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Evaluation of Varying Doses of Magnesium as an Adjuvant to Ropivacaine in Supra Clavicular Brachial Plexus Block

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Abstract

Peripheral nerve blockade is one of the components of comprehensive anaesthesia care because of its distinct advantages over central neuraxial blockade and general anaesthesia. Peripheral Nerve Blockade provides more effective analgesia with fewer side effects than opioid and other oral analgesics. Hence, various adjuvants like opioids, clonidine, neostigmine, dexamethasone, midazolam, etc., were added to local anaesthetics in brachial plexus block to achieve quick, dense and prolonged block, but the results are either inconclusive or associated with side effects Magnesium has been used in intravenous, intrathecal, epidural/caudal routes to improve analgesia. After obtaining permission from our institutional ethical committee, written informed consent was taken from all the study subjects. Totally 90 patients were randomly allocated to three equal groups (n=30 in each group) using computer generated random number list. This study is a prospective double-blinded randomized controlled study. Inclusion Criteria are Both sexes, Aged 18-60 yrs, belonging to ASA I and II, posted for elective upper limb surgeries in sree Mookambika college. Supra clavicular block is administered at the level of nerve trunk of the brachial plexus. The sole sensory, motor and sympathetic supply of upper limb are conducted by three nerve trunks contained in a very small, compact, easily accessible and relatively superficial area. Magnesium sulphate has been used as an adjuvant with local anaesthetics under neuraxial anaesthesia in both spinal and epidural routes, even with different doses. This study it is concluded that on addition of both 100 mg and 150 mg magnesium sulphate to 0.5% ropivacaine in supra clavicular brachial plexus block significantly prolongs the duration of sensory and motor blockade and significantly reduces the requirement of rescue analgesic in postoperative period but delays the onset time of sensory and motor blockade. But both 100 mg and 150 mg magnesium had similar efficacy of postoperative analgesia.

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Key Words
Ropivacine, supra clavicular block

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INTRODUCTION

Peripheral nerve blockade is one of the components of comprehensive anaesthesia care because of its distinct advantages over central neuraxial blockade and general anaesthesia. Peripheral Nerve Blockade provides more effective analgesia with fewer side effects than opioid and other oral analgesics. Its role has expanded from operating room to postoperative and chronic pain management. With careful selection and sedation these techniques can be employed in all age groups. Skilled application of peripheral neuraxial blockade expands anaesthesiologist's variety of options in giving optimal anaesthetic care. In emergency surgeries for full stomach patients, there is less danger of aspiration even if they vomit because they can be awake. Complications and side effects of general anaesthesia such as post-operative nausea vomiting, atelectasis, ileus, delirium and deep vein thrombosis are reduced[1-9]. In peripheral nerve blockade, the sympathetic nerves of anaesthetized limb are blocked, leading to vasodilation and this improves blood flow to the limb and makes microvascular surgeries easy. The anaesthetized hand or foot remains numb for many hours after surgery, thus providing excellent post operative pain relief. Both deep as well as superficial structures in the limb are similarly anesthetized, permitting extensive surgical exploration and repair[10]. This contrasts with locally injected local anaesthetic drugs which tend to numb only the superficial structures close to the site of injection. Brachial plexus blockade provides superior pain control with excellent intraoperative anaesthesia as well as post-operative analgesia, eliminating the need for intra-operative opioids and minimizing the need for post-operative opioids. This results in quicker recovery, shortened hospital stay, increased patient satisfaction as well as surgeon satisfaction and ultimately a decrease in financial burden to the patient when compared to general anaesthesia thus permitting its use in day care surgeries. Peripheral nerve blockade of upper limb includes various methods of brachial plexus block where brachial plexus is blocked at different levels. Supra clavicular block once described as the "spinal of the arm 1" offers dense anaesthesia of the brachial plexus for surgical procedures at or distal to the elbow. At this point, the brachial plexus is compact and a small volume of solution produces rapid onset of reliable blockade of the brachial plexus 2. Historically, supra clavicular block fell out of favour due to high incidence of complications (pneumothorax, accidental intra vascular injection) that occurred with paraesthesia and nerve stimulator techniques. It has seen a resurgence in recent years as the use of ultrasound guidance has improved safety[11-18]. Ropivacaine is a long acting regional anaesthetic that is structurally related to bupivacaine. It was developed for reducing systemic toxicity and improving relative sensory to motor block profiles. Local anaesthetics alone for supra clavicular brachial plexus block provide good operative conditions but have shorter duration of postoperative analgesia 3. Local anaesthetic adjuvants have been studied previously in an attempt to prolong the duration of analgesia after peripheral nerve blockade[19,20]. Hence, various adjuvants like opioids, clonidine, neostigmine, dexamethasone, midazolam, etc., were added to local anaesthetics in brachial plexus block to achieve quick, dense and prolonged block, but the results are either inconclusive or associated with side effects. Magnesium has been used in intravenous, intrathecal, epidural/caudal routes to improve analgesia. Its role in peripheral nerve blocks has only minimal literature and available literature has shown mixed results. Hence this study was designed to evaluate the efficacy of magnesium when added to ropivacaine in supra clavicular brachial plexus block.

Aims and Objectives of the Study: This study is aimed to assess when two different doses of Magnesium added as an adjuvant to Ropivacaine in Ultrasound guided supra clavicular brachial plexus block may enhance the duration of sensory and motor block, duration of analgesia and quality of block and side effects using various parameters and to find out the minimum dose needed to achieve the desired effects. The primary objectives is to assess the onset and duration of sensory and motor blockade and duration of post op analgesia. The secondary objectives is to assess the total rescue analgesics, Visual Analog Scale(VAS) Score and side effects.

MATERIALS AND METHODS

After obtaining permission from our institutional ethical committee, written informed consent was taken from all the study subjects. Totally 90 patients were randomly allocated to three equal groups (n=30 in each group) using computer generated random number list. This study is a prospective double-blinded randomized controlled study. Inclusion Criteria are Both sexes, Aged 18-60 yrs, belonging to ASA I and II, posted for elective upper limb surgeries in GTMCH. (Surgeries of distal humerus, elbow, forearm and hand) Exclusion Criteria are Patient refusal, Pregnant and lactating mothers, ASA III and IV, Known Allergy/ contraindication to local anaesthetic, Patients having peripheral neuropathy and pre existing neurological defects in upper limbs. Known cases of seizure disorder, Patients with co agulopathies and patients on chronic anticoagulation therapy, Patients with psychiatric illness and local skin infections. They are randomly divided into three groups A, B and C.

- **Group A (30 Patients):** Ropivacaine and Normal Saline.

- **Group B (30 Patients):** Ropivacaine and Magnesium (100mg).
- **Group C (30 Patients):** Ropivacaine and Magnesium(150 mg).

- **Group A:** 20 ml 0.5% Ropivacaine plus 1.5 ml of NS.
- **Group B:** 20 ml 0.5% Ropivacaine plus 100 mg MgSO4(diluted in 1.5 ml NS).
- **Group C:** 20 ml 0.5%Ropivacaine plus 150 mg MgSO4 (diluted in 1.5 ml NS) So all the three group of patients received a total of 21.5 ml of the test drug.

The patients were randomly allocated using computer generated random number to one of the three groups of 30 patients each. Visual Analog Scale (VAS)score (0, no pain and 10, worst pain imaginable) was also explained during preoperative visit. Patients were kept Nill Per Oral for 8 hrs before surgery. Patients were premedicated with Inj. Ranitidine 50 mg and Inj. Metoclopramide 10 mg im 45 minutes before surgery. Intravenous line was secured on the limb opposite to surgery. Intravenous infusion of Ringer Lactate(RL) was started and oxygen was given at 4 L/min via face mask. All patients received Inj. Midazolam 0.03 mg/kg iv before procedure. Blocks were performed under standard monitoring with pulseoxymetry, non-invasive BP and ECG. After proper explanation of technique and positioning, a linear high frequency Sonoray USG probe is placed in the supra clavicular fossa just superior to clavicle. The subclavian artery is easily identified by its pulsation. The brachial plexus appears as multiple hypoechoic grape like structures just superficial and lateral to subclavian artery. The 1st rib is identified as hyper echoic line just deep to the artery. The pleura is also found as a hyper echoic line which moves with respiration. By In-plane technique, a 18 gauge venflon needle is used and after careful aspiration of non appearance of blood, drug was injected as per allotment of the group. Local anaesthetic spread was visualized surrounding the plexus. Surgery was started after confirming adequacy of sensory and motor blockade. Sensory and motor blockade were assessed every 3 min after completion of injection till starting of surgery and then every 1 hour after the end of surgery till first 12 hr, or until the block had completely worn off, whichever is earlier. Statistical analysis was done using the statistical package for social sciences (SPSS). Different statistical methods were used as appropriate. Mean±SD was determined for quantitative data and frequency for categorical variables. The independent t-test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group difference for categorical variables. A p-value <0.05 was considered significant.

RESULTS AND DISCUSSIONS

This study comprised of 3 groups. The patients were randomly selected. Group A-30 patients received Ropivacaine and 1.5 ml NS. Group B-30 patients received Ropivacaine and 100 mg MgSO4 Group C-30 patients received Ropivacaine and 150 mg MgSO4. The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer by using SPSS 16 software. Using this software, 'p' values were calculated through Student ‘t’ test for two group comparison and One way ANOVA test for three groups and chi square test for consolidated data to test the significance of difference between variables.'P' value <0.05 is taken to denote significant relationship.

Table 1: ASA Risk Group (A-C)

ASA Risk	Group A	Group B	Group C
I	17	16	22
II	13	14	8
TOTAL	30	30	30
‘P'	0.235 Not significant		

Time for onset of sensory block in Group A varies from the minimum of 6 min to the maximum of 18 min, with the mean of 10.7 min and the standard deviation of 2.693. In group B, it varies from minimum of 6 min to the maximum of 24 min, with the mean of 13.6 min and the standard deviation of 3.41. In group C, it varies from minimum of 9 min, to the maximum of 21 min, with the mean of 14.9 min and the standard deviation of 3.977. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.242 which is not statistically significant.

Onset of Motor Blockade: Time for onset of motor blockade in Group A varies from the minimum of 9 min to the maximum of 24 min, with the mean of 14.767 min and the standard deviation of 3.401. In group B, it varies from minimum of 9 min to the maximum of 27 min, with the mean of 18.1 min and the standard deviation of 3.478. In group C, it varies from minimum of 12 min, to the maximum of 27 min, with the mean of 19.4 min and the standard deviation of 4.709. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.252 which is not statistically significant.

Duration of Sensory Blockade: Duration of sensory blockade in Group A varies from a minimum of 300 min to a maximum of 600 min, with the mean of 442 min, and the standard deviation of 74.713. In group B, it varies from minimum of 360 min to the maximum of 660 min, with the mean of 566 min and the standard

deviation of 64.359. In group C, it varies from minimum of 240 min, to the maximum of 720 min, with the mean of 592 min and the standard deviation of 84.462. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant.

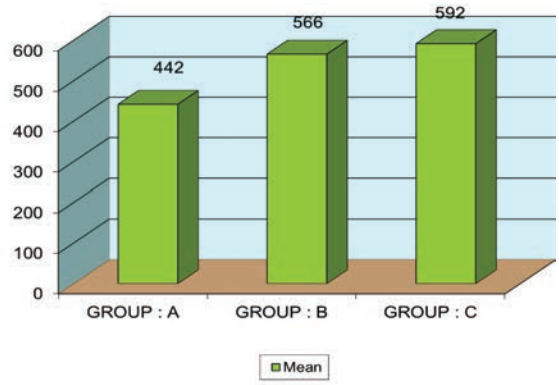

Fig. 1: Duration of Sensory Blockade(min)

Duration of Motor Blockade: Duration of motor blockade in Group A varies from a minimum of 240 min to a maximum of 540 min, with the mean of 352 min, and the standard deviation of 76.762. In group B, it varies from minimum of 240 min to the maximum of 600 min, with the mean of 466 min and the standard deviation of 81.393. In group C, it varies from minimum of 180 min, to the maximum of 600 min, with the mean of 496 min and the standard deviation of 83.278.P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.164 which is not statistically significant.

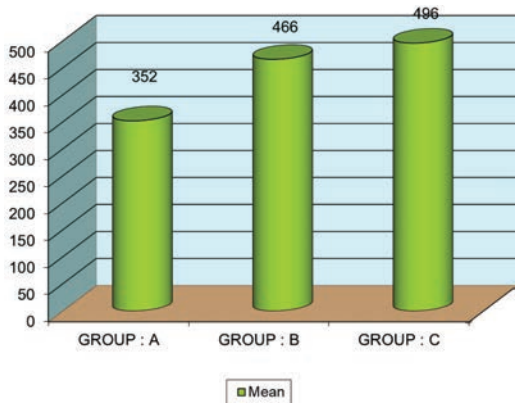

Fig. 2: Duration of Motor Blockade(min)

First Rescue Analgesic Post-Op: The first rescue analgesic given in Group A varied from 310 min-650 min postoperatively with a mean of 474.6 min and Standard deviation of 78.3. The first rescue analgesic given in Group B varied from 375 min-685 min postoperatively with a mean of 599.4 min and Standard deviation of 63.1 The first rescue analgesic given in Group C varied from 280 min-733 min postoperatively with a mean of 613.2 min and Standard deviation of 80.7. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.464 which is not statistically significant.

Number of Rescue Injections in First 24 Hours: The total no of rescue analgesic injections given in first 24 hours in Group A varied from 1-2 injections with a mean of 1.67 injection and Standard deviation of 0.479. The total no of rescue analgesic injections given in first 24 hours in Group B varied from 1-2 injections with a mean of 1.33 injection and Standard deviation of 0.479. The total no of rescue analgesic injections given in first 24 hours in Group C varied from 1-2 injections with a mean of 1.3 injection and Standard deviation of 0.466. P value between Groups A and B is 0.008 which is statistically significant. P value between Groups A and C is 0.004 which is also statistically significant. But P value between Groups B and C is 0.807 which is not statistically significant.

Supra clavicular block is administered at the level of nerve trunk of the brachial plexus. The sole sensory, motor, and sympathetic supply of upper limb are conducted by three nerve trunks contained in a very small, compact, easily accessible and relatively superficial area. As a result of this block, a prompt onset of profound anaesthesia is achieved with high level of certainty. Local anaesthetics alone for supra clavicular brachial plexus block provide good operative conditions but have shorter duration of postoperative analgesia. Magnesium sulphate has analgesic, anti hypertensive, anaesthetic sparing effects when used in systemic route[21-28]. Magnesium sulphate has been used as an adjuvant with local anaesthetics under neuraxial anaesthesia in both spinal and epidural routes, even with different doses. Mixing magnesium sulphate as adjuvant with local anaesthetics during peripheral nerve and nerve plexus blockade has recently been practiced by anesthesiologists[38-40]. The main hypothesis of our study, regarding the dose dependent effect of MgSO4 as an adjuvant to local anaesthetics on peripheral nerves is based on the surface charge theory as explained by Akutagawa *et al.* They proved that modulation of the external magnesium concentration resulted in the synergistic effect on nerve blockade due to local anaesthetics. In our study, we evaluated the efficacy of magnesium as an adjuvant to ropivacaine in supra clavicular block. We compared 2 different doses of 100 mg and 150 mg of magnesium Sulphate added to ropivacaine and

divided the patients into 3 groups, one without magnesium and other two groups with the above doses of magnesium. The demographic profile of all the patients was statistically insignificant between the three groups, quite similar with other research investigators and thus provided us the uniform platform to compare the results obtained[41-45]. Ropivacaine was chosen for our study because it had better sensory to motor block profile and lesser cardiotoxicity than bupivacaine. This was in accordance with the study done by Hofmann[48] and Raeder[51]. Magnesium was chosen for study because it has been used as an adjuvant with local anaesthetics for neuraxial anaesthesia in both spinal and epidural routes, even with different doses and many studies are available. Mixing magnesium sulphate with local anaesthetics during peripheral nerve plexus blockade is recently being practiced by anaesthesiologists and has only limited literature. The doses of 100 mg and 150 mg of Magnesium was chosen based on the previous studies done by Verma[52] where they used $MgSO_4$ in the doses of 125 mg and 250 mg with ropivacaine and Mukher jee *et al* who used 150 mg of $MgSO_4$ with ropivacaine in supra clavicular brachial plexus block.

Onset of Sensory Blockade: The mean time of onset of sensory blockade was 10.7±2.693 min in Group A and 13.6±3.41 min in Group B and 14.9± 3.977 min in Group C. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.252 which is not statistically significant. Thus from our study it was concluded that on addition of magnesium to ropivacaine, the onset of sensory blockade was delayed significantly. This was comparable to the study done by Mukherjee[3] whose time of onset of sensory block was 15.91±1.60 min Vs 16.27±3.07 min and Gupta whose time of onset of sensory block was 16.63±2.79 min Vs 17.33±2.25 min who also had delayed onset but both studies it was not of statistical significance. Also in our study there was no significant difference of onset of sensory blockade between the two groups with 100 mg and 150 mg magnesium[46,47]. (P value 0.252). The mean time of onset of motor blockade was 14.767±3.401 min in Group A and 18.1±3.478 min in Group B and 19.4± 4.709 min in Group C. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.252 which is not statistically significant. Thus from our study it was concluded that on addition of magnesium to ropivacaine, the onset of motor blockade was delayed significantly. This was comparable to the study done by Mukherjee[3] whose time of onset of motor block was 17.80±7.6 min Vs 19.2±6.2 min(P value 0.30) and Gupta whose time of onset of motor block was 18.63±2.79 min Vs 19.76± 2.18 min (P value <0.05) who also had delayed onset. But in our study there was no significant difference of onset of motor blockade between the two groups with 100 mg and 150 mg magnesium[49,50]. (P value 0.252). The mean duration of sensory blockade was 442±74.713 min in Group A and 566±64.359 min in Group B and 592±84.462 min in Group C. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.185 which is not statistically significant. Thus from our study it was concluded that addition of magnesium to ropivacaine, prolongs the duration of sensory blockade significantly. This was comparable to the study done by Mukherjee[3] whose duration of sensory block was 289.67±62.50 min Vs 456.21±97.99 min (P value 0.001) and Verma[52] whose duration of sensory block was also prolonged significantly. But in our study there was no significant difference in the duration of sensory blockade between the two groups with 100 mg and 150 mg magnesium. (P value-0.185). The mean duration of motor blockade was 352±76.762 min in Group A and 466±81.393 min in Group B and 496±83.278 min in Group C. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.164 which is not statistically significant. Thus from our study it was concluded that addition of magnesium to ropivacaine, prolongs the duration of motor blockade significantly. This was comparable to the study done by Mukherjee[3] whose duration of motor block was 242.16 ± 23.86 min Vs 366.62±24.42 min (P value 0.012) and Verma[52] whose duration of motor block was also prolonged significantly. But in our study there was no significant difference in the duration of motor blockade between the two groups with 100 mg and 150 mg magnesium. (P value-0.164)[29-32]. VAS Score was calculated for first 12 hours postoperatively. It was significant in 7th hour (P<0.001), 8th hour (P<0.001), 9th hour (P-0.008) and 10th hour (P value-0.004), It is comparable to the study done by Gupta in which the VAS Score was significant at 6th and 12th hours. The mean time to first rescue analgesic given in Group A was 474.6±78.3 min and in group B it was 599.4±63.1 min and in Group C it was 613.2±80.7min. P value between Groups A and B is <0.001 which is statistically significant. P value between Groups A and C is <0.001 which is also statistically significant. But P value between Groups B and C is 0.464 which is not statistically significant[33-37]. Thus it is strongly

concluded that magnesium prolongs the duration of postoperative analgesia when it is added to the local anaesthetic. This is similar to the studies done by Gupta in which time to first rescue analgesic prolonged from 377.67±73.31 min-491±100.22 min and similar to Mukherjee[3] whose post op analgesia increased from 379.79±145.52 min-461.71±152.57 min and similar to the studies of Verma[52]. But the difference in post op analgesia between 100 mg (599.4 min) and 150 mg (613.2 min) magnesium is not significant. (P value-0.464). So 100 mg magnesium is equally efficacious to 150 mg of $MgSO_4$ when added to ropivacaine in supra clavicular block. The mean no of rescue analgesic injections given in first 24 hours in Group A was 1.67±0.479 injections and in Group B it was 1.33±0.479 injections and in Group C it was 1.3± 0.466 injections. P value between Groups A and B is 0.008 which is statistically significant. P value between Groups A and C is 0.004 which is also statistically significant. But P value between Groups B and C is 0.807 which is not statistically significant. Thus it is inferred that addition of magnesium to ropivacaine significantly reduced the number of rescue injections postoperatively and thereby minimizes the use of systemic opiods. This is in accordance to the study done by Mukherjee[3]. ELShamaa[42] also concluded that much less amount (35.6 mg vs. 113.6 mg) of diclofenac sodium was administered as rescue analgesic in bupivacaine plus magnesium group than in control group. But in our study the no of rescue injections did not differ much between 100 mg and 150 mg magnesium(P value-0.807). So 150 mg of $MgSO_4$ does not have any extra benefit than 100 mg $MgSO_4$ in reducing the post op opiod consumption. The possible side-effects are: Nausea, Vomiting and Hypotension. One patient in group B suffered from nausea which was managed conservatively with iv fluids. One patient in group C suffered from vomiting which was managed with iv fluids and IM metoclopramide 10 mg. In our study, no patient had hypotension. Choi *et al* also found similar side effects (nausea, vomiting, dizziness), but the difference between magnesium and normal saline group was also not significant (P=0.62).

CONCLUSION

From this study it is concluded that on addition of both 100 mg and 150 mg magnesium sulphate to 0.5% ropivacaine in supra clavicular brachial plexus block significantly prolongs the duration of sensory and motor blockade and significantly reduces the requirement of rescue analgesic in postoperative period but delays the onset time of sensory and motor blockade. But both 100 mg and 150 mg magnesium had similar efficacy of postoperative analgesia. Thus it is inferred that 100 mg magnesium is enough in supra clavicular block to achieve the desired effects.

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