RESEARCH PAPER

Comparative Evaluation of Nalbuphine and Buprenorphine as Adjuvants to 0.5% Levobupivacaine in Lateral Approach Supraclavicular Brachial Plexus Block for Elective Upper Limb Orthopaedic Procedures – A Randomised Double Blind Study

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ABSTRACT

Background: Supraclavicular brachial plexus block considered "spinal anesthesia of upper extremity" has gained popularity as the sole anesthetic method for most upper limb surgeries. As literature evidence for mixed opioid agonist-antagonist adjuvants in peripheral nerve blocks and studies on lateral approach supraclavicular block are lacking, we formulated this study to compare the efficacy of an equipotent dose of Nalbuphine with Buprenorphine as an adjuvant to 0.5% levobupivacaine in the lateral approach supraclavicular brachial plexus block.
Methods: A prospective, randomized, double-blind interventional study was conducted in 60 patients with American Society of Anaesthesiologists 1 and 2 physical statuses scheduled for upper limb orthopedic surgeries. Study participants in Group 1(n = 30) received 10 mg Nalbuphine and in Group 2(n = 30) 0.3 mg Buprenorphine as adjuvants along with 0.5% Levobupivacaine (0.5%). Both groups were assessed for block characteristics, hemodynamic parameters, and adverse effects.
Results: The onset of sensory and motor blocks was significantly faster in Group 1 than in Group 2. The duration of sensory block, motor block, and analgesia was significantly longer in Group 2 than in Group 1. Four patients in group 1 had bradycardia, and one patient in group 2 experienced postoperative nausea and vomiting. However, none of the patients in either group had hypotension or respiratory depression.
Conclusion: Equipotent doses of nalbuphine produce a faster onset of sensory and motor blocks, whereas buprenorphine produces prolonged motor blockade and analgesia. This property can be utilized in orthopedic surgeries, which are expected to last longer.

Keywords: Regional anesthesia; Adjuvants; Brachial Plexus block; Levobupivacaine; Nalbuphine, Buprenorphine; Equipotent doses.

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INTRODUCTION

Peripheral nerve blocks are gaining widespread popularity for perioperative pain management because of their distinct advantages over general anesthesia. Patients who undergo surgery under peripheral nerve blocks can bypass the recovery room and be expeditiously discharged following outpatient surgery. Patients can position themselves on the operating table with minimal risk of airway loss and personnel effort. A high degree of patient and surgeon satisfaction results from superior pain control with minimal side effects.

In 1911, Kulenkampff introduced the classic supraclavicular approach to brachial plexus block. [1] Winnie and Collins introduced the subclavian perivascular approach to brachial plexus block.[2] Moorthy introduced a modified lateral paravascular approach to supraclavicular brachial plexus block. Kothari introduced the lateral supraclavicular brachial plexus block in 2010[3]

Constant research and evaluation of adjuvants in regional anesthesia are ongoing, giving more importance to pure opioid agonist agents, with relatively less literature evidence for mixed opioid agonist-antagonist agents. Considering the advantages offered by mixed opioid agonists, we compared the efficacy of Nalbuphine with Buprenorphine as an adjuvant to 0.5% levobupivacaine in lateral approach supraclavicular brachial plexus block.

This study was designed to compare the efficacy of nalbuphine and buprenorphine as adjuvants to 0.5%

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levobupivacaine in peripheral nerve stimulator-guided supraclavicular brachial plexus block using a lateral approach. The primary objective of the study was to compare block characteristics (onset of sensory and motor block, duration of sensory and motor block, and duration of analgesia) among the groups and to evaluate the occurrence of hemodynamic instability and side effects, if any, as secondary objectives.

METHODOLOGY

This prospective, randomized, double-blind interventional study was conducted after receiving approval from the Ethics Committee (approval no. SIMS&RC/IEC/15/2019-20, dated 08/01/2020) and after registering the trial with the Clinical Trials Registry-India (vide registration number CTRI/2021/09/036728, www.ctri.nic.in). Informed written consent for research and educational purposes was obtained from all the patients after explaining the study protocol. The study procedures followed the guidelines of the Declaration of Helsinki,2013. The inclusion criteria were patients with American Society of Anesthesiologists (ASA) physical status 1 and 2, aged 18-60 years, BMI between 20-35 kg/m^2 scheduled for elective upper limb orthopedic surgeries with an expected surgical duration of 1-4 hours duration. Patients who had any contraindication to regional anesthesia, patients who had an arrhythmia, heart failure, renal failure, diabetic neuropathy, history of seizure disorder, or severe bronchopulmonary disease were excluded from the study. Participants who met the inclusion criteria were recruited for the study, randomized using computer-generated random numbers, and allocated to one of the following groups using a sequentially numbered opaque sealed envelope method.

In Group 1 (n = 30), nalbuphine 10 mg and group 2 (n = 30)- Buprenorphine 0.3 mg) were added as an additive with 0.5 ml/kg levobupivacaine (0.5%) in Peripheral Nerve Stimulator (PNS)-guided lateral approach supraclavicular brachial plexus block.

The intravenous line was secured with an 18G cannula and the baseline hemodynamic parameters were recorded for all participants. Intraoperatively, patients were monitored for block characteristics, such as sensory and motor block levels at 3 minutes intervals for an initial 30 min to determine the onset of block.

The onset of sensory blockade was defined as the time interval from completion of drug injection in the supraclavicular brachial plexus block until the achievement of loss of sensation to pinprick, and the onset of motor blockade was defined as the time interval from completion of drug injection in the supraclavicular brachial plexus block until the time to reach a modified Bromage score of 2 was noted in all cases.

Hemodynamic parameters, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), and respiratory parameters such as respiratory rate (RR) and oxygen saturation (SpO2) were monitored at 5 minutes interval until the end of surgery (T0, T1, T2, T3).

Postoperatively, hemodynamic and respiratory parameters were monitored every 30 min for the first 2 hours and then hourly for the next 24 h (PT0, PT1, PT2, and PT3). A numerical analog scale was used to assess pain at 30-minute intervals till the patient had a score of 4. At a numerical rating scale of 4, analgesia was provided with paracetamol 1gram intravenous infusion, and the time of its administration was noted.

The duration of the sensory blockade was defined as the time interval from completion of drug injection to the reappearance of the pinprick response, and the duration of the motor blockade was defined as the time interval from completion of drug injection until restoration of full hand and wrist mobility (modified Bromage score 0). The duration of analgesia, defined as the time interval from completion of drug injection until a numerical analog score of 4 was reached, was noted in all cases.

Patients were also monitored for the occurrence of any side effects such as bradycardia, defined as HR <20% of the baseline value, and were treated with intravenous atropine 0.6 mg intravenously. Hypotension was defined as a BP <20% of the baseline value and was treated with intravenous fluids or ephedrine 6 mg intravenously. Nausea and vomiting were treated intravenously with ondansetron (4 mg). If there was any drop in oxygen saturation to <95%, oxygen was added using a Hudson mask. Respiratory depression, defined as an RR of <8 per minute, was treated with an intravenous injection of naloxone 0.4 mg. The occurrence of other adverse events related to the technique, such as pneumothorax or vascular puncture, was also noted.

Statistical analyses were performed using the statistical program SPSS 20.0. Data were analyzed using descriptive statistics such as mean, standard deviation, percentage, and graphs. All categorical data are presented as frequencies and percentages. All continuous measurements are summarized as the mean ± standard deviation. Independent t-tests and chi-square tests were used to determine significant differences between the two groups. Statistical significance was set at P <0.050 (Confidence interval of 1.96)

RESULTS

Both groups had comparable demographic characteristics, duration of surgery, and ASA of the anesthesiologist physical status distribution (Table 1).

Table 1: Demographic characteristics

Variable	Group 1	Group 2
Age (years)		
18 to 37	16(53.3%)	16(53.3%)
38 to 57	14(46.7%)	14(46.7%)
Mean +/- SD	35.90 +/- 10.4	37.7 +/- 11.6
Gender		
Male	23(76.7%)	19(63.3%)
Female	07(23.3%)	11(36.7%)
Body Mass Index		
Normal	21(70.0%)	22(73.3%)
Overweight	09(30.0%)	08(26.7%)
Mean +/- SD	24.07+/-1.72	23.47+/-2.42
ASA Physical status		
1	26(86.7%)	24(80.0%)
2	04(13.3%)	06(20.0%)
Duration of surgery (minutes)		
</=90	14(46.7%)	12(40.0%)
> 90	16(53.3%)	18(60.0%)
Mean +/- SD	106 +/- 51.50	109 +/- 47.59

Onset of Sensory Block

The onset of sensory block was significantly faster (less than 6 min) in group 1 than in group 2 (P = 0.0001) (Table 2). Motor block onset was significantly faster in Group 1 than in Group 2 (P = 0.0001) (Table 2).

Table 2: Block onset time

Variable	Group 1	Group 2
Sensory block onset time (minutes)		
</=6	28(93.3%)	02(6.7%)
>15	02(06.7%)	28(93.3%)
Mean +/- SD	5.40 +/-1.13	9.17+/-1.23
Motor block onset time (minutes)		
</=6	04(13.3%)	00(0.0%)
>6	26(86.7%)	30(100.0%)
Mean+/- SD	12.40+/-4.90	17.07+/-3.97

Sensory Block Duration

The duration of sensory block, duration of motor block, and analgesia in group 2 were significantly prolonged compared to those in group 1 (P = 0.0001) (Table 3).

Table 3: Duration of block

Variable	Group 1	Group 2
Sensory block duration (minutes)		
</=360	18(60.0%)	03(10%)
>360	12(40.0%)	27(90%)
Mean+/- SD	368+/-51.06	425+/-46.51
Motor block duration (minutes)		
</=360	28(93.3%)	16(53.3%)
>360	02(06.7%)	14(46.7%)
Mean+/- SD	310 +/- 49.0	370+/-29.4
Duration of Analgesia (minutes)		
</=500	30(100.0%)	00(0.0)
>500	00(0.0)	30(100.0%)
Mean+/- SD	425+/- 45.7	656+/-155.1

There were no significant differences in the hemodynamic and respiratory parameters during the intraoperative and postoperative periods between the groups (Table 4 and Table 5).

Table 4: Hemodynamic parameters

Duration (minutes)	Heart rate (beats/min)		P value	MAP (mmhg*)		P value
	Group1	Group2		Group1	Group2	
T0	81.20±11.04	82.13±11.90	0.754	84.60±6.38	86.60±9.12	0.329
T1	81.23±12.80	82.33±11.37	0.726	84.20±6.57	85.17±8.53	0.625
T2	81.00±14.35	83.73±10.99	0.411	85.83±6.02	86.57±8.05	0.691
T3	81.77±12.19	83.13±11.59	0.658	85.73±6.86	87.53±9.09	0.390
PT0	81.93±10.35	83.00±12.17	0.716	85.53±7.09	87.47±8.08	0.329
PT1	81.23±11.14	81.97±11.54	0.803	85.53±6.84	86.73±8.19	0.540
PT2	81.77±10.61	81.90±11.06	0.962	85.67±6.60	86.87±8.83	0.553
PT3	80.69±10.01	81.52±9.98	0.758	84.73±6.97	86.13±9.05	0.505

* mmHg mercury

Table 5: Respiratory parameters

Duration (minutes)	Respiratory rate (breath/minute)		P value	Oxygen saturation (%)		P value
	Group1	Group2		Group1	Group2	
T0	14.90±1.15	14.50±0.97	0.152	98.97±0.56	98.97±0.49	1.000
T1	15.10±0.85	14.60±0.89	0.300	99.30±0.54	99.23±0.57	0.642
T2	15.03±0.81	14.63±1.07	0.170	99.53±0.57	99.33±0.61	0.194
T3	15.10±0.89	14.43±0.94	0.601	99.53±0.57	99.33±0.61	0.194
PT0	15.03±1.03	14.33±0.96	0.901	99.53±0.57	99.33±0.61	0.194
PT1	14.93±0.98	14.50±1.11	0.114	99.53±0.57	99.33±0.61	0.194
PT2	14.93±1.05	14.37±0.99	0.361	99.53±0.57	99.33±0.61	0.194
PT3	14.90±1.13	14.37±0.99	0.571	99.53±0.57	99.33±0.61	0.194

Adverse Effect

Bradycardia was noted in four patients in group 1, whereas none of the patients in group 2 had bradycardia. None of the patients in either group had hypotension or respiratory depression. One patient in group 2 had nausea and vomiting in the postoperative period, which was treated with antiemetics, whereas none of the patients in group 1 had PONV, as shown in Table 6.

Table 6: Adverse Effects

Variable	Group 1	Group 2
Bradycardia	04(13.3%)	00(0.0)
Nausea, vomiting	0(0.0)	01(3.3%)

DISCUSSION

Peripheral nerve blocks are cost-effective anesthetic techniques used to provide good-quality anesthesia and analgesia, while avoiding airway instrumentation and the hemodynamic consequences of general anesthesia. Patient satisfaction and favorable postoperative recovery profiles have resulted in increased popularity of regional anesthetic techniques. Brachial plexus block is an easy and relatively safe procedure for upper limb surgery. The supraclavicular approach to brachial plexus block is associated with rapid onset and reliable anesthesia. The lateral approach to supraclavicular brachial plexus block is a recent update of upper limb blocks, which has proven to be a safe technique with a high success rate, safety, and minimal complications [3]. Hence, this technique was chosen to evaluate its associated safety, which was the secondary objective of this study. The administration of only local anesthetic drugs in peripheral nerve blocks has the disadvantage of a limited duration of action. Thus, increasing the dose of local anesthetic drugs may prolong the duration of anesthesia but may also increase the risk of systemic toxicity of local anesthesia. The use of catheters in nerve blocks can be helpful; however, their placement requires additional time, cost, and skill. Therefore, adjuvants are best used to prolong the block, and thus prolong the duration of analgesia.

Considering the advantages offered by mixed opioid agonist antagonists compared to pure opioid agonists, we decided to compare two drugs that belong to the opioid agonist-antagonist group. Hence, an equipotent dose of

Nalbuphine and Buprenorphine was chosen as an adjuvant to local anesthetics in supraclavicular brachial plexus block to evaluate and compare their effects. The study groups were comparable in terms of demographic characteristics, ASA of anesthesiologist physical status, and duration of surgery (Table 1).

Earlier studies performed by Attri et al., Nazia Nazir et al., and Aruna Vengadessane et al. used nalbuphine as an adjuvant to local anesthetics in supraclavicular brachial plexus block and found a significantly shortened onset of sensory and motor blocks, enhanced duration of sensory and motor blocks, and duration of analgesia. [4-6]

Potency is related to the dose of drug required to produce a given effect. In a study by Abdelhaq et al., an attempt was made to compensate for any differences in the potency of equipotent doses of opioid drugs have been mentioned. Hence, a 10 mg dose of nalbuphine in comparison with a 300 µg dose of buprenorphine was selected in our study [7]. Their study revealed that the onset times of motor and sensory blocks were not statistically significant in either group. Similar results were observed by Nishikawa et al. and Hamed et al. in their studies using buprenorphine as an adjuvant with plain local anesthetic solution in supraclavicular brachial plexus blocks.

In our study, the onset of sensory block was faster in the nalbuphine group than in the buprenorphine group, similar to the study by Patil et al., who found that the onset of sensory block was unaffected by the addition of buprenorphine as an adjuvant, compared to the control group with normal saline.[8]

The onset of motor block in our study was significantly faster in the nalbuphine group than in the buprenorphine group, in contrast to the study by Joshi et al., who did not observe any significant difference in the onset time of motor block between the nalbuphine and buprenorphine groups. This may be attributed to the technique used in our study, in which the lateral approach to block the brachial plexus was used, which resulted in a shorter time to the onset of blockade.

In our study, the buprenorphine group had a prolonged duration of sensory and motor blockade compared with the nalbuphine group. Thus, the duration of analgesia was also prolonged in the buprenorphine group compared with that in the nalbuphine group, similar to the study by Joshi et al. The prolongation of the anesthetic effect and analgesia could be secondary to the stimulation of the kappa receptor by nalbuphine, which inhibits the release of neurotransmitters for pain, such as substance P. Prolonged duration of analgesia by buprenorphine can be due to its high lipophilic nature, binding capacity, and affinity for mu receptors, thus slowing dissociation from the mu opioid receptor. It is also a highly lipophilic drug, resulting in low plasma concentration and prolonged duration [9]. In addition, partial agonist activity of the opioid-receptor-like 1 (ORL-1) receptor, with its endogenous ligand nociceptin or orphanin FQ (N/OFQ), might have contributed to the prolonged analgesic effect of buprenorphine [10].

Kumar et al., in their study using nalbuphine as an additive to supraclavicular brachial plexus block, found a decrease in heart rate in both intraoperative and postoperative periods from baseline values, but was not statistically significant compared to the fentanyl group. Similarly, in our study, four patients treated with nalbuphine had bradycardia that was treated with anticholinergic drugs.[11]

In our study, there was no significant difference in intraoperative and postoperative blood pressure and respiratory rate changes from baseline values in either group, similar to the study by Joshi et al. [9].

In our study, one patient in the buprenorphine group had postoperative nausea and vomiting, which was similar to the study by Thakur et al., who also found an increased risk of post-operative nausea and vomiting in patients with buprenorphine in a regional block compared to intramuscular buprenorphine.[12]

No serious complications, such as pleural puncture, pneumothorax, or any other cardiorespiratory side effects, were observed during the procedure, similar to the findings of Sahu and Kothari, who concluded that minimal adverse effects with a high success rate were observed in the lateral approach compared to conventional techniques [3,13]. The success rate in our study was 95%, as we had to convert to general anesthesia in three patients due to inadequate block, which was similar to the study by Dilip Kothari, where the success rate was 98%, and the study by DK Sahu, who had a success rate of 92%. The main limitation was that we did not assess the sedation score in either group and the sample size of our study was small.

We conclude that nalbuphine 10 mg produces a rapid onset of sensory and motor blockade compared to buprenorphine 0.3 mg in supraclavicular brachial plexus block. At the same time, the duration of sensory and motor blocks was prolonged in the buprenorphine group compared to that in the nalbuphine group. Hence, an equipotent dose of buprenorphine produces prolonged motor blockade and analgesia compared with nalbuphine. This property can be utilized in orthopedic surgeries, where surgeries are expected to be prolonged for longer durations.

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