Comparison of the Anesthetic Efficacy of Mepivacaine and Lidocaine in Patients with Irreversible Pulpitis: A Double-blind Randomized Clinical Trial

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Abstract

Introduction: The objective of this study was to compare the anesthetic efficacy of 2% mepivacaine combined with 1:100,000 epinephrine with 2% lidocaine combined with 1:100,000 epinephrine during pulpectomy of mandibular posterior teeth in patients with irreversible pulpitis. Methods: Forty-two patients with irreversible pulpitis who were admitted to the Emergency Center at the University of São Paulo School of Dentistry volunteered to take part in the study and were randomized to receive conventional inferior alveolar nerve block containing 1.8 or 3.6 mL of either 2% mepivacaine with 1:100,000 epinephrine or 2% lidocaine with 1:100,000 epinephrine. We recorded patients’ subjective assessments of lip anesthesia, absence/presence of pulpal anesthesia tested by using electric pulp stimulation, and absence/presence of pain during the subsequent pulpectomy by using a verbal analogue scale. Results: All patients tested reported lip anesthesia after application of either type of inferior alveolar nerve block. Pulpal anesthesia success rates measured by using the pulp tester were satisfactory for both solutions (86% for mepivacaine and 67% for lidocaine). Success rates according to patient report of no pain or mild pain during pulpectomy were higher for mepivacaine solution (55%) than for lidocaine solution (14%). The differences between mepivacaine and lidocaine were statistically significant. Conclusions: Mepivacaine resulted in effective pain control during irreversible pulpits treatments. The success rates with either solution were not high enough to ensure complete pulpal anesthesia. (J Endod 2016;42:1314–1319)

Key Words

Inferior alveolar nerve block, irreversible pulpitis, lidocaine, mepivacaine

Significance

In this article we report a randomized blind controlled trial that used mepivacaine, which is rarely explored in the literature for this purpose. This article represents original material, which was not previously published.

Pain is an unpleasant sensation of varying intensity associated with a current or potential process of tissue destruction. It is difficult to determine the intensity of pain sensations because there is an emotional element (1), and each patient has a different threshold (2) involving both subjectivity and previous experiences.

In irreversible pulpitis, the cause of pain is acute pulp inflammation. Certain changes can be observed such as vasodilation, increased vascular permeability, and leakage of leukocytes. Because the pulp is unable to expand, inflammation produces a significant increase in internal tissue pressure (3).

Emergency control of irreversible pulpitis involves executing endodontic treatments to relieve pain (3, 4), and pain control is critical in these procedures (1, 2, 5–12).

Mepivacaine and lidocaine are both classified as amides and are the most commonly used solutions in dentistry, and there are 50 years of accumulated experience showing their effectiveness and safety for providing regional anesthesia for dental treatment (13).

Mepivacaine is routinely used in painful clinical situations because it has a lower ionization constant (pKa) than lidocaine and is therefore more compatible with inflamed tissues and has a shorter onset and longer duration of anesthesia.

Even in healthy teeth, inferior alveolar nerve (IAN) blocks are not always successful. Success rates reported in studies vary from 62% to 96% (1, 6–9, 14–16), and they do not always ensure the success of the clinical procedure involved (15, 17), especially in cases of irreversible pulpitis (2, 5, 7, 9, 11, 14–16, 18–25).

The failure rate of IAN blocks is even higher in irreversible pulpitis, ranging from 37% to 85%, according to several different authors (1, 5, 7, 11, 12, 14–16, 18, 19, 22–27).

Many studies (1, 8, 9, 15, 16, 18, 19, 23–25, 28, 29) have shown that achieving soft tissue anesthesia does not guarantee the effectiveness of the block or a painless clinical procedure. The fact that patients often feel pain during endodontic treatment of teeth with irreversible pulpitis is a challenge for the clinician and the patient (1).
Even if the block is confirmed by a negative response to electrical testing, there is still a possibility that supplementary anesthesia will be required. In other words, the block may have been achieved and tested, but only at the time of pulpectomy will the need for additional anesthesia be known on the basis of pain reported by the patient (2, 5, 11, 14, 18, 19, 22).

Even when supplementary techniques are used to increase the effectiveness of the blocking procedure, pulpectomy that is totally painless and comfortable for the patient is unachievable (6, 7, 10, 19, 21, 24, 25, 30).

There are a number of hypotheses to attempt to explain the reduced effectiveness in teeth that are already painful (2, 4, 31–33), such as larger quantities of substance P in teeth with pulpsitis and increased expression of sodium channels. However, the subject still needs to be studied further to achieve a better understanding.

In view of the lack of studies investigating mepivacaine, the objective of this study was to compare the anesthetic efficacy of 2% mepivacaine with that of 2% lidocaine, both administered in conjunction with 1:100,000 epinephrine, for IAN block in patients with irreversible pulpsitis of mandibular posterior teeth.

**Materials and Methods**

Forty-two adult volunteer subjects who presented at the Emergency Center at the University of São Paulo School of Dentistry took part in this prospective, randomized, double-blind study.

Inclusion criteria for volunteers were age from 18 to 50 years, currently feeling pain, good health, and not taking any medication that would alter perception of pain, which were determined by verbal questioning and a written questionnaire. The research was approved by the University of São Paulo School of Dentistry Human Research Ethics Committee (protocol 67/08), and informed consent was obtained from each patient in writing.

In addition, to qualify for our study, patients had to be clinically diagnosed with irreversible pulpsitis on the basis of moderate to severe spontaneous pain and prolonged response exhibited to cold testing with Endo-Frost (Coltene-Roeko, Langenau, Germany) and a positive response to the electric pulp test (Vitality Scanner 2006; SybronEndo, Orange, CA).

Each participant had at least 1 adjacent tooth plus a healthy contralateral canine or, alternatively, a contralateral canine without deep caries damage, extensive restoration, advanced periodontal disease, history of trauma, or sensitivity. Electric pulp stimulation of the contralateral canine, which had not been anesthetized, was used as a control to ensure that the equipment was working properly and that patients were responding as expected. All preinjection and postinjection tests were conducted by trained personnel who were blinded to the anesthetic volumes administered. Electrocardiogram gel was applied to the probe tip, which was placed in the middle third of the buccal surface of the tooth being tested. The current rate was set to take 25 seconds to increase from zero output (0) to maximum output (80 μA). The reading in μA that was shown when the patient reported the first sensation was recorded.

Patients were asked to rate their current pain on the following 4-point scale: 0, no pain; 1, mild pain (ie, pain that was recognizable but did not cause discomfort); 2, moderate pain (ie, pain that was causing discomfort but was bearable); and 3, severe pain (ie, pain that caused considerable discomfort and was difficult to bear). Only patients with moderate to severe pain were included in this study.

Patients were administered standard IAN block injections of 2% mepivacaine or 2% lidocaine, both combined with 1:100,000 epinephrine (DFL Indústrias e Comércio Ltda, Rio de Janeiro, RJ, Brazil). The same person administered all injections.

Blinding was achieved as follows: 3 cartridges (1.8 mL each) of each anesthetic solution were sealed in 42 envelopes by the first author. The senior researcher, who was not involved in the endodontic procedure, administered the anesthesia injection after choosing 1 of the envelopes at random. Electric pulp stimulations to assess pulpal anesthesia and the pulpectomy were performed by a postgraduate student to guarantee that the anesthetic solution remained unknown and thus maintain the double-blindness of the study.

Injections were performed by using a side-loading carpule syringe fitted with 27-gauge 0.4 × 35 mm needle (Injex Indústrias Cirúrgicas Ltda, São Paulo, SP, Brazil) and equipped with a blood aspiration device and a thumb ring (Könken; Kennen Indústria e Comércio Ltda, São Paulo, SP, Brazil). Blood aspiration tests were carried out before each anesthesia injection and after changing needle position.

The first 2 cartridges of the anesthetic solution were administered by using an indirect three-position technique as follows. In the first step of the first attempt to achieve anesthesia (1 cartridge, 1.8 mL), the needle was introduced 3–5 mm deep, blood was aspirated, and approximately 0.3 mL anesthetic solution was injected. In the second step, the syringe was moved to the premolar region on the opposite side, where the needle was inserted until it made contact with bone. The needle was then withdrawn 1–2 mm, blood was aspirated, and the remaining 1.5 mL anesthetic solution was slowly injected. The average injection time for each cartridge was approximately 2 minutes.

Ten minutes after the initial IAN block procedure, each patient was asked whether his/her lip was numb. The electric pulp test was repeated on the tooth with pulpsitis and the adjacent tooth to ensure the nerve blockage had been successful. The criterion used to determine whether pulp anesthesia had been successful was 2 consecutive negative responses to the maximum pulp stimulus (80 μA). Experimentally, the 80 reading is an end point that can be used to measure complete pulp anesthesia over time.

If profound lip numbness was not recorded within 10 minutes and the electric pulp tester did not reach maximum output without the patient reporting pain, the block was considered unsuccessful, and another cartridge (1.8 mL) of the same anesthetic solution was reapplied with the same technique used before. Another 10 minutes were allowed to elapse, and then the electric pulp test was repeated and signs of lip anesthesia were observed. If profound lip numbness was not recorded or, most importantly, the electric pulp tester did not reach 80 μA without provoking sensation, the patients were excluded from the study.

Immediately before the pulpectomy, electric pulp stimulation tests were repeated to determine pulpal anesthesia. Patients were also instructed to report any painful discomfort during the pulpectomy procedure. The intensity of any pain felt during the pulpectomy was evaluated by using the same 4-point scale described above.

Efficacy of anesthesia was defined as successful if the dentist was able to access the pulp chamber without the patient reporting pain (pain scores 0 or 1). In these cases, the pulpectomy procedure was continued. If the patient scored pain as 2 or 3, the efficacy of anesthesia was classified as unsuccessful. In these cases, the extent of access achieved was recorded as within dentin, pulp chamber, or root canal, and intraligamentary or intrapulpal anesthesia was administered, depending on the level of the site of pain, and then the pulpectomy was finalized. The success rates of these complementary techniques are far beyond the scope of this article.

Findings were recorded in a Microsoft Excel spreadsheet (Microsoft Office Excel 2003; Microsoft Corp, Redmond, WA) before statistical evaluation by using the program GMC software, version 2002.
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(FORP-USP, Ribeirão Preto, SP, Brazil). The Fisher exact test (2-tailed) was chosen as an appropriate statistical instrument for the purposes of this study. This test is a form of the $\chi^2$ analysis that only evaluates $P$ values.

Results

There were no statistically significant differences between the patients in the 2 test groups in this study in terms of gender distribution, age (mean age: mepivacaine group, 26 years; lidocaine group, 28 years), the types of teeth with irreversible pulpitis, or the average baseline response to the electric pulp test (Table 1). The groups were therefore considered homogeneous, and thus the results obtained with both anesthetic solutions can be directly compared.

All patients reported subjective lip anesthesia 10 minutes after the IAN block. From the original sample of 42 patients, 10 patients, 3 from the mepivacaine group and 7 from the lidocaine group, did not reach maximum output of the electric pulp tester without feeling pain even after the second cartridge and were excluded from the study (Fig. 1).

After injection of the first cartridge (1.8 mL), 11 patients in the mepivacaine group (52%) and 7 patients in the lidocaine group (33%) exhibited pulpal anesthesia, i.e., a negative response to the electrical stimulus. After the second cartridges, another 7 patients in the mepivacaine group (86%) and 7 patients in the lidocaine group (67%) exhibited pulpal anesthesia. Table 2 contains a comparison of the percentages of IAN block success (pulpal anesthesia) in teeth with pulpitis and healthy teeth after administration of both volumes. There were no statistically significant differences between the 2 experimental groups ($P$ value).

During pulpectomy, 8 patients in the mepivacaine group and 12 patients in the lidocaine group reported pain (pain scores 2 and 3). This time the slight difference was statistically significant ($P < .05$) (Fig. 2).

None of the patients given mepivacaine required an intraligamentary injection; only intrapulpal administration was needed. One of the lidocaine patients needed an intraligamentary injection because he felt pain during dentin access.

Discussion

In this study only lower molars (predominantly the first and second molars) were included to avoid variations in innervation [1], as was also the case in several other studies [1, 12, 16, 23–25, 27], although some authors [8, 11, 14, 19, 22] have investigated lower molars and premolars together. Fowler et al [2] studied the effect of different volumes of 2% lidocaine in 375 premolars and molars with irreversible pulpitis. They concluded that there is no difference between the groups of teeth.

It is difficult to define anesthetic success, and the subject itself is controversial. Many researchers limit their analyses to the superficial effects, but others have been highly meticulous in this respect [24]. Different studies have used a variety of different tests such as numbness of lips and tongue [11, 14, 26, 27], visual analogue pain scales [2, 12, 18], and lack of response to cold stimuli [1, 6, 8, 12, 14, 18, 24] or to electrical testing [7, 9, 15, 21, 25].

There are few studies in the literature that have used the anesthetic salt mepivacaine. Rodriguez-Wong et al [24] compared 2% mepivacaine alone against 2% mepivacaine combined with tramadol (a centrally acting opioid) in irreversible pulpitis cases. In a control group, 1.8 mL 2% mepivacaine used in isolation resulted in pulpal anesthesia efficacy of 67.9% when the criterion was a negative response to a cold test and of 53.6% when the criterion was access to the hard tissues of the tooth with pulpitis without the patient reporting pain [24]. We observed 52% for the electrical test criterion. Rodriguez-Wong et al observed a 46.4% blockage success rate during the pulpectomy, which is very close to the 54% anesthesia efficacy observed in our mepivacaine group.

Cohen et al [1] compared the efficacy of 3% mepivacaine without a vasoconstrictor against 2% lidocaine with 1:100,000 epinephrine in molars with irreversible pulpitis. The efficacy of pulpal anesthesia was assessed by numbness of lip and tongue and negative response to a temperature test, resulting in 61% for the mepivacaine group and 63% for the lidocaine group. They were able to conduct the pulpectomy without pain and without supplementary anesthetic in 55% of the sample for both solutions. In the present study the group that was given the same volume (1.8 mL) of mepivacaine as that administered by Cohen et al exhibited a pulpal anesthesia rate of 53%. This lower rate is the result of the criterion chosen to define successful pulpal anesthesia. Our results for successful, pain-free pulpectomy are similar, because with a single carpule of 2% mepivacaine we achieved 54% success, although we used different concentrations of the anesthetic and of the vasoconstrictor.

There are no other clinical studies in the literature that have compared the efficacy of 2% mepivacaine for cases of irreversible pulpitis, and so we have included studies that used 2% lidocaine combined with epinephrine in the comparative analysis of results.

The anesthetic technique [25] used in this study proved to be adequately effective, because it resulted in pulpal anesthesia in 76% of the whole sample of patients with irreversible pulpitis, 86% of the patients in the mepivacaine group and 67% of those in the lidocaine group (Table 2).

For both solutions, increasing the volume of anesthetic increased the rate of pulpal anesthesia, but without statistical difference between the 2 volumes, as has been reported in previous studies [12, 15, 18, 26]. However, from a clinical perspective, mepivacaine exhibited superior performance. Aggarwal et al [27] observed a statistically significant improvement when volume was increased, which may be because of the larger number of cases assessed (319 molars with irreversible pulpitis). In a recent study by using articaine Abazarpoor et al [18] show that there is an improvement in performance of the block when the second cartridge is injected, although complete control of pain is not always achieved, requiring additional anesthetic during the procedure.

Pain was reported with greater frequency in the lidocaine group, and the difference compared with the mepivacaine group was statistically significant ($P < .05$) when up to 2 carpules were used to achieve IAN block. In contrast, the electric pulp testing results for the healthy control teeth were very similar for lidocaine and mepivacaine at 90% and 95% success, respectively (Table 2). These data, in conjunction with results reported in the literature, lead us to suspect that teeth that are already painful exhibit different nociceptive behavior to

### TABLE 1. Comparison of Age, Sex, Type of Teeth, and Mean Baseline Electric Pulp Tester Results

<table>
<thead>
<tr>
<th></th>
<th>Mepivacaine</th>
<th>Lidocaine</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>26 ± 10</td>
<td>28 ± 11</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Women</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Tooth, molar</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Second</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Third</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Mean baseline electric pulp tester results (µA)</td>
<td>38</td>
<td>39</td>
</tr>
</tbody>
</table>

There were no significant differences ($P > .05$) between the groups.
asymptomatic teeth, but even so, mepivacaine was more compatible and effective.

In this study, lidocaine achieved a pulpal anesthesia rate of 67%, but the IAN block success rate was only 14%. Mepivacaine exhibited greater efficacy for pulpal anesthesia (86%) and a higher IAN block success rate (55%). These rates demonstrate that pulpal anesthesia does not guarantee a painless clinical procedure (2, 6, 8, 11, 14, 16, 19, 22, 23, 25, 30).

Our results for the lidocaine group are in line with data in the literature (7, 22, 23, 25), despite minor variations between different studies. The success of pulpal anesthesia confirmed by the electrical test varies from 43% to 70%, and the pain-free pulpectomy rate falls within the reported range of 13%–31%.

Differences in criteria for initial pulpal anesthesia, types of teeth, populations of patients, and anesthetic volumes and concentrations are probably responsible for the large variations in success rates between different studies (5, 11, 14).

To compile the various results and methodology of irreversible pulpitis, Kung et al (5) conducted a systematic review and meta-analysis to elucidate what is the effectiveness of articaine compared with lidocaine in pain reduction in cases of endodontic treatment for irreversible pulpitis. Following a rigorous methodology and analysis of the results, they concluded that both anesthetics are equally effective when used for mandibular block or maxillary infiltration.

The degree of pulpal anesthesia success observed in this study appears to be sufficient for less invasive procedures, but not to enable intervention in pulpitis (2). Therefore, addition of the second carpule is warranted as long as there is evidence that pulpal anesthesia has been achieved, because this may be better used as supplementary anesthetic, which to date appears to be indispensable in irreversible pulpitis, in contrast with other authors (7, 9, 25) who have started with 3.6 mL. It is safer to use smaller volumes and perform the anesthetic

**TABLE 2.** Comparison of Percentage Success of IANB Block (pulp anesthesia) in Teeth with Pulpitis and in Healthy Teeth

<table>
<thead>
<tr>
<th>Teeth with pulpitis (%)</th>
<th>Healthy teeth (%)</th>
</tr>
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<tbody>
<tr>
<td>Mepivacaine</td>
<td>18 of 21 (86)</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>14 of 21 (67)</td>
</tr>
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</table>

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

**Figure 1.** Outline of the experimental procedures and results for efficacy of anesthesia during pulpectomy. Efficacy of anesthesia, dentist was able to access the pulp chamber without pain; EPT−, electric pulp test negative (pulpal anesthesia successful); EPT+, electric pulp test positive (pulpal anesthesia unsuccessful).

**Figure 2.** Bar graph illustrating proportion of patients feeling pain during pulpectomy after IAN block with 1 of 2 different solutions (2% mepivacaine with 1:100,000 epinephrine or 2% lidocaine with 1:100,000 epinephrine). *P < .05.
technique correctly, thereby reducing the risk of toxicity and providing greater security for patient and professional (13).

With regard to the depth that was attained during endodontic access, mepivacaine made it possible to get closer to the pulp chamber. In 1 case in the lidocaine group it was necessary to perform intraligamental injection before the intrapulpal injection. This contrasts with results reported in the literature (11, 14, 19, 22), where intermittent conditions in the dentin outweighed those in the pulp and root. One possible reason why this may have occurred is that we only analyzed molars, whereas other studies investigated molars and premolars.

The depth attained is of relevance because the type of supplementary analgesia administered depends on the site of pain (11, 14). Each technique has its peculiarities with relation to discomfort during administration, efficacy, and side effects, but these subjects are beyond the scope of this article.

Hypotheses that have been raised to explain the routine lack of success with anesthetic blocks attribute failure to decay of the pain threshold for apprehensive patients (2), to variations in pH (7, 8, 32), successful with anesthetic blocks attribute failure to decay of the pain threshold for apprehensive patients (2), to variations in pH (7, 8, 32). In inflammatory sensitization and in reducing the threshold of the nerve fibers (4, 6, 32; 33), which can be elevated in the pulp of teeth with irreversible pulpitis (35), as seen in vitro study conducted by Potocnik et al (20) showed that local anesthetic provokes total disappearance of the action potential of C fibers, but not of A fibers. These findings may have a connection with anesthetic inefficacy in pulps, because there are large quantities in dental pulp, originating from the trigeminal nerve (34).

The drop in pH seen in inflamed pulp may interfere with dissociation of the anesthetic, and if this is the case, the fact that mepivacaine has an ionization constant (pKa) of 7.6, which is lower than that of lidocaine at 7.9, may mean that a greater quantity of the free base is able to pass the nerve sheath, with the result that the nerve stimulus is more completely interrupted (13, 29). This would in part explain the better performance of mepivacaine.

Further research that correlates the neurophysiology of inflamed pulp with the performance of mepivacaine should be conducted to improve understanding and elucidate failure of anesthesia in irreversible pulps.

Conclusion

At smaller volumes (1 cartridge), mepivacaine was more effective for achieving IAN block (for pulpectomy) than lidocaine. With fewer additional injections and smaller volumes, mepivacaine made it possible to get closer to the pulp tissue (pulp chamber), providing greater clinical comfort than lidocaine. We suggest that the sample should be improved to improve these results.

Acknowledgments

The authors deny any conflicts of interest related to this study.

References


