

Evaluation of magnesium as an adjuvant to ropivacaine-induced axillary brachial plexus block: A prospective, randomised, double-blind study

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ABSTRACT

Background and Aims: Axillary brachial plexus block is commonly performed for surgeries on the hand and forearm. However, there are very few studies on the use of magnesium sulphate in axillary brachial plexus block and, hence, the study was designed to evaluate magnesium as an adjuvant to ropivacaine-induced axillary block with respect to onset and duration of sensorimotor block and postoperative analgesia. **Methods:** Sixty patients of the American Society of Anesthesiologists (ASA) physical status I and II, undergoing surgeries on the hand and forearm were randomly recruited to receive ultrasound-guided axillary block with either 150 mg magnesium sulphate or 1 mL normal saline added to 0.5% ropivacaine. The primary outcome measure was to compare block characteristics including postoperative analgesia and the secondary outcome was to compare the use of rescue analgesia and the side-effect profile. Data were statistically analysed using Statistical Package for Social Sciences (SPSS version 21.0). Categorical variables were compared using the Chi-square test or Fisher's exact probability test; continuous variables compared using unpaired *t*-test or Mann-Whitney U test. **Results:** Onset of sensory (9.93 ± 1.31 vs 8.83 ± 1.12 min) as well as motor block (13.37 ± 1.63 vs 11.57 ± 1.30 min) was significantly hastened with addition of magnesium to ropivacaine ($p < 0.001$) and so was the duration (sensory 386.60 ± 18.26 vs 526.37 ± 27.43 , motor 323.73 ± 15.17 vs 436.97 ± 18.99 min) ($p < 0.001$) and postoperative analgesia (425 ± 21.39 vs 572.83 ± 32.04 min) ($p < 0.001$) which reflected in decreased requirement of rescue analgesic and total postoperative analgesic dosage. **Conclusions:** Magnesium is an effective and safe adjuvant to local anaesthetics and improves all characteristics of axillary brachial plexus block along with postoperative analgesia.

Key words: Axillary block, magnesium, ropivacaine

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INTRODUCTION

The axillary block is one of the most commonly performed regional anaesthesia technique for hand and forearm surgeries. Due to accurate placement of local anaesthetics, in close proximity to the target nerves, ultrasound guidance has shown higher success rate as well as lesser complications especially in the axillary block where the nerves are located around the axillary artery and they may have anatomically variable locations and course.^[1-3] Due to less cardiovascular and central nervous system toxicity, ropivacaine is proven to be a safer alternative to bupivacaine.^[4] Magnesium helps to regulate the amount of intracellular calcium

and is known to be able to control pain. Magnesium sulphate ($MgSO_4$) has analgesic, antihypertensive, anaesthetic sparing effects when used systemically.^[5,6] In recent times, $MgSO_4$ has been commonly used as an adjuvant to neuroaxial block, various peripheral nerve

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blocks as well as plane blocks.^[7-14] However, very few studies exist on MgSO₄ as an adjuvant in the axillary block. Hence, the present study was undertaken to assess the analgesic efficacy of MgSO₄ when added to ropivacaine in ultrasound-guided axillary brachial plexus block. Various studies have used different doses of MgSO₄ by various routes but the optimal dose for brachial plexus block is not yet ascertained. We used a dose of 150 mg based on studies conducted by Mukherjee *et al.* and Verma *et al.*^[15,16] We hypothesised that MgSO₄ improves the characteristics of the axillary block, hastening its onset and prolonging the duration as well as postoperative analgesia. The primary aim of our study was to evaluate the effect of MgSO₄ on the onset and duration of the axillary block along with postoperative analgesia and the secondary aim was to study its side effects if any, and to compare the requirement of rescue analgesics as well.

METHODS

After obtaining clearance from institutional ethical committee (Registration Number: ECR/275/Inst/MH/2013/RR-16), this study was conducted in a prospective, randomised, double-blind manner from July 2017 to June 2019. Sixty patients of either sex, age 18–60 years and American Society of Anesthesiologists (ASA) physical status I and II, undergoing surgeries on the hand and forearm, were recruited for the study. Patients with any contraindication to axillary block, those allergic to local anaesthetics, patients with neuropathies, pregnant and lactating females and patients who refused to participate in the study were excluded from the study [Consort diagram Figure 1].

A thorough assessment was done at preoperative visit including a detailed history, thorough general and systemic examination and review of investigations. Visual analogue scale (VAS) (0, no pain and 10, worst pain imaginable) was also explained during the preoperative visit. After explaining the procedure and the nature of safety of the procedure, a written, valid, informed consent was obtained and adequate starvation confirmed, on the day of surgery.

On arrival to the operation theatre, patient's baseline pulse rate, electrocardiogram and non-invasive blood pressure were recorded and a wide bore intravenous line established and an infusion started with lactated Ringer's solution. Hemodynamic variables were measured every 5 min until the end of surgery. Patients were randomly allocated into two equal

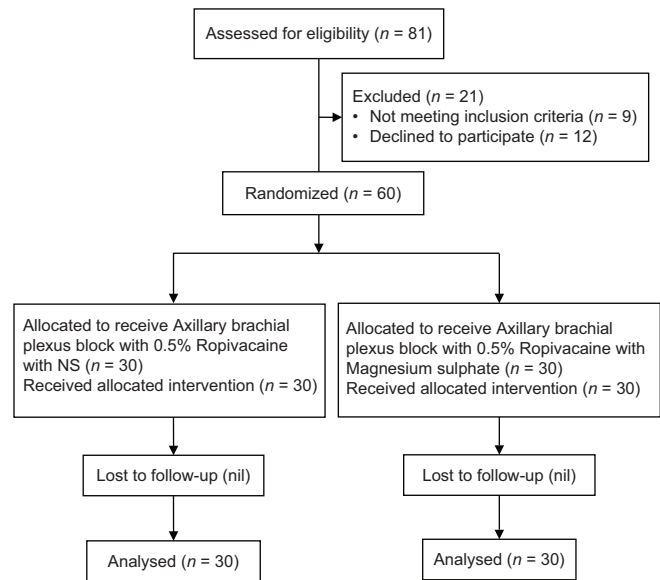


Figure 1: Patient flow (according to consort chart)

groups of 30 each by a computer-generated random number list. Patients in group A (control group) received 30 mL of 0.5% ropivacaine + 1 mL normal saline, and patients in group B (study group) received 30 mL 0.5% ropivacaine + 150 mg (diluted with 0.9% saline to make 1 ml) MgSO₄ for the block. The study drugs were provided in concealed envelopes. The same anaesthetist, who was blinded to the study drug, performed the block as well as observed the block characteristics intraoperatively and postoperatively.

The patient's position was supine and the operative arm was abducted, forearm supinated and elbow flexed with the hand above the head. The axilla was scanned using a high-frequency ultrasound probe (Sonosite NanoMaxx Ultrasound System with L25 13-6 MHz probe) placing it vertically at the level of anterior axillary fold. A preliminary scan was performed to identify structures – axillary artery, veins, nerves and muscles. In relation to the axillary artery, the median nerve lies at 11 O' clock, Ulnar nerve at 2 O'clock and radial nerve at 5–6 O' clock position. Nerves are seen as hyperechoic (bright) structures surrounding the artery. However, the nerves may not always be properly visualised and prescanning should always be done to localise the nerves. Nerve identity can be confirmed by scanning along the course of the nerve. On the lateral side of the axillary artery, biceps brachii (superficial) and coracobrachialis (deep) muscles can be identified. Musculocutaneous nerve usually lies within the coracobrachialis muscle proximally and pierces through it distally to lie between biceps and coracobrachialis. The most common

anatomical variation seen in 18% patients includes the musculocutaneous nerve being adherent to the median nerve and in such cases, a separate injection for the musculocutaneous nerve is not required.^[2,17]

The block was given with 22G hypodermic needle by in-plane approach. Having identified all four nerves, using ultrasound guidance, the local anaesthetic solution was injected around nerves with separate injections. The technique involved the injection of aliquots of 1.5–2 mL of the drug to further enhance the visualisation of the needle tip and increase the safety of injection.

Both the groups were compared with respect to the onset and duration of sensory and motor block, need of rescue analgesic, duration of postoperative analgesia and total dose of postoperative analgesic required in 24 h.

Sensory block was assessed by pinprick method in dermatomes of the sensory regions of the radial, median and ulnar nerves. The onset of sensory blockade was defined as the time interval between the end of injection and loss of sensation to pinprick. Sensory block was considered complete when there was a complete loss of sensation to pinprick. The intensity of the motor block was assessed using the modified Bromage scale at 1-minute intervals.

Assessment of motor block was carried out by the same observer at each minute till complete motor blockade after drug injection. The onset of motor blockade was defined as the inability to move the muscles of the forearm and hand against gravity. Complete motor block was defined as complete inability to move the limb and fingers (grade 0).

After the operation, the pain was assessed hourly by the VAS, with 0 being no pain at all and 10 being the worst imaginable pain. Rescue analgesia was provided by Inj. diclofenac sodium 75mg given intramuscular at VAS ≥ 3 . The total dose of diclofenac sodium given to each patient during the first 24 h of the postoperative period was recorded (maximum three injections in 24 h and duration between two injections at least 8 h).

The time from the end of anaesthetic injection in the operated hand until the first dose of postoperative rescue analgesic was recorded in each patient. The recovery of motor block was defined as the time when the patient regains the strength to move the relevant muscles against gravity. The recovery of sensory block was defined as the time to return of complete sensation.

The duration of sensory block was defined as the time interval between injection and complete recovery of sensation.

The duration of motor block was defined as the time interval between completion of injection and complete recovery of motor power.

The sample size was determined separately for each of the primary outcomes by using the effect sizes from the previously published studies. For each group, a sample size of 29 for the onset of block, 27 for the duration of block and 29 for postoperative analgesia was calculated to be sufficient to detect a clinically significant difference, considering 5% level of significance (type I error probability) and 80% power. As the maximum sample size calculated was 29, we took the sample size for our study as 30 in each group.^[15,18]

The data on categorical variables are shown as n (% of cases). The data on normally distributed continuous variables are presented as mean and standard deviation (SD) across two study groups. For non-normally distributed continuous variables median and min-max is used. Inter-group statistical comparison of the distribution of categorical variables is tested using Chi-square test or Fisher's exact probability test. Inter-group statistical comparison of means of normally distributed continuous variables is done using independent sample *t*-test (or unpaired *t*-test). Inter-group statistical comparison of medians of non-normally distributed continuous variables is done using the Mann-Whitney U test. The underlying normality assumption was tested before subjecting the study variables to *t*-test.

In the entire study, the *p* values less than 0.05 are considered to be statistically significant. The data are statistically analysed using Statistical Package for Social Sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows.

RESULTS

Both groups were comparable with respect to the demographic profile, baseline values of haemodynamic variables and surgical duration [Table 1]. The distribution of the type of surgeries (tendon reconstruction, nerve repair, internal fixation for fractures, contracture release) was comparable in both the groups.

The mean ± SD of the onset of sensory block in group A and group B was 9.93 ± 1.31 min and 8.83 ± 1.12 min, respectively. The mean onset of sensory block among the cases studied was significantly faster in group B compared to group A (*p* value < 0.001) [Table 2].

The mean ± SD of onset of motor block in group A and group B was 13.37 ± 1.63 min and 11.57 ± 1.30 min, respectively. The mean onset of motor block among the cases studied was significantly faster in group B compared to group A (*p* value < 0.001) [Table 2].

The mean ± SD of the duration of sensory block in group A was 386.60 ± 18.26 min while in group B it was 526.37 ± 27.43 min. The duration was sensory block was prolonged significantly in group B as compared to group A. (*p* value < 0.001) [Table 2].

The duration of motor block in group A was 323.73 ± 15.17 min whereas in group B it was 436.97 ± 18.99 min. The difference in the duration of motor block was highly significant statistically (*p* value < 0.001) [Table 2].

The duration of analgesia was significantly prolonged in group B as compared to group A (572.83 ± 32.04 min vs 425.00 ± 21.39 min, respectively) (*p* value < 0.001). Addition of magnesium to ropivacaine, prolonged the duration of analgesia by nearly 150 min [Figure 2].

The median total dosage of postoperative analgesics in group A was 150.00 mg which was double the dose requirement in group B (75.00 mg) (*p* value < 0.001).

Table 1: Demographic variables, baseline haemodynamic parameters and surgical duration			
Parameter	Group A (n=30)	Group B (n=30)	P
Age in years	38.17±12.15	43.33±12.19	0.106 ^{NS}
Sex (M:F)	19:11	18:12	0.999 ^{NS}
ASA (I/II)	22/8	21/9	0.999 ^{NS}
HR (/min)	76.77±8.76	76.00±8.74	0.115 ^{NS}
SBP (mmHg)	120.67±9.32	120.93±9.32	0.912 ^{NS}
DBP (mmHg)	76.47±6.07	77.63±6.85	0.488 ^{NS}
Duration of surgery (min)	123.17±15.85	122.07±14.80	0.782 ^{NS}

Values are mean±standard deviation. NS: Not significant statistically

Table 2: Block Characteristics			
Block characteristics	Group A (n=30)	Group B (n=30)	P
Onset sensory (min)	9.93±1.31	8.83±1.12	0.001*
Onset motor (min)	13.37±1.63	11.57±1.30	0.001*
Duration sensory (min)	386.60±18.26	526.37±27.43	0.001*
Duration motor (min)	323.73±15.17	436.97±18.99	0.001*

Values are mean±S.D. *Statistically significant

DISCUSSION

From the present study, it can be elicited that magnesium sulphate (MgSO₄) 150 mg, when used as an adjuvant to ropivacaine 0.5% (30 ml) in ultrasound-guided axillary brachial plexus block, hastens the onset of block, prolongs the duration of the sensorimotor blockade as well as postoperative analgesia.

Ropivacaine is a pure *S*-enantiomer with better sensorimotor differentiation and makes a safer alternative to bupivacaine, due to lesser cardiovascular toxicity.^[4] Dose selection of ropivacaine was by the recommendation of previous studies.^[14] Bertini *et al.* concluded that ropivacaine 0.5% has beneficial effects over bupivacaine in the axillary block and there is no further added advantage with the use of higher concentration of 0.75%.^[14]

MgSO₄ is an N-methyl-d-aspartate (NMDA) receptor antagonist and has been studied extensively for its analgesic efficacy by different routes.^[7-16,18] Gunduz *et al.* demonstrated that magnesium, when added to prilocaine, prolongs the duration of axillary plexus block.^[9] Dogru *et al.* also found an early onset with prolonged duration of block and postoperative analgesia when magnesium was added to levobupivacaine for axillary brachial plexus block in arteriovenous fistula surgery.^[12] In addition, they also observed that MgSO₄ allows the reduction in dose and concentration of local anaesthetics in chronic renal failure patients. Various studies have used different doses of MgSO₄ by various routes. We used a dose of 150 mg based on studies conducted by Mukherjee *et al.* and Verma *et al.*^[15,16] Mukherjee *et al.* They studied the effect of 150 mg of MgSO₄ with 30 mL ropivacaine in the supraclavicular block and concluded that MgSO₄ prolongs the sensorimotor duration and postoperative analgesia and has no significant side effects.^[16] The results of our study with respect to the duration of block and postoperative analgesia are in concordance with Mukherjee *et al.*,

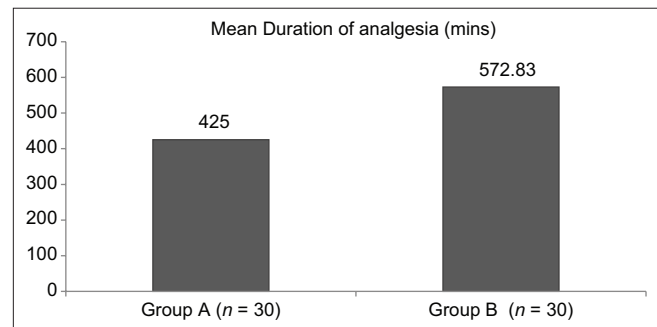


Figure 2: Inter-group comparison of the mean duration of analgesia

Verma *et al.* They studied two different doses (125 mg vs 250 mg) of magnesium sulphate as an adjuvant to bupivacaine in brachial plexus block and found a greater efficacy with higher doses. They found hastening of the onset of the block with MgSO₄ group that was dose-dependent.^[15] Mukherjee *et al.* used a larger volume of ropivacaine which reduces the effective concentration of MgSO₄ which explains the insignificant onset time in their study. We used 30 mL of 0.5% ropivacaine with 150 mg of MgSO₄ and found a faster onset. In our study, the magnesium group required significantly less dose of rescue analgesic, similar to that found in the previous studies.^[15,16] Various mechanisms have been postulated for the antinociceptive effect of MgSO₄. NMDA receptors, which are expressed in the central nervous system, regulate the cellular influx of Na⁺ and Ca⁺⁺ with outflux of K⁺. It has been suggested that calcium channel blockers and NMDA antagonists could play a significant role in the prevention of pain and treatment of established pain states.^[19-21] By blocking NMDA receptors, preventing central sensitisation, abolishing hypersensitivity and muscle relaxing effect, MgSO₄ produces analgesia and anaesthetic sparing effect in the perioperative period.^[5,6,19-21] None of the patients in either group in our study experienced undesirable effects of MgSO₄. Previous studies also stated that patients with MgSO₄ supplementation experienced better comfort levels and quality of sleep in the postoperative period without any major adverse effects.^[22]

There were no block failures or adverse events noted in any of the studied patients which could be attributed to the use of ultrasound and careful aspiration before injection of aliquots.

The limiting factor in our study could be a smaller sample size. Further multicentric studies should be carried out with a larger sample size to investigate efficacy and safety of MgSO₄. However, we found significantly prolonged analgesia with reduced postoperative analgesic consumption without any without any side effects. The beneficial effects on the block characteristics could be partly attributed to systemic absorption of MgSO₄ which we could not quantify in our study. In future, studies can be conducted, which include measurement of serum magnesium levels as well.

CONCLUSIONS

Addition of MgSO₄ 150 mg to 0.5% ropivacaine for USG-guided axillary brachial plexus block is

highly effective. It significantly hastens the onset of sensory as well as motor block, prolongs the duration of anaesthesia and postoperative analgesia. This resulted in a significant reduction in the requirement of systemic analgesics postoperatively, and, thus, conferred a definite therapeutic benefit.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil

Conflicts of interest

There are no conflicts of interest.

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