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A COMPARATIVE STUDY OF THE EFFECTS OF INTRATHECAL MIDAZOLAM(1MG) AND FENTANYL(25 MICROGRAMS) AS ADDITIVES TO INTRATHECAL HYPERBARIC BUPIVACAINE 0.5%(15MG) IN SPINAL ANAESTHESIA

Anasthesiology

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ABSTRACT

Background: Various intrathecal additives are added to local anesthetics to increase the speed of onset, improve the quality, and prolong the influence of spinal anesthesia. Midazolam has a synergistic effect on postoperative analgesia when administered intrathecally with bupivacaine. Opioids such as fentanyl are extensively used as an adjunct to local anesthetics in neuraxial blockade to enhance the duration of postoperative analgesia. **Aim:** The aim of our study was to compare the effects of intrathecal midazolam(1mg) and fentanyl (25 micrograms) as additives to intrathecal hyperbaric bupivacaine 0.5% (15mg) with spinal anesthesia. **Materials and Methods:** Prospective, observational study was conducted at SRI SIDDHARTHA MEDICAL COLLEGE AND RESEARCH INSTITUTE,TUMKUR. from 1st Jan 2021 to 30th June 2022 on 94 patients. **Results:** In Bupivacaine and Midazolam group, mean duration of surgery was 84 ± 12.3 minutes and in Bupivacaine and Fentanyl group, mean duration of surgery was 92 ± 14.4 minutes. In Bupivacaine and Midazolam group, mean time for onset of sensory block was 7.1 ± 0.9 minutes and in Bupivacaine and Fentanyl group, mean time for onset of sensory block was 6.9 ± 1.1 minutes. In Bupivacaine and Midazolam group, mean time for onset of motor block was 7.6 ± 1.3 minutes and in Bupivacaine and Fentanyl group, mean time for onset of motor block was 8.1± 1.2 minutes. In Bupivacaine and Midazolam group, mean duration of sensory block was 213.6 ± 16.1 minutes and in Bupivacaine and Fentanyl group, mean duration of sensory block was 218.3 ± 19.2 minutes. **Conclusion-** The onset of sensory and motor blockade was comparable in Fentanyl with Bupivacaine and Midazolam with Bupivacaine. Additional of intrathecal Fentanyl prolonged the duration of analgesia significantly than that of Midazolam. There was significantly less consumption of rescue of analgesia among patients with Fentanyl with Bupivacaine than Midazolam with Bupivacaine. The duration of postoperative analgesia was also significantly prolonged in the fentanyl and midazolam groups.

KEYWORDS

Intra thecal midazolam, Intra thecal fentanyl, Bupivacaine, spinal anesthesia.

INTRODUCTION

The central neuraxial blockade is one of the most important and most commonly used regional anesthetic techniques for lower abdominal, perineal and lower limb surgeries. There has been growing emphasis on the advantages of combined pharmacological approach for pain relief. Discovery of analgesic effects of spinally administered opioids and other drugs such as benzodiazepines and alpha-2 adrenoreceptor agonists has opened the possibilities of optimizing on useful drug interactions at the level of spinal cord in the management of pain.

Though high dose of bupivacaine provides sensory and motor block, it is also associated with high incidence of hypotension and poor neonatal outcomes. On the other hand, low dose bupivacaine is associated with inadequate anesthesia despite low incidence of hypotension.

Low dose bupivacaine with adjuncts such as fentanyl or midazolam provides adequate anesthesia with stable hemodynamics. (1)By administrating intrathecal combinations of drugs, targeting different spinal cord receptors; prolonged and superior quality analgesia can be achieved by relatively small concentrations of individual drugs. The dose reductions may avoid drug-related side effects. In addition, the simultaneous targeting of several different receptor sites in the spinal cord may lead to improved pain relief. (2)

Fentanyl is the most commonly utilized short-acting opioid in intrathecal injections with local anesthetics. It improves the status of intraoperative and postoperative analgesia by acting synergistically with local anesthetics. The advantage of the use of opioids like fentanyl to facilitate effective postoperative analgesia is well documented in the literature.

Inclusion criteria:

- ASA grade 1 and 2 patients
- Age group of 18 –60 years.
- Patients giving valid informed consent.
- Those patiente scheduled to undergo elective lower abdominal, lower limb, gynaecological and urological surgeries under subarachnoid block.

Exclusion Criteria:

- Patients belonging to ASA grade 3 and grade 4
- Patients physically dependent on narcotics
- Patients with history of drug allergy
- Patients with gross spinal abnormality
- Patients with localized skin sepsis.
- Patients with hemorrhagic diathesis.
- Patients with neurological involvement/diseases.
- Patients with Head injury case.
- Patients with cardiac, pulmonary, hepatic (or) renal disorders.
- Patients having inadequate subarachnoid blockade and who are later supplemented by general anaesthesia and obstetric cases for lower segment caesarean section because of drug dosage discrepancy.
- Patients not willing to participate in the research.

Materials required:

1) Multiparameter monitor with electrocardiogram, pulse oximetry, End tidal carbon dioxide monitoring and noninvasive blood pressure.
2) 25G spinal needle
3) Inj. bupivacaine heavy 0.5%
4) Inj.Midazolam
5) Inj. fentanyl
6) Anaesthesia work station.

Methodology:

- After the approval of institutional ethical clearance committee,
- 94 ASA I and II patients undergo elective lower abdominal, lower limb, gynaecological and urological surgeries under subarachnoid block will be selected for study.
- Time of onset of sensory blockade, the height of sensory blockade, motor blockade as per Bromage scale, total duration of sensory blockade and motor blockade.
- Quality of analgesia (visual analogue score), two segment sensory

regression time, time to first rescue analgesic and rescue analgesics in 24h.

Parameters Measured:

- Heart rate(beats/min)
- Systolic blood pressure(mmHg)
- Diastolic blood pressure(mmHg)
- Mean arterial blood pressure (mmHg)
- End tidal CO2 (mmHg)

Preparation of Patient:

- Patients will be advised overnight fasting – 6hrs for solids, 4hrs for semisolids and 2hrs for liquids. All patients will be given T.Alprazolam 0.5 mg and T.Ranitidine 150 mg on the previous night of surgery.
- On arrival to operating room, IV line will be cited, and lactated ringer solution will be infused 4–6 ml/kg/h.
- All patients will be monitored with non-invasive blood pressure(BP),lectrocardiograph (ECG), pulse oximeter (SpO2) before induction of general anesthesia (GA), capnography for end-tidal CO2(ETCO2).
- Under all aseptic precautions after putting the patient in left lateral position, using25-guage Quincke spinal needle, spinal block will be performed at lumbar third and fourth interspace through a midline approach and the patient will be put to supine position. Patients in Group A will receive 3 ml of 0.5% hyperbaric bupivacaine (15mg) with 25 µg of fentanyl. Patients in Group B will receive 3 ml of hyperbaric 0.5% bupivacaine (15mg) with midazolam (1 mg).
- The vital signs were recorded at time 0, 2, 5 min, then every 10 min for first hour and half-hourly until the end of surgery.

OBSERVATION AND RESULTS

Tab. 1: Age distribution

Age groups	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
18 – 20 years	4	3	Chi square: 0.97 P – 0.8
20 – 40 years	26	25	
40 – 60 years	17	19	
Total	47	47	

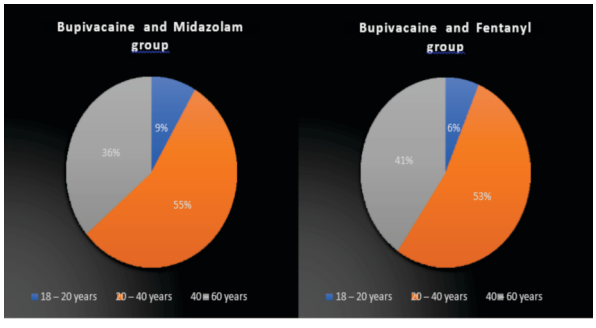

Diagram 2. Age distribution

- Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab. 2 ASA distribution

ASA Gradings	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
I	20	22	Chi square: 0.17 P – 0.68
II	27	25	
Total	47	47	

Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab. 3.Types of surgeries

Types of surgery	No of Patients in Bupivacaine and Midazolam group (n=47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Lower abdominal	8		Chi square: 1.25 P – 0.87
surgeries		6	
lower limb	7		
surgeries		5	
Gynaecological	11		
surgeries		10	
Caesarean	9		
sections		12	
Urological	12		
surgeries		14	
Total	47	47	

Tab.4. Mean duration of surgery

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean duration of surgery (Min)	84 ± 12.3	92 ± 14.4	P – 0.9

Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab. 5. Onset of sensory block

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean onset of sensory block (Min)	7.1 ± 0.9	6.9 ± 1.1	P – 0.23

Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab.6. Onset of Motor block

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean onset of motor block (Min)	7.6 ± 1.3	8.1± 1.2	P – 0.9

Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab.7. Duration of sensory block

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean duration of sensory block (Min)	213.6 ± 16.1	218.3 ± 19.2	P – 0.11

- Chi square test was performed between the 2 groups and p value was observed to be > 0.05 indicating no statistically significant difference between the groups.

Tab. 8. Duration of motor block

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean duration of motor block (Min)	132.6 ± 12.5	143.7 ± 15.3	P – 0.03

Chi square test was performed between the 2 groups and p value was observed to be **< 0.05 indicating statistically significant difference between the groups.**

Tab. 9.Duration of analgesia

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean duration of analgesia (Min)	272.9 ± 31.3	286.1 ± 21.6	P – 0.04

Chi square test was performed between the 2 groups and p value was observed to be **< 0.05 indicating statistically significant difference between the groups.**

Tab. 10. Mean total consumption of rescue analgesia in the first 24 h postoperatively

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Mean total consumption of rescue analgesia in the first 24 h postoperatively	130.6 ± 12.5 mg	121.1 ± 15.7 mg	P – 0.02

- Diclofenac sodium used as rescue analgesia.
- Chi square test was performed between the 2 groups and p value was observed to be **< 0.05 indicating statistically significant difference between the groups.**

Tab. 11 Peri-operative haemodynamic parameters

Time (Min)	No of Patients in Bupivacaine and Midazolam group (n =47)				No of Patients in Bupivacaine and Fentanyl group (n =47)				P values
	HR	SBP	DBP	Mean BP	HR	SBP	DBP	Mean BP	
0	84.2	122.4	79.2	93.60	82.3	117.4	76.5	90.13	P (HR) – 0.81
2	81.3	123.1	78.3	93.23	82.5	118.1	76.8	90.57	
5	80.8	114.5	72.4	86.43	81.7	113.5	72.4	86.10	
10	82.5	112.2	70.5	84.40	81.8	110.7	72.1	84.97	P (SBP) – 0.92
20	83.2	117.8	76.3	90.13	82.5	111.7	73.1	85.97	
30	82.4	118.8	76.8	90.80	82.6	112.4	73.5	86.47	P (DBP) – 0.83
40	83.3	118.3	77.5	91.10	84.6	113.5	73.7	86.97	
50	83.1	118.1	77.7	91.17	83.2	114.3	74.2	87.57	
60	84.2	117.3	76.1	89.83	84.7	116.7	75.1	88.97	P (Mean BP) – 0.88
90	85.2	120.1	76.3	90.90	84.2	116.5	75.2	88.97	
120	85.1	120.4	78.2	92.27	84.9	116.8	76.1	89.67	

In Bupivacaine and Midazolam group and Bupivacaine and Fentanyl group, heart rate, systolic blood pressure, Diastolic blood pressure and mean blood pressure were comparable.

Tab. 12 Adverse events

Variables	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Nausea	2 (4.26%)	3 (6.38 %)	P : 0.63
Vomiting	2 (4.26%)	2 (4.26 %)	
Pruritis	0 (0 %)	4 (8.51%)	

Chi square test was performed between the 2 groups and p value was observed to be **> 0.05 indicating statistically significant difference between the groups.**

Tab. 13 Patients satisfaction score

Variable	No of Patients in Bupivacaine and Midazolam group (n =47)	No of Patients in Bupivacaine and Fentanyl group (n =47)	Statistic
Very satisfied	28 (59.57%)	26 (55.32%)	P : 0.12
Satisfied	9 (19.15%)	10 (21.28%)	
Neutral	10 (21.28%)	11 (23.40%)	

Chi square test was performed between the 2 groups and p value was observed to be **> 0.05 indicating statistically significant difference between the groups.**

DISCUSSION

The present study titled "**A Comparative Study of the Effects of Intrathecal Midazolam(1Mg) and Fentanyl (25 Micrograms) as Additives to Intrathecal Hyperbaric Bupivacaine 0.5%(15Mg) in Spinal Anaesthesia**" was conducted at Sri Siddhartha Medical College and research institute Tumkur, Karnataka for 18 months. The study was a prospective clinical study, total sampling 94 patients of ASA physical status 1 and 2 in the age group of 18 years to 60 years; posted for elective lower limb, lower abdominal, gynaecological and urological surgeries under spinal anaesthesia.

Demography

Patients' demographic characteristics and the duration of surgery were similar among groups. There was no significant difference among groups regarding the type and duration of surgery.

Onset of sensory and motor block

In our study, in Bupivacaine and Midazolam group, mean time for onset of sensory block was 6.9 ± 1.1 minutes and in Bupivacaine and Midazolam group, mean time for onset of sensory block was 7.1 ± 0.9 minutes. In Bupivacaine and Midazolam group, mean time for onset of motor block was 7.6 ± 1.3 minutes and in Bupivacaine and Midazolam group, mean time for onset of motor block was 8.1± 1.2 minutes. There was no statistical difference between the groups.

Similarly, in a study by Bharti et al, they did not observe any significant difference between the onset time of both sensory and motor block among either group. (2) In another study by Adbdelrady et al, the onset of sensory block was comparable in the two groups ($p = 0.710$). (3)

The variation in the onset, though not significant (onset of sensory faster than motor) is because of the fact that though there is fast onset on sensory and motor blockade due to addition of opioid-like fentanyl due to the action on opioid receptors, but there is no potentiation of the effect with the addition of midazolam. Hence, similar difference was noted in onset of sensory and motor blockade in our study and studies by Bharti et al and Adbdelrady et al. (2,3).

Duration of sensory block

In our study, in Bupivacaine and Midazolam group, mean duration of sensory block was 213.6 ± 16.1 minutes and in Bupivacaine and Fentanyl group, it was 218.3 ± 19.2 minutes. There was no statistical difference between the groups.Similarly, in a study by Bharti et al, they did not observe any significant difference between Duration of sensory block among either group.In contrary, in a study by Adbdelrady et al, the time to regression to S1 dermatome wassignificantly shorter in Fentanyl with 199.43 ± 19.77 minutes than in Midazolam with 215.58± 27.94 minutes.(3)

Duration of motor block

In our study, in Bupivacaine and Midazolam group, mean duration of motor block was 132.6± 12.5 minutes and in Bupivacaine and Fentanyl group, mean duration of motor block was 143.7 ± 15.3 minutes. There was no statistical difference between the groups. Similarly, In the study by Bharathi et al, intrathecal midazolam did not affect the duration of motor blockade compared to fentanyl group. (2)In concurrence with ours and other studies, in a study by Adbdelrady et al, total duration of motor block was 182.68 ± 16.27 minutes in Fentanyl group and 189.48 ± 22.48 in Midazolam group. (3)

Durations of analgesia

In our study, in Bupivacaine and Midazolam group, mean duration of analgesia was 272.9 ±31.3 minutes and whereas in Bupivacaine and Fentanyl group, mean duration of analgesia was 286.1 ± 21.6 minutes. The duration of analgesia with fentanyl was statistically significant longer than midazolam group. Study by Adbdelrady et al, the mean duration of analgesia was significantly longer in Midazolam (351.45 ± 11.05 min) than in Fentanyl group (268.83 ± 10.35 min; $p = 0.000$). (3)

Rescue analgesia

In our study, Bupivacaine and Midazolam group, mean consumption of rescue analgesia was 130.6 ± 12.5 mg and in Bupivacaine and Fentanyl group, mean consumption of rescue analgesia was 121.1 ± 15.7 mg. There was statically significant difference between the groups.In contrast to our observation, a study by Adbdelrady et al, the median total consumption of rescue analgesia in the first 24 hours postoperatively was 30 mg in Midazolam group and 60 mg in Fentanyl group ($p = 0.003$). The median VAS scores were significantly lower in Fentanyl than in Midazolam group from the 8th to the 12th hour

postoperatively, with no significant differences between the groups at other studied timepoints. (3)

Hemodynamic profile

In our study, there was no significant difference in the heart rate and blood pressure among groups. No episode of hypotension or bradycardia was recorded. Although the patients receiving intrathecal midazolam were sleepy during intraoperative period, they were easily arousable. No episode of hypoxia or respiratory depression was recorded.Similarly, Adbdelrady et al noted that no significant differences were recorded between the groups in MAP, mean heart rate, or SpO2 at any studied time point. NIBP and HR were stable during the whole procedure. However, no significant differences were detected between the two groups in other side effects (hypotension, bradycardia). (3)

Adverse effects

In our study, Bupivacaine and Midazolam group 4.26% had nausea, 4.26 % had vomiting. In Bupivacaine and Fentanyl group, 6.38 % had nausea, 4.26 % had vomiting and 8.51 % had pruritis. We did not observe any significant difference between those the groups receiving Midazolam and Fentanyl. Similarly, Bharti et al did not any significant difference between the groups in terms of adverse effects. (2)

Post op analgesia and Patient satisfaction

In our study, In Bupivacaine and Midazolam group, 59.57% were very satisfied, 19.15% satisfied, 21.28 % were neutral. In Bupivacaine and Fentanyl group, 55.32 % were very satisfied, 21.28 % satisfied 23.40 % were neutral. There was no significant difference between them.

Adbdelrady et al observed that as assessed by the Likert scale was adequate in 90% of the patients in Midazolam group and 82.5% in Fentanyl group, with no significant difference between the groups. (3)

Contrary to our findings, Sawhney et al reported that adding fentanyl to intrathecal bupivacaine in spinal anesthesia for lower limb surgical procedures led to a better quality of postoperative analgesia than in patients receiving midazolam. (6)

CONCLUSION

The onset of sensory and motor blockade was comparable in Fentanyl with Bupivacaine and Midazolam with Bupivacaine. There was no significant potentiation of the duration of sensory and motor block with the addition of intrathecal midazolam or Fentanyl. Additional of intrathecal Fentanyl prolonged the duration of analgesia significantly than that of Midazolam. There was significantly less consumption of rescue of analgesia among patients with Fentanyl with Bupivacaine than Midazolam with Bupivacaine.There was no significant difference in the heart rate and blood pressure among groups. No episode of hypotension or bradycardia was recorded. Intrathecal Midazolam was associated with mild drowsiness.There was no significant difference between occurrence of nausea and vomiting between those the groups receiving Midazolam and Fentanyl. However, incidence of pruritis was higher in Fentanyl group. Patient satisfaction was comparable in both the groups.Addition of midazolam to intrathecal bupivacaine provides similar potentiation of analgesia as intrathecal fentanyl and appears safe in patients undergoing surgery. The duration of postoperative analgesia was also significantly prolonged in the fentanyl and midazolam groups. However, a larger, multicentre study is required to prove its efficacy and safety in various procedures.

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No

Conflict of Interest:

No conflict of interest

REFERENCES

1. Kayir S, Kisa A. The evolution of the regional anesthesia: a holistic investigation of global outputs with bibliometric analysis between 1980-2019. Korean J Pain. 2021 Jan 1;34(1):82- 93.
2. Bharti N, Madan R, Mohanty PR, et al. Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia Acta Anaesthesiologica Scandinavica. 2003;47:1101–5.
3. Abdelrady MM, Fathy GM, Abdallah MAM, Ali WN. Comparison of the effect of adding midazolam versus fentanyl to intrathecal levobupivacaine in patients undergoing cesarean section: double-blind, randomized clinical trial. Braz J Anesthesiol. 2022 Jun 11:S0104- 0014(22)00072-0. doi: 10.1016/j.bjane.2022.06.001. Epub ahead of print. PMID: 35700752.
4. Ball C, Westhorpe R: Local anaesthesia—early spinal anaesthesia. Anaesth Intensive Care 2003;31(5):493.5. Gorelick PB, Zych D: James Leonard Corning and the early history of spinal puncture.Neurology 1987;37(4):672–674.
6. S. Sawhney .R.K. Singh .S. Chakraberty . Use of intrathecal midazolam or fentanyl as an adjunct to spinal anaesthesia with bupivacaine for lower limb surgery. Department of Anesthesiology, COMMAND hospital , Lucknow, India. medical j o u rna l armed For ce s i ndia 75 (2019) 176 e1837.DevereauxMW.Anatomyandexaminationofthes p i n e . NeurolClin. 2007May;25(2):331-51
8. Waxenbaum JA, Reddy V, Williams C, Futterman B. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 4, 2021.
9. Kalamchi L, Valle C. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 8, 2022. Embryology, Vertebral Column Development.
10. Saifuddin A, Burnett SJ, White J. The variation of position of the conus medullaris in an adult population. A magnetic resonance imaging study. Spine (Phila Pa 1976). 1998 Jul 01;23(13):1452-6
11. Sassack B, Carrier JD. Anatomy, Back, Lumbar Spine. 2022 Aug 25. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan