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Comparative Evaluation of Magnesium as an Adjuvant To 0.5% Bupivacaine and 0.5% Ropivacaine In Ultrasound Guided Interscalene Brachial Plexus Block.

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ABSTRACT

Background: To study the effect of magnesium sulphate as an adjuvant to Bupivacaine and Ropivacaine in ultrasound guided interscalene block in patients scheduled for orthopedic surgeries around the shoulder. **Methods:** Sixty patients (20–60 years) posted for elective orthopedic surgeries around the shoulder under interscalene brachial plexus block were divided into two Groups B and R in a randomized fashion. In group B (n = 30), 20 ml 0.5% bupivacaine plus 150 mg (3 ml of 50:1 solution) magnesium sulfate and in group R (n = 30), 20 ml 0.5% Ropivacaine plus 150 mg (3 ml of 50:1 solution) magnesium sulfate was administered in ultrasound guided interscalene block. After performance of the block it was evaluated for its onset time and duration of sensory and motor block every 3 min up to 30 min and subsequently hourly intervals up to 24hr. The time of first analgesic demand (VAS>4), total analgesic need, hemodynamic stability and side effects were recorded during the study. **Results:** The duration of sensory and motor block and the time to first analgesic demand was significantly longer (P<0.05) in Group B. In addition the total need for rescue analgesics in the post-operative period was also significantly lower (P<0.05) in this group compared to Group R. Intraoperative hemodynamics was comparable and no appreciable side effect was noted in the study. **Conclusion:** This study demonstrates that the addition of magnesium sulfate to Bupivacaine when compared to Ropivacaine in interscalene brachial plexus block provides enhanced sensory and motor block duration, prolonged duration of analgesia and decreased total postoperative analgesic needs with no side effects, hence could be a more rational combination.

Keywords: Magnesium Sulphate, Interscalene brachial block, Bupivacaine, Ropivacaine.

INTRODUCTION

Orthopedic surgeries are one of the most painful procedures associated with severe postoperative pain and discomfort.[1] Compared with general anesthesia, regional anesthesia has the additional advantage of decreased postoperative pain, decreased postoperative opioid requirement, help in early mobilization, decreased overnight hospitalizations, increased operating room efficiency and reduced recovery times.

In anesthesia practice interscalene block is a commonly used technique for shoulder surgery. The interscalene blocks have been shown to offer several advantages over general anesthesia for both open and arthroscopic surgical procedures.[2] Compared with general anesthesia, interscalene blocks decrease postoperative pain, decrease postoperative opioid requirement, helps in early mobilization, decrease overnight hospitalizations, increase operating room efficiency and reduce recovery times.

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An interscalene brachial plexus block is indicated for procedures involving the shoulder and upper arm. Roots C5-7 is most densely blocked with this approach. The principal indication for an interscalene block is surgery on or manipulation of the shoulder. This block provides excellent intraoperative anesthesia, muscle relaxation, and postoperative analgesia.[3,4] Recent studies of interscalene blocks have reported success rates (i.e., postoperative pain score ≤2 of 10) to be >99%.[5]

Ultrasound imaging guidance can potentially improve success rates and reduce the incidence of complications during interscalene brachial plexus block. It allows direct visualization of peripheral nerves, the block needle, and local anesthetic distribution. Many adjuvants have been introduced to improve the efficacy of neuraxial / regional analgesia, including NMDA antagonists (ketamine,

magnesium), GABA agonists (midazolam), and adrenergic agonists (clonidine, adrenaline), COX inhibitors (ketorolac), Ach esterase inhibitors (neostigmine) etc.

Magnesium, a cation existing inside the cell whose quantities are second only to potassium, acts as a physiological calcium antagonist. Magnesium's effects of N-methyl-D-aspartate (NMDA) receptor antagonism and sympathetic blocking have been noted, and magnesium is now used to help reduce the consumption of anesthetics and pain medications. Magnesium blocks the effects of excitatory amino acids (e.g., glutamate, aspartate) on NMDA receptors and contributes to central sensitization.

Bupivacaine and Ropivacaine are longest acting local anesthetics. Various studies have shown that the same volume and concentration of bupivacaine and ropivacaine for brachial plexus block anesthesia produce similar surgical block. In the quest for superior quality and prolonged post-operative analgesia we used magnesium sulphate as an adjuvant to bupivacaine and ropivacaine as studies on its use in ultrasound guided interscalene block had been sparse. In present study, we hypothesized that the difference in the interaction of magnesium, a divalent cation with bupivacaine, a racemic mixture and ropivacaine a pure S (-) enantiomer could be anticipated.

Hence purpose of this study was to evaluate the efficacy of magnesium sulphate (150mg) as an adjuvant to 0.5% Bupivacaine and 0.5% Ropivacaine on onset and duration of sensory and motor block and duration of postoperative analgesia to arrive at an ideal combination.

MATERIALS AND METHODS

Following approval of institutional Ethics Committee a prospective, randomized double blinded study was carried out in 66 consenting patients of both genders, aged 18–65 years, with American Society of Anesthesiologists (ASA) physical status I or II undergoing elective orthopaedic surgery around the shoulder under interscalene brachial plexus block.

The patients excluded from the study were those with severe pulmonary disease or contralateral phrenic nerve palsy, chronic treatment with calcium channel blockers, patients having bleeding disorders, hypersensitivity or allergy to study drugs used, infection at the site where needle for block was to be inserted, patients in whom the block effect was partial and required supplementary anesthesia.

The patients were randomly allocated to one of the two groups using random number chart. The study drug solution was prepared and given to the investigator. The observations were made by a second investigator blinded to the study drug used.

GROUP B (n=32) received 20 mL of 0.5% Bupivacaine + 150 mg MgSO4 (3 mL of 50:1 solution, total volume = 23mL). GROUP R (n=34) received 20 mL of 0.5% Ropivacaine + 150 mg MgSO4 (3 mL of 50:1 solution, total volume = 23mL).

The anesthetic procedure was explained to the patients enrolled for study and thereafter written consent was taken. Before commencing the surgery a case record form was filled for each patient. All patients were kept nil orally for at least six hours before the procedure. They were given premedication in the form of tablet Alprazolam 0.25mg and tablet Ranitidine 150 mg on the night before and at 6:00 am on the morning of surgery. On arrival to operation theatre standard monitoring (five lead ECG, NIBP, SPO2) was established with starting of peripheral I.V. line with normal saline in contralateral hand. Pulse rate, blood pressure, respiratory rate and SPO2 were noted.

The head was positioned, without a headrest, facing 450 to the contralateral side to be blocked. The area was cleaned with chlorhexidine and draped. The ultrasound 4 to16 Hz transducer (linear probe) was placed under sterile conditions in the interscalene groove and positioned in the transverse plane to identify the carotid artery. Once the artery was identified, the transducer was moved slightly laterally across the neck. Then the scalene muscles were identified and the brachial plexus that were sandwiched between the anterior and middle scalene muscles were identified, with typical ‘‘traffic-light sign’’ appearance. A sterile 50 mm 22G insulated needle was advanced using an in-plane technique toward the brachial plexus, typically in a lateral-to-medial direction. As the needle passes through the prevertebral fascia, a certain "give" was appreciated. After a careful aspiration to rule out an intravascular needle placement, 1 to 2 mL of local anesthetic is injected to document the proper needle placement. Injection of prepared local anesthetic solution was injected at various levels of the plexus, both peri-plexus and intra-plexus, tending to start from the deepest bundle and then moving superficially.

Sensory block assessment was done by pin prick with a 23 gauge hypodermic needle.

0 =No block

1 =Analgesia (dull sensation felt)

2 =Anesthesia (no sensation felt)

Motor block assessment was done by Bromage three point score:

0= Normal motor function with full flexion and extension of shoulder and elbow.

1= Decreased motor strength.

2= Complete motor blockade.

The time when motor block was achieved was noted. Block was evaluated every 3 minutes up to 30 minutes after the injection of local anesthetic was completed. Further block assessment was done at hourly intervals up to 24 hours.

Onset of sensory blockade was defined as interval between the end of injection and sensory blockade and was demonstrated as loss of sensation to pinprick i.e. score of 1.Onset of motor blockade was interval between the end of injection and complete motor paralysis i.e. score of 2.
The duration of sensory blockade was time interval between onset of sensory blockade and reappearance of pinprick response. The duration of motor blockade was defined as time interval between maximum motor blockade and complete movement of shoulder.

Pain assessment was done by using Visual Analogue Scale (VAS) which was obtained by asking the patient to rate the intensity of pain perceived by him and express it on a 11 point numerical scale 0-10.
0 = No pain (one extreme)
10 = Worst pain possible (other extreme)
Duration of analgesia was time from completing block to the time demanding first rescue analgesia (VAS>4). Rescue analgesia in the form of injection diclofenac 1.5mg/kg intramuscularly was given to patients with VAS > 4.

Data was collected and entered in MS EXCEL 2007. Statistical analysis was performed using SPSS software 17. The One sample Kolmogorov Smirnov test was employed to determine whether data sets differed from a normal distribution. Normally distributed data was analyzed using a repeat measures general linear model analysis of variance, whereas non normally distributed data was analyzed using the Mann-Whitney U test and categorical data was analyzed using Chi-square test. Level of significance "p" was considered significant < 0.05.

RESULTS

A total of 66 patients were included in the study with 32 patients having received 20ml of 0.5% bupivacaine (Group B) plus 150mg (3 ml of 50:1 solution) magnesium sulphate and the other 34 patients having received 20ml of 0.5% ropivacaine (Group R) plus 150mg (3 ml of 50:1 solution) magnesium sulphate. The number of patients who had partial block was 2 in group B and 4 in group R. After excluding the patients with failed or partial block, number of patients in Group B was 30 and in Group R were 30.

There were no significant differences in the demographic data of the patients and differences in the mean age, weight, height and sex in the two groups were not significant (p>0.05). All block randomization was done successfully. There was no statistically significant difference in the ASA physical status of the patients in the two groups and the mean duration of surgery. [Table 1]
All the patients were stable based on hemodynamic variables. No complications such as hypotension were reported and none were excluded from the study.

Table 1: Demographic Profile

S. No	Parameter	Groups		P value
		Group B	Group R	
1.	Mean age(years) ± SD	44.97±15.897	40.86±13.394	.289
2.	Mean weight(kg) ± SD	57.53±7.851	58.00±6.291	.802
3.	Mean height(m) ± SD	1.576±.0920	1.607±.0595	.131
4.	Mean BMI(kg/m2) ± SD	23.123±2.1597	22.440±2.3472	.249
5.	ASA grade (No. %)			.506
	ASA1	23(76.7%)	26(86.6%)	
	ASA2	7(23.3%)	4(13.3%)	
6.	Mean duration of surgery (min) ± SD	128.83±33.158	114.59±29.215	.086

The onset time for sensory block was 2.40±.675 min in group B and 2.59± .628 min in group R and it was not statistically significant (P>0.05).
The onset time for motor block in group B was 4.23±.817 min as compared to 4.31±.604 minutes in group R and was not statistically significant.(P>0.05). [Table 2]

Table 2: Comparison of mean duration of onset of sensory block and motor block.

	Group B	Group R	Df	F	P Value
Mean duration of onset of sensory block(min) mean±SD	2.40± .675	2.59± .628	57	0.005	.277
Mean duration of onset of motor block(min) mean±SD	4.23±.817	4.31±.604	57	1.347	.683

The mean duration of sensory block in group B was 325.83± 29.714 min as compared to 229.97±21.121 min in group R, which was found to be statistically significant (P value<0.000).Table 4, Figure 7.
Also the mean duration of motor block in group B was 287.50±29.704 min, and 190.48±21.580 min in group R, and the difference between the groups was statistically significant.(P value<0.000) [Table 3]

Table 3: Comparison of mean duration of sensory block and motor block.

	Group B	Group R	DF	F	P Value
Mean Duration Of Sensory Block(Min) Mean±SD	325.83± 29.714	229.97± 21.121	57	2.049	.000
Mean Duration Of Motor Block(Min) Mean±SD	287.50± 29.704	190.48± 21.580	57	2.600	.000

The mean duration of surgery in group B was 128.83±33.158 minutes and in group R was 114.59±29.215minutes. Both the groups were comparable with respect to the duration of surgery. (P>0.05) [Table 4]

The mean duration of analgesia in minutes of group B was 535.50± 42.938 min and in group R was 286.86± 24.213 min and this difference was statistically significant.(P value<0.000) [Table 4]

Also the number of rescue analgesic required in first 24 hours in group B was 1.67±.711, as compared to 2.45±.572 in group R and this was also found to be statistically significant.(P value<0.000). [Table 4]

Table 4: Comparison of mean duration of surgery, mean duration of analgesia and number of rescue analgesic in 24 hours

	Group B	Group R	Df	F	P Value
Mean duration of surgery (min) mean±SD	128.83± 33.158	114.59± 29.215	57	.085	.086
Mean duration of analgesia (min) mean±SD	535.50± 42.938	286.86± 24.213	57	7.734	.000
No. of rescue analgesics in 24 hours	1.67±.711	2.45±.572	57	1.863	.000

DISCUSSION

For many decades magnesium salts have been used as an adjuvant to general anesthesia and in critical care. Magnesium sulphate has been reported to be effective in perioperative pain treatment and in blunting somatic, autonomic and endocrine reflexes provoked by noxious stimuli.[6] Magnesium, by virtue of its NMDA receptor antagonist property, has been investigated in various routes for providing pre-emptive analgesia and also to prolong postoperative analgesia.

The primary hypothesis for the action of magnesium on peripheral nerves is the surface charge theory. Akutagawa and colleagues showed that modulation of the external magnesium concentration bathing a nerve bundle resulted in enhancement of the nerve blockade of the local anesthetics.[7] Mert and colleagues reported that a high concentration of divalent ions (Mg2+ and Ca2+) attracted by the negative charges of the outer membrane surface affected Na+ channel gating and caused hyperpolarization.[8] In the hyperpolarized nerve fiber it is more difficult to achieve the threshold level resulting in nerve conduction block. The mechanism of action of magnesium can also be attributed to its direct action on the peripheral nerve by virtue of its blocking the release of excitatory neurotransmitter at the synaptic junction and hence further potentiating the effect of local anesthetic.

The dose of 150mg of magnesium sulphate in this study was used in accordance to studies done by Goyal and colleagues and Mukherjee and colleagues without any reported side effects and neurotoxicity.[9,10]

Bupivacaine and Ropivacaine are both long acting amino amide type local anesthetic agents. In clinical studies comparing potencies of ropivacaine and bupivacaine administered for brachial plexus, the anesthetic profile of the drugs were almost similar. Both have the clinical advantage of long duration of action, when used in a concentration of 0.25-0.5% and with favorable ratio of sensory to motor neuronal blockade.[11-13]

Ropivacaine is a pure S(-) enantiomer, unlike bupivacaine, which is a racemate and was developed for the purpose of reducing potential toxicity and improving motor and sensory blocking profile.[14] It has propyl group on piperidine nitrogen as compared to butyl group of bupivacaine.

Enantiomers exist in two different spatial configurations. A racemic mixture contains both the enantiomers in equal amounts. The physiochemical properties of two enantiomers are identical, but the two enantiomers can have substantially different behaviors in their site on action or the site for producing side effects.[15] R (+) and S (-) enantiomers of local anesthetics exhibits different affinity for different ion channels of sodium, potassium and calcium; this results in significant reductions in central nervous system and cardiac toxicity with S (-) enantiomer as compared to R(+) enantiomer.[16,17]

The volume of local anesthetic used in this study is 23 mL, which is the volume of drug used in various studies on ultrasound guided interscalene brachial plexus block for providing perioperative anesthesia and analgesia.[18,19]

The onset of sensory block (2.40±.67min for Group B and 2.59±.62min for Group R) and motor block (4.23±.81min for Group Band and 4.31±.60min for Group R) was clinically faster in the present study compared to a similar study done Eroglu A13 who reported a onset of block to be 21±13 min with bupivacaine and18±12min with ropivacaine. This could be attributed to the use of magnesium as an

adjuvant and also to the fact that present study was ultrasound guided. Further the onset of block was faster with ropivacaine compared to bupivacaine as reported by Eroglu A which was in contrast to the present study.

In the present study the addition of magnesium seems to have delayed the onset of both sensory and motor block with ropivacaine compared to bupivacaine but it was not statistically significant($p>0.05$)as also reported by Lee and Bertini.[20,21] The latter had observed that onset of block (16.37min for bupivacaine and 22.3min for ropivacaine) was more delayed for ropivacaine similar to the present study.

The mean duration of sensory block was higher in Group B (325.83±29.715min) as compared to Group R (229.97±21.121min)($p<0.000$) in the present study. This finding is similar to the study done by Kaur who reported sensory block duration significantly higher in bupivacaine group (450.40±54.50min) as compared to ropivacaine group(421.20±38.33min) (pvalue0.033).[22] The comparatively lesser duration of sensory block was in present study can be explained on the basis of lesser volume of local anesthetic 23 ml versus 40 ml used by Kaur and colleagues.

Further the mean duration of motor block was significantly longer in group B was (287.50±29.704 min) as compared Group R (190.48±21.580 min) (P value=0.000).This was consistent with the study by Kaur and colleagues.

The duration of analgesia in group B (535.50± 42.938 min) was significantly prolonged compared to group R was (286.86± 24.213 min) (P value<0.05) in our study. This finding was in agreement with the clinical study by Lee et al who investigated the effect of adding magnesium sulphate to bupivacaine with epinephrine on the duration of sensory and motor blocks along with the analgesic qualities of interscalene nerve blocks in patients undergoing arthroscopic rotator cuff repair.[20] The duration of analgesia was prolonged by nearly two hours in the Magnesium group (664 min) compared with the saline group (553 min) ($p = 0.017$).

The number of rescue analgesic required in the present study in first 24 hours was significant less in group B (1.67±.711) as compared to group R (2.45±.572) (P value<0.05). This was consistent with study done by Mukherjee et al who observed that the time to first analgesic use was significantly longer and the total need for rescue analgesics was lower in group RM than group RN($p=0.026$).[10]

CONCLUSION

The following conclusions were drawn from the study

1) The duration of sensory and motor block was longer when magnesium was combined with bupivacaine as compared to when used with ropivacaine. The duration of postoperative analgesia was also significantly longer in this group leading to decreased frequency and total dose of rescue analgesics requirements up to 24 hr. postoperatively.
2) Both the groups remained hemodynamically stable.
3) No adverse effects were observed with the use of magnesium sulphate in brachial block.

Hence the combination of magnesium sulphate with bupivacaine appears to be superior as compared to magnesium sulphate and ropivacaine, in view of prolonged post-operative analgesia and less analgesic requirement in the post-operative period.

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