



Does the presence and amount of epinephrine in 2% lidocaine affect its anesthetic efficacy in the management of symptomatic maxillary molars with irreversible pulpitis?

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Background: This was a randomized controlled clinical trial that aimed to evaluate the anesthetic efficacy of 2% lidocaine combined with different concentrations of epinephrine (plain, 1:200,000 and 1:80,000) during endodontic treatment of maxillary molars with symptomatic irreversible pulpitis.

Methods: The trial included 144 adult patients who were randomly allocated to three treatment groups. All patients received buccal-plus-palatal infiltration. After 10 min, pulp sensibility testing was performed using an electric pulp test (EPT). If a tooth responded positively, anesthesia was considered to have failed. In the case of a negative EPT response, endodontic access was initiated under rubber dam isolation. The success of anesthesia was defined as having a pain score less than 55 on the Heft Parker visual analog scale (HP VAS), which was categorized as 'no pain' or 'faint/weak/mild' pain on the HP VAS. Baseline pre-injection and post-injection maximum heart rates were recorded. The Pearson chi-square test was used to analyze the anesthetic success rates at 5% significance.

Results: Plain 2% lidocaine and 2% lidocaine with 1:200,000 epinephrine and 1:80,000 epinephrine had anesthetic success rates of 18.75%, 72.9%, and 82.3%, respectively. Statistical analysis indicated significant differences between the groups ($P < 0.001$, $\chi^2 = 47.5$, $df = 2$). The maximum heart rate increase was seen with 2% lidocaine solution with epinephrine.

Conclusion: Adding epinephrine to 2% lidocaine significantly improves its anesthetic success rates during the root canal treatment of maxillary molars with symptomatic irreversible pulpitis.

Keywords: Anesthesia; Buccal Administration; Epinephrine; Irreversible Pulpitis; Lidocaine; Maxilla.

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INTRODUCTION

The maxillary molars are routinely anesthetized using infiltration anesthesia. The porous cortical bone allows the anesthetic solution to diffuse into the affected roots. However, the anesthetic success rate is also affected by

the pulpal status. Teeth with symptomatic irreversible pulpitis, whether mandibular or maxillary, usually have a lower success rate than asymptomatic teeth. Guglielmo et al. [1] achieved successful anesthesia in 95% of asymptomatic maxillary molars using buccal and palatal infiltration. Pfeil et al. evaluated posterior superior alveolar (PSA) nerve blocks in asymptomatic patients and

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documented success rates of up to 100% using 3.6 mL lidocaine solution [2]. In a study evaluating symptomatic teeth, the success rate was 70% [3]. Since symptomatic maxillary molars are comparatively easier to anesthetize than mandibular molars (70% vs. 27%) [2-5], there is relatively less research focused on the variables affecting maxillary anesthesia.

Maxillary anesthesia is affected by various factors, the most important being the local anesthetic solution [6-9]. Lidocaine has an inherent vasodilatory effect that increases the absorption of the anesthetic solution. Vasoconstrictors are, therefore, added to improve the duration of action. Pitt Ford et al. [10] reported that 2% lidocaine with a vasoconstrictor was consistently more successful than plain solution. Another study comparing 3% mepivacaine with 2% lidocaine (1:50,000 and 1:100,000 epinephrine) found that increasing the amount of epinephrine in 2% lidocaine improved the pulpal anesthesia in incisors [7]. The incidence of successful anesthesia was 97% at 45 min. However, this effect was not observed in the first molars. The above-mentioned studies were conducted on healthy pulps. A study comparing 2% lidocaine with 1:80,000 vs. 1:200,000 epinephrine administered as an inferior alveolar nerve block reported that increasing the concentration of epinephrine from 1: 200,000 to 1:80,000 did not improve the anesthetic success rates [8]. However, the results of this study cannot be applied to maxillary posterior teeth.

The present prospective, double-blind clinical trial aimed to comparatively evaluate the anesthetic success rate of 2% lidocaine combined with different doses of epinephrine (plain, 1:200,000 and 1:80,000), given as buccal-plus-palatal infiltration during the endodontic treatment of maxillary molars with symptomatic irreversible pulpitis. The secondary outcome of this study was to evaluate changes in heart rate. This study tested the null hypothesis that varying the amount of epinephrine in lidocaine does not affect the success rates of anesthesia or heart rate.

METHODS

This was a 9-month long prospective randomized clinical trial involving adult patients presenting with a painful, symptomatic maxillary molar, requiring endodontic intervention. Institutional ethical clearance was obtained before recruiting the patients (FODS/EC/FRP/PER/59). All participants provided written informed consent. The sample size calculations were based on the primary and secondary outcomes. The primary outcome was “anesthetic success or failure,” determined by the post-injection response of the involved tooth to the EPT and the ability to perform endodontic instrumentation with mild or no pain. If patients experienced moderate-to-severe pain (pain scores > 54) on the Heft Parker visual analog scale (HP VAS), the anesthesia was considered ‘failed’ [11,12]. The secondary outcome involved measurements of the pre-and post-injection heart rates. Sample size calculations were based on data from a previous study [3]. It was calculated that at least 43 patients should be recruited per to determine a difference of 25% in the success rates. Type 1 error was maintained at 5% and type 2 error at 0.2 (1-0.8) for a two-tailed test, evaluating the increase or decrease in the proportions of successful cases. For heart rate measurements, the sample size calculations were based on data from Susi et al. [13]. The calculations revealed that including 19 patients per group would allow the detection of a difference of 10 beats (resting heart rate at 80 ± 11). A minimum of 48 patients were recruited per group, with a dropout rate of 10% during the treatment.

The inclusion criteria were as follows: symptomatic caries in maxillary first or second molars; positive response to pulp sensibility tests (cold test and EPT) with a prolonged response; mild to moderate pain (on HP VAS); presence of bleeding indicating vital coronal pulp; American Society of Anesthesiologists class I or II medical history; and the ability of the participant to understand the use of pain scales. Each patient had at

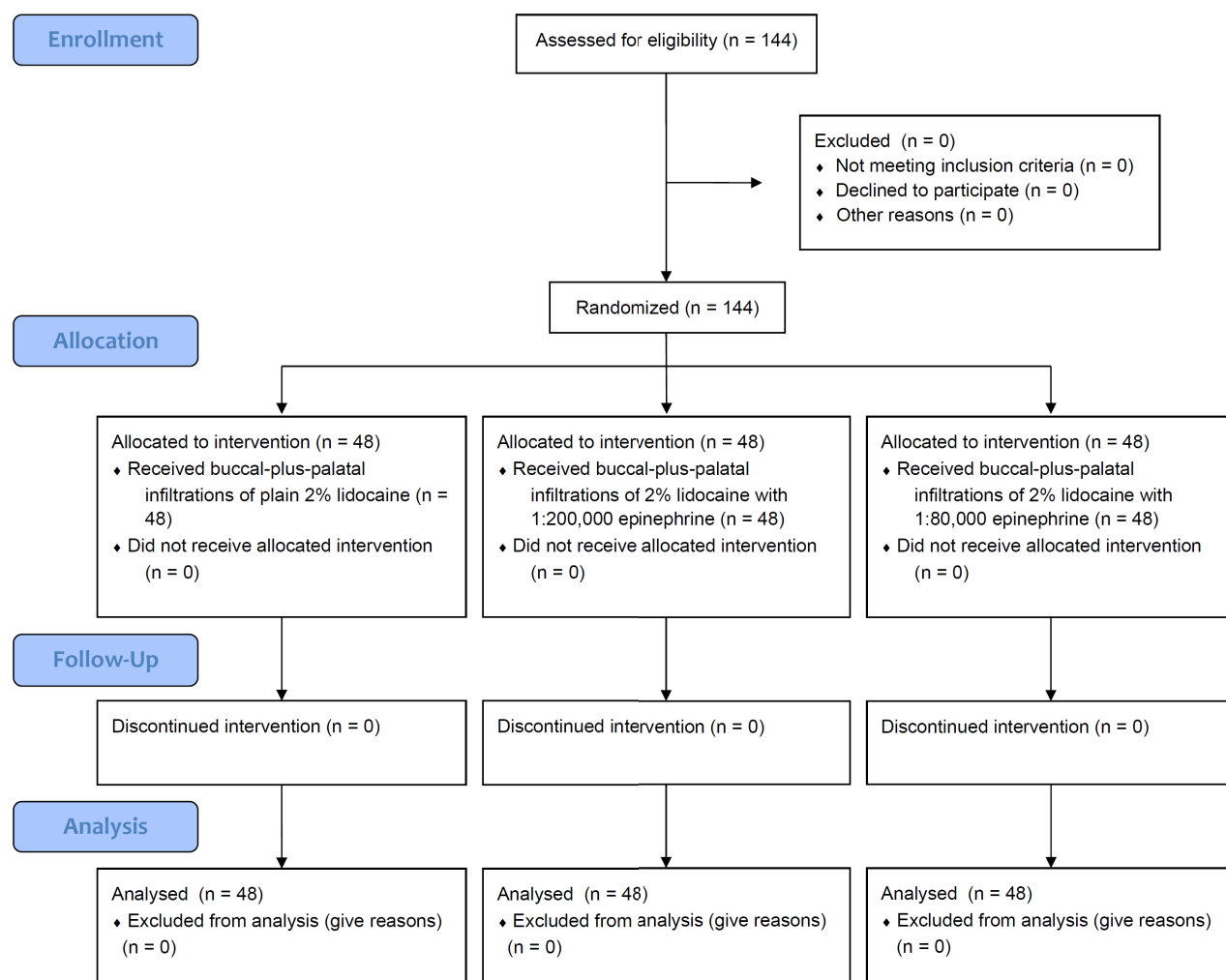


Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram

least one healthy contralateral and adjacent tooth to serve as a control for the thermal and electric tests. The exclusion criteria were any contraindication to the use of any component of the local anesthetic solution, pregnant or breastfeeding patients, patients taking any drug affecting pain perception, which was determined by a written questionnaire and verbal question/answer. Furthermore, patients with active pain in any other tooth, apart from the test tooth, were excluded. Teeth with anatomical variations, such as fused or extra roots, were also excluded. To prevent any bias in recruitment, the diagnosis and inclusion criteria were determined by an individual who was not involved in the clinical management of the patients. Considering the inclusion and exclusion criteria, 144 patients were included in the

study. Pain scales were explained to the patients along with treatment procedures. During treatment, the patients were instructed to mark the HP VAS corresponding to their pain, with cues from the different categorical points. The patients were randomly allocated to three treatment groups (2% lidocaine with no epinephrine, 1:200,000 epinephrine, and 1:80,000 epinephrine). This was obtained from an online random generator (randomization.com), which provided the randomization sequence using the permuted block randomization protocol. The patient allocation sequence was prepared by a clinician from another institute and was involved in performing the treatment. The sequences were enclosed in sealed envelopes and opened just before the individual injections. Standard anesthetic cartridges were emptied,

washed, autoclaved, and filled with different injection solutions using a 5 mL syringe. The solution was taken from commercially available 30 mL dental local anesthetic solutions (Lignox 2%, Indico Warren, Gujrat, India). The cartridges were prepared by three trained dental interns. To ensure blinding, the cartridges were masked and coded. The cartridge code was noted along with the patient code (obtained from a random sequence). The patients received buccal-plus-palatal infiltrations of the anesthetic solutions. Topical anesthetic gel was applied over the buccal sulcus and palatal mucosa of the corresponding tooth. The injection needle was gently inserted into the buccal vestibular sulcus opposite to the furcation area of the involved tooth, with the bevel of the needle towards the bone. The needle was advanced until it reached approximately the level of the apex of the root. A total of 1.8 mL of anesthetic solution was deposited over 1 min after a negative aspiration. Palatal infiltration was administered after 2 minutes. The injection site was located between the gingival margin and mid-palatine raphe of the involved tooth. Fresh cartridges and needles were used in this study. A total of 0.1 to 0.2 mL of the anesthetic solution was deposited over 30 s. Ten minutes after the palatal injection, the teeth were tested using an electric pulp tester. If a tooth responded positively, anesthesia was considered to have failed. In the case of a negative EPT response, endodontic access was initiated under a rubber dam. If the patients experienced any pain during the treatment, they rated the pain on the HP VAS. The patients with failed anesthesia were managed using supplemental anesthesia. Baseline pre-injection heart rate was recorded. Two minutes after the palatal injection, the heart rate was measured at 15-second intervals until the commencement of treatment (Fig. 1).

Age and heart rate changes were analyzed using one-way analysis of variance tests. Gender was analyzed using 3×2 contingency tables and chi-square tests. The anesthetic success rates were analyzed using Pearson's chi-square test at 5% significance. Ninety-five percent confidence intervals were obtained for the difference in

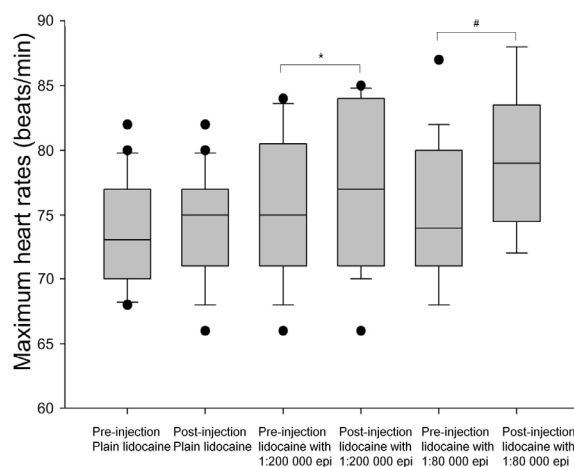


Fig. 2. Pre-injection heart rate was recorded as baseline. Two minutes after the palatal injection, the heart rate was measured at 15-second intervals until the commencement of treatment, and maximum heart rate was recorded. Lidocaine with 1:200,000 and 1:80,000 concentrations of epinephrine significantly increased heart rates (*: $P = 0.006$, #: $P < 0.001$, paired t-tests).

the proportions of success rates in different groups.

RESULTS

A total of 144 patients were included in this study. There were no significant differences between the age, sex, and type of teeth in the different groups (Table 1). There were significant differences between the anesthetic success rates of all groups ($P < 0.001$, $\chi^2 = 47.5$, $df = 2$); hence, the null hypothesis was rejected. Plain 2% lidocaine was successful in 18.8% of cases, while 2% lidocaine with 1:200,000 epinephrine and 2% lidocaine with 1:80,000 epinephrine were successful in 72.9% and 82.3% of cases, respectively. The presence of epinephrine significantly improved the anesthetic success rate ($P < 0.001$), with no significant difference between the amounts of epinephrine ($P = 0.2$) (Table 2). The majority of anesthetic failures with plain lidocaine were observed during the initial post-injection electric pulp testing or dentin penetration (Table 3). Heart rate analysis showed significant differences between the groups ($P = 0.006$). Pair-wise comparison of pre-injection and maximum post-injection mean heart rates was performed using paired t-tests. Plain lidocaine did not affect heart rate. However, solutions with 1:200,000

Table 1. Comparison of age, gender, type of tooth, and success rates

	Plain 2% lidocaine	2% lidocaine with 1: 200 000 epinephrine	2% lidocaine with 1:80 000 epinephrine	P value
Age	32.6 years \pm 10.6 years, range- 19-48 years	34.8 years \pm 8.8 years, range- 21-46 years	35 years \pm 7.7 years, range- 24-50 years	0.587
Gender	34 males 14 females	28 males 20 females	25 males 23 females	0.17, $\chi^2=3.54$, df = 2
Type of tooth	First molar = 20 Second molar = 28	First molar = 30 Second molar = 18	First molar = 23 Second molar = 25	0.11, $\chi^2 = 4.4$, df = 2
Successful anesthesia	9 out of 48 patients (18.75%)	35 out of 48 patients (72.9%)	40 out of 48 patients (83.3%)	< 0.0001, $\chi^2 = 47.5$, df = 2

There was no significant difference between age, gender, and type of teeth. There were significant differences between the anesthetic success rates

Table 2. Group-wise comparison of the anesthetic success rates

vs.	The difference in success rates	P-value	95% confidence intervals		Chi-square, degree of freedom (χ^2 , df)
			Lower bound	Upper bound	
Plain 2% lidocaine	2% lidocaine with 1: 200,000 epinephrine	P < 0.0001	-34.99%	-67.73%	28.1, 1
	2% lidocaine with 1: 80,000 epinephrine	P < 0.0001	-46.12%	-76.28%	39.6, 1
2% lidocaine with 1: 80000 epinephrine	2% lidocaine with 1: 200,000 epinephrine	P = 0.2196	-6.2401%	26.4487%	1.5, 1

Table 3. Comparison of unsuccessful anesthesia based on the stage of treatment

Stage of treatment	Lidocaine group	No of cases with failed anesthesia
During post-injection electric pulp testing/ dentin penetration	Plain 2% lidocaine	30 out of 39
	2% lidocaine with 1: 200,000 epinephrine	5 out of 13
	2% lidocaine with 1: 80,000 epinephrine	3 out of 8
During canal instrumentation	Plain 2% lidocaine	9 out of 39
	2% lidocaine with 1: 200,000 epinephrine	8 out of 13
	2% lidocaine with 1: 80,000 epinephrine	5 out of 8

Table 4. Pair-wise comparison of the change in heart rates before and after injections

	Mean of heart rates at baseline	Mean of maximum heart rate after injections	Difference post-injection vs. Pre-injection	95% confidence intervals		T score, P value
				Lower bound	Upper bound	
Plain 2% lidocaine	73.6	74.3	0.7	1.747	-0.414	T = 1.29 P = 0.2 Non-significant
2% lidocaine with 1 : 200,000 epinephrine	75.7	77.2	1.5	2.568	0.480	T = 3.0 P = 0.006 Significant at 5% and 1%
2% lidocaine with 1 : 80,000 epinephrine	75.2	79.2	4	5.265	0.641	T = 6.9 P < 0.001 Significant at 5% and 1%

and 1:80,000 concentrations of epinephrine significantly increased heart rates (Fig. 2, Table 4).

DISCUSSION

The maxillary molars can be anesthetized using buccal

and palatal infiltrations and the posterior superior alveolar (PSA) nerve block with a success rate of up to 100% in healthy pulps [1,2,8,14-17]. However, symptomatic teeth with irreversible pulpitis pose a challenge, and the success rate decreases to 54% [3]. The present study findings showed success rates of 73-82% using 2% lidocaine with epinephrine. This success rate is lower than

that achieved in uninflamed pulps. Patients with irreversible pulpitis have eight times more chances of local anesthesia failure [4]. The high failure rates can be explained by two mechanisms: first, local inflammation causes acidosis, leading to trapping of the local anesthetic molecules in ionized form. This leads to fewer molecules of the local anesthetic solution crossing through the nerve membrane [4]. Second, inflammation sensitizes nociceptors and activates transient receptors, such as TRPV1 [18,19]. The nociceptors in uninflamed pulps are generally unresponsive to mild changes in temperature or pH. However, inflammatory mediator-induced sensitization reduces their activation threshold to a point where a minor stimulus may activate these neurons [4,18,19]. This leads to a decrease in the action of local anesthetic solutions in inflamed pulps.

Vasoconstrictors, also known as “chemical tourniquet” agents, are a common component of dental local anesthetic solutions [20,21]. Epinephrine stimulates both the alpha and beta-adrenergic receptors [22]. When injected into soft tissues, it causes vasoconstriction of the local peripheral circulation via alpha-adrenergic receptors with limited systemic action [22]. Although a single injection of a local anesthetic solution with epinephrine poses a minimal risk, the use of multiple injections increases the risk of adverse drug reactions [23,24]. This increased risk may be more significant among patients with severe cardiovascular disease or those taking medications that interact with epinephrine [23]. In the present study, the plain 2% lidocaine solution provided unreliable and inadequate anesthesia in over 80% of cases. The pain during treatment in such cases would increase the endogenous catecholamine levels in the systemic circulation, negating any beneficial effects of avoiding epinephrine [25].

Research on the effects of different concentrations of epinephrine on pulpal anesthesia is limited. Knoll-Kijhler and Fortsch [26] evaluated the maxillary infiltrations of plain lidocaine and lidocaine with 1:200,000, 1:100,000, or 1:50,000 epinephrine. The authors reported that plain lidocaine had the lowest success rate. The duration of

anesthesia was increased by increasing the epinephrine concentration from 1:200,000 to 1:100,000. However, there was no further benefit obtained by increasing epinephrine from 1:100,000 to 1:50,000. Dagher et al. [27] compared the degree of anesthesia obtained with 2% lidocaine with 1:50,000, 1:80,000, and 1:100,000 epinephrine concentrations used in inferior alveolar nerve block in healthy volunteers. There was no significant difference between the three solutions in terms of anesthetic success or failure. Another study [28] compared 4% articaine with 1:100,000 and 1:200,000 epinephrine in a mandibular buccal infiltration of the first molar and found no difference in the anesthetic efficacy between the two solutions. Aggarwal et al. [8] evaluated 2% lidocaine with 1:80,000 and 1:200,000 epinephrine in patients with symptomatic mandibular molars and found no difference between the two solutions. In the present study, the plain lidocaine solution had the lowest success rate. However, there was no difference between the solutions containing 1:200,000 epinephrine and 1:80,000 epinephrine. The maximum heart rate was noted 2 min after palatal injections. In a pilot study, it was observed that palatal injections were significantly painful and the heart rate of the patient increased. This was perhaps due to the production and release of catecholamines by the body in response to stress [25]. Therefore, we waited for 2 min after administering the palatal injections. The plain lidocaine did not affect the heart rate. In contrast, both solutions with epinephrine increased heart rate. The increase was transient and the heart rates returned to normal within 5–7 minutes. In a multicenter study, Karm et al. evaluated 2% lidocaine with 1:80,000 or 1:200,000 epinephrine for surgical extraction of mandibular third molars. The authors found that both solutions significantly increased blood pressure and heart rate. Similar results were reported by Kyosaka et al. [29], who found that lidocaine with adrenaline increased the mean heart rate.

Various factors affect the success of infiltration anesthesia in the maxillary molars. The use of 4% articaine may increase the success rates of buccal

infiltrations in mandibular molars [30]; there is no significant increase reported for maxillary molars. Evans et al. [6] and Hosseini et al. [31] compared 2% lidocaine and 4% articaine in asymptomatic and symptomatic teeth, respectively. Both studies reported that there was no significant difference between the two solutions in terms of anesthetic success for the maxillary first molar. However, Evans et al. [6] noted that 4% articaine increased anesthetic success for lateral incisors. Gross et al. [8] evaluated 1.8 mL 0.5% bupivacaine with 1:200,000 epinephrine vs. 1.8 mL of 2% lidocaine with 1:100,000 epinephrine in asymptomatic maxillary lateral incisors and first molars. The authors found that bupivacaine was less successful than lidocaine (64% vs. 82%), but there was no significant difference between the two solutions. Another factor that may affect maxillary infiltration is the amount of injected solution. Brunetto et al. [15] reported that 1.2 mL of 2% lidocaine with epinephrine gave better anesthesia than 0.6 or 0.9 mL of the same solution. Mikesell et al. [16] compared 1.8 mL with 3.6 mL of 2% lidocaine with 1:100,000 epinephrine and reported that 3.6 mL volume provided a longer duration of pulpal anesthesia for the tested teeth. Similar results for maxillary first molars were reported by Pfeil et al. [2], while comparing 3.6 mL with 1.8 mL of 2% lidocaine administered as posterior superior alveolar nerve block. Some authors have compared buccal infiltration with buccal-plus-palatal infiltrations. A study reported success rates of 88% for buccal infiltration and 95% for buccal infiltration with palatal infiltrations in asymptomatic teeth [1]. Another study evaluating symptomatic maxillary molars with irreversible pulpitis showed that buccal infiltrations had lower success rates than buccal-plus-palatal (54% vs. 70%). However, this difference was not statistically significant. A recent study suggested that maxillary molars with longer palatal roots have high failure rates after single buccal infiltrations [32]. The solution may not be able to diffuse from the buccal vestibule to the apex of the palatal root. Hence, it is advisable to provide palatal infiltration during endodontic management of maxillary molars. In the present study,

buccal-plus-palatal infiltrations were successful in 73–82% of cases.

There are a few possible criticisms of the present study. The study included plain 2% lidocaine as the control group. Plain solutions have been shown to present with a lower duration of pulpal anesthesia in asymptomatic teeth, usually 30 minutes [26]. While performing endodontic treatment, this time should be sufficient to debride the canal space. Plain solutions are recommended for patients with cardiac diseases. The purpose of the present study was to comparatively evaluate the plain solutions, with those containing epinephrine, to determine their feasibility in treating teeth with symptomatic irreversible pulpitis. The results of the present study categorically show that plain solutions are not effective in providing anesthesia in symptomatic teeth and should be avoided. Solutions containing a lesser amount of epinephrine (1:200,000) were similar to solutions containing a higher dose of epinephrine (1:80,000).

In conclusion, the presence of epinephrine (irrespective of the concentration 1:80,000 or 1:200,000) significantly improved the anesthetic success rates during the endodontic management of maxillary first molars with irreversible pulpitis.

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Megha Gugnani: Investigation, Methodology, Project administration, Resources
Mandeep Grewal: Investigation, Methodology
Umesh Kumar: Data curation, Formal analysis, Resources, Writing - review & editing
Vivek Aggarwal: Conceptualization, Data curation, Formal analysis, Funding acquisition, Resources, Software, Validation, Writing - original draft, Writing - review & editing

CONFLICTS OF INTEREST: The authors deny any conflicts of interests

CLINICAL TRIAL REGISTRATION: The study has been registered at the clinical trial registry of India REF/2020/07/035288.

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