**Randomized Controlled Trial for Evaluating the Analgesic Effect of Nalbuphine as an Adjuvant to Bupivacaine in Supraclavicular Block under Ultrasound Guidance**

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**Abstract**

**Introduction:** Benefits of regional anesthesia can be prolonged by adding adjuvants to local anesthetics. This study was designed to test the efficacy of adding nalbuphine to bupivacaine in supraclavicular brachial plexus blockade under ultrasound (US) guidance. **Methodology:** This was a prospective, randomized, double-blind study involving sixty patients of either sex undergoing elective orthopedic procedures of upper limb. In control Group C (n = 30), 30 mL of 0.375% bupivacaine + 1 mL normal saline and in study Group N (n = 30), 30 mL of 0.375% bupivacaine + 1 mL (10 mg) nalbuphine were used for giving supraclavicular block under US guidance. Parameters assessed were onset and duration of sensory and motor block, duration of analgesia (DOA), and any adverse events. Data between the groups were analyzed using independent t-test with SPSS 16.0 software. **Results:** In Group N, there was a statistically significant shorter time to onset of sensory blockade (4.89 ± 1.5 vs. 14.62 ± 1.73 min, \( P = 0.000 \)), longer duration of sensory block (373.17 ± 15.56 min vs. 157.82 ± 11.02 min, \( P = 0.000 \)), shorter onset time to achieve motor block (8.83 ± 1.9 min vs. 18.76 ± 1.75 min, \( P = 0.000 \)), longer duration of motor block (313.92 ± 16.22 min vs. 121.87 ± 16.62 min, \( P = 0.000 \)), and prolonged analgesia (389.33 ± 14.52 min vs. 171.65 ± 19.79 min, \( P = 0.000 \)). **Conclusion:** Nalbuphine when added to bupivacaine as an adjuvant in supraclavicular block significantly shortened the onset of sensory and motor block and enhanced the duration of sensory and motor block and DOA.

**Keywords:** Bupivacaine, nalbuphine, postoperative analgesia, supraclavicular block

**INTRODUCTION**

Benefits of regional anesthesia are short-lived because of brief duration of action of local anesthetics (LAs). Various drugs such as opioids, \( \alpha \)-2 agonists, and midazolam have been tried as adjuvants to bupivacaine in supraclavicular block in upper limb surgeries for prolonging the duration of postoperative analgesia.

The primary aim of this study was to evaluate the effect of adding nalbuphine, an opioid agonist-antagonist, to bupivacaine in supraclavicular block in terms of duration of analgesia (DOA), and the secondary aim was to record onset, duration of motor and sensory block, and any adverse events.

**METHODOLOGY**

After approval from the Institutional Ethical Committee and Clinical Trial Registry, sixty adult patients of American Society of Anesthesiology Class I and II of either sex undergoing upper limb orthopedic surgeries under supraclavicular brachial plexus block were enrolled in this prospective, randomized, double-blind study. Patients were explained about the study procedure, and only those who gave written consent were included in the study. Patients with a history of significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal, hepatic disease, alcoholism or drug abuse, morbid obesity, diabetes, peripheral vascular disease, suspected coagulopathy, known allergies, and pregnancy or lactating women were excluded from the study.

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Patients were randomly divided into two groups using computer-generated random number. Patients in Group C received supraclavicular block using 30 mL of 0.375% bupivacaine and 1 mL normal saline and Group N patients received 30 mL 0.375% bupivacaine and 1 mL nalbuphine (10 mg).

All the patients received brachial plexus block through the supraclavicular approach using ultrasonic (US) guidance (The Sonosite Titan™ US machine with a 6–13 MHz linear probe) by an experienced anesthesiologist. A short bevel needle was passed under US guidance. When the tip of the needle was adjacent to the plexus, an aspiration test was done to rule out intravascular placement. Before injecting the drug solution, saline boluses of 0.5 mL were injected to verify the correct position of the needle. After the drug injection, patients were assessed for onset, duration of sensory and motor blockade, postoperative analgesia, and any side effects of the drugs or complications of technique. Both the anesthetist who gave the block and the nursing staff who recorded the duration of block and DOA were blinded about the drug.

The assessment of sensory block was done by the cold sensation method every 3 min after drug injection. A baseline assessment of cold sensation was made in the distribution of each of ulnar, median, radial, and musculocutaneous nerves before the performance of the block. The onset of sensory blockade was the time taken from the end of drug injection to achieving Grade 2 block. The duration of sensory block was the time interval from the end of LA administration to the complete resolution of sensory block in the distribution of each nerve.

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 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.

Failure to achieve complete loss of cold sensation and motor block in the distribution of any of the four nerves was considered as an ineffective block. Patients with ineffective block were excluded from the study, and surgery was done under general anesthesia.

The quality of analgesia was assessed every hour postoperatively in the recovery room and in surgical ward by attending nurse using Numeric Rating Scale (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, the nurse was directed to administer injection diclofenac sodium (1.5 mg/kg) intramuscularly. DOA 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, and postblock neuropathy in the intra- and post-operative periods (Figure 1).

Statistical methods

We conducted a pilot study on seven patients in each group and presuming the difference in the DOA and effect size obtained to be true, calculated that 26 patients in each group would be required for the study with error of 0.05 and error of 0.8. A total of 30 patients were taken in each group to compensate for dropouts. The data were analyzed using SPSS 16.0 (Statistical Package for Social Sciences, Software Inc., Released in 2009, Chicago, USA) for windows. Numerical data were summarized using mean and standard deviations. Demographic data were analyzed by student’s t-test. The time of onset, duration of sensory and motor blocks, and DOA were analyzed using independent t-test and reconfirmed with Mann–Whitney U-tests. P < 0.05 was considered statistically significant.

Results

The demographic data (age, weight, and gender) were comparable for both the groups [Table 1]. Onset time of sensory (4.89 ± 1.5 min vs. 14.62 ± 1.73 min) and motor block (8.83 ± 1.9 min vs. 18.86 ± 1.75 min) in Group N was significantly faster than Group C (P = 0.000) [Table 2]. The mean duration of sensory (373.17 ± 15.56 min vs. 157.82 ± 11.05 min) and motor block (313.92 ± 16.22 min vs. 121.87 ± 16.62 min) in Group N was significantly prolonged than Group C (P = 0.000) [Table 2]. The mean DOA for Group C and Group N was 171.65 ± 9.79 min and 389.33 ± 14.52 min, respectively (P = 0.000) [Table 2]. No side effect was seen in either group.

Discussion

There are several advantages of regional anesthesia over general anesthesia in terms of safety, effective pain relief, and early discharge from the recovery room. However, additional

![Consolid diagram](attachment:Consolid_diagram.png)

**Figure 1:** Consort diagram
Nalbuphine hydrochloride, a potent analgesic,\cite{14} acts as a Kappa agonist and partial mu antagonist.\cite{6,16} Its affinity to \(\kappa\)-opioid receptors results in sedation, analgesia, and cardiovascular stability with minimal respiratory depression.\cite{16,15} In a meta-analysis,\cite{17} 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. Nalbuphine was previously used as an effective adjunct to lidocaine in Intravenous Regional Anaesthesia (IVRA)\cite{18} and to bupivacaine in spinal,\cite{16,19} epidural,\cite{20,21} and caudal\cite{22} anesthesia for increasing DOA.

A volume of 30 mL of 0.375% bupivacaine was taken as this was found to be an adequate volume and concentration for giving supraclavicular block by previous studies.\cite{23} US, a gold standard in regional anesthesia,\cite{24} was used as it enabled visualization of the placement of LA at the precise intended anatomical location. Despite using US guidance, volume lesser than 30 mL was not as previous studies have concluded that recommended volume required for supraclavicular block using US-based or non-US-based nerve localization techniques does not differ.\cite{25}

In our study, we have added 10 mg of nalbuphine to 30 mL of 0.375% of bupivacaine for better efficacy of supraclavicular block. There were several studies in which nalbuphine had been used via various routes without any report of neurotoxicity.\cite{16,18-20} Previously, nalbuphine had been given in the doses of 10–30 mg in combination with LA via the epidural route for postoperative pain relief in orthopedic surgeries and cesarean sections without causing respiratory depression or any other significant side effect.\cite{20,21} Nalbuphine had also been given systemically (IV) for analgesia in a dose of 0.2 mg/kg in medially compromised patients without producing side effects.\cite{20}

The onset and duration of motor and sensory block in Group C was in concordance with the previous studies.\cite{23,27} In Group N, the onset was significantly faster both for sensory and motor block than the Group C. Our result was in agreement with the study in which nalbuphine had been used with lidocaine for IVRA.\cite{18} There were studies in which nalbuphine did not significantly hasten the onset of sensory and motor block when administered with bupivacaine intrathecally.\cite{16,28-30} This could be due to a lesser dose of nalbuphine used in these studies [0.8 mg – 1.6 mg],\cite{16,28-30} as compared to 10 mg in our study.

The patients of Group N had a longer duration of sensory and motor block. Similar prolongation of duration of sensory\cite{28} and motor blocks had been seen when nalbuphine was used as an adjuvant to bupivacaine in spinal,\cite{29,30} epidural,\cite{21} and caudal blocks.\cite{22} The DOA in Group N was also significantly higher than Group C. Similar prolongation of DOA had been obtained in previous studies as well.\cite{16,21,28,29} This prolongation of anesthetic effect and analgesia could be secondary to the stimulation of kappa receptors by nalbuphine, which inhibits release of neurotransmitters for pain such as substance P.\cite{29}

Limitation of our study was that we did not record the hemodynamic changes and sedation score associated with the use of nalbuphine. Due to lack of facility in our institution, we could not measure the level of nalbuphine in blood. Further studies are required to find the optimum dose of nalbuphine in supraclavicular block. To give a better insight of its efficacy, safety profile, and cost-effectiveness, its use needs to be explored in a larger study population and in different nerve blocks.

**Conclusion**

Nalbuphine as an adjuvant to bupivacaine in supraclavicular brachial plexus block prolonged the DOA and duration of block while accelerated the onset of block.

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### Table 1: Demographic and Surgical characteristics

| Demographic characteristics | Mean+SD (n=30) | Group C | Group N | P value |
|-----------------------------|---------------|---------|---------|---------|
| Age (years)                 | 33.4±12.4     | 30.8±13.9 | 0.447   |
| Weight (kilograms)          | 52.8±10.9     | 55.3±8.9  | 0.334   |
| Gender (male/female)        | 20/10         | 18/12    |         |

### Table 2: Onset, duration of sensory and motor blocks, and duration of analgesia in Group C and Group N

| Parameters                        | Mean+SD (n=30) | t   | P   |
|-----------------------------------|----------------|-----|-----|
| Onset of sensory block (min)      | 14.62±1.73     | 4.89±1.5 | 28.275 | 0.000 |
| Onset of motor block (min)        | 18.86±1.75     | 8.83±1.9 | 21.26  | 0.000 |
| Duration of sensory block (min)   | 157.82±11.05   | 373.17±15.56 | 61.805 | 0.000 |
| Duration of motor block (min)     | 121.87±16.62   | 313.92±16.22 | 45.295 | 0.000 |
| Duration of analgesia (min)       | 171.65±19.79   | 389.33±14.52 | 48.575 | 0.000 |

SD=Standard deviation

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Conflicts of interest
There are no conflicts of interest.

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