



A COMPARATIVE STUDY OF INTRATHECAL BUPIVACAINE WITH FENTANYL AND BUPIVACAINE WITH MIDAZOLAM IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES

Anesthesiology

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ABSTRACT

Background: Various adjuvants are being used with local anaesthetics in spinal anaesthesia for prolongation of intraoperative and post-operative analgesia. Fentanyl is a lipophilic μ receptor agonist opioid, neuraxial adjuvant compared with Midazolam, Benzodiazepine used as Neuraxial adjuvant with Bupivacaine.

Aim- To compare and evaluate the onset and duration of sensory and motor blockade, Haemodynamic effect, post-operative Analgesia and adverse effects of fentanyl and Midazolam given intrathecally with hyperbaric 0.5% bupivacaine.

Materials And Methods: 100 patients belonging to ASA Grade-I and Grade-II of both sexes (each group 50 patients, n= 50) were selected for the study. Group-F received 3 mL of 0.5% Hyperbaric Bupivacaine with 0.5 mL (25 micrograms) of Fentanyl. Group-M received 3 mL of 0.5% hyperbaric Bupivacaine with 0.5 mL (25 mg) of Midazolam. The time onset of sensory and motor block, Haemodynamic status, time for two dermatomal segments regression of sensory level to L2 dermatome, time of first request of analgesics, visual analgesic score and adverse effect were compared in both the groups. Data obtained were tabulated and analysed using statistical package for social science (SPSS 16.0 evaluation version). Descriptive data are presented as mean $\pm$ SD. The difference between variables were calculated by student's 't' test and chi square test at 5% level of significance.

Results: Patients in Fentanyl group (Group F) had a significantly longer sensory and motor block than patients in Midazolam group (Group M). The mean time of sensory regression to L2 was (172.30 $\pm$ 5.08 min) in Group F and (147.30 $\pm$ 8.71 min) in Group M. The regression time of motor block to reach Bromage 0 was (201.20 $\pm$ 29.63 min) in Group F and (183.20 $\pm$ 5.88 min) in Group M. The time to rescue analgesia was significantly longer in Group F (381.67 $\pm$ 38.9 min) as compared to Group M (226.67 $\pm$ 15.2 min).

Conclusion: Intrathecal administration of 25 microgram of fentanyl in combination with hyperbaric Bupivacaine 0.5% produces better quality of Analgesia, longer duration of Analgesia with mild sedation and minimal side effects compared to Intrathecal administration of 2.5 mg of Midazolam in combination with hyperbaric Bupivacaine 0.5%.

KEYWORDS

Bupivacaine, Fentanyl, Midazolam, Spinal Anaesthesia.

INTRODUCTION

Subarachnoid blockade is the most commonly used regional anaesthetic technique for lower abdominal surgery. Spinal block is easy to perform, economical and produces rapid onset of anaesthesia. One of the main disadvantages of spinal anaesthesia is its limited duration of action and hence lack of post-op analgesia. A number of adjuvants such as clonidine, fentanyl and others have been studied to prolong the effect of spinal anaesthesia.^{1,2} Fentanyl is a highly lipophilic μ -receptor. Opioid agonist as an adjuvant to hyperbaric bupivacaine in spinal anaesthesia provides good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.^{3,4} We decided to compare the clinical efficacy of intrathecal Fentanyl versus Midazolam when added to hyperbaric Bupivacaine and to evaluate the effect of each on the duration, quality of spinal block, adverse effect and complications.

MATERIALS AND METHODS

A randomised, comparative study was carried out at Netaji Subhash Medical College and Hospital, Bihta, Patna, Bihar. Patients belonging to ASA class I and II, aged 18 - 60 years scheduled for lower limb and lower abdominal surgeries under spinal anaesthesia were enrolled in the study. Patients with h/o uncontrolled hypertension, allergy to the study drug, heart block/dysrhythmias, contraindication for spinal anaesthesia and failure of spinal block were excluded from the study. Based on the results of the study by Naina et al³ and taking a error of .025 and a error of .05, the sample size was calculated. The sample size came to 30 in each arm. Since the study duration was for a period of one year from March 2020 to February 2021, we have included all the patients who gave written consent and fulfilling the criteria during the study period. The sample size came to 100. The study subjects were divided into 2 groups (50 subjects in each arm) based on simple randomisation without replacement. All the subjects who picked even numbers were administered drug F and who picked odd numbers were administered drug M.

All patients were examined and investigated a day prior to surgery and

were familiarised with visual analogue scale (VAS).⁵ They were advised fasting for 6 hours and received alprazolam 0.5 mg the night before surgery.

In the operation theatre, pulse oximetry, electrocardiogram and non-invasive blood pressure were attached and baseline parameters were recorded and monitoring was initiated.

Intravenous access was secured and all patients were preloaded with ringer lactate 10 mL/kg. Under all aseptic precautions, patients in sitting position, lumbar puncture was performed at L3-L4 interspace using 26-Quincke spinal needle. Patients were randomly divided into 2 groups with 50 patients in each group.

Group M- Received 3.0 mL volume of 0.5% hyperbaric bupivacaine and 0.5 mL (2.5 mg) of Midazolam.

Group F- Received 3.0 mL volume of 0.5% hyperbaric bupivacaine and 0.5 mL (25 micrograms) of Fentanyl.

Patients were made supine following the block and oxygen 5 L/min were given through a face mask. The onset and the duration of sensory block, highest level of sensory block, time to reach the highest dermatome level of sensory block, motor block onset, time to complete motor block recovery and duration of spinal anaesthesia were recorded.

The onset of sensory block was defined as the time between injection of drug and the absence of pain to pinprick to highest dermatome level. Then testing was conducted every 10 mins until the point of 2 segment regression of the block was observed. The motor level was assessed according to modified Bromage scale.

Grade 0

The patient is able to move hip, knee and ankle.

Grade 1

Patient is unable to move the hip, but is able to move the knee and ankle.

Grade 2

Patient is unable to move the hip and knee, but is able to move the ankle.

Grade 3

Patient is unable to move the hip, knee and ankle.

Vitals were recorded at 1, 2, 3, 4, 5, 10, 15, 20, 25, 30 mins and subsequently every 30 mins. Hypotension defined as a decrease of systolic blood pressure more than 30% from baseline and was treated with IV bolus of 6 mg Ephedrine and IV fluids as required. Bradycardia defined as heart rate < 50 bpm was treated with IV atropine 0.6 mg. The incidence of nausea and vomiting and sedation were recorded.

Sedation was assessed by modified Ramsay sedation scale-

1. Patient anxious and agitated or restless.
2. Patient co-operative, oriented and tranquil.
3. Responds to verbal commands while sleeping.
4. Exhibits brisk response to light glabellar tap or loud noise while sleeping.
5. Sluggish response to light glabellar tap or loud noise while sleeping.
6. No response to light glabellar tap or loud noise while sleeping.

Post-operatively, the regression time for sensory and motor block were recorded in a post anaesthesia care unit along with the vital signs and Visual Analogue Scale (VAS) score. Any patient showing VAS more than or equal to 3 was given diclofenac intramuscularly as rescue analgesia. All durations were calculated considering the time of spinal injection as time zero. Patients were discharged from PACU after sensory regression to S1 dermatome and Bromage 0.

Data obtained were tabulated and analysed using Statistical Package for Social Science (SPSS 16.0 evaluation version). Descriptive data are presented as mean and SD. The comparison was studied using the chi square test or Fisher's test as appropriate with a 'p' value reported at the 95% confidence interval. P < 0.05 was considered statistically significant.

RESULTS

The groups were comparable with respect to age, height, weight and ASA physical status (Table 1). The characteristics of block and regression time are summarised in (Table 2).

Table 1 : Demography

Variables		Group M	Group F
Age (in years)	Mean	43.37	41.93
	SD	5.149	7.643
	Range	30.56	28.60
Height (cm)	Mean	159.9	160.7
	SD	5.252	5.563
	Range	146-170	148-170
Weight (kg)	Mean	60.40	61.13
	SD	7.587	10.187
	Range	43.75	43.90

Table 2 : Characteristics Of Block

Variables	Group M (Mean±SD)	Group F (Mean±SD)	p-value
Onset of Sensory Block in secs.	165.40±11.61	144.50±14.01	<0.001
Onset of Motor Block to Bromage in secs.	242.80±11.53	220.14±42.71	<0.001
Time for Injection to Highest Sensory Level	12.53±1.2	10.97±1.2	<0.001
Time for two segment Regression (in mins)	81.50±5.41	118.00±4.80	<0.001
Time for sensory Regression to L2 segment (in mins.)	147.30±8.71	172.30±5.08	<0.001
Time (in mins) for complete Motor Recovery	183.20±5.88	201.20±29.63	<0.001
Rescue Analgesia (in mins)	226.67±15.20	381.67±38.09	<0.001

The onset time of block, both sensory up to T10 dermatome and motor to Bromage 3 scale was rapid in the Group F (144.50 ± 14.01 min and 220.14 ± 42.71 min) in comparison with Group M (165.40 ± 11.61 min

and 242.80 ± 11.53 min), P-value < 0.05. There was no difference between Group F and M in the highest level of block achieved. Block regression was significantly slower with the addition of Intrathecal Fentanyl (Group F) as compared with Group M, as both time to two segment regressions and time to L2 segment regression were significantly slower with intrathecal Fentanyl, P-value < 0.05. The regression of motor block to Bromage 0 was significantly slower in Group F (201.20 ± 29.63 min) compared to Group M (183.20 ± 5.88 min), P-value < 0.05. The time to rescue analgesia was significantly longer in Group F (381.67 ± 38.9 min) as compared to Group M (226.67 ± 15.20 min).

There was no significant difference in the mean value of heart rate and mean arterial pressure in the first hour after performing the spinal anaesthesia and the first hour in the PACU between the two groups. The sedation score was more in Group M patients (3.4 ± 0.3), which was statistically significant. The SPO2 was higher than 95% in all patients either in the intraoperative or in the PACU time. 24 hours and 2 weeks followup did not show neurological impairment related to spinal anaesthesia such as back, buttock or leg pain, headache or any neurological deficit.

DISCUSSION

Different agents such as magnesium sulphate, phenylephrine, clonidine has been used as adjuvant for prolonging the duration of spinal anaesthesia. Administration of fentanyl intrathecally is an established method for intraoperative anaesthesia and to supplement postoperative analgesia.⁶ The spread of fentanyl after administration into cerebrospinal fluid include movement from the cerebrospinal fluid into the opioid receptors or other non-specific binding sites in the spinal cord⁷ and rostral migration via the cerebrospinal fluid to supraspinal sites. Because of the high affinity of fentanyl with nonspecific binding sites on the lipid surface, only a small proportion of the administered dose migrates to the cervical region.

BN Biswas et al studied that 12.5 µg of fentanyl added to 2 mL of 0.5% bupivacaine for subarachnoid block would markedly improve intraoperative anaesthesia,⁸ and reduced the demand for postoperative analgesic. We had the same results in our study.

Nocioception action of Midazolam⁹ is well documented. RLM Faull et al showed that spinally mediated analgesia and the segmental analgesia produced by intrathecal midazolam is mediated by the benzodiazepine-GABA receptor complex. They demonstrated that benzodiazepine-GABA receptor were distributed consistently in similar fashion in the grey matter of cervical, thoracic and sacral regions of the spinal cord.

Goodchild and Noble in 1987 observed that 0.3 - 2 mg of intrathecal midazolam¹⁰ interrupts somatic nociceptive afferent pathway of pain. However, it did not significantly block the abdominal visceral nociceptive afferent pathway of pain.

Waldvogel et al investigated the regional, cellular and subcellular distribution of GABA, GABA receptors¹¹ and benzodiazepine receptors. The results showed a close correspondence in the regional distributions of GABA, GABA (GABA-A and GABA-B) receptors and benzodiazepine receptors. The most significant side effect reported about the use of intrathecal Fentanyl is pruritus, but in our study it was not significant.

Better quality of Anaesthesia was noted with the intrathecal Fentanyl group as compared with Intrathecal Midazolam group as Opioid receptors were abundant than GABA receptors in spinal cord.

CONCLUSION

Intrathecal Fentanyl supplementation of spinal block produces earlier onset and prolonged duration of sensory and motor block without associated significant haemodynamic alterations as compared with Midazolam as adjuvant to spinal bupivacaine in lower limb and lower abdominal surgeries.

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