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Original Article

Efficacy of Nalbuphine and Magnesium Sulfate with Ropivacaine for Quality of Supraclavicular Brachial Plexus Block and Post-operative Analgesia

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Abstract

Background: Adequate post-operative analgesia is the prime duty of anesthesiologist and several adjuvants have been used along with local anesthetics to prolong the duration of brachial plexus block. The present study aimed to compare the effect of nalbuphine and magnesium sulfate as an adjuvant to ropivacaine and ropivacaine alone in nerve stimulator guided supraclavicular brachial plexus block in patients scheduled for orthopedic upper limb surgeries.

Materials and Methods: A total of 90 patients of in the age group of 20–65 years of either sex of the American Society of Anesthesiologists Grade I and II were divided into three groups of 30 each. Group R received 30 ml of 0.75% ropivacaine alone, Group RM received 30 ml of 0.75% ropivacaine plus 150 mg of magnesium sulfate, and Group RN received 30 ml of 0.75% ropivacaine plus 20 mg of nalbuphine. All the groups were compared with respect to onset and duration of sensory and motor blockade, post-operative analgesia, need for rescue analgesia, hemodynamics, and side effects.

Results: Onset of sensory and motor block was earliest in Group RN and was highly significant ($P < 0.001$) when compared to Group R and Group RM. Mean duration of post-operative analgesia was 8.70 ± 1.18 h in Group R, 11.73 ± 1.23 h in Group RM, and 14.40 ± 1.25 in Group RN. Duration of sensory and motor block and post-operative analgesia were significantly prolonged ($P < 0.001$) both in Group RM and Group RN when compared to Group R.

Conclusion: Both nalbuphine and magnesium sulfate are effective adjuvant as compared to ropivacaine alone as they prolong the duration of block as well as post-operative analgesia when used for supraclavicular brachial plexus block. However, nalbuphine has proven to be a better adjuvant as compared to magnesium sulfate as it also results in earlier onset of sensory and motor block and better patient and surgeon satisfaction scores.

Key words: Magnesium sulfate, Nalbuphine, Ropivacaine, Supraclavicular brachial plexus block

INTRODUCTION

Skillful application of peripheral neural blockade broadens the anesthesiologist's range of option for providing optimal anesthetic care. It is preferred technique both in emergency and day care surgeries.[1] Supraclavicular block can be used for surgery from midhumerus level down to hand.[2] Ropivacaine is one of the safest and longest acting among various local anesthetics.[3] Extension of analgesia into post-operative period is highly desirable by anesthesiologist, thus various adjuvants have been used along with local anesthetics till date. The current study compared nalbuphine and magnesium sulfate with respect to the duration of block and post-operative analgesia.

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MATERIALS AND METHODS

After the approval of the Institutional Ethics Committee, Government Medical College, Amritsar, written informed

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consent was taken from patients. 90 patients of 20-65 years age were selected for the study. These cases were posted for elective surgeries of humerus, fracture both bone forearm, procedures of wrist and hands. They were randomly divided into three groups of 30 each. All the patients belonged to the American Society of Anesthesiologists (ASA) physical Status I and II. Patients in Group R received 30 ml of ropivacaine, in Group RM received 30 ml of 0.75% ropivacaine plus 150 mg of magnesium sulfate, and in Group RN received 30 ml of 0.75% ropivacaine plus 20 mg of nalbuphine for supraclavicular brachial plexus block under guidance of nerve stimulator (NS).

Using a computer-generated number list, patients were allocated one of the three groups. Sealed envelopes of study drugs were prepared. Staff nurse of the operation theater was handed the envelope and was asked to prepare and fill the drugs in syringes. Those were then handed over to the anesthesiologist performing the block. In this manner, both the anesthesiologist and patient were blinded to the study group. The anesthesiologist, usually the resident recording the parameters and observations, was also blinded to the study group.

Patient refusal, pregnant women, morbidly obese, patients with coagulation disorders and/or on anticoagulation therapy, allergy to any of the three study drug, and any anticipated difficulty in regional anesthesia were considered as exclusion criteria.

A day before surgery, a thorough preanesthetic checkup comprising general physical examination and systemic examination of all patients was conducted. On arrival to operation theater, intravenous line was secured with 18 G angiocatheter and the patients were preloaded with 10 ml/kg body weight of Ringer's lactate solution over 15–20 min. Multipara monitors were applied and baseline respiratory rate, pulse rate, noninvasive blood pressure, SPO_2, and electrocardiogram (ECG) were recorded. Injection midazolam 0.04 mg/Kg body weight was given through intravenous route immediately before the procedure.

With the patient in supine position, head end of the bed was elevated at 30^0. With the upper arm kept by patient's side, elbow flexed and wrist supinated on patients abdomen, clavicular head of sternocleidomastoid was palpated at its clavicular insertion. The positive electrode of the NS was attached to an ECG electrode and stuck on the ipsilateral arm. The subclavian artery was then palpated and immediately lateral to it, an intradermal wheal was raised with 2% lignocaine (2 mL) using a 24 G needle. A 20 G insulated needle attached to the negative electrode of the NS was then inserted through the skin wheal in a backward, inward, and downward direction. NS was set to deliver a current of 1.5 mA in the internal mode. Twitching of shoulder muscles was seen on advancing the needle. Needle was further advanced caudal, parallel to the midline, and perpendicular to the clavicle, at a 10^0 angle. Pectoralis, triceps, wrist, and then finger twitch were seen. Once the desired twitch was obtained at 1.5 mA, amplitude was decreased to 0.4–0.5 mA at frequency of 1–2 Hz, and it was assured that the desired twitch was still present. The goal was isolated twitch of the fingers only. If the desired twitch was not obtained, needle was redirected, keeping in mind that it did not advance >2 cm caudally. When contraction was elicited at a current of 0.5 mA and no twitch with a current of 0.2 mA, needle was fixed and local anesthetic solution injected after negative aspiration for air or blood.

Onset of sensory and motor block was monitored every 5 min till the development of complete surgical anesthesia. Sensory blockade was measured with pin-prick test at a 3-point scale, motor blockade was assessed by technique described by Bromage.

Intraoperatively, respiratory rate, pulse rate, noninvasive blood pressure, and SPO_2 were recorded every 5 min interval till 30 min, every 10 min till 60 min, and then every 15 min till 180 min. Postoperatively, vitals were recorded from monitor every hourly till 8 h, then 2 hourly till 12 h, and then 3 hourly till 24 h.

In case, patient experienced mild pain (visual analog scale [VAS] <3) intraoperative supplementation was given with injection ketamine 0.5–1.0 mg/kg. General anesthesia was given to the patient of failed block or VAS >3 and the case excluded from the study.

Postoperatively, duration of sensory and motor block was assessed every hourly till effect weaned off. Duration of analgesia was measured by interviewing the patients and rescue analgesia was given in the form of injection diclofenac 75 mg i/m when VAS score was >3.

Side effects and complications (procedure or drug related) and if any occurred, were recorded and followed postoperatively.

Operating surgeon was enquired of surgeon satisfaction score (quality of intraoperative muscle relaxation) on a scale of 1–3. Patients were enquired of patient satisfaction score on a scale of 1–5 at 24 h postoperatively.

RESULTS

Duration of analgesia was taken as the outcome measure of interest for sample size calculation. Sample size was

calculated keeping in view at most 5% risk, with minimum 80% power and 5% significance level (significant at 95% confidence interval). Raw data were recorded in a Microsoft Excel spreadsheet and analyzed using the Statistical Package for the Social Sciences (SPSS version 23.00). Continuous data were presented as mean with standard deviation. Categorical data were expressed as percentages. Numerical variables were normally distributed and were compared using Chi-square test for non-parametric data and Student's "*t*" test for parametric data. *P* value was then determined to evaluate the level of significance.

90 patients belonging to ASA Grade I and II of age group 20–65 years of either sex admitted in the orthopedic department of Guru Nanak Dev Hospital, Amritsar and scheduled to undergo surgery of the upper limb or hand were recruited. Group R received 30 ml of 0.75% ropivacaine, Group RM received 30 ml of 0.75% ropivacaine plus 150 mg magnesium sulfate, and Group RN received 30 ml of 0.75% ropivacaine plus 20 mg nalbuphine.

As shown in Table 1, the demographic profile consisting of age, weight, and sex was statistically insignificant among the three groups. The three groups were also comparable with respect to ASA physical status and type of surgery performed.

As shown in Table 2, mean onset of sensory block was 16.90 ± 1.24 min, 16.24 ± 1.45 min, and 11.17 ± 1.26 min in Groups R, RM, and RN, respectively. Mean onset of motor block was 19.23 ± 1.33 min in Group R, 18.73 ± 1.26 min in Group RM, and 12.97 ± 1.22 min in Group RN. Onset of block was comparable in Group R and Group RM, whereas Group RN showed significant early onset as compared to Group R and Group RM.

As shown in Table 3, mean duration of sensory block was 7.93 ± 1.14 h, 10.83 ± 1.18 h, and 13.43 ± 1.19 h in Groups R, RM, and RN, respectively. The mean duration of motor block was 7.14 ± 1.16 h, 9.93 ± 1.20 h, and 11.33 ± 1.24 h in Groups R, RM, and RN, respectively. The difference in the duration of block was found to be statistically highly significant ($P < 0.001$) among Groups RM/R, RN/R, and RN/RM.

As shown in Table 4, mean duration of surgery in Group R was 92.53 ± 21.85 min, in Group RM was 91.87 ± 19.79 min, and in Group RN was 93.37±18.55 min. The difference in the three groups was found to be statistically insignificant ($P > 0.05$). The duration of post-operative analgesia was 8.70 ± 1.18 h, 11.73 ± 1.23 h, and 14.40 ± 1.25 h in Groups R, RM, and RN, respectively. The results showed statistically highly significant ($P < 0.001$) difference within Groups RM/R, RN/R, and RN/RM.

As shown in Figure 1, the mean number of rescue analgesic doses in 24 h was 2.73 ± 0.52 in Group R, 2.47 ± 0.57 in Group RM, and 2.23 ± 0.43 in Group RN.

Table 1: Demographic profile

Variable	Group R	Group RM	Group RN
Mean age (in years)	37.17±12.87*	36.60±11.91*	40.57±11.23*
Mean weight (in kg)	71.90±12.14*	72.07±10.68*	73.57±6.70*
Sex (M/F)	21/9	20/10	19/11
ASA Grade (I/II)	24/6	21/9	25/5

ASA: American Society of Anesthesiology, *: Data are displayed as mean±standard deviation

Table 2: Onset of sensory and motor block

Onset of Block	Group R	Group RM	Group RN	*P* value R/RM	*P* value R/RN	*P* value RM/RN
Onset of sensory block (mins)	16.90±1.24*	16.24±1.45*	11.17±1.26*	0.08;NS	0.00;HS	0.00;HS
Onset of motor block (mins)	19.23±1.33*	18.73±1.26*	12.97±1.22*	0.07;NS	0.00;HS	0.00;HS

NS: Non-significant, HS: Highly significant, *: Data are displayed as mean±standard deviation

Table 3: Duration of sensory and motor block

Duration of Block	Group R	Group RM	Group RN	*P* value R/RM	*P* value R/RN	*P* value RM/RN
Duration of sensory block (hrs)	7.93±1.14*	10.83±1.18*	13.43±1.19*	0.00;HS	0.00;HS	0.00;HS
Duration of motor block (hrs)	7.14±1.16*	9.93±1.20*	11.33±1.24*	0.00;HS	0.00;HS	0.00;HS

HS: Highly significant, *: Data are displayed as mean±standard deviation

Table 4: Duration of surgery, post-operative analgesia, and number of rescue analgesia

Variable	Group R	Group RM	Group RN	*P* value R/RM	*P* value R/RN	*P* value RM/RN
Duration of surgery (mins)	92.53±21.85*	91.87±19.79*	93.37±18.55*	0.45;NS	0.38;S	0.44;NS
Duration of post-operative analgesia (hrs)	8.70±1.18*	11.73±1.23*	14.40±1.25*	0.00;HS	0.00;HS	0.00;HS

NS: Non-significant, S: Significant, HS: Highly significant, *: Data are displayed as mean ± standard deviation

Statistically significant ($P < 0.05$) difference was found in Groups RM/R and RN/RM. Furthermore, statistically highly significant ($P < 0.001$) difference was found in Group RN versus Group R.

As shown in Figure 2, the VAS score was significantly better in Group RM when compared to Group R as well as in Group RN in comparison with both the other groups being Group R and Group RM.

As shown in Table 5, mean patient satisfaction score in Group R was 3.67 ± 0.55, in Group RM was 4.07 ± 0.91, and in Group RN was 4.53 ± 0.68. The mean surgeon satisfaction score was 2.13 ± 0.35, 2.33 ± 0.48, and 2.57 ± 0.50 in Groups R, RM, and RN, respectively. The results were statistically significant between Groups RM/R and RN/RM. Results were statistically highly significant between Groups RN/R.

DISCUSSION

Supraclavicular block, being most commonly used approach for brachial plexus block, has wide variety of implications in upper limb orthopedic surgeries. Minimal requirement of drugs and equipment along with prolonged post-operative analgesia is among the various attractions. Local anesthetics provide excellent intraoperative conditions, but their short duration of action necessitates the use of adjuvants so as to minimize the use of multiple intravenous analgesics postoperatively.

Magnesium, the fourth most abundant cation in the body, is involved in several physiological processes, majority based on voltage-dependent inhibition of calcium influx into cell along with non-competitive antagonism of N-methyl-D-aspartate receptors.[4] Magnesium sulfate also inhibits catecholamine release from adrenal and peripheral nerve endings, thus resulting in sympathetic blockade.[5] Above properties prompted the use of magnesium as an additive to local anesthetics. Magnesium sulfate is routinely used for several therapeutic effects such as antihypertensive, antiarrhythmic, and bronchodilator. It has been used in various anesthetic techniques such as spinal,[6] epidural,[7] intravenous regional anesthesia,[8] and various nerve blocks such as peribulbar and paravertebral.

Demonstration of opioid receptors outside the central nervous system led to studies investigating the efficacy of

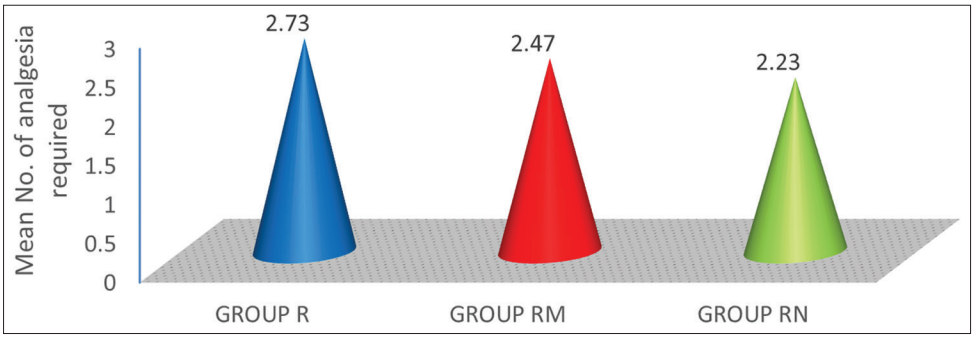

Figure 1: Mean of the total number of doses of rescue analgesia

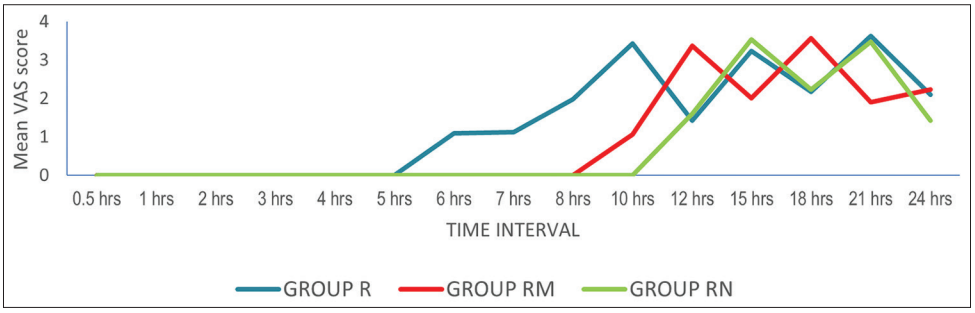

Figure 2: Mean of intra- and post-operative visual analog scale score

Table 5: Patient and surgeon satisfaction score

Variable	Group R	Group RM	Group RN	*P* value R/RM	*P* value R/RN	*P* value RM/RN
Patient satisfaction score	3.67±0.55*	4.07±0.91*	4.53±0.68*	0.02;S	0.01;S	0.00;HS
Surgeon satisfaction score	2.13±0.35*	2.33±0.48*	2.57±0.50*	0.03;S	0.04;S	0.00;HS

S: Significant, HS: Highly significant, *: Data are displayed as mean±standard deviation

combining opioids and local anesthesia for peripheral nerve blocks.[9] Nalbuphine, a synthetic opioid with agonism on κ (kappa) receptor and antagonism on μ (mu) receptor, is equipotent to morphine as analgesic. It additionally possesses ceiling effect on respiratory depression and cardiac stability. Along with the enhancement of μ opioid-based analgesia, nalbuphine also mitigates μ opioid side effects.[10] It has been used extensively as sole analgesic as well as along with local anesthetics.

In search of an ideal adjuvant for local anesthetics, the present study was conducted to compare block characteristics and side effects, if any with magnesium sulfate and nalbuphine.

The dose of ropivacaine used in this study was 30 ml of 0.75% which is well within the maximum recommended dose of ropivacaine as stated by Tripathi *et al.*[11] Dose of magnesium and nalbuphine was also chosen as per recommended and used in of previous studies.[12,13]

The hemodynamic parameters monitored in the study were respiratory rate, systolic blood pressure, diastolic blood pressure, SpO2, and pulse rate. All the monitored hemodynamic parameters were stable throughout surgery.

In this study, the onset of sensory block was comparable in magnesium group, whereas significant shortening was observed in nalbuphine group when compared with control group. Similarly, highly significant difference in onset of motor block was seen in nalbuphine group (12.97 ± 1.22 min) as compared to both control group (19.23 ± 1.33 min) and magnesium group (18.73 ± 1.26 min).

Statistically highly significant prolongation in the duration of sensory and motor block was seen both in group magnesium and nalbuphine as compared to control group. Nalbuphine group also showed highly significant prolongation in the duration as compared to magnesium. Similar were the results for the total duration of analgesia.

Our results were concordant with Haghighi *et al.*[14] and Lee *et al.*,[15] who observed that addition of magnesium sulfate to local anesthetics does not affect the onset of sensory and motor block, whereas it significantly prolongs the duration of sensory and motor block. Lee *et al.* also observed significant prolongation of the total duration of analgesia with magnesium.

Madan *et al.*[16] observed that addition of nalbuphine results in significantly early onset and prolongation in the duration of sensory and motor block. Das *et al.*[17] and Abdelhaq and Elramely[13] also documented that nalbuphine significantly lengthens the duration of sensory and motor block. Das *et al.* also evaluated that addition of nalbuphine to local anesthetic results in significant prolongation of time to request of the first analgesic.

In the present study, VAS score was significantly lower both with magnesium sulfate and nalbuphine as compared to ropivacaine alone. As the duration of analgesia was significantly higher with nalbuphine when compared to magnesium sulfate, VAS score was significantly lower as well. These results correlated well with the study of Reddy *et al.*,[18] who concluded that VAS score was significantly lower at several time intervals with magnesium as additive. For Group RN as well, our results were in concordance with Das *et al.*,[17] who found significantly lower VAS score with nalbuphine.

In the present study, significantly less number of rescue analgesic injection was required in first 24 h in magnesium as well as nalbuphine group as compared to control group. Mukherjee *et al.*[12] and Das *et al.*[17] also found that the number of rescue analgesic injections in the form of diclofenac sodium is significantly less with magnesium sulfate and nalbuphine added to local anesthetic, respectively.

Vascular puncture was seen in 1 (3.33%) patient in Group R, 2 (6.67%) patients in Group RM, and 2 (6.67%) patients in Group RN with an overall percentage of 5.56%. In all these cases, the needle was withdrawn and redirected. The drug was then injected after negative aspiration. Signs and symptoms associated with intravascular injection were not encountered in any of the five patients and the block was successful. Three patients in Group R, two in Group RM, and two in Group RN suffered from nausea. No active intervention was required for the same except increasing the transfusion rate of fluid. Two patients in Group R, one in Group RM, and one in Group RN suffered from vomiting. All the patients were managed with slow intravascular injection ondansetron. A total of two patients experienced mild pruritus, one in Group R and Group RM each. It needed no active management and was self-limiting. Two patients in Group R, two in Group RM, and three in Group RN experienced mild sedation. None of the patients exhibited respiratory distress, arrhythmias, or any other serious complication such as pneumothorax, hoarseness, or neuropathy. All the patients were otherwise hemodynamically stable.

Both magnesium sulfate and nalbuphine displayed significantly better patient and surgeon satisfaction scores as compared to ropivacaine alone, whereas nalbuphine also had significantly better scores than magnesium sulfate.

CONCLUSION

Addition of both magnesium sulfate and nalbuphine to ropivacaine prolongs both sensory and motor blockade duration as compared to ropivacaine alone. Nalbuphine

has a number of beneficial effects such as earlier onset of sensory and motor block which may be desirable in a busy operation room schedule and provides longer duration of sensory and motor block and post-operative analgesia, better patient and surgeon satisfaction scores. Therefore, we concluded that nalbuphine is a better adjuvant than magnesium sulfate in relation to supraclavicular brachial plexus block. The prime limitation of the present study was the unavailability of ultrasonography (USG), thus inability to perform USG-guided supraclavicular brachial plexus block.

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