpal injection,[11] and prescription of medications before the procedure (premedication),[15] are recommended to increase the success rates of anesthesia for the treatment of mandibular teeth. However, if the IANB could serve as a more effective primary anesthesia, it would be beneficial.[1] The most common anesthetic solution used in dentistry is lidocaine, which can be considered the "gold standard" to compare other anesthetic medications.[16] Vasoconstrictor-added anesthetic medications have numerous benefits, such as increase in time and depth of anesthesia,[17] and can be used for most of the patients undergoing dental treatments.[18] However, using them is contraindicated in some patients with systemic problems, such as unstable angina, hypertension, congestive heart failure, and uncontrolled hyperthyroidism. Adrenaline in these patients might cause acute hypertension, angina, arrhythmia, or myocardial infarction.[17,19,20] Therefore, knowledge about medications that can be prescribed in these patients is of utmost importance. In addition, concerns about the possibility of a dose-dependent allergic reaction to sulfite antioxidants in local anesthetics containing vasoconstrictors have been reported in some studies, especially when high doses of antioxidants are used in asthmatic patients and patients with a history of allergy. Anesthetics without vasoconstrictor, such as 3% mepivacaine plain, do not contain antioxidants and can be used without concern in the patients mentioned above.[21,22] Prilocaine anesthetic solution also has less toxicity and achieves vasodilation than most amides, and both types (plain or with vasoconstrictor) provide adequate anesthesia for dental procedures that require moderate anesthesia (30 min).[23] Mepivacaine and prilocaine belong to amide anesthetic medications, which can be used in patients with systemic problems, in which vasoconstrictors are contraindicated.[17,19,20,24,25] Few studies have compared the success rate of these two anesthetic medications. Therefore, the current study aimed to compare the success rate of the IANB in the mandibular first molars with symptomatic irreversible pulpitis using 3% prilocaine with 0.03 IU felypressin and 3% mepivacaine plain.

MATERIALS AND METHODS

The method of this randomized clinical trial study was approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (IR.TBZMED.REC.1398.1159), and the Iranian Center for Clinical Trials (IRCT20200607047680N1).

The sample size calculation, which was based on a type I error of 0.05 ($\alpha = 0.05$) and a power of 0.8 ($\beta = 80\%$), indicated that ideally, a sample size of 50 in each group would be required to detect a 20% difference in the success rate of the test groups. To increase the validity of the study, we considered 112 subjects (56 samples in each group).

Patients who were referred to the Endodontic Department of Tabriz Dental School with the following inclusion criteria were selected:

- Aged 18–65 years
- Lack of allergy to anesthetic agents
- Not consuming any analgesic medications for 6 h before treatment
- Not consuming any medication interacting with anesthetic agents
- Lack of pathosis in the regions considered for injection
- Lack of a history of trauma
- Lack of a pathologic pocket during probing.

Patients with the following conditions were excluded:

- Patients with no response to the cold test
- Teeth with periradicular lesion (excessive PDL widening)
- Teeth with nonvital coronal pulp during the preparation of the access cavity (partial necrosis).

To qualify for the study, patients presented with a permanent mandibular first molar with symptomatic irreversible pulpitis and fully formed roots (confirmed by periapical radiography), exhibiting severe and persistent pain in response to cold testing with Endo-Ice (1,1,1,2-tetrafluoroethane; Hygenic Corp,

Akron, OH, USA).[26] In addition, the periapical area of the concerned tooth in the radiograph was normal. One hundred and twenty patients were assessed for eligibility; eight patients refused to participate, while 112 patients received allocated intervention [Figure 1].

After obtaining signed voluntary informed consent for enrolment in the study, the process was fully explained to each patient, and the necessary consultation and guidance were provided during and after treatment. In the case of illiterate patients, the consent form was read out to them, and left hand thumb impression was obtained. Patients with mental disabilities were not included in the study.

For the purpose of blinding, the anesthetic agent cartridges were covered with a white tape by another person, and the operators who injected the anesthetic agent and recorded pain scores during the treatment were blinded to the groups.

The patients were randomly assigned to two groups. Group 1 entailed the standard IANB with a conventional syringe (Dental Device, Pakistan) and a 27-gauge 3.6-cm needle (Ava, Tehran, Iran). Two cartridges of 3% mepivacaine (Exir Co, Tehran, Iran) were injected 1 min apart after determining the target point of the injection and performing aspiration. Group 2 entailed the standard IANB with a conventional syringe and a 27-gauge 3.6-cm needle. Two cartridges of 3% prilocaine with 0.03 IU felypressin (Exir Co., Tehran, Iran) were injected 1 min apart after determining the target point of the injection and performing aspiration.

Fifteen minutes after the injection, the patients were asked about lip numbness. In case of a negative response, the participant was excluded from the study, and in case of a positive response, first, the tooth was assessed by cold and electric pulp tests (EPT; PT-20, Parkell), and in case of no response to these tests, it was isolated by a rubber dam (Sanctuary Co., Malaysia) and the access cavity was prepared. The patient was asked to raise his/her hand if there was pain during access cavity preparation and intracanal instrumentation and to record his/her pain on visual analog scale (VAS).

For all of the included patients, diagnosis and injection were performed by the same operator; however, another operator created the access cavity and recorded the pain. The pain evaluation scale used was the VAS with a line length of 170 mm, and according to the location of the patient's markup, the pain was classified as follows: 0, no pain; 1–54 mm, mild pain; 55–112 mm, moderate pain; and 114–170 mm, severe pain. Successful anesthesia was defined as painless (0) and mild pain (54 mm) according to the VAS criteria.[27]

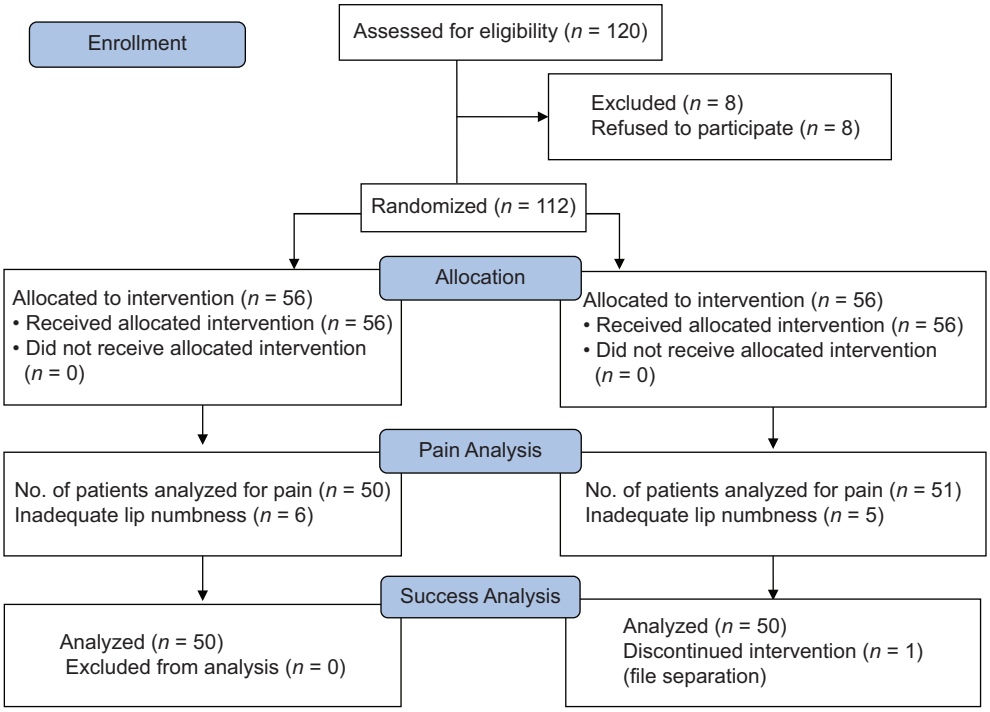

Figure 1: Consolidated Standards of Reporting Trials flowchart.

Statistical analysis

The data of the two groups were reported as A and B codes for statistical analyses. Therefore, the statistician was blinded to the type of anesthetic agent used. The findings of the study were reported using descriptive statistical methods (mean ± standard deviation). Chi-square test was used to compare pain severity between the two groups. SPSS 17 (SPSS version 20.0, SPSS, Chicago, IL, USA) was used, and statistical significance was set at $P < 0.05$.

RESULTS

One hundred and twelve patients with symptomatic irreversible pulpitis of the mandibular first molars participated in this research; 56 patients underwent anesthesia with mepivacaine and 56 with prilocaine. Eleven patients did not feel the lip numbness and were excluded from the study, and one patient was excluded because of file separation during instrumentation.

Finally, 100 patients were selected for success analysis (50 samples in each group).

Means and standard deviations of the patients' age were 32.33 ± 8.78 years (minimum: 15 and maximum: 49).

Table 1 shows the frequency distributions of pain severity reported by patients during access cavity preparation, entry into the pulp chamber, and instrumentation.

Figure 2 shows distribution of pain severity during access cavity preparation in terms of the anesthetic agent type. According to the Chi-square test results, the two groups exhibited significant differences in pain severity during access cavity preparation, and Group 2 (3% prilocaine) showed significant lower pain severities than Group 1 (3% mepivacaine) ($P = 0.001$).

Figure 3 shows the distribution of pain severity of patients upon entry into pulp chamber in terms of the anesthetic agent type. Chi-square test showed significant differences between the two study groups in pain severity upon entry into the pulp chamber, and Group 2 (3% prilocaine) exhibited significant lower pain severities than Group 1 (3% mepivacaine) ($P = 0.0001$).

Figure 4 presents pain severities of patients during instrumentation in terms of the anesthetic agent type. Chi-square test showed significant differences between the two groups in pain severity during instrumentation, and Group 2 (3% prilocaine) exhibited significant lower pain severities than Group 1 (3% mepivacaine) ($P = 0.001$).

The success rates of the IANB with 3% prilocaine with 0.03 IU felypressin and 3% mepivacaine plain during access cavity preparation were 88% and 68%, respectively, indicating a 1.3-time higher success rate with prilocaine. These rates upon entry into the pulp chamber were 78% and 24%, respectively, indicating

Table 1: The frequency distributions of pain severity during access cavity preparation, upon entry into the pulp chamber, and instrumentation (%)

Pain severity	No pain (%)	Mild pain (%)	Moderate pain (%)	Severe pain (%)
Pain during access cavity preparation	17	34	19	30
Pain at entry into the pulp chamber	17	34	19	30
Pain during instrumentation	4	17	19	53

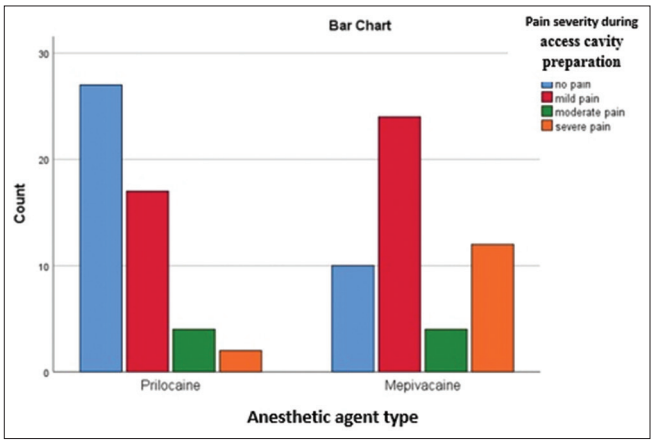

Figure 2: Pain severity of patients during access cavity preparation in terms of the anesthetic agent type.

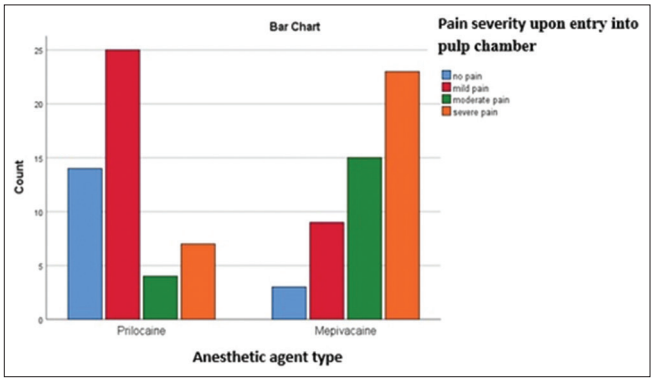

Figure 3: Pain severities of patients upon entry into pulp chamber in terms of the type of anesthetic agent.

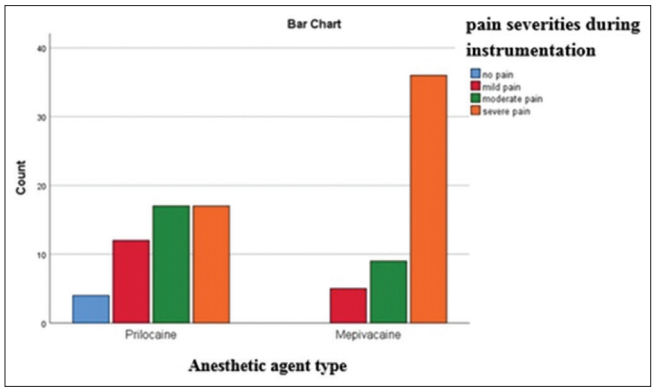

Figure 4: Pain severities of patients during instrumentation in terms of the anesthetic agent type.

that the success rate of prilocaine was 3.25 times higher than that of mepivacaine. In addition, the success rates during instrumentation with prilocaine and mepivacaine were 32% and 10%, respectively, indicating a 3.2-time higher success rate with prilocaine.

DISCUSSION

The effectiveness of local anesthesia during dental procedures affects patient satisfaction directly. The IANB is not always successful in establishing pulpal anesthesia of the mandibular posterior teeth.[28] Therefore, various clinical trials have presented approaches to resolve the shortcomings of this technique in teeth with irreversible pulpitis. One of these approaches is using different anesthetic medications.[11]

Numerous studies have compared the success rate of various local anesthetic solutions with lidocaine as the standard medication.[7,29] A systematic review and meta-analysis by Larocca de Geus *et al*. showed the highest odds of success with articaine (73%) and the lowest with lidocaine (12%) for the IANB. In this study, the success rates of anesthesia with prilocaine was 57%, 55% for mepivacaine and 53% for bupivacaine.[30] In a systematic review and meta-analysis by Nagendrababu *et al*., anesthesia with 2% mepivacaine with 1:100,000 epinephrine was significantly higher in the IANB compared to lidocaine.[1] Accordingly, the highest rate of success was for mepivacaine, followed by 3% prilocaine with felypressin and 4% articaine with 1:100,000 epinephrine, bupivacaine, and lidocaine.[1] Other anesthetic medications are available, such as articaine, prilocaine, and mepivacaine,[4] which have been compared in some studies. For example, some clinical studies reported no significant difference in patients with irreversible pulpitis between 3% mepivacaine[31] and/or 4% articaine containing 1:100,000 epinephrine[32] compared to 2% lidocaine for the IANB.

In addition to the challenge of increasing the success rate of the IANB through changing the anesthetic agent and the necessity of comparing different medications with lidocaine, in some patients with a contraindication to use vasoconstrictors, anesthetic medications without vasoconstrictors must be prescribed. A study by Gazal concluded that prilocaine with felypressin is a proper choice for patients with contraindications to the prescription of lidocaine with epinephrine.[33] Su *et al.* recommended 3% mepivacaine for patients with cardiac problems since this medication leads to more rapid anesthesia and a milder increase in heart rate than 2% lidocaine with 1:100,000 epinephrine.[34] Ezmek *et al*. reported that lidocaine, prilocaine, and mepivacaine without vasoconstrictors could be used safely in patients with hypertension.[18]

Selecting an effective medication to achieve better and deeper anesthesia during endodontic treatments is of most importance in patients with contraindications for vasoconstrictors.

Since 3% mepivacaine and prilocaine-felypressin are prescribed in these patients,[19,24,25,34,35] this study aimed to compare the success rate of the IANB in the mandibular first molars with irreversible symptomatic pulpitis using prilocaine and mepivacaine.

Determining the success rate of anesthesia is challenging. The anesthesia of the IAN is usually confirmed by asking the patient about lip numbness, probing the gingiva around mandibular teeth, and initiating treatment and waiting for the patient's response.[11] Lip anesthesia does not guarantee sufficient pulp anesthesia.[36] Several studies assessed the success rate of anesthesia by applying three tests, including lip anesthesia, lack of response to the cold test or EPT, and the absence of pain during access cavity preparation.[37] This three-step protocol of lip anesthesia, cold test and EPT, and lack of pain or mild pain reported by the VAS scale was used during preparation of access cavity, entry into the pulp chamber, and instrumentation to assess the success rate of anesthesia more precisely.

In patients with irreversible pulpitis, an increase in the volume of anesthetic agent enhanced the success

rate of the IANB.[30] In the current study, similar to previous studies,[38] two cartridges of the anesthetic agents were injected.

The current study showed that the type of anesthetic agents (mepivacaine and prilocaine) significantly affected patients' pain severity during access cavity preparation, upon entry into the pulp chamber, and instrumentation; the success rate of the IANB was higher with prilocaine than mepivacaine. Since prilocaine has lower vasodilatory effects compared to other amides,[33] it exhibits better effects such as longer duration and deeper anesthesia.[21,39,40] Besides, 3% prilocaine was used in the current study along with felypressin, a type of vasoconstrictor. However, this substance restricts venous blood flow;[17] therefore, it has lower vasoconstriction properties than adrenaline.[33]

Currently, a limited number of studies are available on the success rate of mepivacaine and prilocaine. A meta-analysis by Nagendrababu *et al*. showed no significant difference in the success rates of 3% prilocaine/felypressin and 2% mepivacaine/epinephrine.[1] In a meta-analysis by Larocca de Geus *et al*., the odds of success with prilocaine (55%) were a little higher than those with mepivacaine (53%).[30]A study by McLean *et al*. on three anesthetic solutions, 4% prilocaine, 3% mepivacaine, and 2% lidocaine with 1:100,000 epinephrine for the IANB, showed no significant difference between the three anesthetic agents in success or failure rates.[36] Hinkley *et al*. compared three anesthetic agents: prilocaine with 1:200,000 epinephrine, 2% mepivacaine with 1:20,000 levonordefrine, and 2% lidocaine with 1:100,000 epinephrine and reported a lack of significant difference in the success or failure of anesthesia, slow initiation of anesthesia, and short anesthesia between the three solutions.[41] This discrepancy between the above studies and the current study can be attributed to differences in the concentrations of the solutions and use or no use of vasoconstrictors and different manufacturers. Furthermore, different sample sizes and assessment method of the IANB's success rate can be considered the other reasons of the difference in the results of the present study and other studies.

Assessment method of the IANB can also affect the assessment of success rate;[42] in the two studies by Hinkley *et al*. and McLean *et al*., EPT was used to assess pain and success after injection,[36,41] while in the current study, we used the three-step protocol of lip numbness, a lack of response to the cold test and EPT, and pain assessment using VAS during access cavity preparation, upon entry into the pulp chamber, and instrumentation. Direct access to the pulp chamber and instrumentation gives rise to a more painful feeling compared to EPT or cold test,[30] resulting in a significant difference in measuring pain severity.[30] Therefore, further studies are necessary to use more than one method for more precise comparisons.

One of the limitations of the study was the lack of standard method for evaluating the success of IANB. In addition, the difference among the patients, the severity and extent of tissue inflammation, and the patients' dental history could lead to the failure of local anesthesia. Therefore, to provide successful anesthesia, the clinician should consider correct anesthesia technique and other relating factors in addition to proper anesthetic agent.

Similar to this study, some studies have been compared the efficacy of 3% prilocaine and 3% mepivacaine before.[1,2] However, the present study was the first to report the significance of prilocaine to mepivacaine, and previous studies have been stated no significant difference between them according to the success of IANB. According to the present study and considering the importance of prescribing drugs without epinephrine in patients with systemic problems and the interaction of epinephrine with drugs, such as tricyclic antidepressants, nonselective beta-blockers, and cocaine, it seems that the use of 3% prilocaine with 0.03 IU of felypressin can be a good choice in these cases. On the other hand, lidocaine and prilocaine are classified as Group B drugs in pregnant patients, and drugs such as bupivacaine, articaine, and mepivacaine are classified as Group C. Therefore, according to the results of the present study, prilocaine anesthesia can be used in these patients. The number of patients with the above problems is high in the dental office; therefore, dentists should be familiar with all the aspects of specific management protocols in these patients. Meanwhile, anesthesia stress might increase the level of internal catecholamines up to 40 times higher than the resting state in these patients. Therefore, studies, such as the present study and other similar ones, in this regard, can be helpful.

CONCLUSION

The success rate of the IANB in the teeth with symptomatic irreversible pulpitis with 3% prilocaine with 0.03 IU felypressin was higher than 3% mepivacaine plain.

Since it is essential to prescribe a good anesthetic medication during dental procedures in patients with systemic problems, as a stress-decreasing protocol, and to prevent the incidence of acute crises in patients, it seems that prescribing prilocaine would be better than mepivacaine.

Clinical relevance

Use of 3% prilocaine with 0.03 IU felypressin could be a good choice for successful IANB in patients with systemic problems.

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Conflicts of interest

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or nonfinancial in this article.

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