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To Compare the Efficacy of Intrathecal Buprenorphine and Midazolam Added as an Adjuvant to 0.5% Bupivacaine (Heavy) in Lower Abdominal Surgeries

Bhavini B. Shah[1], Chhaya M. Suryawanshi[2], Renny Chacko[3], Ashwini Khamborkar[4], Smruti Govekar[4], Payal Gursahani[5]

[1]Associate Professor [2]Professor [3]Consultant [4]2nd Year Resident [5]1st Year Resident, Department of Anaesthesiology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune Dr. D.Y. Patil Vidyapeeth, Pune, Maharashtra 4011018 India.

Abstract

Background: Opioid like Buprenorphine has been widely used as adjuvant intrathecally for providing prolonged post operative pain relief. Their advantages of neuraxial narcotics over systemic narcotics are well established. IntrathecalMidazolam, abenzodiazepine derivative apart from its own analgesic and sedative effect, it potentiate the analgesic effect of Bupivacaine. This study was conducted to compare the efficacy of intrathecal Buprenorphine (150µg) with intrathecal Midazolam (2.5mg) when used as an adjuvant to 0.5% Bupivacaine for lower abdominal surgeries and also to observe any side effects. *Methods:* After approval from hospital ethical committee, 90 patients between the age group of 20-60 years was taken. Informed consent from the patient was taken. All patients from ASA I and ASA II were allotted in three groups of 30 patients each. Group B was given 3.5 ml of 0.5% bupivacaine (heavy) with 150µg (0.5ml) buprenorphine intrathecally. Group M was given 3.5 ml of 0.5% Bupivacaine (heavy) with 2.5 mg (0.5ml) midazolam (preservative free) intrathecally. Group C was given 3.5 ml of 0.5% bupivacaine (heavy) with (0.5 ml) of Normal Saline intrathecally as controlled group Statistical analysis was performed using ANOVA test and T-test. p value < 0.05 was considered significant. *Result:* Onset of sensory and motor is fastest in Midazolam group while Buprenorphine provided prolonged duration of analgesia post-operatively (827.17+67.77 min.) as compared to Midazolam (297.5+33.21min.). *Conclusion:* Addition of Buprenorphine provides prolonged post-operative analgesia compared to other groups but sensory & motor onset is fastest with Midazolam.

Keywords: Intrathecal Bupivacaine; Buprenorphine; Midazolam.

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Introduction

Spinal block is the first choice of anaesthesia for lower abdominal surgeries. The relative short duration of action of local anaesthesia necessitates supplementation of local anaesthesia with adjuvants [1,2] like opioids, benzodiazepines, ketamine or neostigmine.This reduces the dose of local anaesthetics, minimizes the side effects and prolongs the duration of anaesthesia at a relatively lesser cost to the patient [2,3]. Buprenorphine is a mixed agonist-antagonist narcotic with affinity at both µ and κ opiate receptors [4,5] with both spinal & supraspinal component of analgesia [6]. It is lipophilic long acting and 25 times more potent than morphine. Its cost-effectiveness, easy availability and low abuse potential makes it an attractive option to be used as an adjuvant for spinal anaesthesia [6-9].

Corresponding Author: Chhaya Suryawanshi, Professor, Department of Anaesthesiology, Dr. D.Y. Patil Medical College and Hospital, Dr. D.Y. Patil Vidyapeeth, Pimpri, Pune – 411018.
E-mail: drbhavinishah71@gmail.com

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Midazolam is a short acting, potent, water soluble benzodiazepine [10]. It has been used for potentiating the analgesic effect of local anaesthetic induced neuraxialblockade. The possible mechanism for the antinociceptive action of midazolam is through benzodiazepine/gamma aminobutyric acid- A receptor present in lamina II of dorsal horn of the spinal cord [11].

Therefore we conducted this study to compare the efficacy characteristics and quality of intrathecal buprenorphine and midazolam when added as an adjuvant to hyperbaric bupivacaine for sub-arachnoid block in lower abdominal surgeries.

Materials and Methods

After approval from the hospital ethical committee and informed written consent, this study was carried out in Department of Anaesthesiology, Dr. D.Y. Patil Hospital and Research Centre, Pune.

Ninty (90) patients aged 20-60 years of either sex, weighing 40-70 kg of ASA I and II scheduled for lower abdominal surgeries were included in our study.

Patient having contraindication to regional anaesthesia, opioid dependence, H/O drug allergy and abuse, coagulation disorder and any other major systemic illness were excluded from the study. After detailed pre-anaesthetic evaluation, routine and specific investigation, each patient was informed regarding nature, purpose of the study and visual analogue score (0-no pain, 10-maximum pain). Pre-operative adequate fasting hours (6-8 hrs) were confirmed. Patients were not pre-medicated with any sedative and analgesics. Baseline vital parameters i.e. Pulse Rate (PR), Blood Pressure (BP), Respiratory Rate (RR) and Oxygen Saturation (SpO_2) were recorded.

Patients were randomly allocated into three groups.

Group B- patient were given 3.5 ml of hyperbaric bupivacaine 0.5% along with 150µg (0.5 ml) of Buprenorphine intrathecally.

Group M- patient were given 3.5 ml of hyperbaric bupivacaine 0.5% along with 2.5 mg of (0.5 ml) Midazolam preservative free intrathecally.

Group C- patient were given 3.5 ml of hyperbaric bupivacaine 0.5% along with 0.5 ml of Normal saline intrathecally.

Multipara monitor was attached for monitoring of vitals. All patients were preloaded with 10-15 ml/kg of body weight with Ringer Lactate. All patients were pre-medicated with inj. Ondansetron 4 mg and inj. Ranitidine 100 mg IV prior to spinal anaesthesia. Under all aseptic precautions, lumbar puncture was performed at the level of L3-L4 interspace with 26 G Quincke's spinal needle. The mixture of the drugs according to assigned group was injected intrathecally in a lottery method.

The segmental sensory level of anaesthesia was assessed by patients response to pinprick and motor block was assessed by using modified Bromagescale. PR, BP, RR and SpO_2 were noted every 5 min for first 30 min, every 15 min for next 30 min, at the end of surgery, post-operative and at the time of motor block wear off.

Observations were made at

T0- Time of spinal anaesthesia

T1- Time of onset of sensory block

T2- Time of onset of motor block

T3- Time of peak sensory block

T4- Time of two segment regression

T5- Time of wearing off motor block

T6- Time of first dose of post-operative rescue analgesia

In the intra operative period, patient were closely monitored for pulse rate, blood pressure, respiratory rate, and O_2 saturation. Any side effects such as hypotension, bradycardia, shivering, respiratory discomfort were noted and treated with appropriate drugs. Patients were assessed for quality of sedation and scoring was done with Campbell sedation score as

1. Wide awake
2. Awake and comfortable
3. Drowsy and difficult to arouse
4. Not arousable

Residual sensory blockade was monitored and its wearing off time was noted. Residual motor blockade was monitored and its wearing off time was noted when patient started to lift his legs against the gravity. Patient were monitored for the degree of pain with visual analogue score (VAS). Post-operative rescue analgesiaInj. Diclofenac 75mg IM was given when VAS score was >7 and the time of injection of first analgesic drug noted. This was taken as the time of wearing off of analgesia.

Demographic characteristics, hemodynamic parameters, onset, peak and duration of sensory, motor block and duration of post-operative analgesia, level of sedation were compared between all three groups and data was analyzed. Statistical analysis were carried out with using SPSS software version

10 by ANOVA test. p value < 0.05 was considered significant.

Result

The patient characteristics shown in the Table 1, there was no significant differences in the three groups (p value > 0.05).

As shown in table 2 the time for onset of sensory (16.6±2.95 seconds) and motor block (36.87±3.74 seconds) is fastest in midazolam group compared to control and buprenorphine group.

Peak sensory block is also fastest in midazolam group (149.53±16.8 seconds) compared to buprenorphine and control group.

Average two segment regression timewas significantly prolonged in buprenorphine group (164.17±15.87 min) than control group (130.17±9.69min) and midazolam group (112.43±8.06min) (p value < 0.0001).

Midazolam group had the fastest motor wear off (250.83±9.57min) followed by control (251.67±14.82 min) and buprenorphine group (288.67±15.59min) (p value <0.0001)

Mean time for post operative analgesia was significantly longer in buprenorphine group (827.17±67.77min) followed by midazolam group (297.5±33.21 min) and control group (144.5±26.69 min) (p value < 0.001).

Graph 1,2,3 compares the heart rate, systolic and diastolic blood pressure in all three groups at different time intervals.

There was significant difference in pulse rate when compared to baseline in control and midazolam group. But in buprenorphine groupit was observed only at 0 & 5 min.

As shown in Graph 2, 3 there was a significant difference in systolic & diastolic blood pressure when compared to baseline in control & midazolam group but in buprenorphine group significant difference in systolic blood pressure when compared to baseline only at 5, 20, 25 minutes and in DBP only at 25, 60 min. and at end of surgery.

More patients from buprenorphine and midazolam group showed sedation score of 2 or 3 as shown in Table 5.

There was no significant difference in RR and SpO_2 among all three groups.

Table 1:

Parameter	Control mean (SD)	Buprenorphine mean(SD)	Midazolam mean (SD)	P value
No. of patients	30	30	30	
Age (yrs)	36.87+/- 12.77	39.96+/- 9.83	37.77+/- 14.46	>0.05
Height (cm)	164.33+/- 5.85	164.93+/- 5.03	162+/- 5.38	>0.05
Weight (kg)	63.47+/- 7.09	64.4+/- 3.38	64.87+/-5.10	>0.05
Gender (M:F)	14:16	13:17	13:17	
ASA I : ASA II	28:2	23:7	24:6	

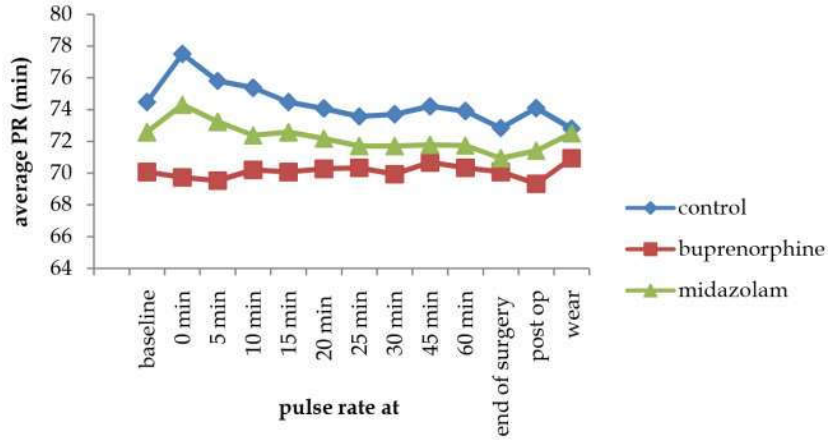
Table 2: Compares time of onset and peak of sensory and motor blockade in all three groups

Parameter	Control group (n =30) Mean+/-SD	Buprenorphine (n=30) Mean +/- SD	Midazolam (n=30) Mean +/- SD	P value
Time in seconds for onset of sensory blockade (T1)	21.97+/- 4.33	24.17+/-5.27	16.6+/-2.95	<0.0001
Time in seconds for onset of motor blockade (T2)	41.97+/-4.82	44.77+/-8.29	36.87+/-3.74	<0.0001
Time in seconds for peak sensory blockade (T3)	169.5+/-9.39	154+/-11.86	149.53+/-16.86	<0.0001
Time in minutes for two segment regression(T4)	130.17+/- 9.69	164.17+/-15.87	112.43+/-8.06	<0.0001
Time in minutes for motor wear off(T5)	251.67+/-14.82	288.67+/-15.59	250.83+/-9.57	<0.0001
Time for first rescue analgesia in minutes (T6)	144.5+/-26.69	827.17+/-67.77	297.5+/-33.21	<0.0001

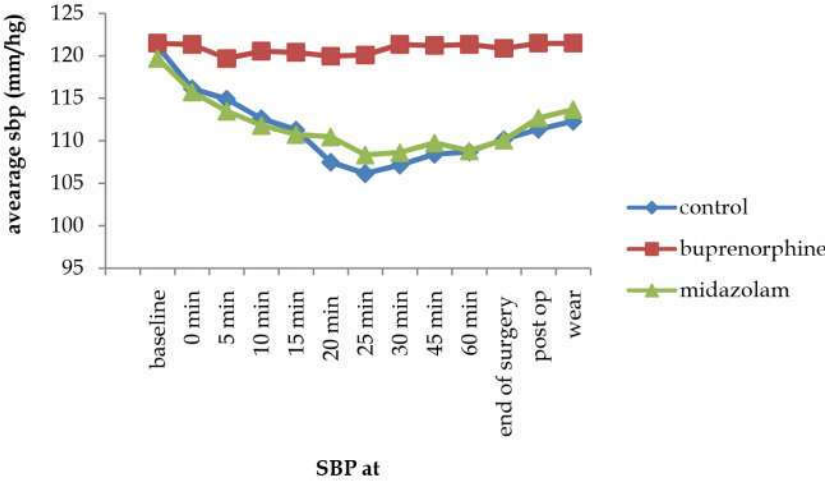
Table 3: Shows the incidence of complicationsin all three groups which were not serious enough to warrant any intervention. There was no morbidity

Side Effects	Control (n=30)	Buprenorphine (n=30)	Midazolam (n=30)
Bradycardia	3(10 %)	0 (0 %)	3 (10%)
Hypotension	7 (23.33 %)	0 (0 %)	3 (10%)

Graph 1:



Graph 2:



Graph 3:

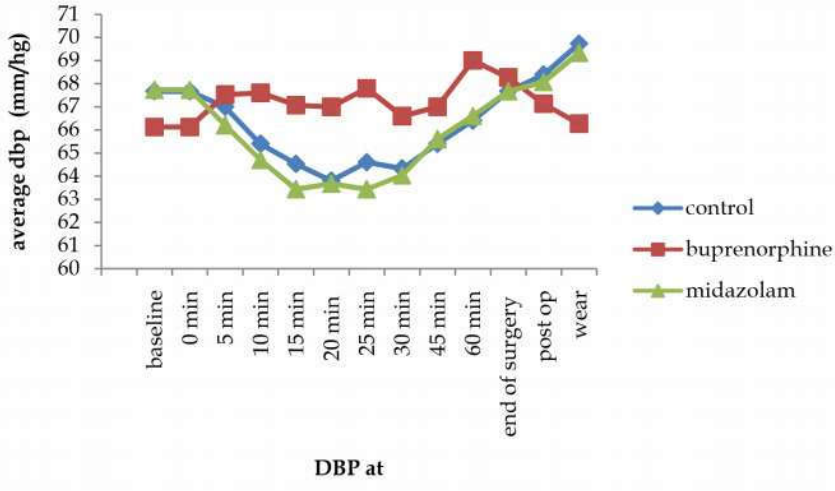


Table 4: Sedation score

Sedation score	Control (%)	Buprenorphine (%)	Midazolam (%)	Total
Wide and awake	20 (22.22)	1 (1.11)	0 (0)	21 (23.33)
Awake and comfortable	10 (11.11)	17 (18.89)	18 (20)	45 (50)
Sedated and arousal	0 (0)	12 (13.33)	12 (13.33)	24 (26.67)
Not arousable	0	0	0	0
Total(4)	30 (33.33)	30 (33.33)	30 (33.33)	30 (33.33)

Discussion

The goal of post operative pain management is to reduce an individual patients pain to a tolerable level with the minimal or no associated suffering or distress. Any method of postoperative analgesia must be simple, clinically appropriate and evidence based [11].

The discovery of opioid receptors in the brain & spinal cord started new era in the field of postoperative analgesia [12,13]. Post-operative pain is most commonly been managed with intra muscular or intra venous opioid analgesics alone or in combinations with the conventional NSAIDs, but they are associated with adverse effects so there clinical utility is limited [14].

The first clinical use of opioids was by Wang et al. and since then, the use of opioids like buprenorphine was found to be more beneficial as a single intrathecal injection produces pain relief of sufficient duration [15].

Both midazolam and buprenorphine if used as an adjuvants with intrathecal bupivacaine are safe and prolongs intraoperative and postoperative analgesia. Present study was designed to directly compare these two drugs for their efficacy, quality of blockand safety. To compare the efficacy we used the duration of effective analgesia measured by time in minutes for requirement of rescue analgesia. For quality of block we used time of onset and peak sensory and motor effects in seconds.

In our study midazolam group had fastest onset of sensory, motor as well as peak sensory than control & buprenorphine group. Similar finding was obtained in Bharati et al. studies [16] and Sajedi [17] studies.

In 2007, Gupta et al. [18] investigated the effect of intrathecal midazolam 2.5mg. as an adjuvant to bupivacaine in lower limb orthopedic surgeries. They concluded that intrathecal 2.5 mg midazolam provided moderate prolongation of postoperative analgesia when used as an adjunct to bupivacaine

In our study we found duration of analgesia was significantly higher in buprenorphine group (827±67.77 min) than in midazolam group (297.5±33.21 minutes) and control group (144.5±26.69 minutes). Similar, effect was found in Caproga [19] and Lanz et al. study [20]. Yet another study by Sapkal Pravin et al., duration of analgesia with buprenorphine was over 800 min. similar results were reported by Dixit & Shah et al. [21,22,23,24].

In consistency to our result above studies also found both drugs to be effective as adjuvants to intrathecal bupivacaine prolonging the duration of analgesia.

In our study, the side effects observed were bradycardia, hypotension, sedation and pruritis as shown in Table 3.

Bradycardia was observed in three patients in control and midazolam group each of which was managed with inj. Atropine 0.6mg I.V.

Hypotension was observed in 7 patients from control group and 3 patients midazolam group which was managed with inj. Mephentermine 6mg I.V.

Bradycardia and hypotension was not observed with buprenophine group.

Nausea and vomiting is one of the most distressing side effect of intrathecal buprenorphine which was prophylactically managed with inj. Ondansetron 4 mg I.V.

Urinary retention could not be assessed as allpatients were catheterized for 24 hours postoperatively.

Limitations of the Study

Since the pain is subjective phenomenon associated with varied individual responses, it is difficult to assess and quantify the pain and this may lead to somebias in the study.

Conclusion

Addition of midazolam to hyperbaric bupivacaine result in faster onset of sensory and motor blockade provides post-operative analgesia for 5-6 hours.

Addition of buprenorphine 150microgram intrathecally to hyperbaric bupivacaine provides a better hemodynamic stability and post-operative analgesia for 13-14 hours and it allows calm, sedated but arousable patients without risk of respiratory depression with stable haemodynamic and minimal side effects.

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Conflict of Interest: None

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