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Original Research Article

To Compare the Effects of Fentanyl and Buprinorphine with Respect_to Sensory and MotorBlock and its Side Effects: A Hospital Based Study

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Abstract:

Background: Intrathecal opioids as adjuvant to local anesthetics, act synergisticallyto overcome the shortcomings of reduced duration and postoperative analgesia. Short acting opioid like fentanyl enhance the sensory blockade of local anesthetics without affecting the sympathetic activity. Buprenorphine a mu receptor partial agonist administered intrathecally with bupivacaine improved the quality and duration of postoperative analgesia. This study was conducted to evaluate and compare the characteristics of spinal block and its side effects in patients undergoing lower abdominal surgeries using intrathecal bupivacaine and its combination with fentanylor buprenorphine.

Methods: In our Prospective Interventional study (March 2023- August 2023), 60 patients aged between 18-70 years of ASA 1 and 2 undergoing lower abdominal surgeries were included, after ethical clearance. Two groups of 30 each were randomly allocated by computer generated random number table, Group A received 3ml of intrathecal hyperbaric bupivacaine with 0.5mcg\KG of fentanyl and group B received 3ml of intrathecal hyperbaric bupivacaine with 2mcg\kg of buprenorphine. Onset and regression of sensory and motor blockade, duration of analgesia was noted in both the groups. Sedation scores and side effects were evaluated. Statistical analysis was by Student's t-test and Chi-square test.

Results: The mean time of onset of sensory, motor blockade and the time to achieve maximum sensory level and sedation scores was comparable in both the groups (p > 0.005). Duration of motor blockade and analgesia, two segment regression time was significantly prolonged in Group B compared to Group F (p < 0.001). Side effects noted were pruritis, nausea and vomiting in both the groups.

Conclusion: Intrathecal Buprenorphine (60mcg) in combination with bupivacaine provides comparable onset of sensory and motor blockade but longer total duration of motor blockade and analgesia as with intrathecal fentanyl (25mcg).

Keywords: Intrathecal, Fentanyl, Buprenorphine, Bupivacaine.

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Introduction

Spinal anesthesia is the most commonly used technique for lower abdominal surgeries as it is very economical and easy to administer [1]. The advantages of subarachnoid block are limited by its short duration of action and lack of postoperative analgesia In recent years, the supplementation of local anesthetics with adjuvants is widely in practice, to reduce the dose of local anesthetic, minimize side effects and prolong the [1.2] duration of anesthesia Opioid added to local anesthetic for spinal anesthesia was first introduced into clinical practice in 1979 with intrathecal morphine as a forerunner. Neuraxial administration of opioids along with local anesthetics improves the quality of intraoperative analgesia and also provide postoperative pain relief for longer duration [3.4].Intrathecal morphine provides prolonged postoperative analgesia but is associated

with increased risk of nausea, vomiting, itching and respiratory depression 5.Fentanyl, a lipophilic opioid, has rapid onset of action following intrathecal administration. It does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered Intrathecally6. Addition of fentanyl to spinal anesthesia produces synergistic analgesia for somatic and visceral pain without increased sympathetic block7 .Therefore, fentanyl provides better intraoperative analgesia and a safer alternative to morphine for management of early postoperative pain Buprenorphine is a centrally acting lipid soluble analogue of alkaloid thebaine. It exhibits analgesic property both at supraspinal level, when used spinal and intrathecally in combination with bupivacaine it has known to improve the quality and [8,9]duration of

postoperative analgesia compared to bupivacaine. This study was conducted to evaluate and compare the characteristics of spinal block and its side effects in adult patients undergoing lower abdominal surgeries who received a subarachnoid block with either bupivacaine with buprenorphine or bupivacaine with fentanyl.

Materials and Methods

Source of Data

In patients posted for major surgeries below umbelical level in Gulbarga Institute Of Medical Sciences Kalaburgi. Study Design: Prospective Interventional Study.

Duration of study: 6 months march 203 to August 2023.

Sample size: 60 patients 30 patients in each group□ Group A will receive 3ml 0.5% hyperbaric bupivacaine + fentanyl 0.5mcg/kg Group B will receive 3ml 0.5% hyperbaric bupivacaine+ buprinorphine 2mcg/kg

Method of Collection of Data

Sixty patients aged between 18 to 70 years of physical status ASA grade 1 and ASA grade 2, undergoing below umbelical surgeries were

included in the study after ethical clearance. evaluation of the patient was done on the day before surgery. After explaining the procedure, written and informed consent was obtained.

Patients were advised overnight fasting and were premedicated with tablet Alprazolam 0.5 mg the night before and on the day of surgery.

Inclusion Criteria

All the patients who were posted for elective lower abdominal surgeries Age group- 18- 70 years.ASA 1 and 2 of either sex

Exclusion Criteria.

Patients with emergency surgery Hypersensitivity to any of the drug Spine deformities.

Bleeding diathesis and coagulopathy.

Data collected was analyzed by IBM SP SS2.0 version software. Data was spread in excel sheet mean, SD and other measures was calculated. For quantitative data analysis t-test and ANOVA test was applied for qualitative data analysis chi-square test was applied for significant if P<0.05 was consider as significant

Results

Table: 1						
Group [Mean(SD)]	n1/n2	Group A	Group B	p value- Student t-test		
Time of onset of sensory block	30//30	2.8(±1.24)	2.8(±1.13)	1.000		





8: Mean duration of onset of sensory block

Heighest sensory level achieved.

The heightest sensory block achieved in both the groups ranged from T6-T10.

Table 2. Heighest sensory lever achieved in the study groups						
Highest sensory level	(Froup	Total	p value		
	Group A	Group A Group B		Chi square		
T6	10(33.33%)	4(13.33%)	14(23.33%)	0.101		
Τ7	1(3.33%)	6(20%)	7(11.67%)			
T8	14(46.67%)	14(46.67%)	28(46.67%)			
T10	5(16.67%)	6(20%)	11(18.33%)			
Total	30(100%)	30(100%)	60(100%)			

Table 2: Heighest sensory level achieved in the study groups

Graph 2: Distribution	of Heighest sensor	y level in the study group
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Time to reach the Heighest Sensory Level The mean time to reach the heighest sensory level in group A to be 10.2+1.77 minutes and in group B to be 10.4+1.22 minutes. The mean time to reach heighest sensory level was comparable in both groups as indicated by p=0.612

Table 3 : Time to reach heighest sensory level						
Group [Mean(SD)] n1/n2 Group A Group B p value- Student						
Time to reach highest sensory level	30//30	$10.2(\pm 1.77)$	10.4(±1.22)	0.612		



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Time to onset of motor block

The mean time to onset of motor block was 7.27+1.78 in group A and 6.93+1.14 in group. Mean duration of onset of motor blockade was comparable in both the groups with p =0.392.

Table 4: Mean duration of onset of motor block						
Group [Mean(SD)] n1/n2 Group A Group B p value- Student t test						
Time of onset of motor block	30//30	7.27(±1.78)	6.93(±1.14)	0.392		



Graph 4: Mean duration of onset of motor block.

Total Duration Of Motor Blockade

The two groups were found to have a significant diffrence in the total duration of motor block with a p value < 0.001. The shortest total duration of motor

blockade in group A was 160 minutes and in group B was 190 minutes. The longest total duration of motor blockade in group A was 200 minutes and in group B was 250 minutes.

Table 5.	Total	duration	of Motor	blockade	in	two groups
Table 5:	TOTAL	uuration		лоскаце	ш	two groups

Group[Mean(SD)]	n1/n2	Group A	Group B	p value- Student t test
Duration of motor blockade	30//30	188.33(±14.58)	214.83(±19.85)	0.000



Graph 5 : Total duration of motor blockade in two groups

The mean duration of motor blockade in group A was 188.33+14.58 minutes and in group B was 214.83+19.85 minutes which is significantly prolonged with p < 0.000

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Group [Mean(SD)]	n1/n2	Group A	Group B	p value- Student t test
Time for 2 segment regression	30//30	92.97(±10.7)	110(±12.87)	0.000

Table 6	5: Time	for	two	segment	regression	of	sensory	bloc	ek
					<u> </u>		•/		

Time for 2 segment regression30//30 $92.97(\pm 10.7)$ $110(\pm 12.87)$ 0.000The mean time for two segment regression in group A was 92.97+10.7 minutes and ingroup B was 110+12.87minutes.

There was a significant difference in the two groups as indicated by p <0.000.



Graph 7: Comparison of the time for two segment regression of sensory level in twogroups

Table 8: Total duration of analgesia							
Group[Mean(SD)] n1/n2 Group A Group B p value- Student t test							
Duration of analgesia	30//30	286.67(±16.57)	386.67(±18.63)	000			

The mean duration of analgesia in group A was 286.67+16.57 minutes and in group B was 386.67+18.63 minutes. The shortest duration in group A was 260 minutes abd in group B was 360 minutes and longest duration in group A was 310 minutes and in group B was 410 minutes. Significant prolonged duration of analgesia was found with Buprinorphine group with p=<0.000.



Graph 8: Total duration of analgesia

Side effects	Group		Total	p value
	Group A	Group B		Chi square
No	23(76.67%)	25(83.33%)	48(80%)	0.745
bradycardia	1(3.33%)	0(0%)	1(1.67%)	
hypotension	2(6.67%)	1(3.33%)	3(5%)	
nausea and vomiting	1(3.33%)	2(6.67%)	3(5%)	
pruritis	3(10%)	2(6.67%)	5(8.33%)	
Total	30(100%)	30(100%)	60(100%)	

Side effects

 Table 9: Comparison of side effects in two groups studied

The incidence of hypotension defined as fall in the mean arterial pressure to less than 20% from baseline was 6% in group A (2 patients) and in group B was 3% (1 patient) which is statistically comparable between the two groups. Hypotension was effectively treated with injection Mephentremine6mg intravenously in increments.

Bradycardia defined as heart rate less than 50bpm was noted in only one patient in group A which was treated with injection Atropine 0.6mg intravenously.





Other common side effects noted in all the patients under the study was pruritis, nausea and vomiting. 3 patients in group Aexperienced pruritis with the incidence of 10% and 2 patients in group B experienced pruritis with the incidence of 6%, but there was no statistical difference in the incidence of pruritis between the two groups ('p' > 0.05). The incidence of nausea and vomiting in group F was 3% (1patients) and that in group B was 6% (2 patients) with no statistical difference between the two groups. ('p'> 0.05)

Discussion

Time to Onset of Sensory Block

In our study, the mean time taken to the onset of sensory block in the Group A was 2.8 ± 1.24 minutes and in the Group, B was 2.8 ± 1.13 minutes. The onset time was comparable in both the groups as indicated by the 'p' value=1.000.

Gajanan Chavan, Aparna Chavan et al [10] in a study titled "Effect of Intrathecal Fentanyl on subarachnoid block with 0.5% hyperbaric bupivacaine" found the onset time of sensory blockade in a group who received 25microgram of fentanyl with 3ml of 0.5% hyperbaric bupivacaine to be 2.2 \pm 0.372 minutes which is in accordance with our study.

Raju G, Priyanka V et al [11] in a study titled "Comparison of analgesic effects of equipotent doses of intrathecal morphine and buprenorphine during spinalanaesthesia with hyperbaric bupivacaine" found that the mean time of onset of sensory block at L1 was 2.62 + 0.525 minutes in group B who received 3cc of 0.5% hyperbaric bupivacaine with 100 µg of buprenorphine, which is similar to our study.

Rashmi Pal, K. K. Arora et al [12] in a study titled "Intrathecal Buprenorphine, Clonidine and Fentany 1 As Adjuvants To 0.5% Hyperbaric Bupivacaine In Lower Abdominal And Lower Limb Surgeries: A Prospective, Randomized And Comparative

Study" found that there was no significant difference in onset time of sensory block in GROUP BF who received 3.0ml of 0.5% hyperbaric bupivacaine +25µg (0.5ml) fentanyl and GROUP BB who received 3.0ml of bupivacaine heavy 0.5% + buprenorphine 75µg (0.25ml). The mean time of onset of sensory block (loss of pin prick at T10) in GROUP BF was 477.6±55.2 seconds, and in GROUP BB was 477.6±61.8 seconds, which is similar to our study as there was comparable clinical onset of sensory blockade in both the groups ('p'= 1.00). [13]

Fauzia A. Khan, Gauhar A. Hamdani16 in a study titled "Comparison of Intrathecal Fentanyl and Buprenorphine in Urological Surgery" found that onset time of sensory blockade in group F who received fentanyl 10 microgram with 2ml of hyperbaric bupivacaine 0.75% was 3.2 ± 2.0 min and that in group B who received buprenorphine 30microgram with hyperbaric bupivacaine 0.75% 2 ml was 3.15 ± 1.0 min which was statistically comparable with 'p' value 0.94. This is in accordance with our study showing comparable clinical onset of sensory blockade in both fentanyl and buprenorphine group.

Time of Onset to Motor Blockade

The mean time to onset of motor blockade (modified Bromage 3) in our study was 7.27 ± 1.78 minutes in Group A and 6.93 ± 1.4 minutes in Group B respectively, which is comparable statistically with a 'p' value of 0.392.

Harbhej Singh et al [14] in a study titled "Intrathecal fentanyl prolongs sensory bupivacaine spinal block" found that the onset to grade III motor block was 8.6+4.1minutes in a group which received 1.8ml hyperbaric bupivacaine 0.75% with (25microgram) fentanyl and Gajanan Gajanan Chavan, Aparna Chavan et al [10] also found 7.37 \pm 2.41 minutes as the mean time to achieve Bromage 3 in a group who received 25microgram of fentanyl with 3ml of 0.5% hyperbaric bupivacaine. The abovementioned studies are in accordance with the mean time of onset of motor blockade of our study group fentanyl, (7.27 \pm 1.78min).

Mahima Gupta et al [15] found the onset time of motor blockade (Bromage 3) in a group who received $60\mu g$ of buprenorphine with 3ml of 0.5% hyperbaric bupivacaine was 3.30 ± 0.97 minutes which did not match with our study as this is much faster.

F A Khan et al [16] in a study titled "Comparison of Intrathecal Fentanyl and Buprenorphine in Urological Surgery" found that time to Bromage 3 in group F who received fentanyl 10 microgram with 2ml of hyperbaric bupivacaine 0.75% to be 10.5 \pm 2.0minutes which was significantly faster when compared to that in group B who received buprenorphine 30microgram with 2ml of hyperbaric bupivacaine 0.75% to be 12.2 \pm 3.0 minutes ('p' value 0.01), which did not match with our study as in our study it was comparable clinical onset of motor blockade observed in both the groups.

Time to reach the highest sensory level Maximum sensory level varied from T6 to T10. In our study, the mean time to reach the highest level of sensory block in group A was 10.20 ± 1.77 minutes and in group B was 10.44 ± 1.22 minutes and was comparable in both the groups with 'p' value 0.612.

Gajanan Chavan, Aparna Chavan et al10 found that the time for maximum cephalic spread was $11.72 \pm$ 3.5minutes in a study group who received 25microgram of fentanyl with 3ml of 0.5% hyperbaric bupivacaine which is similar to our study.

F A Khan et al [16] found that the time taken to achieve maximum sensory level in fentanyl group (fentanyl 10 microgram with hyperbaric bupivacaine 0.75% 2ml) was 10 ± 3.0 minutes which was significantly faster compared to the buprenorphine group (buprenorphine 30microgram with hyperbaric bupivacaine 0.75% 2 ml) which was 15 ± 3.0 minutes which did not match with our study, as the mean time to reach highest sensory level was comparable in both the groups in our study.

Time for Two Segment Regression

In our study, the mean time for two segment regression in the group A was 92.97 ± 10.7 minutes and in group B was 110.12 ± 12.85 minutes. There was a significant difference in the two groups as indicated by the 'p' value < 0.001.

Harbhej Singh et al14 found that the time for two segment regression from the highest sensory level was 93.4±22minutes in a group which received 25microgram of fentanyl with 3ml of 0.5% hyperbaric bupivacaine this is accordance with our study group fentanyl.

Raju G, Priyanka V et all1 found that the 2segment regression time was 122.00 ± 9.85 minutes in a group which received 3cc of 0.5% hyperbaric bupivacaine with 100 µg of buprenorphine which is similar to our study group buprenorphine.

Duration of Motor Blockade

The mean duration of motor blockade in our study in group A was 188.33 ± 14.58 minutes and in group B was 214.83 ± 19.85 minutes which is significantly prolonged. ('p'value 0.001).

Harbhej Singh et al14 found that the duration of motor blockade was 169 ± 37 minutes in a group which received 25microgram of fentanyl with 3ml of 0.5% hyperbaric bupivacaine this is accordance with our study group fentanyl.

Mahima Gupta et al15 found that the duration of motor blockade in a group who received $60\mu g$ of buprenorphine with 3ml of 0.5% hyperbaric bupivacaine was 205.17 ± 63.0 minutes which is in accordance with our study.

Rashmi Pal, K. K. Arora et al17 found that the mean duration of motor blockade in fentanyl group who received 3.0ml of 0.5% hyperbaric bupivacaine $+25\mu g$ fentanyl to be 151.27 ± 12.0 minutes and that in buprenorphine group who received 3.0ml of bupivacaine heavy 0.5% + buprenorphine $75\mu g$ (0.25ml) to be 222.66 ± 24.3 minutes in which it was significantly prolonged ('p' value 0.001), which is in accordance with our study.

Duration of Analgesia

In our study the mean duration of analgesia in group A was found to be 286.67 ± 16.270 minutes and that in group B was 386.60 ± 18.802 which was significantly prolonged as indicated by the ('p' value 0.001)

Mahima Gupta et al15 in a study titled "Comparison of Intrathecal Dexmedetomidine with Buprenorphine as Adjuvant to Bupivacaine in Spinal Anaesthesia" found that the duration of analgesia was 289.66 ± 64.94 minutes in a group which received $60\mu g$ of buprenorphine with 3cc (15mg) of 0.5 % heavy bupivacaine which is slightly lesser than the buprenorphine group in our study.

Gajanan Chavan, Aparna Chavan et al10 found that the duration of analgesia was 207 ± 17.57 minutes in a group who received 25microgram of fentanyl with 3ml of 0.5% hyperbaric bupivacaine which is of a lesser duration compared to the fentanyl group in our study.

Rashmi Pal, K. K. Arora et al12 in a study found that the duration of analgesia in a fentanyl group who received 3.0ml of 0.5% hyperbaric bupivacaine with $25\mu g$ (0.5ml) fentanyl to be 195.83 ± 7.3 minutes and that in buprenorphine group who received 3.0ml of bupivacaine heavy 0.5% with buprenorphine 75µg to be 294 ± 17.0 minutes which was significantly prolonged in buprenorphine group with 'p' value 0.001, which is in accordance with our study.

Fauzia A. Khan, Gauhar A. Hamdani16 in a study titled "Comparison of Intrathecal Fentanyl and Buprenorphine in Urological Surgery" found that the duration of analgesia in group F who received fentanyl 10 microgram with hyperbaric bupivacaine 0.75% 2ml to be 534 ± 35 min and that in group B who received buprenorphine 30microgram with hyperbaric bupivacaine 0.75% 2 ml to be 834 ± 59 minutes, which is significantly prolonged (P <0.01). This is in accordance with our study.

Conclusion

Buprenorphine 2mcg\kg added to 3ml of 0.5% Hyperbaric Bupivacaine produced comparable clinical onset of sensory and motor blockade when compared to 0.5mcg\kg of Fentanyl.The mean time to achieve highest sensory level was comparable in both Buprenorphine and Fentanyl groups.The mean time for two segment regression was significantly prolonged when Buprenorphine was added to Bupivacaine compared to the addition of Fentanyl to bupivacaine.

Total duration of motor blockade and duration of analgesia was of significantly longer duration in Buprenorphine group compared to Fentanyl group. Sedation scores were similar in both Buprenorphine and Fentanyl group. Common side effects noted in both the Fentanyl and Buprenorphine groups were Pruritis, Nausea and vomiting, however there was no statistically significant difference noted between the two groups.

References

- 1. Gupta R, Verma R, Bograj, Kohli M, Raman R, and Kushwaha JK. A comparative studyof intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol. 2011 Jul-Sep; 27(3): 339–343.
- Shaikh SI, Kiran M. Intrathecal buprenorphine for post-operative analgesia: A prospective randomised double-blind study. J Anaesth Clin Pharmacol. 2010; 26:35–8.
- Abouleish E, Rawal N, Shaw J, Lorenz T, Rashad MN. Intrathecal morphine 0.2 mg versus epidural bupivacaine 0.125% or their combination; effects on parturients. Anesthesiology 1991; 74: 711-6-3
- 4. Hunt CO, Naulty JS, Bader AM. Perioperative analgesia with subarachoid fentanyl bupivacaine for Caesarean delivery. Anesthesiology 1989; 71; 535-40.
- Chaney MA. Side effects of intrathecal and epidural opioids. Can J Anaesthesia 1995; 42: 891-903.
- Etches RC, Sandler AN, Daley MD. Respiratory depression and spinal opioids. Can J. Anaesth 1989; 36; 165-85.
- Hamber EA, Viscomi CM: Intrathecal lipophilic opioids as adjuncts to surgical spinal anesthesia. Reg Anesth Pain Med 1999; 24:255– 63.
- Ding Z, Raffa RB. Identification of an additional supraspinal component to the analgesic mechanism of action of buprenorphine. Br J Pharmacol. 2009; 157:831–43
- Capogna G, Celleno D, Tagariello V, Loffreda-Maniculli C. Intrathecal buprenorphine for postoperative analgesia in the elderly patient. Anaesthesia 1988; 43:128-30
- 10. Gajanan Chavan, Aparna Chavan, Alok Ghosh. Effect of Intrathecal Fentanyl on subarachnoid block with 0.5% hyperbaric bupiva-

caine. International J. of Healthcare and Biomedical Research. July 2014; 2(4): 67-76.

- 11. Raju G, Priyanka V, Dayananda V P. Comparison of analgesic effects of equipotent doses of intrathecal morphine and buprenorphine during spinal anaesthesia with hyperbaric bupivacaine. International Medical Journal. September. 2014; 1(9):520-524.
- Rashmi Pal, K. K. Arora, N. S. Doneria. Intrathecal Buprenorphine, Clonidine and Fentanyl as Adjuvants to 0.5% Hyperbaric Bupivacaine in Lower Abdominal and Lower Limb Surgeries: A Prospective, Randomized and comparative study Journal of Evolution of Medical and Dental Sciences. 2015; 4(46): 8009-8017.
- Courtney KR: Structure-activity relations for frequency-dependent sodium channel block in nerve by local anesthetics. J Pharmacol Exp Ther. 1980; 213: P.114-119.
- 14. Singh H, Yang J, Thorton K, Adolph H.

Giesecke. Intrathecal fentanylprolongs sensory bupivacaine spinal block. Canadian journal of anesthesia, 1995; 42:11/ 987-991.

- Gupta M, Shailaja S, Hegde KS. Comparison of Intrathecal Dexmedetomidine with Buprenorphine as Adjuvant to Bupivacaine in Spinal Asnaesthesia. Journal of Clinical and Diagnostic Research. JCDR. 2014;8(2):114-117.
- F A Khan, Hamdani GA. Comparison of intrathecal fentanyl and buprenorphine in urological surgeries.J Pak Med Assoc. 2006; 56(6): 27 7-81.
- Rashmi Pal, K. K. Arora, N. S. Doneria. Intrathecal Buprenorphine, Clonidine and Fentanyl as Adjuvants to 0.5% Hyperbaric Bupivacaine in Lower Abdominal and Lower Limb Surgeries: A Prospective, Randomized and comparative study Journal of Evolution of Medical and Dental Sciences. 2015;4 (46):800 9-8017.