A COMPARATIVE STUDY OF INTRATHECAL BUPIVACAIN AND BUPIVACAIN WITH MIDAZOLAM IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES- A PROSPECTIVE RANDOMISED DOUBLE BLINDED STUDY

Chhaya Joshi¹*, Vinod Hosalli², Anilkumar Ganeshnavar³

Abstract
Background & Objectives:
This study was conducted to compare the differences in the onset, duration of action and complications of intrathecal hyperbaric bupivacaine 0.5% (group I) and intrathecal hyperbaric bupivacaine 0.5% with midazolam 2.5 mg (group II) in lower abdominal and lower limb surgeries

Materials and Methods:
Hundred patients belonging to ASA grade – I and Grade-II (each group, n=50) were randomly selected for the study. The patient and anesthesiologist administering the drug were blinded for the study. The time of onset of sensory and motor block, hemodynamic status, time for two dermatomal segments regression of sensory level, time of first request of analgesics, visual analogue score and adverse effects were compared.

Results:
The time of onset of sensory and motor block was significantly longer in group-II than group-I (P<0.001). Hemodynamic changes did not differ in patient of either group (P>0.05). The time for two dermatomal segments regression of sensory level (group-I 81.50±5.41 minutes and group –II 118.00± 4.80 minutes) were statistically longer in group II (P<0.001). The time of first request of analgesics by the patient in group-I was 208.00±7.55 minutes and in group II was 367.90±8.89 minutes which was statistically significant (P<0.001). The VAS scores were significantly less in group-II at 3 hours (p<0.001), 6 hours (P<0.001) and 12 hours (P<0.001) compared to group-I. The side effects were minimal in both the groups.

Conclusion:
Intrathecal administration of 2.5 mg of midazolam in combination with hyperbaric bupivacaine 0.5% produces better quality of analgesia, longer duration of analgesia, with mild sedation and minimal side effects thus reducing post operative analgesic requirement.

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Keywords: Bupivacaine, Intrathecal, Midazolam, Visual analogue score

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INTRODUCTION
Spinal anesthesia is unparalleled in the way a small mass of drug, virtually devoid of systemic pharmacologic effect, can produce profound, reproducible surgical anesthesia.

The main reasons for the popularity of spinal block are that the block has well defined end points and the anesthesiologist can produce the blocks reliably with a single injection.[1]

The versatility of spinal anesthesia is afforded by a wide range of local anesthetics and additives that allow control over the level, the time of onset and the duration of spinal anesthesia. The distribution of local anesthetic solutions within the subarachnoid space determines the extent of the neural blockade produced by spinal anesthesia.

Spinal anesthesia with hyperbaric bupivacaine 0.5% is a popular method. Addition of opioids to local anesthetics is very commonly practiced. Though the opioids reduce the toxicity and cardiovascular effects of local anesthetics this type of combinations may bring about additional undesirable side effects including itching, nausea and vomiting along with respiratory depression. Instead, there are many clinical studies favouring intrathecal midazolam since it produces sedation, amnesia and antinociceptive effects without any neurotoxicity or other side effects. Hence this study was designed to evaluate the efficacy, to know the duration of pain relief and to know the incidence of adverse effects and complications when midazolam is given along with bupivacaine intrathecally.

MATERIALS AND METHODS:
After obtaining written and informed consent 100 patients of ASA (American Society of Anaesthesiologist) grade 1 and 2, aged 18-60 years undergoing elective and emergency operative procedures under spinal anesthesia for lower abdominal and lower limb surgeries were prospectively enrolled for the study.. This was a double blinded controlled study where neither the patient nor the observer who recorded the parameters was aware of the group allocation and the drug received. The study was approved by the hospital’s ethics committee. Patients with severe systemic disease, metabolic disorder, neurological, congenital or cardiovascular disease were excluded from this study.

On the eve of the surgery all the patients were visited and detailed pre-anesthetic examination including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous systems and examination of spine for deformity, infection was carried out. The anesthetic procedure was briefly explained to the patient.

Routine investigations like haemogram, total leucocyte count, differential leucocyte count, ESR, complete urine examination, random blood sugar, electrocardiogram, chest x-ray, blood grouping, blood urea, serum creatinine were done.

The patients were also introduced to the Visual Analogue Scale (VAS) and were taught how to use it.

Patient’s weight and height was also recorded.

Once the patient was shifted to the operating room, the patient was attached to the routine monitors including sphygmomanometer, pulse oximeter and electrocardiogram.

All resuscitation equipments like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, ephedrine, mephentermine were kept ready. The anesthesia machine was also checked along with the oxygen delivery system.

Patients were categorized into two groups;

Group-I: 50 patients receiving 3ml of hyperbaric bupivacaine 0.5%
Group-II: 50 patients receiving 3ml of hyperbaric bupivacaine 0.5% with 0.5 ml (2.5mg) of midazolam.
Base line pulse rates, blood pressure, respiratory rate, SPO2 were recorded. The patients were then put in left lateral position. Under strict aseptic precautions, lumbar puncture was performed by midline approach by using disposable quincke-babcock spinal needle 25G at L3–L4 intervertebral space.

Patients were continuously monitored using sphygmomanometer, pulse oxymeter and electrocardiogram.

After spinal anesthesia, the patient’s pulse rate and blood pressure were recorded at 0, 5, 10, 20, 30, 45, 60, 90 and 120 minutes.

Visual Analogue Scale:
Since the perception of pain is highly subjective, this variable was standardized by using data from visual analogue scale.

First advocated by Revill and Robinson in 1976, VAS consists of a 10cm line anchored at one end by a label such as no pain and at the other end by a label such as the ‘Worst pain Imaginable’ or ‘Pain as bad as can be’. The patient simply marks the line to indicate the pain intensity and the provider then measures the length of the line to mark on a point scale.

The side effects of intrathecal midazolam like nausea and vomiting, hypotension, respiratory depression, shivering, pruritus, motor weakness and seizures are noted.

RESULTS
The effect of hyperbaric bupivacaine 0.5% (n-50) and hyperbaric bupivacaine 0.5% with midazolam 2.5 mg intrathecally was compared in 100 patients belonging to ASA grade-I and II, posted for elective lower abdominal and lower extremity surgeries.

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Figure 1: Perioperative systolic blood pressure of the patients at different time intervals

Figure 2: Perioperative diastolic blood pressure at different time intervals

Figure 3: Heart rate of the patients perioperatively in both the groups

Figure 4: Onset of sensory blockade (seconds) in either groups. The difference between the groups was statistically highly significant (P<0.001).

Figure 5: Onset of motor blockade (seconds) in either groups.

Figure 6: Two dermatomal segments regression of sensory level (minutes) The difference between the groups was statistically highly significant.
Spinal anesthesia is the most commonly used regional technique. Local anesthetics commonly used for this purpose have various side effects and have less duration of analgesia. There is a need for an adjuvant which increases the duration of analgesia without increasing the duration of motor blockade, thus prolonging post operative analgesia, reducing post operative analgesic requirements. Of all the agents used intrathecal midazolam almost meets the above requirements. The principal mechanism by which intrathecal midazolam provides analgesia is through the GABA-Benzodiazepine system in the spinal cord. This prospective study was conducted to compare intrathecal bupivacaine and bupivacaine with midazolam in lower abdominal and lower limb surgeries. The patients were selected at random, to avoid any kind of bias and to allow comparability of results obtained. This was a double blinded controlled study where neither the patient nor the observer who recorded the parameters was aware of the group allocation and the drug received. The patients studied across the group did not vary much with respect to age, sex , height and the type of surgeries. In the present study, the incidence of hypotension was equal in both groups with 4 patients had a fall in blood pressure in group-I and 4 patients in group-II of the study. Hypotension was corrected by administration of...
injection mephentermine 6mg IV in incremental doses, giving IV fluids and raising the foot end side of the operating table to facilitate venous return. Heart rate, systolic and diastolic blood pressure in both the groups did not vary significantly. Goodchild CS, Noble J in 1987[2], Bahar M and et al 1997[3], Batra Y.K and et al in 1999[4] and Bharti N and et al in 2003[5] found no difference in the hemodynamic responses to the drugs used correlating with the present study. From the above studies we can conclude that use of 2.5 mg of midazolam along with bupivacaine causes no gross hemodynamic disturbances. None of the patients in the present study had respiratory depression (Respiratory depression RR < 10 breaths/min, SPO2< 90%). Bahar M and et al in 1997[3] found no changes in the arterial blood gases or respiratory rate when given intrathecal midazolam in animal model. Sen A and et al in 2001[6] observed that intrathecal midazolam 2mg and 5% lignocaine 1.5 ml produces better tranquility of patients of caesarian section delivery without much sedation and respiratory depression. Apgar score of baby in 1st and 5th minute of delivery was found to be normal. Bharti N and et al in 2003[5] studied the effect of intrathecal 1mg of midazolam with hyperbaric bupivacaine in patients undergoing lower abdominal surgery and found no change in oxygen saturation. The above observations were similar to our study results. We conclude that intrathecal midazolam 2.5 mg is safe to use without causing respiratory depression. It can be safely used in pregnant patients. In the present study the onset of sensory blockade in group-I was 149.50± 14.01 seconds compared to 170.40 ± 11.61 seconds in group-II which was statistically highly significant (P< 0.001). It shows that addition of midazolam to local anesthetic delays the onset of motor blockade. Yegin A and et al 2004[7] have found in their study that addition of 2mg of midazolam to hyperbaric bupivacaine in spinal anesthesia does not delay onset of sensory and motor blockade compared to hyperbaric bupivacaine alone in patients undergoing perianal surgery. From the above study we conclude that there is variation in the onset of sensory and motor blockade in different studies. Though it is statistically significant in our study it does not have any clinical implications. In the present study, the two segment regression of sensory level in group-I was 81.50 ± 5.41 minutes compared to 118.00 ± 4.80 minutes in group-II which was statistically highly significant (P<0.001). This shows that addition of midazolam increases the duration of sensory blockade. Bharti N and et al in 2003[5] found that duration of sensory block (ie., time to regression to S¬2 segment) was significantly longer in the midazolam group than the control group (218 min vs 165min, P< 0.001). Thus we can conclude that intrathecal midazolam increases the duration of sensory blockade. In the present study, the duration of motor blockade in group-I was 181.20±5.88 minutes compared to 198.20 ± 29.63 minutes in group-II which was statistically highly significant (P<0.001). This shows that addition of midazolam potentiates the motor blockade provided by bupivacaine. Bharti N and et al in 2003[5] showed that the duration of motor block was prolonged in the midazolam group as compared with the control group (P< 0.01) and they also showed that in 90% of the patients in the midazolam group the quality of block was adequate during the intraoperative period as compared with only 65% of the patient in the control group (P<0.05). Yegin A and et al in 2004[7] found no statistically significant differences in recovery time of motor blockade in group-I (hyperbaric bupivacaine 0.5% 2ml) and group-II (Hyperbaric bupivacaine 0.5% 2ml + 1ml of 2mg midazolam). From the above studies we conclude that there is variation in the duration...
of motor blockade but the intensity of motor blockade is definitely better in the midazolam group. Though the duration of motor blockade has statistically highly significant result it has no clinical relevance. In the present study, the time of first request of analgesics in group-I was 208.00±7.55 minutes compared to 367.90±8.89 minutes in group-II which was statistically highly significant (P<0.001). This shows that there was significantly longer period of analgesia with intrathecal midazolam. Kim MH and et al in 2001[8] found significantly greater time to first analgesia in the midazolam group in patients undergoing haemorrhoidectomy. Amr M and et al in 2003[9] showed the time required for first postoperative analgesic intake was prolonged when 25 mg preservative free fentanyl or 2mg preservative free midazolam is added to 0.5% heavy bupivacaine in patients undergoing knee arthroscopy. Yegin A and et al in 2004[7] studied the effect of intrathecal midazolam and hyperbaric bupivacaine in comparison to hyperbaric bupivacaine alone and found significantly longer time until the first dose of additional analgesic requirement in midazolam group. Valentine J.M. J and et al in 1996[10], Bharti N and et al in 2003[5], Shah FR[11] and et al in 2003 found prolonged duration of postoperative pain relief in midazolam group. Thus we can conclude that intrathecal midazolam along with bupivacaine prolongs the duration of analgesia thus prolonging the first request of supplemental analgesics in the post operative period.

Visual Analogue Score:

In the present study, there is significant reduction in the visual analogue score of the patients in group-II in comparison with higher VAS in group-I recorded at 3 hours, 6 hours and 12 hours of spinal anesthesia. Shah FR and et al in 2003[11] showed that patients treated with intrathecal midazolam had better pain relief judged by visual analogue score on coughing (P=0.0013) and a nursing mobility score (P<0.0001). Yegin A and et al in 2004[7] found significantly lower visual analogue pain scores in midazolam group at the first 4 hours. Valentine J.M. J and et al in 1996[10], Sen A and et al in 2001[6] Bharti N and et al in 2003[5], Amr M and et al in 2003[9] found significantly decreased frequency of postoperative analgesic intake in those receiving intrathecal midazolam. From the above studies we can conclude that intrathecal midazolam potentiates the sensory blockade of bupivacaine, there by reduce the visual analogue scores in the early post operative period bringing about better post operative outcome.

Adverse Effects:

In the present study, 4 patients had hypotension, 2 patients had shivering and 3 patients had nausea vomiting in group-II compared to 4 patients of hypotension, 3 patients of shivering and 2 patients of nausea vomiting in group-I. This signifies that adverse effects are minimal with intrathecal midazolam.


With all the above observations we conclude that addition of midazolam to bupivacaine provides prolonged analgesia, superior pain relief and better sedation with minimal side effects compared to bupivacaine alone in spinal anesthesia.

CONCLUSION

On the basis of the study, one can draw the conclusion that intrathecal administration of 2.5 mg of midazolam in combination with 0.5% hyperbaric bupivacaine produces better quality of analgesia and sedation without gross hemodynamic disturbances compared to
bupivacaine alone in lower abdominal and lower limb surgeries. The main advantages are its superior quality and longer duration of analgesia, reduced post operative analgesic requirements with minimal side effects.

REFERENCES