Comparison of perineural administration of dexmedetomidine and fentanyl as an adjuvant to 0.5% bupivacaine to enhance the quality of supraclavicular brachial plexus nerve block in upper limb surgeries - A prospective, triple-blind, randomized study

Sayak Patra¹, Ranabir Chanda², Chaitali Biswas³

¹Assistant Professor, ²Professor, Department of Anesthesiology, Bankura Sammilani Medical College, Bankura, West Bengal, India, ³Associate Professor, Department of Anesthesiology, Rampurhat Government Medical College, Rampurhat, West Bengal, India

ABSTRACT

Background: Supraclavicular approach of brachial plexus block (BPB) has been in popular choice in recent years for surgical, diagnostic, and therapeutic management of injury and pathology related to upper limb. Aims and Objectives: In this study, we investigated the effect of dexmedetomidine and fentanyl as an adjuvant to bupivacaine on quality of block and post-operative analgesia in perineural supraclavicular BPB. Materials and Methods: A prospective, randomized, and triple-blind study was done involving 70 patients of age 18–60 years, randomly allocated into two equal groups [group BD- bupivacaine (0.5%) 29 ml with 100 µg (1 ml) of dexmedetomidine and group BF - bupivacaine (0.5%) 29 ml with 50 µg (1 ml) of fentanyl]. The scores of modified Gormley and Hill scale, modified Bromage scale, Ramsay sedation scale, and rescue analgesic requirement were recorded along with hemodynamic parameters. Pearson’s Chi-square test and Mann–Whitney U test were used for statistical analysis. Results: The onset time of sensory and motor blockade was shortened and the duration of the block was significantly prolonged in the BD Group than BF Group (P<0.001). The duration of post-operative analgesia was also longer in the BD Group compared with the BF Group (549.43 ± 10.56 vs. 403.69 ± 10.84) P<0.001. BF Group had more requirements of analgesic postoperatively. Conclusion: Addition of dexmedetomidine to bupivacaine prolonged the duration of perineural supraclavicular BPB and improvement of post-operative analgesia than fentanyl without significant side effects in patients undergoing upper limb surgeries.

Key words: Bupivacaine; Dexmedetomidine; Fentanyl; Post-operative analgesia; Supraclavicular brachial plexus block

INTRODUCTION

The perineural nerve blockade technique, although developed early in the history of anesthesia, remains a well-accepted, versatile anesthetic technique and unavoidable component of today's comprehensive anesthetic management.¹ Brachial plexus block (BPB) is a useful regional anesthetic technique and a superior alternative to general anesthesia for upper limb surgeries as they achieve near-ideal operating conditions by producing complete muscular relaxation, maintaining stable intra-operative hemodynamic and also providing benefits of reduced hospital stay, less financial burden and avoidance of complications due to general anaesthesia.² Once described as the “spinal of the arm” due to its relatively rapid onset and reliability, a supraclavicular BPB offers dense anesthesia of the brachial plexus for any surgery involving the upper
extremity, but not the shoulder. It provides excellent post-operative analgesia but with limited duration. Single shot supraclavicular BPB is more popular since continuous technique using catheter is expensive, requires skill with risk of infection. Many adjuvant drugs such as opioids, α agonists, steroids, and vasoconstrictor agents have been co-administered in BPB with local anesthetic (LA) agents to improve the block quality or duration of analgesia with varying degree of outcome.

Bupivacaine is used frequently for supraclavicular BPB as it has long duration of action from 6 to 12 h. In spite of that, it fails to provide faster onset and prolong postoperative analgesia when used alone. Fentanyl, a synthetic, lipophilic, and potent opioid is known to have an aniciceptive effect which may be mediated via activation of peripheral opioid receptor. The addition of opioid in BPB is reported to improve success rate, post-operative analgesia and also reduce systemic side effects and total dose of anesthetic required. Alpha-2 adrenergic receptor agonist has been the focus of interest for their dose dependent sedation, anxiolysis, analgesia, perioperative sympatholysis and cardiovascular stabilizing effects with reduced anesthetic requirement. Various methods of administration of alpha-2 adrenergic receptor agonists such as epidural, intrathecal, and peripheral injections have been tried either alone or in combination with another drug to prolong the duration of analgesia and intensify the anesthesia. Dexmedetomidine, pharmacologically active d isomer of medetomidine is a highly specific and selective, potent α2 adrenoceptor agonist with α2/α1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine. There are several studies which have proved that, dexmedetomidine as an adjuvant in nerve blocks extends the duration of analgesia. The proposed mechanism is by blocking the hyper-polarization activated cation current.

**Aims and objectives**

A comparison between dexmedetomidine and fentanyl was attempted in this study to evaluate the onset time and duration of sensory blockade, motor blockade, and analgesic efficacy in supraclavicular BPB as an adjuvant to bupivacaine (0.5%).

**MATERIALS AND METHODS**

This prospective, randomized, triple-blind, and comparative study was conducted on seventy (70) patients belonging to American Society of Anesthesiologists (ASA) physical status I and II, and aged 18-60 years, of either sex posted for upper limb surgeries under BPB, during January 2017 – December 2017 at Burdwan Medical College and Hospital, Burdwan, West Bengal India. Exclusion criteria for the study were non-cooperative patients, known allergy to any of the drugs which are used in the study, contraindications of BPB (e.g., coagulation defects, infections at puncture site, and pre-existing neurological deficit in extremities), history of alcohol, antipsychotics, opioid and sedative drug abuse and severe cardiovascular, respiratory, neurological, psychological, hepatic, or renal diseases.

The primary objective was to evaluate and compare the efficacy of dexmedetomidine and fentanyl as an adjuvant to bupivacaine (0.5%) on the onset and duration of sensory and motor block during supraclavicular BPB. The secondary objective was to compare the duration of analgesia, intraoperative sedation and requirement of rescue analgesic in first 24 h postoperatively among the study patients. Assuming P<0.05 to be significant and considering effect to be two sided, we got Zα/2=1.96; assuming power of study to be 90% and Zβ=1.28. Considering an effect size (difference in duration of sensory block between the groups) of 88 to be statistically significant, the sample size (n) was calculated as 31 in each group. A total of 70 patients were recruited in the study to compensate for possible dropouts.

After approval from the Institutional Ethics Committee (Memo No: BMC-2959 dated 1/12/16) and informed written consent from each participant, 70 adult patients presenting for upper extremity surgeries were randomized to two groups: group BD containing 35 and group BF containing 35 patients. Group BD received bupivacaine (0.5%) 29 ml with 100 μg (1 ml) of dexmedetomidine hydrochloride in supraclavicular BPB. Group BF received bupivacaine (0.5%) 29 ml with 50 μg (1 ml) of fentanyl citrate. Randomization was based on a computer-generated randomization table, with group allocation concealed in sealed opaque envelopes. All the selected patients were kept nil per oral for 8 h. On the day of surgery, after confirmation of identity, the patients were shifted to the pre-operative room. Using the multiparameter monitor, basal heart rate (HR), mean blood pressure (MBP), and oxygen saturation were recorded and patients were medicated with 1mg midazolam using an intravenous (IV) line obtained from the non-injured upper limb. All the drug containing syringes were prepared by a 3rd year anesthesia resident not taking part in this study. An independent assistant with good clinical knowledge, but not a part of the study was made available for opening the envelopes with details of the study drugs to be administered. The attending anaesthesiologist, data collection personnel, and the patient were blinded to the group assignment. As dexmedetomidine and fentanyl have sedative properties, no intraoperative sedation was administered to the patients. Regional anesthesia was administered in the operation theatre prior to the starting of surgery. Under proper monitoring and aseptic and antiseptic technique, peripheral nerve stimulator (Stimuplex® A-B Braun) guided single shot brachial plexus nerve block by supraclavicular approach was given.
Onset of sensory block in the injured limb in comparison to normal limb was assessed by changes in pin prick sensation every 2 min interval till no sensations (Grade 2) were achieved, graded according to Modified Bromage and Hill scale (normal sensation 0; blunted sensation 1; and no sensation 2).19 The palmar surface of index and little finger was used to test median and ulnar nerve in the hand, respectively. The dorsal surface of the thumb was to be used to test the radial nerve. Motor block was assessed by using modified Bromage Scale (0=Normal motor function with full flexion and extension of elbow and wrist; 1=Inability of wrist flexion; 2=Inability of elbow flexion; and 3=Complete motor block) and the onset of motor block was considered when Bromage score more than 2.19 Duration of sensory blocks was assessed with testing for return of pin prick sensation at 30 min interval after the end of surgery. Duration of sensory blocks was calculated from the time of drug administration till the complete resolution of anesthesia [Grade 0 in pin prick sensation test] along the distribution of nerves.

Duration of motor block was defined as the time interval between the end of drug administration and the recovery of complete motor function of hand and forearm [Grade 0 in Bromage scale]. Blocks were considered failed when sensory block not achieved within 30 min of delivery of the drugs which was nil among study groups. Intraoperative sedation of the patients were assessed with Ramsay sedation score, (Score 1=Anxious, agitated, non-cooperative, Score 2=Cooperative, oriented, tranquil, Score 3=Respond to verbal commands, Score 4=Brisk response to loud noise or a light tap, Score 5=Sluggish response to loud noise or a light tap, and Score 6=No response to stimuli).28 Vital parameters (HR, MBP, SpO2) and sedation were recorded every 5 min interval for first 30 min from the time of giving block and then every 30 min up to 90 min.

The duration of analgesia was taken from the time of onset of block to the first complain of pain. Inj. dicylofenac sodium intragluteculate deep intramuscular in dose of 1.5 mg/kg was given as rescue analgesic for 24 h postoperatively and number of rescue analgesics required was also calculated. Complain of pain was graded according to visual analog scale (VAS) (0-10) for pain.23 Patient complaining of pain or VAS more than 4, whichever earlier was considered for rescue analgesia. Episodes of perioperative hypotension (MBP <20% of baseline) and bradycardia (HR <60 beats/min) and desaturation (spo2 <90%) and incidence of post-operative nausea vomiting were recorded.

**Statistical analysis**

Data were entered into Microsoft Excel and analysis was performed using Statistical Package for the Social Sciences for Windows, Version 20.0 software (IBM, Bengaluru, India). Categorical variables were expressed as number of patients and percentage and compared across the groups using Pearson’s Chi-square test for Independence of Attributes/Fisher’s Exact Test as appropriate. Continuous variables were expressed as mean, median and standard deviation and compared across the groups using Mann–Whitney U test. An alpha level of 5% has been taken, that is, if any P<0.05 it has been considered as significant.

**RESULTS**

In total 88 patients were screened and 70 patients meeting the inclusion criteria and willing to participate in the study were randomized into two groups (Figure 1).

The study groups were comparable with no statistically significant difference in their demographic profile (Table 1).

When comparing onset and duration of sensory block among patients, Group BD [8.71±1.45 and 536.46±9.54 mean onset and duration in minutes, respectively,] produced statistically significant difference compared to Group BF [11.17±1.48 and 392.20 ±9.96 mean onset and duration in minutes, respectively,] P<0.001 (Table 2).

Onset time of motor block was lower in Group BD (9.83±1.40) compared to Group BF (12.7±11.69) P<0.001. Group BD also demonstrated statistically significant prolonged motor block (521.00±35.06 vs. 381.31±9.97) than Group BF (Table 2). Although, mean duration of surgery was not statistically significant among the groups, mean duration of analgesia was greater in group BD than BF (549.43±10.56 vs. 403.69±10.84) P<0.001 (Table 2).

Intra-operative sedation score was statistically significant in Group BD compared to Group BF (4.11±0.68 vs. 1.91±0.51) P<0.001 (Table 2). Group BD required less post-operative rescue analgesic than Group BF (Table 2).

There was statistically no significant difference regarding intraoperative oxygen saturation among the groups as shown in Table 3.

The hemodynamic parameters (HR and MBP) showed statistically significant differences throughout the perioperative period in group BD when compared group BF (Figure 2 and 3).

**DISCUSSION**

This study primarily demonstrated that significantly earlier onset and prolonged durations of both sensory and motor blocks were achieved with dexmedetomidine compared to...
fentanyl when used as an adjuvant to bupivacaine in perineural supraclavicular BPB along with better post-operative profile.

Regional anesthesia is the preferred choice for upper limb surgeries, and supraclavicular BPB is one of the most commonly used perineural blocks for this purpose. The major consideration for an anesthesiologist while selecting a pharmacological option during regional anesthesia is not only to provide adequate and timely sensory and motor block to facilitate the surgical procedure but also to augment the postoperative analgesic efficacy of the drug being used. Safety of use, speedy and adequacy of block, and post-operative pain control thus decide the usefulness of a pharmacological option. Anesthetists have sought strategies to extend the benefits of single-shot peripheral nerve blocks beyond the duration of commonly available LA. In a systematic review and meta-analysis of randomized controlled trials, Vorobeichik et al. concluded that perineural adjunct was one technically simple strategy that could be used for this purpose.17 Another Systematic Qualitative Review found buprenorphine, clonidine, dexamethasone, magnesium, and dexmedetomidine as promising agents for use in prolongation of local anesthetic peripheral nerve blocks.15 Antinociceptive effect of fentanyl may be mediated through activation of peripheral opioid receptor.22 The use of opioids has been overshadowed by the usage of newer adjuvant drugs like highly selective α2 agonist dexmedetomidine. Dexmedetomidine has the advantage due to its decreased chances of α1 receptor mediated side effects. It successfully prolongs the duration of sensory and motor blockade and duration of analgesia when used as adjuvant to local anesthetics.26 The mechanism of action may be due to its vasoconstrictive property, alteration in locus ceruleus activity decreasing release of norepinephrine. Systemic absorption of drug from injection site results its action over the alpha 2 adrenergic receptors in dorsal horn and reduces the release of pain mediating substances.7,9,11 The augmentation of the effects of local anesthetics may be because of the hyperpolarization of nerve tissues by altering transmembrane potential and K+ ion conductance. This drug also may be the preferable choice for study due to its sedative, anxiolytic, amnestic properties without causing significant respiratory depression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group BD (n=35)</th>
<th>Group BF (n=35)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (57)</td>
<td>19 (54)</td>
<td>0.810*</td>
</tr>
<tr>
<td>Female</td>
<td>15 (43)</td>
<td>16 (46)</td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>35.20 (9.70)</td>
<td>36.00 (8.37)</td>
<td>0.810*</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>67.11 (6.67)</td>
<td>66.80 (5.85)</td>
<td>0.823*</td>
</tr>
<tr>
<td>ASA (n%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>31 (89)</td>
<td>30 (86)</td>
<td>0.721*</td>
</tr>
<tr>
<td>II</td>
<td>4 (11)</td>
<td>5 (14)</td>
<td></td>
</tr>
</tbody>
</table>

ASA: American Society of Anesthesiologists physical status, *Chi-square test, #Mann-Whitney U test, P<0.05 considered statistically significant
In the present study, the study groups, that is, Group BD [29 ml 0.5% bupivacaine + 1 ml of dexmedetomidine (100 µg)] and Group BF [29 ml of 0.5% bupivacaine + 1 ml of fentanyl citrate (50 µg)] were comparable (P>0.05) with each other according to their demographic profile and duration of surgery (Tables 1 and 2). The significant findings were related to onset and duration of sensory and motor blocks after perineural BPB. Group BD showed faster onset and prolonged duration of both sensory and motor blocks (P<0.001) compared to group BF which was clinically and statistically significant (Table 2). There are several studies which have compared the effectiveness of dexmedetomidine and fentanyl as adjuvant to local anesthetics as a single drug or a combination with other drugs. In a previous study conducted by Rajkhowa et al. concluded that the addition of fentanyl (adjuvant) to ropivacaine used for BPB may prolong the duration of sensory and motor block but may delay the onset of sensory and motor block compared to ropivacaine used alone.22 In a study by Kaur et al. adding dexmedetomidine to levobupivacaine for supraclavicular BPB observed that addition of 1 µg/kg dexmedetomidine to 0.25% levobupivacaine for supraclavicular plexus block reduces onset time of sensory and motor block.23 Another study showed that onset of sensory and motor anesthesia was statistically significant for dexmedetomidine as adjuvant for supraclavicular nerve block, which had earlier onset of anesthesia than fentanyl group and control group while fentanyl had earlier onset than control group.24 These findings were comparable to ours study. Kathuria et al. mentioned of a highly significant acceleration on the onset of block with 50 mcg dexmedetomidine to 0.5% ropivacaine in congruence to our findings.25 However, contradictory views have been presented by some workers. However, these contradictions are often caused by several confounders or are marred by the adequacy of sample. A study by Fanelli et al. showed no significant difference in time taken to achieve readiness of surgery between ropivacaine alone and

**Table 2: Description and comparison of onset and duration of blocks (minutes), duration of surgery, duration of analgesia, intra-operative highest Ramsay Sedation score and number of rescue analgesic required within 24 h among the groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group BD (n=35)</th>
<th>Group BF (n=35)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean sensory block onset</td>
<td>8.71 (1.45)</td>
<td>11.17 (1.48)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean sensory block duration</td>
<td>536.46 (9.54)</td>
<td>392.20 (9.96)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean motor block onset</td>
<td>9.83 (1.40)</td>
<td>12.71 (1.69)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean motor block duration</td>
<td>521.00 (35.06)</td>
<td>381.31 (9.97)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean duration of surgery (minutes)</td>
<td>76.20 (14.10)</td>
<td>75.26 (14.25)</td>
<td>0.769*</td>
</tr>
<tr>
<td>Mean duration of analgesia (minutes)</td>
<td>549.43 (10.56)</td>
<td>403.69 (10.84)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mean intra-operative highest Ramsay Sedation score</td>
<td>4.11 (0.68)</td>
<td>1.91 (0.51)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

No. of rescue analgesic required within 24 h (n%)

| 1 | 33 (94.29) | 0 (0) | <0.001* |
| 2 | 2 (5.7) | 28 (80) |
| 3 | 0 (0) | 7 (20) |

*Chi-square test, #Mann–Whitney U test, P<0.05 considered statistically significant

![Figure 2: Comparison of heart rate at time points (P≤0.001)](image2)

![Figure 3: Comparison of mean blood pressure at time points (P≤0.001)](image3)
ropivacaine with fentanyl.\textsuperscript{26} However, this study had only 15 samples in each group and showed a high intra-group variability in the achievement of blockade (5–40 min). In our study, this intra-group variability was shorter and the sample size was more than 2 times larger (n=35 in each group) than the study mentioned.

Present study showed enhanced duration of analgesia in dexmedetomidine group than fentanyl group (549.43±10.56 vs. 403.69±10.84) P<0.001 (Table 2). Intra-operative sedation score was also better in group BD compared to Group BF (4.11±0.68 vs. 1.91± 0.51) P<0.001 (Table 2). Both of these had added advantage of perioperative patient satisfaction. These findings were corroborative to the results of other researchers’ works.\textsuperscript{1,2,9,11,27} Regarding post-operative rescue analgesic requirement, group BD performed better than group BF showing lesser need of administration of repeated doses. About 80% and 20% of fentanyl group patients required 2nd and 3rd of rescue analgesic, respectively, compared to 5.7% and 0% in dexmedetomidine group, respectively, P<0.001 (Table 2). These results were comparable to other study findings.\textsuperscript{5,12,17} It had been observed in the present study that there had been significant (P<0.05) decrease in intraoperative HR and mean arterial pressure in Group BD patients than Group BF patients when measured at 5, 10, 15, 20, 25, 30, 60, and 90 min after administration of block (Figures 2 and 3). However, the decrease in HR and MBP were not clinically significant or alarming for the patients and required no interventions. None of the patients in the study groups had undergone episodes of significant desaturation (Table 3), bradycardia, hypotension, respiratory depression or nausea-vomiting during intraoperative, and post-operative period requiring treatment. Our study accorded emphatically with few previous studies to light on the fact that addition of dexmedetomidine is a surpassing modality in the advent of surgeries under supraclavicular BPB.

**LIMITATIONS OF THE STUDY**

In line with that, we recognized that intake of small number of patients, was a limitation of our study. Nevertheless, ASA physical status I/II patients were included in our study; the effectiveness cannot be repudiated in high-risk patients.

**CONCLUSION**

The study concludes that dexmedetomidine (100 µg) when used as an adjuvant to bupivacaine (0.5%) in perineural supraclavicular BPB enhances the quality of both the sensory and motor blocks producing shorter onset and longer duration along with prolong period of analgesia, better intra-operative sedation and lesser post-operative analgesic requirement than fentanyl (50 µg) with (0.5%) bupivacaine without causing perioperative unwanted side effects.

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