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Research Article

Randomized Controlled Double-Blind Study Comparing Efficacy of Two Doses of Magnesium Sulphate as an Adjuvant to Local Anesthetics in Supraclavicular Block

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ABSTRACT

Background: Magnesium sulphate (MgSO4) is one of the commonly used adjuvant in regional blocks and proved its analgesic efficacy. However, the exact dose of the drug for perineural administration is still debatable. We compared two different doses of Magnesium Sulphate (150mg and 250mg) as an adjuvant to local anesthetics in ultrasound guided supraclavicular block.
Primary objective was to compare block parameters along with postoperative analgesia duration and secondary objectives were comparison of total analgesic requirement and side effects.
Methods: 90 patients posted for elective upper limb surgeries under supraclavicular block with 12 ml 2% adrenalized lignocaine,12 ml 0.5% bupivacaine were divided in two groups. Group M1 received 150 mg and Group M2 received 250 mg magnesium sulphate.
Results: With addition of 250 mg of Magnesium, the duration of sensory (530.37 ± 67.33 min) as well as motor block (492 ± 80.52 min) was prolonged as compared to sensory (478 ± 72.6 min) and motor (442 ± 83.980 min) block durations with 150 mg. Duration of postoperative analgesia was also prolonged with 250 mg (485.33 ± 79.19 min) as compared to 150 mg (538 ± 67.2 min) respectively. Total number of postoperative analgesic doses were lesser with 250 mg magnesium.
Conclusion: Magnesium sulphate as an adjuvant in supraclavicular block in the dose 250 mg significantly prolonged the duration of sensory as well as motor block, duration of postoperative analgesia with reduction in analgesic requirement postoperatively as compared to the 150 mg with no significant side effects.

Introduction

Supraclavicular brachial plexus block is the most preferred peripheral nerve block for upper limb surgeries as it provides dense, predictable anesthesia of the entire upper extremity, with excellent operating conditions. Ultrasound guidance to regional anesthesia helps in real-time imaging of anatomic structures, needle view, drug spread with advantage of lower volumes of drug for successful block. Local anesthetics alone provide limited duration of postoperative analgesia. To increase the success rate and to have longer duration of analgesia many adjuvants have been used like Tramadol, Alpha 2 agonists, Fentanyl, Dexamethasone and Ketamine with varied results.

N- methyl D-aspartate (NMDA) receptors have essential role in nociceptive transmission, modulation, and sensitization in acute pain states. Magnesium ions by blocking calcium influx antagonizes NMDA receptors [1] and prevents central sensitization caused by peripheral nociceptive stimuli. It has proven antinociceptive and anti-inflammatory actions.

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Other than central location, NMDA receptors are found in muscles, skin, [2] knee joints [3] and play a role in the sensory transmission of noxious stimuli. Magnesium owing to its NMDA receptors antagonism [4] has been used as an additive in central neuraxial blocks, peripheral nerve blocks [5] and fascial plane blocks. However, the exact dose of the drug has not been ascertained till now.

So, with this highlighting the role magnesium as NMDA receptor antagonist, this study compared the efficacy of two different doses (150mg and 250mg) of Magnesium Sulphate (MgSO4) when used as an adjuvant to local anesthetics. Our primary objective was to compare duration of sensory and motor block along with duration of postoperative analgesia. Secondary objectives were to compare total analgesic requirement and side effects.

Methods

After approval from institutional ethics committee this prospective, double blind, randomized study (CTRI/2021/07/034681) was conducted within the duration from 2020 to June 2022 in 90 American Society of Anesthesiologist's physical status I and II patients of either gender, aged 18-60 years who were scheduled for elective upper limb surgeries under ultrasound guided supraclavicular block.

Patients not willing to participate, patients on calcium channel blockers, with heart blocks, allergic to local anesthetics and on anticoagulants were excluded from study. Written informed consent was taken from all patients and the study was done in accordance with most recent version of Helsinki declaration. Detailed preoperative anesthesia check up of all participants was done day before surgery. They were explained about block procedure and Visual Analogue Scale (VAS). All were kept nil orally 6 hours prior to surgery.

The sample size was calculated based on standard deviation from previous study done by Verma et al [6] keeping power at 80% and confidence interval 95%, a sample of 90 patients required. They were randomly divided into two groups, Group M1 and Group M2, 45 patients in each group as shown in (Figure 1) by computer generated random number table.

Group M1: received 12 ml of 2% lignocaine with adrenaline, 12 ml 0.5% bupivacaine plus Injection magnesium sulphate 150 mg (50% MgSO4) i.e. 0.3 ml

Group M2: received 12 ml of 2% lignocaine with adrenaline, 12 ml 0.5% bupivacaine plus Injection Magnesium sulphate 250 mg (50% MgSO4) i.e. 0.5 ml

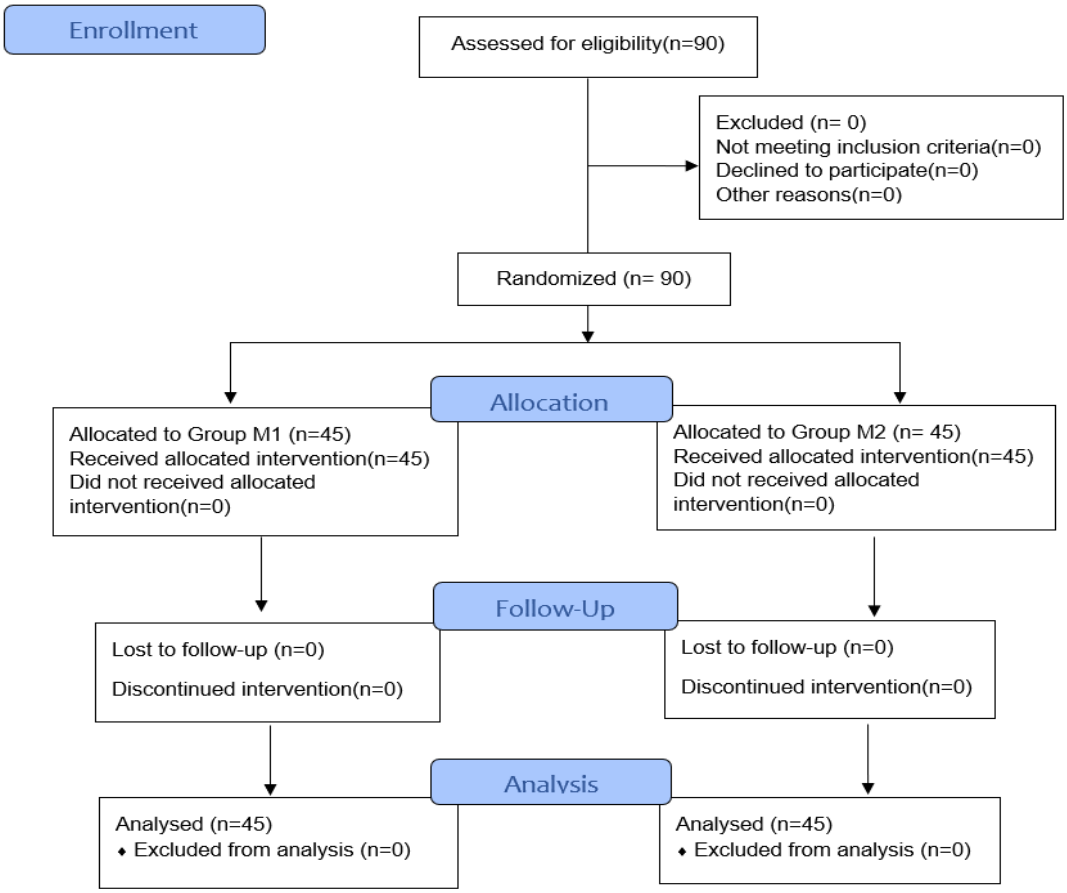

Figure 1- CONSORT flow diagram

On arrival in the operation room baseline heart rate, blood pressure, respiratory rate and oxygen saturation were recorded. An intravenous line was secured in the unaffected limb and Ringer's lactate was started. Anesthesia faculty in the operation theatre only knew about the random number allocated as per computer based randomization table and the study drug administered for block was prepared by same faculty. Both the patient and observer who was assessing the patient intraoperatively and postoperatively were blinded to the drug administered. For accurate calculation of injection magnesium sulphate, it was loaded in tuberculin syringe. All patients received ultrasound guided supraclavicular brachial plexus block by experienced anesthesiologist. Brachial plexus was identified as characteristic 'Honey comb' appearance. After confirming negative aspiration for blood, drug was injected in 5 to 10ml aliquots and homogeneous spread of drug was observed.

Both groups were compared with respect to primary objectives of duration of block along with duration of postoperative analgesia. Total analgesic requirement and side effects were compared as secondary objectives. Pin prick method was used to assess sensory block. After complete drug administration, sensory block was assessed at every minute by three point grading. Sensory onset time was the time interval between drug administration to loss of sensation to pinprick.

Sensory block was graded as:

0: Sharp pain to the prick

1: Analgesia (Loss of sensation to pin prick) but perception of touch feel is present

2: Loss of touch sensation

Assessment of motor block was done every minute after drug injection till complete block by Modified Bromage scale [7]. The onset of motor block was the time interval between the end of drug administration to grade 2 motor blockade.

0: Normal motor function with full flexion and extension of elbow, wrist and fingers

1: Decreased motor strength with ability to move fingers only

2: Complete motor block with inability to move fingers

The duration of sensory blockade was defined as the time interval between onset of sensory block to reappearance of pinprick sensation. The duration of motor blockade was defined as the time interval between complete motor paralysis to complete movement of wrist and fingers. Patients were assessed for duration of analgesia by using VAS score of 0 to 10. Duration of postoperative analgesia was interval between sensory onset till the demand for first rescue analgesia. Time for first rescue analgesia was noted in both groups. Injection paracetamol 1gm IV was given at VAS> 4 as rescue analgesia. All patients were monitored for hemodynamic stability and for side effects like nausea, vomiting, respiratory depression and hypotension.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS software version 25.0 IBM Corporation, USA) for MS windows was used to analyze data. In the entire study, P value less than 0.05 considered as statistically significant. Continuous variables were presented as mean and standard deviation while categorial variables were shown as n (% of cases). For comparison between two groups unpaired t test was used.

Results

At the end of clinical trial, all the data were unblinded and entered into excel sheet according to group they belong. No statistically significant difference was found between the two groups with regards to demographic parameters and surgical duration (Table 1).

The mean onset of sensory block in Group M1 and group M2 was 7.42 ± 2.03 min and 6.91 ± 1.66 min and the mean onset of motor block was 7.78 ± 2.02 min and 7.09 ± 2.48 min respectively (Table2).

The duration of sensory block in Group M1 and Group M2 was 478 ± 72.6 min and 530.37 ± 67.33 min respectively while duration of motor block was 442 ± 83.980 min and 492 ± 80.52 min respectively. Both the block durations were significantly prolonged in Group M2. (P values of 0.001 and 0.004 respectively) as shown in (Table 2).

Also the mean duration of postoperative analgesia in Group M1 and Group M2 was 485.33 ± 79.19 min and 538 ± 67.2 min respectively. It was significantly prolonged in Group M2 with P value of 0.001 (Table 2).

Total number of analgesic doses required in group M1 were 2.42 ± 0.94 compared to 1.91 ± 0.90 in group M2 (P value of 0.010).

As seen in (Figure 2), postoperative VAS score was found to be significantly lower in group M2 at 8th and 10th hour with P value less than 0.001 and 0.04 respectively.

Table1- Demographic parameters

	Group M1 (n=45)	**Group M2 (n=45)**	**P value**
Age(years)	39.17 ± 13.73	41.50 ± 13.15	0.504
Gender: n (%)			
Males	37 (82.2)	29 (64.4)	0.68
Females	8 (17.8)	16 (35.6)	
ASA I	28 (62.2%)	32 (71%)	0.91
ASA II	17 (37.8%)	13 (29%)	

Surgery Duration (min ± SD)	153 ± 56	160 ± 61	0.56

n= sample size, min= minutes, SD= Standard deviation

Table 2- Block characteristics expressed as mean ± standard deviation

	Group M1 (n=45)	Group M2 (n=45)	P-value
Sensory onset (mins)	7.42 ± 2.03	6.91 ± 1.66	0.09
Motor onset (mins)	7.78 ± 2.02	7.09 ± 2.48	0.153
Duration of Sensory Block (mins)	478 ± 72.6	530.37± 67.3	0.001
Duration of Motor Block (mins)	442 ± 83.98	492 ± 80.52	0.004
Time for first rescue analgesia (mins)	485.33 ± 79.19	538.00 ± 67.2	0.001
Total number of Analgesic doses in 24 hours	2.42 ± 0.94	1.91 ± 0.90	0.010

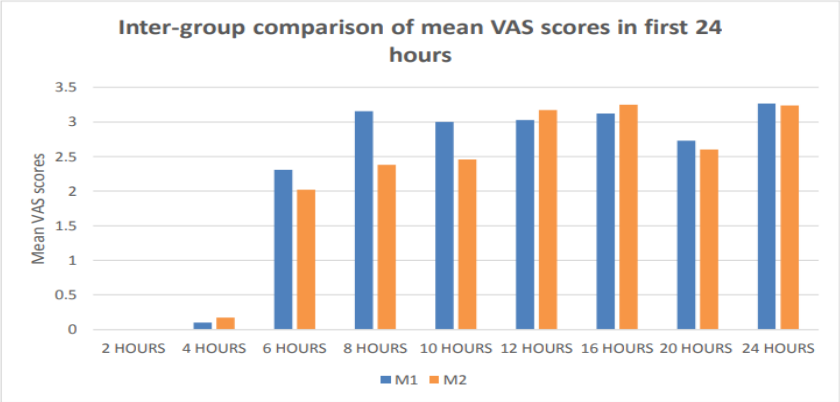

Figure 2- Comparison of mean VAS score

Discussion

During the first 24 hours of orthopedic surgery, patients mainly complain of severe pain, hence they demand for proper analgesia in postoperative period. Supraclavicular brachial plexus block is considered as 'spinal anesthesia' of entire upper extremity with excellent operating conditions. Postoperative duration of analgesia with local anesthetics alone is limited. Amongst the various adjuvants used to enhance the block quality and duration of analgesia, magnesium is one with favorable effects as an analgesic and has anesthetic sparing action in perioperative period. Magnesium being second abundant intracellular cation plays essential role in presynaptic release of acetylcholine from nerve endings and produces effects similar to calcium channel blockers. Owing to its NMDA receptor antagonism, magnesium has proven antinociceptive action. It has been used in different doses in various regional nerve blocks with varied results.

Our study compared two different doses, 150mg (Group M1) and 250 mg (Group M2) of magnesium sulphate when used with 2% lignocaine with adrenaline and 0.5% bupivacaine. Doses selected in this study were based on previous studies conducted by Verma et al [6] who compared 125 mg and 250 mg MgSO4 and Mukherjee et al [8] used 150 mg magnesium.

On comparing both the groups with respect to onset time of sensory and motor blocks, there was no statistically significant difference as shown in Table 2. Priyanka et al [9] compared two doses of magnesium sulphate,125 and 250 mg in interscalene nerve blockade, also obtained findings similar to that of our study. However, in the study conducted by Versha Verma et al [6] they found that when magnesium added to local anesthetic resulted in rapid onset of sensory and motor block. They used 0.5% bupivacaine alone as local anesthetic which has slower onset of action while in our study we used 2% lignocaine with adrenaline which itself has faster onset. This could be the contributing factor why we couldn't appreciate any significant difference in onset time of blocks.

The mean duration of sensory and motor blocks as seen in (Table 2), along with duration of postoperative analgesia, was significantly prolonged in 250 mg magnesium sulphate group as compared to 150 mg magnesium group. Our findings are consistent with studies done by Varsha Verma et al [6], Singh et al [10] and Gunduz et al [11] where they compared two different doses of magnesium and found duration of sensory as well as motor blocks were longer with higher dose. This dose responsive effect of magnesium on peripheral nerve is based on surface charge theory as proposed by Akutgawa [12] which describes the mechanism of action of magnesium on the peripheral neuron. It suggests that

by modulating the external magnesium concentration will have synergistic impact on nerve blockage caused by local anesthetic. Mert et al [13] in his study on effect of magnesium and calcium on nerve conduction showed that negative charges of the outer membrane of nerve surface attracts high concentration of bivalent ions affects Na+ channel gain and leading to hyperpolarization. If the nerve fiber is hyperpolarized, threshold level will not be achieved causing conduction block.

Even with the difference of 100 mg in two doses of magnesium that we used in this study, we found prolongation of block with higher dose. This can be explained by above mentioned theories.

Total analgesic requirement in 24 hours was also less in 250mg magnesium group as shown in Table 2. The lesser requirement of total number of doses of injection paracetamol in Group M2 can be explained by longer duration of sensory block with 250 mg magnesium. Similar results were obtained in studies conducted by Bansal et al [14] and Kalyani et al [15] where total consumption of injection fentanyl and diclofenac were less respectively.

VAS score was also less at 8th and 10th hour in group M2 (p value < 0.01) which shows statistical significance as shown in (Figure 1). Our results were similar with study done by Lee et al [16] where they found lower Numerical Rating Score (NRS) in magnesium group as compared to control group.

The analgesic effects of magnesium are mainly by antagonism of NMDA receptors, it also interferes with calcium mediated release of acetylcholine at synaptic junction and may potentiate the action of local anesthetics. Firing threshold of both myelinated and unmyelinated axons is elevated by magnesium ions. Systemic absorption of magnesium can be another stated mechanism as serum levels are highly associated with reduced postsynaptic activity of slow conducting unmyelinated C fibres which are afferents carrying input signals from periphery.

All our patients remained hemodynamically stable and parameters did not differ significantly from each other. There were no block failures or no any significant side effects as vomiting, hypotension, respiratory depression with both doses.

However there are certain limitations of our study. We have not measured serum magnesium levels. Favorable effects of magnesium on block properties might be partially due to its systemic absorption also along with local action. So further studies can be done comparing systemic versus perineural administration of drug with monitoring of serum magnesium levels.

Conclusion

Addition of Magnesium sulphate as an adjuvant to local anesthetic in supraclavicular block in the dose 250 mg significantly prolonged the duration of sensory as well as motor block, duration of postoperative analgesia with reduction in analgesic requirement postoperatively but no change in onset of sensory and motor blockade as compared to the 150 mg with no significant side effects. So we conclude, magnesium sulphate in dose 250 mg is more effective as compared to 150 mg.

References

[1] Dedek A, Hildebrand ME. Advances and Barriers in Understanding Presynaptic N-Methyl-D-Aspartate Receptors in Spinal Pain Processing. Front Mol Neurosci. 2022; 15.

[2] De Kock MF, Lavand'homme PM. The clinical role of NMDA receptor antagonists for the treatment of postoperative pain. Best Pract Res Clin Anaesthesiol.2007; 21(1):85-98.

[3] Saritas TB, Borazan H, Okesli S, Yel M, Otelcioglu S. Is intra-articular magnesium effective for postoperative analgesia in arthroscopic shoulder surgery? Pain Res Manag. 2015; 20(1):35-38.

[4] Suzuki M. Role of N-methyl D-aspartate receptor antagonists in postoperative pain management. Curr Opin Anaesthesiol.2009; 22(5):618-22.

[5] Khairnar p, Agarwal M, Verma UC, Kumar R. Comparative efficacy of ropivacaine and levobupivacaine in combined femoral and lateral femoral cutaneous nerve block with adjuvant magnesium for post-operative analgesia. Indian J Anaesth.2016; 609(8):584-9.

[6] Verma V, Rana S, Chaudhary SK, Singh J, Verma RK, Sood S. A dose-finding randomised controlled trial of magnesium sulphate as an adjuvant in ultrasound-guided supraclavicular brachial plexus block. Indian J Anaesth. 2017; 61(3):250.

[7] Sarkar DJ, Khurana G, Chaudhary A, Sharma JP. A comparative study on the effects of adding fentanyl and buprenorphine to local anaesthetics in brachial plexus block. J Clin Diagn Res. 2010; 4:3337–43.

[8] Mukherjee K, Das A, Basunia SR, Dutta S, Mandal P, Mukherjee A. Evaluation of magnesium as an adjuvant in ropivacaine-induced supraclavicular brachial plexus block: A prospective, double-blinded randomized controlled study. J Res Pharm Pract. 2014; 3(4):123-9.

[9] Suresh P, Emani A. Effect of two different dosages of adjunct magnesium sulfate on interscalene nerve blockade: A double blind randomized controlled trial. Indian J Clin Anaesth. 2022; 9(1):56-59.

[10] Singh S, Raman R, Singh GP, Singh V, Kumar S, Tewari V. Randomised control trial of dexmedetomidine and magnesium sulfate as an adjuvant to ropivacaine in supraclavicular brachial plexus block. Int J Contemp Med. 2019; 7:39-44.

[11] Gunduz A, Bilir A, Gulec S. Magnesium added to prilocaine prolongs the duration of axillary plexus block. Reg Anesth Pain Med. 2006; 31(3):233-6.

[12] Akutagawa T, Kitahata LM, Saito H, Collins JG,

Katz JD. Magnesium enhances local anesthetic nerve block of frog sciatic nerve. Anesth Analg. 1984; 63(2):111-6.

[13] Mert T, Gunes Y, Guven M, Gunay I, Ozcengiz D. Effects of calcium and magnesium on peripheral nerve conduction. Pol J Pharmcol. 2003; 55(1):25-30.

[14] Bansal P, Baduni N, Bhalla J, Mahawar B. A comparative evaluation of magnesium sulphate and nitroglycerin as potential adjuncts to lignocaine in intravenous regional anaesthesia. Int J Crit Illn Inj Sci. 2015; 5(1):27-31.

[15] Patil KN, Deshpande JP, Menghal R, John L. Evaluation of Magnesium as an Adjuvant in Roipvacaine Induced Interscalene Brachial Plexus Block: A Prospective, Double- Blinded, Randomized Controlled Study. Archives of Anesthesiology and Critital Care. 2022; 8(2):134-8.

[16] Lee AR, Yi HW, Chung IS, Ko JS, Ahn HJ, Gwak MS. Magnesium added to bupivacaine prolongs the duration of analgesia after interscalene nerve block. Can J Anaesth. 2012; 59:21-7.