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A Randomised Comparative Study of Intrathecal Midazolam Versus Fentanyl with Hyperbaric Bupivacaine for Post-Operative Analgesia in Patients Undergoing Orthopedic Surgeries

[1,]Dr. Katakam Swapna, [2,]Dr.Rama Krishna, [3,]Dr. Sudarshan Reddy & [4,]Dr.C.N.Chandra Sekhar
[1,2,3,4,]*Yashoda Hospital, Hyderabad*

ABSTRACT:

Background & Aim: Spinal Anaesthesia / Analgesia is one of the commonest forms of Regional anaesthesia practiced for lower limb surgeries. Local Anaesthetic agent used intrathecally along with certain additives to enhance the block, increase the duration of the block as well as the quality of block. We wanted to compare an opioid and a benzodiazepine as additives in spinal anaesthesia in our study.

Methods: In our study we have enrolled 100 adult patients of ASA physical status 1 & 2 in the age group of 18 years to 60 years, posted for elective orthopaedic surgeries under spinal anaesthesia, divided into two groups **group A** - received 3 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 micrograms) of fentanyl. **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.

Results: Our study concludes that there were no differences in the onset and duration of sensory blockade, maximum level of sensory block achieved, two segment regression, duration of motor blockade, duration of post-operative analgesia; But midazolam was associated with fewer side effects like pruritis and nausea compared to fentanyl.

Conclusion: Midazolam is as good as fentanyl as an adjuvant to intrathecal Bupivacaine for intraoperative sensory blockade, hemodynamic stability and post-operative analgesia. It is better than fentanyl in terms of pruritis and nausea. Further studies should focus on confirming whether these findings have a significant impact on overall satisfaction with their postoperative care.

KEY WORDS: Spinal Analgesia, Spinal Anaesthesia, Midazolam, Fentanyl, Bupivacaine.

I. INTRODUCTION

Relief of Intraoperative & postoperative pain is professionally rewarding and is a subject that has gained attention in past few years.

Pain during surgery or in the postoperative period increases morbidity by causing -

- Sympathetic stimulation increased heart rate, blood pressure, altered regional blood flow, increased oxygen consumption.
- Stress response due to hormonal surge and depressed immune functions.
- Delayed urinary functions.
- Benefits of pain prevention and control is moral and ethical, decreases fear – anxiety, decreases morbidity, early ambulation and discharge, early return of visceral functions and oral intake. Neuraxial analgesia is achieved in the perioperative period with local anesthetic (LA) drugs. Adjuvant drugs modify LA effects and reduce side effects. Preoperatively these drugs affect; time of onset of LA block, Duration of analgesia, Quality of analgesia.

Administration of local anaesthetics with opioids has become a well-accepted practice in the management of spinal anesthesia for surgical procedures. 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. Midazolam is a potent short acting imidazo-benzodiazepine that has been shown to have ant nociceptive effects when administered intrathecal 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[1].

II. MATERIALS AND METHODS

This 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 orthopaedic surgeries under spinal anaesthesia.. After approval from the hospital ethics committee, a prospective randomized controlled study was carried out on 100 adult patients. Patients were randomly divided into two groups of 50 each based on computer generated randomised numbers by simple randomisation method. Patients meeting the inclusion criteria during the pre-anaesthetic evaluation were randomly assigned into **two groups of 50 each** with the help of a computer-generated table of random numbers by simple randomization method.

Group **"A"** - Bupivacaine plus fentanyl group.

Group **"B"** - Bupivacaine plus preservative free midazolam group.

Inclusion criteria:

1. ASA grade 1 and 2 patients.

2. Age group of 18 –60 yrs.

3. Patients giving valid informed consent.

4. Those patients scheduled to undergo elective orthopaedic surgeries under subarachnoid block.

Exclusion criteria:

1) Patient refusal.

2) Patients belonging to ASA grade 3 and grade 4.

3) Patients physically dependant on narcotics.

4) Patients with history of drug allergy.

5) Patients with gross spinal abnormality, localized skin sepsis, haemorrhagic diathesis or neurological involvement / diseases.

6) Head injury cases.

7) Patients with peripheral neuropathy.

8) Extremes of age.

9) Patients having inadequate subarachnoid blockade and who are later supplemented by general anaesthesia.

III. METHOD OF STUDY

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.

• The procedure of subarachnoid block was explained and the patient was informed to communicate to the anaesthesiologist about perception of any pain or discomfort during the surgery.

• They were premedicated with Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg orally 12 hours before giving spinal anaesthesia. 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 interspace with patient in left lateral position and the study solution was injected over 15-20 seconds.

Patients belonging to

group A- received 2.5ml ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 micrograms) of fentanyl.

group B- received 2.5 ml (15 mg) 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.

The total volume injected was 3 ml in all groups. time of injection of drug was noted.

The following parameters were noted:

HAEMODYNAMIC PARAMETERS : Heart Rate, Blood Pressure

SENSORY BLOCK: 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.

MOTOR BLOCKADE: It was assessed by straight leg raising while lying supine and was graded according to **modified Bromage scale**

Bromage 0: Patients is able to move hip, knee & ankle

Bromage 1: Patients is unable to move hip, but able to move knee & ankle

Bromage 2: Patient is unable to move hip & knee but able to move ankle

Bromage 3: Patient is unable to move hip, knee & ankle

The total duration of motor blockade were noted. The time required for raising of ankle from the injection of drug was taken as duration of motor blockade.

POST OPERATIVE ANALGESIA: Post-operative analgesia was assessed using a visual analogue scale (VAS) (Fig.1). 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.

Fig 1 : Linear Visual Analog Scale

VAS Score	**Intensity of pain**
0 – 2	No pain to slight pain
2 – 5	Mild pain.
5 – 7	Moderate pain.
7 – 9	Severe pain.
10	Worst possible pain.

Table 1: **Linear Visual Analog Scale Score**

The duration of complete analgesia was taken from the time of intrathecal drug administration to the first report of pain. The duration of effective analgesia was taken from the time of intrathecal drug administration to the time of first supplementation with rescue analgesic. Injection diclofenac sodium 1.0 mg / kg intramuscular was the rescue analgesic given if VAS was found to be 4 or more.

SEDATION SCORE:

Sedation scores were assessed every 15 minutes both intra and post operatively using a four point score.

Grade 0 – patient wide awake.

Grade 1 – patient is sleeping comfortably, but responding to verbal commands.

Grade 2 – deep sleep but arousable.

Grade 3 – deep sleep, unarousable.

Neurological examination was done to rule out any neurological deficits at discharge.. The Statistical software namely SPSS 15.0, Stata 8.0, MedCalc 9.0.1 and Systat 11.0, t-test, ANOVA test, Fischer exact test were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

IV. RESULTS

GROUP A received 2.5ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.5 ml (25 micrograms) of fentanyl.

GROUP B received 2.5 ml (15 mg) of hyperbaric bupivacaine (0.5 %) + 0.2 ml (1 mg) of preservative free midazolam + 0.3 ml of normal saline.

AGE, HEIGHT, WEIGHT DISTRIBUTION

Parameters	Group A	Group B	P value
	Mean ±SD	Mean ±SD	
Age (years)	38.500 ±9.554	35.080±11.111	0.102
Wt (kg)	64.38 ± 4.78	62.58 ± 6.21	0.104
Height (cm)	161.880 ± 4.860	162.680 ± 4.867	0.413

Table 2: Demographic profile of patients

- **T-test is applied. P value is significant if < 0.05**

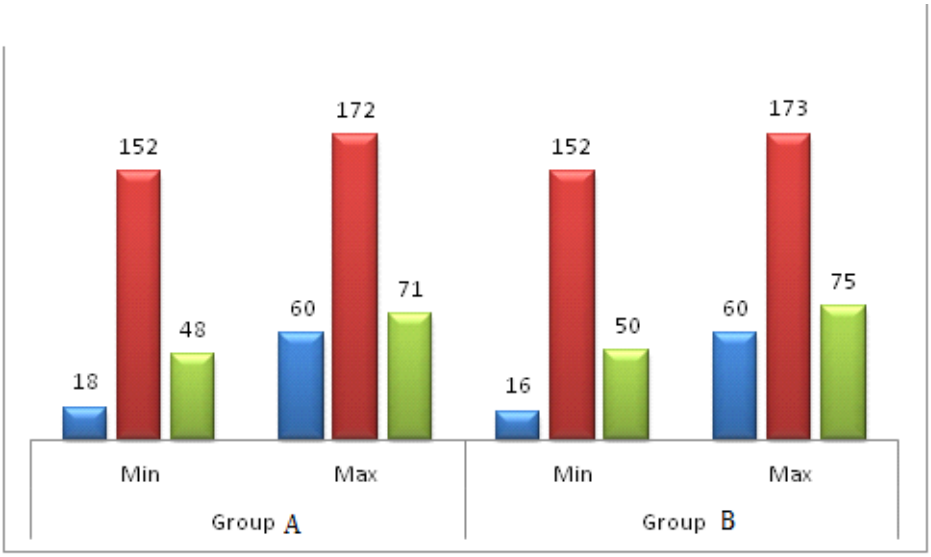

Fig 2: Age, Ht, Weight distribution

In our study, minimum age recorded was 18 yrs. and maximum age was 60 yrs. The mean age of the patients of Group A was 38.50 ± 9.55 years, Group B was 35.08 ± 11.11 years and was comparable in both the groups. Minimum weight recorded in the present study was 48 kg. and maximum weight was 75 kg. The mean weight of the patients of Group A was 64.38 ± 4.78 kgs., Group B was 62.58 ± 6.21 kgs. and were comparable in both the groups. The mean height of the patients of Group A was 161.880 ± 4.860 cms, Group B was 162.680 ± 4.867 cms and was comparable in both the groups.

Thus, the age, weight and height of the patients in both groups were comparable which shows that the patients of equal age, weight and height were enrolled in our study.

Gender COMPARISION:

Groups	Gender		Total	P value
	Male	Female		
Group A (n=50)	37	13	50	0.513
	73.68	26.32	100%	
Group B (n=50)	34	16	50	
	68.42	31.58	100%	
Total	71	19	100	

Table 3: Comparison of Gender in two Groups.

T-test is applied. P value is significant if less than 0.05 : In Group A, 73.68 patients were male and the remaining 26.32% cases were female. In Group B, 68.42% cases were male and 31.58% cases were female. Difference between them was comparable in both groups.

Fig no 3: Gender distribution

SENSORY BLOCKADE-ONSET AND DURATION:

Group		Sensory Block – Onset in seconds	Sensory Block –Duration in min
A (N=50)	Mean ±SD	227. 90±25.557	217.20±24.519
	Minimum	170	160
	Maximum	310	275
B (N=50)	Mean ±SD	223.60±35.313	216.70±28.151
	Minimum	140	150
	Maximum	310	285
	P Value	0.487	0.925

Table 4: Sensory block – onset and duration

T-test applied value significant if<0.05 : The mean onset of sensory block in group A was 227.9±25.557 sec and in group B, mean onset of sensory block was 223.6±35.313sec. There were no differences between the two groups with respect to the onset of block as p value is> 0.05 (here it is 0.487). This means that 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 ±24.51min and in group B, mean duration of sensory block was 216.7±28.15 min. There were no differences between the two groups with respect to duration of sensory block as p value is >0.05 (here it is 0.925). This means that there were no differences in the durations of sensory block between midazolam and fentanyl groups.

Fig no 4: Sensory Block Onset in Sec

Fig 5 : Sensory block – duration in Min

MAXIMUM LEVEL OF SENSORY BLOCK:

MAXIMUM LEVEL SENSORY BLOCK	GROUP A	GROUP B
T6	**2**	**0**
T7	**9**	**9**
T8	**25**	**18**
T9	**10**	**20**
T10	**4**	**3**
T11	**0**	**0**
GRAND TOTAL	**50**	**50**

Table 5: Maximum level of sensory block

T test applied .

P value0.148(>0.05)

Thus in our study we found that there was no significant difference in maximum level of sensory block achieved in between midazolam and fentanyl groups.

Fig no 6: Max Sensory Level Achieved.

TWO SEGMENT REGRESSION AND DURATION OF MOTOR BLOCKADE:

Parameters	Group A	Group B	P value
	Mean ±SD	Mean ±SD	
Time for 2 segment regression in minutes	125.48±10.8	121.8±9.27	0.073
Duration of motor blockade In minutes	161.66 ±15.58	165.120 ± 14.30	0.250

Table 6: Two segment regression and duration of motor blockade

T-test is applied. P value is significant if < 0.05.

Fig no 7: Two Segment Regression & Duration of Motor Blockade

The time taken for two segment regression was 125.48±10.8min in group A and in group B was 121.8±9.27min. There were no differences between the two groups with respect to the time taken for two segment regression as p values >0.05 (here it is 0.073). This means that there were no differences in the durations of motor block between midazolam and fentanyl groups. The duration of motor block in group A was 161.66 ±15.58 min and in group B, mean duration of motor block was165.120 ± 14.30 min. There were no differences between the two groups with respect to the duration of motor block as p values >0.05 (here it is 0.250). This means that there were no differences in the durations of motor block between midazolam and fentanyl groups.

DURATION OF SURGERY:

Parameters	Group A	Group B	P value
	Mean ±SD	Mean ±SD	
Duration of surgery	59.80 ± 20.94	65.80 ± 22.61	0.172

Table 7: Duration Of Surgery

T-test t is applied. P value is significant if < 0.05.

In present study, total duration of the surgery in Group A was 59.80 ± 20.94 mins, in Group B was 65.80 ± 22.61 mins. p value >0.05. These findings were comparable in both groups.

Fig no 8: Duration of Surgery

HEART RATE (beats per minute):

Group		Pre operative reading	5 min	10 min	20 min	30 min	60 min
A	Mean±SD	74.08± 7.87	70.00± 12.936	72.30± 9.677	72.56± 8.291	72.56± 8.437	72.32± 8.095
B	Mean±SD	73.84± 7.427	69.62± 11.719	71.90± 9.545	72.26± 8.506	72.94± 8.016	72.82± 8.285
	P value	0.876	0.878	0.836	0.859	0.818	0.761

Table 8: Heart Rate

ANOVA applied. p value significant if <0.05. There were not much differences in the heart rate observed up to 60 minutes after the administration of the drugs. Statistically there were no significant changes in the heart rates between the 2 groups at corresponding time intervals with p value> 0.05.

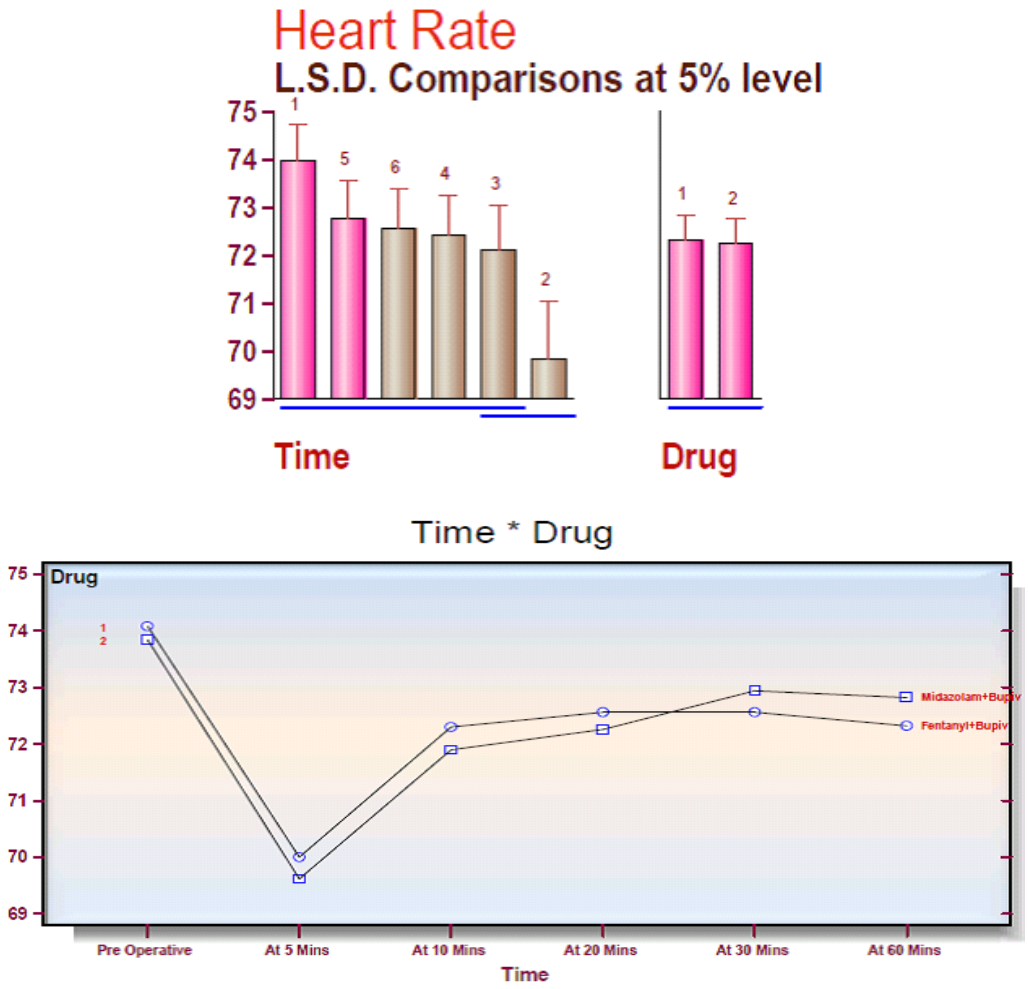

Fig no 9: Heart Rate

BLOOD PRESSURE: SBP(mm of hg):

Group		Pre-operative reading :	5 Min :	10 min	20 min	30 min:	60 min:
A	Mean±SD	116.76± 13.510	106.88± 17.857	110.00± 15.296	113.80± 11.740	115.92± 10.849	113.00± 14.715
B	Mean±SD	116.78±12.960	108.40±16.497	107.96±12.523	113.26±11.423	115.20±10.521	111.68±11.545
	P value	0.994	0.659	0.467	0.619	0.816	0.737

Table 9 : Changes in SBP.

ANOVA applied value significant if <0.05. : There were not much differences in the systolic blood pressure observed up to 60 minutes after the administration of the drugs. Statistically there were no significant changes in the systolic blood pressure between the 2 groups at corresponding time intervals with p value> 0.05.

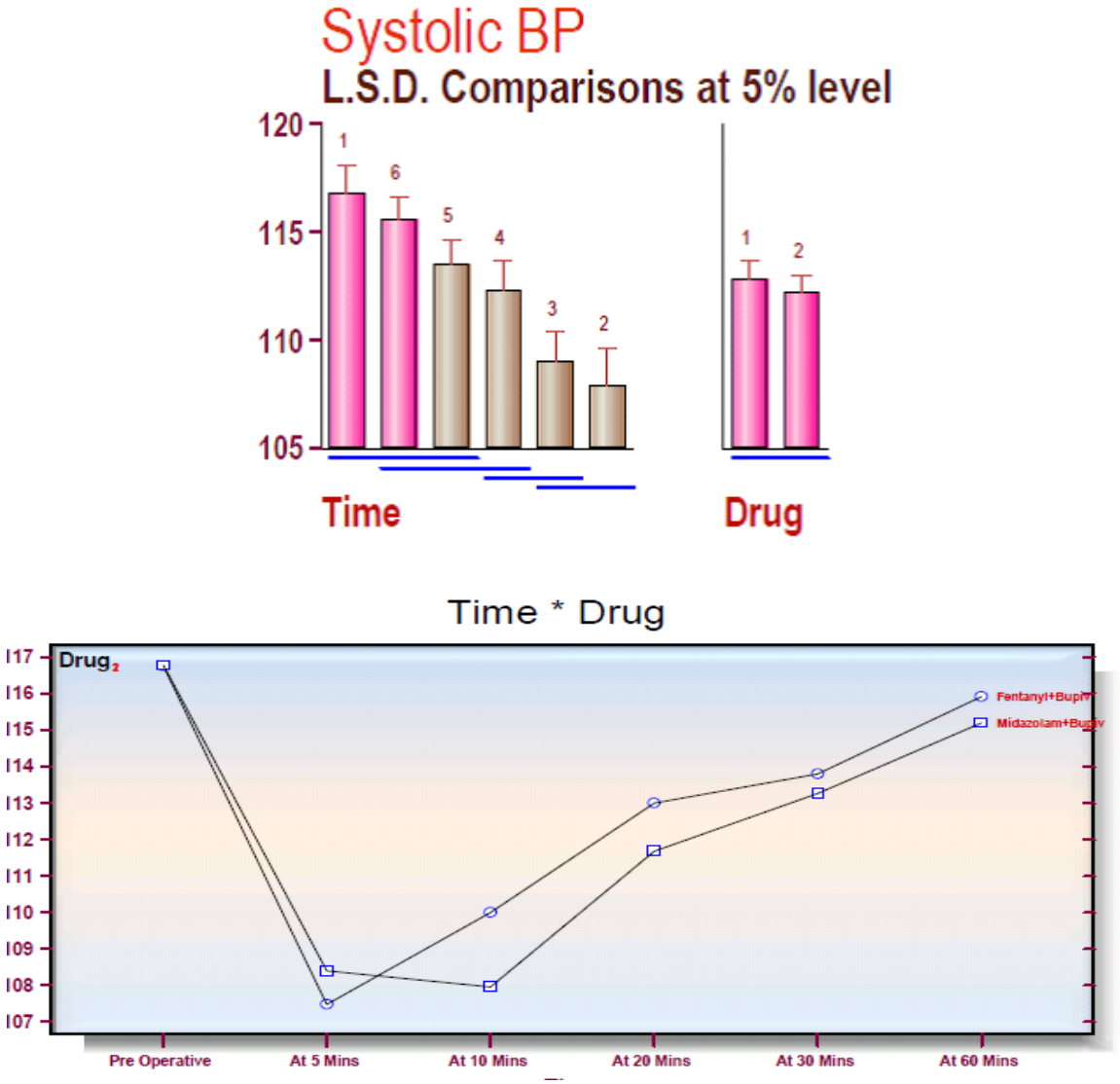

Fig no 10: Systolic BP

BLOOD PRESSURE: DBP(mm of hg):

Group		Pre operative reading	5 min	10 min	20 min	30 min	60 min
A	Mean±SD	74.84± 10.118	68.54±13.123	70.06± 8.863	73.14± 9.342	74.64± 9.102	72.00± 8.953
B	Mean±SD	74.84± 9.749	69.50±11.655	69.04± 9.304	73.30± 8.853	74.04± 8.690	70.84± 8.714
	P value	1.000	0.700	0.576	0.513	0.930	0.737

Table 10 : Changes in DBP.

ANOVA applied. p value significant if <0.05. : There were not much differences in the diastolic blood pressure observed up to 60 minutes after the administration of the drugs. Statistically there were no significant changes in the diastolic blood pressure between the 2 groups at corresponding time intervals with p value> 0.05.

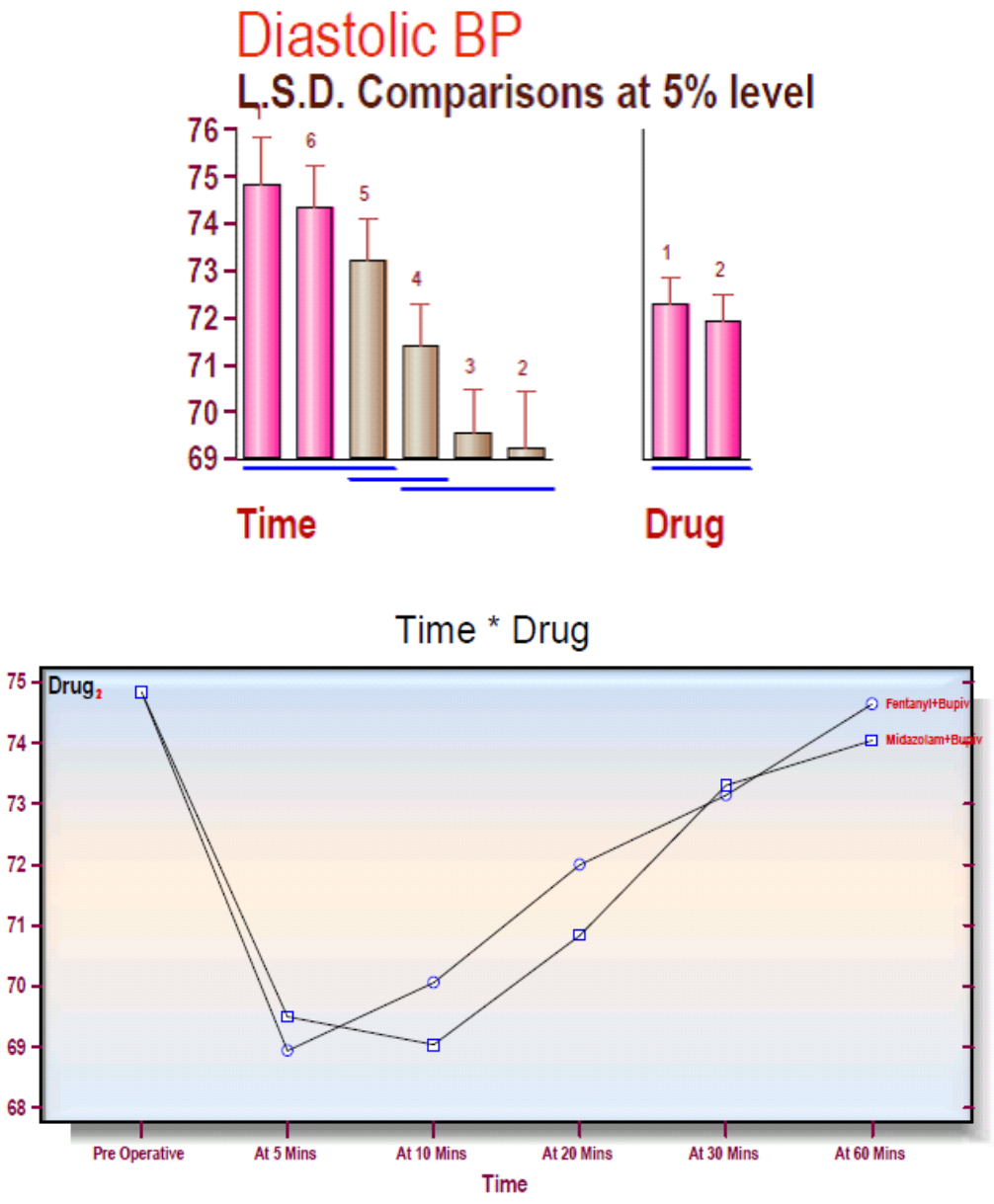

Fig no 11: Diastolic BP

Spo2(percentage saturation of oxygen):

Group		Pre operative reading	5min	10 min	20 min	30 min	60 min
A	Mean±SD	98.46± .908	98.32±1.220	98.34± 1.002	98.44± .884	98.68± .868	98.40± .926
B	Mean±SD	98.34±	98.24±1.205	98.40±	98.62±	98.84±	98.46±

		1.022		1.030	.602	.618	.952
	P value	.536	.742	.768	.750	.237	.291

Table 11 : Changes in spo2.

ANOVA applied. p value significant if <0.05 : There were not much differences in the oxygen saturation observed up to 60 minutes after the administration of the drugs. Statistically there were no significant change in the oxygen saturation between the 2 groups at corresponding time intervals with p value> 0.05.

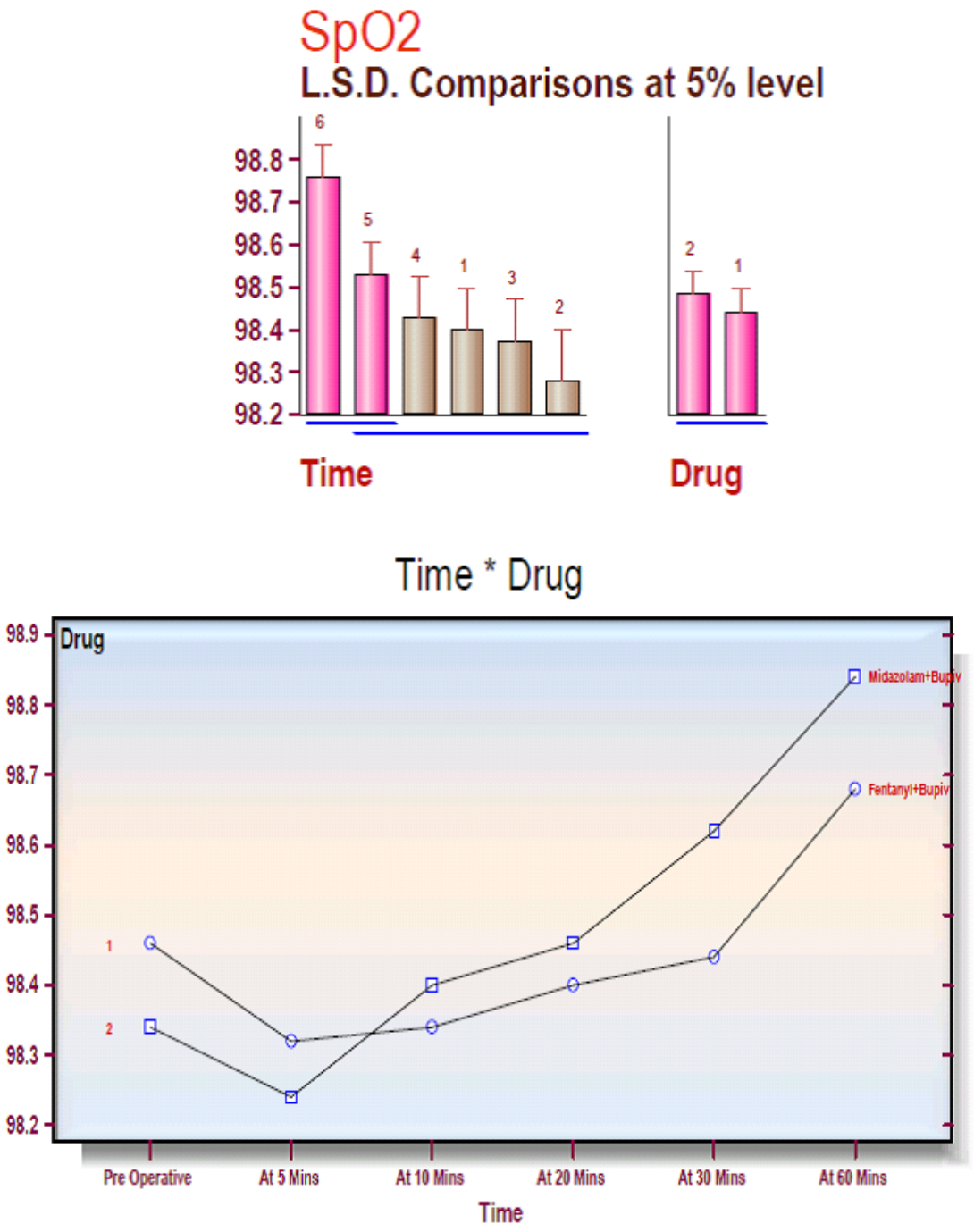

Fig no 12: SpO2

DURATION OF POST OP ANALGESIA:(minutes)

Duration of complete and effective analgesia

Group		Duration of Complete Analgesia (min)	Duration of Effective Analgesia (min)
A (N=50)	Mean ±SD	211. 90±26.876	226.50±26.883
	Minimum	1745	170
	Maximum	270	280
B (N=50)	Mean ±SD	212.50 ±27.091	228.56±30.122
	Minimum	150	160
	Maximum	270	285
	P value	0.912	0.719

Table 12 : Durations of complete and effective analgesia.

Fig no 13: Durations of complete analgesia.

The mean duration of complete analgesia in group A was 211.9±26.876 min and in group B, mean duration of complete analgesia was 212.50±27.091 min. There were no differences between the two groups with respect to the duration of complete analgesia as p value was> 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±26.883 min and in group B, mean duration of effective analgesia was 228.56 ±30.122min. There were no differences between the two groups with respect to the duration of effective analgesia as p value> 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.

Fig no 14: Duration of Effective analgesia.

Side effects

BRADYCARDIA:

Bradycardia	Group		Total
	A	B	
Yes	8	9	17
	16.0%	18.0%	17.0%
No	42	42	83
	84.0%	82.0%	83.0%
Total	50	50	100
	100.0%	100.0%	100.0%

Table 13 : Distribution of bradycardia.

P value from **Fisher's exact test** was 0.5.

It can be seen from the table that 16 % of people in group A and 18 % of people in group B developed bradycardia. Majority of people in both groups (84 % in group A and 82 % in group B) did not develop bradycardia. There were no significant differences between the two groups with respect to the occurrence of bradycardia (p>0.05).

Fig no 15: Bradycardia.

HYPOTENSION:

Hypotension	Group		Total
	A	B	
Yes	8 16.0%	6 12.0%	14 14.0%
No	42 84.0%	44 88.0%	86 86.0%
Total	50 100.0%	50 100.0%	100 100.0%

Table 14 : Distribution of hypotension.

P value from **Fisher's exact test** was 0.387.

It can be seen from the table that 16 % of people in group A and 12 % of people ingroup B developed hypotension. Majority of people in both groups (84 % in group A and 88 % in group B) did not develop hypotension. There were no significant differences between the two groups with respect to the occurrence of hypotension (p>0.05).

Fig no 16: Hypotension.

NAUSEA:

Nausea	Group		Total
	A	B	
Yes	8 16.0%	2 4.0%	10 10.0%
No	42 84.0%	48 96.0%	90 90.0%
Total	50 100.0%	50 100.0%	100 100.0%

Table 15 : Distribution of nausea.

P value from **Fisher's exact test was 0.046(<0.05):** It can be seen from the table that 16 % of people in group A and 4 % of people in group B developed nausea. Majority of people in both groups (84 % in group A and 96 % in group B) did not develop nausea. There were significant differences between the two groups with respect to the occurrence of nausea as the p value obtained from Fisher's exact test was less than 0.05(0.046). Nausea was more commonly associated with fentanyl group though none of the patients in both groups developed vomiting.

Fig no 17: Nausea.

PRURITIS:

Pruritus	Group		Total
	A	B	
Yes	5 10.0%	0 .0%	5 5.0%
No	45 90.0%	50 100.0%	95 95.0%
Total	50 100.0%	50 100.0%	100 100.0%

Table 16 : Distribution of pruritus.

P value from **Fisher's exact test was 0.028(<0.05).**10 % of people in group A developed pruritus where none in group B developed it. The difference was

statistically significant as p value was less than 0.05(0.028).

Fig no 18: Pruritis.

SEDATION SCORE:

Sedation score	Group A	Group B
Zero	42	41
One	8	9
Two	0	0
Three	0	0

Table 17 : Distribution of sedation scores.

Fig no 19: Sedation Score.

P value from **Fisher's exact test** is 0.50.

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(p>0.05).

V. DISCUSSION

Harbhej singh et al[2] in 1995, conducted a study to find out the effect of intrathecal fentanyl 25 micrograms on the onset and duration of hyperbaric bupivacaine induced sensory and motor spinal block, and the early post-operative analgesic requirements in adult male patients undergoing lower extremity or genitourinary surgery. They concluded that fentanyl prolonged the duration of bupivacaine induced sensory block

BN Biswas et al[3] in 2002, conducted a study to evaluate the analgesic effect of intrathecal midazolam and fentanyl as additives to intrathecal hyperbaric lignocaine after inguinal herniorrhaphy. They concluded that both intrathecal midazolam and fentanyl prolonged the duration of post-operative analgesia significantly compared to hyperbaric lignocaine (5 %) alone, but the differences in the duration of post-operative analgesia were not very much significant in fentanyl and midazolam groups.

Khanna MS et al[4] in 2002 conducted a study in which they compared the effects of intrathecally administered, preservative free fentanyl bupivacaine combination versus bupivacaine in geriatric patients. Results showed that 25 micrograms fentanyl during spinal anaesthesia in geriatric patients do not alter the characteristics of motor block. They observed that prolongation in the sensory blockade, (time of analgesia in group 1 191±4.4 versus 219±7.02 in group 2) decrease in post-operative pain intensity and preservation of cognitive function were seen following administration of preservative free fentanyl in geriatric patients. They concluded that caution should be taken when benzodiazepines are used concomitantly because this can lead to fall in oxygen saturation and respiratory depression.

MH Kim et al[5] **in 2001,** conducted a double blind study to evaluate the analgesic effects of intrathecal midazolam bupivacaine combination in comparison with bupivacaine in 45 patients undergoing haemorrhoidectomy. They concluded that the analgesic effect of intrathecal bupivacaine was potentiated by intrathecal midazolam. The addition of 1 or 2 mg of midazolam prolonged the post-operative analgesic effect of bupivacaine by 2 hours and 4.5 hours respectively($p<0.05$). In addition, midazolam treated patients used less analgesics in the first 24 hours after surgery.

Bharti N et al[6] **in 2003,** investigated the addition of midazolam to intrathecal bupivacaine on duration and quality of spinal blockade, on 40 ASA I & II adult patients scheduled to undergo elective lower abdominal surgery. The duration of motor block was also prolonged in midazolam group compared with control group. Quality of block was better with midazolam group when compared with control group. The duration of effective analgesia was longer in midazolam group, than in control group (199 min vs 103 min). Blood pressure, heart rate, oxygen saturation and sedation scores were comparable in both groups.

DEMOGRAPHIC DATA: In present comparative study, minimum age recorded was 18 yrs. and maximum age was 60 yrs. Mean age of the patients in Group A was 38.50 ± 9.55 years, in Group B was 35.08 ± 11.11 years and was comparable in both the groups. Minimum weight recorded in the present study was 48 kg and maximum weight was 75 kg. The mean weight of the patients of Group A was 64.38 ± 4.78kg, Group B was 62.58 ± 6.21 kg and were comparable in both the groups. The mean height of the patients in Group A was 161.880 ± 4.860 cm, whereas in Group B was 162.680 ± 4.867 cm and was comparable in both the groups. In Group A, 73.68% patients were male and the remaining 26.32% cases were female. In Group B, 68.42% cases were male and 31.58% cases were female. Difference between them was comparable in both groups.

The demographic data such as age, sex, height and weight being comparable and seems that it has no influence on outcome of the study.

DURATION OF SURGERY: The duration of surgery with group A was 59.60 ± 20.94 min and that in group B was 65.80 ± 22.61min (P=0.172)

Thus the duration of surgery was comparable in both the groups.

SENSORY BLOCK:

- **Onset sensory block:** In the present study the time of onset of sensory block in group A 227.90±25.55 sec and in group B was 223.60±35.31 sec.(p value 0.487).Similar values were obtained with regard to the onset of sensory block in midazolam group in the studies conducted **by Nidhi Agrawal et al**[7] **in 2005** conducted a double blind study on 53 adult ASA grade I/II patients to compare efficacy of intrathecal bupivacaine with intrathecal bupivacaine midazolam combination for post-operative pain relief. In conclusion intrathecal combination of midazolam and bupivacaine provides longer duration of post-operative analgesia as compared to intrathecal bupivacaine alone, without prolonging duration of dermatomal sensory block.

Aikta Gupta et al[8] in 2008 conducted a prospective, randomized, double blind study to evaluate the analgesic efficacy of intrathecal midazolam bupivacaine combination in comparison to intrathecal bupivacaine alone in patients undergoing lower limb orthopaedic surgery. Time to onset of sensory analgesia, maximum level of sensory block, time to reach it and time to two segment regression were not statistically significant between the two groups. They concluded that intrathecal midazolam 2.5 mg, when used as an adjunct to bupivacaine provides moderate prolongation of post-operative analgesia.

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In their study in 2007, **M Sarkar and L Dewoolkar**[9] conducted a prospective randomised study comparing the effects of intrathecal midazolam 1 mg, fentanyl 25 micrograms and buprenorphine 60 micrograms as additives to intrathecal bupivacaine 17.5 mg. They 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.

Thus in our study we found that there was no significant difference in onset of sensory block in between midazolam and fentanyl groups.

- **Duration of sensory blockade:** In present study the time required for regression of level to L1 was taken as total duration of sensory block. In our study, duration of sensory block in Group A was 217.20 ± 24.51 mins and in Group B was 216.70 ± 28.15 mins .There were no differences between the two groups with respect to the duration of block as p value was more than 0.05 (here it is 0.925). In another study **Vandana et al** [1] in 2008 conducted a comparative study with intrathecal midazolam versus fentanyl as additives to bupivacaine. They concluded that Intrathecal fentanyl in combination with bupivacaine provides a longer duration of sensory and motor blockade as compared to midazolam for elective lower limb surgery. In above study the sensory block was significantly higher in fentanyl group than midazolam group compared to our study.

M Sarkar and L Dewoolkar [9] conducted a prospective randomised study comparing the effects of intrathecal midazolam 1 mg, fentanyl 25 micrograms and buprenorphine 60 micrograms as additives to intrathecal bupivacaine 17.5 mg. They found out that there were no significant differences in the duration of sensory blockade when midazolam and fentanyl were administered as adjuvants to intrathecal hyperbaric bupivacaine.

In our study we found that there was no significant difference in duration of sensory block in between midazolam and fentanyl groups.

3.Maximum level of sensory block achieved: In Group A patients the maximum level reached was up to T6 . In Group B patients maximum level reached was up to T7.

T test applied .

P value0.148

In their study by **Vandana Talwar et al** [1] in 2008 conducted a comparative study with intrathecal midazolam versus fentanyl as additives to bupivacaine. They found that the peak sensory level achieved was same in both fentanyl(T5) and midazolam (T5) groups.($p>0.05$)
In another study done by **Bharti et al** [6] in 2003 investigated the addition of midazolam to intrathecal bupivacaine on duration and quality of spinal blockade. They found that the duration of sensory block was significantly longer in midazolam group than in control group (218 min vs 165 min) $p<0.05$. The maximum level of sensory block achieved was same in both the groups.(T6). They concluded that the addition of intrathecal midazolam to bupivacaine significantly improves the duration and quality of spinal anaesthesia and provides prolonged peri operative analgesia without significant side effects.

Thus in our study we found that there was no significant difference in maximum level of sensory block in between midazolam and fentanyl groups.

TWO SEGMENT REGRESSION AND DURATION OF MOTOR BLOCKADE: The time taken for two segment regression in group A was 125±10.8min and in group B was 121±9.27min.(p value 0.073). Thus in our study we found that there was no significant difference between two groups in terms of two segment regression.

In study done by **Vandana Talwar et al** [1] in 2008 2008 conducted a comparative study with intrathecal midazolam versus fentanyl as additives to bupivacaine .. Duration of sensory and motor blockade was assessed. Time taken for two segment regression was 90.60 ± 22.69min in fentanyl group and 90±17.0min. There was no difference in the time taken for two segment regression in both groups. Duration of motor block in Group A was 161.66 ± 10.8 mins and in Group B was 165.12 ± 14.30 mins with p value of 0.250.The duration of motor blockade was not statistically significant between two groups.

Vandana Talwar et al[1] in 2008 conducted a comparative study with intrathecal midazolam versus fentanyl as additives to bupivacaine. They concluded that Intrathecal fentanyl in combination with bupivacaine provides a longer duration of sensory and motor blockade as compared to midazolam for elective lower limb surgery.
The duration of motor blockade with in our study and in this study conducted was not comparable.

In their study done by **Sarkar and deewolkar [9]** in 2007, conducted a prospective randomised study comparing the effects of intrathecal midazolam 1 mg, fentanyl 25 micrograms and buprenorphine 60 micrograms as additives to intrathecal bupivacaine 17.5 mg. They found out that there were no significant differences in the duration of motor blockade when midazolam (222min) and fentanyl (232min) were administered as adjuvants to intrathecal hyperbaric bupivacaine.

The duration of motor blockade was comparable with our study.

Thus in present study we found that, the time for two segment regression and duration of motor block were clinically and statistically insignificant in between the two groups and were comparable with other studies.

HEART RATE AND BLOOD PRESSURE CHANGES: There were no significant changes with regards to heart rate and blood pressure in between both groups as p value obtained in both was >0.05.**Vandana Talwar et al[1]** in 2008 conducted a comparative study with intrathecal midazolam versus fentanyl as additives to bupivacaine. There were no significant changes with regards to blood pressure and heart rate between groups. They concluded that Intrathecal fentanyl in combination with bupivacaine provides a longer duration of sensory and motor blockade with stable haemodynamics as compared to midazolam for elective lower limb surgery.

Thus in present study we found that, the blood pressure and heart rate changes were clinically and statistically insignificant in between the two groups and were comparable with other studies.

POST OPERATIVE ANALGESIA:

Durations of complete and effective analgesia : The mean duration of complete analgesia in group A was 211.9±26.87 min and in group B was 212.50±27.09 min. There were no differences between the two groups with respect to the duration of complete analgesia as p value was more than 0.05 (p value 0.912).The mean duration of effective analgesia in group A was 226.50±26.883 min and in group B was 228.56± 30.122 min. There were no differences between the two groups with respect to the duration of effective analgesia as p value obtained was more than 0.05 (here it is 0.719).

Biswas BN et al[3] in 2002 conducted a study to evaluate the analgesic effect of intrathecal midazolam and fentanyl as additives to intrathecal hyperbaric lignocaine after inguinal herniorrhaphy. They concluded that both intrathecal midazolam and fentanyl prolonged the duration of post-operative analgesia significantly compared to hyperbaric lignocaine (5 %) alone, but the differences in the duration of post-operative analgesia were not very much significant in fentanyl and midazolam groups.

Vandana Talwar et al [1] in 2008 conducted a comparative study with intrathecal midazolam versus fentanyl as additives to bupivacaine. They found out that the differences in the duration of postoperative analgesia were not very much significant between fentanyl and midazolam groups. Our study finding is in accordance with the study conducted by **Biswas BN[3] et al in 2002 and Vandana Talwar et al [1] in 2008.**

Thus in present study we found that, the duration of post-operative analgesia was clinically and statistically insignificant in between the two groups and were comparable with other studies.

The result of our study shows that addition of optimum dose of 25 mcg Fentanyl or 1mg midazolam to intrathecal Bupivacaine is safe with comparable onset and duration of sensory blockade, two segment regression, duration of motor blockade, stable haemodynamics and duration of post-operative analgesia. Whereas side effects like pruritis, nausea were significantly less with midazolam group.

VI. CONCLUSION

Midazolam is as good as fentanyl as an adjuvant to intrathecal Bupivacaine for intraoperative sensory blockade, hemodynamic stability and post-operative analgesia. It is better than fentanyl in terms of less pruritis and nausea. Further studies should focus on confirming whether these findings have a significant impact on overall satisfaction with their postoperative care.

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