Role of nalbuphine as an adjuvant to ropivacaine in supraclavicular block- a randomized control study

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ABSTRACT

Background: Nalbuphine is a strong analgesic with mixed k agonist and μ antagonist was studied several times as adjuvant to local anesthetics in spinal, epidural and local infiltration but very few studies on brachial plexus block. The aim of this study was to evaluate the effect of nalbuphine as an adjuvant to ropivacaine 0.75% in supraclavicular brachial plexus block.

Methodology: In a prospective, double blind study of sixty patients undergoing elective upper limb surgeries were randomized into two groups. Group R - (n = 30), 29 mL of 0.75% ropivacaine + 1 mL normal saline and in study Group N (n = 30), 29 mL of 0.75% ropivacaine + 1 mL (10 mg) nalbuphine were used for giving supraclavicular block under Ultrasound (US) guidance. Parameters assessed were onset and duration of sensory and motor block, duration of analgesia, and any adverse events. After administration of block with above drugs, the block characteristics were assessed every 2 and 3 min till onset of complete blockade, then hourly till the effect of block persist. Data between the groups were analyzed using independent ttest with statistical package for social science (SPSS) 21.0 software.

Results: The demographic profile of the patients age, sex, weight, ASA grade were comparable in both groups. There were no hemodynamic variations and no complication of technique or adverse effects due to nalbuphine occurred (p > 0.05).

The mean onset times of sensory blocks was 11.58 ± 3.56 vs. 10.84 ± 3.24 (p = 0.40) and onset times of motor block was 13.12 ± 4.98 vs. 11.23 ± 3.29 (p = 0.09) in Group R and Group N respectively. The differences were not statistically significant in both groups.

The mean duration of sensory block [e.g. 512.52 ± 16.47 vs. 588.25 ± 19.63 min (p = 0.0001)] and motor block [467.66 ± 17.34 vs. 518.45 ± 16.65 min (p = 0.0001)] were significantly prolonged in Group R than in Group N. The mean duration of analgesia was significantly more in Group R than in Group N, e.g. 598.21 ± 19.33 vs. 705.39 ± 31.54 min (p < 0.0001)

Conclusion: Nalbuphine significantly extends the duration of analgesia of brachial plexus block under supraclavicular approach when used with 0.75% ropivacaine and has no adverse effects.

Key words: Brachial plexus block; Bupivacaine; Nalbuphine; Supraclavicular approach; Ultrasound guidance

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INTRODUCTION

Brachial plexus block is a reliable alternative for general anesthesia (GA) in upper limb surgery. Regional nerve blocks provide good operating conditions when it is used optimally. They not only provide excellent intraoperative analgesia but also provide good post-operative analgesia. They cause the least interference with the vital physiological functions of the body and reduction in stress response. Disadvantages being inadequate or failed block, local anesthetic toxicity which can be minimized by giving block under ultrasound guidance.

Ultrasound visualization of anatomical structures facilitates safe methods for regional blocks. With the help of USG, the anesthetist secure an optimal needle positioning and can monitor the distribution of local anesthetic in real time.

Ropivacaine is a noble local anesthetic which is considered to be superior over bupivacaine, as it provides more differential block when given via epidural route. It causes less cardiovascular and central nervous system toxicity than bupivacaine. The decreased systemic toxicity makes it suitable local anesthetic agent when used in high concentrations in peripheral nerve block and epidural anesthesia. Ropivacaine has been used in brachial plexus block with substantial advantage. To prolong the duration of analgesia during brachial plexus block, various drugs have been used as adjuvants to local anesthetics. Nalbuphine, an agonist–antagonist opioid, was studied as an adjuvant in procedures like subarachnoid block (SAB), epidural block and found to be effective in increasing the duration of block. It has the potential to maintain or even enhance μ-opioid based analgesia while simultaneously mitigating the μ-opioid side effects. Nalbuphine is cardiac stable with onset of action between 2 and 3 min, duration of action of 3–6 h and has minimal side effects in the dose of 0.2–0.4 mg/kg. Because of its safety profile, nalbuphine can be used for pain management in children with burns, neoplastic or hematological diseases. Despite its known benefits for pain control, nalbuphine has not been studied extensively for its effects as an adjuvant to local anesthetics during brachial plexus blocks.

The primary aim of this study was to evaluate the role of nalbuphine in supraclavicular block with ropivacaine in terms of duration of analgesia, and the secondary aim was to record the effects on onset, duration of motor and sensory block, and any adverse events.

METHODOLOGY

This study was carried out in tertiary center of north India after getting an approval from institutional ethical committee. This study was conducted from December 2017 to October 2018. Sixty patients were selected for this study, divided into 2 groups randomly with help of chit and box method. The two groups were; Group R (n = 30) received 29 mL of 0.75% ropivacaine + 1 mL normal saline and Group N (n = 30) who received 29 mL of 0.75% ropivacaine + 1 mL (10 mg) nalbuphine in supraclavicular block under US guidance. Patients of ASA-I and II, 20-60 y, both sexes and weighing between 50-70 kg, scheduled for mid-humerus, elbow, forearm or hand surgery were included in our study.

Patient refusal, coagulopathy, history of severe cardiovascular, pulmonary, kidney, liver disease, neurological, psychiatric, neuromuscular disorder, infection/sepsis/allergy, and peripheral neuropathy were excluded.

All patients were assessed, examined preoperatively and informed consent was taken day before surgery. On arrival in the preoperative room a 20 gauge intravenous (IV) cannula was secured into a peripheral vein in the contra-lateral arm, procedures was explained in full detail again. Patients were transferred to the operating room and standard monitoring was attached. Baseline heart rate (HR), mean blood pressure (MBP), oxygen saturation and
respiratory rate were recorded as pre-block values.

**Procedure:** All the patients received brachial plexus block through the supraclavicular approach using US guidance (The Sonosite Micromaxx™ Bothell, Washington, USA machine with a 6–13 MHz linear probe) by an experienced anesthesiologist. A 21G 50 mm short beveled insulated needle was inserted under US guidance under all aseptic precaution. When the tip of the needle was adjacent to the plexus, an aspiration test was done to rule out intravascular placement. The local anesthetic solution was injected after careful aspiration. The predetermined volume of 30 ml of the drug solution was administered around the brachial plexus as per group assigned and spread of drug solution was observed in tissue planes under ultrasound imaging. Distension of brachial plexus sheath was regarded as an indication of successful block. All patients were given supplemental oxygen using face mask. Neither the administrator nor the observer were aware about the drug solution used as it was prepared by a different investigator. Drug was to be revealed only on occurrence of any adverse effect.

Block was tested for both sensory and motor block and was compared with the contra lateral side. Sensory block was graded using a 3-point scale by the pin prick method; where 0 = no pain, 1 = blunt pain and 3 = sharp pain. The sensory block was assessed in the dermatome areas corresponding to median nerve, radial nerve, ulnar nerve and musculocutaneous nerve (C5-T1) until the completion of sensory blockade.

Supraclavicular block was considered successful when all dermatomes of brachial plexus (C5–T1) were blocked within 30 min. Onset of sensory block was defined as loss of pinprick sensation in comparison to contralateral limb as a reference. It was evaluated at every 2 min for first 30 min and every 60 min after completion of surgery till the complete resolution of sensory block. Sensory block duration was defined as the time from injection of local anesthetic study solution to complete recovery from pain sensation in all dermatomes of the brachial plexus.

Assessment of motor block was carried out according to modified Bromage scale at every 3 min till complete motor blockade. The onset of motor blockade was the time taken from end of local anesthetic (LA) injection to the development of Grade 3 motor block. The duration of motor block was the time interval between the end of LA administration to the recovery of complete motor function of the hand and forearm. Patients with ineffective block were excluded from the study, and surgery was done under GA.

The quality of analgesia was assessed every hour postoperatively in the recovery room and in surgical ward by attending nurse using numeric rating scale (NRS) (1–10). Zero was considered as no pain, 1–3 as mild pain, 4–6 as moderate pain, and 7–10 as severe pain. At the score of 4, nursing staff was directed to administer injection diclofenac sodium (1.5 mg/kg) intramuscularly as a rescue analgesic. Duration of analgesia was calculated from the time of LA injection to the time of first analgesic requirement. All patients were observed for any side effects such as nausea, vomiting, pneumothorax, hematoma, LA toxicity in the intra- and post-operative periods.

**Statistical analysis:**

Considering two tailed significance sample size was calculated to be at least 26 patients in each group when $\alpha$ error = 0.05, power = 80%, and effect size $d= 0.8$. 30 patients were enrolled in each group to compensate for possible dropouts. Data were presented as a mean and standard deviation. Statistical analysis was performed using t-test for mean and standard deviation (SD) of onset time, duration of sensory and motor blocks, duration of surgery, the total duration of analgesia due to brachial plexus block and hemodynamic variables [HR, systolic BP (SBP), diastolic BP (DBP) and mean arterial pressure (MAP)]. Demographic data (age, weight) were analyzed by student’s t-test. NRS scores between groups were compared nonparametrically using Mann–Whitney U-tests. Statistical significance

![Graph 1: Comparative perioperative heart rates in the groups](image-url)
was accepted for a p-value of < 0.05. All the statistical analysis was performed using Statistical Package for Social Science software version 21.0. (SPSS Inc, Chicago, IL, USA).

RESULTS

69 patients were accessed for eligibility. Consort diagram is shown in Figure 1. The demographic profile of the patients age, sex, weight, ASA grade were comparable in both groups. (Table 1).

The mean onset times of sensory and motor blocks were not statistically significant in both groups (Table 2).

The mean duration of sensory and motor blocks were significantly more in Group R than in Group N (p < 0.0001) as given in Table 2.

The mean duration of analgesia, given in Table 2, was 598.21 ± 19.33 min in Group R and 705.39 ± 31.54 min in the Group N which was statistically significant (p < 0.0001)

Both the groups were hemodynamically comparable at all times of surgery (Graph 1 & 2).

DISCUSSION

Supraclavicular block provides a rapid, dense, and predictable anesthesia of the entire upper extremity in the most consistent manner of any brachial plexus technique. Brachial plexus blockade provides an excellent alternative technique to GA for the upper limb surgical procedures. It not only offers excellent intraoperative pain relief but also good post-operative analgesia. The need was felt of an adjuvant which prolonged the block, was inexpensive and easily available and had least side effects. The chances of systemic toxicity with high concentrations of local anesthetic agents decreased when used with adjuvants in peripheral nerve block.

Nalbuphine hydrochloride, is a potent analgesic which acts as a kappa agonist and partial mu antagonist. Its affinity to κ-opioid receptors results in sedation, analgesia, and cardiovascular stability with minimal respiratory depression. In a meta-analysis, nalbuphine was found to be comparable to morphine in terms of effective pain relief with significantly lower incidences of pruritus, nausea, vomiting, and respiratory depression than morphine.

We added nalbuphine 10 mg to 29 ml of 0.75% of ropivacaine in supraclavicular block as it had been used in same dose in previous studies without any significant side effect or any neurotoxicity. We used 29 ml of 0.75% of ropivacaine which provided complete sensory and motor block without any side effect. Our findings were in accordance to previous studies which showed it to be an adequate volume
nalbuphine as an adjuvant to ropivacaine in supraclavicular block

and concentration. Both 0.5% as well as 0.75% concentration had been successfully in previous studies.\textsuperscript{12-14}

There was no significant statistical difference in the onset of sensory as well as motor block in both the groups in our study. The mean onset of sensory block (11.58 ± 3.56 min) in Group R and Group N (10.84 ± 3.24) were comparable, similarly motor onset was also comparable in both the groups (13.12 ± 4.98 min in Group R vs 11.23 ± 3.29 min in the Group N). Similar findings were noticed by Das A et al. when they used levobupivacaine alone and levobupivacaine with nalbuphine.\textsuperscript{15}

In our study, the duration of sensory block was significantly prolonged in the nalbuphine group in compare to control group. Similarly the duration of motor block was also significantly prolonged in the nalbuphine group than that of control group.

Das A et al. also observed that the duration of sensory and motor block was significantly prolonged in nalbuphine group compared to levobupivacaine group.\textsuperscript{15}

Gupta et al. in their study also observed that nalbuphine 10 mg with bupivacaine significantly enhanced the quality of supraclavicular brachial plexus block and increased the duration of sensory and motor block, but it did not affect the onset time of the blockade.\textsuperscript{11}

In our study the duration of analgesia was significantly higher in Group N (674.83 ± 21.84 min) compared to Group R (598.21 ± 19.33 min) which may be because of synergistic action of nalbuphine with ropivacaine. Gupta et al. as well as Das A et al. both used nalbuphine 10 mg in supraclavicular block along with bupivacaine and found similar results.\textsuperscript{11,15}

The analgesic effect of nalbuphine is explained by several mechanism. Apart from $\mu$-opioid-based spinal and supraspinal analgesia, inhibition of neuronal serotonin uptake leads to augmentation of the spinal inhibitory pathways for pain. Intracellular adenylyl cyclase is inhibited by the stimulation of opiate receptors in central nervous system which causes opening of potassium channels and closing the calcium channels. This leads to hyperpolarization of the cell membrane potential and inhibition of action potential transmission of ascending pain pathways.\textsuperscript{18}

The limitation of our study was that we had not taken any standardized dose of nalbuphine due to non-availability of proper literature reference relating to dose equivalence with other well-known opioid so we had taken the same doses which were used previously with bupivacaine in supraclavicular block.

CONCLUSION

From the current study, we conclude that, using nalbuphine as adjuvant to 0.75% ropivacaine for supraclavicular brachial plexus block prolongs the duration of sensory and motor blockades without any appreciable side effect in postoperative period but does not quicken the onset of sensory and motor blockades.

Conflict of interest: None declared by the authors

Authors’ Contribution:

VKY – Conduction of study work and editing and principal investigator.

AKC - Concept, conduction of study, manuscript editing, data analysis and writing.

MKP - Concept, main reviewer, second investigator, data analysis and processing.

GSJ - Editing and manuscript writing, and overall guidance.

AK – Editing manuscript, investigator and data processor.

RS - Second reviewer, manuscript editing, data collection.
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