



Comparison of Hemodynamic Parameters Between Bupivacaine and Combination of Bupivacaine and Midazolam in Patients Undergoing Lower Limb Surgeries

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KEYWORDS	ABSTRACT:
bupivacaine and midazolam, midazolam, hemodynamic effect	Various intrathecal additives are added to local anesthetics to increase the speed of onset, improve the quality, and prolong the influence of spinal anesthesia. Midazolam has a synergistic effect on postoperative analgesia when administered intrathecally with bupivacaine. Intrathecal midazolam has been reported to have antinociceptive action. ⁴ Evidence indicates that intrathecal midazolam may be useful in the treatment of somatic pain. ^{5,6} The optimum dose of intrathecal midazolam for postoperative analgesia is not identified. In previous studies midazolam has been administered in the dose of 1mg and 2mg intrathecally. 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. 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. SBP, DBP, SPO2 and RR were comparable in both the groups stating no major effect of addition of bupivacaine in midazolam. Conclusion: We observed no significant difference in the effect of two drugs i.e. bupivacaine and combination of bupivacaine and midazolam on hemodynamic parameters like SBP, DBP, SPO2 and respiratory rate in our study.

Introduction

Regional anaesthetic techniques provide an excellent means for managing postoperative pain following orthopaedic procedures. Spinal anaesthesia with bupivacaine is administered routinely for lower limb surgery¹ and provides effective analgesia in the early postoperative period. Various adjuvants have been added to spinal local anaesthetic to prolong postoperative analgesia. Intrathecal morphine provides effective postoperative analgesia but is associated with adverse effects such as itching, nausea, urinary retention, sedation, ileus and life-threatening respiratory depression.² Other adjuvants such as clonidine and ketamine have also been administered but none have become established in regular clinical use because of their adverse effects.³

There has been growing emphasis on the advantages of combined pharmacological approach for pain relief. Discovery of analgesic effects of spinally administered opioids and other drugs such as benzodiazepines^{4,5} and alpha-2 adrenoreceptor agonists⁶ has opened the possibilities of optimizing on useful drug interactions at the level of spinal cord in the management of pain.

By administering intrathecal combinations of drugs, targeting different spinal cord receptors; prolonged and superior quality analgesia can be achieved by relatively small concentrations of individual drugs. The dose reductions may avoid drug-related side effects. In addition, the simultaneous targeting of several different receptor sites in the spinal cord may lead to improved pain relief.⁷



The advantage of the use of opioids like fentanyl to facilitate effective postoperative analgesia is well documented in the literature.⁸⁻¹¹

The administration of intrathecal benzodiazepine has its antinociceptive action mediated via benzodiazepine/GABA-A receptor complex which are abundantly present in lamina II of dorsal horn ganglia of the spinal cord.¹² Intrathecal midazolam also causes the release of an endogenous opioid, acting at spinal delta receptor.¹³ This has been proved as its nociceptive effect has been suppressed by “Naltrindole,” a delta selective opioid antagonist.

Objective: To compare the hemodynamic parameters between bupivacaine and 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 III 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 I-II 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.

Motor block will be checked by Bromage Scale.

0 - Full flexion 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 10 minutes and thereafter every 5 minutes till 20 min and thereafter every 10 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

Results

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.

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.

Table 1: Comparison of intraoperative SBP between bupivacaine and combination of bupivacaine and midazolam

SBP intraoperative	Group B	Group BM	t value	p-value
Duration	MEAN±SD	MEAN±SD		
0 minute	120.56±7.55	122.76±8.42	1.38	0.172
5 minutes	116.44±6.94	119±7.72	1.74	0.084
10 minutes	114.04±6.76	116.2±8.04	1.45	0.149
15 minutes	114.4±7.02	115.38±9.95	0.57	0.571
30 minutes	109.68±7.17	110±7.97	0.21	0.833
45 minutes	107±7.99	110.53±9.36	1.84	0.068
60 minutes	105.81±8.07	109.5±9.50	1.89	0.061
75 minutes	107.57±8.80	112.5±7.61	1.96	0.053
90 minutes	109.43±5.15	113.11±4.80	1.78	0.089
105 minutes	112±4.48	113±3.46	0.36	0.717
120 minutes	113.6±4.56	113.5±3.41	0.04	0.971



Systolic blood pressure in both the groups fell after induction and returned back to near pre-operative level at the end of surgery. The difference of fall in blood

pressures between the groups at different time intervals studied was statistically not significant ($p>0.05$).

Table 2: Comparison of post-operative SBP between bupivacaine and combination of bupivacaine and midazolam

SBP post operative	Group B	Group BM	t value	p-value
Duration	MEAN±SD	MEAN±SD		
Shift	109.7±5.53	112.04±7.55	1.7196	0.0885
30 min	112.8±5.29	115.28±7.16	1.9645	0.0522
1hour	113.4±15.03	117.2±6.14	1.6187	0.1065
2hours	115.4±15.14	117.48±6.68	0.8866	0.3773
4 hours	118.5±4.99	119.2±6.32	0.5964	0.5522
6 hours	115.7±15.81	120.4±6.94	1.9053	0.0596
8 hours	116.8±5.39	118.8±6.31	1.7026	0.0917
10 hours	116.5±5.48	118.1±4.87	1.5036	0.1358
12 hours	1172±5.65	119.08±5.33	1.6504	0.1019
24 hours	115.2±15.16	118.08±5.37	1.2607	0.2103

The post-operative blood pressure showed not much difference from the pre-operative value in both the groups. The difference between the groups at different time intervals studied was statistically not significant ($p>0.05$).

Table 3: Comparison of intraoperative DBP between bupivacaine and combination of bupivacaine and midazolam

DBP post operative	Group B	Group BM	t value	p-value
Duration	MEAN±SD	MEAN±SD		
0 minute	75.88±5.79	76.16±7.11	1.29	0.199
5 minutes	72.12±6.32	74.4±6.49	1.78	0.078
10 minutes	69.84±4.87	71.48±6.24	1.46	0.147
15 minutes	70.4±5.82	68.2±6.40	1.76	0.081
30 minutes	68.4±5.48	67.4±5.62	0.86	0.390
45 minutes	67.36±5.05	69.08±5.25	1.62	0.108
60 minutes	69.43±4.62	70.33±4.95	1.53	0.076
75 minutes	67.25±4.65	70.22±5.39	1.93	0.057
90 minutes	68.67±3.75	71.7±4.40	1.73	0.087
105 minutes	70.34±5.12	70±1.63	0.14	0.887
120 minutes	72±6	70.5±1	0.51	0.610



The intra-operative diastolic blood pressure in both the group at different time intervals were comparable and did not differ much statistically ($p>0.05$).

Table 4: Comparison of intraoperative SPO2 between bupivacaine and combination of bupivacaine and midazolam

SPO2 intra operative	Group B	Group BM	t value	p-value
Duration	MEAN±SD	MEAN±SD		
0 minute	99.2±0.81	99.2±0.80	0.12	0.90
5 minutes	99.06±0.79	99.08±0.80	0.13	0.90
10 minutes	99.06±0.79	99.1±0.814	0.25	0.80
15 minutes	99.36±0.72	99.38±0.70	0.14	0.89
30 minutes	99.06±0.79	99.08±0.80	0.13	0.90
45 minutes	99.16±0.83	99.18±0.72	0.11	0.90
60 minutes	99.33±0.71	99.36±0.72	0.16	0.87
75 minutes	99±0.745	99.05±0.77	0.21	0.83
90 minutes	99.22±0.44	99.33±0.5	0.49	0.62
105 minutes	99±0	98.75±0.5	0.86	0.39
120minutes	100±0	99.6±0.54	1.36	0.12

The peripheral oxygen saturation was well maintained in all the cases intra-operatively. There were no instances of hypoxemia in our study ($p>0.05$).

Table 5: Comparison of intraoperative respiratory rate between bupivacaine and combination of bupivacaine and midazolam

RR intraoperative	Group B	Group BM	t value	p-value
Duration	MEAN±SD	MEAN±SD		
0 minute	14.68±0.55	14.9±0.61	1.88	0.06
5 minutes	14.7±0.61	14.68±0.74	0.15	0.88
10 minutes	14.92±0.69	14.76±0.68	1.16	0.25
15 minutes	14.72±0.60	14.68±0.74	0.30	0.77
30 minutes	14.82±0.82	14.76±0.68	0.40	0.89
45 minutes	14.94±0.68	14.7±0.54	1.94	0.05
60 minutes	14.70±0.71	14.56±0.64	0.90	0.37



75 minutes	14.56±0.76	14.68±0.42	0.65	0.51
90 minutes	14.63±0.58	14.88±0.33	1.48	0.14
105 minutes	14.6±0.54	14.8±0.44	0.61	0.55
120 minutes	14.8±0.44	14.75±0.5	0.15	0.88

The respiratory rate was comparable in both the groups and did not show any significant changes both in intra-operative period ($p>0.05$).

Table 6: Comparison of post-operative respiratory rate between bupivacaine and combination of bupivacaine and midazolam

RR post	Group B	Group BM	t value	p-value
Duration	MEAN±SD	MEAN±SD		
Shift	15±0.49	14.94±0.42	0.65	0.52
30 min	14.7±0.78	14.68±0.79	0.12	0.90
1hour	14.58±0.60	14.6±0.60	0.16	0.87
2hours	14.62±0.69	14.62±0.69	0.00	1.0
4 hours	14.74±0.66	14.72±0.67	0.15	0.9
6 hours	14.94±0.81	14.94±0.81	0.00	1.0
8 hours	15.08±0.72	15.08±0.72	0.00	1.0
10 hours	14.36±0.56	14.96±0.56	0.00	1.0
12 hours	14.92±0.56	14.92±0.56	0.00	1.0
24 hours	14.82±0.48	14.82±0.48	0.00	1.0

The respiratory rate was comparable in both the groups and did not show any significant changes both in post-operative period ($p>0.05$).

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)

Systolic blood pressure in both the groups fell after induction and returned back to near pre-operative level at the end of surgery. The difference of fall in blood pressures between the groups at different time intervals studied was statistically not significant ($p>0.05$). The post-operative systolic blood pressure showed not much



difference from the pre-operative value in both the groups. The difference between the groups at different time intervals studied was statistically not significant ($p>0.05$). (Table 2 and 3)

The intra-operative diastolic blood pressure in both the group at different time intervals were comparable and did not differ much statistically ($p>0.05$). (Table 4)

The peripheral oxygen saturation was well maintained in all the cases intra-operatively. There were no instances of hypoxemia in our study ($p>0.05$). (Table 5)

The respiratory rate was comparable in both the groups and did not show any significant changes both in intra-operative period ($p>0.05$). The respiratory rate was comparable in both the groups and did not show any significant changes both in post-operative period ($p>0.05$). (Table 6 and 7)

There was no significant variation in pulse rate, SBP, and DBP both within the group and between the groups. In none of the studies, there was significant decrease in pulse rate with addition of fentanyl to bupivacaine, however most of the studies were carried out by adding fentanyl in a dose of 25 mcg or less. In this study also there was no significant decrease in pulse rate in Group BFM.^{14,15}

Martyr and Clark¹⁶ found incidences of hypotension as a common complication when intrathecal fentanyl 20 mcg was added to bupivacaine 7.5 mg in elderly patients, but the incidence and severity of hypotension were not significant. Shah *et al.*⁵ observed no significant decrease in mean arterial pressures when intrathecal bupivacaine 15 mg + buprenorphine 0.15 mg was compared with intrathecal bupivacaine 15 mg + buprenorphine 0.15 mg + midazolam 2 mg.

Ben-David *et al.*¹⁴ and Grewal *et al.*¹⁷ found increased incidence of hypotension by adding fentanyl to bupivacaine in SAB. Bhattacharya *et al.*¹⁸ did not find any significant change in blood pressure when intrathecal midazolam 2 mg was added to bupivacaine 15 mg.

Conclusion: We observed no significant difference in the effect of two drugs i.e. bupivacaine and combination of bupivacaine and midazolam on hemodynamic parameters like SBP, DBP, SPO2 and respiratory rate in our study.

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