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# Comparative Evaluation of Clinical Efficacy of Adding Adjuvant to Intrathecal Levobupivacaine or Bupivacaine in Patients Undergoing Surgeries Under Spinal Anaesthesia.

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## ABSTRACT

**Background:** Levobupivacaine has been claimed to have safer cardiovascular profile. However, single injection intrathecally produces limited duration of surgical anaesthesia. Hence we comparatively evaluated the effects of adding fentanyl to levobuivacaine and bupivacaine on spinal anaesthesia characteristics. **Methods:** 50 American Society of Anaesthesiologists grade I-II patients undergoing lower abdominal and lower limb surgeries were divided into two groups of 25 patients each. Intrathecally, 20µgm fentanyl was given with 2.6 ml of levobupivacaine (group L) or bupivacaine (Group B). **Results:** There was no significant difference between the two groups on time of onset and time taken to reach the maximum sensory block level. There was also no significant difference on the maximum levels of sensory block attained between the two groups. The duration of sensory regression to S1 was 262.80±20.13 minutes in group L, while it was 272.40±19.43 minutes in group B (p=0.09). Rescue analgesia was given at 219.80±24.26 minutes in group L, and at 230.00±19.58 minutes in group B (p=0.1). The duration of motor block was 215.60±22.56 minutes in group L, and 217.24±27.04 minutes in group B (p=0.82). **Conclusion:** Our study demonstrated no significant difference existed on time of onset and time taken to reach the maximum sensory block level when fentanyl was added to intrathecal isobaric levobupivacaine or bupivacaine. No significant difference existed on the maximum levels of sensory block attained between the two groups, as well as on the duration of sensory and motor blocks.

***Keywords:*** levobupivacaine, bupivacaine, isobaric, fentanyl, intrathecal.

## INTRODUCTION

Neuraxial blockade has wide range of clinical applications for surgery, obstetrics, acute postoperative pain management, and chronic pain relief. Single-injection spinal or epidural anaesthesia with local anaesthetic is most commonly used for surgery to the lower abdomen, pelvic organs, and lower limbs, and cesarean section.[1]

The arrival of newer local anaesthetic drugs has made spinal anaesthesia more safe and beneficial. The newer local anaesthetics are significantly less cardiotoxic and neurotoxic than the commonly used bupivacaine.[2]

Levobupivacaine (S-1-butyl-2-piperidylformo-2',6'-xylidide hydrochloride), the pure S(-)-enantiomer of racemic bupivacaine, is a new long acting local anaesthetic. Because of its decreased cardiovascular and central nervous system toxicity, levobupivacaine seems to be an attractive alternative to bupivacaine.[3,4] Comparative studies are available for nonobstetric and obstetric epidural anaesthesia, brachial plexus blockade, and infilteration analgesia, but not for spinal anaesthesia.[3]

One of the major disadvantages of single-injection neuraxial anaesthesia is the limited duration of effect. Adding adjuvants to neuraxial block results in prolongation of its effects, without compromising the safety. Wide varieties of adjuvants are used for this purpose, with opioids being the most common.

Levobupivacaine, a new amide local anaesthetic, seems to be equally as potent as racemic bupivacaine, but not many studies are there which can establish their similarity when combined with adjuvants.[5] Hence we undertook this study to demonstrate the efficacy of adding fentanyl to intrathecal isobaric levobupivacaine or bupivacaine on sensory and motor block characteristics.

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## MATERIALS AND METHODS

After taking institutional ethical clearance and informed consent, 50 American Society of

Anaesthesiologist grade I and II patients scheduled for lower abdominal and lower limb surgeries under spinal anaesthesia were randomly divided into two groups of 25 patients each. Group L included intrathecal 2.6ml of isobaric levobupivacaine 0.5%, while Group B included 2.6ml intrathecal isobaric bupivacaine 0.5%. Adjuvant used in both the groups was injection fentanyl 20µg (0.4ml) added to the local anesthetic solution to make the total volume of 3ml for intrathecal injection.

Exclusion criteria included contraindication to spinal anaesthesia; patients on α2-adrenoceptor antagonists, calcium channel blockers, angiotensin-converting enzyme inhibitors; patients having abnormal cardiac rhythm; patients with diabetes, hypertension or other systemic co-morbid conditions.

After obtaining pre-anaesthetic clearance, patients were randomly allocated into two groups. Randomization was done with opaque sealed envelopes using computer generated randomization sequence. On the day of operation, after checking all the preoperative protocols, patients were wheeled into the operation theater and all the necessary monitoring parameters were attached, which included pulse oximetry, electrocardiogram, and non-invasive blood pressure. Patients were preloaded with intravenous ringer lactate at 15ml/kg. Spinal anaesthesia was given in sitting position with 26 gauze Quincke-Babcock spinal needles. The study drugs were prepared by anaesthesiologist who was no further involved in the management of case. The readings were recorded by another anaesthesiologist who was not aware of the nature of the study drug administered and who was also the in-charge of the case. Patients were also unaware of the study group allocation. Hence study proceeded in a double blind fashion. Intraoperatively, fluids were administered according to the institutional protocol. Oxygen was supplemented at the rate of 2l/minute to all the patients. Operation was allowed to commence after the demonstration of adequate block. All the haemodynamics and other additional drugs administered were recorded. Intraoperative bradycardia and hypotension were recorded and managed according to the institutional protocols.

For the comparative evaluation, following parameters were recorded. Maximum level of sensory block was recorded using loss of pin-prick sensation in the mid-clavicular line. Duration of sensory block was recorded by assessing the time taken from the onset of sensory block to regression of block to S1 dermatome. Postoperative analgesia was given on demand and time for first request of analgesia was recorded. Motor block was assessed using modified bromage scale (0 = no paralysis, 1 = unable to raise the extended leg, 2 = unable to flex knee, 3 = unable to flex ankle). Duration of motor block was recorded as the time taken to reach Bromage scale 0 from the maximum motor block.

Statistical evaluation was done using Epi-info 7. T-test was used for continuous variables and Chi-square test was used for categorical variables. Data was presented as Mean±SD or as percentage. P value less than 0.05 was considered significant. To calculate the sample size, a power analysis of alpha= 0.05 and beta = 0.80, showed that 23 patients per study group were needed for 20% difference in sensory regression to two dermatomes. To compensate for the drop-outs and to further increase the power of the study, we enrolled 25 patients in each group.

## RESULTS

50 patients undergoing lower abdominal and lower limb surgeries were divided into two groups. Group L included intrathecal 2.6ml of isobaric levobupivacaine 0.5%, while Group B included 2.6ml intrathecal isobaric bupivacaine 0.5%. Adjuvant used in both the groups was injection fentanyl 20µg (0.4ml). The demographic data was comparable in both the groups with respect to age, weight and gender distribution [Table 1].

**Table 1: Patient Demographics.**

| Patient characteristic | Group I n=25 | Group II n=25 |
|---|---|---|
| Age | 38.00±12.96 | 40.40±10.04 |
| Weight | 60.76±10.56 | 59.56±11.02 |
| Sex (male:female) | 17:8 | 16:9 |

Values as Mean ± SD or ratio.

**Table 2: Sensory and Motor Block Characteristics**

| | Group L | Group B | P value |
|---|---|---|---|
| Onset of sensory block | 5.04±2.01 | 4.64±1.68 | 0.45 |
| Time taken to achieve maximum sensory block (min) | 12.67±3.58 | 12.23±2.74 | 0.72 |
| Maximum level of sensory block | 7.12±2.17 | 6.8±2.08 | 0.6 |
| Duration of sensory regression to S1 level | 262.80±20.13 | 272.40±19.43 | 0.09 |
| Time of rescue analgesia | 219.80±24.26 | 230.00±19.58 | 0.1 |
| Recession to Bromage scale 0 | 215.60±22.56 | 217.24±27.04 | 0.82 |

Our study demonstrated no significant difference between the two groups on time of onset as well as the time taken to reach the maximum sensory block level between the two groups [Table 2]. There was also no significant difference on the maximum levels of sensory block levels attained between the two groups (table2). In our study, the duration of sensory regression to S1 was 262.80±20.13 minutes in group L, while it was 272.40±19.43 minutes in group B (p=0.09). Rescue analgesia was given at

219.80±24.26 minutes in group L, and at 230.00±19.58 minutes in group B (p=0.1). The duration of motor block was also not significantly different in the two groups. It was 215.60±22.56 minutes in group L, and was 217.24±27.04 minutes in group B (p=0.82).

## DISCUSSION

Spinal anaesthesia is preferred over epidural due to its rapid onset, the higher level of muscle relaxation and lower dose requirements. In cesarean section surgeries performed under spinal anesthesia, it has been reported that administration of local anaesthetic alone has short duration of action, that it is insufficient for preventing visceral pain and nausea especially during uterus manipulation and peritoneum closure, and that it leads to postoperative analgesic requirement at an earlier stage.[6] The addition of low dose of opioids to local anaesthesia decreases the incidence of local anaesthesia related side effects, reduces the time of onset of anaesthetic effect and increases the quality of intra- and postoperative analgesia by reducing the administered dose of local anesthetic.[4]

Our study demonstrated no significant difference between the two groups on time of onset as well as the time taken to reach the maximum sensory block level when 20µgm fentanyl was added to 2.6ml of isobaric levobupivacaine (group L) or isobaric bupivacaine (group B) when given intrathecally. There was also no significant difference on the maximum levels of sensory block levels attained between the two groups. In our study, the duration of sensory regression to S1 was 262.80±20.13 minutes in group L, while it was 272.40±19.43 minutes in group B (p=0.09). Rescue analgesia was given at 219.80±24.26 minutes in group L, and at 230.00±19.58 minutes in group B (p=0.1). The duration of motor block was also not significantly different in the two groups. It was 215.60±22.56 minutes in group L, and was 217.24±27.04 minutes in group B (p=0.82).

Camorcia found that among the parturients who had effective analgesia, the duration of analgesia showed no difference between the groups of levobupivacaine, ropivacaine and bupivacaine intrathecally; though their study was not designed to assess the duration of analgesia.[7]

Bupivacaine is available as plain and hyperbaric solutions. Plain bupivacaine is hypobaric when compared to cerebrospinal fluid. Although hyperbaric bupivacaine is the most commonly used drug for spinal anaesthesia, it too, has been known to cause sudden cardiac arrest after spinal anaesthesia due to extension of sympathetic block and may cause hypotension and bradycardia after mobilization, especially with abrupt position changes. Like other benefits, hypobaric solutions also produce less position sensitive blocks.[8]

Varcauteren et al, like in our study, demonstrated the same onset time and duration of analgesia. However, they showed less motor block in levobupicvacaine group. However here they have administered as a combined spinal- epidural procedure and used dilute concentration of the solutions.[2]

Attri et al, in their study showed similar prolongation of spinal anaesthesia when fentanyl was added to levobupivaciane. Total duration of analgesia (regression to S1) was 265minutes, similar to our study. However, they showed early onset T10 dermatome and the total duration of motor block was also less. They further demonstrated no significant difference in hemodynamics by addition of opioid to intrathecal local anaesthetic. Similarly Chattopadhyay et al concluded that addition of fentanyl to levobupivacaine does not increase the incidence of bradycardia.[9,10] Lee et al also further reported no significant difference in study groups in the hemodynamic changes, and the quality of sensory and motor block when 2.6ml of 0.5% levobupivacaine was compared with 2.3ml of 0.5% levobupivacaine with fentanyl 15µgm.[5]

Owing to the lower affinity of the S (-) isomer to cardiac sodium channels compared to the R isomer, levobupivacaine is associated with less cardiac side effects. In contrast to our study, Erdil et al found time to reach T10 and peak sensory block level were significantly shorter with intrathecal fentanyl in bupivacaine group vs levobupivacaine group. Peak sensory block level was significantly higher in bupivacaine group. However they have studied aged population (more than 65 year age). Hence there was a difference in the study-sample characteristics as compared to our study. The time to sensory regression to L5 was almost similar to our study. We had evaluated sensory regression to S1.[11]

Contrasting results were also shown by Goyal et al. However, they have compared levobupivacaine with hyperbaric bupivacaine which could have resulted in results dissimilar to that of our study. Although hyperbaric local anaesthetic solutions are have a remarkable record of safety, their use is not without risks.[4]

Recent advances in anesthesia have allowed more surgeries to be performed on day case basis. Opioids are hypobaric and when added to a hypobaric solution will make the mixture more hypobaric thus altering the density of resulting solution which effects the direction and spread of local anaesthetic.[9] It has been suggested that 0.5% levobupivacaine, i.e. 5mg/ml, will contain 13% more local anaesthetic than 0.5% racemic bupivacaine, because this corresponds with milligrams of bupivaciane-hydrochloride per milliliter.[12]

Although we have studied the effect of adding fentanyl to local anesthetics, there are studies also which show that adding sufentanyl results in better efficacy as compared to fentanyl.[6] Hence further

studies are needed to establish the efficacy of sufentanyl to more commonly used fentanyl.

## CONCLUSION

Our study demonstrated that no significant difference existed on time of onset as well as the time taken to reach the maximum sensory block level when 20µgm fentanyl was added to 2.6ml of isobaric levobupivacaine or bupivacaine when given intrathecally. There was also no significant difference on the maximum levels of sensory block levels attained between the two groups, as well as on the duration of sensory and motor blocks.

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