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A Comparative Study of Efficacy of Intrathecal Fentanyl and Butorphanol as an Adjuvant to Bupivacaine 0.5% Heavy for Lower Limb and Lower Abdominal Surgeries

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Original Research Article

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Abstract: Opioids have an important place as adjuvant to local anaesthetic agents in the management of spinal anaesthesia, the most commonly used being fentanyl. Other alternatives like opioid agonist antagonist agents like nalbuphine, butorphanol and buprenorphine are now being studied as adjuvants to prolong the duration of sensory and motor block with lower incidence of opioid related side effects. 60 patients belonging to ASA status I and II of either sex were randomly divided into three groups of 30 each to receive either butorphanol25 µg (Group A) or fentanyl 25 mcg (Group B)) with 2.5 mL 0.5% hyperbaric bupivacaine, making intrathecal drug volume to 3mL in each group. . Sensory and motor block characteristics in terms of time to onset and duration were recorded for each group. Drug-related side effects of pruritus, nausea/vomiting, and respiratory depression were also recorded. The two groups were comparable regarding the demographic profile. The fentanyl group showed delayed onset of sensory block (274 ± 73.39 sec) as well as a longer duration of sensory block (145.07 ± 5.34 mins vs 141.33 ± 3.51) than butorphanol. The duration of motor block was also prolonged in the fentanyl group(149 ± 7.13 vs 140.37 ± 2.31) . Both the findings were significant. Butorphanol provided a significantly longer duration of postoperative analgesia (250.10 ± 4.05 vs 244 ± 7.11 min) . No drug related side effects were observed in either group. Addition of 25 µg of butorphanol as adjuvant to hyperbaric bupivacaine 0.5% provides a faster onset of sensory block as compared to 25 µg fentanyl. Fentanyl provided a significantly greater duration of both sensory and motor block than butorphanol. The duration of postoperative analgesia was significantly greater with butorphanol.
Keywords: Intrathecal, butorphanol, fentanyl.

INTRODUCTION

The successful conduct of spinal anaesthesia includes deposition of local anaesthetic into the subarachnoid space with effective blockade of transmission through spinal nerves. The history of spinal anesthesia in clinical practice dates back to 1898 when Karl August Bier[1] injected 3 ml of 0.5% cocaine solution into a 34-year-old labourer to administer the first spinal anaesthesia, in Kiel.

Spinal anesthesia using local anesthetics like cocaine, procaine, lignocaine, bupivacaine, ropivacaine is one of the most popular techniques for both elective and emergency surgical procedures.

Adding adjuvant drugs to intrathecal local anesthetics improves or prolongs analgesia, decreases the adverse effects associated with high doses of single local anesthetic, increases the speed of onset of neural blockade(reduce latency) and increases analgesic gap[2,3].

A number of drugs that have been used as adjuvants adjuvants to local anesthetics include - Opioids (Morphine, Fentanyl, Butorphanol, Nalbuphine, Pentazocine, etc.), Alpha-2 Agonists (clonidine, dexmedetomidine) GABA Agonists (Midazolam), NMDA Receptor Antagonists (Ketamine), Neostigmine, NSAIDS, Neuromuscular Blocking Drugs, Adenosine and Dextrans[3,4].

Opioids are extensively used as an adjuvant in neuraxial blocks. In 1979, Wang *et al.* published the first controlled clinical study of intrathecally administered opioid in humans. Fentanyl is a synthetic, lipophilic phenylpiperidine opioid agonist with analgesic and anesthetic properties which selectively binds to the mu-receptor in the central nervous system. It is widely used as an adjuvant drug via intrathecal

and epidural approaches for postoperative pain relief [5]. But Fentanyl was found to have higher incidence of pruritus. Butorphanol was found to be effective in alleviating neuraxial opioid-induced itch Butorphanol is a synthetic opioid agonist antagonist of phenanthrene group with affinity at both μ and κ opioid receptors.

The effects of opioids within the CSF are complex, because of a combination of direct spinal cord dorsal horn opioid receptor activation, cerebral opioid receptor activation after CSF transport, and peripheral and central systemic effects after vascular uptake. The effect at each of these sites depends on both the dose administered and the physicochemical properties of the opioid, particularly lipid solubility. Highly lipid-soluble drugs such as fentanyl and sufentanil have a more rapid onset and shorter duration of action than more hydrophilic opioids. In addition to increasing uptake into neural tissue, greater lipid solubility results in rapid uptake into both blood vessels (with a resultant systemic effect) and fatty tissue. The spread of lipophilic opioids within the CSF is therefore more limited than hydrophilic opioids such as morphine, which demonstrate greater spread as a result of slower uptake and elimination from the CSF. As a result, hydrophilic opioids have a greater risk of late respiratory depression, which is one of the rare but most serious consequences of intrathecal opioid administration.

Opioid receptors belong to G- protein coupled receptors superfamily. Agonist binding to opioid receptors leads to several events that inhibit the activation of neuron by:

- Inhibition of adenyl cyclase
- Inhibition of activation of voltage-gated Ca^+ channels which will decrease neurotransmitter release
- Membrane hyperpolarization by increasing K^+ conductance resulting in reduced excitability.

The present study was undertaken to compare the effects of adding fentanyl or butorphanol as adjuvant to bupivacaine 0.5% heavy intrathecally on the characterstics of sensory and motor block and postoperative analgesia, in patients undergoing lower limb and lower abdominal surgeries.

AIM AND OBJECTIVES

The study aims to compare the efficacy of Fentanyl and Butorphanol as adjuvant to bupivacaine 0.5% heavy for lower limb and lower abdominal surgeries with respect to:

- Onset of sensory and motor block.
- Duration of motor block.
- Duration of Post-operative analgesia
- Adverse effects – like hypotension, nausea, vomiting, bradycardia, respiratory depression, shivering and pruritus.

MATERIALS AND METHODS

Study design

The study"A Comparative Study of Efficacy of Intrathecal Fentanyl and Butorphanol as an Adjuvant to Bupivacaine 0.5% Heavy for Lower Limb and Lower Abdominal Surgeries"was a Randomised Controlled Trial done on 60patients of age between 18-60 years with ASA physical status grade I and II.

After obtaining approval from the institutional ethics committee, 60 patients scheduled for lower limb or lower abdominal surgery were randomly selected and divided in two groups of 30 each.

Inclusion criteria

- ASA physical status I and II of either sex
- Age in between 18 to 60 years
- Patient with written valid consent
- Patient undergoing elective lower limb or lower abdominal surgery.

Exclusion criteria

- Refused by patient
- Allergy to any drug
- Infection at injection site
- Patient on anticoagulants or bleeding disorder
- ASA III and IV
- Patients on tranquilizers, hypnotics, sedatives, and other psychotropic drugs.
- Duration of surgery > 2 hours

Pre anesthetic check-up was done a day before and reviewed on the day of surgery.
Patients were randomly allocated into 2 groups each having 30 patients.
GROUP A - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + Fentanyl 25μg (0.5 ml)
GROUP B - Intrathecal bupivacaine 0.5% heavy (2.5 ml) + butorphanol 25ug (0.5 ml)

All the patients were kept fasting overnight prior to the scheduled day of operation. Sedatives and hypnotics, inclusive of Opioids were avoided in pre medication as well as intra operatively. Patients received Inj. Ranitidine 50mg IV as premedication after entering the operation theatre. All standard monitors (ECG, NIBP, SpO2) were applied. Baseline BP, PR, RR was recorded. All patients were preloaded through 18 G cannula with 10 ml/kg of RL solution over 15-20 min. Under all aseptic precautions, lumbar puncture was performed in the L_{3-4} Interspace using 25 G Quincke's spinal needle in sitting position. The patient received either one of the drug solution. Patient was turned supine and position of table was kept horizontal. Recording of HR, SBP, DBP, MAP, SpO2 and RR was done every 3 mins for 15 min, every 5

mins for 30 mins, and every 15 mins till 3 hours. In the intra operative period, crystalloid solutions (Ringer Lactate) 4ml/kg/hr was infused. Sensory onset was tested by pin-prick method every 2 minutes using a 23 G hypodermic needle until the level had stabilized for 3 consecutive times. Motor block was assessed using modified Bromage scale. VAS was noted when the patient first complained of pain. VAS>3 was treated with inj. Diclofenac 75mg IV.

The following parameters were noted

1) Time of onset of sensory block (i.e. time taken from intrathecal injection of drug to complete loss of sensation to pin prick at T10).
2) The highest level of sensory block achieved.
3) Time taken to achieve the highest level achieved by sensory block (time from intrathecal injection to highest level of sensory block).
4) The time required for regression of sensory level by two dermatomal segments .
5) Time required to achieve complete motor block by Modified Bromage Score (time from intrathecal injection of drug to achievement of Bromage 3).
6) Motor block duration was noted (time from Bromage 3 to Bromage 2).

Modified Bromage Scale (for grading of motor block)

1. Grade 0 - No motor block
2. Grade 1 – not able to raise extended leg but able to move knees and feet
3. Grade 2 - not ability to raise extended leg and move knees but able to move feet
4. Grade 3 – complete motor block of lower limbs.

7) Duration of analgesia (time required for the onset of sensory block to first complaint of pain by patient).
8) Post-operative pain was assessed using 10 point Visual Analogue Scoring method (0- means no pain, 10- means worst pain)

Pain score '0' to '3' - Mild pain, Pain scores '3' to '7' - Moderate pain, Pain scores> 7 - Severe pain

9) Adverse effects

A. If Hypotension occurred (MAP fall below 20% of base line) – was treated by following methods, till blood pressure normalized.
   - Bolus of 100 – 200 ml of crystalloid solution
   - Sympathomimetics
     Inj. Mephenteramine IV 6mg to begin with and repeated if necessary, to the maximum of 30mg.
     Inj .dopamine 3-10 mcg / kg / min I.V. infusion if no response to mephenteramine
   - Colloid/Blood transfusion in case hypovolemia ensued due to bleeding.

B. If Bradycardia(HR<50) was encountered,
   - Inj. Atropine 0.5mg IV was given

C. If Respiratory depression RR<10/min.
   - Oxygenation and IPPV if required.

D. If Nausea and vomiting
   - Inj. Ondansetron 4 mg i.v.

E. Shivering
   - Use of patient warming system-baer hugger.

F. Pruritus
   - Inj hydrocortisone 100mg iv

RESULTS

Observations and results of the study were compared and then statistical analysis was done. Data being managed in an excel spreadsheet.

SPSS program was used for statistical analysis for Windows, version 17.0. Continuous variables are presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. For comparing the two main groups Paired t test was applied.

In this study p value<0.05 have been considered as statically significant.
Data is presented as Mean±SD

Table-1: Comparison of age, weight, height and sex in study groups

		Group F	Group B	P Value
Age in years		35.10 ± 12.17	33.53 ± 11.39	0.880
Height in cm		162 ± 4.63	163.23 ± 4.23	0.357
Weight in Kg		65.93 ± 4.97	64.43 ± 6.66	0.239
Sex	F	4 (13.3%)	8 (26.7%)	0.186
	M	26 (86.7%)	22 (73.3%)	

Table-2: Comparison of ASA physical status grades in study groups

ASA	Group F	Group B	P Value
	Frequency (%)	Frequency (%)	
I	19 (63.3%)	16 (53.3%)	0.659
II	11 (36.7%)	14 (46.7%)	
Total	30 (100%)	30 (100%)	

Table-3: Comparison of preoperative vitals in study groups

	Group F	Group B	P Value
	Mean ± SD	Mean ± SD	
SBP	125.6 ± 12.76	124.07 ± 10.73	0.366
DBP	78.33 ± 8.17	75.63 ± 7.78	0.446
PR(bpm)	79.43 ± 9.94	80.83 ± 10.76	0.812
SPO2	100.00 ± 0.00	100.00 ± 0.00	–
RR(cpm)	14.23 ± 1.72	14.23 ± 1.72	0.539

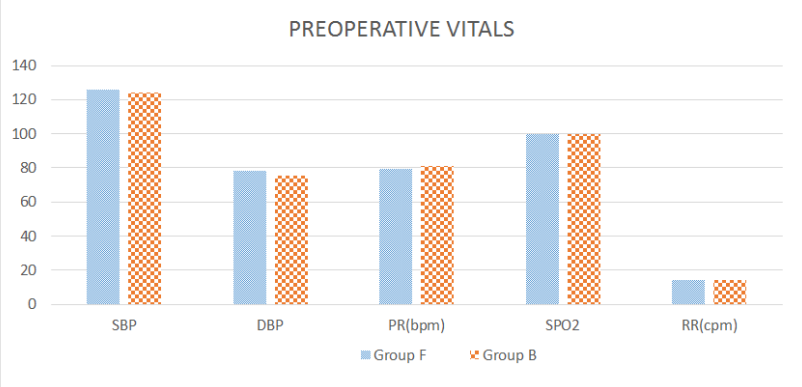

Fig-1: Comparison of preoperative vitals in study groups

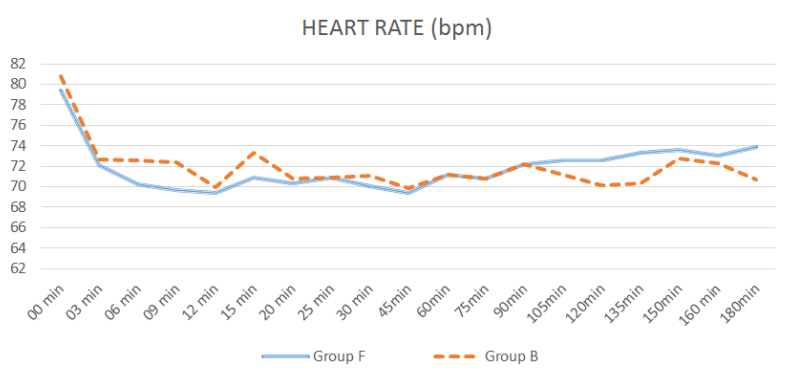

Fig-2: Heart rate (beats/min) of the two studied groups

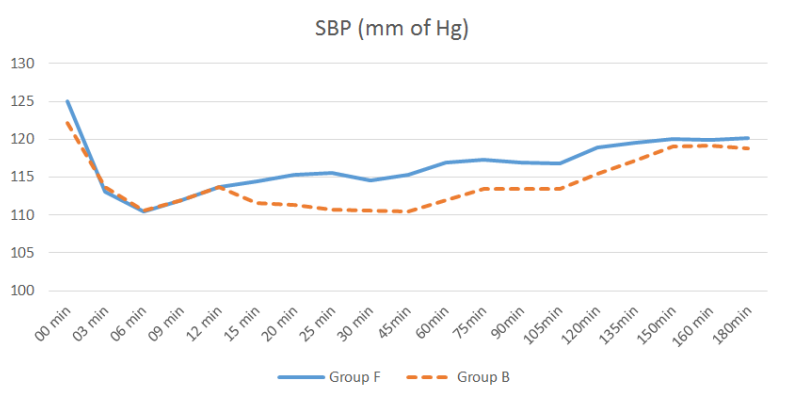

Fig-3: SBP (mmHg) of the two studied groups

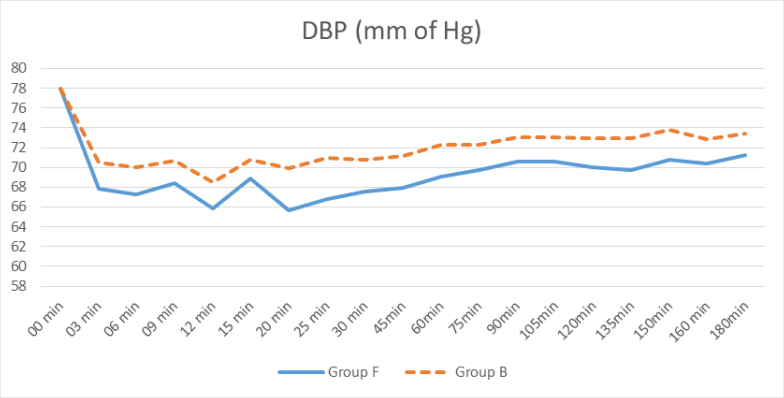

Fig-4: DBP (mmHg) of the two studied groups

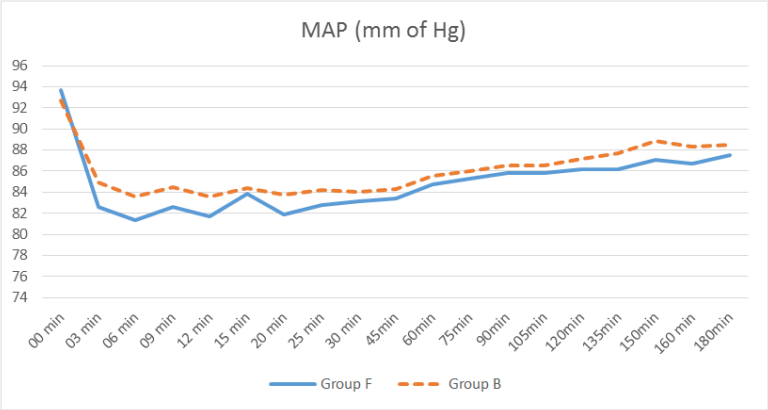

Fig-5: MAP (mmHg) of the two studied groups

Table-4: Comparison of various objectives of the study groups

	Group F	Group B	P Value
	Mean ± SD	Mean ± SD	
Time of onset of sensory block (T10)(sec)	274 ± 73.39	148.63 ± 2.54	<0.001
Time to highest sensory (MIN)	5 ± 1	4.3 ± 0.92	0.007
Time of 2 dermatomal regression (MIN)	145.07 ± 5.34	141.33 ± 3.51	0.002
Time to motor bromage 3 (MIN)	5 ± 1.12	4.53 ± 0.86	0.06
Duration of motor block (MIN)	149 ± 7.13	140.37 ± 2.31	<0.001
Duration of analgesia (VAS>3) (MIN)	244 ± 7.11	250.10 ± 4.05	<0.001

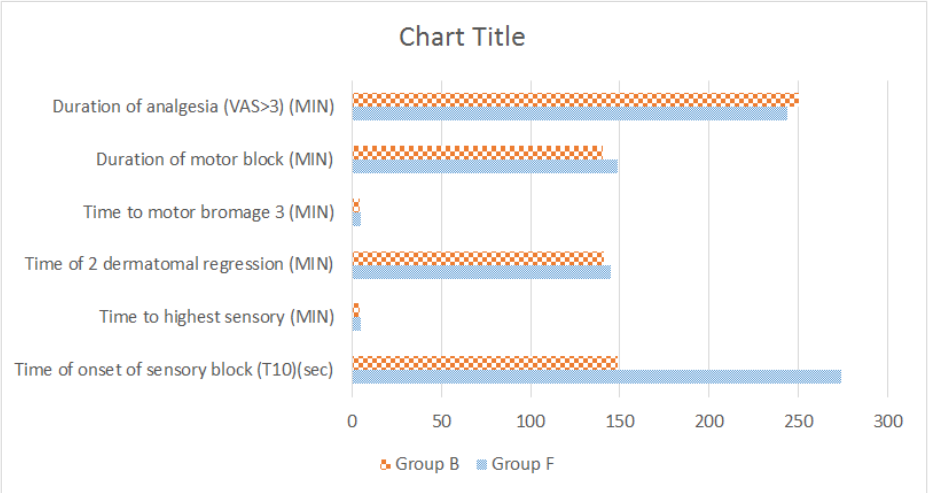

Fig-6: Comparison of various objectives of the study groups

The two groups were found to be comparable in terms of demographic variables such as age, sex, weight and height. All the patients in both the groups remained hemodynamically stable through the conduct of anaesthesia with no significant deviation in heart rate, systolic and diastolic BP and mean arterial pressure.

Sensory blockade onset time and time to attain highest sensory level were rapid and statistically significant with Butorphanol as compared to Fentanyl. The onset of motor block was comparable in both the groups and the difference was not statistically significant. Maximum sensory level achieved was T6.A sensory level up to T10 could be achieved in all the cases.

Time for two segment regression and motor block duration were significantly prolonged with fentanyl as compared to butorphanol and were statistically significant.

Analgesia was prolonged and was statistically significant with Butorphanol as compared to Fentanyl.

DISCUSSION

The salient findings in our study are that addition of 25 µg of butorphanol as adjuvant to hyperbaric bupivacaine 0.5% provides a faster onset of sensory block as compared to 25 µg fentanyl. Fentanyl provided a significantly greater duration of both sensory and motor block than butorphanol. The duration of postoperative analgesia was significantly greater with butorphanol.

Also in the present study, there was no statistically significant difference between both groups as regards the duration of motor block, hemodynamics and oxygen saturation. Neither bradycardia nor oxygen desaturation was recorded.

The onset of sensory block was delayed in fentanyl group (274 ± 73.39 sec) when compared to butorphanol group (148.63 ± 2.54sec) by about 120 sec. It was both statistically and clinically significant. The duration of sensory block as well as motor block was prolonged in fentanyl group (145.07 ± 5.34 mins) and (149 ± 7.13 min) respectively as compared to butorphanol group (141.33 ± 3.51 min) and (140.37 ± 2.31 min) respectively, which were both statistically and clinically significant.

Vinita Singh *et al*. [7], in their study compared intrathecal fentanyl and butorphanol in combination with bupivacaine for lower limb surgeries and concluded that 25µg intrathecal butorphanol is superior to 25µg intrathecal fentanyl in respect to duration of sensory block Kumar B *et al*. [6], in their study compared intrathecal bupivacaine-fentanyl and bupivacaine-butorphanol mixtures for lower limb orthopedic procedures, concluded that intrathecal bupivacaine-butorphanol mixture provides longer duration and superior analgesia than intrathecal fentanyl-bupivacaine mixture.

The time for highest level of sensory block was also delayed in fentanyl group (5 ± 1 mins) when compared to butorphanol group (4.3 ± 0.92 mins). It was also both statistically and clinically significant.

The complete motor block onset was comparable in both fentanyls than butorphanol group. The duration of motor block was significantly prolonged by addition of fentanyl, though this was not observed in any of the previous studies.

The duration of analgesia was more in butorphanol group (250.10 ± 4.05 min) as compared to fentanyl group (244 ± 7.11 min) which was both statistically and clinically significant. Vinita Singh *et al*.**[**7], in their study compared intrathecal fentanyl and butorphanol incombination with bupivacaine for lower limb surgeries and concluded that 25µg intrathecal butorphanol is superior to 25µg intrathecal fentanyl regarding the duration of analgesia and requirement of analgesia was reduced in the early postoperative period which was in concordance to the present study. Kumar B *et al*. [6], in their study compared intrathecal bupivacaine-fentanyl and bupivacaine-butorphanol mixtures for lower limb orthopedic procedures, observed decreased pain scores and reduced analgesic requirements in the butorphanol group. Vangipuram RC *et al*. [8], in their study compared addition of butorphanol to hyperbaric bupivacaine intrathecally to patients undergoing lower segment caesarean section and concluded that addition of butorphanol gives longer duration of post-operative analgesia compared with control without serious side effects.

CONCLUSION

Addition of 25 mcg fentanyl to bupivacaine0.5% heavy in spinal anaesthesia prolongs duration of sensory and motor block, whereas addition of 25 mcg of butorphanol to bupivacaine0.5% heavy in spinal anaesthesia provides the advantage of faster onset of sensory block and longer duration of postoperative analgesia as compared to 25 mcg fentanyl. None of the two adjuvants are associated with significant side effects.

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