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A study of intrathecal fentanyl and butorphanol as an adjuvant to 0.5% bupivacaine [heavy] for lower limb surgeries: Randomized control study

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***Abstract*---**The most commonly used technique for lower limb surgeries is Spinal anesthesia, as it is economical, easy, effective and has less complications. Adjuvants are added with local anaesthetics intrathecally. Opioids as adjuvants to local anaesthetics improves the quality of intraoperative analgesia and prolongs postoperative analgesia. To observe and compare the effect of intrathecal bupivacaine with fentanyl and bupivacaine with butorphanol on onset and duration of sensory and motor block, haemodynamics, duration of post-operative analgesia, requirement of rescue analgesia and side effects/complications. In this study 72 patients were selected with 36 patients [group BF & BB] in each group. Patients aged 18-70 years,

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ASA Grade I and II of either gender, undergoing elective lower limb surgeries were included in our study. All patients were monitored for onset and duration of sensory block and motor block, haemodynamics and duration of analgesia, time to rescue analgesia and complications. Mean onset of sensory & motor block was significantly faster in BF group than BB group [p<0.05]. Mean duration of analgesia and rescue analgesia in BB was significantly longer than BF [p<0.05]. Haemodynamic parameters were comparable in both groups. We concluded that onset of sensory & motor block was faster in BF group than BB group and the duration of sensory and motor block along with postoperative analgesia and duration to rescue analgesia was longer in BB group. Both the groups had minimal side effects.

***Keywords*---**opioids, additive, subarachnoid block, post-operative analgesia.

Introduction

Spinal anaesthesia is the most commonly used technique for lower abdominal and lower limb surgeries because of its rapid onset of blockade, low failure rates and cost effectiveness. After the introduction of local anaesthetic drugs, various diverse classes of drugs like epinephrine, ketamine, fentanyl, butorphanol, dexmedetomidine, nalbuphine etc have been added as adjuvants to local anaesthetics in an attempt to prolong the duration of anesthesia and postoperative analgesia and reduce the incidence of side effects. Opioids are widely used adjuvants as they reduce the requirement of local anesthetics while providing adequate anesthesia and analgesia. The first published report on opioids for intrathecal anesthesia belongs to a Romanian surgeon, Racoviceanu–Pitesti, who described his experience at Paris in 1901[1]. The use of opioids in conjunction with local anesthetic for spinal anesthesia has been associated with decrease in pain scores and reduction in analgesic requirement in the post-operative period [2]. Fentanyl is highly lipid soluble, pure μ agonist opiod with rapid onset and short duration of action. Butorphanol is a lipophilic opioid agonist-antagonist analgesic with an affinity for opioid receptors in vitro of 1:4:25 [mu: delta: kappa]. Hence, the present study was undertaken to evaluate the onset, duration of sensory and motor block and postoperative analgesia of fentanyl and butorphanol given intrathecally as adjuvant with hyperbaric bupivacaine.

Aim and Objectives

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

- Onset and duration of sensory and motor block.
- Haemodynamics- Heart rate [HR], Systolic blood pressure [SBP], Diastolic blood pressure [DBP], Mean Arterial Pressure [MAP] and Respiratory Rate [RR].

- Duration of Post-operative analgesia.
- Adverse effects – like hypotension, nausea, vomiting, bradycardia.

Material and Methodology

After permission and clearance from the ethical committee this study was conducted at Dhiraj Hospital in Department of Anaesthesiology. It is an observational and comparative study**.** The Study duration was 18 months.

Sample size

Keeping the power of study as 80% and confidence limit at 95%, the minimum sample size required is 36 in each group.
Total = 72 patients

Sample size was calculated using formula below:

nA=κnB and nB=[1+1κ][σz1−α/2+z1−βμA−μB]2nA=κnB and nB=[1+1κ][σz1−α/2+z1−βμA−μB]2
1−β=Φ[z−z1−α/2]+Φ[−z−z1−α/2],z=μA−μBσ1nA+1nB√1−β=Φ[z−z1−α/2]+Φ[−z−z1−α/2],z=μA−μBσ1nA+1nB.

References: Chow S, Shao J, Wang H. 2008. *Sample Size Calculations in Clinical Research*. 2nd Ed. Chapman & Hall/CRC Biostatistics Series. page 58.
All the patients participating in the study were clearly explained about the purpose and nature of the study in the language they can understand. They were included in the study only after obtaining a written informed consent.
Patients were randomly divided into two groups with chit method– Group BF and Group BB.

Group BF- Inj 3ml Bupivacaine [0.5% hyperbaric] + 0.5ml Fentanyl 25mcg [Inj Fentanyl 1ampoule contains 2ml, each ml contains 50mcg, hence 0.5ml = 25mcg.]

Group BB - Inj 3ml Bupivacaine [0.5% hyperbaric] + 0.5ml Butorphanol 25mcg [Inj Butorphanol 1ampoule contains 1ml, each ml contains 1mg. 0.5ml is diluted upto 10ml with sterile normal saline which makes each ml of 50mcg strength and hence 0.5ml = 25mcg.]
Both Fentanyl and Butorphanol drug used were preservative free.

Inclusion criteria

- Patients willing to sign the informed written consent.
- Patients of ASA Grade I and II of either gender.
- Undergoing elective lower limb surgeries.
- Aged 18-70 years.

Exclusion criteria

- Patient refusal to give informed consent.

- Patients with systemic disease like heart disease, liver disease, kidney disease.
- Patients with anaemia, shock, septicemia, uncontrolled hypertension.
- Patients with coagulation disorders or on anticoagulant therapy.
- Local infection at the site of proposed puncture for spinal anaesthesia, spinal deformities.
- Known allergy to study drug.
- Caesarean section.
- Aged less than18 and more than 70 years.
- ASA III & IV.

Methodology

Preoperative assessment

All the patients posted for elective lower limb surgeries were examined for weight, pulse rate, blood pressure, respiratory rate and complete systemic examination. All the patients were examined for skin condition, any gross abnormalities of the spine and any visible defects at the back. Routine blood investigations were carried out with ECG and chest X-Ray. All the patients were kept nil by mouth for 8 hours. The patient's consent was taken for their agreement to accept spinal anaesthesia and to be included in the study group and the procedure of the anaesthesia was explained.On the day of surgery, the patients were shifted to the operating room.

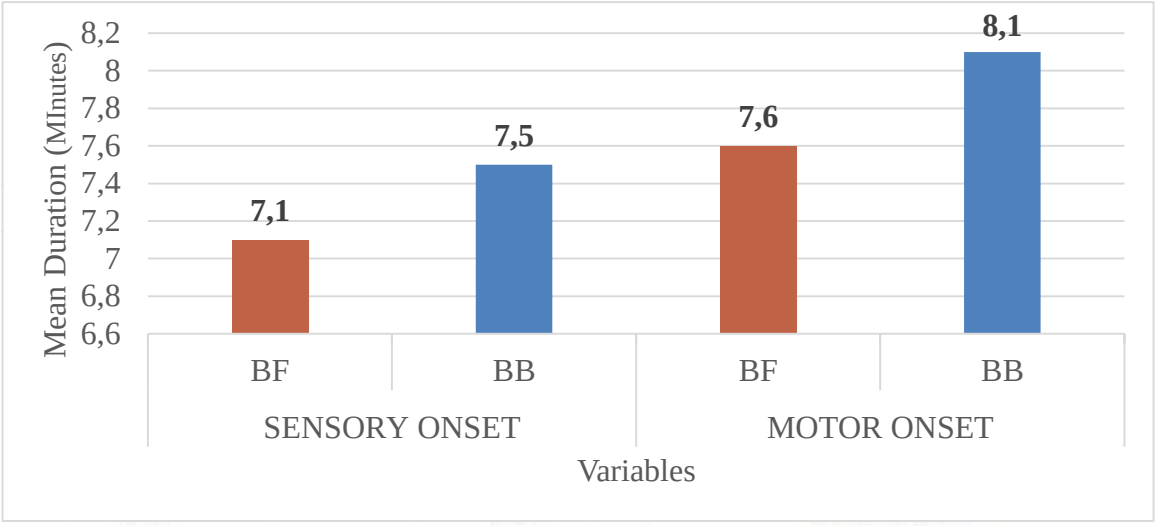
On arrival of the patient in the operating room, an 18-gauge intravenous line was secured in upper limb and inj. Ringer's lactate was started. The patients were connected to a multipara monitor which records Heart rate [HR], non-invasive measurements of systolic, diastolic and mean arterial pressure [SBP, DBP, MAP], continuous ECG monitoring and oxygen saturation[SpO_2]. All patients were pre medicated with Inj. Glycopyrrolate 0.004mg/kg, Inj. Ondansetron 0.1mg/kg intravenously and preloaded with crystalloids 10ml/kg iv before spinal anaesthesia over 20 minutes. Patients were randomly divided into two groups by chit method: BF & BB. Patients were given position for spinal anaesthesia and under all aspetic and antiseptic precautions 25 G Quincke spinal needle was inserted in the midline at L3-L4 intervertebral space. After free flow of clear cerebrospinal fluid, study drug was injected over 10-15 seconds. The patients were placed supine immediately after injecting the test drug.

Intraoperative vitals was recorded at regular intervals for the first 30 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. Side effects and complications were noted and treated intra and postoperatively as an when required with appropriate drugs.

Intra operative

All patients were monitored for:

- Haemodynamics in form of Heart rate, SBP,DBP, MAP



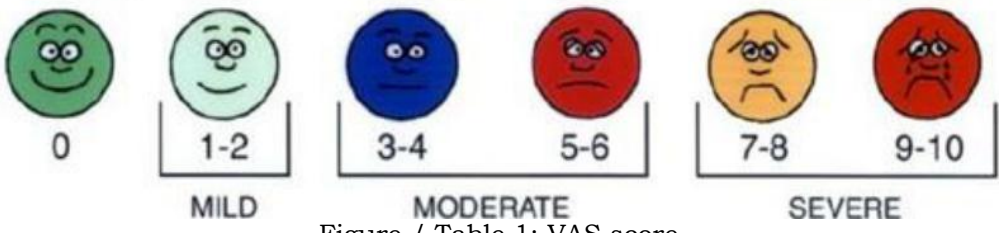


Figure / Table 1: VAS score

Time of supplemental analgesia was noted. Patients were given Rescue analgesia of Inj. Diclofenac 75 mg iv when VAS score was more than 4 and Inj. Paracetamol 1gm iv when demanded by patient as supplemental analgesia when VAS score than 5. The frequency of analgesia required during the first 24 hours after the surgery was noted.

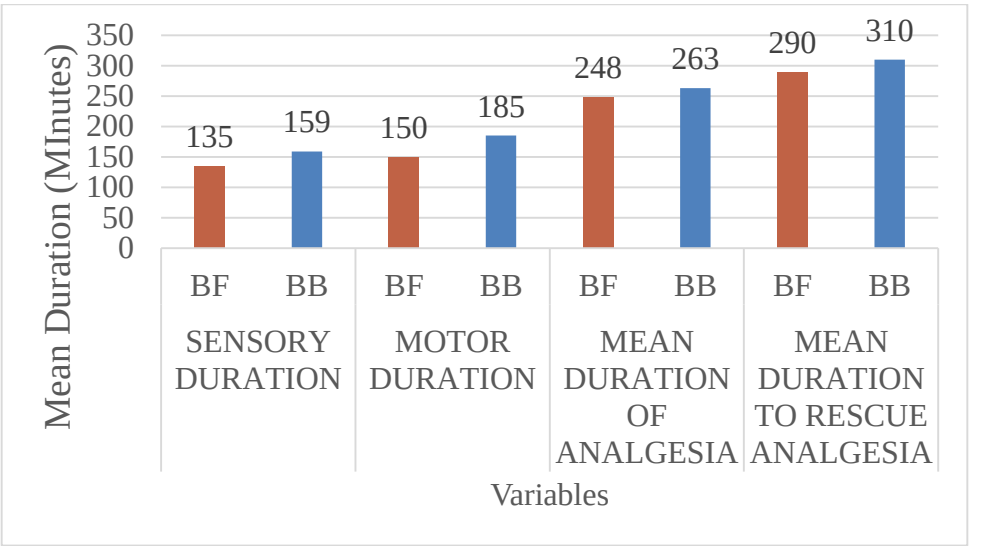
Results and Observation

The present study was carried in the patients who were given intrathecal fentanyl with bupivacaine and intrathecal butorphanol with bupivacaine for lower limb surgeries.

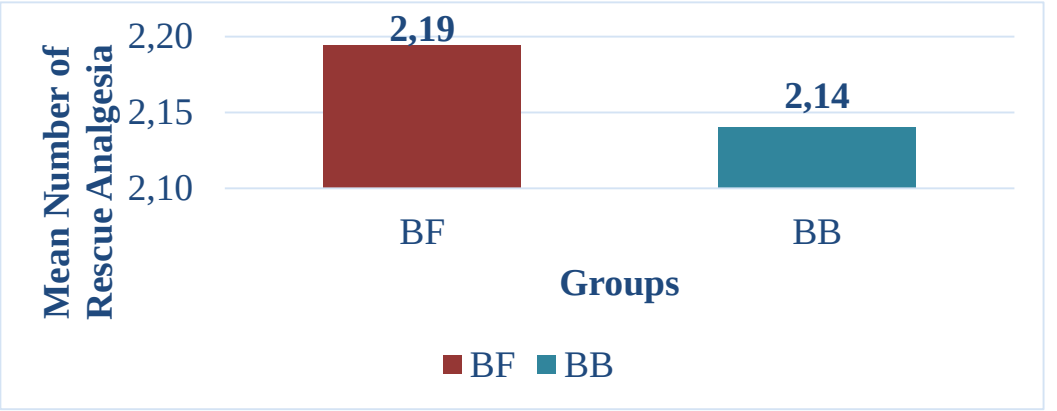
- Data was collected, tabulated and then analyzed.
- The numerical variables were presented as mean, standard deviation [SD] and categorical variables presented as percentage
- For numerical variables and for in-between groups comparison, unpaired student – t test, while for categorical variables; chi – square test was used. A difference with P value < 0.05 was considered statistically significant.

Graph 1a: Mean duration of various parameters (mins)

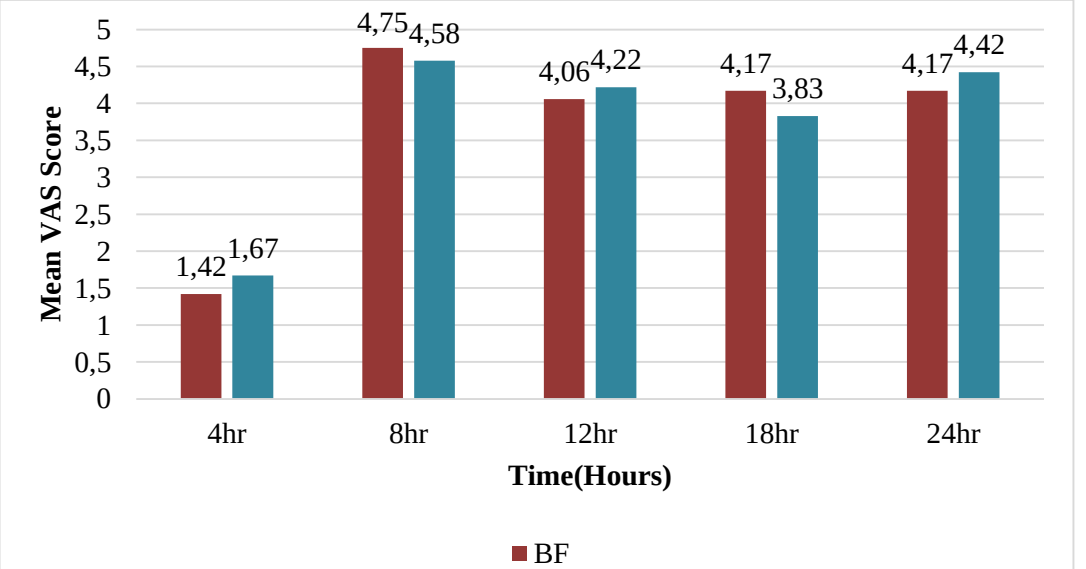
Graph 1b: Mean duration of various parameters(mins)



Graph 2. Mean number of Rescue analgesia requirement post-operatively



Graph 3. Mean VAS score between the two groups post-operatively



Discussion

The results of our study indicated that the mean onset of sensory block as well as motor block was significantly faster in the fentanyl group [BF] than butorphanol group [BB]. Similar findings were seen in Kumar B et al [4] and Kumar A et al [1] in their studies. Study by Arora N et al. [5] was in contrast to our study. In our study, mean time for two segments regression from highest level of sensory block was found to be faster with fentanyl. Gupta V et al.[3] reported significantly slower two segment regression in butorphanol. However, Reddy NG et al [6] observed faster regression with butorphanol. The mean duration of sensory block and motor block was longer with butorphanol compared to fentanyl. These findings were consistent with the study conducted by Basunia RS et al.[7], Reddy R et al and Bhatia U et al [2, 3] and in contrast to the findings of Kumar B et al.[4], who had found no statistical significant difference.

Mean heart rate was statistically significantly increased in intrathecal butorphanol group at 5, 10, 15, 20, 25, 30, 60, 90 minute intraoperatively. Consistent to our finding in the study by Reddy R et al[2] mean heart rate was higher in Butorphanol group than Fentanyl group. In contrast, Bhatia U et al.[3] and Reddy R et al [2] observed significantly lower mean heart rate from 45-90 minutes in Butorphanol group than Fentanyl group. Fentanyl has action on the heart which leads to bradycardia, reduction in systemic vascular resistance leading to hypotension and decrease in the cardiac output. It also causes reduction in AV conduction and prolongation of R-R interval. In our study the mean SBP was significantly higher in patients receiving intrathecal butorphanol at 90 and 120 minutes. The mean DBP was significantly higher in patients receiving intrathecal butorphanol at 60 and 90 minute. Similarly Kumar B et al [4] observed that mean SBP and mean DBP were higher in butorphanol group. Esampalli S et al. [8] observed that the mean systolic pressure was maintained in butorphanol group but the mean diastolic pressure was found higher compared to fentanyl group.

In contrast, Reddy R et al. [2] and Basunia RS et al. [7] in their study observed that SBP, DBP and MAP were decreased. In our study the mean MAP [in mm Hg] was significantly higher in patients who received intrathecal butorphanol at 60, 90 and 120 minutes. In most of the studies, MAP was comparable on studies carried out by Reddy R *et al*[2], Gupta V et al and Reddy NG et al. [9]. In contrary to our findings, Bhatia U et al. [3] observed that the MAP was significantly lower in Group B from 45 minutes to 90 minutes. In our study effect of intrathecal fentanyl and butorphanol on respiratory rate and oxygen saturation were similar during the intraoperative period and consistent with the previous studies of Reddy NG et al [9], Bhatia U et al [3], Basunia et al [7], Kumar B et al [4] and Reddy R et al [2]. Opiods have respiratory depression due to μ receptor agonism. Fentanyl, a highly lipophilic opioid does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally [10]. Butorphanol is a competitive antagonist at μ opioid receptor and partial agonist at the opioid receptor. It binds to kappa

receptor present in the CNS which is responsible for nociception producing analgesia and devoid of μ receptor related side effects.
In our study **mean duration of analgesia** was longer in the group receiving butorphanol compared to fentanyl. Similar to our findings Reddy NG et al [9], Bhatia U et al [3], Gupta V et al [3], Reddy R et al [2],Arora N et al [5] had observed similar results in their studies. In our study mean demand for rescue analgesia was higher in the group receiving butorphanol compared to fentanyl. Similar to our findings, Kumar B et al [4], Basunia et al [7], Reddy R et al [2], Arora N et al [5] had similar results in their studies. The best medication is one with the highest safety and least side effects. In our study, 3 [8.33%] patients in BB group were observed to have hypotension as side effect intraoperatively. In BF group 2 [5.56%] patients had bradycardia and 1 patient [2.78%] reported to have nausea intra operatively. Similar to our findings, Kumar B et al [4], Bhatia U et al [3] had reported side effects in form of pruritis, sedation and hypotension. In contrast to our study, studies by Reddy NG *et al* [9], Kumar A *et al* [1], Arora N *et al* [5], Reddy R *et al* [2] found no drug related side effects. Bromage PR suggested that lipid-soluble, highly protein bound narcotic analgesics might have lesser probability to exhibit the effects of vomiting, pruritus, respiratory depression, urinary retention and this hold true for butorphanol and fentanyl [11]. Additional side effects like a possible serotonin syndrome related to intrathecal fentanyl has been reported [12].

Limitations

Our present study had a few limitations:

- The absence of a control group in which patients would have received 3 ml of hyperbaric bupivacaine along with 0.5 ml of saline intrathecally. The inclusion of a control group would have further supported our findings.
- A bigger sample size could have been taken which would have resulted in lesser sampling bias.
- The wide range in the age of the patients included in the study is a confounding factor to perception of pain as pain perception varies for various age groups.

Conclusion

From our study we were able to conclude that the onset of sensory and motor block was faster in fentanyl group while, duration of sensory and motor block and duration of post operative analgesia was significantly longer in butorphanol group. Both 25 μg fentanyl and 25 μg butorphanol given intrathecally with 15 mg of hyperbaric bupivacaine are equally efficacious in patients undergoing lower limb surgeries.

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