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Efficacy of Midazolam in Patients Undergoing Lower Limb Surgeries: A Study from Tertiary Care Centre

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KEYWORDS

bupivacaine and midazolam, midazolam, side effect, efficacy

ABSTRACT:

Introduction: Co-administration of drugs with synergistic effects is considered as one of the methods to increase the effectiveness of intrathecal anaesthesia and to reduce the need for injectable analgesics. The purpose of this study was to investigate the efficacy of intrathecal midazolam on enhancing the analgesic effect of fentanyl in patients undergoing lower limb surgery.

Objective: To compare the hemodynamic parameters between bupivacaine and combination of bupivacaine and midazolam.

Materials and Methods: The present Descriptive observational study was carried out at Department of anaesthesia with simple Random sampling method. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. **Results:** We included 50 patients in each group. Mean age of the patients from Group B and Group BM was 41.19(13.27) and 36.50(13.70) years. We found no significant difference in the duration of surgery between bupivacaine and combination of bupivacaine and midazolam ($p>0.05$). We found significant difference in the onset of peak sensory analgesia between bupivacaine and combination of bupivacaine and midazolam ($p<0.05$).

Conclusion: We found significant difference in the onset of peak sensory analgesia between bupivacaine and combination of bupivacaine and midazolam ($p<0.05$). We observed incidence of bradycardia in Group B as 6% and in Group BM as 4%. Incidence of hypotension in Group B as 0% and in Group BM as 4%. Incidence of vomiting in Group B as 2% and in Group BM as 6%.

Introduction

Post-operative pain is considered as one of the common problems in patients. Failure to control pain can thus result in physiological complications, such as hypertension, tachycardia, cardiac dysrhythmia, and even cardiac ischemic events.[1,2]

One of the most effective procedures to relieve post-operative pain is systemic opiate injection. [3]

Given that injection of systemic intravenous analgesics leads to extensive side effects, including hypotension, respiratory arrest, pruritus and urinary retention[4], the use of central nervous block is thought to be an appropriate

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approach to control pain in patients undergoing lower limb surgery. [1]

This method is a type of regional anaesthesia in which drugs are injected into the subarachnoid space. Therefore, adding low doses of fentanyl to an anaesthetic agent may increase the duration of the sensory nerve block and that of the analgesia following surgery. However, it can also cause complications, such as pruritus and respiratory depression. [5]

However, a combination of drugs with synergistic effects can enhance the anticipated impacts, and the patient may suffer from fewer side effects due to insignificant concentrations of each drug. [6]

Following the use of intrathecal midazolam for prolongation of spinal anaesthesia, *in vitro* autoradiography has shown a high density of benzodiazepine (GABAA) receptors in Lamina II of the dorsal horn of the human spinal cord, suggesting a possible role of midazolom in pain modulation. [7]

Intrathecal midazolam also causes the release of an endogenous opioid, which acts on the spinal delta receptor. [8]

Various studies have found that adding midazolam to bupivacaine increases the duration of post-operative analgesia in a significant manner. [9]

Objective: To compare the side effects and efficacy of midazolam with the combination of bupivacaine and midazolam.

Materials and Methods

Study setting: Department of anaesthesia**.**

Study design: Descriptive observational study

Sample size:

Sampling technique: Simple Random sampling method

Inclusion criteria:

1. ASA Grade I/II physical status.
2. Weight 30-80 kg.
3. Age 18-60 yrs.

Exclusion criteria:

1. ASA Grade Ill and IV patients
2. Patients with history of known allergy to the drugs to be used.
3. Patients on chronic analgesic therapy.
4. Gross spinal deformity.
5. Patients in whom regional anesthesia Is contraindicated.
6. Patients with peripheral neuropathy. 7.Surgeries lasting for more than 2 hours.

Methods of data collection:

After approval from the local ethics committee and with written Informed consent from patient, a randomized controlled prospective study is carried out in the medical college and hospital from November 2009 to October 2010. During this one-year study, total 100 ASA Grade 1111 patients aged 18- 60 years were studied who were scheduled for the lower limb surgeries up to two hours duration.

These patients were randomly allocated in-

Group B: who received 3ml (15mg) hyperbaric 0.5% bupivacaine hydrochloride.

Group BM: who received 3ml (15mg) hyperbaric 0.5% bupivacaine hydrochloride +0.2 ml (1mg) of preservative free midazolam.

Detailed preoperative evaluation was carried out in all patients with detailed history, physical examination including height, weight, evidence of spinal deformity or presence of any neurological disease and mental status of the patient Vital parameters were noted and systemic examination was performed along with general and spine examination.

Anaesthetic Procedure: After explaining the patient about the procedure, subarachnoid block was given in sitting position with midline approach with strict aseptic precautions using 25G Quincke's spinal needle. The study drugs I.e. either bupivacaine alone (Group. B) or combination of bupivacaine and midazolam (Group BM).

The highest level of sensory block will be checked by pinprick method caudal to cephalad direction every 2 minutes.

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Motor block will be checked by Bromage Scale.

0 - Full flex.ion of knees and feet (0% block)

1 - Just able to flex knees, full flexion of feet possible

2 - Unable to flex knees but some flexion of feet possible
3 - Unable to move legs or feet

Vital parameters like heart rate, blood pressure, respiratory rate, peripheral oxygen saturation and sedation score will be noted every 2 minutes for first 1O minutes and thereafter every 5 minutes till 20 min and thereafter every10 min till the end of surgery.

Intra operatively sedation was assessed by Ramsay Sedation Score as follows:

1. Patient is anxious and agitated or restless. or both.
2. Patient is co-operative, oriented, and tranquil.
3. Patient responds to commands only.
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
5. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient exhibits no response.

Statistical analysis:

Data was collected by using a structure proforma. Data entered in MS excel sheet and analysed by using SPSS 24.0 version IBM USA. Qualitative data was expressed in terms of proportions. Quantitative data was expressed in terms of Mean and Standard deviation. Comparison of mean and SD between two groups was done by using unpaired t test to assess whether the mean difference between groups is significant or not. A p value of <0.05 was considered as statistically significant whereas a p value <0.001 was considered as highly significant.

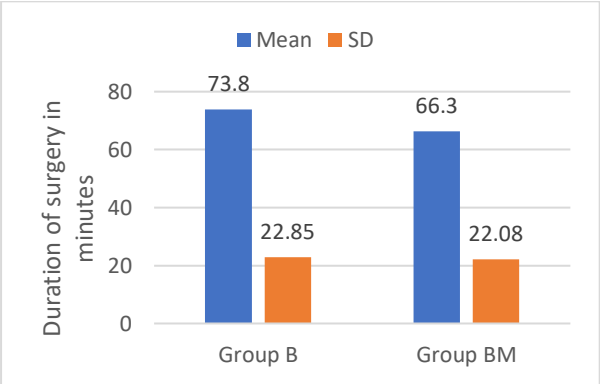
Results

Table 1: Distribution according to age and gender

	Group B	Group BM
Mean age	41.19(13.27)	36.50(13.70)
Male	38 (76%)	42 (84%)
Female	12 (24%)	8 (16%)

We included 50 patients in each group. Mean age of the patients from Group B and Group BM was 41.19(13.27) and 36.50(13.70) years. 76% and 84% of the males were from Group B and Group BM. 24% and 16% of the females were from Group B and Group BM.

Figure 1: Bar diagram showing comparison of duration of surgery between bupivacaine and combination of bupivacaine and midazolam



The mean duration of surgery for bupivacaine and combination of bupivacaine and midazolam was 73.8±22.85 and 66.3±22.08 minutes respectively. We found no significant difference in the duration of surgery between bupivacaine and combination of bupivacaine and midazolam (p>0.05).

Table 2: Comparison of onset of peak sensory analgesia between bupivacaine and combination of bupivacaine and midazolam

	Group B	Group BM
Mean	4.3	3.9
SD	0.4	0.14

t-2.56, p-0.043

The onset of peak sensory analgesia for bupivacaine and combination of bupivacaine and midazolam was 4.3±0.4 and 3.9±0.14 minutes respectively. We found significant difference in the onset of peak sensory analgesia between bupivacaine and combination of bupivacaine and midazolam (p<0.05).

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Table 3: Comparison of duration of sensory blockade between bupivacaine and combination of bupivacaine and midazolam

	Group B	Group BM
Mean	177.6	197.3
SD	10.51	16.23

t-7.206, p-0.0001

The duration of sensory blockade for bupivacaine and combination of bupivacaine and midazolam was 177.6±10.51 and 197.3±16.23 minutes respectively. We found significant difference in the duration of sensory blockade between bupivacaine and combination of bupivacaine and midazolam ($p<0.01$) stating duration of sensory blockade was significantly less in bupivacaine as compared to combination with midazolam.

Table 4: Comparison of duration of rescue analgesia between bupivacaine and combination of bupivacaine and midazolam

	Group B	Group BM
Mean	190.2	298.8
SD	19.74	59.99

t-12.15, p-0.0001

The duration of rescue analgesia for bupivacaine and combination of bupivacaine and midazolam was 190.2±19.74 and 298.8±59.99 minutes respectively. We found significant difference in the duration of rescue analgesia between bupivacaine and combination of bupivacaine and midazolam ($p<0.01$) stating duration of rescue analgesia was significantly less in bupivacaine as compared to combination with midazolam.

Table 5: Comparison of side effects between bupivacaine and combination of bupivacaine and midazolam

	Group B	Group BM
Bradycardia	3 (6%)	4 (4%)
Hypotension	0 (0%)	2 (4%)
Vomiting	1(2%)	3(6%)

We observed incidence of bradycardia in Group B as 6% and in Group BM as 4%. Incidence of hypotension in Group B as 0% and in Group BM as 4%. Incidence of vomiting in Group B as 2% and in Group BM as 6%.

Discussion

Mean age of the patients from Group B and Group BM was 41.19(13.27) and 36.50(13.70) years. 76% and 84% of the males were from Group B and Group BM. 24% and 16% of the females were from Group B and Group BM. **(Table 1)**

The mean duration of surgery for bupivacaine and combination of bupivacaine and midazolam was 73.8±22.85 and 66.3±22.08 minutes respectively. We found no significant difference in the duration of surgery between bupivacaine and combination of bupivacaine and midazolam ($p>0.05$). **(Figure 1)**

The duration of sensory blockade for bupivacaine and combination of bupivacaine and midazolam was 177.6±10.51 and 197.3±16.23 minutes respectively. We found significant difference in the duration of sensory blockade between bupivacaine and combination of bupivacaine and midazolam ($p<0.01$) stating duration of sensory blockade was significantly less in bupivacaine as compared to combination with midazolam. **(Table 2)**

The onset of peak sensory analgesia for bupivacaine and combination of bupivacaine and midazolam was 4.3±0.4 and 3.9±0.14 minutes respectively. We found significant difference in the onset of peak sensory analgesia between bupivacaine and combination of bupivacaine and midazolam ($p<0.05$). **(Table 3)**

The duration of rescue analgesia for bupivacaine and combination of bupivacaine and midazolam was 190.2±19.74 and 298.8±59.99 minutes respectively. We found significant difference in the duration of rescue analgesia between bupivacaine and combination of bupivacaine and midazolam ($p<0.01$) stating duration of rescue analgesia was significantly less in bupivacaine as compared to combination with midazolam. **(Table 4)**

We observed incidence of bradycardia in Group B as 6% and in Group BM as 4%. Incidence of hypotension in Group B as 0% and in Group BM as 4%. Incidence of vomiting in Group B as 2% and in Group BM as 6%. **(Table 5)**

Martyr and Clark[10] found incidences of hypotension as a common complication when intrathecal fentanyl 20

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mcg was added to bupivacaine 7.5 mg in elderly patients, but the incidence and severity of hypotension were not significant.

Ben-David *et al*[11] and Grewal *et al*[12] found increased incidence of hypotension by adding fentanyl to bupivacaine in SAB**. Bhattacharya *et al*[13]** did not find any significant change in blood pressure when intrathecal midazolam 2 mg was added to bupivacaine 15 mg.

Conclusion:

1. We found significant difference in the onset of peak sensory analgesia between bupivacaine and combination of bupivacaine and midazolam ($p<0.05$).
2. Duration of rescue analgesia was significantly less in bupivacaine as compared to combination with midazolam.
3. Duration of sensory blockade was significantly less in bupivacaine as compared to combination with midazolam.
4. We observed incidence of bradycardia in Group B as 6% and in Group BM as 4%. Incidence of hypotension in Group B as 0% and in Group BM as 4%. Incidence of vomiting in Group B as 2% and in Group BM as 6%.

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