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Original Article

Effect of Magnesium Sulphate Added to Mepivacaine Hydrochloride on Inferior Alveolar Nerve Block Success in Patients with Symptomatic Irreversible Pulpitis in Mandibular Molars: A Randomized Clinical Trial

Alaa Ibrahim Mekhimar[1], Randa Elboghdadi[1], Dina A. Morsy[1]

[1] Endodontics Department, Faculty of Dentistry, Cairo University, Egypt

Email: alaa.ibrahim@dentistry.cu.edu.eg

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Abstract

Aim: The aim was to assess the success of inferior alveolar nerve block when adding magnesium sulphate to mepivacaine HCl in comparison to mepivacaine HCl alone in patients with symptomatic irreversible pulpitis in mandibular molars. **Subjects and methods**: Patients diagnosed with symptomatic irreversible pulpitis were assigned randomly into 2 groups (n=24). Initial pain data were diagnosed with cold spray and collected on a numerical rating scale chart. Both groups received 1.8 ml of local anaesthetic solution as a standard inferior alveolar nerve block (IANB). In the control group, the local anaesthetic solution contained 1.8% mepivacaine HCl while in the experimental group contained 1% magnesium sulphate and 1.8% mepivacaine HCl. Pain was assessed 15 minutes after injection using cold spray, during access and canal negotiation. Success of local anaesthesia was defined as recording no or mild pain. **Results:** The success of IANB was 70.8% for the magnesium sulphate group compared to 50% in the control group. There was no significant difference between the 2 groups ($P > 0.05$). **Conclusion:** The combination of mepivacaine– magnesium sulphate achieved a higher success rate for IANB than that of mepivacaine alone, but there was no significant difference between both groups.

Keywords: magnesium sulfate; anesthesia; dental; mandibular nerve; pulpitis; root canal treatment; nerve block

I. INTRODUCTION

One of the most difficult issues in endodontics is achieving a sufficient depth of local anaesthesia, particularly during inferior alveolar nerve block (IANB) for mandibular posterior teeth with symptomatic irreversible pulpitis (SIP). This is a significant clinical challenge, since a poorly anaesthetized hot tooth in acute pain will increase the patient's apprehension and trigger the suffering of the clinician. The most popular anaesthetic approach utilized for posterior mandibular root canal therapy is conventional IANB. However, it has a high failure rate of 44%–81% in mandibular posterior teeth with SIP [1].

Reduced concentration of the local anaesthetic solution (LAS) caused by increased blood flow, lowered pH, activation effect on the peripheral free terminals of nociceptive neurons and the associated

central mechanisms, as well as psychological factors, may contribute to higher failure rates in patients with inflamed pulp [2]. Various strategies and procedures were searched for to improve the anaesthetic efficacy of IANB, such as using premedication [3], alternative LAS [4], supplemental injection techniques [5], changing the volume of LAS [6] or using additives to LAS [7].

Magnesium sulphate ($MgSO_4$) is one of the additives that have been used during anaesthetic practice. It reduces central sensitization because it is a noncompetitive antagonist of N-methyl-D-aspartate (NMDA) receptors. Additionally, it disrupts calcium channels, It also impairs calcium channels, which provide voltage-dependent regulation of calcium influx into the cells. LA and magnesium have additive inhibitory effects on calcium transport[8].

Mepivacaine hydrochloride (HCl) is widely used in dentistry. It is more compatible with inflamed tissues as compared to lidocaine, it has a lower ionization constant (pKa) and therefore is routinely used in painful clinical situations [9].

To our knowledge, there is no previous clinical study that assessed the combination of mepivacaine HCl and $MgSO_4$. Therefore, this study evaluated the success of IANB in patients with SIP in mandibular molars treated with MgSO4 added to mepivacaine HCl to that of mepivacaine HCl alone.

II. SUBJECTS AND METHODS

A. Trial Design

The clinical trial has a two-arm, parallel, randomized, triple-blinded design. It was approved by the Ethics Committee of the Faculty of Dentistry, Cairo University, Cairo, Egypt. The study's purpose, the procedure's nature, and any potential discomforts were all explained to each patient before they were asked to sign a printed consent. The study was registered at www.clinicaltrials.gov (NCT04561921).

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B. Sample Size

The sample size was determined based on a previous study by **El Marakby et al., 2018**[10], the primary outcome used was incidence of success of IANB. Proportion of comparator group was 0.39 while proportion of intervention group was estimated to be 0.8. Using power 80% and 5% significance level, it was determined that a total sample size of 42 cases (21 cases per group) was adequate. To account for a 15% dropout, this number was adjusted to 48 cases (24 per group). The G*Power program (University of Düsseldorf, Düsseldorf, Germany) was used to determine the sample size.

C. Participants

Only healthy individuals (ASA I or II) between the ages of 18 and 55 with SIP involving mandibular molars and normal periapical radiographic appearance or slight lamina dura widening were included. Patients who had taken any form of analgesic medicine within the last 12 hours of treatment, pregnant women, or nursing mothers, as well as having a contraindication for the use of $MgSO_4$ or mepivacaine HCl and patients with sensory impairment or paresthesia were all excluded from the study.

Between May and November 2021, patients were enrolled and treated. One operator screened 107 patients who had been referred to the Dental Clinic of the Endodontic Department at the Faculty of Dentistry, Cairo University, Urban area, Cairo governorate, Egypt. Patients who were enrolled in the study gave their consent as well. From the chief complaint and the clinical examination, the diagnosis of SIP was reached for each tooth. Pulp sensibility was done by applying cold-sprayed (ethyl chloride) cotton on the tested tooth and comparing it to the contralateral tooth. The patient was asked to record his pain on a numerical rating scale (NRS) chart which is an 11point scale consisting of numbers from 0 through 10 as follows: “0” represents no pain, “1 - 3” represent “mild pain”, “4 - 6” represent moderate pain, “7 - 10” represent severe pain[11]. Reporting moderate to severe pain on the NRS scale and prolonged sharp, intense painful response to cold testing (>10s) was considered a diagnostic criterion.

D. Anaesthetic Solution Preparation

The anaesthetic solution was prepared by withdrawal of 0.18ml from the 2% mepivacaine HCl with Levonordefrin HCl 1:20000/ 1.8 ml carpule (Mepecaine – L, Alexandria Co.-Egypt) by using a 100 IU insulin syringe. For the intervention group (Group A), 0.18 ml of 10% $MgSO_4$ (Magnisol, Memphis Co. -Egypt) were added to the mepivacaine carpule. The cartridge was mixed by inverting the cartridge five times, with no precipitation produced. The final concentration in the carpule was 1% $MgSO_4$, and 1.8% mepivacaine HCl with 1:22000 Levonordefrin HCl. While the solution for the comparator group (Group B) was prepared by adding 0.18ml of sterile distilled water to the mepivacaine carpule. The final concentration in the carpule was 1.8% mepivacaine HCl with 1:22000 Levonordefrin HCl. This preparation technique was in accordance with **Mousavi et al. 2020 [12].**

E. Anaesthetic Injections and Data Collection

The conventional IANB was used to administer the injections, with aspiration coming first. The injections used the solutions described in the section above. All injections were given by the operator slowly (over 100 seconds) using a 27-G, long needle (1.5-inch) connected to a standard aspirating dental injection syringe. Fifteen minutes after the injection, the numbness of the lip was assessed and compared to the opposite lip. Cold test by ethyl chloride spray was performed to determine whether a painful response exists or not. The patient was given instructions to fill out the NRS chart with his pain score. In case the patient didn't feel lip numbness or recorded moderate or severe pain, she/he was omitted from the study (the injection was repeated and the endodontic treatment was completed but the patient was excluded from the study). The ability to perform coronal access and to negotiate the canals with no pain (NRS =0) or mild pain (NRS ranges from 1-3) was used to determine the success of pulpal anaesthetic. If the patient reported moderate or severe pain, the anaesthetic blockade was categorized as a failure and a supplemental buccal articaine infiltration was given. Single-visit endodontic treatment was performed for all participants by crown-down technique using rotary M-PRO and irrigation with 2.5% NaOCl subsequent to each file and 1 ml EDTA 17% as a final irrigant with saline in between and as a final flush. The modified single-cone technique was performed. A temporary filling material was used to fill the cavity. Patients were redirected for final restoration in the restorative department and given postoperative instructions.

F. Randomization

The assistant supervisor made the sequence generation for the patients' numbers using a computer-generated random sequence number (http://www.random.org/) and the table was kept with her. The operator was in charge of diagnosing the patients, describing the process to them, and obtaining their written informed consent. After the individual was confirmed to be enrolled in the study, he was given sealed envelopes numbered from 1 to 48 and was asked to choose one. Based on this number, the patient was then allocated to either intervention or comparator group after contacting the assistant supervisor to prepare the anaesthetic solution accordingly.

G. Blinding

The study was triple-blinded, where the patient, operator and outcome assessor (data analyst) didn't know the group to which the patients were assigned.

H. Statistical Analysis

Categorical and ordinal data were presented as frequency and percentage values. By examining the data distribution and utilizing the Shapiro-Wilk test, numerical data were examined for normality and provided as mean and standard deviation values. Categorical data were analyzed using Fisher's exact test. Independent t-test was used to analyze parametric data (age) for intergroup comparisons. For all tests, the significance level was set at $p<0.05$. R statistical analysis software version 4.1.3 for Windows 20. Was used to conduct statistical analysis.

III. RESULTS

A total of 48 patients who met the inclusion criteria, were enrolled in the study. Patients were assigned randomly into two groups (n=24). All patients were included in the analysis. Flow of the patients is summarized in the CONSORT 2010 Flow diagram of the trial design presented in Figure (1). Regarding age, gender, and the number of treated teeth, there was no statistically significant difference between the two groups (P=0.534, P=0.510, and P=1 respectively) (Table 1). Baseline data showed that 100% of participants in both groups had severe pain. Results of anaesthetic efficacy presented in (Table 2) showed that all cases (100%) in both groups were successful after 15 minutes where all patients reported numb lips and no response to the cold test. Success rate during access preparation was 75% for the intervention group and 62.5% for the control group. The intervention group's success rate during canal negotiation was 94.4%, whereas the other group's rate was 80%. For the overall success, adding $MgSO_4$ to mepivacaine HCl increased the success rate of IANB in comparison to mepivacaine HCl alone (70.8% and 50% respectively), but this increase was not statistically significant.

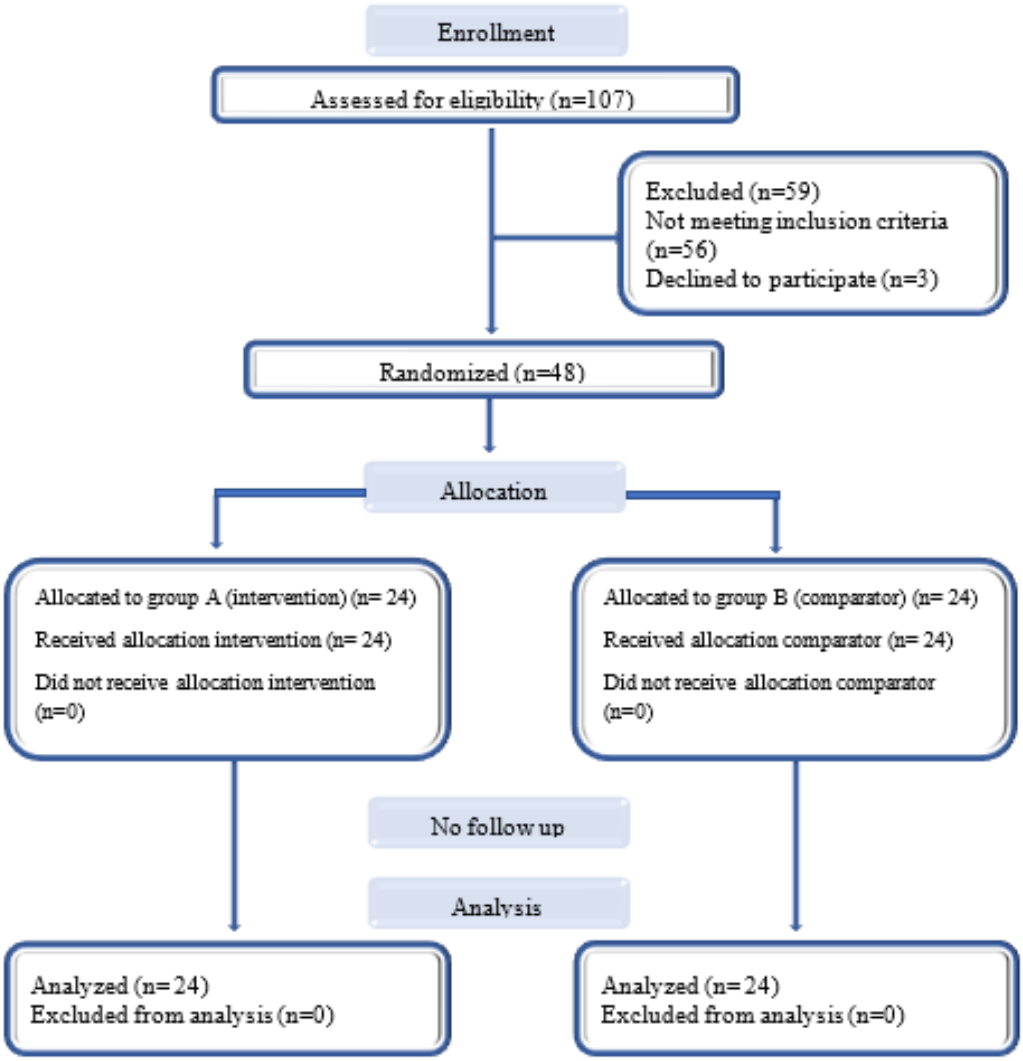

Figure (1): CONSORT 2010 flow diagram

Table (1): Summary of statistics of Demographic Data for Group A and Group B

Parameter			Group (A)	Group (B)	p-value
Gender	Male	N	6	9	0.534ns
		%	25.0%	37.5%	
	Female	N	18	15	
		%	75.0%	62.5%	
Age	Mean±SD		35.88±10.83	33.92±9.56	0.510ns
Treated tooth	First molar	N	19	20	1ns
		%	79.2%	83.3%	
	Second molar	N	5	4	
		%	20.8%	16.7%	

Table 2: Frequency and percentage values for anaesthetic outcome in both groups

Interval	Anaesthetic outcome		Group (A)	Group (B)	p-value
After 15 minutes	Success	N	24	24	NA
		%	100.0%	100.0%	
	Failure	N	0	0	
		%	0.0%	0.0%	
During access preparation	Success	N	18	15	0.533ns
		%	75.0%	62.5%	
	Failure	N	6	9	
		%	25.0%	37.5%	
Canal negotiation	Success	N	17	12	0.465ns
		%	94.4%	80.0%	
	Failure	N	1	3	
		%	5.6%	20.0%	
Overall	Success	N	17	12	0.238ns
		%	70.8%	50.0%	
	Failure	N	7	12	
		%	29.2%	50.0%	

IV. DISCUSSION

This study evaluated the efficacy of IANB when adding $MgSO_4$ to mepivacaine HCl in comparison to mepivacaine HCl alone in patients with SIP in mandibular molars**.** The best technique for diagnosing SIP is cold thermal stimulation **[13].** Unlike electrical pulp testing, cold stimuli are easily available and do not necessitate extensive tooth drying. They are also simple and reliable in determining pulpal state **[14].**

MgSO4 was employed to enhance the quality of anaesthesia in this experiment and numerous other research projects in the field of anaesthesia. Its role in intra-operative analgesia has been studied during general and spinal anaesthesia. For example, in neuraxial, epidural, femoral, and paravertebral blockades, MgSO4 is administered as an adjuvant to block anaesthesia [12,15,16].

$MgSO_4$ is a noncompetitive NMDA receptor antagonist with antinociceptive effects. In the central nervous system (CNS), the NMDA receptor is a membrane-bound, voltage-dependent ion channel that is expressed on primary sensory neurons. It contributes to the induction and maintenance of pathological pain conditions and central sensitization **[17]**. MgSO4 inhibits these NMDA receptors, deactivating hypersensitivity after it has evolved and preventing cerebral sensitization from peripheral nociceptor activation **[8,12,18]**. In addition, $MgSO_4$ helps control the calcium

influx in the neurons, which may be important in the mechanism of antinociception [8,12,18].

Using $MgSO_4$ as an adjuvant to local anaesthetics in a single IANB injection might be advantageous [12]. In this study, we added $MgSO_4$ to mepivacaine carpule to decrease the patient's discomfort from multiple injections and reduce the probability of mishaps at the site of injection. The MgSO4 concentration chosen was consistent with previously established reports and all used dosages of no more than 150 mg of magnesium as an adjuvant to establish nerve blocks, with no documented side effects and they reported an increase in anaesthetic success [15,16,19,]

Results of anaesthetic efficacy showed that all cases (100%) in both groups were successful after 15 minutes. During access preparation, there were 6 (25.0%) failed cases in $MgSO_4$ + mepivacaine group and 9 failed cases (37.5%) in the comparator group. During canal negotiation, there was 1 (5.6%) failed case in $MgSO_4$ + mepivacaine group and 3 failed cases (20.0%) in the other group. This is in accordance with **Aggarwal et al.,**[20] who reported higher failure rate during access without significant difference. The failure to achieve fully successful anaesthesia may be explained by lowered pH values, overexpression of aberrant sodium channels, a rise in inflammatory pain mediators, and excessive vasodilation. Overall adding $MgSO_4$ to mepivacaine HCl increased the success rate of IANB more than mepivacaine HCl alone (70.8% and 50% respectively), however, the results lacked statistical significance. This is per the results of **Mousavi et al.,**[12] who found that adding MgSo4 increases the efficacy of local anaesthetic agents. However, their results were statistically significant unlike the findings of this study, and this might be related to the difference in the type of local anaesthetic employed.

It should also be noted that in our study the failure rate after adding MgSO4 (29.2%) is lower than that mentioned in previous studies that reported a failure rate of (44-81%) in patients with SIP in lower molars[12,21].

Our results are consistent with those of **Rodriguez-Wong et al.**[22], who showed no statistically significant difference between mepivacaine group and the experimental group (tramadol was added as an adjuvant to mepivacaine. Although the results of mepivacaine group in both studies are comparable (50% and 46.4%), $MgSO_4$ as an adjuvant to mepivacaine showed much higher success rate (70.8%) than tramadol as an adjuvant to mepivacaine (57.1%). This makes $MgSO_4$ a promising additive to mepivacaine and more studies with different concentrations and higher sample sizes need to be conducted.

V. CONCLUSION

Within the confines of this study, it can be concluded that using magnesium sulphate as an additive to mepivacaine HCl increased the anaesthetic success rate of IANB in patients with SIP related to mandibular molars, however this success was not statistically significant when compared to using mepivacaine HCl alone. Neither of the local anaesthetic solutions achieved 100% anaesthetic success in patients with SIP of mandibular molars.

Conflict of interest:
The authors declare no conflict of interest.

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Ethics:
This study protocol was approved by the ethical committee of the faculty of dentistry- Cairo University on: 27-10-2020, approval number 4 10 20.

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