Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(4): 505-511
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5418.1

Comparative Clinical Study of 0.5% Hyperbaric Bupivacaine Alone and 0.5% Hyperbaric Bupivacaine with Midazolam Intrathecally for Lower Limb and Lower Abdominal Surgeries

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Abstract

Aim: 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. *Materials and Methods:* The present study was conducted on 100 patients aged between 18 to 60 years belonging to ASA Grade I and II of both the sexes posted for lower limb and lower abdominal surgeries. *Results:* In 100 patients duration of sensory blockade in both group B and group M. the mean duration of sensory blockade in group B is 89.1±2.95 minutes were as in group M, it is 118.94±10.83 minutes, $p<0.05$, hence statistically significant. ($t = 18.5918$, $p= 0.000$, statistically significant). The mean duration of maximum motor blockade in B is 163.3±16.6 with a range being 135 to 210 minutes. In group M, the mean duration of maximum motor blockade is 180.24±27.40 minutes with a range being 152 to 245 minutes. As p value is 0.0004 it is statistically significant. (T=3.693, P value-0.0004, highly significant). 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. In group B, the mean VAS 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. *Conclusion:* It can be inferred that inj. midazolam 1 mg in combination with inj.bupivacaine 0.5% hyperbaric can be safely administered intrathecally for better postoperative analgesia.

Keywords: Bupivacaine; Midazolam; Intrathecal; Lower Abdominal Surgeries.

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 end 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 centrineuraxial 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 anaesthetics. Morphine prolongs the post -operative analgesia but is associated with major side effects, in particular delayed respiratory depression [1]. The other

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Received on 24.11.2017, **Accepted on** 07.12.2017

adjuvants like clonidine, ketamine have also been tried but none has become established in regular clinical practice because of their adverse effects. The subarachnoid midazolam was originally shown to have anti-nociceptive properties in studies performed in animals in early 1980's [2]. The subarachnoid midazolam is being used in humans since 1986 and doses up to 2 mg have been described [3]. 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].

The subarachnoid midazolam is also devoid of complications such as, bradycardia, hypotension, post-operative nausea and vomiting, pruritus, urinary retention and neurotoxicity. 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.

Methodology

The present study was conducted on 100 patients aged between 18 to 60 years belonging to ASA Grade I and II of both the sexes posted for lower limb and lower abdominal surgeries. The study was conducted at Konaseema institute of medical sciences and research foundation, Amalapuam, Andhra Pradesh during the period of December 2014 to October 2016.

Inclusion Criteria

Patients belonging to ASA grade I and II, Patients of either sex aged 18 to 60 years, patients undergoing lower limb and lower abdominal surgeries.

Exclusion Criteria

Patients with ASA grade III and IV physical status, Patients in extreme age, who had undergone chronic analgesic therapy, with gross spinal abnormality, localized skin sepsis, haemorrhagic diathesis, neurological involvement or disease, patients with peripheral neuropathy.

Pre-Anaesthetic Evaluation

A detailed history was taken from each patient subjected for study. The data such as age, sex, weight, hospital registration number, date of admission were noted. The general physical examination was performed and baseline data i.e., general condition, pulse rate, blood pressure, respiratory rate were recorded. 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 were performed. Tablet Alprazolam 0.5mg on the night before surgery to relieve anxiety. Tablet Ranitidine 150mg on the night before surgery. Informed written consent was taken from the patient. A minimum of 6 hours Nil per oral status was confirmed. The patients were randomly allocated by simple randomization in to control Bupivacaine group(B) and Midazolam (group M) + Bupivacaine group(B), each group consisting of 50 patients.

The monitoring was established with electrocardiography display, pulse oximetry, and non invasive blood pressure. The baseline pulse rate, blood pressure, rate of respiration, oxygen saturation and ECG were recorded in each patient before subarachnoid block.

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.

Bradycardia: A pulse rate of less than 60 beats per minutes was considered as bradycardia and, if any was treated with injection atropine 0.6 mg intravenously.

Hypotension: A systolic blood pressure of less than 90mm Hg or decrease in 30% below the baseline blood pressure was considered as hypotension. It was corrected with rapid infusion of IV fluids, oxygen with face mask, foot end elevation and injection mephentemine 6mg IV was given. Any untoward effects like nausea and vomiting were noted and treated appropriately.

Post-Operative Analgesia

The patients were monitored in post anaesthesia care unit. Duration of sensory blockade, duration of maximum motor blockade, total duration of analgesia.

Sedation Score

0: Wide awake,

1: Sleeping comfortably responding to verbal commands,

2: Deep sleep arousable,

3: Deep sleep not arousable.

The effectiveness of pain relief in the post operative period was assessed by Visual Analogue Score. The patient makes a mark on a 10cm scale horizontal or vertical one end of which is marked as 'No pain' and the other end as 'The worst pain one can image.

The position of the mark on the line measures how much pain the patient experiences. The patients were observed for 24 hours and any post-operative side effects such as nausea, vomiting, head ache, respiratory depression, drowsiness urinary retention and Neurological deficits were noted. 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.

Results

The present clinical study was conducted on 100 patients of either sex belonging to different age group. These patients belonged to ASA grade I or II and underwent lower limb orthopaedic surgeries under subarachnoid anaesthesia. The study was undertaken to evaluate the efficacy of intrathecally administered Inj. Midazolam (preservative free) and 0.5% hyperbaric bupivacaine in improving the quality of anaesthesia and providing post operative pain relief.

The following observations were made during the study. Group B consisted of 50 patients and the drug administered is 3 ml of 0.5% hyperbaric bupivacaine, Group M consisted of 50 patients and the drug administerd is 3 ml of 0.5% hyperbaric bupivacaine and 0.2 ml (1 mg) midazolam.

Age wise distribution in both group b and group M. The minimum age was 19 years and maximum age was 60 years. The mean age in group B is 40.14±11.6023 and group M is 49.72±11.708 years. This table shows sex distribution of the study population. There were 34 male patients and 16 female patients in group B. The group M had 33 male patients and 17 female patients (Table 1).

Time of onset of Sensory Block. t value is 8.3512 and p value being 0.000($p<0.05$), hence statistically significant. Duration of sensory blockade in both group B and group M. the mean duration of sensory blockade $p<0.05$ hence statistically significant. ($t = 18.5918$, $p= 0.000$, statistically significant). The mean duration of maximum motor blockade p value is 0.0004 it is statistically significant. (T=3.693, P value-0.0004, highly significant). The duration of analgesia in both the groups p value is 0.000 ($p<0.05$), hence statistically highly significant. (t=32.4063, P value-0.000, Significant) (Table 2).

Table 1: Demographic distribution

Age in years	Group B	Group M
Below 30	13	18
31-40	14	14
41-50	12	12
51-60	11	6
Mean age in years ± SD	40.14±11.6023	49.72±11.708
Sex (Group)		
Male	34	33
Female	16	17
Maximum Sensory level		
T6	2	9
T7	9	17
T8	25	21
T9	10	3
T10	4	0

Table 2: Variables in study

Onset of Sensory Blockade	Range	Mean	SD
Group –B	4-6	4.62	0.62
Group –M	2-6	3.26	1.01
Duration of sensory blockade (mins)			
Group –B	86-98	89.1	2.95
Group –M	106-140	118.94	10.83
Duration of motor blockade (mins)			
Group –B	135-210	163.32	16.6
Group –M	148-250	180.24	27.40
duration of analgesia			
Group –B	110 to 142	125.46	7.18
Group –M	173 to 273	243.26	24.41

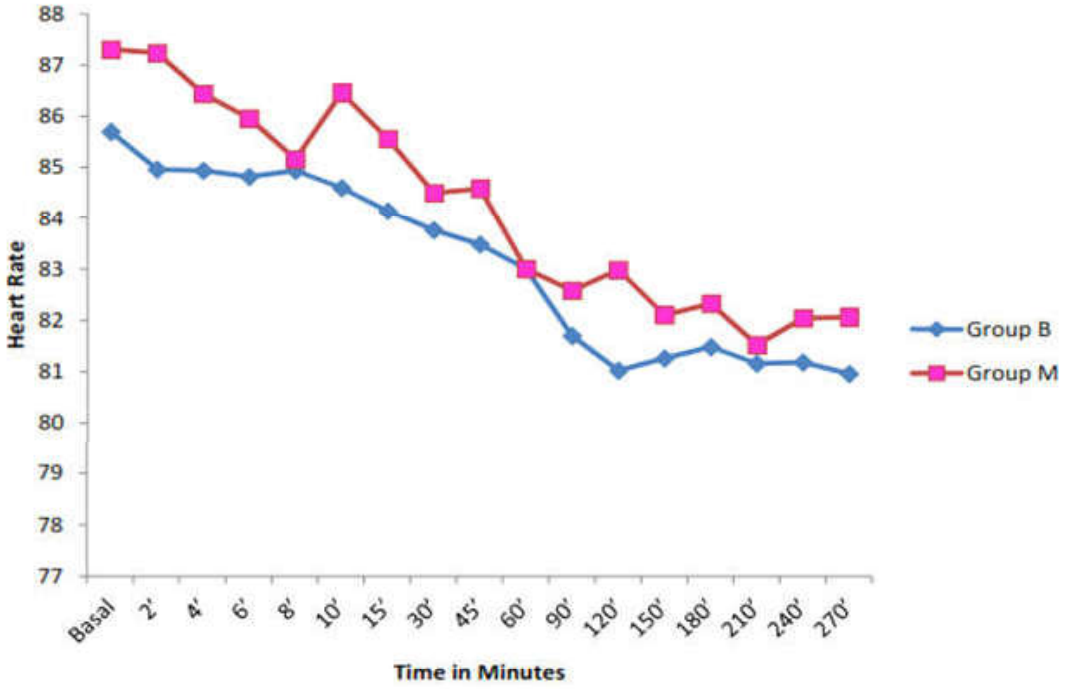

Fig. 1: Heart rate in both groups

Heart rate is not significant in comparision in both groups

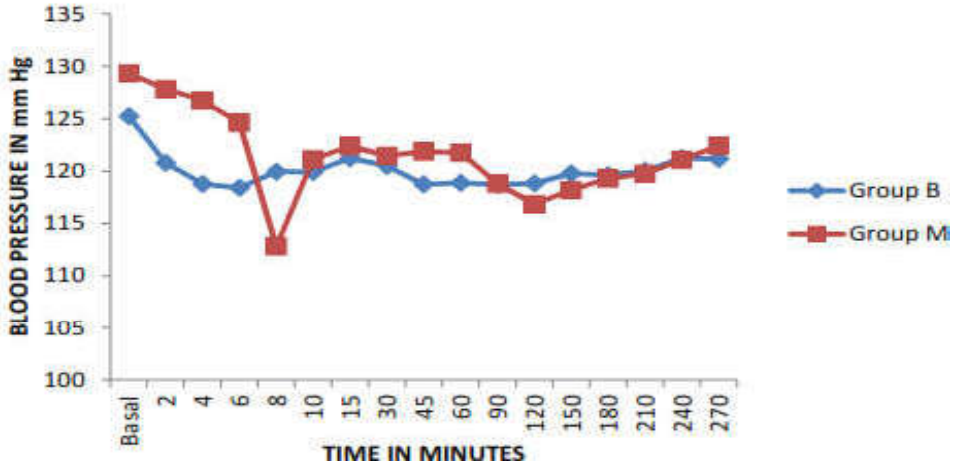

Fig. 2: Mean Systolic blood pressure (mm of Hg).

Systolic blood pressure is not significant in comparision in both groups

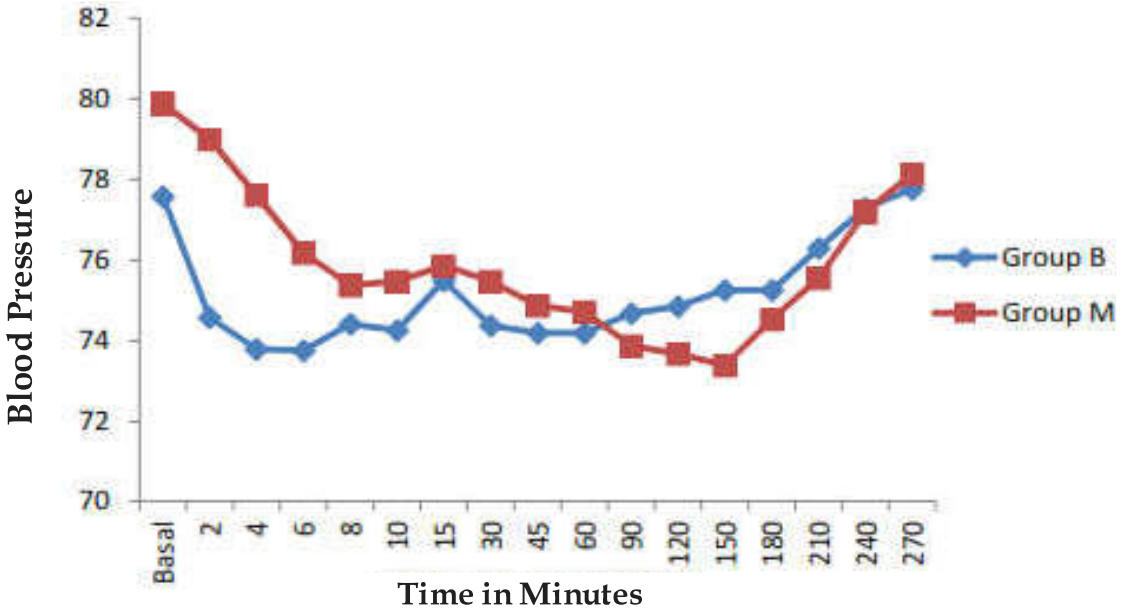

Fig. 3: Mean Diastolic blood pressure (mm of Hg).

Mean Diastolic blood pressure is not significant in comparision in both groups

Table 3: Time of first voiding and VAS score

Group	Duration of first voiding (mins) Range	Mean	SD
B	225-400	285.56	38.10
M	236-410	295.06	55.74
VAS (Scores)			
B	3-5	3.98	1
M	3-5	3.6	0.6

The mean duration of first voiding time is 285.56 ± 38.1 minutes in group B and 295.06 ± 55.74 in group M. Since p value is >0.05, this is statistically not significant. (t=0.98473, p=0.3275, not significant). The Visual Analogue score for effectiveness of pain relief is shown in the table. In group B, the mean VAS 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. The complications (side effects) encountered in the group B and M. 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. (Table 3).

Discussion

The subarachnoid blockade is the common form of centrineuraxial 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. Midazolam is a newer water soluble imidazo-benzodiazepine derivative which has been tried since early 1980's. It had been tried widely and antinociceptive effect with neurological safety had been well established in animals and humans. 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 orthopaedic 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 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.

Vaswani et al [6] have reported that the addition of midazolam intrathecally has reduced the onset of sensory blockade from 3'41''±0.41 minutes in control group (groupI) to 2.00±0.25 minutes in midazlam group (Group II) (p<0.001). The results of present study are consistent with Vaswani et. al. [6] with regards to onset time.

Duration of Sensory Blockade

The study conducted by Batra Y. K et. al. [7] 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 present study the duration of sensory blockade was prolonged from is 89.1±2.95 minutes in group B to 118.94±10.83 minutes in Group M and it was found to be statistically significant as p<0.05. It can be attributed to the lipophilicity of midazolam and its synergism with local anaesthetics. The benzodiazepines and exert their antinociceptive effect at the spinal cord by different mechanism. Midazolam excerts its action through GABA on getting bound, opens ligand gated chloride channels. Chloride conductance is increased leading to hyperpolarisation and presynaptic inhibition of afferent terminal in spinal cord and hence reduction in neuronal activity [4]. Our study consistent with both Batra et. al. [7] with regards to duration of sensory blockade.

Duration of Maximum Motor Blockade

The study of Batra et. al. [8]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 al [7] 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 [8] Anjana Sen. et. al. [9], Batra Y.K et. al. [7], Nidhi Agarwal et al [10] and Bharti N et. al. [11] and Vaswani et. al. [6] 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.

Time of First Voiding

The early trials conducted by Goodchild and Nobel [3] showed that the intrathecal administration of midazolam causes depression of sympathetic nervous system activity in humans. The study of Batra et. al. [7] showed no difference in the time of first voiding in control group (252±29.8minutes) and in study group (258.8±25.4) (p>0.05). Kim et. al. [8] reported that time to the episode of first self-voiding (control group:4.99h, BM1 group: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 Batra et. al. [7] and Kim et. al. [8]. In the present study the sedation score ranged from 0 to 1 in both the groups.

Most of the patients in group M were calm and sleeping comfortably were as most of the patients in the group B were awake and alert. Midazolam is used in a variety of clinical setting for pre and post operative settings for sedation. The studies of have shown that the sedation scores were higher in the patients receiving midazolam the epidural or intrathecal route. Vaswani et. al. 6 reported that sedation was earlier with maximum sedation level of short duration if midazolam is given

intravenously. The sedation scores were less but more sustained when the midazolam is administered intrathecally. Anjana Sen et. al. [9] also reported the higher sedation scores with intrathecal midazolam.

Conclusion

It can be inferred that inj. midazolam 1 mg in combination with inj.bupivacaine 0.5% hyperbaric can be safely administered intrathecally for better postoperative analgesia.

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