Original Research Paper Anesthesiology

SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK: USING MIDAZOLAM AS AN ADJUVANT TO BUPIVACAINE: A DOUBLE BLIND RANDOMIZED TRIAL

Gopal lal Bansal Departments of Anaesthesiology, SMS Medical College, Jaipur.

Anupama Gupta Departments of Anaesthesiology, SMS Medical College, Jaipur.

ABSTRACT

Objectives: To assess and compare onset and duration of sensory and motor block, sedation score, duration of analgesia and requirement of rescue analgesia in postoperative period.

Methods: After approval from the ethical committee a prospective randomized, double blind study of 100 patients of ASA I/ II, aged 18 to 60 years, undergoing upper limb orthopaedic surgeries under PNS guided supraclavicular brachial plexus block were taken and randomly allocated into 2 groups.

Group A (n=50): Inj. Bupivacaine (0.5%) 20 ml+ Inj. Normal Saline 10 ml (Total vol.30 ml)

Group B (n=50): Inj. Bupivacaine (0.5%) 20 ml+ Inj. Midazolam (preservative free) 0.05 mg/kg in 10 ml normal saline (Total vol.30 ml).

Results: The mean onset of sensory and motor block was significantly fast (P value < 0.05) in Group BM (sensory 11.2±3.3min, motor 8.8±3.4 min) compared to Group B (sensory 16.2±4.3 min, motor13.4±4.0min). The mean duration of analgesia was significantly longer in Group BM (12.4±3.7Hrs) compared to Group A (6.4±2.2 hrs).The mean duration of motor block in Group B (5.18±2.032 Hrs) was comparable to Group BM (5.16±1.338hrs).The mean number of rescue analgesic doses required in Group BM (3.0±0.4) was significantly less than in Group B (1.88±0.6273).

Conclusion: The addition of Midazolam (0.05mg/kg) as an adjuvant to Bupivacaine has faster onset of sensory and motor block, higher sedation scores, longer duration of analgesia and less number of rescue analgesics requirement in postop-24 hours with stable haemodynamic variables.

KEYWORDS : Midazolam, Bupivacaine, Supraclavicular brachial plexus block, Nerve stimulator.

INTRODUCTION

Brachial plexus block is a useful alternative[1] to general anaesthesia for upper limb surgeries as it provides ideal operating conditions with adequate relaxation of muscles of upper limb, stable intraoperative hemodynamic[2] and postoperative period free from nausea, vomiting, cerebral depression and pain. Sympathetic blockade of blood vessels lessens postoperative vasospasm, pain and edema.[2, 3] There are many approaches to the brachial plexus block have been described plexus namely the interscalene, supraclavicular, infraclavicular and axillary approach.

The supraclavicular approach for blockade of the brachial plexus was first described by Kulenkampff [4] in 1911.It is technically easy to perform because of reliable and fixed landmark but association of pneumothorax is a profound complication.[5]With use of peripheral nerve stimulator (PNS),incidence of complications have reduced drastically.

Bupivacaine is most frequently used local anaesthetics as it has long duration of action, several adjuvant have been studied so far, including opioids, clonidine, dexmedetomidine neostigmine, hyaluronidase, bicarbonate, dexamethasone and midazolam. Addition of various adjuvant to local anaesthetics is supposed to prolong the analgesic effect without any unwanted systemic effects.

Midazolam a water soluble, short acting benzodiazepine, produces antinociception by acting on gamma –amino butyric acid receptors (GABA).[6,7] Extra synaptic receptors for GABA are present on myelinated axons of peripheral nerves. Midazolam when used with local anaesthetics is known to enhance the effect of local anaesthetic when given epidurally or intrathecally.

Hence, the present study was conducted with primary aim of assessing the onset and duration of sensori-motor blockade, duration of analgesia; when midazolam 0.05mg/kg was added to 0.5 % bupivacaine in comparison to plain bupivacaine 0.5%, in patients posted for upper limb orthopaedic surgeries under supraclavicular brachial plexus block. The secondary outcomes measured were haemodyanamic variables and adverse effects in both the group.

METHODS

After approval from institutional ethical committee, written informed consent from patients, total 100 patients of ASA physical status I and II, aged 18-60 years undergoing upper limb surgeries were taken in this prospective, randomized double blinded trial. Patient with cardiovascular, cerebrovascular, coagulation disorder, neuropathy, allergy to LA, local infection at injection site and any other chronic illness were excluded from the study.

One hundred patients were randomised using computer generated randomisation list. Group assignment was enclosed in a sealed opaque envelope; this envelope was opened by an anaesthesiologist not involved in the study who then prepared the drug solution according to randomisation. Patients were randomly assigned to one of the equal groups. Patients in Group A received 20 ml of bupivacaine 0.5% and 10 ml normal saline (total 30 ml). Patients in Group B received 20 ml of bupivacaine 0.5% along with preservative free midazolam 0.05 mg/kg for supraclavicular brachial plexus block. Normal saline was added to make total solution to 30 ml.

After shifting the patients to the operation table, all the standard monitors like NIBP, pulse oximeter, ECG were attached, and baseline parameters were recorded. Intravenous access was secured using 18G cannula. Patient was placed in supine position, arms by the side and head turned to opposite side. Inter scalene groove was be identified at its most inferior point and marked by rolling of fingers from lateral head of sternocleidomastoid muscle and midpoint of clavicle. Neural localisation was achieved using nerve stimulator technique. The stimulation frequency was set at 1 Hz, and the intensity at 1.5 mA. Then 22G insulated stimulating needle was inserted and directed in a caudal, slightly medial and posterior direction, needle was advanced until paraesthesia is felt or muscle contraction of forearm is noted. Once identified stimulation current is reduced to < 0.5 mA. On negative aspiration for blood, the local anaesthetic solution was injected in incremental 5ml boluses with intermittent aspiration.

Assessments of sensory and motor blockade were done every 2 minutes after the completion of injection till 30 minutes and then for every 30 minutes minute after the end of surgery till the effect of

block is completely worn off. Sensory block was assessed by pinprick test with a 3 point scale: 0-no block, 1-analgesia (loss of sensation to pin prick) and 2-loss of touch. Motor blockade was assessed by ability to flex the elbow and hand as: Complete - inability to elevate arm against the gravity, Partial- motor activity is diminished but not totally absent, And Failed: if motor activity conserved. Failure of block was defined as inadequate or patchy analgesia after 30 minutes of drug injection.

Onset of sensory blockade was defined as the interval between the injection and sensory blockade evidenced by loss of sensation to pin prick. Onset of motor blockade was the interval between the end of injection and complete motor paralysis of wrist and hand. Motor block was assessed by asking the patient to elevate the arm. The duration of sensory blockade was defined as the time interval between sensory blockade and reappearance of the pinprick response. The duration of motor blockade was defined as the time interval between maximum motor blockade and complete movement of wrist and fingers. Duration of analgesia was taken as the time interval between the onset of sensory blockade and the first dose of rescue analgesic given to the patient.

Postoperative monitoring including heart rate, systolic and diastolic blood pressure,SpO2 and sedation score were recorded for every 1h for 6 hrs, then every 2 h for next 6 hrs & then 4 h till the need for rescue analgesia. Postoperative pain was assessed using Visual analogue scale (0- no pain to 10-worst possible pain).Inj diclofenac sodium (75 mg) IM was given as rescue analgesic when patient complained of pain (VAS score >4).The number of rescue analgesic doses given in 24 h were recorded. Sedation was assessed using sedation score as (described by Culebras et al[8]);1 -Patient awake and alert, 2- Patient sedated, but responding to verbal command, 3 - Patient sedated, but responding to mild physical stimulus, 4- Patient sedated, but responding to moderate or severe stimulus and 5- Patient not arousable.

Statistical data analysis was done using SPSS version 17. Quantitative data were represented as mean +/- standard deviation; number and percentage were used for qualitative data. Quantitative data was analyzed by student's t-test. Qualitative data was analyzed by Chi-square test. P value <0.05 was considered as statistically significant.

RESULTS

Both groups were comparable with respect to age, sex ratio, weight, ASA physical status and duration of surgery (Table I).There was no statistical difference in baseline haemodynamic parameters.

Onset of sensory and motor blockade was significantly faster in Group BM than in Group B (P < 0.05). In Group BM, onset of sensory block occurred in 11.2 ± 3.3 min compared to 16.2 ± 4.38 min in group B. Onset time of motor block in Group BM was 8.8 ± 3.4 min compared to 13.4 ± 4.0 min in Group B. In both groups, motor block occurred earlier than sensory block (P < 0.05) but the duration of motor block was not significantly different between groups (Table II).

Postoperatively, lower pain scores were observed in Group BM compared to Group B for the 2 to 8 hr postoperative period (Table 3). All patients in both of the group required rescue analgesia but there was less no. of rescue analgesic doses required in first 24 hrs postoperative period in group BM as compare to group B. (P < 0.0001)

Sedation scores differed between the groups as patients in Group B were all awake and alert (score 1) throughout the intraoperative period, while in Group BM, sedation score 2 was observed in some patients, 10 min. from time of injection to 50 min. Statistical analysis of sedation score shows that p value between 10 min to 50 min was statistically significant. After 50 min all patients in group BM also had sedation score 1. No patient in Group BM required assistance for airway maintenance due to sedation. Sedation scores did not differ between groups in the postoperative period.

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation were comparable between groups and did not change significantly in the intraoperative or postoperative period. No adverse events were encountered in either group of patients.

Table 1: Demographic data

Variables	Group B	Group BM	P value
Age (year)	33.5 ± 11.4	35.1 ± 11.7	0.503
Gender(male/female)	42/8	39/11	
ASA (I/II)	45/5	46/4	
Weight (kg.)	59.5 ± 11.7	58.5 ± 11.0	0.669
Duration of surgery (min)	59.6 ± 14.4	59.8 ± 14.6	0.945

Table 2: Characteristics of block in each group

Parameters	Group B	Group BM	P value
Onset of sensory block (min)	16.2 ± 4.3	11.2 ± 3.3	< 0.0001
Onset of motor block (min)	13.4 ± 4.0	8.8 ± 3.4	<.0001
Duration of sensory block (hrs)	6.4 ± 2.2	12.4 ± 3.7	<0.0001
Duration of motor block (hrs)	5.18 ± 2.03	5.16 ± 1.33	0.9538
Duration of analgesia(hrs)	6.2 ±1.9	13.7 ± 3.6	< 0.0001
Number of rescue analgesic doses in 24 hrs postop	3.0 ± 0.4	1.8 ± 0.6	< 0.0001

Table 3: Postoperative pain score in two groups.

	Group B	Group BM	P value
Time	VAS (Mean±SD)	VAS (Mean±SD)	
2 hrs	0.03 ± 0.92	0	0.080
4 hrs	1.68 ± 1.64	0.14 ± 0.40	<0.0001
6 hrs	3.02 ± 2.085	0.62 ± 0.66	<0.0001
8 hrs	3.16 ± 2.37	1.5 ± 1.18	<0.0001
10 hrs	2.64 ± 1.98	2.16 ± 1.14	0.1677
12 hrs	4.04 ± 2.35	4.28 ± 2.3	0.6117
16 hrs	4 ± 2.39	3.2 ± 2.42	0.1004
20 hrs	3.9 ± 2.26	4.18 ± 2.48	0.6751
24 hrs	4.06 ± 2.32	3.38 ± 1.88	0.1112

DISCUSSION

Brachial plexus block has been used for upper limb surgeries[4] for many decades over the years, but, even with long acting[3] local anaesthetic like bupivacaine, the duration of postoperative analgesia is often inadequate. Various adjuncts have been used in conjunction with local anaesthetics to prolong the duration of analgesia.[9] Midazolam used with local anaesthetic in intrathecal[10], caudal[11] and epidural routes in various studies has shown to prolong post operative analgesia. In our prospective, randomised, double blinded study we found that the onset of sensory and motor blocks was significantly faster in patients who received a combination of midazolam and bupivacaine. This could be due to a local anaesthetic property of midazolam and its synergistic action with local anaesthetics.[10-11] our observations are consistent with Koj J et al,[12]that midazolam added to bupivacaine in supraclavicular brachial plexus block, enhanced the onset of sensory block and motor block which was statistically significant (p<0.05).

Onset of motor block was found to be faster than onset of sensory block in both groups. Winnie et al[13] observed same, it could be attributed to the somatotrophic arrangement of fibres in a nerve bundle at the level of trunk, motor fibers are located more peripherally than sensory fibers, hence a local anaesthetic injected perineurally will reach early at motor fibers in comparison to centrally located sensory fibers.

In our study, we observed that sensory blockade lasted longer as compared to motor blockade which is in coherence with the observation made by De Jong et al[2]. They explained that large fibers require a higher concentration of local anaesthetic than small fibers. The minimal effective concentration of local anaesthetic for large (motor) fibers is greater than for small (sensory) fibers. Thus, motor

function returns before pain perception and duration of motor block is shorter than the sensory block.

The duration of motor block was not different between the groups (group B 5.18 ± 2.03) and group BM 5.16 ± 1.33 hr). NasreenLaiq et al[15] also observed same findings.

In our study we observed significantly lower VAS scores postoperatively in Group BM at 2hr, 3hr, 4hr, 5hr, 6hr, 8 hr as compared to Group B ($P < 0.05$), similar phenomena was observed in studies done by Koj J et al[12], Shaikh SI et al[15], NasreenLaiq et al[14] and Ritesh M et al[16] They also observed that midazolam prolongs the duration of analgesia and reduces pain score significantly. The prolonged analgesia in group BM could be due to the action of midazolam on GABA-A receptors present in brachial plexus and thus producing antinociception as demonstrated by Brown and Marsh.[17] All patients in both of the group required rescue analgesia but the mean total number of rescue analgesic doses required in first 24 hrs postoperatively was less in group BM as compared to group B ($P < 0.0001$). Same results were obtained in a study conducted by Aggrawal et al.[18]

We observed that addition of midazolam increases sedation scores in intraoperative period, higher sedation score was noted from 10 min of drug injection till 50 min but none of the patient required any ventilatory assistance. Partial vascular uptake of midazolam and its transport to CNS, where it acts might have accounted for it.

Sedation was of limited duration, transient effect may be due to rapid, high rate of clearance of midazolam (6-11 ml/kg/min).[22] In post operative period patients were awake and alert in both the groups, this correlates with the study by Koj J et al[12] and Nishiyama[19] et al.

There were no statistically significant hemodynamic changes observed in both groups. Heart rate, mean arterial pressure, respiratory rate and SpO2 were comparable between both groups intraoperatively as well as postoperatively. This is in correlation with studies conducted by Koj J et al[12,] Batra et al[20] and Singh J et al.[21]

CONCLUSION

In conclusion, addition of Midazolam 0.05 mg/kg as adjuvant to Bupivacaine 0.5% for supraclavicular brachial plexus block significantly enhances the onset of sensory and motor blockade. This combination provides prolonged superior analgesia, resulting in reduced requirements for rescue analgesics and also has desirable properties of stable haemodynamics and lesser sedation.

Financial support and sponsorship
Nil.

Conflicts of interest There are no conflicts of interest.

REFERENCES

1. Brown, Anthony R. et al. Interscalene block for shoulder arthroscopy: Comparison with general anesthesia. Arthroscopy, Volume 9, Issue 3, 295- 300
2. De Jong RH. Axillary block of brachial plexus. Anesthesiology 1961; 22: 215-25
3. Lund PC, Cwik JC, Vallesterons F. Bupivacaine-A new long acting local anesthetic agent. A preliminary clinical and laboratory report. AnesthAnalg 1976; 49: 103-13.
4. Kulenkampf D. Anesthesia of the brachial plexus. ZentralblChir. 1911; 38:1337-50.
5. Brown Dl, Cahill DR, Bridenbaugh LD. Supraclavicular nerve block: Anatomic analysis of a method to prevent peumothorax. Anesth Anal 1993; 76:530-4. 32.
6. Edwards M, Serrao JM, Gent JP, Goodchild CS. On the mechanism by which midazolam causes spinally mediated analgesia. Anesthesiology 1990; 73:273-7.
7. Cairns BE, Sessle BJ, Hu JW. Activation of peripheral GABAA receptors inhibits temporomandibular joint-evoked jaw muscle activity. J Neurophysiol 1999; 81:1966-9
8. Culebras X, Van Gesse lE, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anaesthetic does not prolong post operative analgesia after brachial plexus block but does induce hemodynamic changes. Anesth Analg 2001; 92:199-204.
9. Liske S, Morris ME. Extra synaptic effects of GABA agonists on myelinated axons of peripheral nerves. Can J Physiol Pharmacol. 1994; 72(4):368-74.
10. Batra YK, Jain K, Chari P, Dhillon MS, Shaheen B, Reddy GM. Addition of intrathecal midazolam to bupivacaine produces better postoperative analgesia without prolonging recovery. Int J Clin Pharmacol Ther 1999; 37:519-23.
11. Naguib M, Gammal M, Elhattab YS, Seraj M. Midazolam for caudal analgesia in children: Comparison with caudal bupivacaine. Can J Anaesth. 1995; 42(9):758-64.
12. Koj J, Yatindra KB, Nidhi BP. Brachial plexus block with midazolam and bupivacaine improves analgesia. Can J Anesth 2005; 52:822-826
13. Winnie AP. Interscalene brachial plexus block. Anesthanalog 1970; 49:455-66.
14. NasreenLaiq, Mohammad Naeem Khan, Mohammad Arif et al Khan Midazolam with Bupivacaine for Improving Analgesia Quality in Brachial Plexus Block for Upper Limb Surgeries Journal of the College of Physicians and Surgeons Pakistan 2008, Vol. 18 (11): 674-678 677
15. Shaikh SI, Veena K. Midazolam as an adjuvant in supraclavicular brachial plexus block. Anaesth, pain &intensive care; 2012; 16(1):7-11
16. Ritesh M. Karia, Ravi N. Agrawal, Pramila S. Jha, Deepshikha C. Tripathi.Role of midazolam as an adjuvant to local anaesthetic in supraclavicular brachial plexus block. Asian Journal of Medical Research2013 » Volume 2, Issue 1 pp. 1-41
17. Brown DA, Marsh S. Axonal GABA – receptors in mammalian peripheral nerve trunks. Brain Res 1978; 156: 187-91.
18. Aggarwal N, Usmani A, Sehgal R, Kumar R, Bhadoria P. Effect of intrathecal midazolam bupivacaine combination on post operative analgesia. Indian J Anaes 2005; 49:37–39.
19. Nishiyama T, Yokoyama T, HanokaK. Midazolam improves postoperative epidural analgesia with continuous infusion of local anaesthetics. Can J Anesth 1998; 45:551-55.
20. Batra YK, Jain K, Chari P, Dhillon MS, Shaheen B, Reddy GM. Addition of intrathecal midazolam to bupivacaine produces better post-operative analgesia without prolonging recovery. Int J ClinPharmacol Ther 1999; 37:519-23.
21. Singh J, Verma V, Sood P, Thakur A, Rana S, Thakur L. Midazolam as an adjunct to lignocaine at two different doses in ultrasound-guided supraclavicular brachial plexus block: a randomized controlled trial. Ain Shams J Anaesthesiol2016;9:549-57
22. Raghu R, Indira P, Kiran M, Murthy R. A comparative study of 0. 375% bupivacaine with midazolam and 0. 375% bupivacaine for brachial plexus block in upper limb surgeries. Asian Pac J Health Sci 2015; 2:129–135