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MAGNESIUM SULFATE AS A LIDOCAINE ADJUVANT IN INFERIOR ALVEOLAR NERVE BLOCK – A SYSTEMATIC REVIEW

Aswathi B*1, Rajmohan M*2, Gousalya V*3, Bharathwaj VV*4, Sindhu R*5, Dinesh Dhamodhar*6, Prabu D*7

*1,2,3,4,5,6Third Year, Bachelor Of Dental Surgery, Department Of Public Health Dentistry, SRM Dental College, Ramapuram, Chennai, India.

*7Head Of The Department, Phd., Department Of Public Health Dentistry, SRM Dental College, Ramapuram, Chennai, India.

ABSTRACT

BACKGROUND: Accomplishing adequate anaesthesia is imperative for performing invasive dental procedures. Hence adjuvants are administered via various routes to hasten the onset and facilitate the efficacy of anaesthesia. Magnesium sulfate is one such promising agent used as an adjuvant to anaesthesia.

AIM: To appraise the effectiveness of magnesium sulfate as an adjuvant to Lidocaine in inferior alveolar nerve block.

METHODS: A literature search was conducted using PubMed, Google Scholar, Elsevier science direct, Ovid Medline, Lilacs, Scopus, Cochrane, Wiley online library using MeSH terms- Magnesium sulfate, Adjuvant, Inferior Alveolar Nerve Block, Lidocaine. Out of 45 total articles, 13 full-text articles were screened, and three were included in qualitative analysis. This review has been reported according to PRISMA guidelines. Three randomized control trials were included in the review process.

RESULTS: The effect of magnesium sulfate added to Lidocaine was compared with plain local anaesthetic solutions in all three trials. The magnesium sulfate group showed a statistically significant difference from the other groups ($P<0.05$). Magnesium having analgesic effects also enhances the effectiveness of established analgesics when used as an adjuvant.

CONCLUSION: Magnesium having an antinociceptive, anaesthetic, and neuroprotective properties can be used as an adjuvant to Lidocaine. Yet large, well-designed clinical trials are needed to evaluate its true efficacy in pain management as an adjuvant.

Keywords: Magnesium Sulfate, Adjuvant, Inferior Alveolar Nerve Block, Lidocaine.

I. INTRODUCTION

Pain is a distressing physical and emotional sensation. [1] that is inherently subjective and can be debilitating, which brings the need for sedative techniques to aid treatment. To prevent the patients from experiencing discomfort during invasive procedures, local anaesthesia must be administered [2]. Local anaesthesia (LA) functions by producing blockade of nerve conduction in a circumscribed area and causes reversible loss of sensation, which is achieved by inhibiting ionic fluxes required for propagation of neuronal impulses. In addition, it blocks the nociceptive action potentials in sensory nerve fibres, resulting in loss of pain without loss of consciousness [3].

Inferior alveolar nerve block (IANB) involves the deposition of a solution of local anaesthetic (often Lidocaine) near the nerve before it enters the foramen and is the most common type of anaesthesia given in dentistry [4]. Lidocaine, an amino amide prototype drug, was the first sodium channel blocker identified and used since 1948 [5]. Lidocaine blocks voltage-gated sodium and potassium channels and ligand-gated calcium channels, thereby causing decreased excitability of neurons and reduced pain sensitization [6]. However, even though 2% Lidocaine along with 1:100,000 epinephrine is considered the gold standard [7], achieving profound anaesthesia in symptomatic cases is more challenging [8]. This might be attributed to inflammation that would have resulted in central sensitization that causes upregulation of NMDA receptors [9].

For this reason, local anaesthetics are frequently amalgamated with adjuvants (substances that have synergistic properties) in clinical practice to improve the anaesthetic efficacy. Various adjuvants like dexamethasone,

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clonidine, tramadol, dexmedetomidine, midazolam, NSAIDs, buprenorphine, ketamine, magnesium, neostigmine, sodium bicarbonate, and epinephrine have been studied [10].

'The forgotten electrolyte'- magnesium [11] plays a fundamental role in many cellular functions, and as a result, interest in its significance in clinical medicine is growing [12]. The principle behind the effects of magnesium is physiological calcium antagonism, which is voltage-dependent regulation of calcium influx into the cell, and non-competitive antagonism of (NMDA) N-methyl-D-aspartate receptors [13]. Magnesium reduces the peripheral nerve excitability and augments the ability of Lidocaine to increase the excitation threshold of A- β fibres [14]. In addition, magnesium inhibits the activation of NMDA receptors, obstructing the excitatory postsynaptic currents and reducing C fibre stimulation [15]. It also prevents induction of central sensitization by inhibiting the activation of NMDA receptors in the dorsal horn via amino acid transmitters such as glutamate and aspartate [16] and abolishes hypersensitivity. This paper reviews Magnesium sulfate's ($MgSO_4$) therapeutic use and efficacy as an adjuvant medication to Lidocaine in IANB.

OBJECTIVE:

To appraise the effectiveness of magnesium sulfate as an adjuvant to Lidocaine in inferior alveolar nerve block.

II. MATERIALS AND METHOD

STUDY DESIGN:

Systematic review of randomized control trials on the effectiveness of magnesium sulfate as an adjuvant to Lidocaine in IANB. A total of 45 articles were referred, of which three articles were finally chosen based on inclusion and exclusion criteria according to PRISMA guidelines.

SEARCH STRATEGY:

The electronic databases used to find published articles on the effectiveness of magnesium sulfate as an adjuvant to Lidocaine in inferior alveolar nerve block are as follows:

- PubMed
- Google Scholar
- Elsevier science direct
- Ovid Medline
- Lilacs
- Scopus
- Cochrane
- Wiley online library

Each database was combed to obtain the articles using specific MeSH representatives. The MeSH terms used were Magnesium sulfate AND Adjuvant, Lidocaine, and Inferior Alveolar Nerve Block. The articles were collected using the Cochrane database following PRISMA guidelines and bias assessment.

INCLUSION CRITERIA:

- Articles related to the topic
- Articles focussing on magnesium sulfate as an adjuvant
- Articles that were only randomized control trials
- Full-text articles
- Articles in English

EXCLUSION CRITERIA:

- Articles not related to the topic
- Articles with other adjuvants
- Articles in other languages
- Articles with magnesium sulfate used in other anaesthesia
- Articles other than Randomized control trials.

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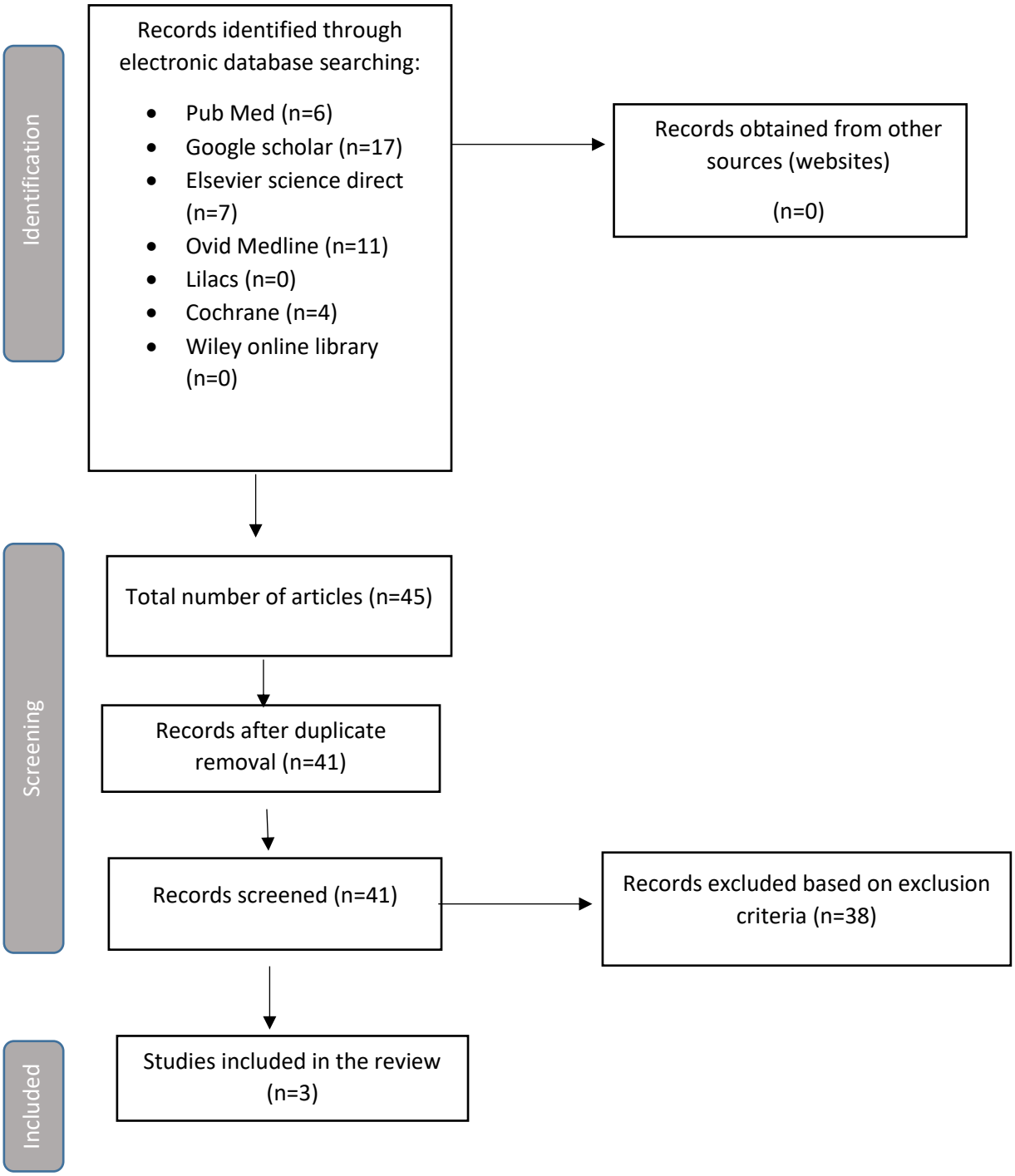

Fig 1: Flow diagram depicting the number of studies identified, screened, evaluated for eligibility, excluded, and included in the systematic review:

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Table 1: Characteristics Of Interventions In The Study

AUTHOR NAME	YEAR	SAMPLE SIZE	PATIENT CHARACTERISTICS	(NUMBER CASE/CONTROL)
Krishna Prasad Shetty et al. [17]	2015	100	Patients aged below 18 years	Group 1- 1ml magnesium sulfate 60 minutes before administration of IANB Group 2- 1ml distilled water 60 minutes before administration of IANB
Charanya Chandrashekaran et al. [18]	September 2016 to 2019	33	Patients aged 20 to 60 years	Group 1- 1.5 ml of 2% LA only Group 2- 1.5 ml of 2% LA with 0.15 ml of $MgSO_4$ containing an osmolar concentration of approximately 4.060 mmol/ml that is equivalent to 75 mg of $MgSO_4$ Group 3- 1.5 ml of 2% LA with 0.3 ml of $MgSO_4$ equivalent to 150 mg of $MgSO_4$
S.A. Mousavi et al. [19]	2017	68	Patients aged 16-18 years of age Female - 42 Male - 26	Group 1- IANB with 1.8% lidocaine/ 1:88,000 epinephrine (control) Group 2- 1% magnesium sulphate, 1.8% lidocaine/ 1 : 88 000 epinephrine (test group)

Table 2 describes the characteristics of the interventions in the included studies. In all three studies, the effect of IANB using Lidocaine with and without magnesium sulfate was compared. The studies differed individually based on sample size and age of the population.

Table 2: Characteristics Of Outcome And Effect Measures

AUTHOR NAME	YEAR	EFFECT MEASURE	OUTCOME	RESULT
Krishna Prasad Shetty et al. [17]	2015	Heft–Parker visual analogue scale (HP-VAS)	The success of anaesthesia was For magnesium sulfate was 58%, and that of the placebo-group is 32% (P = 0.016).	The increase in the success of IANB was statistically significant.
Charanya Chandrashekaran et al. [18]	September 2016 to 2019	Heft–Parker visual analogue scale (HP-VAS) Electric pulp tester (EPT) – Diagnostic	In comparison to the control group, there was a significant difference in terms	The trial showed that combining $MgSO_4$ with LA was more effective than 2% LA alone.

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		aid to determine the vitality of the pulp.	of onset, duration, and anaesthetic effectiveness. HP-VAS scores : Group 1 - 3.29 Group 2 - 9.14 Group 3 – 35.79 (P < 0.05)	
S.A. Mousavi et al. [19]	2017	Heft–Parker visual analogue scale (HP-VAS)	The success of anaesthesia for magnesium sulfate was 82%, and that of the placebo group was 53% HP-VAS scores : $MgSO_4$ group -23.35 Placebo group -63.7 (P < 0.001)	The authors found that the magnesium sulfate group's IANB effectiveness was significantly higher.

Table 3 shows the outcome of the effectiveness of $MgSO_4$ in the studies mentioned above. The success rate of anaesthesia was significantly increased compared to the control group with (P<0.05).

Table 3: Bias Assessment As Included In The Study

Author name, year	Random sequence generation	Allocation concealment	Blinding of outcome	Incomplete outcome data	Blinding of participants and personnel	Selective reporting
Krishna Prasad Shetty et al. [17]	+	?	+	?	+	+
Charanya Chandrashekaran et al. [18]	+	+	+	+	+	+
S.A. Mousavi et al. [19]	+	+	+	+	+	+

+ = Low risk of bias; - = High risk of bias; ? = Unclear risk of bias

III. DISCUSSION

Magnesium, the second most prevalent intracellular cation, is responsible for the activation of about 300 enzyme systems. [20]. By blocking NMDA glutamate receptors, which is the main excitatory neurotransmitter in the central nervous system, magnesium inhibits neuronal activity. Magnesium has been used for the prophylaxis of seizures, treatment of pulmonary hypertension, the management of asthma and tetanus, pheochromocytoma, myocardial infarction, etc., [21]. Reports demonstrate the efficacy of $MgSO_4$ as an adjuvant to IV regional anaesthesia in septorhinoplasty, cholecystectomy, upper limb surgery, hysteroscopy, trans abdominis plane block, caesarian section, mastectomy, hysterectomy, infra umbilical surgeries, spinal anaesthesia in knee arthroscopy, axillary brachial plexus block in arteriovenous fistula surgery, etc. In dentistry, magnesium sulfate has been used as an adjuvant to Lidocaine in IANB in cases of symptomatic irreversible pulpitis.

In this systematic review, three randomized control trials were carefully selected and assessed for the efficacy of magnesium sulfate as an adjuvant to Lidocaine in IANB. Severe pain, a lingering response to the cold test, and

the absence of radiographic signs of apical periodontitis were deemed to represent symptomatic irreversible pulpitis. A successful Inferior alveolar nerve block was described as the tooth being painless (HP-VAS score equal to 0 mm) or having mild pain (HP-VAS rating ≤ 54 mm).

Krishna Prasad Shetty et al. conducted a randomized, double-blind, placebo-controlled study in the year 2015. Side effects of magnesium sulfate begin to appear when plasma magnesium levels cross 6–7 mEq/mL (21). The total dosage of magnesium sulfate in our present study (1 mL = 500 mg = 4.06 mEq/mL) was substantially lower than the dose needed to initiate side effects. The study concluded that there was a statistically significant increase in the success of IANB. (P = 0.016).

The randomized, double-blind controlled clinical trial conducted by Charanya Chandrashekaran et al. from 2016 to 2019 consisted of 33 patients aged 20 to 60 years. A smaller dose of 75 mg was used in addition to 150 mg of $MgSO_4$ in the trial as the inferior alveolar nerve is a peripheral nerve without a multiple plexus of nerves. The study showed that 150 mg of $MgSO_4$ when added to lignocaine, provided faster and extended duration of anaesthesia, maximum anaesthetic efficacy, and enhanced postoperative analgesia compared to 2% LA. From the study's findings, we can deduce that 75 mg $MgSO_4$ is sufficient in endodontics since the duration of anaesthesia with this group was estimated to be 190 +/- 37.250, which is copious for the endodontic procedure to be completed. HP-VAS scores: Group 1 - 3.29, Group 2 - 9.14, Group 3 – 35.79 (P < 0.05).

S.A. Mousavi et al. conducted a double-blind clinical trial in 2017. He reported that the IANB effectiveness was much greater for the magnesium sulfate group. HP-VAS scores: (23.35) for the $MgSO_4$ group and (63.7) for the placebo group. (P < 0.001). The magnesium sulfate concentration employed in this investigation was based on previously published data. None of the studies that included doses of 150 mg magnesium or less as an adjuvant reported any adverse effects. The success of anaesthesia was found to be significantly improved.

The outcome obtained from the study suggests that magnesium sulfate, when added to the local anaesthetic lidocaine, acts as an adjuvant in IANB procedures and causes favourable improvements in onset, duration and anaesthetic efficacy.

IV. LIMITATIONS

This study is based on fewer clinical trials included in the systematic review. Several articles were excluded due to various reasons that did not fit the criteria of the study. Considering other databases can provide more appropriate results.

V. CONCLUSION

There is strong evidence that magnesium sulfate when used in IANB as an adjuvant to Lidocaine, has significant positive outcomes. Therefore, magnesium sulfate could be administered as an adjuvant for achieving profound pulpal anaesthesia in formidable cases. However, to establish an appropriate conclusion before routine clinical use, more studies with larger sample sizes and different dose concentrations must be conducted.

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