ORIGINAL RESEARCH PAPER

Anaesthesiology

A COMPARATIVE STUDY OF THE EFFECTS OF INTRATHECAL HYPERBARIC BUPIVACAINE WITH BUPRENORPHINE AND HYPERBARIC BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES

KEY WORDS: Spinal Anaesthesia, Intrathecal Hyperbaric Bupivacaine, Buprenorphine, Fentanyl.

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ABSTRACT

BACKGROUND: Spinal anaesthesia is the most commonly used technique for lower abdominal, lower limb surgeries. In clinical practice both Fentanyl and buprenorphine have been used as adjuvants with bupivacaine for spinal anesthesia. So, this present study has been conducted to assess the better drug between these two adjuvants with regard to post-operative analgesia and haemodynamic stability.

OBJECTIVE: To study the effects of 0.5% hyperbaric bupivacaine with buprenorphine and 0.5% hyperbaric bupivacaine with fentanyl in spinal anaesthesia for lower abdominal and lower limb surgeries.

SETTINGS & DESIGN: This comparative study included 50 patients in two groups, of ASA class I & II undergoing lower abdominal and lower limb surgeries under spinal anesthesia after approval from hospital ethics committee with written informed consent of patients.

MATERIALS AND METHODS: Patients were categorized into two groups (n=50) A & B. Group A received 75 g of buprenorphine and Group B received 25 g of fentanyl as adjuvants to 15mg of 0.5% hyperbaric bupivacaine (3.0ml). Onset of sensory block and motor block, two segment regression, time of sensory and motor block, duration of sensory & motor block, duration of analgesia, haemodynamic changes and side effects were recorded.

RESULTS: There was no significant difference in onset of sensory block in two groups ($P>0.05$), but onset of motor block was significantly earlier in buprenorphine group. Two segment regression time, duration of sensory & motor block, duration of analgesia were significantly longer for group A as compared to group B ($P< 0.05$).

CONCLUSION: The duration of sensory block, motor block and duration of post-operative analgesia was better in buprenorphine group in comparison to fentanyl group. Both the drugs prolong the duration of analgesia on giving intrathecally along with bupivacaine heavy. These drugs can be used to prolong duration of analgesia in lower abdominal and lower limb surgeries without having any significant side effect.

INTRODUCTION:

Pain is a complex distressing feeling often caused by intense and damaging stimuli. Pain is defined by the International Association for the Study of Pain (IASP) as an "Unpleasant sensory and motor experience associated with actual or potential tissue damage or described in terms of such damage".[1] Spinal anaesthesia is the most commonly used technique for lower abdominal, lower limb surgeries. It is the first choice of anaesthesia because of its rapid onset, superior blockade, less failure rates and cost effectiveness. Local anaesthetic applied for neuraxis can provide potent, long lasting analgesia including intra-operative analgesia, acute post-surgical pain, and severe chronic pain associated with malignancy but the duration of block and analgesia is not satisfactory to many of the patients. Opioid was first used as spinal additive in 1979 with morphine as forereunner.[2] Opioids and local anaesthetic administered together have synergistic analgesic effect in control of post-operative pain.[3] It improves the quality of intraoperative analgesia and prolongs the duration of post-operative analgesia. Intrathecal opioids enhance sensory block without affecting sympathetic activity.[4] Intrathecal administration of additive drugs along with local anaesthetic is beneficial as no extra technique is required, dose required is less as compared to IV/ IM and side effect of systemic absorption is avoided.

Fentanyl, a lipophilic opioid, has a rapid onset of action following intrathecal administration but duration of action is dose dependent with no respiratory depression. It improves the quality of sensory block intra-operatively without increasing sympathetic or motor blockade, it also enhances the quality and duration of post-operative analgesia to a significant extent[5] and has been found to be safe and effective for neonatal and maternal outcome for both normal parturient and also in severe pre-eclampsia patients for labour analgesia and cesarean section.[6]

Buprenorphine, a semi synthetic opioid is a μ-receptor agonist-partial or full δ-receptor agonist and competitive antagonist at receptor. It is an effective analgesic, as morp hine in nearly all clinical situations and 25- 40 times more potent than morphine.[7, 8, 9] Buprenorphine is compatible with CSF and produces no adverse reactions when administered intrathecally.[9] Its high lipid solubility, high affinity for opioid receptor, and long duration of action make buprenorphine a good choice as a spinal adjuvant with local anaesthetic for managing both intra and post-operative pain. In clinical practice both Fentanyl and buprenorphine has been used as adjuvants with bupivacaine for spinal anesthesia.[10] So, this present study has been conducted to assess the better drug between these two adjuvants with regard to post- operative analgesia and haemodynamic stability.

OBJECTIVE

To compare the efficacy of Buprenorphine and Fentanyl added to bupivacaine as additives :

1. Onset and duration of sensory and motor block.
2. Highest Level of Sensory Block.
3. Duration of post operative analgesia.
4. Any side effects present during the procedure.

MATERIALS AND METHODS

This study was conducted under the Department of Anaesthesiology and Critical Care, Silchar Medical College and Hospital, Silchar for a period of 1 year from 1st June 2018 to 31st May 2019 after approval from the hospital ethical committee.

The inclusion criteria was patients of ASA I & II, aged between 18 - 60 years scheduled for elective surgery for lower abdo minal and lower limb surgeries lasting less than 180 min. The exclusion criteria were patient refusal, ASA III and IV physical status, patients with known allergy to any local anaesthetic or opioid like fentanyl, buprenorphine & patients where subara chnoid block was contraindicated like bleeding tendencies

and local infection.

Pre-anaesthetic evaluation on the day prior to surgery was done for all 100 patients. All general and systemic examinations were done including airway and the surface anatomy of the lumbar spine. Basic laboratory investigations were conducted including complete haemogram, urine analysis, blood sugar, kidney function test, chest X-ray & ECG. The anaesthetic procedure to be carried out was explained. A written informed consent was taken explaining the risks associated to the patients. The patients were made familiar to the methodology for sensory and motor block assessment during the pre-anaesthetic check-up. All the patients were fasted overnight for at least 6 hours and received 0.5 mg Alprazolam the night before surgery. On arrival of the patients in operation theatre, all routine monitors were applied (non invasive blood pressure, pulse oxymetry, electrocar diography and temperature) and oxygen was delivered via face mask at 5lts/min. An infusion was started after insertion of 18 G intravenous cannula on non dominant hand. Pre loading was done with 500 ml of ringer's lactate solution. Baseline recording of heart rate, systolic and diastolic blood pressure, SpO_2 were taken. Patients were instructed about Visual Analouge Score (VAS) and also a scale of 10 cm length with 0 on the scale corresponding to "NO PAIN" and 10 corresponding to "MAXIMUM INTOLERABLE PAIN EXPERIENCED."

The patients were randomly divided into two groups of 50 patients each.

Group A (n=50) receiving 3ml of 0.5% hyperbaric bupivacaine plus 0.25ml buprenorphine (75µg) and 0.25ml normal saline intrathecally (a total of 3.5 ml).

Group B (n=50) received 3.0ml of 0.5% heavy bupivacaine and 0.5ml (25 mcg) of preservative free Fentanyl, a total of 3.5ml.

The patients were placed in the left lateral position. After all preparations under all aseptic precautions, a 25-gauge Quincke's point needle was introduced in the L3-L4 interspace and the duramater was punctured for the administration of the local anaesthetic solution in the subara chnoid space. Patients in Group A received 3 ml of 0.5% hyperbaric bupivacaine (15 mg) and 75 microgram of buprenorphine solution, a total volume of 3.5 ml. Those in Group B received 3 ml of 0.5% hyperbaric bupivacaine (15 mg) and 0.5 ml of preservative free Fentanyl (25µg) intrathecally. The anaesthetist administering the study drugs as well as the patients were blinded to the group allocation.

The highest level of sensory block was asessed by pin prick method in caudal to cephalic direction every 2 minutes, the time taken to achieve absence of pinprick response at T10 level in midclavicular line was taken as onset of sensory block. Motor block was assessed by modified bromage scale. Intraoperative assessment of sedation was done as par modified Ramsay's sedation scale at 1st, 2nd, 3rd, 4th, 6th, 8th and 12th hours.

Satisfactory block was defined as sensory level of T10 and Bromage score of 3. Duration of sensory block was defined from completion of drug injection to reappearance of response to pinprick at L-1 level. Duration of motor block was recorded as time from injection of drug into subarachnoid space to achieve Bromage- 0. Postoperative pain was assessed by visual analogue scale (VAS). Duration of analgesia was taken from the time of intrathecal drug administration to the time when patient, first complained of pain. At that point the study was terminated with respect to analgesia and inj. Diclofenac was given at the dose of 75 mg IM. Post operatively the patients were evaluated for motor and sensory recovery. Pain was assessed by standardized Visual analogue scale (VAS) at hours from the time 1st hour, 2 hours, 3 hours ,4 hours, 5 hours, 6 hours, 8 hours, 12 hours of intrathecal injection of the test drug. The supplemental analgesia was given in the form of inj. Diclofenac 75mg when VAS score was more than four. Time to first dose of rescue analgesic required was noted.

Statistical analysis were analysed with Graphpad Instat® 3 statistical software. For qualitative data, Fisher's exact test was used. Quantitative data were analysed using student t-test. For non-parametric data Mann-Witney test was used. P value < 0.05 was considered statistically significant. Data are presented as mean values ± SD.

RESULTS:

Demographic profile – both the groups were comparable with regard age, height weight and ASA grading. The duration of operation is also comparable in two groups statistically.

Table 1: Showing demographic profile

Parameters	Group A (Mean ± SD)	Group B (Mean ± SD)	P Value
Height(cms)	161.64 ± 4.323	160.46 ± 4.793	0.1964
Weight(Kg)	62.82 ± 7.537	62.34 ± 7.383	0.7653
Age (years)	38.78 ±9.316	37.00 ± 9.934	0.3819.
ASA-PS	43.50 ± 2.121	6.50 ± 2.121	0.3333
Duration of operation (mins)	112.90 ± 9.040	113.40 ± 7.384	0.7626

In our study there was no significant variation in the onset of sensory blockade but onset of motor blockade for group A was 3.896±0.4495 minutes and group B was 3.706±0.4142 minutes which was statistically significant. The blockade was earlier in buprenorphine group. The highest level of sensory blockade was similar in both groups.

The duration of sensory block in Group A was 268.94 ± 10.306 minutes and group B was 168.46 ± 26.265 minutes. The duration of motor block for group A was 222.68 ± 15.213 minutes and group B was 152.56 ± 18.853 minutes. In both the cases the duration of sensory and motor block for buprenorphine group was more and was found to be statistically significant. The duration of analgesia in Group A was 295.82 ± 10.352 and group B was 196.16 ± 10.309. The duration of analgesia was more for buprenorphine group in comparison to fentanyl group.

Table 2: Subarachnoid Block Characteristics between two group

	Group A	**Group B**	**P value**
	Mean ± SD	**Mean ± SD**	
Onset of sensory block(minutes)	7.304 ±0.6104	7.420±0.575	0.3306
Onset of motor block(in minutes)	3.896±.4495	3.706±0.4142	0.0303
Two segment regression Time of sensory block (minutes)	97.72±1.750	96.12±2.561	0.0004
Duration of Sensory block(in minutes)	268.94±10.306	168.46±26.265	0.001
Duration of motor block(in minutes)	222.68±15.213	152.56±18.853	0.001
Duration of Analgesia(in minutes)	295.82±10.352	196.16±10.039	0.001
Time for highest level of sensory block(in minutes)	16.67±4.163	16.67±5.508164	0.9999

Figure 1: Graphical representations of mean comparison Intra-operative sedation (Ramsay scale) in two groups

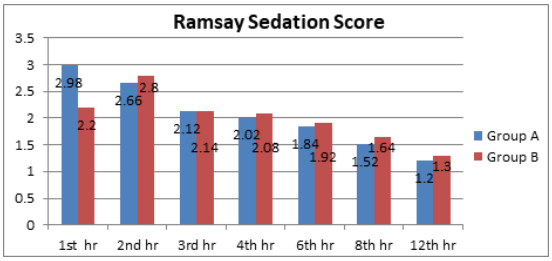
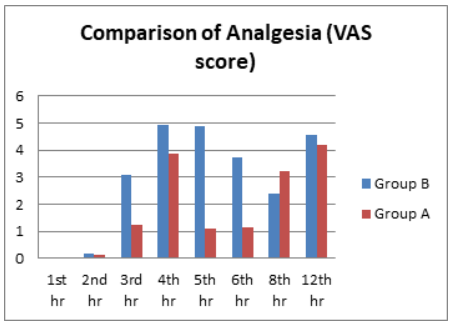


Figure-2. Graphical representations of mean comparison analgesia (VAS score) in two groups



DISCUSSION:

Buprenorphine a semi-synthetic opoid is a μ- receptor agonist-partial or full δ-receptor agonist and competitive anatagonist at the -receptor. It has a long half life and it is 25-40 times more potent than morphine.[7, 8, 9] It is available as preservative free solution and has high lipid solubility. It is a lipid soluble analogue of the alkaloid thebaine with both spinal and supra spinal component of analgesia. The anti hyperalgesic effect of buprenorphine helps in preventing central sensitization. Its high lipid solubility, high affinity for opoid receptor, and long duration of action make buprenorphine a good choice as a spinal adjuvant to intrathecal local anaesthetic for managing moderate to severe post operative pain. Being more lipophilic than morphine, buprenorphine has low medullary bioavailability after neuraxial administration so that occurrence of side effects is less, making it an attractive alternative. As suggested by Capogna et al[10] duration of analgesia is dose dependent and was found to be 430 minutes where as in our study duration of analgesia was 295.82±10.352 minutes.

Fentanyl is a lipophilic μ- receptor agonist. Intrathecally fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord and may have a supraspinal spread and action. Fentanyl given intrathecally in combin ation with local anaesthetic prolongs the duration of spinal anaesthesia in comparison to local anaesthetic given alone in both obstetric and non obstetric surgeries. Reuben et al [11] used different doses (5, 10, 20, 40, 50 μg) of fentanyl in their study and found that even 20μg of fentanyl in combination of 0.5 % of bupivacaine gave good amount of analgesia. So, we have used 25μg of fentanyl in our study.

There was no significant difference in onset time of sensory block in both the groups (7.304 ± 0.6140 and 7.42±0.5753 minutes for Group A & B (P >0.05). The mean onset of motor blockade in both the group (3.896± 0 .4495 & 3.706± 0.4142 minutes for Group A & B) minutes (P 0.05). The mean time for onset of motor bock was found to be significantly earlier in fentanyl group in comparison to buprenorphine group. Rashmi Pal et al[12], Naresh Bukya et al.[13], Krishnakumar shrinivasagam et al.[14] found similar result to the present study. Fauza A Khan et al[15], Kamal Sonya &Davies C.V[16] in their study found no significant difference between the two groups.

In the present study, the P value for the Highest Level of Sensory Block was found to be 0.9999 (>0.05) which was statistically not significant. Borse et al[21], found similar result in their study comparing intrathecal bupivacaine and bupiv acaine with buprenorphine. Singh et al[18], in their study found no significant difference in maximum level and time required for reaching maximum level of sensory block in between the groups receiving fentanyl and CSF with bupivacaine.

The mean time duration for two segment regression in our study for group A was 97.72 ± 1.750 min whereas in group B it was 96.12±2.561 min (P= 0.0004) , the difference being statistically significant. The two segment regression time for fentanyl is earlier than buprenorphine group. Singh et al[18], in their study found that the two segment regression time for intrathecal administration of 13.5 mg hyperbaric 0.75 % bupivacaine and 25μg fentanyl were 93 ± 22 mins which is comparable with the present study. Acharya et al.[19],in their study found that the two segment regression time for intrathecal administration of 2ml hyperbaric 0.5 % bupivacaine and 12.5μg fentanyl were 95.17±16.5mins which is comparable with the present study. Borse et al[21], in their study found that the two segment regression time for intrathecal administration of 2.5ml hyperbaric 0.5 % bupivacaine and 150μg preservative free buprenorphine were 84 ± 12.0 mins. The duration is significantly different than the present study which may be due to the difference in the dose of buprenorphine (75μg) used in our study. Kaur et al[20], in their study found that the two segment regression time for intrathecal administration of 1.8ml hyperbaric 0.5 % bupivacaine and 60μg buprenorphine were 74 ± 25.3 mins. The duration is significantly different than the present study which may be due to the difference in the dose of bupivacaine 2.5ml and buprenorphine (75μg) used in our study. The duration of sensory block in Group A was 268.94 ± 10.306 minutes and group B was 168.46 ± 26.265 minutes and the duration of motor block for group A was 222.68 ± 15.213 minutes and group B was 152.56 ± 18.853 minutes. The study done by Khan et al[15], Pal et al[12], Krishnakumar Shrinivasagam et al.[14], Kamal Sonya, Davis C.V [16], Naresh Bukya et al.[13] found significant difference in the duration of sensory block and motor block between the two groups which is similar to the present study and the duration of sensory and motor block was more for buprenorphine group in comparison to fentanyl group. The duration of analgesia in the present study showed no requirement of additional analgesic intra-operatively. The mean duration of analgesia for group A was 295.82 ± 10.352 and for group B was 196.16 ± 10.039 minutes statistically significant in between the two groups (P=0.001 i.e P <0.001). The duration of analgesia was longer for buprenorphine group in comparison to fentanyl group. Khan et al[15], Pal et al[12], Krishnakumar Shrinivasagam et al.[14], Bukya et al.[13] found significant difference in duration of sensory block and motor block between the two groups which is similar to the present study and the duration of sensory and motor block was more for buprenorphine group in comparison to fentanyl group. VAS (Visual Analouge Scale) SCORE In the present study VAS score at rest for pain was measured at 1st, 2nd, 3rd, 4th, 5th, 6th, 8th and 12th hours. It was observed that VAS score for fentanyl group was more than buprenorphine group and the difference was found to be statistically significant (p<0.05). The study corresponds to Nelamangala et al[22], Bhukya et al[13], found significant difference in VAS between the two groups which is similar to the present study and the VAS was more for fentanyl group in comparison to buprenorphine group. Krishnakumar Srinivasagam et al [14], found significant differ ence in VAS score between the two group but did not mention which group had higher VAS score. Assessment of sedation as per modified Ramsay's sedation scale was done at 1st, 2nd, 3rd, 4th, 6th, 8th and 12th hours in the present study for the intrathecal injection of bupivacaine and bupren orphine

(group-A) and bupivacaine and fentanyl (group B). The sedation score group A(mean= 2.98 ± .1414) is more in comparison to group B(mean=2.20±.5741) and was statistically significant during the 1st hour but in later hours, sedation score was more for fentanyl group in comparison to buprenorphine but the difference was statistically non-significant. In the study done by Bhukya et al[13], The sedation score group A is more in comparison to group B and was statistically significant during the 1st hrs but later sedation score was more for fentanyl group in comparison to buprenorphine but was statistically non-significant. The result was similar to the present study. Bogra et al.[17] after intrathecal inj.of bupivacaine with fentanyl, found that patient was drowsy but arouseable state intraoperatively. Dixit et al [23], after intrathecal inj.of bupivacaine with buprenorphine found that patient was drowsy state intraoperatively. Gupta et al[24], on administering 60µg of buprenorphine with hyperbaric bupivacaine intrathecally found a sedation score of less than 3 in 28 out of 30 patients.

In this study hypotension is considered if there is fall in mean blood pressure of more than 20% of base line and Heart rate less than 60 beats per minutes was considered bradycardia. No case of Hypotension or bradycardia was noted in the present study. Initially after spinal anaesthesia there decrease in blood pressure but neither of them caused hypotension the decrease in blood pressure is maximum at around 50 to 60 minutes. In the present study there were no any incidences of hypotesion or bradycardia. There was initial decrease in SBP, DBP and MAP but was not statistically significant between the two groups and the fall in SBP, DBP and MAP is more for fentanyl in comparison to buprenorphine group but was not significant. In the study conducted by Pal et al[12], Shriniv asagam etal.[14], similar result was found. Khan et al.[15] found significant difference in systolic and diastolic blood pressure intraopertively but none of the patient required ephedrine. Few cases of decrease in heart rate was found intra-operatively but there was no significant difference in systolic and diastolic blood pressure. Nilamangla et al[22] found few incidences of bradycardia and hypotension but was statistically not significant. Few incidences of complication like nausea & vomiting, pruritus, urinary retention & shivering were found but not statistically significant. In the present study there was no incidence of respiratory depression for both fentanyl and buprenorphine group. The limited sample size and absence of control group to compare the drugs separately is the limitation of the study.

CONCLUSION:

On the basis of our clinical comparative study, we can conclude that the addition of 75µg buprenorphine and 25µg fentanyl with 0.5% hyperbaric bupivacaine intrathecally for spinal anaesthesia in patients undergoing lower abdominal and lower limb surgeries caused no significant difference in onset of sensory block but onset of motor block was significantly earlier in buprenorphine group. The duration of sensory block, motor block and duration of post operative analgesia was longer in buprenorphine group in comparison to fentanyl group. Both the drugs prolonged the duration of analgesia on giving intrathically along with bupivacaine heavy. So, these drugs can be used to prolong duration of analgesia in lower abdomen and lower limb surgeries without having any significant side effect. But further study is necessary to find out the optimum dose of the drugs which can be used for intra operative as well as post operative analgesia without any side effect.

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