Efficacy and potency of intrathecally administered bupivacaine and bupivacaine with midazolam in lower limb surgery at Ahmadabad, India

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Abstract

Background and Aim: Many drugs have been used for spinal anaesthesia in lower limb surgery e.g. Lignocaine, bupivacaine, ropivacaine etc. Bupivacaine is still considered as a standard drug as far as therapeutic and side effect profile is concerned. The aim of present study to evaluate efficacy and potency of intrathecally administered bupivacaine and bupivacaine with midazolam on sensory and motor blockade, hemodynamic stability, side effects and post operative pain relief in lower limb surgery.

Methods: A randomized controlled study was conducted on 50 patients aged 20-70 years at AMC MET Medical College, Ahmadabad, Gujarat, India. Patients were scheduled for lower limb surgeries after taking informed consent. Patients who were selected and posted for surgeries were randomly allocated in two groups. Group A received 3 ml (15 mg) hyperbaric bupivacaine 0.5% plus 0.2 ml 0.9% saline and Group B received 3 ml (15 mg) hyperbaric bupivacaine 0.5% plus 0.2 ml (1 mg) preservative free midazolam. Duration of surgery for each case was noted. Pain measurement was done using VAS scale.

Results: No statistically significant difference in duration of surgery was observed between the two groups. Difference between time to onset of sensory block and time to achieve maximum block height was not statistically significant between two groups ($P > 0.05$) maximum level of sensory block in both groups was between $T_6 – T_{10}$.

Conclusion: Addition of preservative free midazolam to intrathecal bupivacaine prolongs sensory blockade and postoperative analgesia without increasing motor blockade and any adverse effects.

Keywords: Ahmadabad, Anaesthesia, Bupivacaine, Midazolam, Surgery

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Introduction

It is universally agreed that the anesthesia of choice for lower limb surgeries is subarachnoid block. Regional anaesthesia is generally well tolerated by all patients, producing less post-operative complications like confusion and delirium than general anaesthesia. It is also associated with lesser incidence of post-operative thromboembolism. However, subarachnoid block has got its own inherent complications, especially related to cardiovascular stability.[1]

Many drugs have been used for spinal anaesthesia in lower limb surgery e.g. Lignocaine, bupivacaine, ropivacaine etc. Bupivacaine is still considered as a standard drug as far as therapeutic and side effect profile is concerned.

The adjuvant's action is directed towards decreasing sensory input to central nervous system. Their site of action is different from that of local anaesthetic agent.

"Pain" is an unpleasant sensory and emotional experience associated with actual / potential tissue damage or described in terms of such tissue damage. Many factors modify pain. Goal of pain management is to eliminate pain with minimum side effects. One of the modality is neuraxial anaesthesia.[2]

Neuraxial anaesthesia suppresses the nociceptive transmission at the 1st synaptic relay in the spinal cord. It greatly expands anaesthesiologist's armamentarium and provides alternative to general anaesthesia.

It blunts "neuroendocrine" stress response to surgery, reduces the risk of aspiration in the patient with full stomach, preserves spontaneous respiration, reduces intraoperative blood loss and provides excellent muscle relaxation.[1,3]

Discovery of benzodiazepine receptors in the spinal cord triggered the use of intrathecal Midazolam as an adjuvant to local anaesthetic. Midazolam produces an analgesic action through the benzodiazepine gamma-aminobutyric acid (GABA-A) complex in the spinal cord. Previous pre-clinical studies have demonstrated that midazolam either intrathecally or epidurally produces a dose dependent modulation of pain and not associated with neurotoxicity, respiratory depression or sedation.[4]

The aim of present study to evaluate efficacy and potency of intrathecally administered bupivacaine and bupivacaine with midazolam on sensory and motor blockade, hemodynamic stability, side effects and post-operative pain relief in lower limb surgery.

Material and Methods

A randomized controlled study was conducted on 50 patients **(ASA grade I- A normal healthy patient or II-**

A patient with mild systemic disease) aged 20-70 years at AMC MET Medical College, Ahmedabad, Gujarat, India. Patients were scheduled for lower limb surgeries after taking informed consent. Ethical clearance was taken from the institutional ethics board.

All the patients were evaluated pre-operatively and laboratory investigations complete blood count, blood sugar, renal function tests, serum bilirubin, serum electrolytes and chest x-ray, ECG was reviewed.

Exclusion Criteria:

- Patient's age less than 20 years and above 70 years.
- Pregnant patients.
- Infection at site of block.
- History of allergy to local anaesthesia drug.

Patients who were selected and posted for surgeries were randomly allocated in two groups. Group-A: 0.5% heavy bupivacaine 3 ml (15 mg) + 0.9% normal saline 0.2 ml.

Group-B: 0.5% heavy bupivacaine 3 ml (15 mg) + preservative free midazolam 0.2 ml (1 mg).

The rate of giving bupivacaine is according to Ben-David B at al[5].

Procedure

In all the patients, under strict aseptic and antiseptic precautions, lumber puncture was performed after giving local anaesthesia with a 26G needle, using a 23-gauge Quincke is point needle positioned midline at the L3-L4 interspace.

Group A received 3 ml (15 mg) hyperbaric bupivacaine 0.5% plus 0.2 ml 0.9% saline and Group B received 3 ml (15 mg) hyperbaric bupivacaine 0.5% plus 0.2 ml (1 mg) preservative free midazolam. Injected total volume for both groups was 3.2 ml. After completion of injections the patients were immediately returned to the supine position and time of injection was noted.

Sensory block was assessed by the loss of sensation to pinprick. Time to onset of sensory block, maximum level of sensory block achieved and time to achieve maximum sensory block were noted in minutes. Sensory level in between T6-T10 was achieved. Time from subarachnoid injection to second sacral dermatome (S_2) was assessed by pinprick and recorded in minutes (T_1).

Motor block was assessed by Modified Bromage score.[6]

Grade 0: Free movements of legs and feet with ability to raise extended leg

Grade 1: Inability to raise extended leg and knee flexion is decreased, but full flexion of feet and ankles is present.

Grade 2: Inability to raise leg or flex knees, but flexion of ankle and feet is present.

Grade 3: Inability to raise leg, flex knees or ankle or move toes

Time for onset of grade-3 motor blockade was noted. Total duration of grade-3 motor blockade was noted. Pulse, BP, SPO2 and RR were recorded on 5, 10, 20, 30, 45, 60 and 90 minutes after giving spinal anaesthesia. Sedation levels were assessed using the observer's Assessment of Alertness/ Sedation (OAA/S) scale as used by Chernik et al. Duration of surgery for each case was noted. Pain measurement was done using VAS scale.

Statistical Analysis

Statistical analysis was done using the SPSS software. **Data were first categorized in to nominal and ordinal and then intergroup comparison was done. Data were analyzed using paired 't' test as well as comparing mean and standard deviation.** A 'p' value < 0.05 was taken as significant.

Results

Table 1: Demographic characteristics

Demographic Data	Group-A (mean±SD)	Group B (mean±SD)
Age (years)	40.96±13.28	43.64±14.49
Height (cms)	163.44±4.56	163.16±5.08
Weight (kg)	63.4±7.16	61.92±7.30

The patients in both groups were comparable with respect to their age, height and weight

Table 2: Distribution of sex

Sex	Group A	Group B
Male	20	20
Female	5	5
Total	25	25

Above table shows equal distribution of males and females in both groups.

Table 3: ASA Grades

ASA Grade	Group A	Group B
I	20	20
II	5	5

Above table shows ASA grades.

Table 4: Duration of surgery

	Group A (mean±SD)	Group B (mean±SD)
Duration of surgery (min)	104.6±23.74	101.4±21.65

No statistically significant difference in duration of surgery between the two groups (p>0.05).

Table 5: Preoperative vital parameters

	Group A (mean±SD)	Group B (Mean±SD)
Pulse (beats per min)	88±10	85.6±11.3
BP (SBP/ DBP mmHg)	127.36±10.16 / 80.72±7.4	127.76±8.12 / 79.92±5.46
Respiration Rate (per min)	16.12±1.60	16.72±2.0
SPO_2 (%)	98.26±0.66	98.4±0.63

The above table shows that both the groups were comparable with regards to preoperative vitals – pulse, blood pressure, respiratory rate and SPO_2.

Table 6: Characteristics of sensory blockage

	Group A (mean±SD)	Group B (mean±SD)
Time to onset of block (min)	7.2±1.14	6.64±0.97
Time to achieve highest level of block (min)	11.4±1.54	10.76±1.36
S_2 regression time (T_1) (min)	207.8±17.3	229.4±18.77

Difference between time to onset of sensory block and time to achieve maximum block height was not statistically significant between two groups ($P > 0.05$) maximum level of sensory block in both groups was between $T_6 – T_{10.}$

Time to regression of sensory block to S_2 dermatomal level (T_1) was significantly prolonged in Group B than Group A, which was statistically significant, (p value < 0.05)

1 mg (0.2 ml, 5 mg/ ml) preservative free midazolam was chosen along with 15 mg (3 ml, 0.5%) bupivacaine heavy for current study which produced longer sensory regression time And Perioperative hemodynamic stability.

No significant difference was observed in vital parameters during intraoperative period in both groups. Oxygen saturation and respiratory rate remain relatively constant in both groups. It was also noted that use of intrathecal midazolam did not increase rate of perioperative complication.

Our findings also suggest that intrathecal midazolam did not increase rate of perioperative complication like urinary retention, nausea vomiting, hypotension, bradycardia, shivering, respiratory depression.

Discussion

Primary objective of this study was to evaluate the efficacy of intrathecal bupivacaine and intrathecal bupivacaine plus preservative free midazolam in lower limb surgery. Intrathecal midazolam has been shown to have analgesic properties and potentiates the effects of intrathecal local anaesthetics. The mechanism by which midazolam provides analgesia has been explored in several studies. Good child CS et al[7]studied that intrathecal midazolam is involved in the release of an endogeneous opioid acting at spinal delta receptor. Edward M[8], Serrao et al[9] observed that antinociception actions of intrathecal midazolam are mediated via BZD/ GABAA receptor complex which are abundantly present in dorsal horn of spinal cord.

1 mg (0.2 ml, 5 mg/ ml) preservative free midazolam was chosen along with 15 mg (3 ml, 0.5%) bupivacaine heavy for this study. Kim M.H and Lee YM studied that 1-2 mg intrathecal midazolam is rare and efficacious.[10]

In this study, different types of surgical cases were selected and randomly allocated in the two groups. Both the groups were comparable with regards to age, height, weight, ASA grading and gender ratio. There was also no statistically significant difference between the two groups regarding duration of surgery ($p>0.05$). Preoperatively there was no significant difference in mean pulse rate, BP, RR and SPO2 between both groups.

No statistically significant difference was found between two groups regarding time to achieve maximum block height ($p>0.05$).

Similar to present study Gupta et al[11] reported no significant difference between the two groups regarding time to onset of sensory block and time to achieve maximum block level. Maximum level of sensory block achieved was T6 – T10 in both group. Time taken for regression of sensory block to second sacral dermatome (S2) was significantly longer in Group B than in Group A ($p<0.05$). Batra et al[12] who found that L5-S1 regression time was longer in Midazolam group as compared to Bupivacaine group.

There is no statistically significant difference was found between two groups regarding duration of motor blockade. Similar to our study, B. K. Shadangi and Pandy R[13] in June 2011 studied that the addition of preservative free midazolam to bupivacaine intrathecally resulted in prolonged postoperative analgesia without increasing motor block.

No significant difference was observed in vital parameters during intraoperative and postoperative monitoring between the two groups. N Bharti R. Madan et al[14], also reported no significant difference in mean pulse rates, blood pressures, oxygen saturation and respiratory rate.

Mean time to first rescue analgesic drug was significantly prolonged in Group B ($p<0.001$). Effective analgesia was significantly prolonged in Group B than Group A. Similar to our study duration of postoperative analgesia was found increased in study by Kim M.H. and Lee Y.M[9]. They found that addition of 1 or 2 mg of intrathecal midazolam prolonged the postoperative analgesic effect of bupivacaine by approximately 2 hours and 4.5 hours respectively, compared with controls.

Conclusion

In the present study, we observed that addition of 1 mg preservative free midazolam to intrathecal 15 mg (3 ml) hyperbaric 0.5% bupivacaine produces. Longer sensory regression time, Perioperative hemodynamic stability, No significant adverse effects, prolonged postoperative analgesia without increasing motor block. Addition of preservative free midazolam to intrathecal bupivacaine prolongs sensory blockade and postoperative analgesia without increasing motor blockade and any adverse effects.

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