



Original Research Article

Effect of two different dosages of adjunct magnesium sulfate on interscalene nerve blockade: A double blind randomized controlled trial

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ABSTRACT

Background: Interscalene nerve block is very commonly performed for clavicle & proximal humerus surgeries. However very few studies have evaluated the effect of add on magnesium sulphate to local anaesthetic for interscalene nerve block.

Materials and Methods: Sixty patients of American Society of Anaesthesiologist (ASA) physical status I and II undergoing surgeries for fracture clavicle and proximal humerus were recruited in this trial. Following randomisation, ultrasound guided interscalene block was performed with 10ml of 2% lignocaine and 20ml of 0.5% bupivacaine either with adjunct 125 mg (MS 125 group, n=30) or 250 mg (MS 250 group, n=30) magnesium sulphate. Primary outcome was to measure and compare the postoperative analgesia, duration of sensory and motor blockade.

Results: There was no significant difference between the groups in the duration of sensory blockade [MS 125 v/s MS 250; Mean±SD [Median]; 505.3±44.6 (500) minutes v/s 501.1±45.9(498) minutes; p=0.65], duration of motor blockade [MS 125 v/s MS 250; Mean±SD [Median]; 314.9±31.1(307) minutes v/s 311.4±34.2(305) minutes; p=0.7] and the duration of post-operative analgesia [MS 125 v/s MS 250; Mean±SD [Median]; 519±46.1(512) minutes v/s 498±95.8(507) minutes; p=0.43].

Conclusions: Magnesium sulfate at the dose of 125 mg is equally effective as 250 mg for prolonging sensory and motor blockade as well as for post-operative analgesia when used as an adjunct to bupivacaine and lignocaine during interscalene brachial plexus blockade. Our study is limited by small sample size. Further studies with larger sample size are needed.

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1. Introduction

Peripheral nerve blocks (PNBs) using local anaesthetics are commonly practiced for many surgeries. Although PNBs carry the advantage of providing postoperative analgesia, the duration of action of these anaesthetics is very short when used alone and it prevents the smooth transition of the patient to oral/parenteral analgesics.¹ To enhance the duration of action of anaesthetics many adjunct medications have been tried. The agents like magnesium sulfate, dexmedetomidine have been used as adjunct to

local anaesthetics in PNBs.^{2,3} Enhancing the duration of analgesia carries many advantages, as postoperative pain management is an integral part of the management of any surgical patient. Inadequate pain management has been shown to be associated with delayed surgical recovery, decreased patient satisfaction and increased health care costs.^{4,5}

Magnesium sulfate, as an adjunct, has been shown to enhance postoperative analgesia. Magnesium is an N-Methyl-D-Aspartate (NMDA) antagonist and moderates the influx of calcium to neurons. Magnesium decreases the excitability of peripheral neurons and is been shown to enhance the ability of lidocaine to raise the excitation

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threshold of A-beta fibers.⁶ Magnesium sulfate does not let catecholamines be released from the adrenal and peripheral nerve endings and results in sympathetic block.⁷ Magnesium sulfate has been found to be useful as an adjunct with local anesthetics in prolonging postoperative analgesia and decreasing the time for onset of action of local anesthetic. In a recently conducted meta-analysis, add on magnesium sulfate was found to significantly prolong postoperative analgesia, sensory and motor blockade.⁸ However, the role of magnesium sulfate in inter scalene nerve blockade for clavicular and proximal humerus shaft surgeries has not been studied well. Only a single study is available on the role of add on magnesium sulfate for inter scalene nerve block in patients undergoing shoulder arthroscopy surgery, done by researchers from Korea.⁹ Overall, only very few studies from India have looked at the impact of add on magnesium sulfate during PNB across different surgeries. The dose of the magnesium sulfate used in these studies has varied from 125 mg to 1000 mg. However, nausea appears to be most common side effect, it was two to three times more likely in the first 12 hours after interscalene blocks with 200mg magnesium in the study done in Korea.⁹ Nausea seems to be dose dependent side effects as it was not reported in another study that used add on 150 mg of magnesium sulfate.

So, in this study we studied and compared the impact of two different doses of magnesium sulfate (125 mg and 250 mg) on inter scalene nerve block when used as an adjunct to local anesthetic (bupivacaine and lignocaine) during clavicular and proximal shaft humerus fracture surgeries. We measured the duration of postoperative analgesia, sensory and motor blockade and the incidence of nausea/vomiting of add on magnesium sulfate at 2 different doses. In addition, the time required for the onset of motor and sensory blockade as well as the pain at the surgery site in the post-operative period was also measured.

2. Materials and Methods

The institute ethics committee approved the study. All the consenting patients meeting the inclusion and exclusion criteria were included in the study. Patients of age between 18 years and 60 years, physical status ASA grade 1 and 2 undergoing elective clavicular and proximal shaft humerus fracture surgeries lasting more than 30 minutes were included in the study. Patients on antiplatelet or anticoagulant drugs, having local infection at the site of block, bleeding coagulopathy, neurological ailments such as peripheral neuropathy, chronic neuropathic pain, and nerve injury allergy to local anaesthetic were excluded from the study. Pregnant women and lactating mothers were also excluded from the study. Each patient was visited pre-operatively and the procedure explained and written and informed consent was obtained. All the routine investigations required for pre-operative evaluation and the

proposed surgery were done. All the patients were pre-medicated with tablet Alprazolam 0.5 mg a night before and on the morning of the surgery. Patients were on absolute fasting for at least 8 hours before surgery.

On arrival in the operating room, intravenous line was secured with 18G Intravenous cannula and patients were preloaded with lactated ringer's solution at 15ml/kg. Patients were randomized to two groups of 30 each by simple randomization sampling and the allocation concealment was done using sealed envelope technique. One group of patients (MS 250) received 20 ml of 0.5% bupivacaine + 10 ml of 2% lignocaine + 250 mg of magnesium sulfate (0.5 ml of 50% of magnesium sulfate with 0.5 ml of normal saline) and the patients in the other group (MS 125) received 20 ml of 0.5% bupivacaine + 10 ml of 2% lignocaine + 125 mg of magnesium sulfate (0.25 ml of 50% of magnesium sulfate with 0.75 ml of normal saline).

Patient being in supine position, under the aseptic precautions, under the guidance of ultrasound, inter scalene nerve plexus was identified. The anaesthetic agents and the magnesium sulfate was deposited perineurally to the inter scalene plexus using one inch and half inch 23 G hypodermic needle under ultrasound guidance. Monitoring of the vitals was done using automated multi-parameter monitor. Vital parameters like heart rate, non-invasive blood pressure, SPO₂ were recorded every 5 minutes till the end of surgery. Patients were assessed every 5 minutes until 30 min from the time of drug deposition by the anaesthesiologist who was blinded to randomisation. Sensory block was elicited by pinprick test using a three-point scale in the sensory dermatome distribution and compared with the contralateral arm as a reference: 0 = normal sensation; 1 = loss of sensation of pinprick (analgesia); and 2 = loss of sensation of touch (anesthesia).⁹ Motor block was elicited in accordance to shoulder movement using a three point scale: 0 = normal movement; 1 = diminished but not totally absent motor strength (paresis); and 2 = unable to elevate the arm (lack of movement).⁹ The sensory and motor blockades onset were defined as the time interval between the end of local anesthetic administration and the loss of sensation to pinprick (sensory score = 1) and absent movement (motor score = 2), respectively.

Post-surgery, the anaesthesiologist who monitored the patients intra operatively, assessed the patients every ten minutes until complete reversal of sensory and motor blockade. The duration of sensory block was defined as the time interval between the end of local anaesthetic administration and restoration of normal sensation. The motor block duration was taken from the end of local anaesthetic administration to the complete recovery of motor function. The duration of analgesia was the time between end of local anaesthetic administration to the demand of first rescue analgesic in the

postoperative period.

Postoperative pain was measured using a visual analogue scale (VAS) numeric rating-scale (VAS, from 0 = no pain to 10 = worst pain ever experienced) at 4, 8, 12, and 24 hours after the end of surgery. Rescue analgesia in the form of injection diclofenac 1.5mg/kg intramuscularly or Injection paracetamol 15 mg/kg was given to patients with VAS >4. The incidence of nausea/vomiting within the first 12 hours of post-operative period was noted down by interviewing the patients. The preparation of the local anaesthetic agent and magnesium sulfate was done by trained anesthesia assistants/nurses. They were aware of group allocation but took no further part in study. The patients and the anesthesiologists performing interscalene nerve block were blinded from the group allocation. The study was registered with clinical trial registry of India (CTRI/2018/11/016394). Data analysis was performed using R statistical software.¹⁰ Before the analysis, the data was screened for the normal distribution. Since the data was not normally distributed, the continuous variables across the groups were compared using Mann-Whitney U test. The categorical variables between the groups were compared using chi-square test. Associations with p-values less than 0.05 (2 sided) were considered statistically significant.

3. Results

There was no significant group difference in the distribution of the gender ($\chi^2 = 0.373$) and age (MS 125 v/s MS 250; Mean $\pm$ SD [Median]; 37.3 $\pm$ 13.2[35.5] years v/s 41.3 $\pm$ 13.4 [44] years) and the ASA physical status ($\chi^2 = 1.1$; p=0.3). There was no significant difference between the groups in the duration of sensory blockade [MS 125 v/s MS 250; Mean $\pm$ SD [Median]; 505.3 $\pm$ 44.6 (500) minutes v/s 501.1 $\pm$ 45.9(498) minutes; p= 0.65], duration of motor blockade [MS 125 v/s MS 250; Mean $\pm$ SD [Median]; 314.9 $\pm$ 31.1(307) minutes v/s 311.4 $\pm$ 34.2(305) minutes; p= 0.7] and the duration of post-operative analgesia [MS 125 v/s MS 250; Mean $\pm$ SD [Median]; 519 $\pm$ 46.1(512) minutes v/s 498 $\pm$ 95.8(507 minutes); p=0.43].

The mean and the median values of the onset of the sensory and motor blockades, VAS scores of pain at different post-operative intervals are mentioned in the Table 1. There was no significant difference between the groups in all the above parameters as assessed with Mann-Whitney U test. The incidence of nausea/vomiting within the first 12 hours of the post-operative period did not differ between the groups (Fisher's exact test: p=0.254).

4. Discussion

The findings of the current study suggest that the duration of sensory and motor blockade as well as the duration of post-operative analgesia in interscalene block is not different

when either 125 mg or 250 mg of adjunct magnesium sulfate is given along with local anaesthetic agent (20 ml of 0.5% bupivacaine + 10 ml of 2% lignocaine). Time needed for the onset of sensory and motor blockade was also not different between the groups.

Since we did not have a control group (without magnesium sulfate group) it is not possible from this study to infer whether the adjunct magnesium sulfate increase the motor and sensory nerve blockade period. But, the earlier findings consistently suggest increase in the motor and sensory blockade whenever magnesium sulfate is used as an adjunct to the local anaesthetic agent during PNB.⁸ But, an earlier study from India in patients undergoing upper limb surgeries with supra clavicular brachial plexus block found that the adjunct magnesium sulfate increases the duration of sensory and motor blockade but the difference was not statistically significant.¹¹ However, the finding that the either of 125 mg or 250 mg of adjunct magnesium sulfate could be used as an adjunct for interscalene nerve block without much difference in the nerve blockade and post-operative analgesia periods is a clinically relevant observation. In addition, the onset of nerve blockade as well as the pain scores within first 24 hours following surgery was also not different between the groups suggesting that the adjunct 125 mg magnesium sulfate may be as much useful as 250 mg of magnesium sulfate.

Although adjunct magnesium sulfate has been found to be having favourable effects, the exact dose to be used is still debated. In the literature, magnesium sulfate dose has ranged from 100 mg to 1000 mg.^{9,12} There has been an argument that the effect of adjunct magnesium sulfate is dose dependent and at high doses tolerability issues may come up. Higher doses of magnesium sulfate have been reported to be associated with adverse effects.¹³ So, the findings of the current study suggest that there is no dose dependent effect of magnesium sulfate on nerve blockade and other parameters measured in the study in the range of 125 to 250 mg. However, considering the smaller sample size of the current study, authors are cautious about the findings of the current study. Further randomised trials having more than 2 arms looking at the effect of adjunct magnesium sulfate with a larger sample size would be able to answer definitively the dose dependent nature of the magnesium sulfate effects on sensory and motor blockade as well as the post-operative analgesia.

The most commonly reported side effect with adjunct magnesium sulfate, nausea/vomiting, also did not differ between the groups, although MS 250 group patients had numerically higher incidence of nausea/vomiting. Overall, the findings of our study favour using 125 mg of adjunct magnesium sulfate for interscalene blockade, especially for the Indian subjects, as higher dose is not been shown to have any additional advantages.

Table 1: The comparison of baseline clinico-demographic factors and study objectives between the groups

Variable	Magnesium Sulphate 125 mg group (MS 125)Mean $\pm$ SD (Median) or n (%)	Magnesium Sulphate 250 mg group (MS 250)Mean $\pm$ SD (Median) or n (%)	P value
Age	37.3 $\pm$ 13.2 (35.5)	41.3 $\pm$ 13.4(44)	0.25
Sex			
Male	24 (80%)	22 (73.3%)	0.54
Female	6 (20%)	8 (26.7)	
ASA Physical status			
Grade I	20	16	0.3
Grade II	10	14	
Onset of sensory blockade	9.2 $\pm$ 1.3(10)	9.5 $\pm$ 1.2(10.2)	0.53
Onset of motor blockade	13.5 $\pm$ 2.4(14)	13.9 $\pm$ 1.17(14)	0.87
Duration of sensory blockade	505.3 $\pm$ 44.6(500)	501.1 $\pm$ 45.9(498)	0.65
Duration of analgesia	519 $\pm$ 46.1(512)	498 $\pm$ 95.8(507)	0.43
Duration of motor block	314.9 $\pm$ 31.1(307)	311.4 $\pm$ 34.2(305)	0.7
Visual Analogue Score			
4 hours	0.2 $\pm$ 0.4	0.2 $\pm$ 0.4	1
8 hours	3.5 $\pm$ 0.5(4)	3.5 $\pm$ 0.5(3.5)	0.8
12 hours	5.5 $\pm$ 0.5 (5.5)	5.3 $\pm$ 0.6(5.5)	0.45
24 hours	7.4 $\pm$ 0.56(7)	7.3 $\pm$ 0.6(7)	0.26
Nausea/Vomiting in the first 12 hours of the post-operative period			
Yes	2 (6%)	6 (20%)	0.25
No	28 (94%)	24 (80%)	

As mentioned earlier the primary limitation of our study is the limited sample size. Having had an additional arm of patients who were not given adjunct magnesium sulfate would have helped us to quantify the effect of magnesium sulfate on the duration nerve blockade and post-operative analgesia. To conclude, 150 mg magnesium sulphate is as much effective as 250 mg as an adjunct for the bupivacaine and lidocaine in interscalene blockade in prolonging nerve blockade and post-operative analgesia during upper limb surgeries. Both the doses are tolerated well. Further studies are needed with larger sample sizes to confirm our findings.

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