

A Comparative Study Of Intrathecal 0.5% Hyperbaric Bupivacaine Alone And 0.5% Hyperbaric Bupivacaine with Midazolam for Lower Limb and Lower Abdominal Surgeries.

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Abstract

BACKGROUND: Spinal anaesthesia gives intra and postoperative pain relief with full preservation of mental status and normal reflexes. The spinal blockade is the commonest form of centrineuraxial blockade. The objective of this study is to assess the efficacy and analgesic effect of mixture of midazolam-bupivacaine as compared to bupivacaine alone in patients undergoing lower limb and lower abdominal surgeries under subarachnoid block.

Materials and Methods: 100 adult patients of ASA grade I-II scheduled for lower limb and lower abdominal surgeries were randomly allocated to two groups to receive either 3.0ml of 0.5% hyperbaric bupivacaine in (group B) or 3ml of 0.5% hyperbaric bupivacaine with 0.2ml(1mg) of intrathecal midazolam in (group M). The statistical data like Time for Onset of Sensory Blockade, Maximum sensory level, Duration of sensory blockade and Maximum Motor blockade, Total duration of Analgesia and side effects were analysed.

Results: The mean onset of Sensory Blockade is decreased. Duration of Sensory Blockade, Maximum Motor Blockade and Analgesia is increased. No significant complications.

Conclusions: The present study concluded that subarachnoid blockade using midazolam in addition to bupivacaine decreases the onset time of sensory blockade, increase the duration of analgesia and the motor blockade without prolonging the sympathetic recovery or any significant hemodynamic changes.

Keys words: Group B- Bupivacaine group, Group M- Midazolam Group, CSF-cerebrospinal fluid.

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I. Introduction

Regional anesthesia for lower limb and lower abdominal surgeries surgery is held generally to be safer than general anaesthesia. It avoids general anesthesia related problems such as poly-pharmacy, airway manipulation, misplacement of endo tracheal tube, hypo or hyperventilation, vomiting, pulmonary aspiration. It reduces surgical stress and attenuates increase in plasma catecholamine and other hormones. Regional anaesthesia gives intra and postoperative pain relief with full preservation of mental status and normal reflexes. The subarachnoid blockade is the common form of neuraxial blockade performed for lower limb surgeries. The ensuing nerve block ensures the patient well being, while motor block facilitates the surgeon's work. The 0.5% hyperbaric bupivacaine is the most commonly used drug. It produces longer duration of anaesthesia with good muscle relaxation. It provides effective pain relief in initial post-operative period. In order to maximize post operative analgesia, a number of adjuvants have been added to spinal local anaesthetics¹. The subarachnoid midazolam was originally shown to have anti-nociceptive properties in studies performed in animals in early 1980's². The subarachnoid midazolam is being used in humans since 1986 and doses up to 2 mg have been described³. It abolishes pain of somatic origin, produces selective sensory block and blocks somatosympathetic reflexes without any neurotoxicity. The subarachnoid midazolam potentiates the blocking actions of local anaesthetics. It improves the quality of sensory and motor block, without prolonging the recovery.

It also provides prolonged post-operative pain relief without producing sedation^{4,5,6,7,8,9}. The subarachnoid midazolam is also devoid of complications such as, bradycardia, hypotension, post-operative nausea and vomiting, pruritus, urinary retention, and neurotoxicity^{4,5}. The present study was conducted to evaluate the efficacy and analgesic effect of mixture of midazolam-bupivacaine as compared to bupivacaine alone in patients undergoing lower limb and lower abdominal surgeries under subarachnoid block.

II. Materials And Methods

Study design

This study was a prospective cross-sectional study, performed in the department of anaesthesia at a tertiary care centre in Andhrapradesh, India, over a period of two years.

Study population

The present study was conducted on 100 patients of both sexes posted for lower limb and lower abdominal surgeries who were selected by adhering to the inclusion and exclusion criteria.

Inclusion criteria

1. Patients belonging to ASA Grade I and 2
2. Patients of either sex aged between 18 to 60 years.
3. Patients undergoing lower limb and lower abdominal surgeries after written consent.

Exclusion criteria

1. Patients with ASA Grade III and IV physical status.
2. Patients in extremes of age.
3. Patients on chronic analgesic therapy.
4. Patients with gross spinal abnormality, localized skin sepsis, haemorrhagic diathesis, neurological involvement or disease.
5. Patients with peripheral neuropathy.

The study was approved by the institutional ethics committee.

Pre-anaesthetic evaluation:

A detailed history was taken, the general physical examination was performed to record pulse rate, blood pressure, respiratory rate. The cardiovascular, respiratory and central nervous system were thoroughly examined clinically. The back and vertebral column of the patients were examined to rule out any spinal deformity and infection.

Laboratory investigations like complete blood picture, urine routine, blood urea, serum Creatinine, coagulation profile, ECG and chest X-ray chest P/A view, HbsAg and HIV were done.

Procedure:

The patients were randomly allocated by simple randomization into control Bupivacaine group(B) and Midazolam (groupM) + Bupivacaine group(B), each group consisting of 50 patients. On arrival in the operating room, each patient was put on standard monitoring that included ECG, non invasive BP, pulse oximetry (spo₂) and baseline readings were recorded. A suitable intravenous line with 18 G intravenous cannula was secured and preloaded with 500mL of Ringer lactate solution. The patients were then put in lateral position with head, neck, spine, hip and knees flexed and back arched. The hip and shoulder were maintained in vertical plane and patient was brought to the edge of the table.

The following data were collected.

Onset of sensory analgesia

Quality of motor blockade was assessed using modified Bromage scale 1978

Intra-operative period:

After the subarachnoid blockade, all the patients were monitored for pulse rate, blood pressure, respiratory rate, oxygen saturation at 2, 4, 6, 8, 10, 15, 30, 45, 60,90, 120,150,210,240 and 270 minutes intra-operatively and every hour till 4 hours post operatively until the effect of subarachnoid block was disappeared. During the procedure all the patients were infused with appropriate quantity of intravenous fluids. Any untoward side effects were noted like bradycardia and hypotension.

Post-operative period:

The patients were monitored in post anaesthesia care unit.

Duration of sensory blockade

Duration of Maximum Motor blockade

Total duration of Analgesia

Effectiveness of pain relief:

The effectiveness of pain relief in the post operative period was assessed by Visual Analogue Score.

Statistical analysis:

The collected data was analyzed by using Statistical Presentation System Software for windows version10, SPSS 16.0 ; SPSS Inc New York.

The interval data were expressed as Mean and Standard Deviation. The Student’s t-test was used for comparing two groups. Chi-Square test was used for analysis of statistical data. A ‘p’ value less than 0.05 was considered significant for statistical difference.

III. Results

Distribution according to age, sex and number of patients, ASA grading, type of surgeries in both the study groups were comparable(table 1).

Table 1: patient demographics in both group B and group M

	Group B	GROUP M
Number of Patients	50	50
Female/Male	34/16	33/17
Mean age in years±SD	40.14±SD11.6023	49.72±SD11.708
ASA I/II	23/27	21/29
Type of Surgery		
Lower limb orthopaedic	25	25
Lower abdominal	25	25

Table 2: characteristics of subarachnoid blockade and side effects

	Group B	Group M	P-value
Mean duration for onset of sensory blockade	4.62±0.62*	3.62±1.01*	0.000**
Maximum level of sensory blockade	T6/T7	T6/T7	0.0046**
Mean duration for sensory blockade	89.1±2.95*	118.94±10.83*	0.000**
Mean duration of maximum motor blockade	163.3±16.6*	180.24±27.40*	0.0004**
Mean duration of analgesia	125.46±7.18*	243.26±24.41*	0.000**
Time of first voiding	285.56±38.1*	295.06±55.74*	0.3275
Visual analogue score	3.98±1*	3.6±0.6*	0.005**
Side effects			
Bradycardia	3	2	1.86
Hypotension	3	3	
Nausea/vomiting	2	3	

*Data is expressed as mean±standard deviation.

**Statistically significant.

The mean duration for onset of sensory block in group B is 4 to 6 minutes with mean onset time being 4.62 ± 0.62 minutes. In the group M the range for onset of sensory blockade is 2 to 6 minutes with a mean onset time of 3.26±1.01 minutes. The t value is 8.3512 and p value being 0.000 (p<0.05), hence statistically significant.

The above table shows maximum sensory level attained in the group B and group M in different patients . By applying the Chi-Square test, p value 0.0046, hence highly significant. (p<0.005) (figure 1).

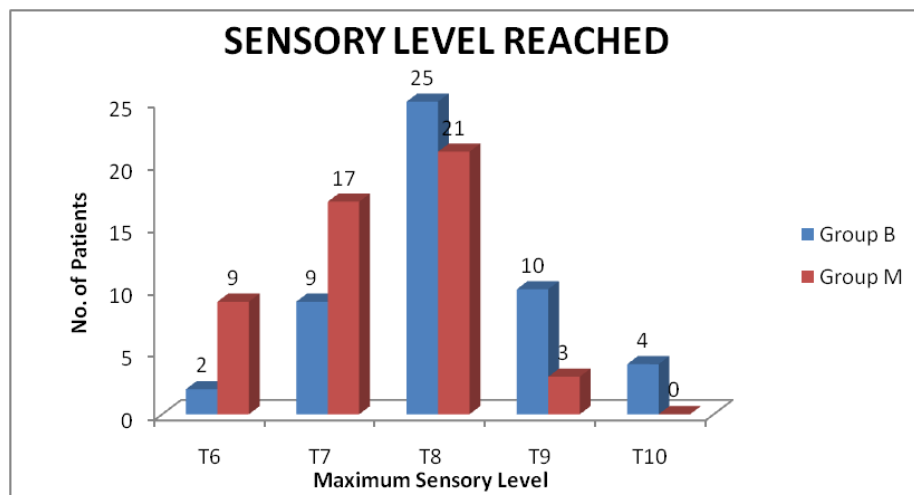
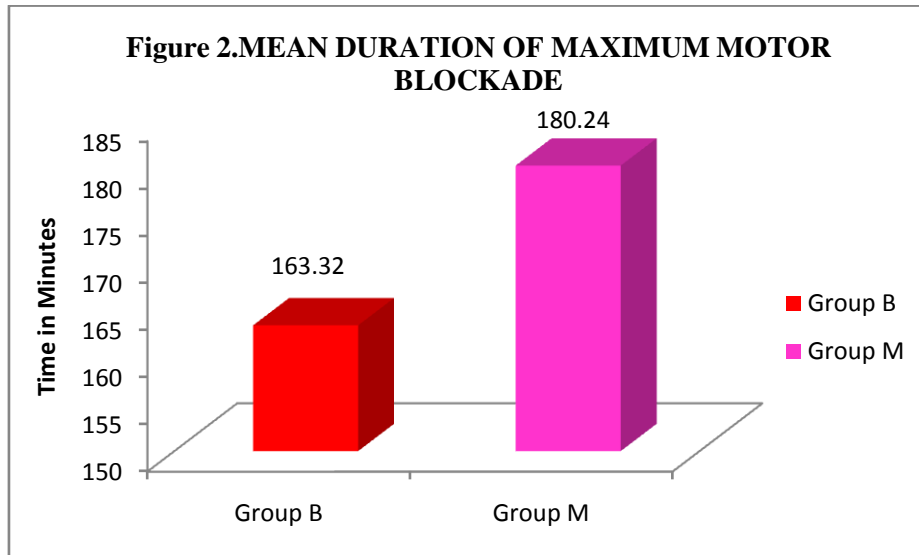


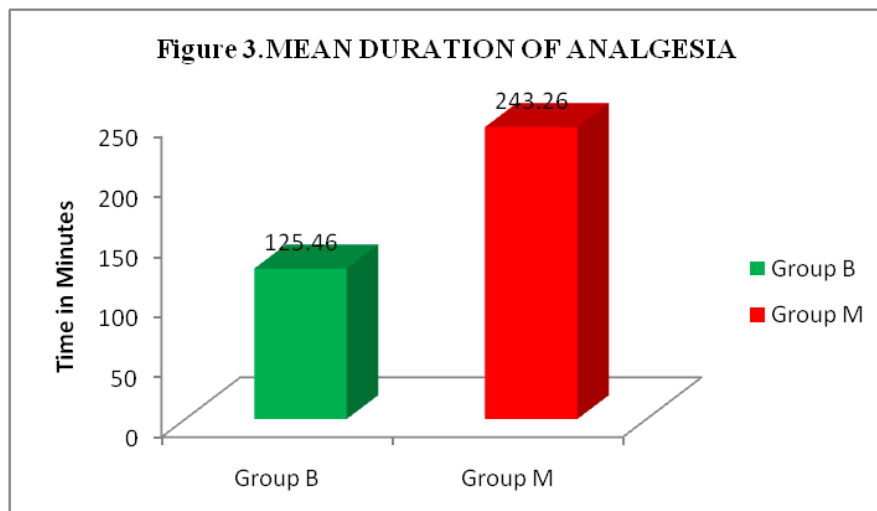
Figure 1. Distribution of highest dermatomal level of sensory block

The mean duration of sensory blockade in group B is 89.1 ± 2.95 minutes whereas in group M it is 118.94 ± 10.83 minutes, $t=18.5918$, $p=0.000$. $p<0.05$ hence statistically significant.

The mean duration of maximum motor blockade in B is 163.3 ± 16.6 with a range being 135 to 210 minutes (figure 2). In group M, the mean duration of maximum motor blockade is 180.24 ± 27.40 minutes with a range being 152 to 245 minutes. $t=3.693$ P value 0.0004. As p value is (<0.05), it is statistically significant.



The above table 2 shows the duration of analgesia in both the groups. In group B, the mean duration of analgesia is 125.46 ± 7.18 minutes with a range of 110 to 142 minutes. In group M, the mean duration of analgesia is 243.26 ± 24.41 minutes with a range of 173 to 273 minutes (figure 3). The duration of analgesia has been increased from 125.46 minutes to 243.26 minutes. $t=-32.4063$ the p value is 0.000 ($p<0.05$), hence statistically highly significant.



The mean duration of first voiding time is 285.56 ± 38.1 minutes in group B and 295.06 ± 55.74 in group M. $t=0.98473$ $p=0.37275$ Since p value is >0.05 , this is statistically not significant.

The Visual Analogue score for effectiveness of pain relief in group B, the mean score is 3.98 ± 1 and in group M, it is 3.6 ± 0.6 . The t value is 2.869 and the p value is 0.005, hence there is statistical significance between them.

Complications

There was no serious complications encountered. In group B, 3 patients had bradycardia, 3 patients had hypotension, and 2 patients had nausea and vomiting. In group M, 2 patients had bradycardia, 3 had hypotension, and 3 patients had nausea. Here $p=1.86$ and hence there is no statistical difference between the groups.

IV. Discussion

The spinal blockade is the common form of neuraxial blockade performed for lower limb and lower abdominal surgeries. The ensuing nerve block ensures the patient well being, while motor block facilitates the surgeon's work. 0.5% hyperbaric bupivacaine produces longer duration of anaesthesia with good muscle relaxation. It provides effective pain relief in initial post-operative period.

In order to maximize post operative analgesia, a number of adjuvants have been added to spinal local anaesthetics. After established safety trails Midazolam has been using from 1982. It had been tried widely and antinociceptive effect with neurological safety had been well established in animals and humans.

The intrathecal benzodiazepine induced analgesia is spinally mediated. The binding sites benzodiazepine molecules are GABA receptors which are abundant in dorsal root nerve cells of spinal cord. The maximum concentration of GABA receptors are found within lamina II of dorsal nerve cells, a region which plays prominent role in processing nociceptive and thermoceptive stimulation. Acting over the GABA receptors benzodiazepines induce changes in chloride conductance and enhance GABA induced presynaptic inhibition of primary afferent terminals.

The present clinical study is a randomized prospective study in 100 patients belonging to age group 18 to 60 years of both the sexes and of ASA Grade I and II who were scheduled to undergo various elective lower limb and lower abdominal surgeries under subarachnoid anaesthesia. The patient group B received 3.0mL of 0.5% hyperbaric bupivacaine and the patient Group M received 3.0mL of 0.5% hyperbaric bupivacaine with 0.2mL (1mg preservative free) midazolam intrathecally.

The result of the present clinical study were discussed under the following headings.

Time of onset of sensory Blockade:

In present study, the time for onset of sensory blockade for the two groups was not statistically significant when compared. In Group B, it was 4.62 ± 0.62 minutes minutes were as in Group M it was 3.26 ± 1.06 minutes, Were p value 0.000 ($p < 0.05$) significant. So the addition of the midazolam to bupivacaine has made apparent difference with regard to time of onset which was similar to Vaswani et al⁶ who reported that the addition of midazolam intrathecally has reduced the onset of sensory blockade from $3'41'' \pm 0.41$ minutes in control group(groupI) to 2.00 ± 0.25 minutes in midazolam group(Group II) ($p < 0.001$).

Maximum level of Blockade:

DERMATOMAL LEVEL	GROUP B		GROUP M	
	NO. OF PATIENTS	% WITHIN GROUP	NO OF PATIENTS	% WITHIN GROUP
T6	2	4	9	18
T7	9	18	17	34
T8	25	50	23	42
T9	10	20	13	6
T12	4	8	0	0

The table shows the maximum level of sensory blockade in both the groups. Maximum level of blockade achieved in more patients of group M than group B. when compared statistically, by applying Chi Square test $p = 0.0046$, Hence it is highly significant.

Duration of sensory blockade:

The study conducted by Batra Y.K et al,¹⁰ showed that the duration of sensory blockade being increased from 229.8 ± 41.4 minutes in bupivacaine group to 267.6 ± 67.38 minutes in midazolam group with p value < 0.05 and thus, being statistically significant.

In the present study the duration of sensory blockade was prolonged from 89.1 ± 2.95 minutes in groupB to 118.94 ± 10.83 minutes in group M and it was found to be statistically significant as p value < 0.05 .

Duration of maximum motor blockade:

The study of Batra et al,¹⁰ on the patients undergoing knee arthroscopy, reported that the mean ambulation time as a measure of complete recovery from motor blockade was 242 ± 30.9 minutes in the bupivacaine group and 258.3 ± 25.4 minutes in Midazolam group($p > 0.05$). This study shows that intrathecal midazolam has no significant effect on motor blockade.

In present study, the duration of maximum motor blockade in group B is 163.3 ± 16.6 with a range of 135 to 210 minutes, and 180.24 ± 27.40 minutes in group M with a range being 152 to 245 minutes. As p value is 0.0004 it is statistically not significant.

The results of our study are consistent with that of Batra et al¹⁰ with respect to maximum duration of motor blockade.

Duration of Analgesia:

Midazolam is a potent short acting benzodiazepine in aqueous solution has been reported to provide antinociceptive effect in animals and in humans.

M.H Kim and Y.M. Lee,⁴ Vaswani et al,⁶ Bharti N et al,⁷ Nidhi Agarwal et al,⁸ Batra Y.K et al,¹⁰ and Anjana Sen. et al.¹¹ and showed that the mean duration of analgesia significantly prolonged in patients receiving intrathecal midazolam.

In present the duration of analgesia was prolonged from 125.46 ± 7.18 minutes in bupivacaine group to 243 ± 24.41 minutes in midazolam group. This is statistically highly significant as p value is 0.000.

Midazolam acts through the GABA receptors which are present in the dorsal horn of spinal cord. Addition of midazolam through epidural intrathecal infusion provides better analgesia, than local anaesthetics, which confirms by A Sen, A Rudra study.¹²

Time for first voiding:

The early trials conducted by Good child and Nobel³ showed that the intrathecal administration of midazolam causes depression of sympathetic nervous system activity in humans.

The study of Batra et al¹⁰ showed no difference in the time of first voiding in control group(252 ± 29.8 minutes) and in study group(258.8 ± 25.4) ($p > 0.05$). Kim et al⁴ reported that time to the episode of first self-voiding(control group: 4.99h, BM1group:4.95h, MB2 group:5.31h), was similar in all groups. The analgesic effect of intrathecal midazolam was segmental, with no alteration in sympathetic tone or reflexes.

In present study, the time of first voiding, when compared with two groups were statistically not significant. The time of first voiding is 285 ± 38.10 minutes in group B and 295.06 ± 55.74 minutes in group M ($p = 0.3275$) ($p < 0.05$ to be statistically significant). The results of our study are consistent with the study of Kim et al⁴ and Batra et al.¹⁰

V. Conclusion

The results of the present study suggests that the combination of inj.midazolam 1mg with inj. bupivacaine 0.5% (hyperbaric). Decreases the onset time of sensory blockade and prolongs the duration of analgesia and the motor blockade, Does not have any significant hemodynamic changes, Does not increases the incidence of complications such as bradycardia, drowsiness, hypotension, post operative nausea and vomiting, urinary retention and neurotoxicity.

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Conflict of Interest: None declared

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