MIDAZOLAM AS AN ADJUVANT TO BUPIVACAINE IN SUPRACLAVICULAR APPROACH OF BRACHIAL PLEXUS BLOCK

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ABSTRACT

BACKGROUND

Brachial plexus block in supraclavicular approach is a very good postoperative analgesia. Midazolam, a water-soluble benzodiazepine has been used by various routes to prolong analgesia. The analgesic efficacy of midazolam with bupivacaine in brachial plexus block produces significantly faster onset of sensory and motor blockade and prolongs the duration of sensory and motor block and duration of analgesia.

The aim of this study is to compare the effectiveness of addition of midazolam as an adjuvant to bupivacaine in supraclavicular approach of brachial plexus block in upper limb surgery.

MATERIALS AND METHODS

60 patients were recruited to two groups. Group B received 30 mL of 0.375% Bupivacaine and Group BM received 30 mL of 0.375% Bupivacaine and 50 mcg/kg of Midazolam.

RESULTS

On addition of midazolam to bupivacaine, there was significant difference in onset of sensory and motor block compared to bupivacaine. There is prolongation in duration of analgesia, duration of sensory and motor blockade. There is no significant difference in haemodynamics and no side effects like hypotension, bradycardia or respiratory depression.

CONCLUSION

The addition of midazolam to LA solution in supraclavicular approach to brachial plexus block produces significantly faster onset of sensory and motor blockade and prolongs the duration of sensory and motor block and duration of analgesia.

KEYWORDS

Supraclavicular, Brachial Plexus Block, Midazolam.

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BACKGROUND

Pain is a fundamental biological phenomenon, always underestimated and undertreated. The relief of pain during surgery is the main part of anaesthesia. In 1911, Kulenkampff introduced the classical approach to brachial plexus block. Winnie and Collins introduced the lateral perivascular approach.

Midazolam is known to produce antinociception and potentiates the effect of local anaesthetic when given in neuraxial block. The effect is produced by its action on GABA-A receptors and peripheral nerves containing these receptors. This study was designed to compare the effectiveness of adding midazolam to bupivacaine in supraclavicular approach of brachial plexus block for prolonging the duration of sensory and motor block and duration of analgesia in upper limb surgery.

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MATERIALS AND METHODS

This study was conducted at Government Rajaji Hospital, attached to Madurai Medical College. After getting approval from the Institution's Ethical Committee and obtaining high-risk informed consent, the study was conducted on 60 patients. Sample size calculation was not done for sake of convenience and this study was non-randomised control study.

Inclusion Criteria

- Age more than 20.
- Both sex.
- ASA Grading I and II.
- Undergoing upper limb surgery.

Exclusion Criteria

- Patients allergic to local anaesthetic.
- Contraindications to the use of midazolam.

Patients were allocated randomly to two groups, Group B and Group BM. Each group having 30 patients, surgery was done under supraclavicular approach of brachial plexus block.

No premedications were given. IV access was obtained, Anaesthesia machine checked, Resuscitative drugs and

equipment kept ready. Supraclavicular block was performed by subclavian/lateral perivascular approach by using peripheral nerve locator.

Group B- 30 mL of 0.375% Bupivacaine alone.

Group BM- 30 mL of 0.375% Bupivacaine with 50 mcg/kg of midazolam.

Parameters Observed

1. Onset of Sensory Blockade

Abolishment of pain (pin prick) over distribution of ulnar and median nerve assessed every minute after performance of block.

2. Onset of Motor Blockade

Assessed every 2 mins after block using 4-point scale.

- 0– Normal power.
- 1– Weakness present, but able to move arm.
- 2– Not able to move arm, but able to move fingers.
- 3– Complete motor block.

Attaining a score of 2 was considered as onset of Motor block.

3. Duration of Surgery.

4. Duration of Sensory block.

5. Duration of Motor block.

When 3 in four-point scale changes to 2, the blockade is said to reverse giving the duration of motor block.

6. Duration of Analgesia

The pain was assessed by VAS (Visual Analogue Scale) numbered from 0 - 10.

VAS 0– No pain.

VAS 10– Worst pain.

Pain was observed for every 30 mins after surgery is over, till motor block reverses thereafter hourly for every 6 hrs. and then 2nd hourly for next 6 hrs. Duration of Postoperative analgesia is the period of time after surgery till the time when patient needs analgesics (VAS > 5).

7. Vital Parameters

Pulse rate, BP and respiratory rate were monitored every 5 mins.

8. Sedation Score

Brain and ready scoring was employed,

- 0– Fully awake.
- 1– Drowsy.
- 2– Drowsy, but arousable on touch or call.
- 3– Drowsy and arousable on deep stimuli.
- 4– Somnolent.

9. Side effects noted are Sedation, Hypotension, Bradycardia.

Patients in whom the block was unsuccessful due to total failure/missed dermatomes/ which needed IV supplementation/ need for GA were excluded from the study.

Statistical Tools

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with

the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Independence 'T' test was done and Kruskal-Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi-square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS

Demographic Data

Age Distribution

Patients are categorised into 5 groups, 20 yrs., 21 – 30 yrs., 31 - 40 yrs., 41 – 50 yrs. and above 50 yrs. in both groups which is shown in Table 1.

There is no significant difference in two groups ('p' value 0.1131).

Weight Distribution

As shown in Table 2.

There is no significant difference in two groups (P value 0.0721).

Sex Distribution

Shown in Table 3, male patients are 63.3% and females are 36.7%. There is no significant difference in both groups (P value 0.7842).

Onset of Sensory Block

Sensory block was taken within 8 - 10 mts in Group BM and it was within 15 - 19 mts in Group B, which is shown in Table 4. The onset of block was significantly faster in midazolam group (p value < 0.0001).

Onset of Motor Block

Motor block was taken within 13 - 20 mts and 20 - 25 mts in Group BM and Group B respectively, which is shown in Table 5.

The onset of motor block was significantly faster in midazolam group (p value < 0.0001).

Duration of Surgery

As shown in Table 6, it was 0.53 hrs. in both groups.

Duration of surgery was comparable in both groups (p value < 0.5511).

Duration of Motor Block

It was 7 - 9 hrs. and 5 - 7 hrs. respectively in both groups as shown in Table 7.

Duration of Motor block was prolonged significantly in midazolam group (p value < 0.0001).

Duration of Sensory Block

As shown in Table 8, it was 11 - 15 hrs. and 5 - 9 hrs. respectively in both groups.

Duration of sensory blockade was prolonged significantly in midazolam group (p value < 0.0001).

Duration of Analgesia

It was prolonged in Group BM, which was 15 - 18 hrs. which is shown in Table 9.

Duration of analgesia was prolonged significantly in midazolam group (p value < 0.0001).

Sedation Score was shown in Table 10.

Midazolam group has significant sedation score than bupivacaine group (p value 0.0001).

Haemodynamic Changes

Was shown in Table 11.

The 'p' values are not statistically significant.

There was no significant haemodynamic changes after administration of midazolam and bupivacaine. In both the groups, there was no incidence of side effects like hypotension or bradycardia.

Age in Yrs.	BM Group		B Group	
	No.	%	No.	%
Up to 20 yrs.	4	13.3	1	3.3
21 - 30 yrs.	11	36.7	6	20
31 - 40 yrs.	7	23.3	12	40
41 - 50 yrs.	6	20.0	5	16.7
Above 50 yrs.	2	6.7	6	20
Total	30	100	30	100
Range	15 - 60 yrs.		16-75 yrs.	
Mean	33.6 yrs.		39.5 yrs.	
SD	12.4 yrs.		14 yrs.	
P value		0.1131		
Table 1. Age Distribution				

Table 1. Age Distribution

Weight (Kg)	Group BM	Group B
Range	45-60	42-60
Mean	52.7	54.6
S.D	4.4	5.3
P value	0.0721	

Table 2. Weight Distribution

Sex	Group BM		Group B	
	No.	%	No.	%
Male	21	70	19	63.3
Female	9	30	11	36.7
Total	30	100	30	100
P value	0.7842			

Table 3. Sex Distribution

Onset of Sensory Block	Group BM	Group B
Range	8 - 10 mins	15 - 19 mins
Mean	8 mins	17.9 mins
S.D	0.8 mins	0.8 mins
P value	0.0001	

Table 4. Onset of Sensory Block

Onset of Motor Block	Group BM	Group B
Range	13 - 20 mins	20 - 25 mins
Mean	16.4 mins	21.8 mins
SD	1.7 mins	1.5 mins
P value	0.0001	

Table 5. Onset of Motor Block

Duration of Surgery (hrs.)	Group BM	Group B
Range	0.5 - 3 hrs.	0.5 - 3 hrs.
Mean	1.49 hrs.	1.41 hrs.
S.D	0.64 hrs.	0.64 hrs.
P value	0.5511	

Table 6. Duration of Surgery

Duration of Motor Block	Group BM	Group B
Range	7 - 9 hrs.	5 - 7 hrs.
Mean	7.38 hrs.	6.03 hrs.
SD	0.46 hrs.	0.32 hrs.
P value	0.0001	

Table 7. Duration of Motor Block

Duration of Sensory Block	Group BM	Group B
Range	11 - 15 hrs.	5 - 9 hrs.
Mean	13.5 hrs.	8 hrs.
SD	2.6 hrs.	0.7 hrs.
P value	0.0001	

Table 8. Duration of Sensory Block

Duration of Analgesia (hrs.)	Group BM	Group B
Range	15 - 18 hrs.	8 - 16 hrs.
Mean	16.8 hrs.	10.1 hrs.
SD	0.9 hrs.	1.8 hrs.
P value	0.0001	

Table 9. Duration of Analgesia

Sedation Score	Group BM	Group B
Range	1 - 3	0 - 1
Mean	2.1	0.33
SD	0.48	0.28
P value	0.0001	

Table 10. Sedation Score

	Pulse Rate		Systolic BP		Diastolic BP		SPO2	
	GpBM	GpM	GpBM	GpM	GpBM	GpM	GpBM	GpM
Mean	87.7	87.8	121.0	122	70.7	71.6	98.7	98.5
S.D	6.3	4.7	5.9	4.1	5.9	4.3	0.6	0.6
P value	0.8244		0.8591		0.6840		0.01724	

Table 11. Haemodynamic Changes

DISCUSSION

GABA A receptor (GABA A R) is an ionotropic receptor and ligand-gated ion channel. Its endogenous ligand is Gamma-Aminobutyric Acid (GABA), the major inhibitory neurotransmitter in the central nervous system. Upon activation, the GABA receptors selectively conducts chloride through its pores, resulting in hyperpolarisation of the neuron. This causes an inhibitory effect on neurotransmission by diminishing the chance of a successful action potential occurring ligands which contribute to receptor activation typically having anxiolytic, anticonvulsant, amnesic, sedative, hypnotic, euphoriant and muscle relaxant properties. Ligands which decrease receptor activation have opposite effects including anxiogenesis and convulsions.^{1,2,3}

Midazolam was synthesised in 1976 by Fryer and Walser. First used in 1986, by Nilsson and colleagues. Midazolam acts on GABA receptors in the spinal cord. When used as an adjuvant with local anaesthetic in intrathecal, epidural and

caudal blocks, it prolonged the duration of analgesic effect of local anaesthetics.^{4,5,6}

By statistical analysis of two groups the age, sex, weight and duration of surgery was comparable in both groups.

Onset of Sensory Block

Mean onset of sensory block in Group BM was 8.0 ± 0.8 mins and in Group B was 17.9 ± 0.8 . The difference between the two groups was statistically significant with a 'p' value of 0.0001 ($p < 0.05$).

Onset of Motor Block

Mean onset of motor block in Group BM was 16.4 ± 1.7 mins and in Group B it was 21.8 ± 1.5 mins. The difference between the two groups was statistically significant with a 'p' value of 0.0001 ($p < 0.05$).

On addition of Midazolam to LA solution, there is difference in onset of sensory and motor block.

Nasreen Laiq et al study also reported similarly that the onset of sensory block was 14 ± 3.1 mins, 18.5 ± 3.5 mins in Group BM and Group B and motor block of 10.5 ± 2.4 mins, 18.5 ± 3.5 mins in Group BM and B respectively.^{7,8,9}

Duration of Motor Block

Mean duration of motor block from score 3 - 3 in Group BM was 7.83 ± 0.46 hrs. and in Group B was 6.03 ± 0.32 hrs. The difference between the two groups was statistically significant with a 'p' value of 0.0001 ($p < 0.05$).

This result correlates with studies conducted by Nasreen et al. In Midazolam group it was 7.65 ± 3.20 hrs. compared to bupivacaine group it was 5.20 ± 2.10 hrs.

Duration of Sensory Block

The mean duration of sensory block in Group BM was 13.5 ± 2.6 hrs. and in Group B was 8.0 ± 0.7 hrs. The difference between the two groups was statistically significant with a 'p' value of 0.0001 ($p < 0.05$).

This is comparable with study done by Koj Jarbo, Yatindra Kumar Batra et al in which the duration of sensory block was 7 ± 4.32 hrs. in midazolam group compared to 5.95 ± 1.4 hrs. in plain bupivacaine group.^{10,11,12}

Duration of Analgesia

The mean duration of analgesia is till VAS score > 5 and in Group BM it was 16.8 ± 0.9 hrs. and in Group B it was 10.1 ± 0.9 hrs. The difference between the two groups was statistically significant with a 'p' value of 0.0001 ($p < 0.05$).

These results correlate favourably with studies conducted by Nasreen Laiq et al. The mean duration of complete analgesia was significantly prolonged ($p = 0.002$) in the bupivacaine-midazolam group.

Sedation Score

The sedation score in Group BM was 2.1 ± 0.48 , and in Group B was 0.33 ± 0.28 . In midazolam group since the sedation score was not more than 3, the respiratory function was not compromised. So, intraoperative sedation is well observed in midazolam group.

Haemodynamics

In this study, no significant difference was observed with respect to pulse rate, systolic and diastolic blood pressure and SPO₂. This finding is consistent with the observations made by Nasreen Laiq et al, who concluded that there were no significant haemodynamic changes after administration of midazolam with bupivacaine.

Side Effects

Patients were observed for the side effects such as sedation, hypotension and bradycardia. No complications related to brachial plexus block were observed.

Gulec et al reported that bupivacaine-midazolam prolonged postoperative analgesia compared to bupivacaine-morphine combination when given caudally.

Tucker and Associates reported the analgesic effects of intrathecal midazolam in combination with intrathecal fentanyl in labouring patients.^{13,14,15}

In this study, the addition of midazolam to local anaesthetic solution produce difference between the onset of sensory and motor blockade when compared to bupivacaine group.

The duration of analgesia is significantly higher in midazolam group when compared to bupivacaine group.

The duration of sensory blockade is also increased in midazolam group. These inferences provide midazolam producing a prolonged sensory and motor blockade.

CONCLUSION

The addition of Midazolam to Local anaesthetic solution in supraclavicular approach to brachial plexus-

- Produces significantly faster onset of sensory and motor block.
- Prolongs the duration of sensory and motor block and duration of analgesia.

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