

A Comparative Study of the Effects of Intrathecal Midazolam(1Mg) and Fentanyl(25 Micrograms) as Additives to Intrathecal Hyperbaric Bupivacaine (0.5%) for Spinal Anaesthesia

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ABSTRACT

Aim and Objectives: The purpose of study was to compare the effects of intrathecal midazolam (1 mg) and fentanyl (25 micrograms) as additives to intrathecal hyperbaric bupivacaine (0.5 %) with spinal anaesthesia.

Materials and Methods: The study was prospective clinical study, total sampling 100 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.

Results: The mean onset of sensory block in group A was 227.9 sec and in group B, mean onset of sensory block was 223.6 sec. There were no differences between the two groups with respect to the onset of block as significance value obtained from independent sample's t test was more than 0.05.

Conclusion: In conclusion, there were no differences in the durations of complete and effective analgesia when fentanyl 25 micrograms or midazolam 1mg was used as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia.

Keywords: Intrathecal Midazolam, fentanyl, intrathecal hyperbaric bupivacaine, spinal anaesthesia

INTRODUCTION

Spinal anesthesia for cesarean delivery is the best anesthetic technique as it is simple to perform with rapid onset of anesthesia and complete muscle relaxation. Its benefits of simplicity, reliability, low rates of airway complications and aspiration, facilitation of postoperative analgesia, less neonatal exposure to potentially depressant drugs, and awake mother at the time of the birth of the child that establishes maternal-infant bonding and successful breast feeding. However, spinal anesthesia has been associated with an incidence of maternal hypotension of 60-94%. [1]

Midazolam is an imidazobenzodiazepine with unique properties when compared with other benzodiazepines. It is water soluble in its acid formulation but is highly lipid soluble in vivo. It has been reported to have a spinally mediated antinociceptive effect. [2] Previous studies have shown that intrathecal administration of midazolam added to bupivacaine improves the duration and quality of spinal anesthesia. [3]

Fentanyl is a lipophilic opioid with a rapid onset following intrathecal injection. It does not migrate to the 4th ventricle in sufficient concentration to cause respiratory depression. It is commonly added to

intrathecal bupivacaine in cesarean delivery by many anesthesiologists.^[4] It improves quality of anesthesia without producing significant side effects and improves post-operative analgesia and hemodynamic stability.^[5]

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%) with spinal anaesthesia.

MATERIALS AND METHODS

The prospective clinical study was conducted on 100 adult patients of ASA physical status 1&2 in the age group of 18 years to 60 years, of either sex, posted for elective lower limb, lower abdominal, gynaecological and urological surgeries under spinal anaesthesia at Department of Anesthesiology, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar during from November 2013 to November 2014.

After approval from the Institute ethics committee, CAIMS, Karimnagar, a prospective double blind randomized controlled study was carried out on 100 adult patients. Patients were randomly divided on an alternative basis into two groups of 50 each.

Group A: Bupivacaine plus fentanyl group.

Group B: Bupivacaine plus midazolam group.

Inclusion criteria

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

Exclusion criteria

Patients belonging to ASA grade 3 and grade 4, Patients physically dependent on narcotics, history of drug allergy, gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis or neurological involvement/diseases, Head injury cases, 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.

Pre anaesthetic check up was carried out pre operatively with a detailed history, general physical examination and systemic examination. Airway assessment and spinal column examination were done.

In each case, spinal anaesthesia was performed under

strict aseptic precautions by inserting 25 gauge Quincke's spinal needle into subarachnoid space at L3,4 inter space with patient in left lateral position and the study solution was injected over 15-20 seconds.

Patients belonging to group A received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 micrograms) of fentanyl. Patients of group B received 3ml (15mg) of hyperbaric bupivacaine (0.5 %) + 0.2 ml (1 mg) of preservative free midazolam + 0.3 ml of normal saline. After injection, patient was immediately turned to supine position.

Sensory block was assessed by pin pricks in mid clavicular line bilaterally using 27 gauge hypodermic needle. The onset of sensory block was considered as the time taken from intrathecal injection to the highest level of the sensory block.

The duration of sensory block was taken from the time of intrathecal injection to regression of the level of sensory block to L1 dermatome.

Post operative analgesia was assessed using a visual analog scale (VAS). The patient was asked to mark on a 10 cm horizontal scale with no pain corresponding to 0 at one end and the worst unbearable excruciating pain to 10 at the other end. This was explained to the patient in his vernacular language. The patient's mark of severity of pain on the line was measured.

STATISTICAL ANALYSIS

The SPSS 15.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

RESULTS

Total 100 adult patients of ASA physical status 1 & 2 in the age group of 18 years to 60 years, of either sex, posted for elective lower limb, lower abdominal, gynaecological and urological surgeries under spinal anaesthesia were selected for the study.

Patients were randomly divided on an alternative basis into two groups of 50 each. Patients belonging to group A received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 micrograms) of fentanyl.

Patients of group B received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.2 ml (1 mg) of preservative free midazolam + 0.3 ml of normal saline. This randomized study was conducted to compare the effects with regards to the onset and duration of sensory block, durations of complete and effective analgesia, and associated side effects.

Table 1: Age and sex distribution

Age Groups	Number of patients	Percentage (%)
18 to 30	12	12.0
30 to 40	28	28.0
40 to 50	28	28.0
50 to 60	32	32.0
Total	100	100.0

Table 1 shows that the Majority of patients in the both the groups (16 each in group A and group B) belonged to the group 50 to 60 years. Samples were age matched.

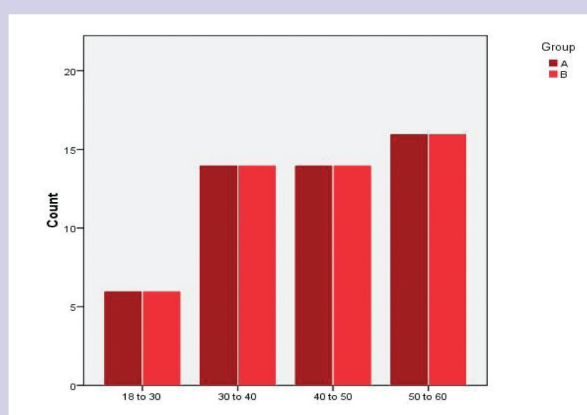


Figure 1: Age composition

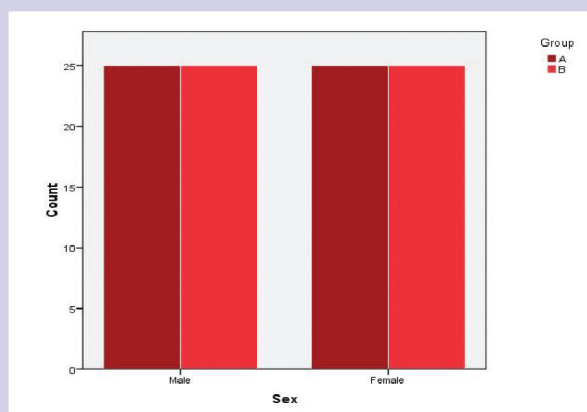


Figure 2: Gender distribution

Figure 1 and 2 showed the number of males and females in each group was same (n=25) and samples in both groups were matched with respect to sex.

Table 2 The mean onset of sensory block in group A was 227.9 sec and in group B, mean onset of sensory block was 223.6 sec. There were no differences between the two

Table 2: Sensory block-onset and duration

Group		Sensory block onset in sec	Sensory block onset in sec
A	Mean	227.90	217.20
	Standard Deviation	25.557	24.519
	N	50	50
	Minimum	170	160
	Maximum	310	275
B	Mean	223.60	216.70
	Std.Deviation	35.313	28.151
	N	50	50
	Minimum	140	150
	Maximum	310	285
Total	Mean	225.75	216.95
	Std.Deviation	30.743	26.265
	N	100	100
	Minimum	140	150
	Maximum	310	285
Independent T-test	T	.698	.095
	df	98	98
	Sig.(2-tailed)	.487	.925

groups with respect to the onset of block as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.487). There were no differences in the onset of sensory block between midazolam and fentanyl groups.

The mean duration of sensory block in group A was 217.2 min and in group B, mean duration of sensory block was 216.7 min. There were no differences between the two groups with respect to the duration of block as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.925).

There were no differences in the durations of sensory block between midazolam and fentanyl groups.

Table 3 showed the mean duration of complete analgesia in group A was 211.9 min and in group B, mean duration of complete analgesia was 212.50 min. There were no differences between the two groups with respect to the duration of complete analgesia as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.912). This means that there were no differences in the durations of complete analgesia between midazolam and fentanyl groups.

The mean duration of effective analgesia in group A was 226.50 min and in group B, mean duration of effective analgesia was 228.56 min.

Table 3: Duration of complete and effective analgesia

Group		Duration of complete Analgesia (min)	Duration of effective analgesia (min)
A	Mean		226.50
	Standard Deviation		26.883
	N		No
	Minimum		170
	Maximum		280
B	Mean		228.56
	Std.Deviation		30.122
	N		50
	Minimum		160
	Maximum		285
Total	Mean		227.53
	Std.Deviation		28.423
	N		100
	Minimum		160
	Maximum		285
Independent T-test	T		.361
	df		98
	Sig.(2-tailed)		.719

There were no differences between the two groups with respect to the duration of effective analgesia as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.719).

This means that there were no differences in the durations of effective analgesia between midazolam and fentanyl groups.

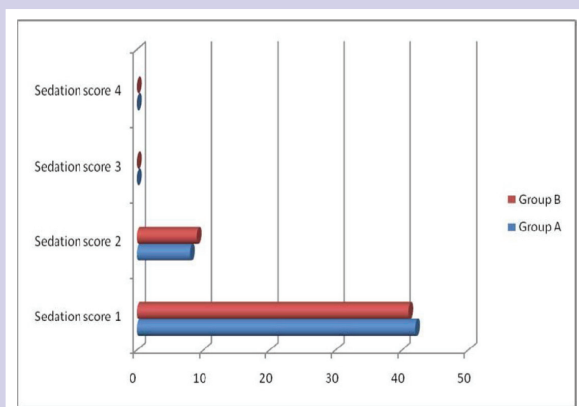
**Figure 3: Distribution of sedation scores**

Figure 3 showed that the majority of people in both groups did not have any significant sedation. There were

no statistical differences in the sedation scores between the two groups.

DISCUSSION

Fentanyl, a highly lipophilic opioid, has rapid onset of action following intrathecal administration. It is associated with fewer side effects compared to morphine. It has become very popular additive to hyperbaric bupivacaine in recent times. However, fentanyl has side effects like pruritus, nausea and vomiting and even a possible serotonin syndrome related to intrathecal fentanyl has been reported.

Midazolam is a potent short acting imidazo benzodiazepine that has been shown to have antinociceptive effects when administered intrathecally both in laboratory animals and in humans.

Preservative free midazolam is also being used in recent times as an additive to intrathecal hyperbaric bupivacaine to prolong the quality and duration of analgesia. It is said to be associated with less side effects compared to neuraxial opioids. [7]

Intrathecal midazolam in doses upto 2 mg has been used without significant side effects in various studies such as those conducted by MH Kim and YM Lee in 2001. [8]

Yegin et al reported that addition of 25 µg fentanyl to 18mg hyperbaric ropivacaine in spinal anaesthesia for patients undergoing transurethral resection of prostate provided postoperative analgesia of approximately 3.5 hour 4 out of 15 in fentanyl group patients had pruritis. [9]

Onset of sensory blockade

The mean onset of sensory block in fentanyl group was 227.9 sec and in midazolam group, mean onset of sensory block was 223.6 sec. Similar values were obtained with regard to the onset of sensory block in midazolam group in the studies conducted by Nidhi Agrawal et al and Aikta Gupta et al. [10,11]

There were no differences between the two groups with respect to the onset of block as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.487).

Sarkar M et al study described to comparing the effects of intrathecal midazolam 1 mg, fentanyl 25 micrograms and buprenorphine 60- 90 micrograms as additives to intrathecal bupivacaine 17.5 mg also found out that there were no significant differences in the onset of sensory blockade when midazolam and fentanyl were administered as adjuvants to intrathecal hyperbaric bupivacaine. [12]

Duration of sensory blockade

The mean duration of sensory block in group A was 217.2 min and in group B, mean duration of sensory block was 216.7 min. There were no differences between the two groups with respect to the duration of block as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.925).

The mean duration of effective analgesia in group A was 226.50 min with a standard deviation of 26.883 and in group B, mean duration of effective analgesia was 228.56 min with a standard deviation of 30.122. There were no differences between the two groups with respect to the duration of effective analgesia as significance value obtained from independent sample's t test was more than 0.05 (here it is 0.719).

There were no significant differences between the two groups with respect to the occurrences of bradycardia, hypotension and in sedation scores as the significance values obtained from Fisher's exact test were more than 0.05 for each of these variables. None of the patients in our study had any post operative complications like urinary retention, respiratory depression, lower limb weakness or any other neurological deficits.

CONCLUSION

The present study concludes that there were no differences in the onset and duration of sensory blockade, and durations of complete and effective analgesia, when fentanyl 25 micrograms or midazolam 1mg was used as additive to intrathecal hyperbaric bupivacaine for spinal anaesthesia. But midazolam was associated with fewer side effects compared to fentanyl.

CONFLICT OF INTEREST :

The authors declared no conflict of interest.

FUNDING : None

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