International Journal of Anesthesia and Clinical Medicine
2019; 7(1): 13-19
http://www.sciencepublishinggroup.com/j/ijacm
doi: 10.11648/j.ijacm.20190701.13

The Effect on Outcome of Adding Magnesium Sulphate to Bupivacaine in the Ultrasound-guided Supraclavicular Brachial Plexus Block Anesthesia

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To cite this article:

Ashraf Mohamed Ghali, Khalid Mohamad Awid Molokhia, Sameh Abdelkhalik Ahmed. The Effect on Outcome of Adding Magnesium Sulphate to Bupivacaine in the Ultrasound-guided Supraclavicular Brachial Plexus Block Anesthesia. *International Journal of Anesthesia and Clinical Medicine*. Vol. 7, No. 1, 2019, pp. 13-19. doi: 10.11648/j.ijacm.20190701.13

Received: December 28, 2018; **Accepted**: February 19, 2019; **Published**: March 5, 2019

Abstract: This study evaluated the motor and sensory block durations and the postoperative analgesic effects of adding Magnesium Sulphate to Bupivacaine HCL for Ultrasound-guided supraclavicular brachial plexus block. Sixty ASA I-II patients subjected to elective forearm or hand surgery were randomly divided equally into 1 of 2 groups depending upon the local anesthesia (LA) solution used to receive either 23 mL of bupivacaine HCL 0.5% plus 2 mL normal saline (group B) or 23 mL of bupivacaine HCL 0.5% plus Magnesium Sulphate 100 mg diluted with 2mL normal saline (group BM). Motor and sensory block durations were evaluated until the return of normal motor and sensory function. The degree of pain was assessed during the surgery period and 24 hours postoperatively. The results of this study showed that Magnesium Sulphate provided significantly longer motor block duration (329.33 ± 86.54 min vs 237.46 ± 62.91 min, P = 0.001) and significantly longer sensory block duration (356.00 ± 117.02 min vs 278.00 ± 87.23 min, P = 0.005) when compared with bupivacaine alone. Furthermore, the patients in the Magnesium Sulphate group achieved significantly (P < 0.001) lower values of Visual Analogue Scale (VAS) of pain between the periods from 4 to 12 hours postoperatively. There was significantly less diclofenac consumed (mg) in the Magnesium Sulphate group. The patients in the Magnesium Sulphate group reported significantly higher rates of good sleep quality on the first postoperative night (75%) compared with the patients in the bupivacaine group (25%). Also, the patient satisfaction was significantly higher in the Magnesium Sulphate group compared with the bupivacaine group (75% vs 25%). We concluded that Magnesium Sulphate 100 mg to bupivacaine HCL extended the motor and sensory block durations, provided more effective postoperative analgesia with improvement in the sleep quality of the first postoperative night, and provided better patient satisfaction compared to bupivacaine HCL alone.

Keywords: Magnesium Sulphate, Supraclavicular Brachial Plexus Block Anesthesia

1. Introduction

The supraclavicular approach to the brachial plexus provides more consistent and effective regional anesthesia to the upper extremity than other approaches to brachial plexus blockade. However, the fear of pneumothorax is often cited by anesthetists as a reason to avoid this approach. [1] With increasing affirmation on patient safety and better patient outcomes, ultrasound guided regional anesthesia (UGRA) is becoming more widely popular. Ultrasound provides clinicians with a real-time image suitable for visualizing anatomical structures, needle placement, and local anesthetic spread. [2] Ultrasound-guidance to supraclavicular brachial plexus block has shown to increase success rates, reduce the volume of local anesthetic (LA) used and has the potential to minimize the risk of complications. [3]

Although there are many treatment choices for postoperative pain, a gold standard has not been established. Prolonging the duration of peripheral nerve blocks using long-acting LA or perineural catheters can be used. However,

perineural catheters are more time-consuming, costly, has possible higher complication rates (e.g. Infection), and needs more postoperative care. [4]

Several adjuvants such as fentanyl, alpha-2 adrenergic agonists (clonidine or dexmedetomidine), tramadol, and magnesium have been used to extend the duration of peripheral nerve blocks. [5-7] Magnesium has antinociceptive effects in animal and human models, principally related to blocking the N-methyl-D-aspartate (NMDA) receptors and regulation of calcium influx into cells. Calcium influx leads to a sequence of central sensitization such as windup phenomenon and long term potentiation which are crucial mechanisms that determine the duration and intensity of post-operative pain. Magnesium prevents central sensitization triggered by peripheral nociceptive stimulation in response to painful stimuli. [8, 9]

We designed this study to evaluate the effect of adding magnesium sulphate to bupivacaine in the ultrasound-guided supraclavicular brachial plexus block anesthesia. The sensory and motor block durations were evaluated as primary endpoints and the postoperative analgesic effects as a secondary endpoint.

2. Patients and Methods

2.1. Approval

This study was approved by the Research Ethics Committee at Tanta University (the approval code 30471/08/15) and was registered in the Clinical Trials. Gov (NCT02752334). Written informed consent was obtained from all the patients. Sixty adult patients, between the ages of 20-60 years, ASA physical status I to II, listed for elective forearm or hand surgery using supraclavicular brachial plexus block anesthesia, participated in this prospective, double-blind, randomized study.

2.2. Exclusion Criteria

Exclusion criteria included evidence of severe cardiovascular, renal, or hepatic diseases, preexisting neurological or psychiatric illnesses, patients have allergy to the study drugs, patients who have any contraindications to brachial plexus block anesthesia, pregnant or lactating women, or if the BMI was > 35 kg/m^2.

2.3. Study Design

The patients were randomly divided into 1 of 2 groups (using a computer-generated list) depending on the LA solution used: either 23 mL of Bupivacaine HCL 0.5% (Marcaine, 5 mg per mL; Hospira, USA) in addition to 2 mL normal saline (group B, *n*=30) or 23 mL of Bupivacaine HCL 0.5% in addition to 2 mL (100 mg) Magnesium Sulphate (Magnesium Sulphate 50%, 500 mg per mL; Hospira, USA) diluted with normal saline (group BM, *n*=30). The total volume of the local anesthetic solution used was 25 mL, which was prepared at the bedside before the injection and provided in patient-specific, sealed packaging by a member of the staff not involved in the study. All ultrasound-guided supraclavicular brachial plexus blocks were performed by the same anesthetist experienced in the technique. Both the patient and the surgeon were blinded to the solution used.

2.4. Ultrasound-Guided Supraclavicular Brachial Plexus Block Anesthesia Technique

Patients admitted to the operating room fasted for 8 hours and were not premedicated. A peripheral IV cannula was inserted in the contralateral arm, and intravenous infusion of normal saline 5 mL/Kg/hr was started. Standard monitoring was applied and recorded heart rate, noninvasive arterial blood pressure, electrocardiogram (5 leads), and peripheral capillary oxygen saturation. Supplemental oxygen was given through nasal cannula at 4 L/min. The patient was positioned supine with the head turned gently to the contralateral side, and a pillow was placed under the head and shoulders. Ultrasound imaging was performed using Philips (Philips CX 50 Compact-Xtreme ultrasound system, USA) with a linear array transducer (3-12 MHz, 160 elements, 38 mm). Under complete aseptic technique, the ultrasound probe was positioned in the supraclavicular fossa to visualize the subclavian artery and brachial plexus in the transverse sectional view (i.e., at approximately 90°). The brachial plexus, a cluster of hypoechoic nodules, was often found lateral to the round pulsating hypoechoic subclavian artery lying on top of the hyperechoic first rib. After local skin infiltration with 3 mL xylocaine 1%, a 22 gauge 50 mm insulated block needle (Stimuplex ®, Braun Medical, Germany) was placed on the outer (lateral) end of the probe and advanced along the long axis of the probe and in the same plane as the ultrasound beam. Needle movement was observed in real time. Once the needle reached the brachial plexus cluster, the LA solution was injected incrementally over 3–5 min. LA spread at the time of injection was observed in real time. If spread did not reach some parts of the brachial plexus, the needle was repositioned once before depositing the remaining half of the LA dose.

2.5. Measurements

After that, Patients were evaluated every 5 minutes until 30 min after the end of LA injection by the anesthesiologist who performed the nerve block and was blinded to group allocation. Sensory block was assessed by a pinprick test using a three-point scale in the ulnar, median, radial, and musculocutaneous nerve dermatome distribution and compared with the contralateral arm as a reference: 0 = loss of sensation of touch (anesthesia); 1 = loss of sensation of pinprick (analgesia); and 2 = normal sensation. Motor block was evaluated by the ability to flex the elbow and hand against gravity as the following; Grade 0 (inability to move the forearm, wrist, and fingers), Grade 1 (ability to flex or extend only the fingers), Grade 2 (ability to flex or extend only the wrist and fingers), and Grade 3 (ability to flex and extend the forearm). The onset times of the sensory and motor blockades were defined as the time interval between

the end of local anesthetic administration and the loss of sensation of touch (sensory score = 0) and inability to move the forearm, wrist, and fingers (motor score = 0), respectively. A successful block was defined as complete sensory and motor block (0%) in all regions assessed within 30 min of local anesthetic injection. In case that block success was not achieved after 30 min, general anesthesia was applied and the patient would then be excluded from data analysis.

Postoperatively, all measures were assessed by an observer who was blinded to the aim of the study. The sensory block duration (the time interval between the end of local anesthetic administration and restoration of normal sensation i.e., sensory score 2 compared with the contralateral arm as a reference) and motor block duration (the time interval between the end of local anesthetic administration and the recovery of complete motor function i.e., motor score 3) was evaluated every 1 hour. The degree of postoperative pain was assessed via a 10-cm visual analog scale (VAS) for pain where: 0=no pain and 10=intolerable pain at 1, 2, 3, 4, 6, 8, 12, 18 and 24 hours postoperatively. The patient was given diclofenac 1 mg/kg intramuscularly (IM) if the VAS for pain was > 4. Tramadol 100 mg was given intravenously by infusion over 15 minutes as rescue analgesia medication along with the diclofenac if the patient complained of severe pain (VAS was >7). Both analgesic drugs were given in a maximum frequency of 6 h, and 3 doses maximally per 24 hours. The total diclofenac consumption (mg) and the number of patients (%) who required tramadol were recorded. The sleep quality on the first postoperative night was assessed in the day after surgery using the CSD [10] which is a self-monitor questionnaire to be recorded by the patients on a night-by-night basis. The CSD has been regarded as the "gold standard" for subjective sleep assessment. At the end of the questionnaire, the patient rated the quality of sleep to be either very good, good, fair, bad, or very bad. Moreover, patients were asked about their overall satisfaction concerning the pain management to be either very good, good, fair, bad, or very bad.

2.6. Statistical Analysis

A preliminary study was conducted on 10 patients (5 in each group). Supraclavicular brachial plexus block anesthesia using 23 mL of Bupivacaine HCL 0.5% resulted in prolongation of the sensory block duration from 289 ± 95 minutes in group B to 375 ± 104 minutes in group BM when 100 mg Magnesium Sulphate was added. On the basis of this study, it was calculated that a total number of 60 patients (30 pairs) would be required to have a 90% power of detecting a 30% prolongation in the sensory block duration at a significance level of 0.05. Altman's nomogram for the calculation of sample size or power was used (Altman DG. Practical Statistics for Medical Research. London: Chapman & Hall, 1991). Data were presented as mean ± SD or number (%). In the intergroup comparison, Pearson $\chi 2$ test was used to analyze the nominal categorical data; the ordinal categorical data were compared using the Mann–Whitney *U* test. Comparison of quantitative/numerical variables between the 2 groups was performed with an independent 2-sample *t* test. The significance level was set at $P < 0.05$. Statistical analysis of the results was conducted using the computer program SPSS version 16.0 for Windows (SPSS, Chicago, IL).

3. Results

Siventy-three patients were assessed for eligibility for this study. Eliven were excluded from enrollment either because of failure to meet the inclusion criteria (n = 5) or because they declined to participate in the study (n = 6). Sixty patients were randomly divided equally into 1 of 2 groups depending on the LA solution used. Afterward, all patients were followed up and analyzed (Figure 1). This study demonstrated comparable results concerning age, gender, BMI, and ASA classification in the group BM compared with the group B (Table 1). Magnesium Sulphate provided significantly longer motor block duration (329.33 ± 86.54 min vs 237.46 ± 62.91 min, P = 0.001) and significantly longer sensory block duration (356.00 ± 117.02 min vs 278.00 ± 87.23 min, P = 0.005) when compared with bupivacaine alone. There was significantly less diclofenac consumed (mg) in the Magnesium Sulphate group (76.66 ± 17.48 mg vs 156.33 ± 43.98 mg, P = 0.001) when compared with bupivacaine alone (Table 1).

Furthermore, the patients in the Magnesium Sulphate group achieved significantly (P < 0.001) lower values of Visual Analogue Scale (VAS) of pain between the periods from 4 to 12 hours postoperatively (figure 2).

The patients in the Magnesium Sulphate group reported significantly higher rates of good sleep quality on the first postoperative night (75%) compared with the patients in the bupivacaine group (25%). Also, the patient satisfaction was significantly higher in the Magnesium Sulphate group compared with the bupivacaine group (75% vs 25%) (figure 3).

Table 1. *Demographic data, surgical characteristics, and descriptive statistics for the quality of brachial plexus block anesthesia and the postoperative analgesia.*

	Group B N = 30	**Group BM N = 30**	***P* value**
Age (years)	39.16 ± 11.26	40.53 ± 10.96	0.636
Sex (F/M)	14/16	13/17	0.795
BMI (kg/m^2)	24.66 ± 4.48	25.16 ± 4.96	0.684
ASA I / II	17/13	19/11	0.598
Duration of surgery (min)	93.76 ± 34.54	87.36 ± 33.63	0.470
Onset time of sensory block (min)	19.00 ± 4.84	14.46 ± 4.06	0.001*

	Group B N = 30	**Group BM N = 30**	***P* value**
Onset time of motor block (min)	24.86 ± 5.82	18.63 ± 4.74	0.001*
Duration of sensory block (min)	278.00 ± 87.23	356.00 ± 117.02	0.005*
Duration of motor block (min)	237.46 ± 62.91	329.33 ± 86.54	0.001*
Total diclofenac consumption (mg)	156.33 ± 43.98	76.66 ± 17.48	0.001*
The number of patients (%) requiring tramadol as rescue analgesia medication	7 (23.3%)	1 (3.3%)	0.023*

Data are displayed as mean ± SD or *n* (%).
* indicate statistically significant ($p < 0.05$) compared to B group.

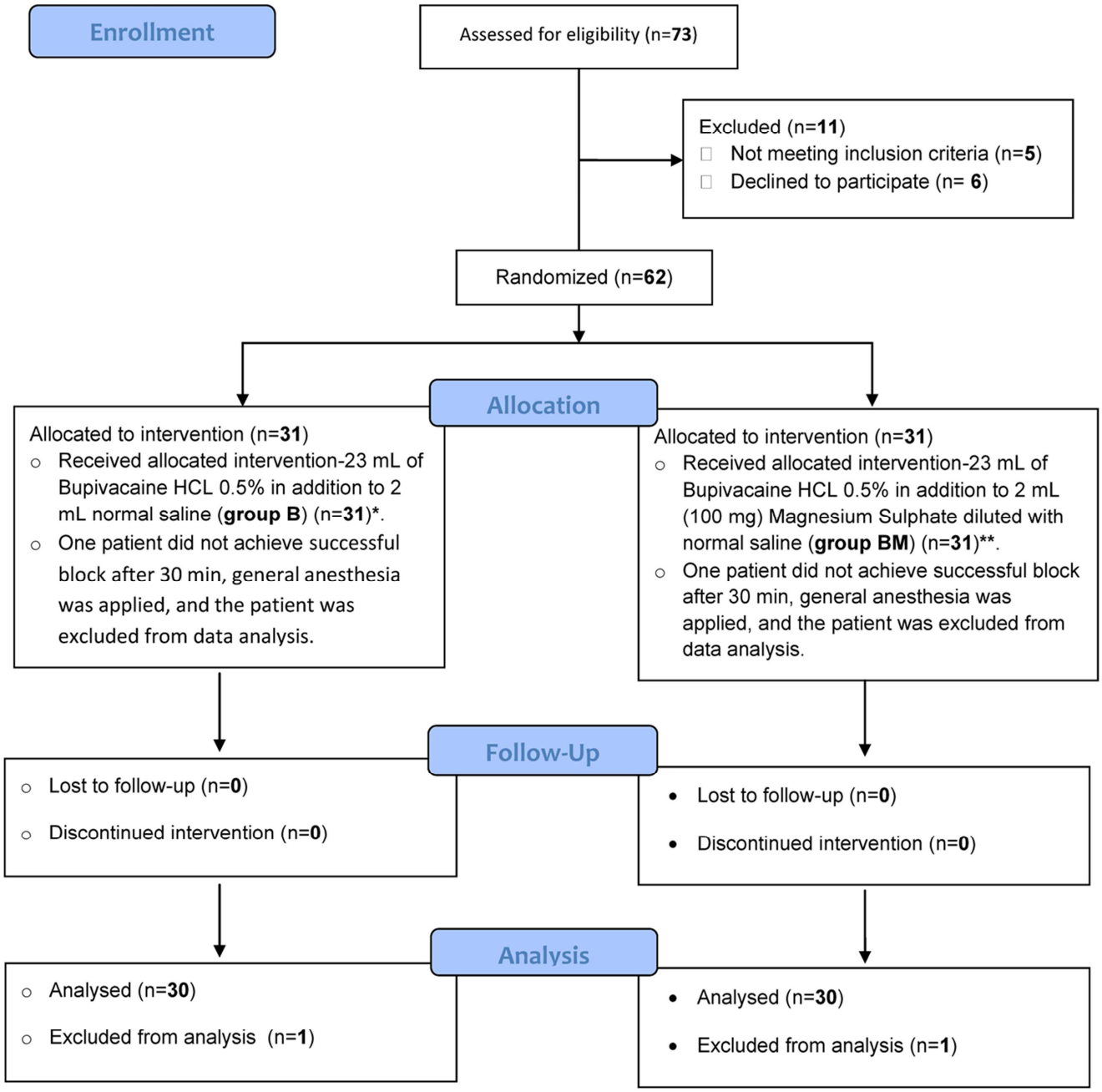

Figure 1. *Consolidated Standards of Reporting Trials (CONSORT) flow diagram.*

* Group B = received bupivacaine HCL plus normal saline.
** Group BM = received bupivacaine HCL plus Magnesium Sulphate.

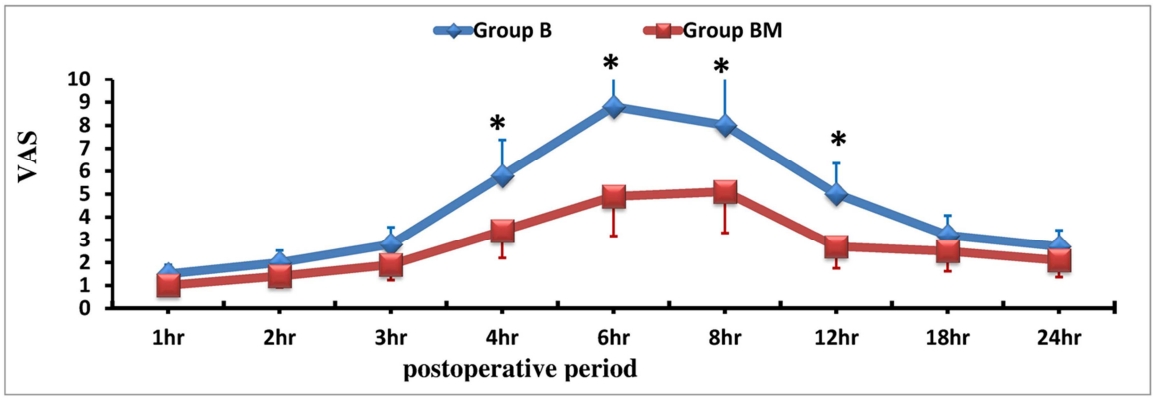

Figure 2. *Verbal analog scale of pain (VAS) 24 hours postoperatively. * indicate statistically significant (p < 0.05) compared to B group.*

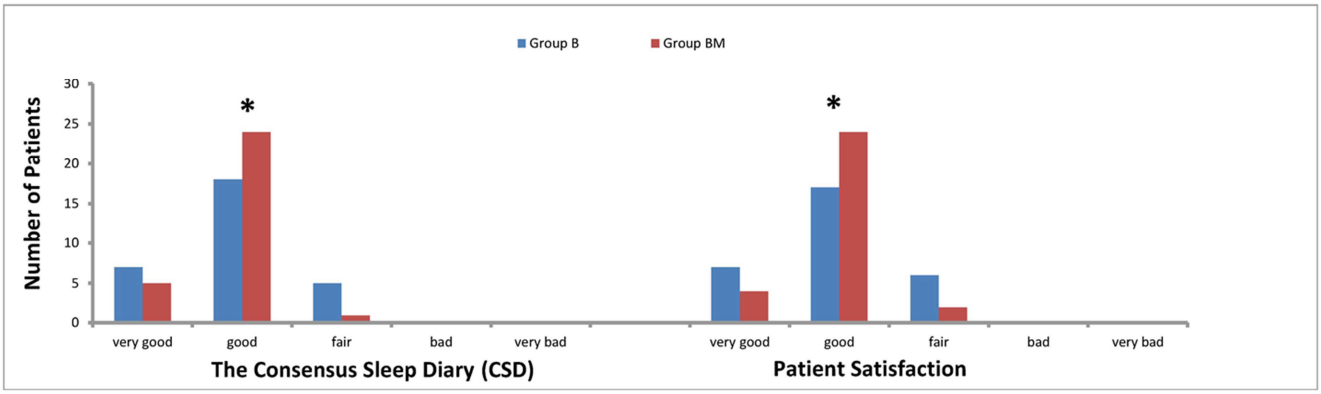

Figure 3. *Consensus Sleep Diary (CSD) of the first postoperative night and patient satisfaction. * indicate statistically significant (p < 0.05) compared to B group.*

4. Discussion

This study demonstrated that the use of 100 mg Magnesium Sulphate as an adjuvant to Bupivacaine HCL 0.5% in patients undergoing elective forearm and hand surgeries under ultrasound guided supraclavicular brachial plexus block anesthesia extended the motor and sensory block durations and delivered more effective postoperative analgesia, as shown by lower diclofenac consumption, fewer patients requiring tramadol as a rescue analgesia medication, and lower pain scores at the periods from 4 h till 12 h postoperatively. Moreover, it improved the quality of the sleep in the first day of the postoperative period and the satisfactions of the patients.

Similar results had been described in previous studies. [11–16] However, most of these studies were designed for different clinical applications and used different local anesthetics. The meta-analysis of Li, et al [11] that included 7 randomized controlled trials (490 patients) and aimed to evaluate the effect of the use of magnesium sulphate as an adjuvant in peripheral nerve block revealed that the use of magnesium in peripheral nerve block shortened the onset and increased the duration of sensory and motor blocks and decreased the postoperative analgesic requirements. Furthermore, Haghighi, et al [12], investigated the effect of addition of magnesium sulphate to lidocaine on the duration of sensory and motor blocks of the axillary block anesthesia in patients presented for orthopedic surgeries and detected significantly prolonged motor and sensory block durations with the use of magnesium sulphate. Also, Ekmekci, et al [13] found significant prolongation of the duration of sensory and motor blocks with the addition of magnesium to Levobupivacaine in femoral block anesthesia. Comparable results were found by Mukherjee, et al [14] who concluded that the addition of magnesium sulphate to ropivacaine 0.5% in supraclavicular nerve block extended the sensory and motor block durations, the postoperative pain score, and the rescue analgesia consumption. Gunduz, et al [15] studied the effect of adding different doses of magnesium to prilocaine in brachial plexus nerve block for hand and forearm surgeries and found significant prolongation of the motor and sensory block durations with the use of higher doses of magnesium.

Moreover, this study demonstrated that Magnesium Sulphate improved the quality of the sleep in the first day of the postoperative period and the satisfactions of the patients which can be explained by the more effective postoperative analgesia delivered by Magnesium Sulphate.

Quite the reverse, the randomized trial of Lee, et al [8] evaluated the effect of the addition of magnesium to bupivacaine-epinephrine mixture in interscalene brachial plexsus block and concluded that the use of magnesium as an additive improved the postoperative pain score and the duration of the postoperative analgesia without significant effect on the onset or the duration of sensory or motor

blockade. This may be attributed to the use of epinephrine in both groups that may prolong the duration of the block.

The mechanism by which Magnesium Sulphate extended the motor and sensory block durations of the LA and delivered more effective postoperative analgesia is not fully clear, but it is likely to be multifactorial. It was noticed that the use of magnesium decreased the required doses of anesthetics when used with general anesthesia and prolonged the sensory and motor blocks when added to the regional anesthesia mixtures. [16] The analgesic effect of Magnesium can be explained by a noncompetitive NMDA receptor antagonism and at the same time competitive blocking of the entry of calcium in presynaptic endings leading to reduced release of acetylcholine at the synaptic gaps and therefore strongly reducing the post synaptic activity of slow conducting unmyelinated C-fibers which are the main afferent fibers transmitting the input signals from periphery to CNS. [17, 18] Also, Magnesium inhibits the activation of NMDA receptor induced by excitatory amino acid neurotransmitters, such as glutamate and aspartate which causes calcium and sodium influx into the cell with an efflux of potassium and initiation of central sensitization and wind-up leading to propagation of peripheral nociceptive stimulation. [19] Another explanation is that Magnesium is the second most abundant intracellular cation and physiological calcium channel antagonist. In animal models of pain, calcium channel antagonists have been demonstrated to provide analgesic effects. [20]

The study was limited by the use of a single dose of magnesium sulphate (100mg). Also, it did not evaluate its effect on the continuous nerve block.

5. Conclusion

In conclusion, we found that the addition of 100 mg Magnesium Sulphate as an adjuvant to Bupivacaine HCL 0.5% in patients undergoing elective forearm and hand surgeries under ultrasound guided supraclavicular brachial plexus block anesthesia extended the motor and sensory block durations and provided more effective postoperative analgesia. Furthermore, Magnesium Sulphate improved the quality of postoperative recovery which is evinced by the improvement in the sleep quality on the first postoperative night and patients satisfaction.

Acknowledgements

We thank Dr. Mahmoud M. Ibrahim, Assistant Professor of Educational Psychology (statistical education), Sultan Qaboos University, Oman, for his statistical assistance.

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