**Original Research Article**

# EFFECT OF NALBUPHINE AS ADJUVANT TO 0.5% BUPIVACAINE IN ULTRASOUND-GUIDED SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

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## Abstract

**Background:** Regional anaesthesia provides effective and reliable anaesthesia and analgesia for upper extremity surgeries, requiring precise localization, accurate drug deposition, and avoiding intra-arterial injection and pneumothorax. The present study aimed to evaluate the effect of nalbuphine as an adjuvant to 0.5% Bupivacaine in ultrasound-guided supraclavicular brachial plexus block for patients undergoing elective upper limb surgeries. **Materials and Methods:** This single-centre, prospective, randomized, double-blinded control study was conducted at Srinivasan Medical College and Hospital. Sixty patients were divided into Group C: In the Control group, 30 patients received 20 ml of 0.5 % bupivacaine and 2 ml of normal saline. Group-N: Nalbuphine group, 30 patients received 20 ml of 0.5 % bupivacaine and nalbuphine 2 ml (10 mg/ml). Patients were assessed in pre-anaesthetic assessment before surgery. **Result:** There was no statistically significant difference in gender, age, weight, ASA, and the duration of the surgery between the groups. There was a statistically significant difference between the two groups, with Group N having an earlier onset of sensory (36%) and motor block onset (16%) than Group C. There was a statistically significant difference between the two groups, with Group N having a longer duration of motor block (33%) and longer duration of analgesia (42%) than Group C. Group C showed a dip in SBP and DBP at 45, 60, 75 and 90 min, suggesting peak effect of nalbuphine. **Conclusion:** Nalbuphine is a safe, economic, and better adjuvant for peripheral nerve blocks, with faster onset, longer duration, and calm patients.

## INTRODUCTION

Regional anaesthesia benefits patients, surgeons and Anaesthesiologists because of its inherent simplicity, preservation of consciousness, avoidance of airway instrumentation, rapid recovery, prevention of undesirable effects of general anaesthetic drugs and improved postoperative analgesia.[1] Regional blockade at the brachial plexus provides effective and reliable anaesthesia and analgesia for upper extremity surgeries.[2] Success depends on the precise localization of neural structures, accurate drug deposition around the plexus, and avoiding intra-arterial injection and pneumothorax. Historically, this was accomplished by elicitation of the paraesthesia technique, which is replaced by a peripheral nerve stimulator. Now ultra-sonography guided supraclavicular brachial plexus block is widely used because it is quick to perform and offers improved safety and accuracy in identifying the position of the nerves to be blocked.[3]

Back in history, where it started with the discovery of cocaine till the recent updates in local anaesthetics, the mechanism of action remains the same: blockade of voltage-gated sodium channels, which inhibits the excitation of nerve endings or blocking conduction in peripheral nerves.[4] Having a wide array of applications in local anaesthetics, bupivacaine maintains its stand because of its long duration and high potency compared to other local anaesthetics. Adding adjuvants increases the quality and duration of the blockade and decreases the incidence of local anaesthetic toxicity.[1] Recently, nalbuphine, a semisynthetic opioid with mixed κ agonist and μ antagonist, was studied frequently as an adjuvant to local anaesthetics, and the results of all studies conclude that nalbuphine is effective when used as an adjuvant to local anaesthetics in spinal, epidural, and

IV block as it significantly prolongs the block duration.[5]

Nalbuphine is a 14-hydroxy morphine derivative that has a strong analgesic effect.[6] The analgesic effect of nalbuphine is equal to that of morphine, but unlike morphine, it has a ceiling effect on respiration. Nalbuphine can potentially maintain or even enhance μ-opioid-based analgesic effect while mitigating the μ-opioid side effects. Nalbuphine has been proven to prevent hemodynamic stress response associated with endotracheal intubation.[5,6] Like fentanyl and propofol, nalbuphine is also popular in producing analgesia during monitored anaesthesia care. The drug is also very effective in subarachnoid and epidural routes for prolonging sensory and motor block duration and postoperative analgesia. Success and nontoxicity of the drug in the subarachnoid and epidural route ensure that the drug can safely be used perineurally in any peripheral nerve block. Though nalbuphine has side effects like sedation, clamminess, nausea and vomiting, dizziness, xerostomia, and headache, it is much less than other additives.[4,7] The present study aimed to evaluate the effect of nalbuphine as an adjuvant to 0.5% Bupivacaine in ultrasound-guided supraclavicular brachial plexus block for patients undergoing elective upper limb surgeries.

## MATERIALS AND METHODS

This single-centre, prospective, randomized, double-blinded control study was conducted at the Department of Anaesthesiology and Critical Care in Srinivasan Medical College and Hospital from Jan 2023 to June 2023. All patients who attended the orthopaedic and plastic surgery outpatient clinic planned for surgical treatment were assessed in pre-anaesthetic assessment. Written informed consent was obtained from all patients.

**Inclusion Criteria**
ASA physical status I and II patients of both sex, ages between 18 and 60 years, weight between 40 and 70 Kg, and patients undergoing elective forearm and hand surgery in orthopaedic and plastic surgical operating theatre were included.

**Exclusion Criteria**
Patient refusal for the procedure, any bleeding tendency or patient on oral anticoagulants, neurological deficits involving brachial plexus, history of allergy to local anaesthetics or opioids, local infection at the site of injection, and patients on any sedatives or antipsychotics and chronic analgesics were excluded.

Patients were divided into two groups. Group-C: In the Control group, 30 patients received 20 ml of 0.5 % bupivacaine and 2 ml of normal saline. Group-N: Nalbuphine group, 30 patients received 20 ml of 0.5 % bupivacaine and nalbuphine 2 ml (10 mg/ml).

On the day of surgery, all the patients were verified for their systematic preoperative assessment, including history taking, physical examination and review of the results of routine investigations. On arrival at the preparation room, an 18-gauge IV cannula was inserted into a peripheral vein in the contralateral arm. The patient was sedated by 0.01-0.05 mcg/kg of intravenous midazolam. Additional intravenous fentanyl 1mcg/kg was added as needed (to keep moderate sedation arousable on command). The patient was then transferred to the operating room where basic monitoring [Electrocardiography (ECG), Non-invasive Blood Pressure (NIBP) and pulse Oximetry (SpO2)] were attached. Baseline heart rate, blood pressure, and oxygen saturation were recorded as pre-block values. All the patients were supplemented with oxygen via a poly mask. The patient was supine, and an ultrasound machine was used to locate the subclavian artery, first rib, pleura and brachial plexus cluster. A 23-gauge, 5 cm echogenic needle was advanced to the corner pocket, and half the prepared local anaesthetic mixture was injected. The onset of sensory and motor blockade, duration of motor blockade and duration of analgesia were recorded by interviewing the patient. Heart rate, blood pressure, and Spo2 were noted during the intraoperative period every 5 min.

The onset of sensory block was assessed by pinprick method using a 25‑G hypodermic needle in the appropriate area using a 3‑point scale for pain compared to the same stimulation on the contralateral upper limb. Motor block was also assessed by thumb abduction (radial nerve), thumb adduction (ulnar nerve) and thumb opposition (median nerve). The duration of motor block and analgesia was determined by asking patients to move their fingers. The patient was monitored periodically for up to 120 minutes. Side effects like nausea, vomiting, euphoria, sedation, hypotension and bradycardia were noted, and if any of the above signs and symptoms were mentioned, it was planned as follows.

Sp02 monitored sedation, and oxygen supplementation was given. Oral and nasopharyngeal airways were used in case of deeper sedation. Inj. Ondansetron, 4mg IV, was given to manage nausea and vomiting, and reassurance was provided to manage euphoria. Inj. Dexamethasone 8 mg IV and Inj. Chlorpheniramine 40mg IV were given to manage pruritis. Inj. Ephedrine, 6mg IV bolus, was given to manage hypotension. Inj. Atropine 0.6 mg IV was given to manage bradycardia if the heart rate was less than 50 /min. In the postoperative period, if a patient had started to complain of pain (VAS > 3), rescue analgesia was given in the form of pethidine 1mg/kg, paracetamol 1 gm IV drip and or diclofenac 75 mg IM till VAS ≤ 3.

The statistical analyses were performed by using SPSS version 21. Data were presented as mean with Standard deviation for normal distribution. The unpaired t-test and Chi-square test were used to compare the means between the groups, and a P value <0.05 was considered statistically significant.

## RESULTS

Among 60 patients, 24 males and five females were in Group N, while 24 males and six females were in Group C.

The mean age in average years was $39.00 \pm 14.83$ (years) in group N and $36.43 \pm 11.53$ (years) in group C. The mean weight in Kg was $58.56 \pm 6.55$ (Kg) in group N and $59.53 \pm 4.24$ (Kg) in group C. In group N, 12 patients (40%) with ASA I and 18 patients (60%) with ASA II. In group C, ten patients (33%) had ASA I, and 20 (67%) had ASA II. There was no statistically significant difference in gender, age, weight, ASA, and the duration of the surgery between the two groups.

There was a statistically significant difference between the two groups, with Group N having an earlier onset of sensory (36%) and the onset of motor block (16%) than Group C ($P<0.001$). There was a statistically significant difference between the two groups, with Group N having a longer duration of motor block (33%) and longer duration of analgesia (42%) than Group C ($P < 0.001$).
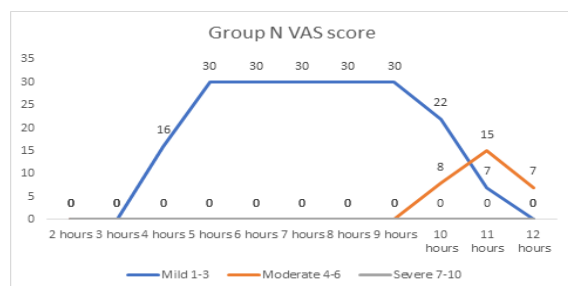


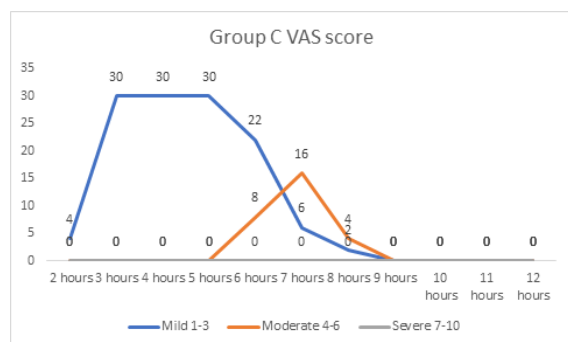**Figure 1: VAS score in Group N**



**Figure 2: VAS score in Group C**

The VAS score in Group C had four patients with mild pain at 2 hours and 30 patients with moderate pain at 3 hours. At 4 hours, Group C had 30 patients with moderate pain, and Group N had 16 patients with moderate pain. At 5 hours, Group C and Group N had 30 patients with moderate pain. At 6 hours, Group C had 22 patients with mild pain, 8 with moderate pain, and in Group N, 30 patients with moderate pain.

At 7 hours, Group C had six patients with mild pain, 16 with moderate pain, and in Group N, 30 patients with moderate pain. At 8 hours, Group C had two patients with mild pain, 4 with moderate pain, and in

Group N, 30 patients with moderate pain. In Group N, 30 patients with moderate pain at 9 hours. Twenty-two with mild, and 8 with moderate at 10 hours. At 11 hours, Group N had seven patients with mild pain and 15 with moderate pain. At 12 hours, Group N had seven patients with moderate pain, while Group C had none [Figure 1 and 2].
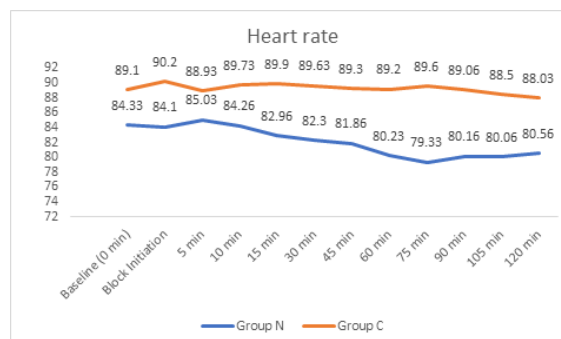


**Figure 3: Heart rate between groups**

The heart rate variation between the two groups was significant at block initiation and post-block at 15, 30, 45, 60, 75, 90, 105 and 120 min with a p-value of <0.05 [Figure 3].
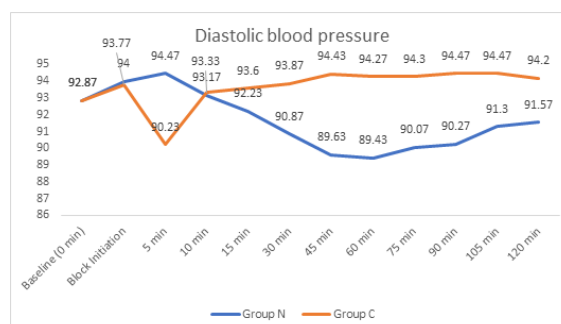


**Figure 4: Diastolic blood pressure between groups**

Systolic BP variation between the two groups was not statistically significant. Diastolic BP variation between the two groups was statistically significant at 15, 30, 45, 60 mi, 75, 90, 105 and 120 min intervals with a p-value of <0.05. Baseline values were comparable, and the diastolic blood pressure in group C increased in each interval from the 5th minute, whereas in group N, the values decreased [Figure 4].
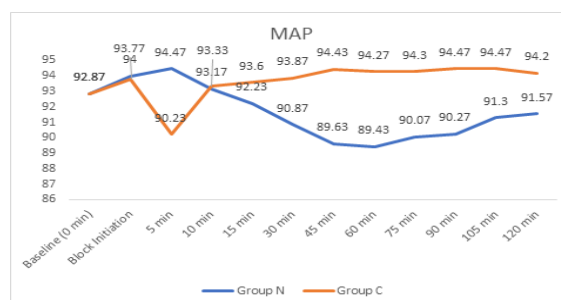


**Figure 5: Mean arterial pressure between groups**

MAP variation between the two groups was statistically significant at 45, 60, 75 and 90 min with

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a p-value of <0.05. At these intervals, group N also shows a dip in SBP and DBP, which would be considered the peak effect of nalbuphine [Figure 5].

SPO2 between the two groups was not statistically significant.

**Table 1: Distribution of patient's characteristics**

| | | Group N | Group C | P-value |
|---|---|---|---|---|
| Gender (M/F) | | 24/5 | 24/6 | 0.551 |
| Age (Years) | | 39.00 ± 14.83 | 36.43 ± 11.53 | 0.457 |
| Weight (Kg) | | 58.56 ± 6.55 | 59.53 ± 4.24 | 0.501 |
| ASA | I | 12 (40%) | 10 (33%) | 0.599 |
| | II | 18 (60%) | 20 (67%) | |
| Duration of surgery (min) | | 120.00 ± 0.47 | 120.00 ± 0.00 | 0.321 |
| Mean onset time of sensory block | | 6.16 ± 1.782 | 8.90 ± 1.688 | <0.001 |
| Mean onset time of motor block | | 12.167 ± 2.506 | 14.30 ± 1.803 | <0.001 |
| Mean duration of the motor block | | 445.26 ± 35.154 | 316.56 ± 28.816 | <0.001 |
| Mean duration of analgesia | | 687.50 ± 36.287 | 444.30 ± 38.198 | <0.001 |

## DISCUSSION

Our study shows gender, age, ASA and duration of surgery were comparable between group N and group C, and they were statistically insignificant. The mean onset time for the sensory block was 6.16 ± 1.782 in group N and 8.90 ± 1.688 in group C, which was statistically significant (p < 0.001), with 36 % earlier in group N than group C. Nazir N et al,[8] have shown that 10 mg of nalbuphine as an adjuvant to 0.375 % bupivacaine gives a significantly faster onset (66%) than the control group. In contrast, Gupta et al. and other studies have a faster onset than the control group with no statistical significance.[1,2,7]

In our study, the mean onset time for the motor block was 12.167 ± 2.506 in group N and 14.30 ± 1.803 in group C, which is statistically significant (p < 0.001), with 16 % earlier in group N than group C. Nazir N et al,[8] have shown that 10 mg of nalbuphine as an adjuvant to 0.375 % bupivacaine gives a significantly faster onset (54 %) than the control group. Gupta et al,[2] have shown a significantly faster onset (33%) with nalbuphine compared to a control group. The results of Abdelhaq MM et al,[1] and Chiruvella S et al,[7] have shown faster onset in nalbuphine than the control group with no statistical significance. The rapid onset was attributed to the partial kappa agonist nalbuphine, which has lipophilic properties that make local anaesthetics attach to the neuronal receptors faster.[9]

In our study, the mean duration of motor block was 445.26 ± 35.154 in group N and 316.56 ± 28.816 in group C, which was statistically significant (p<0.001), with 33 % longer in group N than group C. Similar findings have been noted with Chiruvella S et al,[7] (33%) and Nazir N et al,[8] (61%) with statistically significant.

In our study, the mean duration of analgesia was 687.50 ± 36.287 in group N and 444.30 ± 38.198 in group C. This was statistically significant (p < 0.001), with 42 % longer than in group N than in group C. The duration of analgesia in studies conducted by Gupta et al,[2] (30%), Chiruvella S et al.7 (36%), Nazir N et al,[8] (56%), and Abdelhamid BM et al.10 (52%) were also significantly prolonged compared to control groups.

Chiruvella S et al,[7] conducted a study comparing various adjuvants like nalbuphine 10 mg, dexmedetomidine 100 mcg and 10 % magnesium sulfate with 0.5% bupivacaine (30 ml) in supraclavicular brachial plexus block. They showed that all adjuvants prolonged the duration of analgesia and decreased the analgesic requirement. They also concluded that compared to the nalbuphine group, dexmedetomidine and magnesium sulfate produced significant sedation and may extend to the postoperative period.

Kumar R et al,[4] conducted a study comparing fentanyl (100 mcg) which was the maximum dose, and nalbuphine 20 mg as an adjuvant to 0.5% bupivacaine in supraclavicular brachial plexus block showed a faster onset of sensory and motor block, longer duration of sensory and motor block and prolonged duration of analgesia in nalbuphine group. A study conducted by Abdelhamid BM et al,[11] to evaluate the efficacy of nalbuphine (10 mg) and dexmedetomidine (1 mcg/ kg) with 0.5 % bupivacaine (0.3 ml/kg) in a thoracic paravertebral block. Though the duration of analgesia was longer in dexmedetomidine (15%) than in nalbuphine, it was statistically insignificant. The drug nalbuphine was cost-effective compared to dexmedetomidine with stable hemodynamics.

Shakooh S et al,[11] in their study conducted on patients undergoing lower abdominal and lower limb surgeries, intrathecal nalbuphine (0.8 mg) was an effective adjuvant with 0.5% hyperbaric bupivacaine for postoperative analgesia. Intrathecal nalbuphine hastened the onset of sensory (53%) and motor block (23%), duration of sensory (44%) and motor block (46%), provided effective postoperative analgesia (54%) with desirable sedation and minimal side effects. Rawal N et al,[9] studied the behavioural and histopathological effects following intrathecal administration of butorphanol, sufentanil and nalbuphine in sheep. They found that nalbuphine was the least irritating to neural tissue, even when used in large doses and was associated with minor behavioural and EEG changes.

In our study, the mean Systolic BP values between the two groups were not statistically significant (P value > 0.05). Baseline diastolic BP baseline values

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were comparable. The diastolic BP variation between the two groups was statistically significant at eight intervals from $15^{th}$ to 120 minutes (P value < 0.05). Diastolic BP in group C increased in each interval from the $5^{th}$ minute, whereas in group N, the values decreased. MAP variation between the two groups was statistically significant at 45, 60, 75 and 90 minutes (P value < 0.05). Group N also showed a dip in SBP and DBP at these intervals. Absorption of nalbuphine by its lipophilic characteristics is insidious and produces mild sedation with stable hemodynamics. Its peak action would appreciate this, and though the blockade was adequate to proceed with surgery, Group C patients had significantly elevated diastolic BP and MAP.

Kumar R et al,[4] showed in their study clinically manageable side effects like bradycardia (10%), hypotension (10%) and sedation (3.3%) in the nalbuphine group. Abdelhamid BM et al,[10] observed median values for heart rate, and both groups had a decline in heart rate. Still, in the nalbuphine group, it raised to preoperative values at the end of the surgery. In contrast, in dexmedetomidine groups, heart rate values were below the baseline values throughout the surgery.

In this study, no sedation was given in either group before the initiation of the block. The significance noted at different intervals in heart rate, diastolic BP and mean arterial BP could be attributed to the systemic absorption of nalbuphine, causing calm and sedated patients with a peak effect in MAP between 45 and 90 minutes.[12] At the end of 120 minutes, the mean variation of hemodynamic parameters was narrowed and became insignificant. SPO2 between the two groups was not statistically significant, with a p-value> 0.05.

## CONCLUSION

The study concludes that the nalbuphine group had a faster onset of sensory and motor blockade, longer duration of motor blockade and analgesia, and calm patients with stable hemodynamics. 20 mg of nalbuphine is a safe, economical, and better adjuvant in peripheral nerve blocks.

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