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ORIGINAL ARTICLE

Anaesthetic efficacy of 2% lidocaine with different concentrations of epinephrine (1:80,000 and 1:200,000) in intraligamentary injection after a failed primary inferior alveolar nerve block: a randomized double-blind study

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ABSTRACT

Introduction: The present study evaluated the anaesthetic efficacy of 2% lidocaine with 1:80,000 epinephrine vs. 2% lidocaine with 1:200,000 given as supplemental intraligamentary injections after a failed inferior alveolar nerve block (IANB) in patients with symptomatic irreversible pulpitis. The effect of these solutions on the heart rate was also evaluated.

Methods: One-hundred-eighteen adult patients with symptomatic irreversible pulpits in a mandibular first or second molar, received an initial IANB with 2% lidocaine with 1:80,000 epinephrine. Pain during the endodontic treatment was assessed using a visual analogue scale (Heft-Parker VAS). Eighty-eight patients with unsuccessful anaesthesia were randomly allocated to one of the two treatment groups: one group received 0.6 mL/root of supplementary intraligamentary injection of 2% lidocaine with 1:80,000 epinephrine; while the second group received 2% lidocaine with 1:200,000 epinephrine. Endodontic treatment was re-initiated. Success after primary injection or supplementary injection was defined as no or mild pain (pain score $\leq$54 mm on HP VAS) during access preparation and root canal instrumentation. Heart rate was monitored using a finger pulse oximeter. The anaesthetic success rates were analyzed with the Pearson chi-square test at 5% significance levels. The heart rate changes were analyzed using the t-test.

Results: The anaesthetic success rate in patients receiving supplementary intraligamentary injections in 1:80,000 epinephrine group was 82%, while the intraligamentary injections with 2% lidocaine with 1:200,000 epinephrine were successful in 57% of cases. The difference was statistically significant (χ^2=6.4, p = .011). There was no significant effect of both the anaesthetic agents on the mean heart rate.

Conclusions: Both 2% lidocaine with 1:80,000 epinephrine and 2% lidocaine with 1:200,000 epinephrine improved the success rates after a failed primary anaesthetic injection. The 1:80,000 epinephrine group was significantly more successful.

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Introduction

Successful local anaesthesia is the basis of endodontic management of symptomatic teeth. However, the dental anaesthetic injections have a limited success rate in the first attempt [1,2]. The success rate further decreases with the presence of preoperative pain [3]. The inferior alveolar nerve block is particularly notorious with high anaesthetic failure rates especially in teeth associated with symptomatic pulpitis [1–10]. To achieve painless treatment in patients with a failed primary IANB, supplementary anaesthesia has been advised [2]. Supplementary intraligamentary (or periodontal injections) and intraosseous injections have shown promising results [1,2,11]. The aim of the supplementary injections is to deposit the local anaesthetic solution in the cancellous bone close to the root apex [11]. An intraligamentary injection is actually a form of intraosseous injection since the local anaesthetic solution is forced *via* perforations in the dental socket to the cancellous bone around the root [11–14].

The intraligamentary injection was introduced by Malamed in 1982 as an alternative to the conventional inferior alveolar nerve block [12]. Since then it has been evaluated both as primary injection and as a supplementary injection [15–18]. Success rates of up to 92% have been reported with both pressure type and conventional syringes [2,11]. It has been reported that the presence of a vasoconstrictor significantly increases the duration and efficacy of intraligamentary injections [2]. Kaufman et al. [19] compared the anaesthetic efficacy of plain 2% lidocaine with 2% lidocaine with 1:50,000 epinephrine. The authors reported that the duration of anaesthesia with plain lidocaine was 1.02 min, while lidocaine with epinephrine had pulpal

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anaesthesia of 27.05 min. Johnson et al. [20] compared the duration of anaesthesia of 1.5% etidocaine with 1:200,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine given as an intraligamental injection. Etidocaine gave 35% whereas lidocaine gave 55% success rates. The authors suggested that the anaesthetic efficacy in intraligamentary injections is more related to the concentration of epinephrine than the type of anaesthetic agent. A recent study compared the efficacy of 4% articaine with 1:100,000 epinephrine vs. 2% lidocaine with 1:80,000 epinephrine given as a supplemental intraligamentary injection after a failed IANB [21]. The authors reported that there was no significant difference between the anaesthetic efficacy of the two agents. Meechan [18] evaluated the anaesthetic efficacy of 2 different concentrations of plain ropivacaine vs. lidocaine containing epinephrine when given as a primary intraligamentary injection and reported that lignocaine with epinephrine was more effective than ropivacaine. The results of these studies are in accordance of the fact that the presence of vasoconstrictors will decrease the absorption of local anaesthetic solution from the highly vascular cancellous bone, thus increasing the depth and the duration of anaesthetic agent. Majority of the studies evaluating intraligamentary injections have been performed on asymptomatic teeth. Very limited research has been dedicated to the evaluation of different variables in intraliagmentary injections in patients with symptomatic irreversible pulpitis.

The aim of this prospective, randomized, double-blind clinical trial was to compare the anaesthetic efficacy/success rate of 2% lidocaine with different concentrations of epinephrine (1:80,000 and 1:200,000) given as a supplemental intraligamentary injection after a failed primary inferior alveolar nerve block during the endodontic management of symptomatic mandibular first/second molar. The secondary outcome was the evaluation of heart rate during and after intraligamentary injections. The null hypothesis was that different anaesthetic solutions have no effect on the anaesthetic success rate or the heart rate.

Materials and methods

After obtaining ethical clearance from the institutional ethics committee (FOD/IRRC/06/150319), 118 patients participated in this randomized double-blind clinical trial. The trial was prospectively registered with the clinical trial registry of India (REF/2019/04/018643). The treatment was explained to each patient and informed consent was taken from all the patients. Following inclusion criteria were adopted: symptomatic carious exposed mandibular 1st or 2nd molar which tested positive and gave a prolonged response to thermal sensitivity test; the presence of vital coronal pulp during endodontic access preparation; and American Society of Anaesthesiologists class I or II medical history. Patients who were unable to understand the use of pain scales were excluded from the study. Other exclusion criteria were: patients having active pain in multiple teeth, known contraindications to any content of the local anaesthetic solution, pregnant patients, patients with known cardiac disease, and patients taking any drugs which could have affected the pain perception.

The pain was evaluated using a Heft-Parker visual analogue scale (HP-VAS) [22]. The HP-VAS comprises of a 170 mm VAS line with 6 categories (faint, weak, mild, moderate, severe and intense). The ends of the line were labelled 'no pain' and 'unbearable pain'. During the treatment, if the patient experienced any pain, he/she marked it on the VAS line with the help of pain categories mentioned on the scale [17]. The anaesthesia was marked successful if the patient marked no pain or mild pain (which corresponded pain up to 54 mm on VAS line). If the patient marked more than 54, it was considered a failure.

The patients received an inferior alveolar nerve block (IANB) of 1.8 mL of 2% lidocaine with 1:80,000 epinephrine. The injections were given using a direst Halsted approach. The anaesthetic solution was slowly deposited at the target area over a period of 60 s. After 10 min of the IANB injection, the patients were asked about the presence of lip numbness. If the patient reported the absence of a profound lip numbness, the patient was excluded from the study. Three patients were excluded due to absence of lip numbness. In the remaining 115 patients, conventional endodontic access opening was initiated. The patients were asked to inform any pain during the procedure. In case of pain, patients were asked to rate the severity of the pain on the HP-VAS. Of the initial 115 patients, 88 patients marked more than 54 score on HP-VAS during the treatment (during dentine penetration or endodontic instrument placement). These patients were considered as 'patients with failed primary IANB'. These patients received supplementary intraligamentary injections of 2% lidocaine with either 1:80,000 or 1:200,000 epinephrine. To prepare the anaesthetic cartridges, 88 cartridges were emptied, washed with distilled water, autoclaved and filled with 1.8 mL of 2% lidocaine solution with either 1:80,000 epinephrine or 1:200,000 epinephrine. The solution was taken from a commercially available 30 mL dental local anaesthetic solution (Xylocaine, AstraZeneca, Bangalore, India). The cartridges were masked with an opaque tape and were coded with an alpha-numeric code. The code was broken only after the completion of the study. The cartridge preparation was carried out by two trained dental interns who were not aware of the study design. The patients were randomly allocated to two treatment groups ($n = 44$) with the help of an online random generator, using permuted block stratified randomization protocol (randomization.com). To give intraligamentary injections the rubber dam was removed and the gingival sulcus was cleaned with an antiseptic solution. The patients in the first group received intraligamentary injections of 2% lidocaine with 1:80,000 epinephrine. The intraligamentary injections were given using a pressure type syringe (Osung Deosy, Pearland, TX, USA) and 30 gauge short needles (Septojet needles, Septodont). The injecting needle was bent for easy placement. The needle was firmly wedged between the alveolar bone and the tooth in the mesial gingival sulcus near the mesiobuccal line angle of the tooth. The handle of the syringe was firmly squeezed to complete three squeezes (which

deposited $0.2 \times 3 = 0.6$ mL solution) under strong backpressure. If no backpressure was felt, the needle was repositioned and the injection was repeated until a firm back pressure was achieved. The needle was maintained for another 20 s to prevent the backflow of the anaesthetic solution. Similar injections were given at the distobuccal line angle of the tooth. The patients in the second group received an anaesthetic solution with 1:200,000 epinephrine. Both groups received 1.2 mL of anaesthetic solution. All injections were performed by a single operator. The resting heart rate was recorded just before the intraligamentary injection. Subsequently, the heart rate was measured at 15-second interval till 5 min after intraligamentary injections. The heart rate measurements started after distal injections. The rubber dam was applied and the treatment was re-initiated. Success was again defined as no pain or faint/weak/mild pain during endodontic access preparation and instrumentation (pain score $\leq$54 mm on HP VAS). The failed cases were managed by intra-pulpal or intra-osseous anaesthesia.

Statistical analysis

The primary and secondary outcomes were defined for the calculation of the total number of patients to be recruited in the study. The primary outcome was defined as 'success or failure' which was indicated as the ability of the clinician to perform endodontic access and root canal preparation with no or mild pain (HP-VAS score <55 mm). The secondary outcome was the evaluation of heart rate after intraligamentary injections. The sample size was calculated using data from a previous study [15], keeping the α level type I error at 0.05 for a single-tailed test and β level type II error at 0.20. The analysis indicated that a sample size of 39 subjects would give 80% power to detect a 25% difference in the success rates of the two different supplemental intraligamentary injections. For heart rate analysis, it was calculated that a minimum of 23 patients per group shall be required to detect a difference of 10 beats per minutes (with the baseline heart rate of 72 beats per minutes).

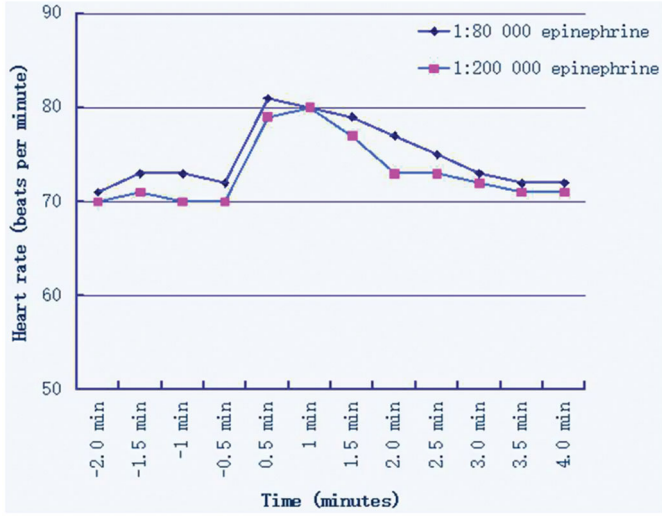
The age of patients was analyzed using Mann–Whitney *U* test at $p<.05$. The gender and distribution of teeth were analyzed using 2×2 contingency tables and chi-square tests (Table 1). The anaesthetic success rates were analyzed with the Pearson chi-square test. The heart rate changes were analyzed using the *t*-test.

Results

A total of 118 patients participated in this study. Three patients did not have profound lip anaesthesia after initial IANB and were excluded from further evaluation. The success rate of IANB was 23% (27 patients). However, 88 patients (73%) reported moderate-intense pain (more than 54 scores on HP-VAS) during the endodontic intervention and received supplementary intraligamentary injections of 2% lidocaine with either 1:80,000 or 1:200,000 epinephrine in two equal groups of 44. There was no significant difference between the age, gender, and tooth type of patients participating in both the groups. The success rate of intraligamentary injections were 82% and 57% in the 1:80,000 and 1:200,000 epinephrine groups, respectively. The difference was statistically significant (χ^2=6.4, p=.011). The mean heart rate was measured every 15 s after the end of distal intraligamentary injections for a 5 min period (Graph 1). There was a transient increase in the heart rates in both the groups at the 30–180 s intervals. However, the increase was statistically insignificant for both groups.

Discussion

The inferior alveolar nerve block has a low success rate especially in patients with symptomatic irreversible pulpitis [1–10]. In the present study, the initial IANB was successful in



Graph 1. Means of patients heart rate before and after intraligamentary injections.

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

	2% Lidocaine with 1:80,000 epinephrine	2% Lidocaine with 1:200,000 epinephrine	*p* Value
Age[$]	39 ± 11 years, range: 25–52 years	37 ± 9 years, range: 23–48 years	>.05
Gender[$]	28 males 16 females	27 males 17 females	.82, χ^2=0.05
Type of tooth[$]	First molar = 41 Second molar = 3	First molar = 36 Second molar = 8	.1, χ^2=2.5
Successful anaesthesia*	36 out of 44 patients (82%)	25 out of 44 patients (57%)	.011, χ^2=6.4

*There was a significant difference between the groups ($p < .05$).
[$]There were no significant differences ($p > .05$).

24% of the cases (27 out of 115 patients). In these clinical scenarios, the supplementary injections are used to overcome the anaesthetic failure. A viable option is to deposit the anaesthetic solution near the tooth [1]. However, the nerve the apex of mandibular teeth is surrounded by thick cortical bone [2]. The presence of cortical bone impedes the diffusion of anaesthetic solution. To overcome this barrier, intraligamentary or intraosseous injection can be used [2,11]. The intraosseous requires perforation of the cortical bone near the root apex followed by directly depositing the anaesthetic solution into the cancellous bone [11]. The intraligamentary injection involves deposition of the local anaesthetic solution in the periodontal ligament space around the root [11]. The injection is given under strong backpressure. It was assumed that the presence of backpressure provided pulpal anaesthesia similar to intra-pulpal anaesthesia. However, it was refuted by Moore et al. [23]. The authors injected either 2% lidocaine or normal saline as intraligamentary injection in mandibular premolars and reported that the intraligamentary injection of saline did not provide any effective anaesthesia, thus emphasizing on the fact that it was the local anaesthetic solution and not the pressure which provided the anaesthesia [23].

The name of the technique (intraligamentary) may be a misnomer [2,14]. The anaesthetic solution is deposited in the coronal portion of the periodontal space, however, it does not force down till the root apex. The solution is redirected, under force, to the surrounding cancellous bone through the natural perforations in the alveolar socket wall [14]. Smith and Walton [14] used a dog model to evaluate the distribution of the anaesthetic solution after an intraligamentary injection. The authors injected colloidal carbon particles in the periodontal space and authors reported that the injected material was found in the soft tissue and the adjacent hard structures. The distribution was consistently more widespread when the injections were given under strong backpressure. The authors finally concluded that intraligamentary injections are a form of intraosseous injections [14]. Since the injections are administered under strong back pressure, it can lead to an increase in the interstitial pressure inside the periodontal space. A study evaluated the change in the interstitial tissue pressure during the administration of local anaesthesia using a fixed flow rate of 0.005 mL/sec injected *via* a fluid-pressure computed controlled local anaesthetic delivery system [24]. The mean interstitial pressure during intraligamentary injections was 294 psi compared to 68, 11.5 and 9.8 psi for palatal injections, supraperiosteal buccal infiltrations, and inferior alveolar nerve block respectively. Some authors have raised their concerns on the deleterious effects of strong back pressure on the periodontal ligament. Roahen and Marshall [25] utilized a dog model to histologically assess the effect of intraligamentary injections on the pulp and the periodontal tissues. The results showed no apparent effect on the pulp tissue from the injection. However, the periodontal ligament in several cases showed some signs of injections, ranging from tissue disruption to some areas of active external root resorption. Peterson et al. [26] in a similar study on monkeys reported that in 3 out of 16 cases showed some changes in the root cementum approximately at the level of needle tip penetration. Out of 3 cases, 2 cases had areas of cementum resorption. The authors noted that the areas of resorption were shallow with indications of repair. The third case, however, showed areas of hypercementosis. The authors hypothesized that the three factors may induce tissue damage during an intraligamentary injection: 1, mechanical trauma from the injection needle; 2, increased interstitial pressure during the injection and; 3, the caustic effect of the anaesthetic solution. Another histological study reported limited supraosseous inflammation 24 h after the intraligamentary injections. The periodontal ligament appeared to be within normal limits after 7 days [27]. In the present study, the patients were recalled after 48 hrs. None of the patients reported any tenderness or labial swelling due to intraligamentary injections.

According to Meechan [2], the efficacy and the duration of anaesthesia of intraligamentary injection are dependent upon the type of the anaesthetic solution, type of the operative procedure and the type of tooth. Various studies have evaluated the different type of anaesthetic solutions for intraligamentary injections. Berlin et al. [16] compared the anaesthetic success of 1.4 mL intraligamentary injections of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine in asymptomatic mandibular posterior teeth. Using a pulp tester, the articaine gave 86% successful anaesthesia and lidocaine gave 74% successful anaesthesia with no significant difference between both the solutions. Grey et al. [28] evaluated 3% plain mepivacaine and 3% prilocaine with felypressin with 2% lidocaine with and without 1:80,000 epinephrine and reported that both mepivacaine and prilocaine were not as effective as lidocaine with epinephrine. However, the success rates of these three solutions were not statistically different. Grey et al. [29] reported that lidocaine with adrenaline, given as intraligamentary injection, was effective in 91.6% of cases vs. 42% when given without adrenaline.

The vasoconstrictors or 'chemical tourniquet' agents are added to increase the duration of local anaesthetic agents [30,31]. Epinephrine is the most commonly used vasoconstrictive agent. It stimulates both alpha and beta-adrenergic receptors [20,30–33]. The present study compared the effect of concentration of epinephrine in 2% lidocaine given as supplementary intraligamentary injections after a failed IANB. The 2% lidocaine injections with 1:80,000 epinephrine were significantly more successful than 2% lidocaine with 1:200,000 epinephrine. Johnson et al. [20] evaluated 1.5% etidocaine with 1:200,000 epinephrine vs. 2% lidocaine with 1:100,000 epinephrine in asymptomatic maxillary canines and reported that 2% lidocaine provided a longer duration of anaesthesia than 1.5% etidocaine. The authors suggested that the anaesthetic duration after the intraligamentary injections is more dependent upon the presence of a vasoconstrictor, rather than the type of anaesthetic solution itself. Similarly, Kaufman et al. demonstrated a relation between the anaesthetic duration and the vasoconstrictor concentration [19]. The result of the present study suggests that the efficacy of intraligamentary injections is affected by the

concentration of the epinephrine in the local anaesthetic solution.

There was a transient increase in the heart rate after giving the intraligamentary injections. The heart rate increased after the injections, however, it came to normal within 3 min in the majority of the cases. Two patients in the 1:80,000 group and one patient in 1:200,000 group reported palpitations after the injections. The condition subsided within a few minutes and the treatment was uneventful. Various studies have reported minimal cardiovascular risk with intraligamentary injections. Nusstein et al. [17] injected 1.4 mL of 4% articaine with 1:100000 epinephrine or 2% lidocaine with 1:100000 epinephrine and reported that there were no significant changes in the heart rate. Zarei et al. [34] compared the effect of intraligamentary injections and intraosseous injections on the anaesthetic efficacy and the mean heart rate. The authors found that intraligamentary injections did not affect the heart rate. On the other hand, Smith and Pashley [35] reported that intraligamentary injections cause a transient increase in heart rate and this increase was similar to an intravenous injection of the anaesthetic solution. The change in the heart rate was due to rapid absorption of the anaesthetic solution with epinephrine from the highly vascularized cancellous bone. In the present study, there were non-significant changes in the heart rates after the intraligamentary injections. A possible limitation of the present study is the lack of standardization of pain obtained by the Heft-Parker VAS of the primary anaesthesia failure in both the groups. However, there is no evidence of any correlation between the VAS scores of primary anaesthesia failure and success of supplementary injections. This is a very important aspect and it can be undertaken in future clinical studies.

Conclusions

The present study evaluated the use of 2% lidocaine with 1:80,000 epinephrine and 2% lidocaine with 1:200,000 epinephrine, given as supplementary intraligamentary injections after an unsuccessful primary IANB. The 1:80,000 group was significantly more successful. There was no significant difference between the mean heart rates in both groups.

Disclosure statement

No potential conflict of interest was reported by the authors.

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