Original Article

# Comparison of morphine, dexmedetomidine and dexamethasone as an adjuvant to ropivacaine in ultrasound-guided supraclavicular brachial plexus block for postoperative analgesia—a randomized controlled trial

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## Abstract

**Background and Aims:** An ideal adjuvant to local anesthetic in a nerve block should prolong the duration of analgesia, and hasten the onset of sensory and motor blockade without significant adverse effects. The aim of this study was to compare morphine, dexmedetomidine, and dexamethasone as an additive to ropivacaine in ultrasound-guided supraclavicular brachial plexus block (SBPB) for postoperative analgesia.

**Material and Methods:** In this randomized, double-blinded study, 150 patients undergoing upper extremity surgery were randomly divided into three groups: group A (morphine 5 mg), group B (dexmedetomidine 50 μg), and group C (dexamethasone 8 mg). The additives were added to 30 ml of 0.5% ropivacaine solution and administered in SBPB. The duration of postoperative analgesia, onset of sensory and motor blockade, sedation, and adverse effects were observed. The pain was assessed by visual analog scale (VAS) and sedation by Ramsay sedation score. The duration of postoperative analgesia was taken as time consumed from block completion to administration of rescue analgesia (VAS >3).

**Results:** The demographic profile was similar in both groups. The duration of analgesia was significantly longer in dexamethasone (867.2 ± 217.6 min) than morphine (739. 2 ± 162.5 min) and dexmedetomidine (654.2 ± 179.9 min) ($P < 0.001$). The onset of sensory and motor blockade was quicker with dexmedetomidine than dexamethasone and morphine. Three cases of block failure were reported with morphine. No major adverse effects were reported.

**Conclusion:** Dexamethasone is an ideal adjuvant to ropivacaine in brachial plexus block to prolong postoperative analgesia and devoid of adverse effects. Dexmedetomidine has a quicker onset of sensory and motor blockade.

**Keywords:** Brachial plexus block, dexamethasone, dexmedetomidine, morphine

## Introduction

A regional anesthetic technique provides multiple advantages like avoiding multiple drugs, conscious patient, and most importantly excellent postoperative analgesia.[1] Brachial plexus block (BPB) provides excellent postoperative analgesia but with limited duration. Continuous catheter techniques, while effective can present technical challenges, infection, and failure due to catheter migration.[2]

Many adjuvants have been added to local anesthetics (LA) to enhance postoperative analgesia.[2,3] But search for an ideal additive that has good postoperative analgesia with a quicker onset of sensory and motor blockade and fewer

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side effects continues. The studies have revealed that duration of analgesia for different additives to LA was as follows: dexamethasone (22.2 h),[4] dexmedetomidine (776.4 ± 130.8 min),[5] clonidine (491.8 ± 3.9 min),[6] tramadol (313 ± 21.4 min),[6] buprenorphine (8.64 h),[7] magnesium sulphate (598.7 ± 51.5 min),[8] and fentanyl (7.5 ± 0.5 h).[9] The literature revealed that the duration of analgesia was longer when clonidine, dexmedetomidine, and dexamethasone were used as adjuvants to local anesthetics. A meta-analysis has revealed that perineural dexmedetomidine was more effective than clonidine.[10] Hence, we decided to include dexmedetomidine in our study. The duration of action of morphine was found to be as high as 20 h when used as an adjuvant.[11]

We hypothesized that morphine will be as effective as dexamethasone and dexmedetomidine when used as an additive in the supraclavicular nerve block. In this prospective, randomized, double-blinded study, the primary aim was to compare morphine, dexmedetomidine, and dexamethasone as adjuvant to ropivacaine in supraclavicular brachial plexus block for the duration of postoperative analgesia in upper extremity surgeries. The secondary objectives were to compare the onset of sensory and motor blockade, total analgesic consumption in 24 h, and complications such as nausea, vomiting, bradycardia, hypotension, and pruritus.

## Material and Methods

After approval by the Institutional Review Board, this study was registered with the Clinical trial registry of India (CTRI/2017/08/009374). This prospective, randomized, and double-blinded study was done in 150 patients undergoing elective upper limb surgeries in a tertiary medical college hospital between September 2017 to August 2018. Patients of the American Society of Anesthesiologists' (ASA) Physical status I or II, in the age group of 18–60 years and weighing between 60 and 100 kg were included in the study. Patients with chronic cardiac, renal and pulmonary pathology, uncooperative patients, and those who refused to participate were excluded from the study. Patients with the clavicle fracture, coagulation abnormalities, and pregnancy were also not included in the study. The informed written consent was obtained from each patient for participating in the study.

The patients were randomized to receive either morphine 5 mg (Group A: $n = 50$), dexmedetomidine 50 μg (Group B: $n = 50$) or dexamethasone 8 mg (Group C: $n = 50$) as adjuvant to ropivacaine in ultrasound-guided supraclavicular brachial plexus block by computer-generated random numbers and closed-envelope method. The commonly used doses of drugs as per literature evidence were selected.[3,4,12] All the patients received alprazolam 0.5 mg premedication overnight and 2 h before surgery. A randomization envelope was opened at this stage and the patient was allocated to Group A, B, or C. The first anesthesiologist opens the envelope and makes the study solution to 5 ml. It was mixed with ropivacaine 0.75% 20 ml and normal saline 5 ml. After preparing this 30 ml of 0.5% of ropivacaine with the study drug, he takes no further part in the study.

All the patients were monitored continuously with an electrocardiogram, noninvasive blood pressure (NIBP), and pulse oximetry intraoperatively and postoperatively for 24 h. Under aseptic precautions, BPB was performed with ultrasound guidance. A GE Vivid Ultrasonogram Machine, with a 6–12 MHz linear probe with color Doppler, was utilized for the study. The second anesthesiologist, who was blinded to the group allotted, administered ultrasound-guided supraclavicular brachial plexus block. All the blocks were performed by an experienced anesthesiologistas per the recommendations of The New York School of Regional Anesthesia (NYSORA).[13] The patient was placed in the supine position with the head turned to the opposite side. Under strict aseptic precautions, the transducer was positioned in the transverse plane immediately in the center of the supraclavicular notch. The subclavian artery, pleura, and first rib were visualized along with brachial plexus. The needle was placed in the brachialplexus sheath and ropivacaine was injected to visualize the spread within the brachial plexus and the centrifugal displacement of the trunks and divisions. If the spread was satisfactory, then 30 ml of 0.5% ropivacaine including the study solution was injected.

The second anesthesiologist monitored all the study parameters and decided on further management of the patient. The onset and degree of sensory and motor block were observed every 2 min for the first 10 min and every 5 min for the next 20 min. If complete sensory blockade was not achieved after 30 min and patient perceived pain, then it was considered as a failed block. The patient was administered general anesthesia or given a rescue block of spared nerve and excluded from the study. The sensory score was assessed using the pin-prick method by testing the five individual nerves: radial nerve, median nerve, musculocutaneous nerve, ulnar nerve, and medial cutaneous nerve of the forearm every 5 min for first 30 min.[1] The sensory block was assessed using the scoring system adapted from Koscielniak-Nielsen *et al.* (0: sharp pain, 1: touch sensation only, and 2: no sensation).[14] The onset of sensory block was defined as the time between complete drug administration and complete loss of pinprick sensation. The motor block was assessed using the scoring system adapted

from Lahori *et al.*: 0—Flexion and extension in both the hand and arm against resistance, 1—Flexion and extension in both the hand and arm against gravity but not against resistance, 2—Flexion and extension movements in the hand but not in the arm, and 3—No movement in the entire upper limb.[15] The onset of motor blockade was defined as the time from injection of the drug to complete motor blockade.

The postoperative analgesia was assessed utilizing the visual analog scale (VAS) scoring of one to ten. The duration of postoperative analgesia was defined as the time from completion of drug administration to the first request for postoperative analgesia (VAS >3).[16] VAS was assessed every 4 h postoperatively for 24 h. The patients received Inj. paracetamol 1 g intravenously (IV) when VAS was between 3 to 5 and Inj. tramadol 100 mg IV if VAS ≥6. These doses of paracetamol and tramadol were taken as a single dose and total doses consumed in 24 h were recorded. The maximum allowable doses in 24 hours for paracetamol and tramadol were 4 g and 300 mg respectively. If the patient had persistent VAS ≥6 after receiving paracetamol and tramadol, morphine 0.1 mg/kg IV was given as a rescue analgesic. Sedation score was assessed as per modified Ramsay Sedation Scale (RSS) from 1–6.[5] Since it is a known fact that dexamethasone does not cause sedation, RSS was compared only between morphine and dexmedetomidine every 4 h postoperatively for 24 h. The following adverse effects were observed: nausea, vomiting, bradycardia, hypotension, and complications of block like pneumothorax, Horners' syndrome, and vascular puncture.

The sample size calculation was based on an initial pilot study involving thirty patients with the duration of postoperative analgesia as the primary endpoint of the study. Time to first analgesic request was 720 ± 117.7 min for morphine, 657 ± 148.5 min for dexmedetomidine, and 846 ± 192.5 min for dexamethasone groups. With $\alpha$ error of 0.05 and power of the study $(1-\beta)$ at 80%, to detect a minimum of 60 min difference in time needed for rescue analgesia between the two groups, the sample size was calculated to be approximately 44 in each group. We included fifty patients in each group to compensate for possible dropouts. The patients, who were part of the pilot study, were not included in the study. Data were entered in the MS-Excel spreadsheet (2010) and were analyzed using the Statistical Package for Social Sciences version 20 (trial version). Descriptive statistics including proportions, measures of central tendency, and measures of dispersion were used to describe the data. Further, one-way analysis of variance (ANOVA) test was used to compare means and proportions between the groups. The Chi-square test was utilized to analyze categorical data. A $P < 0.05$ was considered to be statistically significant.

## Results

One hundred and sixty patients were recruited into the study. A CONsolidated Standards of Reporting Trials (CONSORT) flow diagram depicting the passage of participants through the study has been provided in Figure 1. There were no difference in demographic characteristics like age, sex, weight, ASA physical status, and site of surgery among the three groups [Table 1].

There were three cases of an incomplete block in the morphine group after 30 min and they were converted to general anesthesia (one patient) or given distal rescue block of the spared nerve (two patients). The data from these three patients were also included in the study based on intention to treat rather than per-protocol basis.[17] The duration of postoperative analgesia was significantly longer in the dexamethasone group than morphine and dexmedetomidine. The intergroup analysis between the three groups also revealed a statistical significance. The onset of sensory and motor blockade was found to be quicker with dexmedetomidine than dexamethasone and it was prolonged in morphine than the other two groups. The consumption of tramadol and paracetamol in 24 h was less in morphine and dexamethasone than dexmedetomidine. However, there was no significant difference between morphine and dexamethasone. The results are summarized in Table 2. Morphine as a rescue analgesic was not needed in any of the patients.

There were significant variations in VAS score between the groups and is given in Figure 2. The sedation achieved with dexmedetomidine was better than morphine and is depicted in Figure 3. The hemodynamic parameters were comparable between the two groups during the intra-and postoperative period. Nausea and vomiting occurred in two patients in the morphine group and bradycardia was encountered in one patient in the dexmedetomidine group. There were no other side effects postoperatively for 24 h and the results are tabulated in Table 3.

## Discussion

Brachial plexus block is the preferred anesthetic technique for surgeries of the upper limb. Bupivacaine was long used as a local anesthetic for BPB. However, because of its cardiac toxic property, it has now been replaced by ropivacaine and levobupivacaine. But, the duration of analgesia with these agents is limited. Hence, several agents have been added as an adjuvant to local anesthetic to enhance postoperative analgesia. In this randomized control trial, we decided to compare morphine, dexmedetomidine, and dexamethasone as

adjuvants to ropivacaine in ultrasound-guided brachial plexus block for postoperative analgesia in upper extremity surgeries.

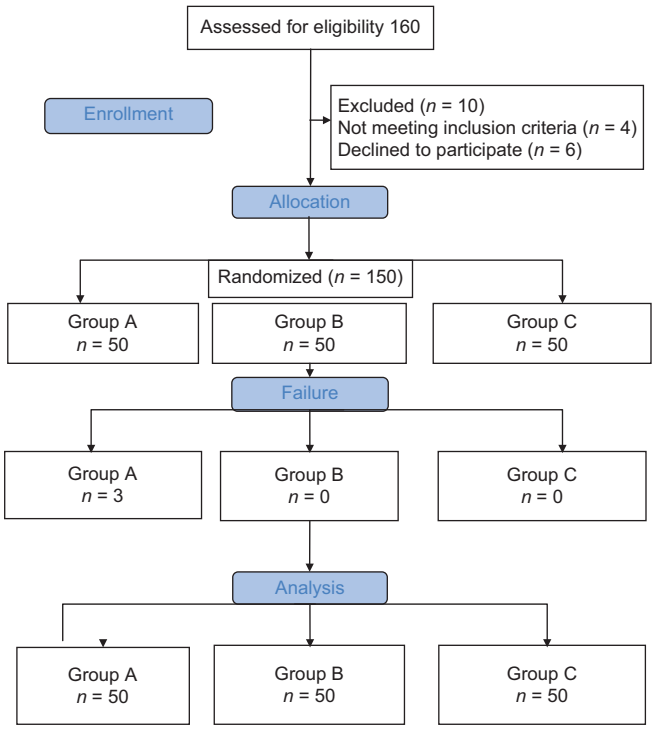


**Figure 1:** Consolidated Standards of Reporting Trials (CONSORT) flow chart

Morphine is a long-acting opioid and has been used as an adjuvant in both central and peripheral neuraxial blockade. The exact mechanism of action of morphine in nerve blocks is not known. Several mechanisms like central action after absorption, presence of opioid receptors in the peripheral nerves, and impairing sodium and potassium conduction on the nerves have been described.[11] Dexmedetomidine has eight times higher affinity and $\alpha_2$ agonist property compared with clonidine.[18,19] The mechanism of action varies from

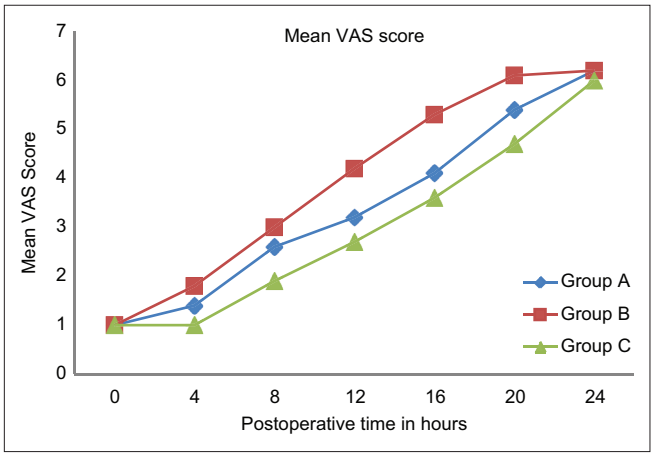


**Figure 2:** Mean VAS scores in the two groups

**Table 1: Patient demographical profile and surgical characteristics**

| Group | A-Morphine (*n*=50) | B-Dexmedetomidine (*n*=50) | C-Dexamethasone (*n*=50) | *P* |
|---|---|---|---|---|
| Gender (Male/Female) | 39/11 | 39/11 | 41/9 | 1.0 |
| Age (years) | 31.2±8.6 | 30.9±10 | 31.7±9.7 | 0.909 |
| Height (cm) | 167.2±7.9 | 165.2±10.1 | 167.8±7.8 | 0.317 |
| Weight (kg) | 75.2±12 | 72.1±13.7 | 73.5±13.4 | 0.504 |
| ASAPSI/II | 35/15 | 38/12 | 31/19 | 0.7 |
| Duration of surgery (min) | 78.4±12.9 | 82.3±19.3 | 85.8±22.5 | 0.149 |

*Data are expressed as mean±SD, or as number of patients. P-values were determined by $\chi^2$ test (gender, ASA PS) and Bonferroni-corrected analysis of variance (ANOVA) (age, height, weight, block onset and duration, duration of surgery, type of block).*

**Table 2: Onset and duration of block, and postoperative analgesic drug consumption**

| Group | A-Morphine (*n*=50) | B-Dexmedetomidine (*n*=50) | C-Dexamethasone (*n*=50) | *P* |
|---|---|---|---|---|
| Duration of post operative analgesia (min) | 739.2±162.5 | 654.2±179.9 | 867.2±217.6 | <0.001*,†,§ |
| Onset of sensory block (min) | 14.3±6 | 7.6±3.1 | 9.4±4.3 | <0.001*,†,§ |
| Onset of motor block (min) | 16.2±6.4 | 9.0±3.5 | 9.0±3.5 | <0.001*,†,§ |
| Success rate | 47 (94%) | 50 (100%) | 50 (100%) | 1 |
| Paracetamol consumption (1dose=1000 mg) | 2±0.9 | 1.68±0.6 | 1.4±0.5 | <0.001 |
| Tramadol consumption (1dose=100 mg) | 1.8±0.8 | 1.2±0.7 | 0.7±0.7 | <0.001 |

**P<0.05 Morphine versus dexmedetomidine, †P<0.05 Dexmedetomidine versus dexamethasone, §P<0.05 Morphine versus dexmedetomidine, Bonferroni-corrected analysis of variance (ANOVA)*

**Table 3:Complications and side effects**

| Group | A-Morphine (*n*=50) | B-Dexmedetomidine (*n*=50) | C-Dexamethasone (*n*=50) |
|---|---|---|---|
| Bradycardia | 0 | 1 (2%) | 0 |
| Nausea | 2 (4%) | 0 | 0 |
| Vomiting | 2 (4%) | 0 | 0 |

*Data are expressed as numbers of patients (percentage)*

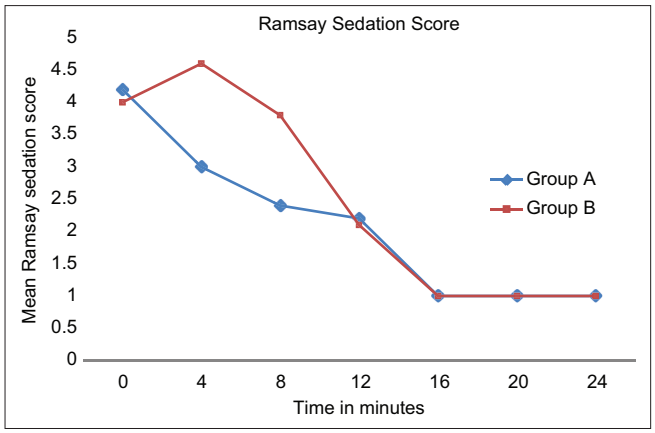


**Figure 3:** Ramsay sedation scores in the two groups

peripheral $\alpha_{2A}$ action, blockade of hyperpolarization-activated cation current, and inhibition of compound action potential.[5] Dexamethasone is a glucocorticosteroid exerting its action by attenuating the release of inflammatory mediators, inhibiting potassium channel-mediated discharge of nociceptive C-fibers, and reducing ectopic neuronal discharge.[20] No major long-term adverse effects have been reported with any of these adjuvants.

There were three cases (6%) of block failure with morphine and no failure in other groups. This success rate is similar to 90% to 95% reported in other studies.[1] This incomplete blockade after 30 min in the morphine group may be due to its delayed onset of the sensory blockade and can be taken as a drawback for use of morphine as an adjuvant. In our study, the duration of postoperative analgesia was significantly prolonged in the dexamethasone (14.5 h) group than morphine (12.4 h) which was longer than the dexmedetomidine (10.9 h) group. Choi *et al*. had reported that dexamethasone prolonged duration of postoperative analgesia with long-acting LA from 730 to 1306 min.[20] Bazin *et al*. stated that morphine in a dose of 75 μg/kg produced analgesia of 21 h (median value). Gurajala *et al*. had reported dexmedetomidine 50 μg produced analgesia for 960 min (median value).[3] There was a significant reduction in the consumption of tramadol and paracetamol for the first 24 h in morphine and dexamethasone when compared to the dexmedetomidine group.

The onset of sensory and motor blockade was quicker with dexmedetomidine than dexamethasone. Morphine had delayed onset among the three groups. The faster onset of sensory and motor blockade with dexmedetomidine has been confirmed by many studies.[3,5,21] Agarwal *et al*. found that dexmedetomidine reduced the onset of sensory blockade from 19.0 ± 3.2 min to 13.2 ± 1.8 min and onset of motor blockade from 22.7 ± 2.8 min to 16.3 ± 1.7 min.[5] In our study, dexmedetomidine provided an even faster onset of sensory and motor blockade. The sedation achieved with dexmedetomidine was better than morphine. Gurajala *et al*. demonstrated that RSS was atleast one point higher in the dexmedetomidine group.[3] There were no major adverse effects of drugs like nausea, vomiting, bradycardia, or hypotension. No other adverse effects attributable to brachial plexus block were observed in our study.

There are a few limitations to this study. First, doses selected for these agents are based on commonly used doses available in the literature. Another study may be needed to find out if increased doses of any of these drugs might prolong analgesia. Second, the use of patient-controlled analgesia (PCA) with 24 h consumption of opioids is the ideal method to assess postoperative analgesia. But, due to the unavailability of the PCA pump in our institute, we used 24 h consumption of paracetamol and tramadol. Third, the long-term follow-up of patients was not done in our study due to technical feasibility. However, no other studies have documented any long-term adverse effects with any of these drugs.

To summarize, dexamethasone had the longest duration of analgesia when used as an additive to ropivacaine in brachial plexus block, followed by morphine and dexmedetomidine had the shortest duration of action. The onset of sensory and motor blockade was quicker with dexmedetomidine than dexamethasone and morphine. Hence, we conclude that dexamethasone is an ideal adjuvant to ropivacaine in brachial plexus block with prolonged analgesia, relatively faster onset of sensory and motor blockade, and devoid of adverse effects.

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## Conflicts of interest
There are no conflicts of interest.

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