Effect of 2% lignocaine with and without magnesium sulfate for inferior alveolar block in symptomatic mandibular molars

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Abstract

Background and Aim: Magnesium sulphate is used in the field of anaesthesia to increase the quality of anaesthesia. The aim of our prospective randomized, double-blind, controlled clinical trial was to combine MgSO\(_4\) with 2% lignocaine in two different concentrations (75 mg and 150 mg) to evaluate the onset, duration and anesthetic efficacy, and postoperative analgesia during routine root canal treatment in patients with symptomatic irreversible pulpitis and symptomatic apical periodontitis.

Material and Methods: The study consisted of three groups: 1.5 ml of 2% LA only (group 1), 1.5 ml of 2% LA with 0.15 ml of MgSO\(_4\) containing an osmolar concentration of approximately 4.060 mosmol/ml, that is equivalent to 75 mg of MgSO\(_4\) (group 2). Group 3 consisted of 1.5 ml of 2% LA with 0.3 ml of MgSO\(_4\) equivalent to 150 mg of MgSO\(_4\). Pre-operative vitals and Heft Parker–Visual Analogue Scale (HP–VAS) pain scores were recorded. The onset of anaesthesia, anesthetic efficacy, and duration of anesthesia were evaluated post administration of the local anesthetic solution. The post-operative analgesia was examined at intervals of 2, 6, 12, 24, and 48 h.

Results: Both experimental groups showed a significant difference in the onset, duration, and anesthetic efficacy compared to the control group. There was no significant difference between groups 2 and 3 in terms of the onset and anesthetic efficacy, but a significant difference was observed in the duration of anesthesia. Friedman non-parametric test showed significant reduction in pain from the 12th hour in the experimental groups.

Conclusion: Present study shows that both 75 mg and 150 mg of MgSO\(_4\) in combination with LA are more effective than 2% LA alone. The anesthetic duration achieved with 75 mg of MgSO\(_4\) is more than adequate for most of the dental procedures. Pertaining to the post-operative analgesia, both 75 mg and 150 mg did not have significant difference from 24 h onwards.

Keywords: Anaesthesia, irreversible pulpitis lignocaine, magnesium sulphate

Introduction

One of the primary challenges faced by the clinician during endodontic therapy of mandibular teeth is the accomplishment of a successful anesthesia in patients with irreversible pulpitis using the inferior alveolar nerve block (IANB). This poses major difficulty from a clinical point of view as an inadequately anesthetized hot tooth with severe pain will not only lead to elevation of apprehension by the patient but also cause distress in the practicing clinician. Studies reported that the failure ratio of a single IANB block injection of local anesthetic in patients with irreversible pulpitis ranges between 30 and 90 percent \([1,3]\). The success rate of the inferior alveolar nerve block (IANB) routinely used to anesthetize the mandibular’s posterior region is only approximately 75-90% due to the large surface area covered by the inferior alveolar nerve \([4]\). However, it becomes inadequate in inflamed tissues, where the success rate is approximately 30-80% in patients with symptomatic irreversible pulpitis, which is challenging \([5]\). This lower success rate of local anesthetics (LA) could be attributed to anatomical variations, local tissue pH, acute tachyphylaxis, effect of nociceptors, central sensitization, psychological reasons, and more.

To overcome such failures, various supplementary anesthetic techniques such as intraligamentary, intraosseous, and intrapulpal are used routinely \([6]\). However, the additional needle prick may have a negative effect on the patient’s psychology. Instead, an adjuvant such as epinephrine, mannitol, or ketorolac added to the LA produces synergistic anesthetic effect \([7]\). A thorough review of the literature showed that only limited drugs that are potent inhibitors of N-methyl D-aspartate (NMDA) glutamate receptor are available that provide...
central sensitization and block pain perception. Previous studies have also reported that the use of preoperative medication increases the success rate of IANB in symptomatic irreversible pulpitis \cite{8,9}. Inflammation is a result of inflammatory mediators like prostaglandins. Ketorolac which is a pyrrolo-pyridederviative inhibits the enzyme cycloxygenase thereby decreasing pain and inflammation \cite{10}.

Magnesium sulphate is used in the field of anaesthesia to increase the quality of anaesthesia \cite{11}. Local anaesthetics inhibit the phospholipid facilitated calcium transport in order to achieve anaesthesia. Magnesium reversibly binds to phospholipid molecules and acts in a synergistic effect with the local anaesthetic solution, thereby improving the quality of anaesthesia \cite{12}.

Narang et al. \cite{13} evaluated the use of MgSO\textsubscript{4} added to lignocaine as a single dose in intravenous regional anesthesia for upper limb surgery and concluded that MgSO\textsubscript{4} had better anesthetic and analgesic effects \cite{13}. In dentistry, Shetty KP et al. \cite{14} showed that administering pre-injection of MgSO\textsubscript{4} before giving IANB increased the anesthetic efficacy \cite{14}. However, this requires two needle pricks for the patient, which may be a psychological deterrent. There are no clinical studies evaluating MgSO\textsubscript{4} combined with lignocaine as a single dose. Hence, the aim of present prospective randomized, double-blind, controlled clinical trial was to combine MgSO\textsubscript{4} with 2% lignocaine in two different concentrations (75 mg and 150 mg) to evaluate the onset, duration and anesthetic efficacy, and postoperative analgesia during routine root canal treatment in patients with symptomatic irreversible pulpitis and symptomatic apical periodontitis.

**Material and Methods**

Patients classified under the American Society of Anesthesiologists (ASA) categories I and II, within the age groups of 18 to 60 years were screened in the study. The study consisted of three groups: 1.5 ml of 2% LA only (group 1), 1.5 ml of 2% LA with 0.15 ml of MgSO\textsubscript{4} containing an osmolar concentration of approximately 4.060 mosmol/ml that is equivalent to 75 mg of MgSO\textsubscript{4} (group 2). Group 3 consisted of 1.5 ml of 2% LA with 0.3 ml of MgSO\textsubscript{4} equivalent to 150 mg of MgSO\textsubscript{4}. After thorough clinical and radiographic examination along with sensitivity tests, those who were diagnosed with symptomatic irreversible pulpitis and symptomatic apical periodontitis of mandibular molar teeth were recruited into the study. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants.

Patients with pain of moderate-to-severe intensity (American association of endodontists guidelines) \cite{85,86,87} were included in the study. Patients younger than 18 years, patients allergic to local anaesthesia and ketorolac, patients who have a significant medical history, those who are pregnant or lactating, patients who have taken medication for pain within 8 hours of treatment and those patients who are unable to give informed consent were excluded from the study.

On basis of the results of the pilot study and individual power calculation, 15 subjects per group (N = 45) would provide a minimum of 90% power in all categories. Considering 20% drop-outs, the total sample size was calculated to be 20 per group. The recruited 60 patients were randomly allocated to three groups using block randomization. The experimental solutions were freshly prepared by an anesthesiologist (operator 1) who maintained the master coded list of the patients with the respective solutions. The patients, endodontist (operator 2) who performed the treatment and evaluator (operator 3) who recorded the pre and post-operative parameters were blinded to the anesthetic solution used. Before starting the procedure, the evaluator recorded the baseline pain values using the HP-VAS pain score. The endodontist then injected the coded anesthetic solution prepared by the anesthesiologist, on the landmark of corresponding operating IANB quadrant on the affected site. After negative aspiration, the local anesthetic solution was slowly deposited at the rate of 1.5 ml over 60 seconds. The Electric pulp tester (EPT) is a device to determine the vitality of the pulp. The onset of anesthesia was evaluated by EPT for every 1 min until the corresponding vital tooth stopped responding. Root canal treatment was initiated and access cavity preparation was done under rubber dam isolation. The anesthetic efficacy was calculated using HP-VAS pain score on placement of the first 10 size K file (Mani Inc., Japan). Cleaning and shaping of the root canal system was performed subsequently, sterile cotton pellet was placed, and closed dressing given using Cavit-G (3M ESPE, Germany). The duration of anesthesia was evaluated every 15 min using EPT till the adjacent normal tooth responded on the working side. In this study, none of the patients experienced pain during the procedure and thus no other supplementary injection was required in both groups. Post-operative analgesic efficacy was assessed up to 2 h after the procedure at the operating site. Subsequently, the patient was handed a HP-VAS pain scale and was requested to respond to our telephonic evaluation at 6, 12, 24, and 48 h. Post-operative instructions were given to all the patients along with the prescription of an anti-inflammatory drug, to be consumed only if pain arises. On the subsequent visit, the endodontic therapy was completed.

**Statistical analysis**

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

**Results**

The patients were equally distributed between the groups and show no significant difference. The mean and standard deviation of onset, duration and anesthetic efficacy of the three groups are mentioned in Table 2. Both experimental groups showed a significant difference in the onset, duration, and anesthetic efficacy compared to the control group. There was no significant difference between groups 2 and 3 in terms of the onset and anesthetic efficacy, but a significant difference was observed in the duration of anesthesia. The mean HP-VAS scores of post-operative analgesic efficacy at different time points for all the three groups are given in Table 3. Friedman non-parametric test showed significant reduction in pain from the 12th hour in the experimental groups.
Table 1: Demographic data and pre-operative vital signs

| Groups          | Group 1          | Group 2          | Group 3          | P value
|-----------------|------------------|------------------|------------------|---------|
| Pulse rate      | 70.50 ±6.10      | 68.50 ± 5.12     | 72.40 ± 5.47     | P > 0.05|
| Peripheral Oxygen saturation level (SpO2) | 94.40 ±2.76     | 95.20 ±3.12      | 94.11 ± 4.12     | P > 0.05|
| Respiratory rate| 12.10 ± 1.01     | 12.01 ± 0.92     | 12.04 ± 0.10     | P > 0.05|
| Blood pressure  | 96.9 ± 5.10      | 97.10 ± 5.47     | 99.02 ± 2.66     | P > 0.05|
| Gender distribution (M:F) | 6:04     | 8:01             | 4:03             | P > 0.05|
| Pre-operative HP-VAS pain score | 123.40 ± 22.30 | 122.51 ±14.02    | 122.59 ± 18.10   | P > 0.05|

Statistically significance at p≤0.05

Table 2: Onset, duration and anesthetic efficacy of the 3 groups

| Groups          | Onset (Mins) | Duration (Mins) | Anesthetic efficacy (HP-VAS Pain score) |
|-----------------|--------------|-----------------|----------------------------------------|
| Group 1         | 3.33 ± 0.85  | 109.10 ± 37.50  | 34.90 ± 31.50                          |
| Group 2         | 2.10 ± 0.50  | 189.10 ± 37.25  | 9.01 ± 13.12                           |
| Group 3         | 1.25 ± 0.62  | 246.90 ± 26.30  | 3.30 ± 8.3                            |

Statistically significance at p≤0.05

Table 3: Onset, duration and anesthetic efficacy of the 3 groups

| Groups          | 2       | 6       | 12      | 24      | 48      |
|-----------------|--------|--------|--------|--------|--------|
| Group 1         | 50.10 ± 51.10 | 32.70 ± 32.70 | 21.50 ± 25.14 | 21.01 ± 18.8 | 15.01 ± 16.99 |
| Group 2         | 24.99 ± 34.25 | 24.12 ± 35.1 | 13.10 ± 32.6 | 4.10 ± 11.0 | 1.20 ± 6.11 |
| Group 3         | 30.90 ± 41.9 | 12.01 ± 24.15 | 1.62 ± 6.10 | 0      | 0      |

Statistically significance at p≤0.05

Discussion

Inferior alveolar nerve block is the most common nerve block used to provide anaesthesia of the mandibular molar teeth. As proposed by Malamed, it is the nerve block that fails usually. This could be due to the accessory innervations, inaccurate injection technique, needle deflection and cross innervations. The action of local anaesthetics is by diffusion across the cell membrane and blockade of the sodium channel. This action requires a shift of the form of the local anaesthetic between charged and uncharged forms. The pH of the local anaesthetic in the cartridge is made low (pH 4), because at a lower pH, the shelf life is longer and the solution is more stable. When injected into the tissues, its transition into base form depends upon the tissue pH. In inflamed tissue, the low pH of the tissue leads to greater portion of the local anaesthetic being trapped in its charged form thus making it unavailable to cross the cell membranes. This hypothesis of “ion trapping” is considered the major mechanism of failure of local anaesthetics in inflamed tissue. Lidocaine hydrochloride has been the widely used local anaesthetic agent since its introduction because of its proven efficacy, low allergenicity and minimal toxicity. Articaine has gained popularity due to its enhanced anaesthetic property. Many studies comparing the anaesthetic efficacy of articaine over lidocaine including those done by Aggarwal et al. [15], Kanaa et al and Poorni et al. [16] reported a higher success rate of articaine when compared with lidocaine. Articaine is 4- methyl-3,2-thiophene carboxylic acid, methyl ester hydrochloride that is the only amide local anaesthetic containing thiophene ring in its structure. The higher lipid solubility of this agent allows for its easier penetration through the nerve membrane and the surrounding tissues. Hence the higher lipid solubility of Articaine could contribute to the enhanced efficiency of this agent [17].

In this study, patients diagnosed as symptomatic irreversible pulpitis with symptomatic apical periodontitis were included because inflamed pulp causes pain, but once the inflamed pulp is treated, the pain progressively subsides. Whereas, in case of symptomatic apical periodontitis, the inflammatory mediators that are present increase the neuropeptides such as prostaglandins E2 and bradykinin and can cause exaggerated central sensitization even in the presence of a small stimulus. This results in more post-operative pain. For IANB, 1.5 ml of 2% lignocaine without methylparaben and adrenaline was used in this study. This is to standardize the anesthetic solution, rule out hypersensitivity reaction in patients, avoid any interaction between methylparaben and MgSO₄, and avoid the influence of adrenaline on the heart rate and blood pressure, respectively. Literature states that even 1.0 ml of 2% lignocaine is an effective volume for obtaining clinical success in IANB. Usual regimen of MgSO₄ administered as intravenous injection were a dose of 30–50 mg/kg followed by a continuous dose of 6–20 mg/kg/h till the end of surgery. According to the literature, 150 mg is the lowest concentration used in regional anesthesia for plexus block [21]. Since the inferior alveolar nerve is a peripheral nerve without a myelin sheath, a smaller dose of 75 mg was also chosen along with 150 mg of MgSO₄ in this randomized controlled clinical trial. The experimental anesthetic solution was freshly mixed to retain the chemical properties of the drug. However, Houlihan S et al. earlier observed that freshly mixed anesthetic solution showed no precipitation for up to 168 days when stored at 25°C and 40°C [22]. There was no significant difference in the demographic data and pre-operative vitals, indicating a random and an even distribution of subjects between the three groups (Table 1). This is in accordance to the statement of Wolff (1940) and Mumford (1965) who stated that the perception of pain is independent of age and sex [23, 24]. The results of this study show that 150 mg of MgSO₄ when added to lignocaine provided faster and longer duration of anesthesia, maximum anesthetic efficacy, and better post-operative analgesia as compared to 2% LA. Hence, the null hypothesis was rejected. In addition, 75 mg of MgSO₄ also showed better results comparable to those of 150 mg MgSO₄, though there
was a significant difference between the 2 experimental groups in terms of the anesthetic efficacy. Hargreaves and Keiser have proposed several hypotheses to explain local anesthetic failure including effect of inflammation on central sensitization. Central sensitization is due to upregulation of N-methyl-D-aspartate (NMDA) receptors. Magnesium sulphate interfere with these NMDA receptors and prevent the induction of central sensitization due to peripheral nociceptor stimulation and eliminate the hypersensitivity. This study also proves that the addition of MgSO4 to 2% LA has a dose dependent increase in the onset, duration, anesthetic efficacy, and post-operative analgesia. From the results of the study, we can extrapolate that 75 mg MgSO4 is sufficient in endodontics, since the duration of anesthesia with this group was found to be 189.10 ± 37.25, which is more than adequate for the endodontic procedure to be completed. It was further observed that the patients of the control group had lesser pain relief at 2 and 6 h compared to groups 2 and 3, though not statistically significant. Siqueira JF and Barnett F stated that the highest peak of post-operative pain was present at the 6th hour due to the action of the inflammatory mediators as a result of the local immune response. It can be inferred that action of MgSO4 on the NMDA receptor and calcium channel blockers progressively reduced the postoperative pain and also proved to be effective at the 6th hour time point in Table 3. MgSO4 in both concentrations proved to be effective in post-operative analgesia at 12, 24, and 48 h with significant reduction in pain compared to group 1. However, contradictory results were reported in the literature by few authors who showed that MgSO4 has limited or no effect on post-operative pain in patients undergoing abdominal hysterectomy and caesarean delivery. Tramer MR and Glynn CJ also observed that the pre-treatment of MgSO4 for ambulatory ilioinguinal hernia repair or operation of varicose vein had no effect on postoperative analgesia because of the heterogeneous populations and dose variation. In our study, the pre-serum values of Mg2+ were not taken into consideration, although they may have an influence on the results. In a study done by Krishna Prasad Shetty et al. 14, there was a significant increase in the success rate of IANB in patients with symptomatic irreversible pulpitis when anaesthesia was achieved along the a pre-operative magnesium sulphate compared with a pre-operative placebo group. This is in accordance with this study where magnesium sulphate showed significant decrease in the pain values compared to the other two groups. Further studies with increased number of samples are required to validate the results of the current study.

**Conclusion**

Present study shows that both 75 mg and 150 mg of MgSO4 in combination with LA are more effective than 2% LA alone. The anesthetic duration achieved with 75 mg of MgSO4 is more than adequate for most of the dental procedures. Pertaining to the post-operative analgesia, both 75 mg and 150 mg did not have significant difference from 24 h onwards. Hence, considering the dental procedure that requires only half the duration compared to general surgery, a lower concentration or dose should be more than adequate for most dental procedures.

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