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# A Comparative Study Of Bupivacaine With Midazolam And Bupivacaine Only In Brachial Plexus Block For Upper Limb Surgery

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**Abstract**

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## Introduction

In recent times, Brachial plexus block (BPB) is the most useful technique of regional anaesthesia for upper limb surgeries.[1] It is chosen in preference to general anaesthesia as it avoids the risks associated with general anaesthesia, provides postoperative pain relief, shortens recovery time, and reduces hospital stay. Brachial plexus block provides an optimum condition of the operating field by complete muscular relaxation, stable intraoperative hemodynamic parameters and associated sympathetic block which helps to reduce postoperative pain, vasospasm and limb edema.[2,3] It is also called 'spinal anaesthesia' of the upper limb.

Amongst various approaches, Supraclavicular approach involves blockade of the Brachial plexus at its trunk on the first rib where all the sensory, motor, and sympathetic nerve fibres supplying the upper extremity are confined in only three nerves.[4] At this place brachial plexus is most compact over a small surface area so that only a small volume of local anaesthetic produces predictable block with rapid onset. Moreover, the technique is easy to perform as the landmark used during performing the block such as midclavicular point and lateral insertion of sternocleidomastoid are very constant in position and easily discernible. Diedrich Kulenkampf first performed this technique on himself in 1911.[5]

Bupivacaine is the most commonly used local anaesthetic for this procedure as it's effect lasts longer than others[6] . Sometimes, the duration of action of a single dose of Bupivacaine may not be adequate for the duration of operation. The effects of single-injection BPB dissipate after several hours unmasking the moderate-to-severe pain of the surgical insult. Efforts to prolong BPB duration by increasing LA dose are limited by their narrow therapeutic window and indeed may not be effective as recent studies have demonstrated equivalent analgesic duration with volumes as low as 5 ml[7].

Midazolam is known to produce antinociception and potentiate the effect of LA when given in neuraxial block. It produces this effect by its action on Gamma Aminobutyric Acid-A (GABA-A) receptors [8,9,10,11]. Gaba receptors have also been found in peripheral nerves.

Several studies showed midazolam to be effective when used in intrathecal, epidural and caudal blocks and now recently midazolam with bupivacaine has been found to improve analgesic characteristics in peripheral blocks compared to bupivacaine alone[12 - 20]. Due to the high blood concentration of benzodiazepine through conventional routes and

profound sedation, proper assessment of analgesic effect was difficult to obtain. With the advent of the less toxic water soluble benzodiazepine (midazolam), it became possible to use it directly over the nerve tissues. We therefore, like to evaluate the effects of adding midazolam to bupivacaine during brachial plexus blocks in regard to the onset duration and intensity block along with its analgesic efficacy.

Primary objective of the study is to compare onset , duration and intensity of both sensory and motor blocks between bupivacaine alone and bupivacaine midazolam combination. Secondary objective is to compare pain and sedation score between the two groups.

**Methodology:**

After getting institutional ethical clearance for the present prospective randomized double blind clinical study hundred adults of either sex aged between 18 to 60 years, American society of Anaesthesiologist (ASA) physical status l and ll scheduled to undergo upper limb operation under brachial plexus block in Nil Ratan Sircar Medical College were selected and randomly allocated by sealed envelope technique into two groups . Group B ( n= 50 ) to receive plain Bupivacaine 0.25% 30 ml and Group BM ( n= 50 ) to receive Midazolam 0.05 mg/kg with Bupivacaine total 30 ml during Brachial plexus block. Patients with history of allergy to the drugs under study, ASA > II, weight > 80kg, having local site infection pregnancy ,coagulopathy patients with pneumothorax or pneumonectomy on the opposite side , with neuromuscular and respiratory disease were excluded from the study.

After taking the patient in OT baseline monitors were applied to every patient and baseline hemodynamic parameters recorded. For the brachial plexus block the patient was placed in supine position with head turned to opposite side. A rolled towel was placed between the shoulders along the spine so as to expose the block site properly . The patient was asked to lift the head so as to bring the sternocleidomastoid into prominence. The index finger was placed behind the lateral border of the sternocleidomastoid and interscalene groove was palpated. The subclavian artery pulsation was palpated in the lower part of interscalene groove . After all aseptic preparation, a skin wheal was raised at this point with 2 ml of lignocaine, 2 to 3 cm midpoint, and perpendicular to the clavicle. The pulsation of the subclavian artery against the needle or the palpating finger was the surest guide to the Supraclavicular block. The needle entered at the C7 level in the groove and was directed caudally. A 22G 4 cm long needle is inserted through the skin and directed posterior laterally and parallel to the scalene muscles and towards the patient's feet. Needle progression was stopped once the sheath was entered. After confirming negative aspiration 30 ml anesthetic solution was injected.

Group B patients received only Bupivacaine 0.5% 30 ml. Group BM patients received Bupivacaine with preservative-free Midazolam 0.05 mg /kg total 30 ml. Both the anaesthetic solution was prepared in similar-looking syringes by an independent anaesthesiologist not involved in the study. The patient and observer both were blinded about the nature of the drug solution used for performing the block.

The onset of both sensory and motor block was assessed with an alcohol-soaked cotton swab and by assessing ability to raise a hand and flex forearm against gravity using the Hollmen scale. Onset was set at grade 2 [time elapsed between block injection and attainment of grade 2 sensory or motor block] and complete block at grade 3 [ time between block injection to the attainment of grade 3 sensory or motor block ]in the Hollmen's scale. Duration of sensory and motor block was considered as the time interval between injection of local anaesthetic and onset of paresthesia for sensory and the time interval between injection of local anaesthetic and recovery from motor block.

Postoperatively , every patient was assessed for pain and sedation score at 0 min, 15 min, 30 min 60 min 2 hr, 6 hr, 12 hr and 24 hrs. Sedation was monitored by Ramsay sedation scale and pain was assessed using Visual Analog Scale [VAS]. Injection diclofenac 75 mg was given as rescue analgesic as soon as VAS score exceeded 3. Duration of postoperative analgesia [ time of first dose of rescue analgesia after completion of operation] and presence of any complication were also noted for every patient.

Statistics: Sample size was calculated using software assuming 90% statistical power wit a level of significance at 5%. A sample size of 45 in each group came out to be an adequate size to denote any improvement in pain scores. Considering 10% as



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dropout and incomplete studies we took 50 patients for enrolment in each group.

The study was conducted over 1 year period. Data from 100 patients were analyzed using SPS for window [ version 20.0; SPS Inc., Chicago IL, USA ]

Continuous data were expressed as mean ± SD . Discrete categorical data were expressed as n [ % ]. Differences in demographic, anaesthetic intraoperative, and postoperative data are tested by Independent Student's t-test [ continuous data ] or by Pearson Chi-square test [ discrete data]. For statistical purposes, P-value differences of <0.05 have been considered significant.

**Results :**

**Table 1: Demographic Properties**

| | Group B [n = 50 ] | Group BM [n= 50 ] | P value [ < 0.05] | Significance | |
|---|---|---|---|---|---|
| Age ( mean±SD) In years | 39.78 ± 13.721 | 36.10 ± 12.564 | 0.165 | NS | |
| Sex ( M/F) (%) | 16/34 (32%/68) | 26/24 (52%/48) | | | |
| Height(mean±SD) in years | 150.46 ± 6.637 | 157.18 ± 7.381 | 0.249 | NS | |
| Weight(mean±SD) in kg | 62.24 ± 9.023 | 64.52 ± 7.135 | 0.164 | NS | |
| ASA (I/II )(%) | 22/28 ( 44/56%) | 24/26 (48%/52) | 0.346 | NS | |

Demographic characteristics of both the groups that are age, sex, height weight, and ASA status were similar between the groups (Table1)

**Table 2: Intra and postoperative hemodynamic parameters**

| | Group B | Group BM | P value | Significance |
|---|---|---|---|---|
| HR Baseline | 72.46 ± 7.282 | 77.22 ± 5.604 | 0.000 | HS |
| SBP Baseline | 126.52 ± 9.671 | 123.52 ± 6.783 | 0.076 | NS |
| DBP Baseline | 83.00 ± 4.674 | 77.48 ± 6.139 | 0.000 | HS |
| SpO2 Baseline | 99.48 ±.505 | 99.20 ± .808 | 0.040 | S |
| HR 15 min | 75.14 ± 7.282 | 77.22 ± 5.604 | 0.000 | HS |
| SBP 15 min | 130.32 ± 8.537 | 122.36 ± 6.561 | 0.000 | HS |
| DBP 15 min | 83.88 ± 4.415 | 76.56 ± 6.299 | 0.000 | HS |
| SpO2 15 min | 99.46 ± .613 | 99.40 ±.728 | 0.657 | NS |



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| | | | | |
|---|---|---|---|---|
| HR 30 min | 74.76 ± 6.536 | 70.70 ± 5.800 | 0.001 | HS |
| SBP 30 min | 124.92 ± 9.741 | 121.80 ± 5.718 | 0.054 | S |
| DBP 30 MIN | 83.72 ± 3.855 | 76.60 ± 6.824 | 0.000 | HS |
| SpO2 30 min | 99.48 ± .580 | 99.16 ± .681 | 0.013 | S |
| HR 60 MIN | 75.50 ± 6.341 | 69.36 ± 5.348 | 0.000 | HS |
| SBP 60 MIN | 125.88 ± 9.471 | 121.44 ± 5.643 | 0.005 | HS |
| DBP 60 MIN | 82.08 ± 4.517 | 75.96 ± 6.484 | 0.000 | HS |
| SpO2 60 MIN | 99.56 ± 0.541 | 99.12 ± 0 .895 | 0.004 | HS |
| HR 2 HRS | 74.34 ± 6.906 | 67.84 ± 5.369 | 0.000 | HS |
| SBP 2 HRS | 129.16 ± 10.078 | 120.32 ± 5.274 | 0.000 | HS |
| DBP 2 HRS | 83.28 ± 4.272 | 76.04 ± 6.214 | 0.000 | HS |
| SpO2 2 HRS | 99.38 ± 0.490 | 99.70 ± 0.505 | 0.002 | HS |
| HR 6 HRS | 74.20 ± 6.382 | 66.62 ± 5.054 | 0.000 | HS |
| SBP 6 HRS | 125.60 ± 9.596 | 119.76 ± 5.370 | 0.000 | HS |
| DBP 6 HRS | 82.80 ± 4.729 | 75.96 ± 7.188 | 0.000 | HS |
| SpO2 6 HRS | 99.38 ± 0.602 | 99.38 ± 0 .725 | 1.000 | NS |
| HR 12 HRS | 74.30 ± 6.112 | 65.40 ± 4.513 | 0.000 | HS |
| SBP 12 HRS | 125.68 ± 9.146 | 119.12 ± 4.645 | 0.000 | HS |
| DBP 12 HRS | 83.76 ± 4.113 | 76.28 ± 6.490 | 0.000 | HS |
| SpO2 12 HRS | 99.66 ± 0 .479 | 99.38 ± 0 .753 | 0.029 | S |
| HR 24 HRS | 74.72 ± 6.224 | 75.40 ± 5.485 | 0.564 | NS |
| SBP 24 HRS | 126.92 ± 9.100 | 142.12 ± 16.802 | 0.506 | NS |
| DBP 24 HRS | 84.00 ± 4.536 | 75.96 ± 6.803 | 0.000 | HS |
| SpO2 24 HRS | 99.50 ± 0.544 | 99.44 ± .644 | 0.616 | NS |

Table 2 shows that baseline hemodynamic characteristics intra and postoperatively. Intraoperative mean HR ranges from72.46 ± 7.282 to 74.72 ± 6.224 in group B and from 77.22 ± 5.604 to 75.40 ± 5.485 in group BM. Differences were not statistically significant. Similarly other hemodynamic parameters such as SBP, DBP SpO2 also were similar between the groups without any statistical significance.



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**Table 3 : Block characteristics**

| Parameter (time in min) | Group B (mean ± SD) | Group BM (mean ± SD) | P value | Significance |
|---|---|---|---|---|
| Onset sensory block | 11.67 ± 1.4 | 9.14 ± 1.6 | <0.001 | HS |
| Onset motor block | 6.46 ± 1.3 | 4.82 ± 1.5 | <0.001 | HS |
| Complete sensory block time | 19.84 ± 2.94 | 13.57 ± 1.71 | 0.000 | HS |
| Complete motor block time | 14.8 ± 3.495 | 11.29 ± 1.215 | 0.000 | HS |
| Duration of sensory block | 286.16 ± 8.445 | 369.94 ± 34.181 | 0.000 | HS |
| Duration of motor block | 264.94 ± 8.749 | 8.749 ± 28.966 | 0.000 | HS |

Table 3 shows that onset time and time of complete motor and sensory blocks were significantly shortened in Group BM i.e. Bupivacaine and midazolam group than in group B i.e. bupivacaine only group. On the other hand duration of both motor and sensory blocks was significantly prolonged in the Bupivacaine midazolam group than in the bupivacaine-only group.

**Table 4 : Intensity of blockade**

| | Grade | Group B | Group BM |
|---|---|---|---|
| MOTOR | 4 | 8 (16%) | 14 (28%) |
| | 3 | 42 (84%) | 36 (72%) |
| | 2 | 0 | 0 |
| | 1 | 0 | 0 |
| SENSORY | 4 | 21 (42%) | 17 (34%) |
| | 3 | 29 (58 %) | 33 (66%) |
| | 2 | 0 | 0 |
| | 1 | 0 | 0 |

Table 4 shows In group BM 28% and 34 % patients had grade 4 and 72% and 66% patients had grade 3 motor and sensory blocks respectively.in Group B 16% and 42% patients had grade 4 and 84% and 58% patients had grade 3 motor and sensory blocks respectively. These differences were not statistically significant (motor : $\chi 2=2.098$, $p = 0.148$ and sensory : $\chi 2= 0.679$, $p = 0.410$).

In group B patients 8 (16 %) patients and in Bupivacaine midazolam group 5 (10%) patients required one dose of rescue analgesic. Postoperative pain scores (VAS) of Group BM patients recorded a lower mean than group B This difference in requirement of rescue analgesic and pain (VAS) were statistically significant. Patient



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sedation scores: Group BM: 38% of patients were sedated and required mild physical stimulus to awaken. Group B: Only 8% of patients were sedated. The rest of the patients were awake and alert.

**Discussion :**

In Anesthetizing, the upper limb for surgical procedures the brachial plexus block is an excellent alternative to general anaesthesia. Various approaches have been described for this blockade. The brachial block has been performed here by the supraclavicular method.

Adequate postoperative analgesia can be obtained even when a long-acting anaesthetic agent like bupivacaine is used alone and when concomitant adjuvants such as opioids, clonidine, hyaluronidase are used, the period of analgesia is prolonged, and minimum adverse effects have been seen. In the present study, midazolam was added as an adjuvant to bupivacaine, and the hemodynamic variables, onset, and duration of the block, sedation, pain score, and need for rescue analgesia were studied at regular intervals over a period of 24 hours.

In our study hundred patients were selected within the age group of 18 to 60 years Out of the 50 patients present in the first group received bupivacaine only whereas the second group received bupivacaine plus Midazolam for the brachial plexus block. A demographic profile such as mean age, height, weight, male to female ratio was comparable in both groups. The study showed that the onset of sensory and motor blocks was significantly faster in the group BM who received midazolam as an adjuvant, along with bupivacaine. The onset of motor block in Group B which received bupivacaine only was, 6.46 ± 1.3 minutes, and in the bupivacaine midazolam group ( group B) was 4.82 ± 1.5 minutes. Whereas the onset of sensory block the bupivacaine group had a mean time of 11.67 ± 1.4 minutes. And the bupivacaine midazolam group had a mean time of 9.14 ± 1.6 minutes.

Winnie et al had observed that in a nerve trunk the motor fibres are arranged peripherally and the sensory fibres are towards the core. Hence, when the drug is injected perineurally, the motor fibres are blocked much faster than the sensory ones. The results in our study also showed the same. Our study results also showed that the sensory block lasted longer than the motor block. Jong et al in their theory had proved the fact. There have been various studies in which midazolam when used in central neuraxial block or epidural infusion, improved analgesia and significantly lowered VAS scores. Our present study also showed similar results.

In our study, the total requirement of rescue analgesia was significantly lower in the group BM which received midazolam along with bupivacaine in the brachial plexus block. This can be explained by its action on the GABA- A receptors present on the brachial plexus causing antinociception. The presence of such receptors in the peripheral nerves has been proved by many scientists in the past.

Sedation scores in the group BM which received midazolam were higher than the other group. Partial vascular uptake of midazolam from the block site and its transportation to the CNS probably caused this sedative effect. The high lipid solubility, the faster diffusion, rapid clearance, and the shorter half-life of midazolam explain why the sedative effect was short-lived. No patient in the study experienced airway compromise or needed airway assistance.

**Conclusion:** We can conclude that midazolam 0.05 mg/ kg, when added to supraclavicular brachial plexus block along with bupivacaine in upper limb surgery, hastens the onset of sensory and motor blocks, produces a prolonged effect, improves analgesia, and reduces the requirement of rescue analgesics. It also provides comfortable sedation intraoperatively without any need for airway assistance.

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