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DOES ADDITION OF MIDAZOLAM TO BUPIVACAINE PROLONG THE ANALGESIC CHARACTERISTICS OF BRACHIAL PLEXUS BLOCK ?

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ABSTRACT

To evaluate the effect of adding midazolam to bupivacaine to prolong the analgesia characteristics of brachial plexus block. After pre- anaesthetic assessment all the patients were premedicated with diazepam 0.1mg/kg orally one hour before the surgery. Patients were randomly divided into group1 & 2. Group -1 patients received supraclavicular brachial plexus block with 30ml of 0.5% bupivacaine & group -2 patients received a mixture of 30ml of 0.5% bupivacaine & midazolam 50µg/kg body weight. On arrival in the operating room, standard base line vital signs readings were recorded. Intra –operatively HR, BP, oxygen saturation & sedation, time of establishment of sensory & motor block were recorded in all patients. Post-operatively HR, BP, sensory & motor block, pain score & sedation score, time of requirement of rescue analgesia were assessed at 0,30min,2hr,6hrs,12 hrs & 24 hrs in all patients. Demographic variables were comparable. There was no significant difference in monitoring of intra-operative & post-operative Vital signs (HR, SBP, DBP, MAP & oxygen saturation). Post–operative sedation score, pain score, requirement of rescue analgesia, sensory & motor block were significantly less in group-2 (p –value-<0.05). Conclusion-addition of midazolam to bupivacaine in brachial plexus block produces early onset of sensory and motor block, increased sedation score intraoperatively & prolongs postoperative analgesia.

KEYWORDS- BRACHIALPLEXUS, SENSORY BLOCK, MOTOR BLOCK, SEDATION SCORE, PAIN SCORE, RESCUE ANALGESIA

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INTRODUCTION

Brachial plexus block is a useful alternative to general anaesthesia for upper limb surgeries. It provides ideal operating condition; complete relaxation of muscles of upper extremities, intra-operative haemodynamics are not altered significantly, sympathetic block of blood vessels which lessens post-operative vasospasms, pain and postoperative period free from nausea, vomiting, cerebral depression .[1] A large number of local anaesthetics have been used for brachial plexus block. Bupivacaine is one of the most frequently used local anaesthetics for brachial plexus block by virtue of its long duration of action. Studies have shown that the duration of analgesia produced by bupivacaine when injected into brachial plexus sheath varies from 3 hrs to 15 hrs.[1] Several studies have been done to find a suitable adjunct to local anaesthetics to improve and prolong the analgesia produced by local anaesthetics. Opioids, Clonidine, neostigmine, hyaluronidase, bicarbonate, etc have been tried as adjuncts. The results have been inconclusive. Hence, the search for the suitable agents to be used along with local anaesthetics to potentiate their action is still going on. Midazolam (preservative free), a water-soluble benzodiazepine, when administered centroneuraxially has been shown to produce segmental anti-nociception and the midazolam induced analgesia has been found to enhance the effects of local anaesthetics given in combination epidurally or intrathecally without any adverse effects. Midazolam produces this additive effect on local anaesthetics by its action on the benzodiazepine - $GABA_A$ receptor complexes present in the spinal cord.[2-5] $GABA_A$ receptors have been demonstrated in peripheral nerves and it has been shown that the activation of peripheral $GABA_A$ receptors decreases the transmission of nociceptive signals and this results in local analgesic effect. However, the effect of adding midazolam to local anaesthetic solution on analgesia characteristics in peripheral nerve blocks has not been sufficiently studied. This study aims to evaluate the effect of midazolam on analgesia characteristics produced by bupivacaine 0.5% in brachial plexus block .

METHODOLOGY

After obtaining the permission from Institutional Ethical Committee and informed consent from 40 ASA I and II adult patients undergoing upper limb surgeries this prospective, randomized study was conducted to evaluate the effect of adding Midazolam 50μg/kg to Bupivacaine to prolong the analgesia characteristics of Brachial Plexus Block. All patients were kept nil per oral after midnight & on the day of operation. All the patients were premedicated with diazepam 0.1 mg/kg orally 1 hr. before the surgery. Patients were randomly divided into two groups by closed envelope technique. Patients in group 1 (n=20) were given supraclavicular brachial plexus block with 30 ml of 0.5% Bupivacaine. Patients in group II (n=20)were given supraclavicular brachial plexus block with a mixture of 30ml of 0.5% Bupivacaine and Midazolam 50μg/kg. On arrival in the operating room, standard monitoring of vital signs (H.R., ECG, NIBP, SpO_2) was instituted and baseline readings were recorded. The patients received oxygen by ventimask (4L/min) throughout the procedure and all patients were monitored Intraoperatively for heart rate, blood pressure, electrocardiography, pulse oximetry and sedation every 5 minutes. The assessment for sensory and motor block was done every minute from the time of injection of the drug(s) until the blocks were established.Sensory block was evaluated by temperature test using spirit-soaked swab. Onset time of sensory block was defined as the time between injection of drug(s) and complete loss of cold perception in C_4 and C_5 dermatomes. Motor block was assessed by asking the patient to elevate the arm. It was graded as:(Complete : If patient was unable to elevate his arm against gravity,partial: If motor force was diminished but not totally absent, Failed: If motor force

was conserved. Onset time of motor block was defined as the time between injection of drugs(s) and complete or partial motor block. Sedation was assessed using sedation score as(1.If the patient was awake and alert 2.If the patient was sedated, responding to verbal stimulus 3. If the patient was sedated responding to mild physical stimulus. 4 If the patient was sedated, responding to moderate or severe physical stimulus.5 If the patient was not arousable). Postoperative monitoring included heart rate, blood pressure, sensory and motor block, pain score and sedation score. All the parameters were assessed at 0, 30 min, 2 hr, 6 hr, 12 hr, & 24 hrs postoperatively. Duration of sensory block was defined as the time elapsed between the time of injecting the drug(s) and appearance of pain requiring analgesia. Duration of motor block was defined as the time elapsed between the time of injecting the drug(s) and the complete return of motor power. Pain was assessed using NRS-101 pain score scale, wherein zero (0) means "no pain" and one hundred (100) means, "pain as bad as it could get". Patients were asked to indicate on line the number that best describes his/her pain. Fentanyl 2 µg/kg I.V. was given as rescue analgesic when the NRS-101 pain score is > 40. The comparison between the two groups with respect to demographic variables , Intraoperative H.R., B.P. & SpO_2 ., the onset, quality and duration of sensory and motor blocks were compared between two groups using unpaired t-test. Sedation score and Pain score were analyzed by Mann-Whitney 'U' test. Rescue analgesics required was compared by Chi-square test. P value <0.05 was considered significant.

RESULTS

A total 40 cases were included in the study & divided into Group-1 & Group-2.Table -1 shows the demographic data & average duration of surgery in both group were no significant difference. Intraoperative monitoring of HR, Mean arterial pressure & Post operative monitoring of HR & MAP shown in graph 1-4 respectively. Intraoperative sedation score remain unchanged in group-1. But in Group -2, 7 (35%) patients were sedation score of three. Mean sedation score in Group -2 is higher compared to Group-1.(p--<0.05). Post-operative period sedation score was one in all patients till 24hrs after surgery in Group-1. But in group -2 in 1 (5%) patients it was 2 at 2hrs,6 hrs & 24 hrs respectively (p value--<0.05). post-operative pain score was shown in table -2. Requirement of Fentanyl as a rescue analgesic is shown in table-3. Onset time of sensory & motor block & its duration is shown in table -4.

Table1
Demographic Data (Mean ± SD)

	Group I (Bupivacaine) n=20	Group II (Bupivacaine -midazolam) n=20
Age (years)	33.2±9.288	33.65±9.34
Weight (kg)	60.00+5.3	58.U5.2
M/F	15/5	13/7
Duration of Surgery (min)	92.8±27.815	88.58+25.840

p> 0.05.

Figure 1

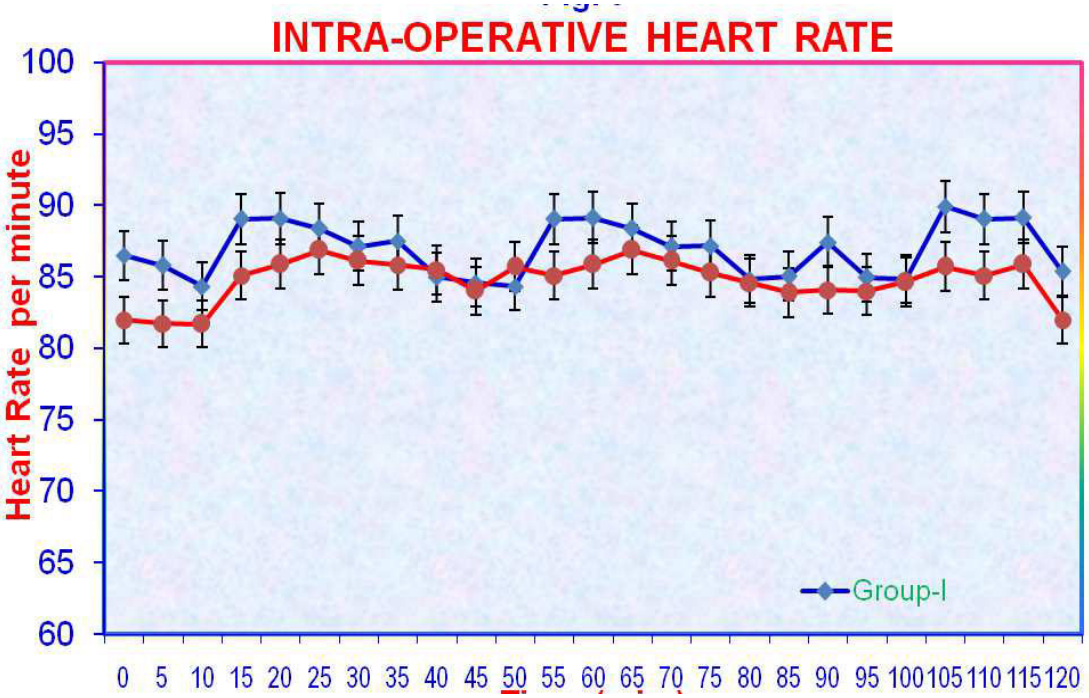

Fig. 2

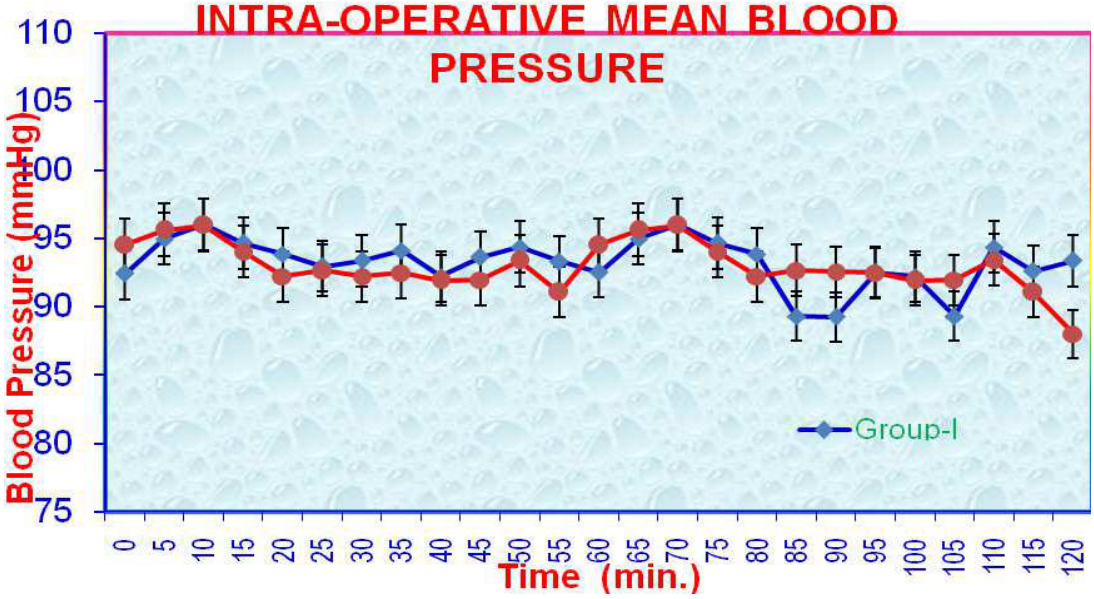

Figure 3

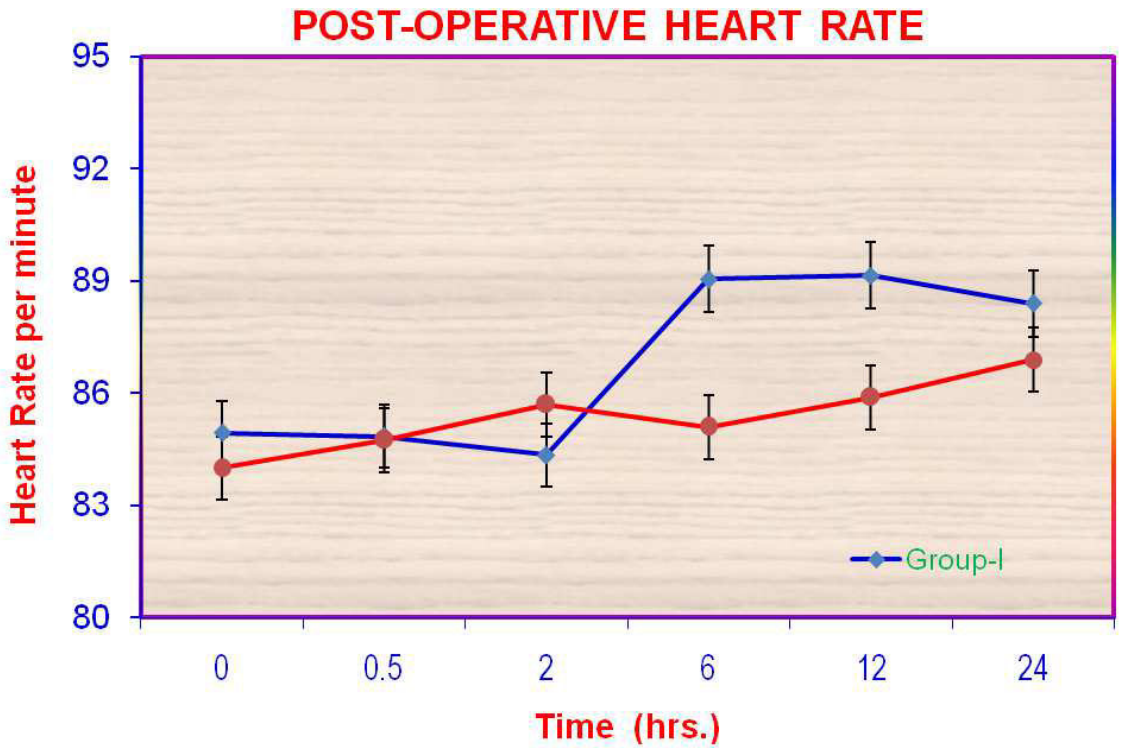

Figure 4

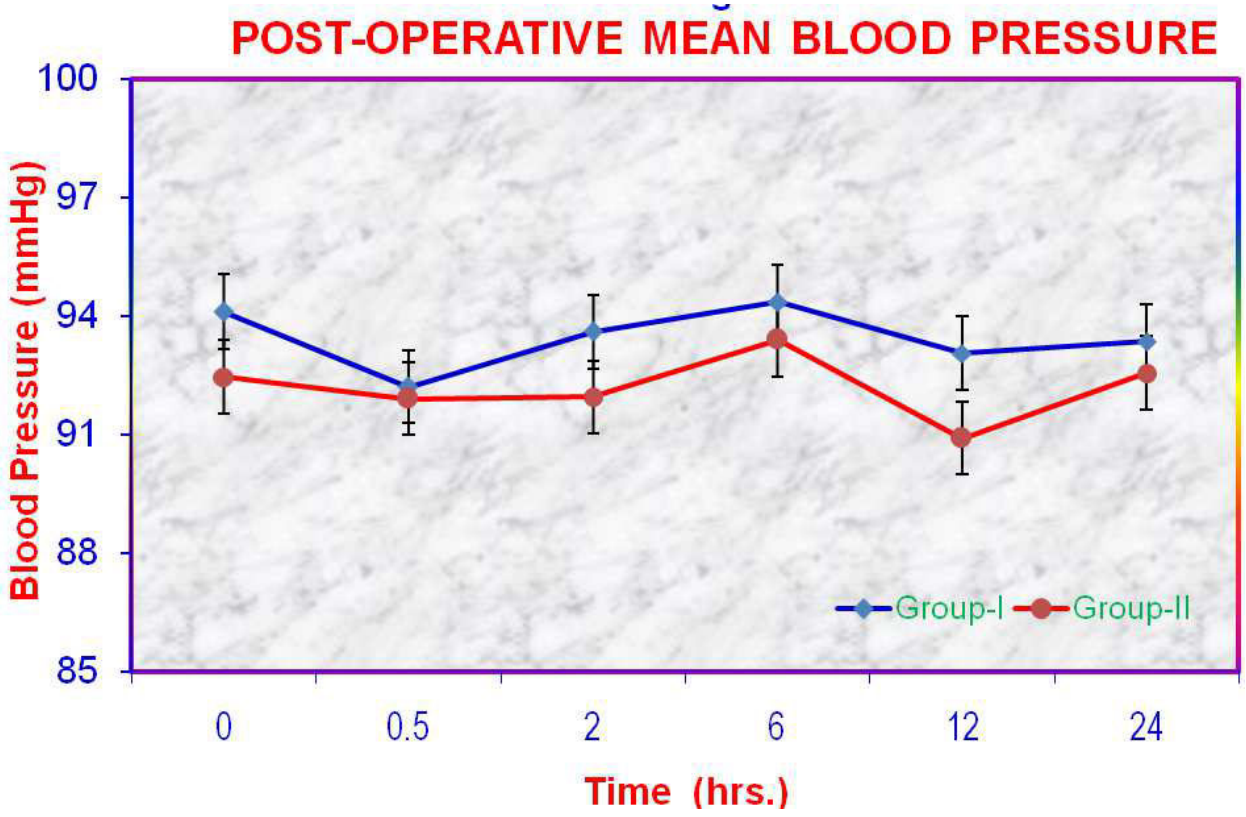

Table 2
Post –operative pain score

Time (hrs)	Group-1 (N=20)	Mean pain score	Group-2 (N=20)	Mean pain score	p-value
2	13(65%)	21.5±18.24	2(10%)	10±3	<0.05
6	19(95%)	53±25.32	9(45%)	12±15.03	
12	20(100%)	69.5±12.44	19(95%)	23.5±13.51	
24	20(100%)	66±15.62	19(95%)	25.5±12.03	

One patients did not experience any pain for 24 hrs post operative period.

Table 3
Rescue analgesia requirement

Time (hrs)	Group-1(N=20)	Group-2(N=20)	P-value
0	Nil	Nil	<0.05
0.5	Nil	Nil	
2	4(20%)	Nil	
6	14(70%)	2(10%)	
12	20(100%)	3(15%)	
24	20 (100%)	3(15%)	
Mean dose	2.9±0.718	0.994±0.4	

Table-04
Onset & duration of sensory & motor block

Parameters	Group-1 (N=20)	Group-2(N=20)	p-value
Sensory block			
Onset time (min)	20±3.8	12±2.9	<0.05
Duration (hrs)	5.95±1.4	7±4.32	
Motor block			
Onset time (min)	17.1±3.83	9.2 ± 2.38	
Duration(hrs)	5.1±1.14	5.65 ± 3.32	

DISCUSSION

Brachial plexus block is a good alternative to general anaesthesia for upper extremity surgeries. It provides anaesthesia of the upper limb and a good surgical condition without the attendant complications associated with general anaesthesia. supraclavicular approach produces most complete block of all the branches of brachial plexus and hence is suitable for arm, forearm and hand surgeries. Complications are pneumothorax (0.5-6%), phrenic nerve block (40-60%), Horner's syndrome and neuropathy [6]. It also provides variable postoperative analgesia, depending on the local anaesthetic used for the blockade. But, even with long-acting local anaesthetic like bupivacaine, the duration of postoperative analgesia is often inadequate. The intraoperative and postoperative MAP, HR, SpO_2 remained stable and did not change significantly in both the groups because bupivacaine at this dose when used for brachial plexus block and midazolam 50 µ/kg used for centroneuraxial blocks don't produce any significant alterations in the respiratory and cardiovascular system. Lund et al[1] reviewed number of series on different types or

conduction anaesthesia. They found that bupivacaine 0.25% or 0.5% solution at a dose of 10 to 30 ml does not produce any significant changes in the haemodynamic parameters. Gulec et al[7], Nishiyama et al[3,8,9],Batra et al[10] and Mahajan et al[11] showed that the addition of midazolam to bupivacaine when administered caudally or intrathecally does not alter blood pressure, heart rate or oxygen saturation significantly. Pain score was significantly higher in group I as compared to group II. The number of patients who required rescue analgesic and the number of supplemental analgesic doses that each patient required was significantly higher in group I as compared to group II. This, again, probably could be attributed to the action of midazolam on $GABA_A$ receptors located in the brachial plexus and thus producing antinociception[2,12-16,]. Gulec et al [7] found that midazolam 50 µg/kg body weight when added to bupivacaine produces a significantly longer postoperative analgesia than a bupivacaine-morphine mixture and bupivacaine alone. Nishiyama et al[8] observed that adding midazolam to a continuous epidural infusion of bupivacaine provides better analgesia. Mohamed Naquib et al[17] showed that caudal midazolam in a dose of 50 µg/kg provides equivalent analgesia to bupivacaine 0.25%, when administered postoperatively in a volume of 1 ml/kg for children following unilateral inguinal herniotomy. In a study by Batra et al[10], a significantly higher VAS score was seen in patients receiving bupivacaine alone as compared to those who received both midazolam and bupivacaine intrathecally. Rescue analgesic requirement was significantly higher in patients who received bupivacaine alone. Mahajan et al[11] compared caudal anaesthesia with 0.25% bupivacaine 0.5 ml/kg and 0.25% bupivacaine with midazolam 50 µg/kg. Lowest pain scores were observed with the addition of midazolam to caudal bupivacaine. Duration of analgesia was longer and fewer patients required additional analgesia in those who received both bupivacaine and midazolam.

Sedation score was significantly higher in group II from 15 min after Injection of drugs till 30 min postoperatively as compared to group I. This could be explained by the vascular uptake of part of the drug (midazolam) from the site of injection and transport to central nervous system where it acts and causes sedation. Nishiyama[3,8,9] showed that, in addition to increasing duration of analgesia, midazolam increases sedation score when combined with bupivacaine for epidural anaesthesia. The results of our study are similar to the observations made by Winnie et al[18] in which the onset of motor block occurred earlier than sensory block. Our study results showed that the sensory block tended to last longer as compared to motor block, which agrees with the prediction made by DeJong[19]. But the difference in duration of blocks was not statistically significant. Both the sensory and motor block occurred earlier in group II as compared to group I. This could be attributed to the local anaesthetic property of midazolam and its enhancement of action of the local anaesthetic (bupivacaine). The duration of sensory and motor block did not differ significantly between the groups.

CONCLUSION

To summaries addition of Midazolam to Bupivacaine in Brachial plexus block produces early onset of sensory and motor block, increased sedation score intraoperatively and prolongs postoperative analgesia.

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