

## Efficacy of Adding Midazolam to Bupivacaine in Supraclavicular Technique of Brachial Plexus Block for Upper Limb Surgeries

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### Abstract

**Background:** Brachial plexus blocks provide a wonderful alternative to general anaesthesia for upper limb surgeries. Various adjuvants like opioids, midazolam and  $\alpha_2$  agonists have been used to improve the quality of block. **Aim:** To compare the efficacy of adding midazolam to 0.375% bupivacaine in supraclavicular technique of brachial plexus block for upper limb surgeries. **Methods:** 100 patients undergoing upper limb surgeries under supraclavicular block were randomized to receive 30ml of 0.375% bupivacaine Group B or 30ml of 0.375% bupivacaine with midazolam 0.05 mg/kg (Preservative free) Group BM. The onset and duration of sensory and motor block, sedation score and number of rescue analgesics needed during 24 hours post-operative period was assessed. **Results:** The mean time of onset of sensory and motor block was significantly faster in Group BM (11.26 $\pm$ 1.5min, 9.56 $\pm$ 1.32 min) than Group B (19.08 $\pm$ 1.7min, 15.30 $\pm$ 2.09 min) respectively. The mean duration of sensory and motor block in group BM (13.81 $\pm$ 1.23hrs, 5.25 $\pm$ 0.45hrs) were found to be significantly longer than in group B (5.84 $\pm$ 0.49 hrs, 5.25 $\pm$ 0.45 hrs). **Conclusion:** The addition of Midazolam as an adjuvant to bupivacaine when compared to plain bupivacaine resulted in rapid onset of sensory block and motor block, prolonged duration of sensory block, reduced number of rescue analgesics in the post-operative period of 24 hours.

**Keywords:** Brachial Plexus Block; Bupivacaine; Midazolam; Upper Limb Surgery.

### Introduction

Brachial plexus blocks provide a wonderful alternative to general anaesthesia for upper limb surgeries. They provide complete and prolonged pain relief, muscle relaxation, maintaining stable intraoperative hemodynamics and adequate sympathetic block. The sympathetic block decreases postoperative pain, vasospasm and edema [1]. of various local anaesthetics, Bupivacaine is used most frequently, as it has a long duration of action varying from 3 to 8 hours. However, there are many limiting factors like delayed onset, patchy or incomplete analgesia, sometimes of short duration etc. Various drugs like opioids, midazolam and  $\alpha_2$  agonists [2-3] have been added to local anaesthetics to improve

the block in terms of quicker onset, good quality, prolonged duration and postoperative analgesia. Midazolam, a water-soluble benzodiazepine is known to produce antinociception and enhance the effect of local anaesthetic when given epidurally or intrathecally.

Midazolam produces this effect by its action on gamma aminobutyric acid-A (GABA-A) receptors. GABA receptors have also been found in peripheral nerves [4].

So the present study is being undertaken in a randomized single blinded manner to evaluate the onset time and analgesic efficacy of Midazolam (preservative free)- Bupivacaine combination compared to plain Bupivacaine (0.375%) for brachial plexus block by supraclavicular approach.

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**Materials and Methods**

After obtaining Ethics Committee approval and written consent, 100 patients undergoing elective upper limbs surgeries were prospectively enrolled. Block randomization was performed. Each patient was randomly allocated into one of the two groups of 50 patients each.

a. *Control group:* Group B: Received 30 ml of Inj. Bupivacaine (0.375%).

*Study group:* Group BM: Received 30 ml of mixture of Inj. bupivacaine (0.375%) and midazolam (0.05 mg/kg) (Preservative free).

*Exclusion Criteria were*

Patients with a previous history of allergy to Midazolam and bupivacaine, Local infection, Patient refusal, Patients with coagulation disorders, Patients with systemic illness

*Pre Operative Preparation*

Patients were preoperatively assessed and ASA risk stratified. Basic investigations were done. Premedication with Control group - Group B: Received 30 ml of Inj. bupivacaine (0.375%)

*Study Group-Group BM:* Received 30 ml of mixture of Inj. bupivacaine (0.375%) and midazolam (0.05 mg/kg) (Preservative free) I.M 45 min prior to the procedure. Peripheral venous line was accessed using 18G I.V cannula. Preloading was done with 10ml/kg of Ringer lactate solution.

All patients were premedicated with Inj. Glycopyrrolate on the morning day of surgery. Peripheral venous line was accessed using a 18G intravenous cannula and all patients were preloaded with 10 ml/kg of Ringer lactate solution just within 30 minutes before performing the supraclavicular block. ECG, pulse oximeter and NIBP monitors were connected and baseline parameters were recorded.

Patient was laid supine with the head turned to the opposite side. Brachial plexus block was

performed using supra clavicular approach by classic technique. All patients were monitored for onset of sensory blockade, motor blockade and for any complications. Onset of sensory block was assessed as the time interval between administration of drug and absence of sensation to pin prick. Duration of sensory block was defined as the time elapsed between injection of drug and appearance of pain requiring analgesia was also noted. Onset of motor block was assessed as the time interval between administration of drug and loss of flexion/extension movements in the arm. Duration of motor block was defined as the time elapsed between injection of drug and complete return of muscle power was also noted. The effect on the following parameters were observed onset of sensory blockade, onset of motor blockade, duration of sensory blockade, duration of motor blockade, sedation score, hemodynamic variables, number of rescue analgesics given during 24 hours post-operative period.

Heart rate, non-invasive blood pressure and O<sub>2</sub> saturation were monitored and recorded. Number of rescue analgesics in 24 hours of post-operative period was also recorded. All patients were monitored for 24 hours post-operatively. All patients were given rescue analgesics if they complained of pain or any discomfort.

**Results**

As shown in Table 1 the mean time for onset of sensory block in group BM was 11.26 ±1.53 min and in group B was 19.07±1.7 min. The statistical analysis by student’s unpaired ‘t’ test showed that, the time for onset of sensory block in group BM was faster when compared to group B and was statistically highly significant (p< 0.001).

As shown in Table 2 the mean time for onset of motor block in group BM was 9.56 ±1.32 min and in group B was 15.3±2.09 min. The statistical analysis by unpaired student’s ‘t’ test showed that, the time for onset of motor block was significantly faster when compared to group B (p< 0.001).

**Table 1:** Comparison of Group B and Group BM On the Basis of Time for Onset of Sensory Block (Minutes)

Study Group	Onset time	P value
B	19.08 ± 1.7	0.001*
BM	11.26 ±1.5	

Test applied Student t test

\* indicates statistically significant difference at p<0.05

**Table 2:** Comparison of Group B and Group BM on the basis of time for onset of motor block (min)

Study Group	Onset time	P value
B	15.30 ± 2.09	0.002*
BM	9.56 ± 1.32	

Test applied Student t test

\* indicates statistically significant difference at  $p < 0.05$

Patients of both groups were observed for 24 hours. Time was noted when the patient asked for rescue analgesics. The mean duration of sensory block in group BM was  $13.81 \pm 1.23$  hours and in group B was  $5.84 \pm 0.49$  hours. The statistical analysis by students unpaired 't' test showed that the duration of sensory block in group BM was significantly longer when compared to group B ( $p < 0.001$ ).

The mean duration of motor block in group BM was  $5.25 \pm 0.45$  hours and the group B was  $5.13 \pm 0.45$  hours. The statistical analysis by students unpaired 't' test showed that the difference between duration of motor block in group BM and group B was not significant statistically ( $p > 0.05$ ).

In group BM, 74% patients required only 1 rescue analgesic dosage and 26% of patients required 2 rescue analgesic doses in post-op 24 hours. In group B 76% of patients required 2 and 24% of patients required 3 rescue analgesic doses in post-op 24 hours. This difference in number of rescue analgesic doses required by patient of both groups is statistically highly significant by chi-square test ( $\chi^2 = 61.25$ ,  $p < 0.001$ ).

In group B all patients were awake and alert and had sedation score of 1. In group BM, sedation corresponding to score 2 was observed in some patients between 15 minutes from time of injection to 60 minutes. 20% of patients at 15 minutes, 32% of patients at 30 minutes and 26% of patients at 60 minutes had sedation score of 2. None of the patients had sedation score of 3 and above during the study period. Statistical analysis of sedation score by chi-square test showed that the difference in sedation score was significant ( $p < 0.05$ ) during 15, 30 and 60 minutes.

## Discussion

This was a prospective, randomized single blinded study carried out at Hospital. 100 ASA I and ASA II patients undergoing elective upper limb surgeries were included in the study.

The patients in our study groups did not vary much with respect to age. The p value for age-wise

distribution among the groups was 0.83 ( $p > 0.05$ ), hence not significant statistically.

There were no significant differences between the study groups with respect to haemodynamic changes. Nasreen et al [5], Koj Jarbo et al [6] and Shaikh et al [7] also found no significant difference in hemodynamic changes, in concordance with our study.

### Onset Time of Sensory Block

In our study, Onset of sensory block for group BM was  $11.26 \pm 1.5$  minutes; while in group B was  $19.08 \pm 1.7$  minutes. The p value was 0.0007, which was statistically highly significant ( $p < 0.05$ ). In Koj Jarbo et al [6] study the onset of sensory block in group BM was  $12 \pm 2.9$  minutes and in group B was  $20 \pm 3.8$  minutes. Nasreen et al [5] found BM  $14 \pm 3.1$  minutes and B  $22 \pm 3.5$  minutes. These values were in concordance with our study. This could be due to a local anaesthetic property of Midazolam and its synergistic action with that of local anaesthetics. Midazolam a water soluble benzodiazepine is known to produce antinociception and to enhance the effect of local anaesthetic when administered intrathecally and epidurally. Midazolam produces this effect by its action GABA receptors. GABA receptors are also found in peripheral nerves.

In our study Onset of motor block for group BM was  $9.56 \pm 1.32$  min and in group B was  $15.30 \pm 2.09$  min, which was statistically highly significant ( $p = 0.0009$ ). In Koj Jarbo et al [6] study BM was  $9.2 \pm 2.38$  minutes and B was  $17.1 \pm 3.83$  minutes. In Nasreen et al [5] BM was  $10.5 \pm 2.40$  minutes and B was  $18 \pm 3.50$  minutes. The onset of motor block was found to be faster than the onset of sensory block in both groups.

In the present study, the mean duration of sensory block in group BM was  $13.81 \pm 1.23$  hours and it was  $5.84 \pm 0.49$  hours in group B which was statistically highly significant ( $P = 0.0003$ ). In Koj Jarbo et al [6] study duration in BM group was  $7 \pm 4.32$  hours and in B group it was  $5.95 \pm 1.4$  hours. These values were comparable with the study conducted by Nasreen et al [5] and Shaikh et al [7].

### *Duration of Motor Blockade*

In our study, the mean duration of motor block in group BM was  $5.25 \pm 0.45$  hours and the group B was  $5.13 \pm 0.45$  hours. This result was not found to be statistically significant ( $p = 0.12$ ). These values were comparable with the study conducted by Koj Jarbo et al [6] in which they found out that the mean duration of motor blockade in group BM was  $5.65 \pm 3.32$  hours while in group B was  $5.1 \pm 1.14$  hours.

The mean time from onset of block to request of analgesics was taken as total duration of analgesia. The duration of analgesia was  $13.81 \pm 1.23$  hours with Group BM and it was  $5.84 \pm 0.49$  hours with Group B and it is statistically highly significant ( $p=0.01$ ). This observation is supported by Nasreen et al [5] ( $9.30 \pm 4.30$  hours and  $6.20 \pm 1.80$  hours) and Shaikh et al [7] ( $805.04 \pm 175.75$  minutes and  $502.24 \pm 52.68$  minutes). The addition of Midazolam in doses of approximately 1 to 2 mg intrathecally has a positive effect on perioperative and chronic pain therapy [9]. Studies in animals have revealed no neurotoxic effects of intrathecally administered

### *Midazolam [10-12].*

In our study, in group BM, 74% patients required only 1 rescue analgesic dosage and 26% of patients required 2 rescue analgesic doses in post-op 24 hours. In group B 76% of patients required 2 and 24% of patients required 3 rescue analgesic doses and this difference is statistically highly significant ( $p < 0.001$ ). Our study correlates with the study conducted by Jarbo et al [6], Naguib et al [8].

In our study, in group B all patients had a sedation score of 1. In group BM, sedation score of 2 was observed in some patients and the difference was statistically significant ( $p < 0.05$ ). Our study correlates with the study conducted by Shaikh et al [7]. This could be due to partial vascular uptake of Midazolam, and its transport to the central nervous system where it acts and produces sedation. Adding midazolam not only provides prolonged post-operative analgesia but also sedation.

### **Conclusion**

From our study, it was concluded that, the addition of Midazolam (0.05 mg/kg) as an adjuvant to bupivacaine (0.375%) when compared to plain bupivacaine (0.375%) resulted in Rapid onset of

sensory block and motor block, Prolonged duration of sensory block. And Reduced number of rescue analgesics in the post-operative period of 24 hours.

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