ORIGINAL ARTICLE

Midazolam as an adjuvant in supraclavicular brachial plexus block

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ABSTRACT

Background & Aims: Brachial plexus block is a useful alternative to general anaesthesia. Postoperative analgesia is an added advantage. Midazolam, a water soluble benzodiazepine has been used by various routes to prolong analgesia. The present study was undertaken to assess the analgesic efficacy of midazolam with bupivacaine in brachial plexus block.

Methods: A prospective, randomized, double blind study was done 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 and scheduled for various upper limb surgeries. Patients were divided into two groups of 25 each. Group B received 30ml of inj. bupivacaine 0.5% +2ml normal saline and group BM received 30ml 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.

Results: Post operative 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. 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. 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 min. Hence there was not statistically significant difference Mild respiratory depression and sedation occurred intraoperatively in group BM which required no active intervention.

Conclusion: 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.

Key words: Bupivacaine; Midazolam; Supraclavicular brachial plexus block; Postoperative analgesia.

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INTRODUCTION

Brachial plexus block is a useful alternative to general anesthesia for upper limb surgeries providing complete muscle relaxation, stable intraoperative hemodynamics and smooth transition to postoperative pain relief.[1] Hence the need of the hour today for postoperative analgesia is the one which requires minimum technical intervention and expertise, gives good quality of analgesia, requires easily available drugs and equipments, cost effective, and has least side effects thereby has good patient and surgeon acceptance.

Midazolam, a water soluble, short acting benzodiazepine, produces analgesia by acting on gamma –amino butyric acid receptors (GABA). Extrasynaptic receptors for GABA are present on myelinated axons of peripheral nerves. Midazolam used with local anesthetics (LA) through various routes in many studies has been shown to prolong post-operative analgesia. An earlier study was

done by Koj Jarbo et al.[1] With this in mind, we conducted a study to evaluate the effects of adding midazolam to bupivacaine in brachial plexus block.

METHODOLOGY

After approval by the hospital ethical committee, a prospective, double blind, randomized study was carried out in KIMS (Karnataka Institute of Medical Sciences) Hubli (India), from 01 March 2008 to 01 March 2009. Fifty adult patients of either sex, aged 18-60 years, ASA physical status 1 and 2 and scheduled for various upper limb surgeries were recruited for the study. We checked praevious year(i.e year 2007) hospital statistics. Considering 95% confidence interval and 9% allowable error and prevalence of 13%, worked out sample size was 54, hence we decided for a sample size to be 50. Patients having known allergy to test drugs, ASA grade 3 and 4 patients, patients on drugs that might have modified the pain perception, patients who refused to be enrolled in the study, patients with a history of substance abuse, coagulopathies, contralateral phrenic nerve or recurrent laryngeal nerve palsy, contralateral pneumothorax or infection at the site of injection were excluded from the study.

All enrolled patients were assessed by preanaesthetic examination. Informed consent was taken. Patients were premedicated with tab. diazepam 5mg orally 1 hour before surgery. Emergency drugs and equipments including facilities for GA were kept ready. Brachial plexus block was performed by supraclavicular approach. Double blind randomization was done. The trial was so planned that neither the doctors (investigator) nor the participants (patients) were aware of the group allocation and drug received. The study drugs were prepared by an anesthesiologist not involved in performing the block, patient care or in data collection.

Patient was made to lay supine with head turned to opposite side with ipsilateral arm adducted. After aseptic preparation, midpoint of clavicle and interscalene groove was identified. At a point 1-1.5 cm posterior to midpoint of the clavicle, skin wheal was raised with local aneasthetic. A 22 gauge 4 cm short beveled needle was passed through the same point in a caudad, slightly medial and posterior direction until paresthesia was elicited. After negative aspiration for blood study medication was inj. ected.

Patients in group B received inj. bupivacaine 0.5% 30 ml + NS 2ml, patients in group BM received inj. bupivacaine 0.5% 30ml + inj. midazolam (preservative free) 0.05mg/kg. Heart rate, blood pressure and respiratory rate were recorded pre operatively, intra op every 10min upto the end of surgery and post operatively at 2h, 6h, 12h and 24 hrs. Onset of sensory block-time elapsed between injection of drug and complete loss of cold perception was tested by spirit soaked cotton on skin dermatomes C4-T2. Onset of motor block- time elapsed between injection of drug to complete motor block was tested by adduction of shoulder and flexion of forearm and hand against gravity. Sedation was assessed using sedation score described by Culebras et al.[2] (Awake and alert -1; Sedated and responding to verbal command-2; Sedated responding to mild stimulus-3; Sedated & responding to moderate to severe physical stimulus-4; Not arousable-5). Duration of sensory block-time elapsed between injection of drugs to appearance of pain requiring rescue analgesia. Duration of motor block-time elapsed between injection of drug to complete return of motor power. Pain was assessed by an anaesthesiologist performing the block, who was unaware of the study medications injected. Pain was assessed by numerical rating pain scale where zero represents no pain and 10 means worst possible pain. Duration of pain relief was taken from time of onset of sensory block to time of administration of rescue analgesic. Rescue analgesic was administered when pain score was 4 and above. Inj. diclofenac 75 mg IM was the rescue analgesic. At the end of 24 hours, anaesthesiologist who loaded the drugs revealed the contents of study medications and hence the group to which patient belonged could be notified.

Interval data are expressed as mean and standard deviation. Student's 't' test was used to compare the two groups. Chi square test was used for analysis of nonparametric data. A p value of < 0.05 was considered statistically significant.

RESULTS

Mean age was 34.40 yrs with a range of 18-60 years. Mean weight of group B and group BM patients was 58.4 ± 6.07 and 59.3 ± 6.79 kg respectively and was comparable between two groups. Duration of surgery was 65.6 ± 16.84 min and 67 ± 14.43 min in group B and group BM respectively and was comparable between two groups.

Table 1: Demographic data of the patients

Parameter	Group B	Group BM	P value
Mean age (years)	32.52±12.69	33.28±10.91	>0.05
Mean weight (kgs)	58.4±6.07	59.3±6.79	>0.05
Male:Female			

P value < 0.05- Statistically significant

P value < 0.001- Statistically highly significant

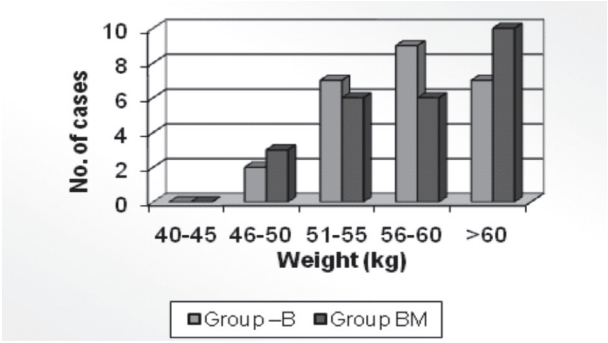

Figure I: Weight distribution of the patients

Table 2: Comparison of main outcomes in two groups

Outcome	Group B	Group BM	P value
Mean duration of surgery (min)	65.6±16.84	67±14.43	>0.05
Mean onset of sensory block (min)	8.36±3.58	8.52±4.18	>0.05
Mean onset of motor block (min)	9.96±5.69	7.92±5.68	>0.05
Mean duration of motor block (min)	450.48±57.95	608.96±157.75	<0.001
Duration of pain relief (min)	502.24±52.68	805.04±175.75	<0.001
Sedation score	One	Three	>0.05
Numerical rating pain scale score at 12 hours	4.36	1.44	<0.001

P value < 0.05- Statistically significant

P value < 0.001- Statistically highly significant

The mean onset of sensory block in two groups was equivalent with statistically no significant difference (p > 0.05) (8.36 ± 3.58 min vs. 8.52 ± 4.18 min). The mean onset of motor block was faster in group BM (7.92 ± 5.68 min) as compared to group B (7.96 ± 5.69 min) but it was not statistically significant (p > 0.05). Mean duration of motor block in group BM patients was significantly longer (608.96 ± 157.75 min) compared to patients in group B (450.48 ± 57.95 min).

There was a statistically significant decrease in the respiratory rate from base line in group BM from 10min to 30min after injection (P < 0.001). During remaining time respiration remained normal between two groups and was comparable.

Table 3 : Respiratory rate (per min)

Time (min)	Group B Mean ±SD	Group BM` Mean ±SD	't' value	'p' value
Baseline	14.8 ± 1.5	14.6 ±0.92	0.57	>0.05
5	14.8 ±1.5	14.6 ±1.22	0.51	>0.05
10	10.8 ±1.47	13.2 ±1.0	4.57	<0.001
20	15.1 ±1.83	12.4 ±0.76	6.75	<0.001
30	14.8 ±1.41	13.0 ±1.02	5.14	<0.001
60	14.0 ±2.2	14.0 ±0	0	>0.05
120	13.9 ±1.42	14.0 ±1.32	0.263	>0.05
360	13.9 ±1.44	14.1 ±0.40	0.66	>0.05
720	13.9 ±1.42	14.1 ±0.40	0.66	>0.05
1440	14.8 ±1.49	13.1 ±0.40	0.33	>0.05

Patients in group BM had significantly high sedation score (2.2 ± 0.5) than patients in group B.

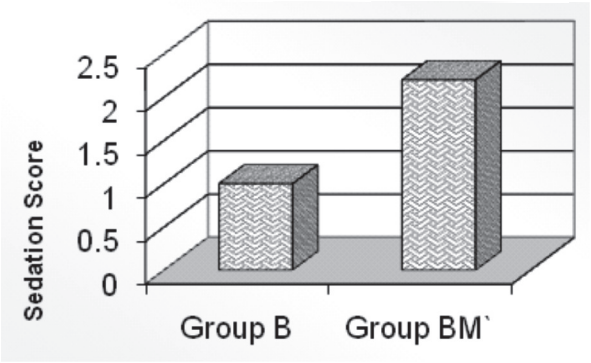

Figure II: Comparison of sedation score

Duration of pain relief in group BM was significantly longer than in group B (805.04 ± 175.75min vs. 502.24 ± 52.68min). Time to analgesia was more in group BM than in group B. In immediate post operative period and at two hours the pain score was zero in both groups and was comparable. Patients in group BM had significantly less pain scores at 6hr, 12hr and 24hrs compared to patients in group B.

Table 4: Numerical Rating Pain Scale Scores

Time	Group B	Group BM	p value
6hr	4.12	0.24	<0.001
12hr	4.36	1.44	
24hr	2.84	1.56	

DISCUSSION

Pain is an inevitable consequence of surgery. Opioids and nonsteroidal anti inflammatory drugs (NSAIDs) singly or in combination provide good analgesia but cause various side effects. Most surgeries on forearm and hand are intermediate and minor surgeries and have relatively short duration of severe postoperative pain.[2] Supraclavicular approach is attractive due to its effectiveness, cost, performance, margin of safety.[3] It is carried out at the level of nerve trunks where it is more compact, resulting in homogeneous spread of anaesthetic throughout the plexus with a fast onset and complete block.[4] Of various local anaesthetics used for brachial plexus block bupivacaine[5] is a reliable, versatile, long acting local anaesthetic, when used in correct dosage for caudal, spinal, epidural and peripheral nerve blocks. Various adjuncts like midazolam,[1] tramadol,[6,7] clonidine,[8] buprenorphine,[9] morphine,[10] pethidine,[11] fentanyl, sufentanyl have been shown to prolong post operative analgesia. Addition of hyaluronidase[12] has produced significant decrease in duration of anaesthesia. Midazolam, a water soluble, short acting benzodiazepine, produces analgesia by acting on gamma amino butyric acid (GABA) receptors.[13] Extrasynaptic receptors for GABA are present on myelinated axons of peripheral nerves.[14,15] Midazolam used with local anaesthetic in intrathecal,[16] caudal[17] and epidural[18] routes in various studies has shown to prolong post operative analgesia.

Pain remains undertreated in developing countries.[19] Acute pain of surgery if poorly managed leads to various hemodynamic respiratory and autonomic changes that disturb the physiological homeostasis of various organ systems.[20] Development of chronic pain and psychological trauma are the long term squeals of acute post-op pain. Since long, physicians have tried to alleviate pain in patients by various drugs and techniques, each having its own advantages and disadvantages.

Brachial plexus block provides intense analgesia, motor blockade without significant hemodynamic changes, airway manipulation and polypharmacy. Bupivacaine is the most commonly used long acting LA that is safe, effective and versatile if used in proper doses.[5] Midazolam is a water soluble, short acting BZD that has a PH dependent ring opening phenomenon. The ring remains open at pH < 4 making it highly water soluble approximately 5 mg/ml,21 the ring closes at pH > 4 making it more lipid soluble at physiological pH.

My Most Unforgettable Experience

Being a senior consultant anesthesiologist did not offer him any immunity to coronary blocks, rather it proved to be a major contributor towards epigastric discomfort coupled with scapular and interscapular pain, which suddenly developed one fateful evening. Knowing fully well, the emergency handling routines of his own hospital as well as some other neighboring hospitals, he suffered in silence for hours, till sleep overwhelmed and peace engulfed him. The next morning all was well, except the pricking memory of the pain and discomfort of yesterday. He took some time out of busy OR schedule and went to emergency for an ECG. The trace was unremarkable, but he never put a glance at it. Was it really his heart, who was at fault? Not finding the cardiologist in his office, he returned to operating rooms to continue his routine anesthesia and pain management duties. An attempt to trace the desired cardiologist by phone failed again, so he visited cardiology OPD by himself. He must see the cardiologist soon. The cardiologist greeted him and escorted him for an ETT. ETT could not be completed due to long procedural rituals. He developed perspiration, epigastric discomfort and dizziness. Felt like lying down. At this point the cardiologist entered the ETT room, saw his condition and asked the attendant to escort him to CCU, which he did. The echo was normal but trop-T test suggested immediate angiography was needed. From hereafter, the time took up a lightening pace. He was shifted to a cardiac cath lab, angiography done, the blockades identified, coronary stents offered and passed in the same sitting. Shifted back to his old CCU. Observation period started only to be interrupted occasionally by staff nurse who came for automated BP and pulse check. His wife brought him some tea and snacks. A crowd of sympathetic colleagues and co-workers paid him a visit, for which he was more than grateful. The deep concern shown by them touched his heart. For him it was like being a character in a drama, a drama in real life. He was filled with satisfaction. He was in expert hands.

The bed to his right side was occupied by an old aged male with a white beard. He guessed he must had had diabetes in addition to cardiac disease, as his grandson of about 12 years of age, who accompanied him as an attendant, had to bring in a

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In a study by Koj Jorbo et al[1] midazolam added to bupivacaine in supraclavicular brachial plexus block has enhanced the onset of sensory block and motor block which was statistically significant ($p < 0.05$). In the present study, there was no statistically significant difference in onset of sensory block between the two groups. The onset of motor block was earlier in Group BM but it was not statistically significant ($p > 0.05$). This could be due to location of motor fibers in the mantle layer and sensory fibers in the core.[4]

There were no statistically significant hemodynamic changes in both groups. This is in correlation with a study by Koj Jarbo et al.[1] In another study by Batra et al16 when midazolam was added to intrathecal bupivacaine, there were no statistically significant difference in hemodynamic or respiratory parameters between two groups.

The mean respiratory rate decreased in group BM from baseline between 10-30 min. This did not require any ventilatory assistance except for face mask oxygenation for that period. Maximum sedation seen was 3 (three), most of other patients were asleep and responding to verbal commands. All patients in group B were awake with sedation score of 1(one). There was no sedation in both groups in the postoperative period. This correlates with the study by Koj Jarbo et al.[1] Adding midazolam increased not only analgesia but also provided sedation which was an added advantage. This effect was also observed in a study by Nishiyama.T et al.[18]

Sedation and respiratory depression in group BM could be due to systemic absorption and depression of respiratory center. Transient effect may be due to rapid, high rate of clearance of midazolam (6-11 ml/kg/min).[15]

There was statistically significant prolongation of motor block in group BM than in group B. This observation is in contrast to observation by Koj Jabo et al[1] in which duration of motor block was similar in both groups.

Group BM had prolonged analgesia which was statistically significant ($P < 0.001$), this also correlates well with vatious studies.[1,16,18] Patients in group BM had significantly less pain scores than patients in group B. Only one patient required rescue analgesia in group BM. Time to administration of rescue analgesia was delayed in group BM than in group B as also observed in a study by M Naguib et al.[17] This observation also correlates with a study by koj Jarbo et al.[1] Midazolam may produce antinociception by acting on GABA receptors located on peripheral nerves.[14,15]

In the present study there was no adverse effects, either

My Most Unforgettable Experience (*Contd from page 10)*

plastic urinal every two hours or so, help him pass his water and took the urinal to some toilet outside CCU for disposal. The boy also brought lunch and dinner for his grandfather from the cafeteria and helped him with the food. The NIBP arm band and SpO_2 probe were conveniently removed by the boy to allow unrestricted feeding by the old man. All these rituals were performed free from any outside interference as the nursing staff seemed quite pleased with the routine. A middle aged lady occupied a bed in front of him. Two attendants remained at the bedside to take care of her. The melodious mobile phone ring tones filled the space of the CCU time and again, perhaps to soothe the nerves of all. Some outdoor cardiac patients narrated their long stories to the doctors at the nursing station. He slept heartily, having disturbed a day before due to compulsion to lie down still in supine position for hours.

At about 4 am in the morning, he needed to go to toilet. He rose up and put on his slippers. The lone male nurse was fast asleep cuddled up and wrapped up in white sheets by joining two easy chairs at their front side. The central monitor on the nursing station displayed coloured graphic lines continuously moving. He went to the toilet without disturbing the male nurse. He opened the door and hustled back almost fainting off the stinking smell, slamming the door shut behind him. He went to the other toilet. Left unlocked by mistake, it was meant for the staff use; was also filled with foul smell but with less ferocity. He pressed the switch to put on the exhaust fan, but it refused to obey. He forcefully spinned it and it came to life like an old turboprop aeroplane. He was so gratified to see the toilet seat broken and repaired with the sticking plaster (often called 'amrit dhara', as it is used to bond all broken things or to seal every hole in operating rooms). The drain pipe of the wash basin was broken and leaking and the door lock almost prolapsed out of its socket. Perhaps someone had forgotten to use the sticking plaster over there, or perhaps this commodity was also in short supply at there.

The night passed and the male nurse hurried to dress the things up before the medical staff arrived. He was kind enough to fetch him a cup of hot tea from the hospital cafeteria before leaving. The time ticked and he wished he was sent home as early as possible. Someone advised him to collect his discharge certificate later on and to go home. He was so happy to see that the discharge certificate bore his actual age and not the usual 110 years or 0 years.

(Quoted to Khadim Hussain)

due to drugs or the technique, except for mild respiratory depression, which was treatable with oxygen supplement via face mask and few incidences of vascular tap while performing brachial plexus block for which a transient topical pressure was applied. This can be minimized by the use of a nerve stimulator or ultrasound guided technique.

CONCLUSION

In conclusion, addition of midazolam to bupivacaine 0.5% for supraclavicular brachial plexus block prolongs sensory blockade and post-operative analgesia without increasing the risk of adverse effects.

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