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A CLINICAL COMPARATIVE STUDY BETWEEN 0.5%BUPIVACINE, MIDAZOLAM COMBINATION AND 0.5% BUPIVACAINE ALONE FOR BRACHIAL PLEXUS BLOCK BY SUPRACLAVICULAR APPROACH.

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ABSTRACT Regional anaesthetic techniques like peripheral nerve blocks are essential components of anaesthetist's armamentarium for comprehensive anaesthetic care. Regional anaesthesia benefits patients by reducing immediate postoperative pain as well as postoperative complications.

Bupivacaine is the most frequently used local anaesthetics for brachial plexus block due to its long duration of action . Adjuvant drugs like dexamethasone and clonidine were used to prolong the effect of Bupivacaine, but they are associated with the delay in the onset of action and no sufficient prolongation of postoperative analgesia. Midazolam, a water-soluble agent, prolong the effect of local anaesthetics by its action on GABA- A receptors when given by epidural or intrathecal route. The same effect is expected on peripheral nerves . This study is intended to determine the effects of adding midazolam to 0.5% Bupivacaine in brachial plexus blockade by supraclavicular approach about the onset, intensity and duration of the blockade along with its analgesic efficacy.

Based on our study, we conclude that at equal volumes bupivacaine 0.5% with Midazolam has an advantage over Bupivacaine 0.5% alone for supraclavicular brachial plexus block in terms of Early-onset of sensory & motor blockade, Prolonged duration of sensory & motor blockade, Prolonged duration of postoperative analgesia.

KEYWORDS : Brachial plexus block by Subclavian Perivascular Technique, Bupivacaine, sensory and motor blockade, Midozolam

INTRODUCTION

Regional anaesthetic techniques like peripheral nerve blocks are essential components of anaesthetist's armamentarium for comprehensive anaesthetic care. Regional anaesthesia benefits patients by reducing immediate postoperative pain as well as postoperative complications[1]. Peripheral nerve blocks have superior recovery profile in comparisons general anaesthesia when carefully selected[2]. Halsted and Hall in the 1880s used a cocaine injection that produced a sensory block in the ulnar, musculocutaneous, supratrochlear and infraorbital regions[3]. A supraclavicular approach for the blockade of the brachial plexus was first described by Kulenkampf in 1911[4]. The supraclavicular block has gained popularity due to its less chance of significant complication[5]

Bupivacaine is the most frequently used local anaesthetics for brachial plexus block due to its long duration of action [6]. Adjuvant drugs like dexamethasone and clonidine were used to prolong the effect of Bupivacaine, but they are associated with the delay in the onset of action and no sufficient prolongation of postoperative analgesia[7,8]. Midazolam, a water-soluble agent, prolong the effect of local anaesthetics by its action on GABA- A receptors when given by epidural or intrathecal route[9,10]. The same effect is expected on peripheral nerves[11]. This study is intended to determine the effects of adding midazolam to 0.5% Bupivacaine in brachial plexus blockade by supraclavicular approach about the onset, intensity and duration of the blockade along with its analgesic efficacy.

AIMS AND OBJECTIVES OF STUDY

This study was a randomized, double-blinded, prospective study conducted at the Department of Anaesthesiology, Konaseema institute of medical sciences and research foundation, Amalapuram from June 2017 to June 2019. This study was to compare the efficacy of supraclavicular brachial plexus block, with 0.5% Bupivacaine & 0.5% Bupivacaine with Midazolam with respect to

- Onset & duration of sensory blockade
- Onset & duration of motor blockade
- Duration of postoperative analgesia

REVIEW OF LITERATURE

Halsted [28] performed the first brachial plexus nerve block when he found the cords and nerves of the brachial plexus, after blocking the roots in the neck with a cocaine solution 0.1% under direct vision.

Harvey Cushing[28], who was at that time one of Halsted's surgical residents applied cocaine to the brachial plexus before dividing it, during a forequarter amputation for sarcoma.

George Hirschel [29] later in the same year, described a percutaneous approach to the brachial plexus from the axilla. He made separate injections above and below the axillary artery with a four-inch needle directed towards apex of the axilla.

Kulenkampff and Persky[30] published their experiences with thousand blocks without apparent major complications. They described their technique with the patient in the sitting position or the supine position with a pillow between the shoulders. The needle was inserted above the midpoint of the clavicle where the pulse of the subclavian artery could be felt, and it was directed medially towards the second or third thoracic spinous process.

Patrick [31] in 1940 published his modification of Kulenkamff technique. Alon Willie and Collins [32] first developed the subclavian (Supraclavicular) perivascular technique with a reported incidence of pneumothorax less than 1%.

McGlade et al. [22], Compared the effectiveness of 0.5% ropivacaine and 0.5% bupivacaine for brachial plexus block. They appeared equally effective in providing brachial plexus anaesthesia.

Batra et al. [33] used Bupivacaine with Midazolam intrathecally and found a significantly lower visual analogue score compared to Bupivacaine alone. Midazolam produces this additive effect on local anaesthetics by its action on the GABA-A receptor complexes present in the spinal cord.

Bharti et al. [10] found out that the addition of intrathecal midazolam to bupivacaine significantly improves the duration and quality of spinal anaesthesia and provides prolonged perioperative analgesia without significant side-effects.

Yegin et al. [34]demonstrated the use of intrathecal midazolam combined

with intrathecal bupivacaine producing a more effective and more extended analgesia with a mild sedative effect in perianal surgery.

Nishiyama et al. [9,35] observed that adding midazolam increased not only analgesic but also sedative effect with increasing dose of bupivacaine in a postoperative continuous epidural administration.

Nishiyama et al. [36] observed that adding midazolam (10 to 20 mg per 12 h) to continuous epidural infusion of bupivacaine for postoperative pain can provide better analgesia, amnesia and sedation than bupivacaine alone.

Kim et al. [37] observed that intrathecal midazolam increases the analgesic effects of the spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy.

Nasreen Laiq et al. [38] in 2007 studied Bupivacaine vs Midazolam & Bupivacaine for the supraclavicular block. It concluded that there was no significant change in the hemodynamic variables (heart rate, noninvasive blood pressure, oxygen saturation). The onset and duration of sensory and motor block were significantly faster and, pain scores were significantly lower in those who received Midazolam along with Bupivacaine. Demand for rescue analgesia was considerably less in the study group.

Safiya I Shaikh, Veena K [39] conducted a prospective, randomized, double-blind study at Karnataka Institute of Medical Sciences (KIMS), Hubli (India), from 01 March 2008 to 01 March 2009, on 50 adult patients of ASA 1 and 2, aged between 18-65 years scheduled for various upper limb surgeries.

Patients were divided into two groups of 25 each. Group B received 30 ml of inj. Bupivacaine 0.5% +2 ml normal saline and group BM received 30 ml of inj. bupivacaine 0.5% + inj. midazolam (preservative-free) 0.05mg/kg. Patients were observed for sedation, respiratory depression, pulse rate, SBP, DBP, duration of motor block, duration of pain relief and occurrence of any complications.

Postoperative analgesia was significantly longer (805.04± 175.75 min) in group BM, as compared to group B (502.24± 52.68 min) with p-value <0.001. Pain score was significantly low in group BM (mean 1.6), compared to group B (mean 4.92) at 12 hours postoperatively. The onset of sensory block was 8.36 ±3.58 min and 8.52 ±4.18 min in group B and group BM respectively with p-value > 0.05. Hence there was no statistically significant difference. The onset of motor block in group B was 9.96 ± 5.69 min and in group BM 7.92 ± 5.68 min. and p-value was > 0.05. Hence there was no statistically significant difference. Mild respiratory depression and sedation occurred intraoperatively in group BM, which required no active intervention.

Addition of midazolam 50mcg/kg to 30ml of bupivacaine 0.5% for supraclavicular brachial plexus block prolonged sensory blockade and post- operative analgesia without increasing the risk of adverse effects. Dhwani Nalwaya et al. [40] conducted a randomised, double-blind study was carried out on 70 patients of ASA grade I and II undergoing upper limb orthopaedic surgeries, were divided into two groups. Group A (n=35) received Inj. Bupivacaine (0.5%) 20 ml + Inj. Lignocaine with adrenaline (1:200000) 10 ml. Group B (n=35) received Inj. Bupivacaine (0.5%) 20 ml + Inj. Lignocaine with Adrenaline (1:200000) 10 ml + Inj. Midazolam 50 jig/kg as an adjuvant in supraclavicular brachial plexus block. The duration of sensory block, motor block, duration of postoperative analgesia, sedation score and visual analogue score were obtained in both groups and values were compared with 'unpaired t-test'.

The onset and duration of sensory and motor block were significantly faster and longer in group B compared to group A ($p < 0.05$). The onset of sensory and motor block was faster in group B. The mean time for onset of sensory block in group B was 11. 6 ± 1.39 minutes and in group A was 19.02 ± 1.8 mins.

The mean time for onset of motor block in group A was 15.6 ±1.8 min, and in the group, B was 11.15 ± 0.8 min. The mean time duration of motor block in group A was 4.6 ± 0.69 and in group B 4.9 ± 0.48. There was no significant difference in the duration of motor block in both groups. ($p>0.05$) Pain scores were significantly lower in group B for 24 hours postoperatively ($p < 0.001$). Demand for rescue analgesia was significantly less in group B. ($p<0.05$).

The addition of midazolam to local anaesthetics in supraclavicular block quickens onset and prolongs the duration of the blockade, enhances post-op analgesia with stable hemodynamic and desirable sedation score without any adverse effects.

Bhattacharya D et al.[41] also observed the faster onset of sensory and motor block in midazolam group II (XBM). Sensory block in group IfBupivacaine) was 12 ±4.2 minutes, in group II was six ± 3.1 minutes, motor block in group I was 11 ± 2.3 minutes, group II was 5 ± 4.2 minutes.

Nishiyama et al.[35] added Midazolam to a continuous epidural infusion of Bupivacaine and observed improved analgesia. The addition of Midazolam in doses of approximately 1 to 2 mg intrathecally has a positive effect on perioperative and chronic pain therapy.

Koj Jarbo et al.[42] conducted a prospective, randomised, double-blind study was conducted on 40 ASA I or II adult patients undergoing upper limb surgeries under supraclavicular brachial plexus block. Patients were randomly divided into two groups. Patients in Group B (n = 20) were administered 30 mL of 0.5% bupivacaine and Group BM (n = 20) were given 30 mL of 0.5% bupivacaine with midazolam 50 ug-kg-1. Haemodynamic variables (i.e., heart rate, noninvasive blood pressure), pain scores and rescue analgesic requirements were recorded for 24 hr postoperatively. Sensory and motor block appeared earlier in Group BM than in Group B ($P < 0.05$). In Group BM, the onset of sensory block occurred in 12 ± 2.9 min compared to 20 ± 3.8 min in Group B. Onset time of motor block in Group BM was 9.2 ± 2.38 min compared to 17.1 ±3.83 min in Group B. In both groups, motor block occurred earlier than a sensory block ($P < 0.05$) but the duration of motor block was not different between groups (Table II). Postoperatively, lower pain scores were observed in Group BM compared to Group B for the 2 to 24 hr postoperative period ($P < 0.05$). All patients in Group B required rescue analgesia, while only three patients (15%) of group BM required rescue analgesics ($P < 0.05$). The number of rescue analgesic doses required was significantly higher (n = 58) in Group B compared to Group BM (n = 8, $P < 0.05$) during the study period.

Midazolam (50 ug-kg-1) in combination with 30 mL of bupivacaine (0.5%) hastened the onset of sensory and motor block and improved postoperative analgesia when used in brachial plexus block, without producing any adverse events.
Gulec et al. [43] found that a Bupivacaine and midazolam combination prolonged postoperative analgesia compared to a bupivacaine-morphine combination when administered caudally.

MATERIALS AND METHODS:

Study design:

This study was a randomised, double-blinded, prospective study conducted at Konaseema institute of medical sciences and research foundation, Amalapuram during 2020.

Study setting and population:

The study approval was obtained from both academic and ethics committee of the hospital. After a valid informed written consent, patients were enrolled for the study. The study population included patients of 18-60 yrs of either sex with, ASA grade I & II who were undergoing surgical intervention for upper limb pathologies under brachial plexus block by supraclavicular approach.

Sample Size:

A total of 80 patients were consented and participated, who were undergoing surgical intervention for upper limb injuries under regional anaesthesia through brachial plexus blockade by supraclavicular approach.

Inclusion criteria:

- Age group 18-60 years
- ASA grade I & II
- Patients were undergoing supraclavicular block for Upper limb surgery below the shoulder joint.

Exclusion criteria:

- Age <18 yrs or >60 yrs
- ASA Grade III & IV
- Any bleeding disorder and patient on anticoagulants
- Neuro deficit involving brachial plexus
- Local infection at the injection site
- History of allergy to local anaesthetic drug
- Pneumothorax or previous pneumonectomy on the opposite side

❖ Patients who did not consent for the study

After a thorough history, clinical examination and laboratory investigations (Complete Blood Count, X-ray chest, & Blood urea nitrogen) patients were randomized into one of the two groups(Group BM or B) through standard randomization methods.

Group BM: Patients in this group received 0.5% Bupivacaine (27.5 ml) + Midazolam 2.5 mg (2.5ml), making a total volume of 30 ml.
Group B: Patients in this group received 0.5% Bupivacaine (27.5ml) + distilled water (2.5ml), making a total volume of 30 ml.

Drug solution used and dosage:
Bupivacaine 0.5% was used with a dose not exceeding 3 mg/kg. Midazolam (1 mg/ml) 2.5 ml was added to Bupivacaine in group BM patients. A total volume of each dose was adjusted to 30 ml in both groups. Drug solutions were prepared by an independent anesthesiologist not involved in the study.

Monitoring:
Standard monitors were attached-
❖ Pulse oximeter
❖ ECG
❖ NIBP

Initially, the pre-procedure parameters were recorded, i.e. pulse rate, BP, SpO2 and Ecg. Then the block was administered. All through the study, these parameters were monitored continuously except the NIBP, which was recorded intermittently and continued postoperatively for 24 hours. Patients were observed vigilantly for development of various complications and necessary instructions given.

Brachial plexus block by Subclavian Perivascular Technique [32]
Position
- The patient was fully explained about the procedure, and then placed in the supine position with the head turned to the side opposite to the side that is to be injected.
- The arms were at the patient's side with the hands pointing towards the knee. The arm on the side to be injected may be pulled to depress the clavicle and the shoulder.
- A rolled towel was placed lengthwise between the shoulders along the spine to give the best exposure to the area.

Landmarks
- The anesthesiologist stands at the head end of the table. The patient was asked to lift the head slightly to bring the clavicular head of the sternomastoid muscle into prominence.
- The index finger was placed lateral to the muscle, and the patient was told to relax. Roll the index finger laterally across the belly of the muscle until the interscalene groove was palpated.
- The finger was then moved inferiorly down the groove until the pulse of the subclavian artery was palpated between the scalene muscles.
- After aseptic preparation, a skin wheal was raised at this point with 2ml of lignocaine with a 24G needle about 2 - 3 cms above the midpoint of and perpendicular to the clavicle.
- The pulsation of the subclavian artery against the palpating finger or needle was the surest guide to supraclavicular block.

Procedure
- After sterile preparation of the region, the 22G, 4cm needle was inserted through the skin wheal and above the palpating finger immediately lateral to the subclavian artery.
- It was directed dorsolateral and paralleled to the scalene muscles and towards the patient's feet. There would be a click once the sheath was entered and there was a give way. The needle advancement was stopped at this level and conducted subclavian pulsation was observed. If the needle was pulsating, then the anaesthetic solution was injected.
- If the needle pulsation was not satisfactory, then the needle was advanced further until it hits one of the three trunks of the plexus.
- Paraesthesia to any part of the upper extremity as long as it was below the shoulder indicates that the needle was in the perivascular space.
- In this technique, paraesthesia was obtained before the first rib was contacted. If paraesthesia was not elicited, then the needle was withdrawn and tried once again.
- A cough by the patient is a warning that the pleura is being irritated by the needle.
- When the desired endpoint was reached, (i.e. paraesthesia elicited in the arm and fingers or loss of resistance with "click" sensation and transmitted pulsations were observed as needle movement, the needle was halted, and the success of the procedure now depends on holding the needle tip near the nerve during the injection.
- Potential pitfalls include patient movement and failure to hold the needle firmly in place.
- The local anaesthetic solution was injected once the position of needle within the sheath was confirmed. Accidental intravascular injection and trauma to the nerves were avoided.
- After injecting the local anaesthetic, the block was tested for both sensory (using pinprick) and motor (using muscle power) and was compared with the same stimulation or power in the contralateral arm.
- Motor block was evaluated by thumb abduction (Radial nerve), thumb adduction (Ulnar nerve), thumb opposition (Median nerve) and flexion of the elbow in supination and pronation of the forearm (musculocutaneous).

Hollmen's scale : The Hollmen's scale was used in the study for assessing both sensory, and motor blockade and the onset of blockade means minimum grade 2 and complete blockade means minimum grade 3.

Hollmen's scale
Sensory blockade (Grade)
- 0 – Normal sensation of a pinprick.
- + - Pinprick felt as sharp-pointed but weaker compared with the same area in other extremities.
- ++ - Pinprick felt as touch with a blunt object.
- +++ - No perception of a pinprick.

Motor blockade(Grade)
- 0 – Normal muscle function
- + - Slight depression in muscle function as compared with pre-anaesthetic power.
- ++ - Very weak muscular action persisting in muscle.
- +++ - Complete block with absent muscular function.

Nerves studied in the block
- The lateral cutaneous nerve of the arm
- The medial cutaneous nerve of the arm
- The medial cutaneous nerve of forearm
- The posterior cutaneous nerve of forearm
- The lateral cutaneous nerve of forearm
- Median nerve
- Ulnar nerve
- Radial nerve

The evaluation was carried for every minute after completion of the injection, and the time of onset was noted for both sensory and motor blockade. The onset of the blockade, both sensory and the motor, is defined as a minimum of grade 2 in Hollmen's scale. The blockade was considered complete when sensory and motor scores were at least grade 3 in Hollmen's scale. Only patients with complete motor block were included in the study. Once the block was complete; the patient was wheeled into the theatre and surgery was allowed to proceed.

Duration of sensory blockade was considered as the time interval between the local anaesthetic administration and the onset of paraesthesia (during recovery) while the duration of motor block was defined as the time interval between the local anaesthetic administration and the recovery of motor block.

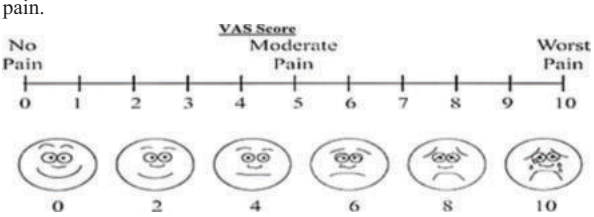
Sedation was assessed using the sedation score described by Culebras et al. [7] where sedation was graded on a scale of 1 to 5 as follows:
1. awake and alert
2. sedated, responding to verbal stimulus
3. sedated, responding to mild physical stimulus
4. sedated, responding to moderate or severe physical stimulus
5. Not arousable.

Monitoring
Monitoring during regional anaesthesia focuses on delayed local anaesthetic toxicity from excessive tissue absorption (usually 40 – 60 min), ventilation and oxygenation and the consequences of surgical stress such as tourniquet pain or blood loss.

Baseline vital signs pulse rate, respiratory rate, blood pressure and

saturation were recorded and monitored every 5 min till the procedure was over and after that every hour for 24 hours postoperatively. Onset, completion of the blockade, duration of the blockade was assessed as described earlier.

The pain was assessed using a numerical rating pain score scale(VAS scale)(44) where 0 represents no pain and 10 means the worst possible pain.



Possible side effects of brachial plexus block:
Incidence of drowsiness, pruritus, nausea/vomiting, Horner's syndrome, phrenic nerve palsy, pneumothorax, respiratory depression and sign and symptoms for local anaesthetic toxicity were looked for and noted if any. The above assessments were carried out by the principal investigator who was blinded to the drugs administered in the plexus block.

Management of unsuccessful block:
In the circumstance of inadequate or patchy action of the block, it would be supplemented with general anaesthesia. Patchy, failed block or prolonged surgery requiring general anaesthesia supplementation were eliminated from our study.

Statistical analysis:
Sample size:
$X = Z_{\alpha/2}^{\ 2} * p*(1-p) / (p-p_0)^2$

Z score =1.96 at 5% significance level

Using the above formula, the sample size calculated as 80 patients for the required study, 40 patients in each group. The Student's t-test used to compare intergroup differences like onset, completion, duration & intensity of blockade. The X^2 test and Fisher's exact test were used for categorical variables, comparison of more than two means did with ANOVA test. Values of P corrected by the Bonferroni method, and P values <0.05 were considered to indicate statistical significance.

Chi square value = $\sum^{(O-E)2}/E$, degree of freedom= (r-1)(c-1)
O= observed frequency E= expected frequency.

RESULTS AND ANALYSIS :
This study was a prospective randomized double-blinded study done in a total of eighty patients with ASA grade I & II of either sex aged between 18-60 years, who were posted for upper limb surgeries under brachial plexus block through the supraclavicular approach.

All the patients were selected after matching for both exclusions and inclusion criteria. The study assessed the efficacy of Midazolam as an adjuvant to 0.5% Bupivacaine along with as compared to 0.5% Bupivacaine alone for brachial plexus block by supraclavicular approach. The results were tabulated as follows :

Table 1: Comparison Of Age In Two Groups

Groups	N	Mean Duration (min)	Standard Deviation	P-Value
GroupMB	40	118	10.33	0.103
GroupB	40	115	5.12	

In our study, the mean age of Group MB was 30.70+10.46 years, and that of Group B was 35.06+11.49 years, with p-value > 0.05, which was not significant. Hence both group MB & B are comparable for study.

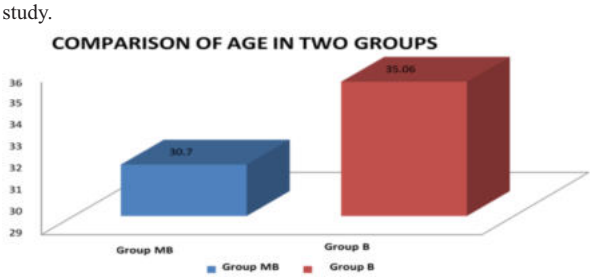


Table 2: Comparison Of Weight In Two Groups

Groups	N	Mean Weight (Kg)	Standard Deviation
Group MB	40	65.16	8.17
Group B	40	63.83	8.13

Our study shows, the mean weight of Group MB was 65.16+8.17 Kg, andthat of Group B was 63.83+8.13 Kg, with p-value > 0.05. Hence both group MB ,B are comparable for study.

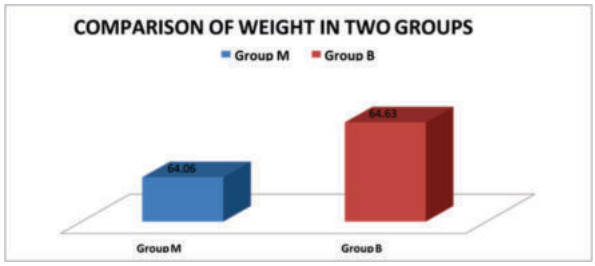


Table 3: Sex Distribution In Two Groups

Groups	Male	Percentage	Female	Percentage
Group MB	32	80	8	20
Group B	28	70	12	30

The total number of males in group MB was 32(80%), and the total number of females in group MB was 8(20%). The total number of males in group B was 28(70%), and that of females was 12(30%).

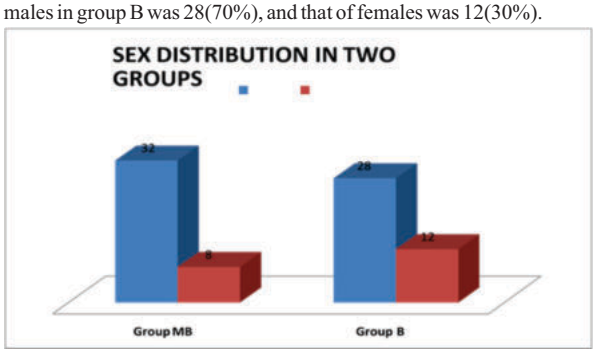


Table 4: Duration Of Surgery

Groups	N	Mean age (years)	Standard Deviation
Group MB	40	30.70	10.46
Group B	40	35.06	11.49

In our study, the mean duration of surgery for group MB was 118+10.33, and that group B was 115+5.12, with no statistically significant difference (p>0.05) between both groups.

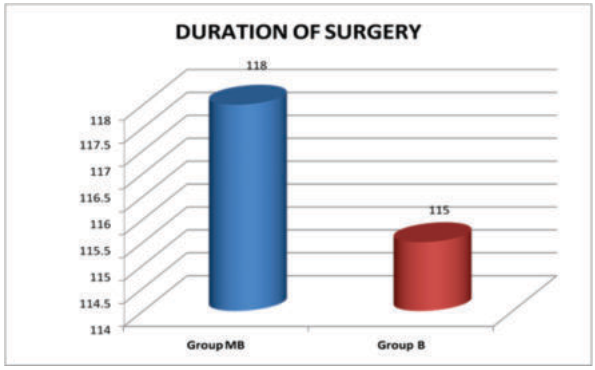


Table 5: Comparison Of Heart Rate In Two Groups

Heart Rate (Minutes)	Group MB (beats/min)	Group B (beats/min)	P-Value MB vs B
0 min	74.26±6.27	73.24±5.67	0.447
5 min	73.56±4.23	74.23±6.33	0.579
15 min	75.32±5.23	74.56±4.56	0.490
30 min	73.59±2.36	75.63±8.47	0.146
60 min	77.56±5.63	74.63±8.77	0.079
90 min	75.26±6.63	73.13±6.55	0.152
120 min	76.86±8.33	75.66±5.12	0.440

As shown in the above table, our study showed there was no statistically significant difference (p>0.05) in the heart rate between both groups measured at regular intervals from 0-120 min.

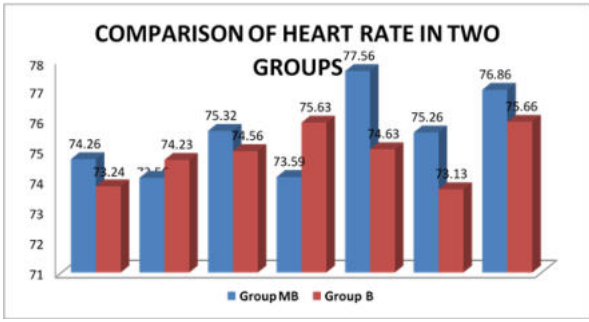


Table 6: Comparison Of Systolic Blood Pressure (mm Hg) In Two Groups

Heart Rate (Minutes)	Group MB (mm Hg)	Group B (mm Hg)	P-Value MB vs B
0 min	107.00±7.94	106.33±6.14	0.576
5 min	113.00±8.36	110.33±8.50	0.342
15 min	120.66±11.42	119.66±11.29	0.782
30 min	120.33+9.27	119.00±10.93	0.302
60 min	113.00±11.49	114.66±13.32	0.129
90 min	117.66±11.65	116.33±10.66	0.278
120 min	113.66±10.33	111.00±10.61	0.811

As shown in the above table, our study showed there was no statistically significant difference (p>0.05) in Systolic Blood Pressure between both groups measured at regular intervals from 0-120 min.

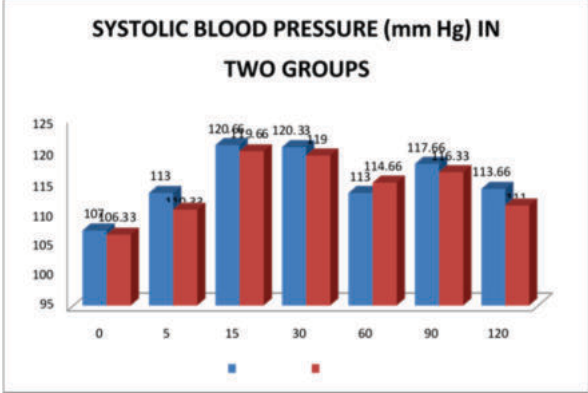


Table 7: Comparison Of Diastolic Blood Pressure (mm Hg) In Two Groups

Heart Rate (Minutes)	Group MB (mm Hg)	Group B (mm Hg)	P-Value MB vs B
0 min	74.33±5.68	73.33±4.79	0.120
5 min	77.66±5.68	75.66±5.04	0.607
15 min	77.66±7.27	78.33±5.92	0.209
30 min	80.00±6.43	79.00±7.11	0.260
60 min	77.00±6.51	75.66±9.35	1.000
90 min	77.00±6.51	75.00±5.72	0.281
120 min	75.66±7.27	76.00±8.13	0.487

As shown in the above table, our study showed there was no statistically significant difference (p>0.05) in Diastolic Blood Pressure between both groups measured at regular intervals from 0-120 min.

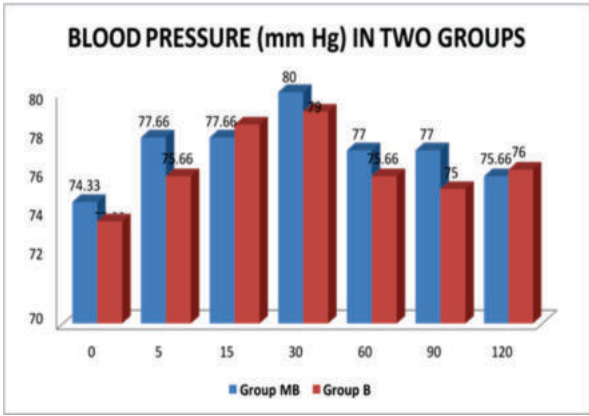


Table 8: Comparison Of Onset Fo Motor Block In Two Groups

Groups	N	Mean Duration (min)	StandardDeviation	P-Value
Group MB	40	5.13	2.36	<0.0001
Group B	40	12.87	3.12	

In our study group, MB has early onset of the motor blockade with a mean duration of 5.13 + 2.36 minutes, in comparison to group B which has the mean duration of 12.87 + 3.12 minutes which was statistically significant(p-value was <0.0001).

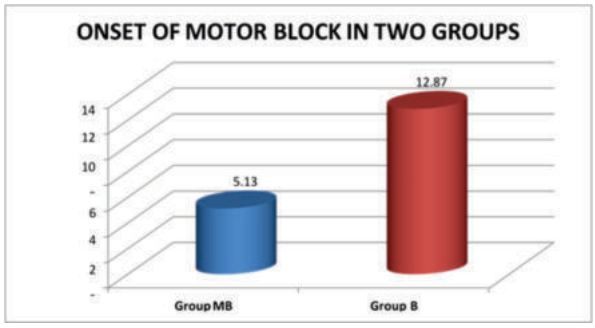


Table 9: Comparison Of Onset For Sensory Block In Two Groups

Groups	N	Mean Onset (min)	Standard Deviation	P-Value
Group MB	40	7.56	0.58	<0.0001
Group B	40	14.25	2.15	

In our study group, MB has early onset of sensory blockade, with a mean duration of 7.56 + 0.58 minute, in comparison to group B which has the mean duration of 14.25 + 2.15 minutes which was statistically significant(p-value<0.0001).

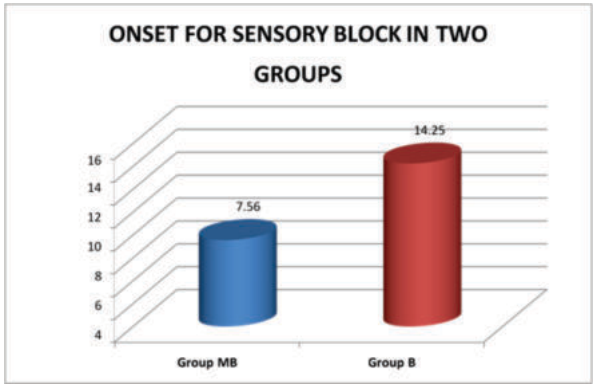


Table 10: Comparison Of Duration Of Motor Block In Two Groups

Groups	N	Mean Duration (hours)	Standard Deviation	P-Value
Group MB	40	10.62	0.34	<0.0001
Group B	40	6.40	0.72	

The duration of motor blockade was 10.62 + 0.34 hours for Group MB and 6.40 + 0.72 hours for Group B. It was prolonged in Group MB when compared with Group B, which was statistically significant. (p-value <0.01).

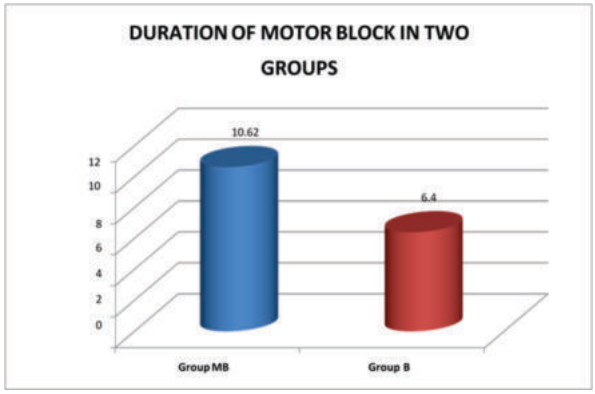


Table 11: Comparison Of Duration Of Sensory Block In Two Groups

Groups	N	Mean Duration (hours)	Standard Deviation	P-Value
GroupMB	40	11.68	1.44	<0.0001

GroupB	40	5.88	1.22	

In our study, the duration of sensory blockade for Group MB was 11.68+1.44 hours, and for Group B was 5.88 + 1.22 hours. It was prolonged in GroupMB when compared with Group B, which was statistically significant. (p-value<0.0001)

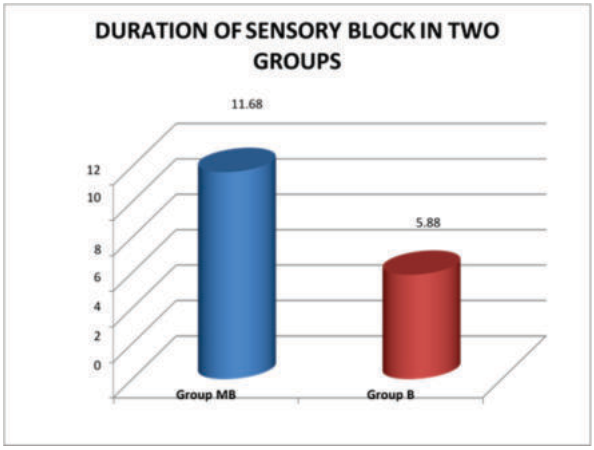
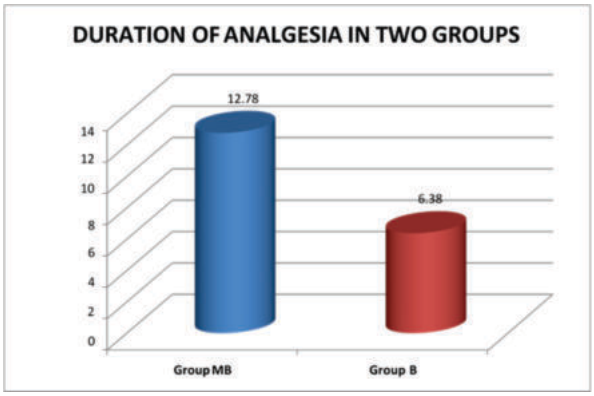


Table 12: Comparison Of Duration Of Analgesia In Two Groups

Groups	N	Mean Duration (hours)	Standard Deviation	P-Value
GroupMB	40	12.78	1.34	<0.0001
GroupB	40	6.38	0.22	

In our study, the duration of analgesia for Group MB was 12.78+ 1.34 hours, and for Group B was 6.38 + 0.22 hours. Duration of Analgesia was prolonged in Group MB when compared with Group B, which was statistically significant. (p-value <0.0001)



DISCUSSION

Regional anaesthesia has gained popularity in recent years due to its versatility over general anaesthesia in the indicated cases. It provides analgesia postoperatively apart from intra-operative anaesthesia and anaesthesia. One can avoid systemic stress response and complications of general anaesthesia with proper regional anaesthetic techniques.

Regional anaesthesia should always be considered whenever the general condition of the patient is poor, or the patient is not adequately prepared for general anaesthesia. It is also a preferred technique over general anaesthesia, as it doesn't cause stress on the cardio-respiratory system. It is also useful when the patient prefers to retain his consciousness during surgery and when the patient needs to remain ambulatory. The frequent use of pneumatic tourniquet[45] to provide a bloodless field during surgery makes individual nerve blocks impractical. Brachial plexus block[46] is the answer in such a situation.

We selected the supraclavicular approach to the brachial plexus block. It provides rapid, dense and predictable anaesthesia of the entire upper extremity in the most consistent manner. It is the most effective block for the entire the upper extremity and is carried out at the "division" level of the brachial plexus; with high volume, the "trunk" level of the plexus may also be blocked in this approach. Perhaps that is why there was often little or no sparing of peripheral nerve, if "adequate" paresthesia is obtained.

The alleviation of the suffering is, of course, a primary concern of the anesthesiologist. Any method of postoperative pain relief must meet three basic criteria. It should be effective, safe, and feasible. Currently available local anaesthetics can provide analgesia for a limited period when used as a single injection. Various methods have been tried to extend the postoperative analgesia period beyond the operating rooms, with the aim of prolonging the local anaesthetic action, like a continuous infusion of local anaesthetics via indwelling catheters, use of different additives in local anaesthetics.

In our study, Midazolam was used as an adjuvant in local anaesthetic bupivacaine. After exclusion of six patients who failed to achieve a satisfactory level of analgesia and required general anaesthesia, a total of 80 patients posted for upper limb surgeries received brachial plexus block by supraclavicular approach. The standard randomization code used, and patients were divided into group M and group MB. One group of patients received 0.5% Bupivacaine (27.5 ml) with Midazolam 2.5 mg (2.5 ml). They formed Group BM or Midazolam group. Group 'B' or Bupivacaine group received 0.5% Bupivacaine (27.5 ml) with distilled water (2.5 ml).

The principal investigator has assessed the onset and duration of the block. Parameters observed included onset time of the sensory block, onset time of the motor block, duration of motor & sensory block, duration of analgesia and side effects.

In our study, the mean age of Group MB was 30.70+10.46 years, and that of Group B was 35.06+11.49 years, with p-value > 0.05, which was not significant. The mean weight of Group MB was 65.16+8.17 Kg, and that of Group B was 63.83+8.13 Kg, with p-value > 0.05. Both groups were comparable concerning age and weight, as there was no statistically significant difference.

Changes in the perioperative hemodynamic parameters

Previous studies were done by Nasreen Laiq et al[38], Safiya I Shaikh[39], and Koj Jarbo et al[42] showed the addition of midazolam as an adjuvant to bupivacaine does not change the hemodynamic parameters, which make both the study groups were comparable.

Our study also showed that there was no statistically significant difference between the study groups concerning the pattern of changes in heart rate, systolic blood pressure, and diastolic blood pressure peri-operatively.

Onset time of Sensory and Motor block

In our study group, MB(Midazolam) had early onset of the motor blockade with a mean duration of 5.13 + 2.36 minutes, in comparison to group B which had the mean duration of 12.87 + 3.12 minutes which was statistically significant (p-value was <0.0001). So also true for the onset of the sensory blockade. MB(Midazolam) had early onset of sensory blockade, with a mean duration of 7.56 + 0.58 minute, in comparison to group B which had the mean duration of 14.25 + 2.15 minutes which was statistically significant (p-value <0.0001).

In the study conducted Safiya, I Shaikh et al[39] and Koj Jarbo et al[42] found that the onset of sensory and motor blocks was significantly faster in patients who received a combination of midazolam and bupivacaine. Our study also showed that the onset of sensory and motor blockade was significantly faster those who received midazolam as an adjuvant in comparison to those who receive bupivacaine alone.

Duration of Sensory block and Motor block

The duration of Motor blockade was prolonged in Group MB(10.62 + 0.34 hour) when compared with Group B(6.40 + 0.72 hours), which was statistically significant.(p-value <0.01). It was also true for sensory blockade with the duration of sensory blockade for Group MB was 11.68+ 1.44 hours and for Group B was 5.88 + 1.22 hours, which was statistically significant. (p-value <0.0001)

The study conducted by Nasreen Laiq et al. [38], Safiya I Shaikh,Veena.K[39] Bhattacharyya D et al [41] concluded that the duration of Motor and Sensory blockade was prolonged when Midazolam added to Bupivacaine compared when Bupivacaine used alone. Our study also showed similar results in comparison to previous studies.

Duration of Analgesia

The mean time from onset of the block to the request of rescue analgesia was taken as the total duration of analgesia. In our study, the duration of analgesia for Group MB was 12.78+ 1.34 hours, and for Group B was 6.38 + 0.22 hours. Duration of Analgesia was prolonged in Group MB when compared with Group B, which was statistically

significant. (p-value <0.0001)

Previous studies were done by Safiya I Shaikh, Veena K [39], and Gulec et al. [43], showed adding Midazolam as an adjuvant to Bupivacaine prolonged the postoperative analgesia in comparison to Bupivacaine alone. Our study results also go with the studies mentioned above.

SUMMARY

This was a randomized, double-blinded, prospective study conducted at Department of Anaesthesiology, Konaseema institute of medical sciences and research foundation, Amalapuram from June2017 to June 2019, with the objective to compare the effect between Bupivacaine (0.5%) with Midazolam & Bupivacaine (0.5%) alone used for supraclavicular approach to brachial plexus block. A total of eighty patients with age of 18-60yrs and ASA grade I & II of either sex which underwent brachial plexus block through supraclavicular approach for upper limbs have participated.

Patients were divided into two groups of 40 each. (Group MB and Group B). Group MB received supraclavicular brachial plexus block with 27.5 ml of 0.5% bupivacaine with 2.5 ml Midazolam. Group B received 27.5 ml of 0.5% bupivacaine with 2.5 ml distilled water. Parameters observed included onset time of the sensory block, onset time of the motor block, duration of sensory block, duration of motor block and duration of analgesia, side effects.

Under all asepsis, all the patients were administered supraclavicular brachial plexus block. All necessary equipment and drugs needed for the administration of general anaesthesia were kept ready to manage the failure of the block.

The patients in our study groups did not vary much concerning Age, Sex and weight. The type of surgeries performed was almost identical in both the groups and the difference in the duration of surgeries also not statistically significant that made both groups were comparable with each other.

There was no significant difference between the study groups concerning the pattern of changes in heart rate, systolic, and diastolic blood pressure peri-operatively.

In our study, Group MB(Midazolam) had early onset of the motor blockade with a mean duration of 5.13 + 2.36 minutes, in comparison to group B which had the mean duration of 12.87 + 3.12 minutes which was statistically significant (p-value was <0.0001). It was also true for the onset of the sensory blockade. MB(Midazolam) had early onset of sensory blockade, with a mean duration of 7.56 + 0.58 minute, in comparison to group B which had the mean duration of 14.25 + 2.15 minutes which was statistically significant(p-value <0.0001).

Motor blockade duration was prolonged in Group MB(10.62 + 0.34 hour) when compared with Group B(6.40 + 0.72 hours), which was statistically significant.(p-value <0.01). It was also true for sensory blockade with the duration of sensory blockade for Group MB was 11.68+ 1.44 hours and for Group B was 5.88 + 1.22 hours, which was statistically significant. (p-value <0.0001).

Our study also showed less need of postoperative analgesia in the patients who received Midazolam along with Bupivacaine (12.78+ 1.34 hrs) in comparison to those who received Bupivacaine alone(6.38 + 0.22 hrs), which was statistically significant (p-value <0.0001).

From our study, we could establish that the addition of Midazolam to 0.5% Bupivacaine for supraclavicular brachial plexus block resulted in the early onset of sensory and motor blockade and prolonged duration of postoperative analgesia. Our study also showed stable hemodynamics, and there were no side effects with doses used in our study.

CONCLUSION

Based on our study, we conclude that at equal volumes bupivacaine 0.5% with Midazolam has an advantage over Bupivacaine 0.5% alone for supraclavicular brachial plexus block in terms of

- Early-onset of sensory & motor blockade.
- Prolonged duration of sensory & motor blockade.
- Prolonged duration of postoperative analgesia.

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