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Original Article

A Comparative Study of Efficacy of Anesthesia and Analgesia between Intrathecal Fentanyl and Butorphanol with Bupivacaine 0.5% Heavy for Lower Limb Orthopedic Surgery: A Prospective Randomized Study in a Tertiary Care Teaching Hospital

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ABSTRACT

Background: Subarachnoid block is a common anesthesia procedure for lower abdominal or lower limb surgeries including perineal surgeries. Usage of opioids in conjunction with local anesthetic for spinal anesthesia has been associated with decreased pain scores and reduced analgesic requirement in the post-operative period.
Objectives: To assess the efficacy of anesthesia and analgesia between intrathecal fentanyl and butorphanol with bupivacaine heavy 0.5% for lower limb orthopaedic surgery.
Design: Prospective randomized control trial
Method of collection of data: This prospective, randomized, double blind study was conducted after approval from the institutional ethics committee and written informed consent of patients. About 100 patients, aged 18-75 years, belonging to American society of anesthesiologists (ASA) physical status 1 or 2 and scheduled for elective, lower limb orthopedic surgeries was randomized into two groups. Group A received 2.5ml of 0.5% hyperbaric bupivacaine with 0.5ml (25µg fentanyl) a total volume of 3ml intrathecally. The Butorphanol was diluted using distilled sterile water to obtain 25µg in 0.5ml. This was then added to 2.5ml of 0.5% hyperbaric bupivacaine to make a total volume of 3ml which was given to group B.
Results: The times required for onset of sensory and motor blockade were comparable among the two groups. Significantly slower block regression to S2 level was observed in the group receiving intrathecal butorphanol as compared to intrathecal fentanyl (P<.001). A higher number of patients in group A requested for rescue analgesia during the postoperative period than in group B (9 versus 2; P=0.0238). The average times to first request for rescue analgesia were 245.74±9.22 minutes and 282±8.66 minutes in group A and B, respectively (P<0.001).
Conclusion: Both 25µgfentanyl and 25µgbutorphanol given intrathecally along with 12.5 mg of hyperbaric bupivacaine provide effective anesthesia for lower limb surgeries. Intrathecal bupivacaine-butorphanol mixture provides longer duration of sensory blockade and superior analgesia than intrathecal fentanyl-bupivacaine mixture.

Keywords: Intrathecal, Hyperbaric Bupivacaine, Fentanyl, butorphanol, lower limb orthopedic surgery.

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INTRODUCTION

Subarachnoid block (SAB) a popular is a common anesthesia procedure practiced worldwide and was first performed by August Bier more than a century ago by injection of cocaine into CSF of a patient. It is the anesthesia of choice and gold standard for lower abdominal /lower limb surgeries including perineal surgeries.[1] Lidocaine has been the most widely used local anesthetic for SAB because of its faster onset and shorter duration of action but it has been associated with higher incidence of transient neurologic symptoms and cauda equina syndrome.[1, 2] Postoperative pain after spinal anesthesia is a common complication in patients undergoing lower limb orthopedic surgeries. Neuraxial opioids are widely used in conjunction with local anesthetics as they permit the use of lower dose of local anesthetics, while providing adequate anesthesia and analgesia.[2] Neuraxial opioids also allow prolonged analgesia in the postoperative period and faster recovery from spinal anesthesia.[3]

The use of opioids in conjunction with local anesthetic for spinal anesthesia has been associated with decreased pain scores and reduced analgesic requirement in the post-operative period.[4,5] The Animal studies have also demonstrated antinociceptive synergism between intrathecal opioids and local anesthetics during visceral and somatic nociception.[6, 7] Present study was undertaken to compare the efficacy of anesthesia and analgesia of intrathecal bupivacaine-butorphanol mixture with intrathecal bupivacaine-fentanyl mixture for lower limb orthopedic procedure, as there are only a limited number of studies have explored the use of intrathecal butorphanol in human subjects previously.[3-7] Hence our aim was to compare the effectiveness of intrathecal hyperbaric bupivacaine with fentanyl and hyperbaric bupivacaine with butorphanol for lower limb orthopedic surgeries.

MATERIALS AND METHODS

Source of Data: This prospective randomized double blind study was conducted on 100 patients undergoing various lower limb orthopaedic surgeries under subarachnoid block at Chalmeda Anand Rao Institute of Medical Sciences and Research centre, Karimnagar from December 2016 to December 2017 over period of 12 months.

Inclusion criteria:

1. Patients belonging to American society of anesthesiologists (ASA) physical status 1 or 2.
2. Patients aged between 18 to 75 years.
3. Patients scheduled for elective lower limb orthopedic surgery.
4. The patients willing to give informed written consent.

Exclusion criteria:

1. Patients in whom spinal anesthesia or the study drugs are contraindicated.
2. Patients with neurological disease, spinal deformities, local skin infection or mental disorders; those who are morbidly obese, hemodynamic unstable or having coagulation disorders, or patients with liver disease, impaired renal functions,
3. ASA Physical status >2 or a history of opioid dependence.

Examination and Preparation: Preanesthetic check up was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations were recorded. The procedure of SAB was explained to the patients and written informed consent was obtained.

Method

After meeting inclusion criteria 100 patients were randomly divided into 2 groups, 50 each based on computer generated randomization table.

Group A: Received 2.5ml of 0.5% hyperbaric bupivacaine with 0.5ml(25µg fentanyl) a total volume of 3ml intrathecally.

Group B: Butorphanol was diluted using distilled sterile water to obtain 25µg in 0.5ml. This was then added to 2.5ml of 0.5% hyperbaric bupivacaine to make a total volume of 3ml.

Anesthetic Procedure: Intrathecal drugs were prepared beforehand to maintain the blinding process. Baseline heart rate, systolic blood pressure, diastolic blood pressure respiratory rate and peripheral arterial oxygen saturation were recorded for all subjects. All patients received 10ml/kg of lactated ringer solution as preload within 20-30 minutes. Subarachnoid block was performed under strict aseptic conditions in the lateral position at the level of L3-4 or L4-5 Inter vertebral space using 25G Quincke spinal needle. The midline approach was used to perform the spinal blocks after infiltrating the skin with 1ml of 2% Lidocaine.. Following the SAB, the patient was put in supine position.

Intraoperative, vitals was recorded at 5 minutes intervals for the first 15 minutes from the time of injection of spinal solution and there after every 30 minutes for the complete period of surgery and every thirty minutes in the postoperative period. This data was recorded by the primary investigator, who was unaware of the patient allocation.

Hypotension less than 20% of base line was treated with fluid boluses and 6 mg IV boluses of Mephenteramine, while bradycardia (HR<50bpm) was treated with 0.6 mg IV atropine. The highest level of sensory block was determined in the midclavicular line bilaterally, by pinprick test using a 20-G hypodermic needle every 2 minutes till the level was stabilized for four consecutive tests. The highest level of sensory block and the time taken to attain it from the time of the intrathecal injection was recorded. Further sensory testing was performed at 20 minutes intervals till the recovery of S2 dermatome. Motor block was assessed using the modified Bromage scale , till achievement of the highest motor level; at the end of the surgery and then at 30min. Side effects such as hypotension, bradycardia nausea vomiting, sedation, pruritus, shivering and respiratory depression was recorded. The quality of postoperative analgesia was assessed using LVAS at 15min, 30min and thereafter every 30minutes, till 2 hours postoperatively; and then every hour, till 4 hours postoperative duration. The time of first request of rescue analgesia was recorded.

Parameters Evaluated:

1. Duration of sensory block: Defined as the time from intrathecal injection to regression of pinprick sensation to S2 level.

2. Degree of motor block: was assessed using Modified Bromage score

A. 0=full movement
B. 1=inability to raise extended leg, can bend knee
C. 2=inability to bend knee, can flex ankle,
D. 3=no movements

3. Duration of motor block: Defined as the time from intrathecal injection to the regression of motor block to Bromage score 0.

4. Hemodynamic parameters: HR, systolic BP, Diastolic BP, Mean arterial pressure was assessed every 5 minutes till 30minutes then every 30 minutes till end of study period.

The segmental level of sensory block to pin-prick was assessed on both sides. The surgery was allowed to start once sensory block had reached at least T10 dermatome. General anesthesia was induced when the case was labelled as failure. A fall of Systolic BP <20% of baseline was considered as hypotension and was treated with intravenous mephentermine 6 mg bolus and lactated Ringer's solution as required. Heart rate of <50 beats/minute was considered as bradycardia and was treated with Inj atropine 0.6mg IV. The end of study period was defined as the time at which the sensory block had regressed below the S2 dermatome or at which the Bromage score was 0 , whichever occurred later.

Assessment of analgesia: Pain was assessed by visual analogue score (VAS).[29] Duration of complete analgesia was defined as the time from the intrathecal injection to VAS >0 - <4 and duration of effective analgesia as the time to VAS >4. Analgesics were avoided until demanded by the patient and the time taken for the first pain medication was also noted (when VAS >6). VAS was also recorded every 30 minutes postoperatively.

Post operatively, monitoring of vital signs, VAS scores and sedation scores was continued every 30 minutes until the time of regression of sensory block to S2 dermatome. The incidence of hypotension was recorded,(arterial blood pressure < 20 % of baseline), and was treated with Inj. Mephentermine 6 mg intravenous increments and bradycardia as pulse rate < 50/ min was recorded and treated by atropine 0.6 mg intravenous stat. Side effects like hypotension, bradycardia, respiratory depression (RR<10), shivering, nausea, vomiting, pruritis were recorded in the perioperative period. Neurological examination was done to rule out any neurological deficits at discharge.

Statistical Analysis:

Statistical analysis was done using SPSS software 16.0. Data obtained was tabulated in the Excel sheet and Chi-sqaure test for proportion, t – test for Quantitative data. Block characteristics were compared using Mann – Whitney U test.

RESULTS

Both the groups were comparable with respect to Age, Sex, Height, Weight, BMI, level of SAB, ASA score and types of surgery (P values >0.05) (**Tables 1 and 2**).

We found the following observations (**Tables 3, 4 and Graphs 1-3**)

1. A statistical significant difference in duration for regression of sensory block to S2 with Group A 119.0±24.0 minutes compared to group B 153±20.4 minutes (P<0.001).
2. A statistically significant difference in time for regression of motor block to Bromage score 0 with group A 144.5±26.1 minutes as compared with group B 181.0±21.3 minutes (P<0.001).
3. A Bromage score of 3 was achieved in 100% of group B and 80% of group A.
4. Statistical significant difference in time for first rescue analgesia with group A 245±40.9 minutes to group B 290±47.6 minutes (P<0.001).

5. HR, Systolic BP, Diastolic BP and MAP decreased after the block in both the groups but were comparatively lower in group B than in group A. Intraoperative hemodynamic parameters were well within normal limits.

Table 1: Patient characteristics and types of surgery

Parameter	Group A (n=50)	Group B (n=50)	P
Age (Years)	41.56 ± 17.53	38.42 ± 16.07	0.353 **NS**
Weight (kgs)	69.68 ± 4.6	70.08 ± 4.351	0.656 **NS**
Height (cm)	169.02 ± 7.72	170.06 ± 6.903	0.479 **NS**
BMI	23.3±1.23	22.9±1.34	0.07 **NS**
LP Value (2-3)/(3-4)	25/35	21/39	0.42 **NS**
ASA status I/II	46/14	52/39	0.15 **NS**
Type of surgery Fracture femur Fracture tibia Fracture of bb of leg Arthroscopy	 5 16 23 14	 16 9 17 8	0.09 **NS**

NS: Non Significant: Student 't' test applied

Table-2 : Gender distribution in frequency and percentage

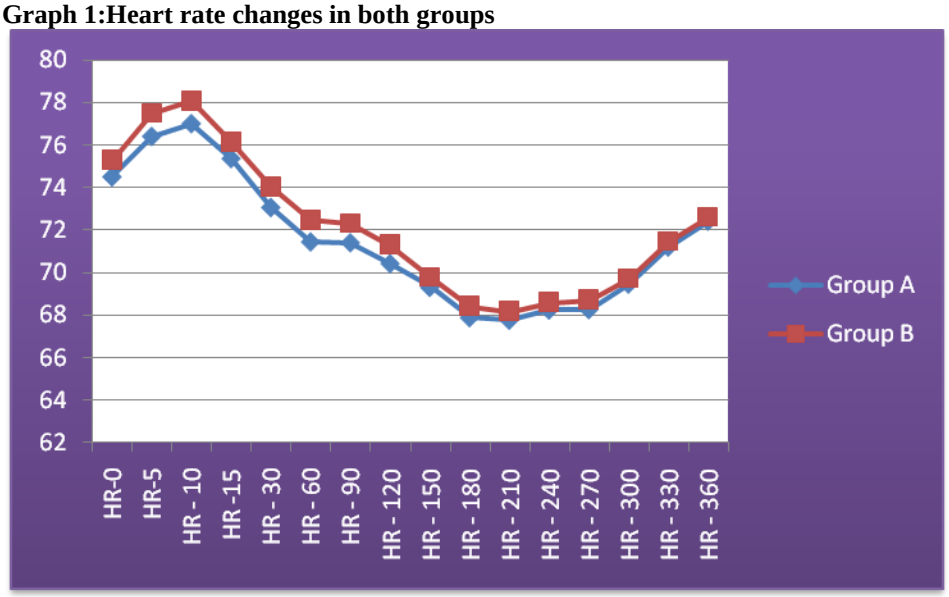
Gender	Group A		Group B		Total	
	Frequency	**Percentage**	**Frequency**	**Percentage**	**Frequency**	**Percentage**
Male	46	92%	38	76%	84	84%
Female	4	8%	12	24%	16	16%

Table -3: Block characteristics

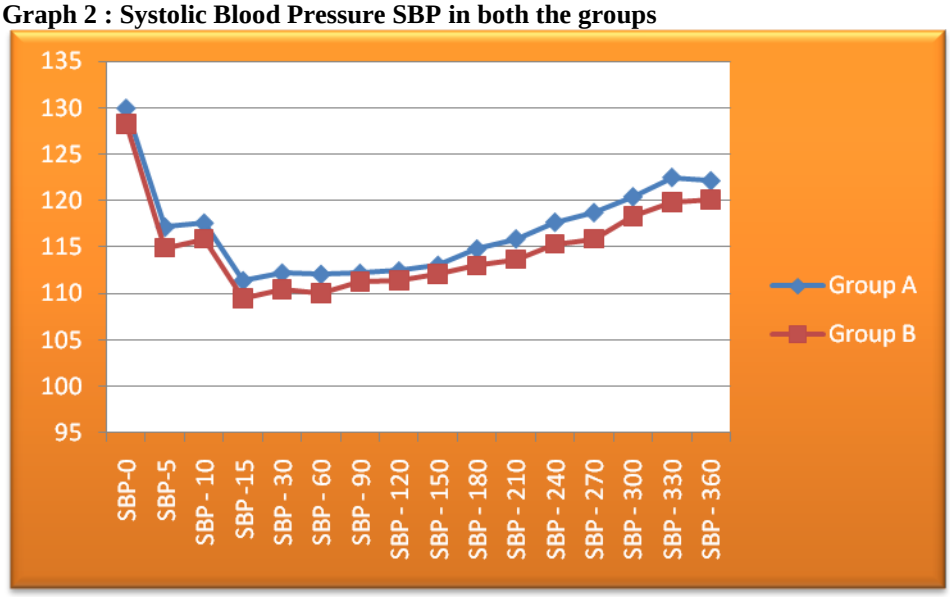
Parameter	Group A	Group B	P
Duration of Surgery	135.52 ± 5.679	133.48 ± 4.871	0.057 **NS**
Duration of motor blockade	168.8 ± 9.180	178.99 ± 13.327	<0.001 **HS**
Duration of analgesia	245.74 ± 9.220	282.40 ± 8.666	<0.001 **HS**
Time for sensory regression to s2 level (min)	160.36 ± 8.810	171.14 ± 13.77	<0.001 **HS**

HS-highly significant, student 't' test applied

Graph 1:Heart rate changes in both groups



Graph 2 : Systolic Blood Pressure SBP in both the groups



Graph 3: Diastolic Blood Pressure in both the groups

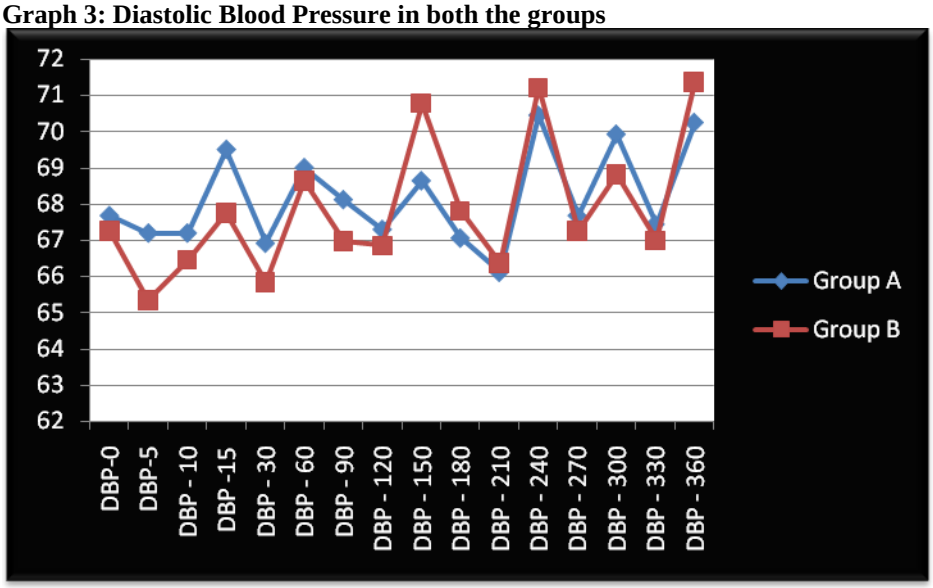


Table 4 : Level of block in the groups

Highest Level Of Sensory Blockade	Group A		Group B		Total	
	Frequency	%	Frequency	%	Frequency	%
T1	0	0	13	26	13	13
T6	12	24	1	2	13	13
T7	10	20	8	16	18	18
T8	14	28	13	26	27	27
T9	14	28	15	30	29	29
Total	50	100	50	100	100	100

P-value = 0.00

DISCUSSION

The use of opioids in conjunction with local anesthetic for spinal anesthesia has been associated with decreased pain scores and reduced analgesic requirement in the postoperative period.[5] Opioids as epidural adjuvants to local anesthesia improve the quality of the block and provide a dose sparing effect.[8] The principal findings of this study are that intrathecal butorphanol-bupivacaine mixture provides longer duration of sensory blockade and superior analgesia (with lesser requirement for

rescue analgesia) as compared to intrathecal fentanyl-bupivacaine mixture.

The observed duration of analgesia with 20 ml 0.5% Bupivacaine alone to be 2-7 hours (mean 4.76) in our study is consistent with studies of Modig and Paalzov (mean 4.3 hours) and Paech et al (mean 5.2 hours).[9, 10] We found that the duration of analgesia was prolonged with the addition of 100 μg fentanyl (3-9 h; mean 5.96), consistent with that given by Kim et al and Paech et al.[10, 11]

The duration of analgesia was longest with B-butorphanol combination (5-10 h; mean 7.64). Studies by Abboud et al, Tan and Gupta et al, using epidural butorphanol for post-operative analgesia have reported the duration of analgesia to be 4-6 h, 5 h and 5.35 h with 0.5 mg, 1 mg, 2 mg and respectively.[12-14] Malik et al have also reported in their study that butorphanol provided a longer duration of analgesia than fentanyl, similar to our study.[15]

In our study, both fentanyl and butorphanol along with bupivacaine, provided adequate anesthesia and analgesia; but significantly lesser analgesic requirement was observed in the group receiving intrathecal butorphanol and bupivacaine mixture compared to intrathecal fentanyl and bupivacaine mixture. The time for first request of analgesia with the use of intrathecal butorphanol and fentanyl, in conjunction with bupivacaine, in our study was about 5 hours and 4 hours respectively from the time of spinal injection. Kim et al. have reported the duration of analgesia of approximately 7 hours after the use of 4 mg bupivacaine with 25 μ fentanyl for TURP.[10]

Singh V et al have reported that lesser number of patients receiving intrathecal butorphanol requested for rescue analgesia as compared to those receiving intrathecal fentanyl.[16] We studied the 25 μg dose of intrathecal fentanyl and butorphanol and the results of our study are consistent with experimental evidence of synergistic interaction between spinal opioids and local anesthetics, which are characterized by enhanced somatic analgesia without effect on the degree or level of the local anesthetic induced sympathetic or motor blockade.[7] The synergism between intrathecal opioids in addition to local anesthetics may be due to the drugs' separate mechanism of action; blockade of Na+ channel by local anesthetics36 and voltage-gated Ca++ channels with opioids.[17] The combination of opioids with LA allows for a reduction in doses of the LA, thus lessening the likelihood of side effects.[18]

A low incidence of side effects was observed in our study. We noticed seven patients (17.5%) in the fentanyl treated group and two patients (5%) in the butorphanol-treated group having hypotension requiring treatment with small doses of intravenous mephenteramine (6 mg in 7 and 12 mg in 2 patients) in addition to crystalloid bolus. Earlier studies comparing 25 μg intrathecal fentanyl and butorphanol with hyperbaric bupivacaine, have reported the instance of hypotension as 20% in the fentanyl group and 17% in the butorphanol group.[16] However, animal studies have reported that fentanyl does not potentiate the effect of Bupivacaine on efferent sympathetic pathways.[7] Furthermore, the addition of fentanyl (20-25 μg) to low-dose bupivacaine (4 mg) has been reported to increase the perioperative quality of spinal blocks with fewer cardiovascular changes in elderly patients.[18]

Five patients (12.5%) in the group receiving fentanyl- bupivacaine had pruritis compared with none in the group receiving butorphanol-bupivacaine. The pruritis was mild in nature and did not required any treatment. Mallik et al reported an incidence of pruritus with epidural fentanyl to be 23% and with epidural butorphanol as 1.4%.[15]

The patients were continuously observed for respiratory depression with SpO2 (< 90%) and RR (< 10). No case of respiratory depression was observed in any group, consistent with other studies.[15] Although six patients had sedation in the group receiving butorphanol-bupivacaine, as compared with none in the group receiving fentanyl; none of them had respiratory depression. Sedation is a reported side effect of neuraxially administered butorphanol.[19]

Seven patients were catheterised during the postoperative period due to difficulty in voiding, although the average times to voiding were comparable among both the study groups. Previous studies have reported that intrathecal bupivacaine is associated with a clinically significant disturbance of bladder function and spontaneous voiding may not be expected until the sensory blockade has regressed to the S3 level.[20]

No patient had urinary retention in either of the groups, consistent with the study by Ackerman et al. The side-effect observed in the majority of patients with butorphanol was somnolence as observed by other authors as well.[12, 15] None of the patients in the study experienced nausea or vomiting as we promptly treated all episodes of hypotension.

Limitations of the study:

1. Absence of a control group (in which patients would have received 2.5 ml of hyperbaric bupivacaine along with 0.5 ml of saline intrathecally). The inclusion of a control group would have further supported our findings.
2. The wide variability in the age of the patients included in the study is a confounding factor in relation to perception of pain as pain perception varies for various age groups.
3. We studied postoperative analgesia in the subjects for duration of 4 hours only and did not record the number of doses and the total dose of rescue analgesic required to relieve pain.

Hence further studies can be aimed at finding the minimal possible doses of intrathecal fentanyl and butorphanol in conjunction with hyperbaric bupivacaine that will provide adequate anesthesia and analgesia for lower limb surgeries.

CONCLUSION

Both 25-µg fentanyl and 25-µg butorphanol given intrathecally with 12.5 mg of hyperbaric bupivacaine are equally efficacious in patients undergoing lower limb surgeries instead of bupivacaine alone with minor side effects because:

1) Both opioids Fentanyl or Butorphanol are easily available in the market first one with license as schedule drug other without it when compared, hence useful in peripheral and rural hospital setups.
2) Haemodynamic stability with these combinations is good.
3) Effective Prolonged duration of sensory analgesia.
4) Less side effects compared to morphine.
5) Less addiction potential because of diaphoresis.

Hence intrathecal bupivacaine-butorphanol mixture provides longer duration of sensory blockade and better quality of analgesia than intrathecal fentanylbupivacaine mixture.

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