

## Original Research Article

# POSTOPERATIVE ANALGESIC EFFICACY AND SAFETY OF BUPRENORPHINE VERSUS CLONIDINE ADDED TO BUPIVACAINE FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK: A RANDOMIZED COMPARATIVE STUDY

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Received : 28/08/2026  
Received in revised form : 21/09/2026  
Accepted : 03/10/2026

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DOI: 10.70034/ijmedph.2026.4.60

Source of Support: Nil,

Conflict of Interest: None declared

**Int J Med Pub Health**  
2026; 16 (4); 408-415

**ABSTRACT**

**Background:** Adjuvant drugs are commonly added to local anaesthetics in brachial plexus block to prolong block duration and reduce postoperative analgesic requirement, but comparative postoperative data on buprenorphine and clonidine specifically in the supraclavicular approach remain limited. **Objectives:** To compare the postoperative analgesic efficacy and safety of buprenorphine and clonidine, each added to bupivacaine, for supraclavicular brachial plexus block.

**Materials and Methods:** In this prospective, randomised, observer-blind, comparative study, 60 ASA I/II patients aged 20–60 years undergoing unilateral upper-limb surgery below the elbow were randomly allocated to three groups of 20 each: Group B (bupivacaine 0.5%, 20 mL, plus normal saline), Group BB (bupivacaine 0.5%, 20 mL, plus buprenorphine 100 mcg), and Group BC (bupivacaine 0.5%, 20 mL, plus clonidine 50 mcg), each to a total volume of 30 mL, for peripheral-nerve-stimulator-guided supraclavicular block. Primary outcomes were duration of postoperative analgesia, time to first rescue analgesic, and 24-hour rescue analgesic consumption. Secondary outcomes were postoperative visual analogue scale (VAS) trajectory, quality of anaesthesia, haemodynamic parameters, and adverse effects. Continuous variables were compared using one-way ANOVA and categorical variables using the chi-square test;  $p < 0.05$  was considered significant.

**Results:** Mean duration of analgesia was significantly longer with buprenorphine ( $815.20 \pm 266.06$  min) than with clonidine ( $432.35 \pm 96.40$  min) or bupivacaine alone ( $367.75 \pm 36.26$  min) ( $p < 0.05$ ). Time to first rescue analgesic was similarly delayed with buprenorphine ( $17.10 \pm 6.64$  h) and clonidine ( $16.35 \pm 5.90$  h) compared with bupivacaine alone ( $8.15 \pm 2.56$  h;  $p < 0.05$ ), with no difference between the two adjuvants ( $p > 0.05$ ). Twenty-four-hour rescue analgesic consumption fell from  $2.50 \pm 0.76$  doses with bupivacaine alone to  $1.45 \pm 0.60$  (buprenorphine) and  $1.45 \pm 0.89$  (clonidine) doses ( $p < 0.05$ ). VAS scores were significantly higher with bupivacaine alone at 6, 8, and 10 hours ( $p < 0.05$ ). Sedation, nausea, vomiting, and pruritus were numerically more frequent with buprenorphine, but the overall between-group difference in adverse effects was not statistically significant ( $p > 0.05$ ); haemodynamic parameters and  $SpO_2$  remained comparable throughout.

**Conclusion:** Both buprenorphine and clonidine, added to bupivacaine for supraclavicular brachial plexus block, provided significantly prolonged and comparably delayed postoperative analgesia with reduced rescue analgesic

consumption relative to bupivacaine alone, without a statistically significant increase in adverse effects; buprenorphine produced the longest overall duration of analgesia.

**Keywords:** Brachial Plexus Block; Buprenorphine; Clonidine; Pain, Postoperative; Bupivacaine.

## INTRODUCTION

Regional anaesthesia via brachial plexus block provides reliable surgical anaesthesia and superior early postoperative pain control for upper-limb surgery while reducing the systemic opioid-related side effects associated with general anaesthesia, although this early analgesic advantage does not always persist beyond the immediate postoperative period.<sup>[1]</sup> Peripheral nerve blocks have also been shown to provide superior postoperative pain control compared with systemic opioids alone.<sup>[2]</sup> A single-shot technique is generally preferred over continuous catheter-based approaches because the latter carry a higher risk of catheter-related infection and require additional expertise and equipment.<sup>[3]</sup> The supraclavicular approach, performed at the level of the trunks and divisions of the brachial plexus, provides dense and consistent blockade of the entire upper limb, and ultrasound- or nerve-stimulator-guided techniques have further improved its safety by reducing the risk of vascular puncture and pneumothorax.<sup>[4]</sup>

Because plain local anaesthetics provide only a finite duration of postoperative analgesia, adjuvant drugs are frequently added to the local anaesthetic solution used for brachial plexus block to prolong block duration and reduce the postoperative rescue-analgesic requirement.<sup>[5]</sup> Opioids such as buprenorphine, acting on peripheral opioid receptors that are upregulated at sites of tissue injury, have been shown to significantly prolong postoperative analgesia when added to local anaesthetics for supraclavicular brachial plexus block.<sup>[6,7]</sup> Alpha-2 adrenergic agonists such as clonidine, acting through both peripheral and possibly spinal mechanisms, have similarly been reported to prolong the duration of analgesia and delay the requirement for rescue analgesia when combined with local anaesthetics for brachial plexus block, in a dose-dependent manner.<sup>[8,9]</sup> Individually, both buprenorphine and clonidine have therefore been validated as effective adjuvants to local anaesthetics in brachial plexus blockade.<sup>[10]</sup>

However, direct head-to-head comparisons of buprenorphine and clonidine as adjuvants to bupivacaine specifically in the supraclavicular approach remain limited, and available comparative studies have focused predominantly on intraoperative block characteristics — onset and duration of sensory and motor blockade — with comparatively less emphasis on the postoperative analgesic trajectory, rescue-analgesic burden, and safety profile that determine a patient's overall postoperative recovery experience.<sup>[11,12]</sup> Reports comparing postoperative

pain scores, time to first rescue analgesic, and cumulative 24-hour analgesic consumption between these two adjuvants in supraclavicular block are sparse, and the relative magnitude of postoperative analgesic benefit as well as the comparative adverse-effect burden of buprenorphine versus clonidine in this setting has not been well characterised.<sup>[13]</sup> A clearer understanding of these postoperative outcomes would help anaesthesiologists select the more clinically appropriate adjuvant for supraclavicular brachial plexus block in routine upper-limb surgical practice.

The present study was therefore designed to compare the postoperative analgesic efficacy and safety of buprenorphine and clonidine, each added to bupivacaine, against bupivacaine alone, in patients undergoing supraclavicular brachial plexus block for unilateral upper-limb surgery. The primary objectives were to compare the mean duration of postoperative analgesia, the time to first rescue-analgesic requirement, and the total analgesic consumption in the first 24 postoperative hours between the three groups. The secondary objectives were to compare the postoperative visual analogue scale (VAS) pain-score trajectory, the overall quality of anaesthesia, and the incidence of adverse effects and haemodynamic changes associated with each adjuvant.

## MATERIALS AND METHODS

### Study design

This was a prospective, randomised, observer-blind, comparative clinical study conducted to compare the postoperative analgesic efficacy and safety of buprenorphine and clonidine, each added to bupivacaine, against bupivacaine alone, for supraclavicular brachial plexus block.

### Study setting and duration

The study was conducted in the Department of Anaesthesiology of a tertiary care teaching hospital over a period of 18 months, among patients attending the outpatient and inpatient services of the department who were scheduled for unilateral upper-limb surgery.

### Study population

Adult patients of either sex, aged 20–60 years, of American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective unilateral upper-limb surgery below the lower end of the humerus under supraclavicular brachial plexus block, were considered for enrolment.

### Eligibility Criteria

#### Inclusion Criteria

- Age between 20 and 60 years

- ASA physical status grade I or II
- Either sex
- Unilateral upper-limb surgery below the lower end of the humerus

#### Exclusion Criteria

- Suspected coagulopathy
- Infection at the proposed injection site
- Age below 20 or above 60 years
- Co-existing systemic disease such as hypertension, diabetes mellitus, seizure disorder, hepatic disease, renal disease, or coronary artery disease
- Patient refusal
- Known allergy to local anaesthetics or the study drugs
- Pregnancy
- ASA physical status grade III or IV
- Bilateral upper-limb procedures
- Pneumothorax on either side

#### Sample size and sampling technique

The sample size was calculated using the formula  $n = [Z^2 p(1-p)]/d^2$ , where  $Z$  (1.96) corresponds to a two-sided alpha error of 0.05,  $p$  (0.80) is the anticipated proportion based on the reported proportion of patients achieving a favourable postoperative analgesic outcome with adjuvant use in a comparable study by Paliwal B, et al,<sup>11</sup> and  $d$  (0.18) is the acceptable absolute precision of estimation. This yielded a minimum requirement of approximately 19 patients per group; 20 patients per group (total  $N = 60$ ) were enrolled to allow for anticipated attrition. Eligible consecutive patients attending the anaesthesiology outpatient and inpatient services who satisfied the eligibility criteria were enrolled and randomly allocated in a 1:1:1 ratio to one of the three study groups.

#### Participant recruitment and study groups

After approval from the Institutional Ethics Committee, eligible patients underwent a detailed pre-anaesthetic history and physical examination as per a structured proforma, and written informed consent was obtained from all participants prior to enrolment. Enrolled patients were randomly allocated to one of the following three groups of 20 patients each:

- Group B: bupivacaine 0.5% (isobaric), 20 mL, plus normal saline 10 mL (total volume 30 mL)
- Group BB: bupivacaine 0.5%, 20 mL, plus buprenorphine 100 mcg (1 mL), plus normal saline 9 mL (total volume 30 mL)
- Group BC: bupivacaine 0.5%, 20 mL, plus clonidine 50 mcg (1 mL), plus normal saline 9 mL (total volume 30 mL)

The study drug for each patient was prepared and coded by an anaesthesiologist not otherwise involved in the study, and was administered by an anaesthesiologist blinded to the group allocation, so that both the block procedure and the subsequent postoperative outcome assessments were conducted without knowledge of the adjuvant used.

#### Study procedure and data collection

On arrival in the operating room, standard ASA monitoring — electrocardiography, non-invasive blood pressure, and pulse oximetry — was established, and an 18G intravenous cannula was secured. Baseline heart rate, blood pressure, respiratory rate, and peripheral oxygen saturation ( $SpO_2$ ) were recorded, and the 10-point visual analogue scale (VAS) for pain was explained to each participant. Patients were positioned supine or semi-sitting with the head turned away from the side to be blocked and slightly elevated. Under strict aseptic precautions, the interscalene groove and subclavian artery pulsation were identified as landmarks, and a peripheral-nerve-stimulator-guided supraclavicular block was performed using a 22–25G, 5 cm stimulating needle inserted in a parasagittal plane; a target motor response (finger flexion/extension) at a stimulating current of 0.3–0.5 mA was confirmed before injecting the total study drug volume of 30 mL. Sensory and motor block were assessed at regular intervals until complete block was achieved, and the surgical procedure was allowed to proceed once adequate anaesthesia was confirmed. Postoperatively, patients were assessed at 30-minute intervals for the first two hours and thereafter hourly up to 24 hours for pain (VAS), time to first rescue analgesic requirement, quality of anaesthesia, haemodynamic parameters, and adverse effects, following a pre-defined assessment schedule and structured proforma.

#### Study variables

**Independent (exposure) variable:** the adjuvant added to bupivacaine (buprenorphine, clonidine, or none).

**Primary outcome (dependent) variables:** duration of postoperative analgesia; time to first rescue analgesic requirement; total rescue-analgesic doses required in the first 24 postoperative hours.

**Secondary outcome variables:** postoperative VAS pain score at 0, 6, 8, 10, 14, 18 and 24 hours; quality of anaesthesia; heart rate, systolic/diastolic/mean arterial blood pressure and  $SpO_2$  at baseline through 2 hours; incidence of sedation, nausea, vomiting, and pruritus.

**Potential confounding variables:** age, sex, ASA physical status, and body mass index (BMI), which were recorded and compared as baseline characteristics between groups.

#### Operational definitions

- Duration of analgesia: the time interval from onset of sensory blockade to the patient's first spontaneous complaint of pain warranting rescue analgesia.
- VAS score: a 10-point visual analogue scale, where 0 denotes no pain and 10 denotes the worst imaginable pain.
- Rescue analgesic criterion: injection diclofenac 75 mg intramuscularly, administered when the VAS score exceeded 3.
- Quality of anaesthesia: graded as Excellent (no complaints), Good (few vague complaints not

requiring supplementation), Moderate (complaints necessitating supplemental analgesia), or Unsuccessful (conversion to general anaesthesia).

#### Data quality assurance

A structured, pre-tested proforma was used for data collection. All postoperative outcome assessments were performed by a single blinded observer following the pre-defined assessment schedule described above, to minimise inter-observer variability, and data were cross-checked against the proforma before entry into the analysis dataset.

#### Statistical analysis

Data were entered in Microsoft Excel and analysed using SPSS version 20.0. Continuous variables (age, BMI, duration of analgesia, time to first rescue analgesic, VAS score, and haemodynamic parameters) were summarised as mean  $\pm$  standard deviation (SD) and compared among the three groups using one-way ANOVA, with pairwise (post-hoc) comparison between groups where the overall ANOVA result was significant. Categorical variables (sex, ASA grade, quality of anaesthesia, and adverse effects) were expressed as frequency and percentage, n (%), and compared using the chi-square test. A two-tailed p value of less than 0.05 was considered

statistically significant. No formal method for handling missing data was required, as no missing data occurred. Graphical representation of the results was performed using Microsoft Excel 2010.

#### Ethical considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants, or their legally authorised attendant, prior to enrolment; participants were informed of their right to withdraw from the study at any stage without any effect on their subsequent clinical care, and patient confidentiality was maintained throughout the study.

## RESULTS

Sixty patients were assessed for eligibility, and all 60 were randomised and analysed (20 per group); there were no dropouts, protocol deviations, or losses to follow-up (Figure 1).

#### Baseline demographic and clinical characteristics

The three groups were comparable with respect to age, sex distribution, ASA physical status, and body mass index (BMI), confirming adequate baseline matching (Table 1).

**Table 1: Baseline Demographic and Clinical Characteristics**

| Characteristic                         | Group B (n=20)    | Group BB (n=20)   | Group BC (n=20)   | p value            |
|----------------------------------------|-------------------|-------------------|-------------------|--------------------|
| Age, years (mean $\pm$ SD)             | 39.25 $\pm$ 11.20 | 39.75 $\pm$ 11.01 | 38.85 $\pm$ 11.69 | >0.05 <sup>a</sup> |
| Male sex, n (%)                        | 12 (60%)          | 11 (55%)          | 13 (65%)          | >0.05 <sup>b</sup> |
| ASA grade I, n (%)                     | 13 (65%)          | 16 (80%)          | 14 (70%)          | >0.05 <sup>b</sup> |
| ASA grade II, n (%)                    | 7 (35%)           | 4 (20%)           | 6 (30%)           |                    |
| BMI, kg/m <sup>2</sup> (mean $\pm$ SD) | 25.53 $\pm$ 3.61  | 26.31 $\pm$ 4.18  | 25.34 $\pm$ 3.59  | >0.05 <sup>a</sup> |

<sup>a</sup>One-way ANOVA test. <sup>b</sup>Chi-square test. ASA, American Society of Anesthesiologists; BMI, body mass index; SD, standard deviation.

#### Primary postoperative analgesic outcomes

The mean duration of postoperative analgesia was significantly longer in Group BB than in Group BC and Group B ( $p < 0.05$  for both comparisons); no significant difference was observed between Group B and Group BC ( $p > 0.05$ ) (Table 2, Figure 3A). The time to first rescue-analgesic requirement was significantly delayed in both Group BB and Group BC compared with Group B ( $p < 0.05$  for both), with no significant difference between the two adjuvant

groups ( $p > 0.05$ ) (Table 2, Figure 3B); the majority of Group B patients (90%) required their first rescue analgesic within 6–12 hours, whereas most Group BB and Group BC patients required it later, between 13 and 24 hours (Table 3). The total number of rescue-analgesic doses required in the first 24 postoperative hours was significantly higher in Group B than in Group BB and Group BC ( $p < 0.05$  for both), with no significant difference between the two adjuvant groups ( $p > 0.05$ ) (Table 2).

**Table 2: Primary Postoperative Analgesic Outcomes**

| Outcome                           | Group B (n=20)     | Group BB (n=20)     | Group BC (n=20)    | p value <sup>a</sup> |
|-----------------------------------|--------------------|---------------------|--------------------|----------------------|
| Duration of analgesia, min        | 367.75 $\pm$ 36.26 | 815.20 $\pm$ 266.06 | 432.35 $\pm$ 96.40 | <0.05 <sup>bc</sup>  |
| Time to first rescue analgesic, h | 8.15 $\pm$ 2.56    | 17.10 $\pm$ 6.64    | 16.35 $\pm$ 5.90   | <0.05 <sup>bc</sup>  |
| 24-hour rescue-analgesic doses, n | 2.50 $\pm$ 0.76    | 1.45 $\pm$ 0.60     | 1.45 $\pm$ 0.89    | <0.05 <sup>bc</sup>  |

Values expressed as mean  $\pm$  SD. <sup>a</sup>One-way ANOVA test. <sup>b</sup>Group B vs Group BB,  $p < 0.05$ . <sup>c</sup>Group B vs Group BC,  $p < 0.05$  (for duration of analgesia and 24-hour rescue-analgesic doses) /  $p > 0.05$  (for time to first rescue analgesic, Group BB vs Group BC comparison only was non-significant). SD, standard deviation.

**Table 3: Distribution of Patients by Time to First Rescue Analgesic**

| Time to first rescue analgesic | Group B, n (%) | Group BB, n (%) | Group BC, n (%) | p value            |
|--------------------------------|----------------|-----------------|-----------------|--------------------|
| < 6 hours                      | 2 (10%)        | 0 (0%)          | 0 (0%)          | <0.05 <sup>a</sup> |
| 6–12 hours                     | 18 (90%)       | 4 (20%)         | 5 (25%)         |                    |
| 13–18 hours                    | 0 (0%)         | 9 (45%)         | 7 (35%)         |                    |
| 19–24 hours                    | 0 (0%)         | 4 (20%)         | 8 (40%)         |                    |
| > 24 hours                     | 0 (0%)         | 3 (15%)         | 0 (0%)          |                    |

<sup>a</sup>Chi-square test for trend,  $p < 0.05$  across groups.

### Postoperative VAS score trajectory

VAS scores were comparable across the three groups at 0 hours and from 14 hours onward (all  $p > 0.05$ ), but were significantly higher in Group B at 6 hours, 8

hours, and 10 hours compared with both Group BB and Group BC ( $p < 0.05$  at each interval); VAS scores did not differ significantly between Group BB and Group BC at any time point (Table 4, Figure 2).

**Table 4: Postoperative Visual Analogue Scale (VAS) Score by Time Interval**

| Time | Group B     | Group BB    | Group BC    | B vs BB | B vs BC | BB vs BC |
|------|-------------|-------------|-------------|---------|---------|----------|
| 0 h  | 3.93 ± 1.20 | 3.47 ± 0.66 | 3.36 ± 0.85 | >0.05   | >0.05   | >0.05    |
| 6 h  | 3.42 ± 1.38 | 2.13 ± 0.82 | 2.07 ± 0.52 | <0.05   | <0.05   | >0.05    |
| 8 h  | 3.37 ± 0.72 | 1.74 ± 0.90 | 1.68 ± 0.41 | <0.05   | <0.05   | >0.05    |
| 10 h | 2.56 ± 0.63 | 1.04 ± 0.90 | 0.98 ± 0.12 | <0.05   | <0.05   | >0.05    |
| 14 h | 1.03 ± 0.63 | 0.81 ± 0.19 | 0.51 ± 0.32 | >0.05   | >0.05   | >0.05    |
| 18 h | 0.62 ± 0.35 | 0.33 ± 0.24 | 0.27 ± 0.14 | >0.05   | >0.05   | >0.05    |
| 24 h | 0.24 ± 0.15 | 0.17 ± 0.08 | 0.14 ± 0.04 | >0.05   | >0.05   | >0.05    |

Values expressed as mean ± SD; comparisons by one-way ANOVA with post-hoc pairwise testing.

### Quality of anaesthesia

The overall quality of postoperative anaesthesia, graded as Excellent, Good, or Moderate, was significantly better in Group BB than in Group B and

Group BC ( $p < 0.05$  for both comparisons), with no significant difference between Group B and Group BC ( $p > 0.05$ ) (Table 5). No patient in any group required conversion to general anaesthesia.

**Table 5: Quality of Anaesthesia by Study Group**

| Quality of anaesthesia | Group B, n (%) | Group BB, n (%) | Group BC, n (%) | p value            |
|------------------------|----------------|-----------------|-----------------|--------------------|
| Excellent              | 3 (15%)        | 12 (60%)        | 2 (10%)         | <0.05 <sup>a</sup> |
| Good                   | 12 (60%)       | 6 (30%)         | 11 (55%)        |                    |
| Moderate               | 5 (25%)        | 2 (10%)         | 7 (35%)         |                    |
| Unsuccessful           | 0 (0%)         | 0 (0%)          | 0 (0%)          |                    |

<sup>a</sup>Chi-square test; Group B vs Group BB,  $p < 0.05$ ; Group BB vs Group BC,  $p < 0.05$ ; Group B vs Group BC,  $p > 0.05$ .

### Haemodynamic parameters, oxygen saturation, and adverse effects

Heart rate, systolic and diastolic blood pressure, mean arterial pressure, and SpO<sub>2</sub> remained comparable between the three groups at all recorded time points from baseline through 2 hours postoperatively, without any statistically significant inter-group difference at any interval ( $p > 0.05$  throughout), indicating stable haemodynamic status with both adjuvants. Sedation was observed only in

the adjuvant groups (25% in Group BB and 15% in Group BC); nausea, vomiting, and pruritus were noted infrequently across groups (Table 6). Although the overall incidence of adverse effects was numerically highest in Group BB, the between-group difference did not reach statistical significance ( $p > 0.05$ ). No episode of clinically significant respiratory depression, bradycardia, or hypotension requiring intervention was recorded in any group.

**Table 6: Adverse Effects by Study Group**

| Adverse effect | Group B, n (%) | Group BB, n (%) | Group BC, n (%) | p value            |
|----------------|----------------|-----------------|-----------------|--------------------|
| Sedation       | 0 (0%)         | 5 (25%)         | 3 (15%)         | >0.05 <sup>a</sup> |
| Nausea         | 1 (5%)         | 3 (15%)         | 1 (5%)          |                    |
| Vomiting       | 1 (5%)         | 2 (10%)         | 2 (10%)         |                    |
| Pruritus       | 0 (0%)         | 2 (10%)         | 0 (0%)          |                    |

<sup>a</sup>Chi-square test, overall between-group comparison.

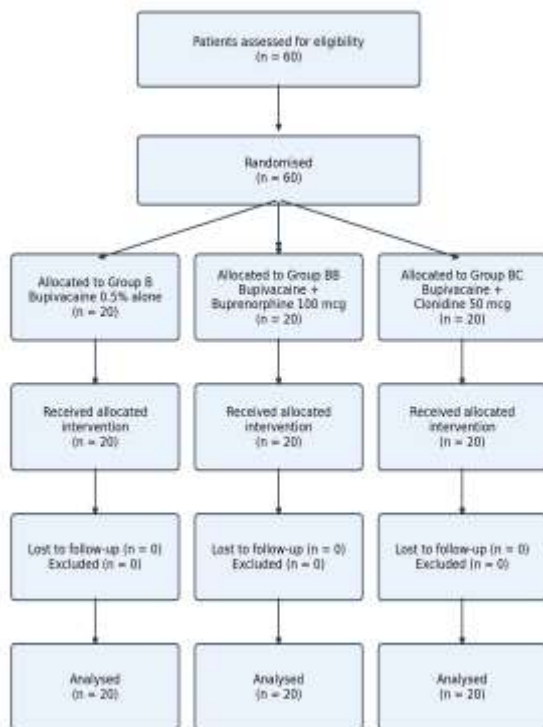


**Figure 1: CONSORT-style participant flow diagram**

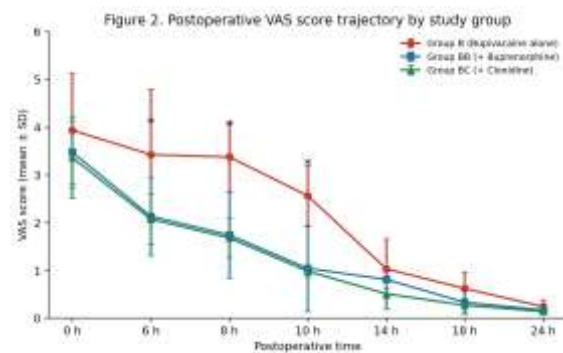


**Figure 2: Postoperative VAS score trajectory by study group (mean ± SD). \*p<0.05, Group B vs Group BB and Group BC**

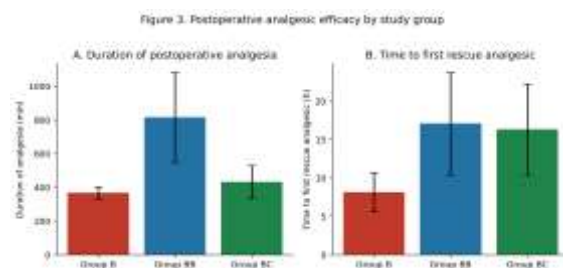


**Figure 3: (A) Duration of postoperative analgesia and (B) time to first rescue analgesic by study group (mean ± SD)**

## DISCUSSION

In this prospective, randomised, comparative study, both buprenorphine and clonidine, when added to bupivacaine for supraclavicular brachial plexus block, produced significantly longer postoperative

analgesia, delayed the requirement for rescue analgesia, and reduced 24-hour analgesic consumption compared with bupivacaine alone, without a significant increase in clinically important adverse effects. Buprenorphine produced the longest overall mean duration of analgesia among the three groups, whereas the time to first rescue-analgesic requirement was comparably delayed with both adjuvants.

The prolongation of analgesia observed with buprenorphine in the present study is consistent with the findings of Paliwal B, et al,<sup>[11]</sup> who similarly reported that buprenorphine prolonged the duration of analgesia to a greater extent than clonidine when added to bupivacaine for supraclavicular block, and with Tulsyan V, et al,<sup>[14]</sup> who reported significantly prolonged analgesia with buprenorphine compared with plain local anaesthetic in lumbar plexus block. Mathew A, et al,<sup>[7]</sup> and Jain N, et al,<sup>[6]</sup> have similarly documented a marked prolongation of postoperative analgesia with buprenorphine as an adjuvant to local anaesthetics in supraclavicular block. The magnitude of prolongation with clonidine observed in the present study is comparable to that reported by Chakraborty S, et al,<sup>[10]</sup> who found a significantly longer time to first analgesic request with clonidine compared with plain bupivacaine in supraclavicular block, and by Singh A, et al,<sup>[13]</sup> who reported lower postoperative pain scores with clonidine than with bupivacaine alone.

The overall incidence of adverse effects, although numerically higher with buprenorphine (sedation, nausea, and pruritus), did not reach statistical significance in the present study, a pattern also reported by Paliwal B, et al,<sup>[11]</sup> Abhishek R, et al,<sup>[12]</sup> and Tulsyan V, et al,<sup>[14]</sup> each of whom observed a higher but statistically non-significant incidence of opioid-related side effects with buprenorphine compared with clonidine or plain local anaesthetic. Chakraborty S, et al<sup>[10]</sup> similarly reported greater sedation with clonidine compared with control, without accompanying haemodynamic instability. Haemodynamic parameters and SpO<sub>2</sub> remained stable throughout the postoperative period in all three groups in the present study, in agreement with the observations of Abhishek R, et al,<sup>[12]</sup> and Tulsyan V, et al,<sup>[14]</sup> supporting the overall safety of both adjuvants at the doses used.

The prolonged analgesic effect of buprenorphine is attributable to its high affinity and slow dissociation from peripheral mu-opioid receptors that are upregulated at sites of tissue injury and inflammation, in addition to a possible direct local anaesthetic-like effect on nerve conduction.<sup>[5]</sup> Clonidine, in contrast, is thought to prolong block duration predominantly through a direct, peripherally mediated action on axonal ion channels rather than through a purely systemic alpha-2 adrenoceptor effect, since perineural administration has been shown to be more effective than systemic administration at equivalent doses.<sup>[15]</sup> Peripheral antinociception with clonidine has also been attributed to alpha-2-adrenoceptor-

mediated local release of endogenous enkephalin-like substances.<sup>[16]</sup> Clonidine administered as the sole analgesic agent within the brachial plexus sheath, without a co-administered local anaesthetic, has been shown not to provide clinically useful analgesia,<sup>[17]</sup> which suggests that the prolongation effect observed in the present study reflects a genuine synergistic interaction with bupivacaine rather than an independent analgesic action of clonidine alone.

These findings suggest that both buprenorphine and clonidine are clinically useful adjuncts for supraclavicular brachial plexus block when the goal is to extend the postoperative pain-free interval and reduce the requirement for systemic rescue analgesics, which is particularly relevant in the context of opioid-sparing, multimodal perioperative analgesia protocols and ambulatory upper-limb surgery. Given its longer overall duration of analgesia and superior quality-of-anaesthesia profile, buprenorphine may be preferred where prolonged postoperative analgesia is the primary clinical priority, whereas clonidine, with its comparable delay in first rescue-analgesic requirement and a numerically lower incidence of sedation, may be an acceptable alternative in settings where opioid-related sedation is undesirable.

The principal strengths of this study are its prospective, randomised, comparative design; blinding of the treating anaesthesiologist to group allocation; the use of a standardised postoperative pain-assessment protocol with pre-defined rescue-analgesic criteria; and the inclusion of a plain-bupivacaine control arm, which allowed the analgesic contribution of each adjuvant to be assessed against a common reference rather than only against each other.

The study is limited by its relatively modest sample size (20 patients per group), single-centre design, and the absence of blinding of patients and outcome assessors to group allocation beyond the injecting anaesthesiologist, which could not entirely exclude observer- or patient-related bias in VAS scoring. Plasma or perineural drug-concentration measurements were not performed, so a purely peripheral versus a combined peripheral-systemic mechanism of action could not be definitively distinguished. The study was not specifically powered for the postoperative-analgesia endpoints reported here, and longer-term outcomes such as chronic postsurgical pain or patient-reported functional recovery were not assessed.

Future multicentric trials with larger sample sizes, dose-ranging comparisons of buprenorphine and clonidine, and patient- and assessor-blinded designs are warranted to confirm these findings. Studies incorporating plasma drug-level sampling, longer follow-up for chronic pain outcomes, and cost-effectiveness analyses would further help define the optimal adjuvant choice for supraclavicular brachial plexus block in routine clinical practice.

## CONCLUSION

In this prospective, randomised, comparative study, both buprenorphine and clonidine, when added to bupivacaine for supraclavicular brachial plexus block, significantly prolonged the postoperative pain-free interval, delayed the time to first rescue-analgesic requirement, and reduced 24-hour rescue-analgesic consumption compared with bupivacaine alone, directly answering the study's primary objective. Buprenorphine provided the longest overall duration of postoperative analgesia and the best quality-of-anaesthesia profile, while clonidine achieved a comparable delay in first rescue-analgesic requirement with a numerically lower incidence of sedation. Neither adjuvant was associated with clinically significant haemodynamic instability, respiratory depression, or a statistically higher burden of adverse effects compared with plain bupivacaine. These findings support the use of either buprenorphine or clonidine as clinically effective and reasonably safe adjuvants to bupivacaine for supraclavicular brachial plexus block, with the choice between the two guided by the relative clinical priority given to duration of analgesia versus a lower sedation profile. Confirmation in larger, multicentric, patient- and assessor-blinded trials is recommended before these findings can be generalised to routine perioperative practice.

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