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RESEARCH ARTICLE
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EFFICACY OF INTRATHECAL BUPRENORPHINE AS AN ADJUVANT TO HYPERBARIC LEVOBUPIVACAINE IN INFRA-UMBILICAL SURGERIES: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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ABSTRACT

Background: Subarachnoid block is a widely used anesthetic technique for infraumbilical surgeries due to its rapid onset and effective blockade. Levobupivacaine, a safer enantiomer of bupivacaine, is commonly employed in spinal anesthesia. However, single-agent spinal anesthesia may not always provide optimal analgesia. Intrathecal adjuvants like buprenorphine have been explored to enhance spinal anesthesia quality and prolong analgesia. This study compares intrathecal levobupivacaine 0.5% (heavy) alone versus with 60 mcg buprenorphine in terms of sensory-motor blockade, hemodynamic stability, side effects, and postoperative analgesia.

Methods: This prospective, randomized, double-blind, unicentric study was conducted in a tertiary care center in Maharashtra from September 2022 to August 2024. A total of 100 ASA grade I & II patients (18-65 years, 40-80 kg) scheduled for elective lower abdominal or limb surgeries were included and divided into two groups: Group L (levobupivacaine 3.3 ml + 0.2 ml NS) and Group L+B (levobupivacaine 3.3 ml + 60 mcg buprenorphine). Hemodynamic parameters, sensory and motor block characteristics, intraoperative side effects, and postoperative analgesia were assessed.

Results: Both groups were comparable in demographics and surgical duration. Sensory and motor block onset was significantly faster in Group L+B, with prolonged blockade duration ($p<0.05$). VAS scores were significantly lower in Group L+B at 1 and 2 hours ($p=0.0001$). Hemodynamic parameters remained stable, with no significant differences ($p>0.05$). The need for rescue analgesia was significantly delayed in Group L+B ($p=0.0001$).

Conclusion: Intrathecal buprenorphine 60 mcg enhances the effects of levobupivacaine, leading to faster onset, prolonged sensory-motor blockade, and superior postoperative analgesia without significant hemodynamic instability or adverse effects. It is a viable alternative to levobupivacaine alone for infraumbilical surgeries.

Keywords: Subarachnoid block; Infraumbilical surgeries; Levobupivacaine; Buprenorphine; Sensory and motor block.

INTRODUCTION

Spinal anaesthesia consists of temporary interruption of nerve transmission produced by the injection of a local anaesthetic solution in the subarachnoid space. Subarachnoid blockade is often popular technique of choice for infraumbilical surgeries due to its rapid onset, effective sensory and motor blockade, minimal systemic effects, and several advantages over general anesthesia.[1] Hyperbaric racemic bupivacaine is commonly used for spinal anesthesia due to its prolonged duration of action and effective sensory-motor blockade. However, it has drawbacks, including a high risk of hypotension, bradycardia, and potential cardiotoxicity due to its strong affinity for cardiac myocytes.[2,3]

Levobupivacaine, the S-enantiomer of racemic bupivacaine, is a safer alternative with a lower risk of cardiac toxicity, reduced affinity for cardiac sodium channels, and greater plasma protein binding, leading to improved hemodynamic stability and a faster recovery profile. Reports of toxicity with levobupivacaine are scarce, and occasional toxic symptoms are usually reversible with minimal treatment without any fatal outcome. However, levobupivacaine has not entirely replaced bupivacaine in clinical practice.[4,5] In comparative trials, although its clinical effects were not significantly different from those of bupivacaine, there was some variability in efficacy findings in different clinical populations.[6] The clinical studies available on intrathecal anaesthesia with levobupivacaine suggest that it achieves satisfactory surgical anaesthesia but with an unpredictable spread of sensory blockade.[5]

Adjuvants are commonly added to local anesthetics to enhance sensory-motor blockade, reduce dose requirements, and minimize side effects. Neuraxial opioids provide intraoperative and postoperative analgesia without prolonging motor or sympathetic block.[7]

Buprenorphine, a potent agonist-antagonist opioid, offers spinal and supraspinal analgesia, a ceiling effect on respiratory depression, and antihyperalgesic properties that prevent central sensitization. Its high lipid solubility, strong opioid receptor affinity, and long duration of action make it an effective adjuvant for managing postoperative pain. Given its low medullary bioavailability, intrathecal buprenorphine (30–150 μg) prolongs analgesia with minimal side effects.[8,9] This study aims to compare intrathecal levobupivacaine 0.5% (heavy) 3.3 ml with and without 60 mcg intrathecal buprenorphine in terms of sensory-motor block quality, hemodynamic stability, side effects, and postoperative analgesia in adults undergoing infraumbilical surgeries.

MATERIALS AND METHODS

This prospective, randomized controlled, Double blind, unicentric, interventional study was carried out in the Department of Anaesthesiology at a Tertiary care center in Maharashtra during the period between September 2022 to August 2024, after approval from the hospital ethics committee. After obtaining written informed consent 100 patients of either sex, ASA grade I & II, age between 18 and 65 years and weight 40 to 80kg posted for elective lower abdominal or lower limb surgeries, predicted to last from 30-120 mins were included in the study and were equally divided into 2 groups- Group L - Control group and Group L+B- Study group. Patients who refuse to participate and those with contraindications to spinal anesthesia (local infection, bleeding diathesis, coagulation disorders, or vertebral column deformities/surgeries), patients with comorbid conditions like hypertension, ischemic heart disease, COPD, CNS disorders, liver disorders, psychiatric disorders, or a history of pruritus, itching, or allergies, pregnant and lactating women were excluded from the study.

Preanesthetic evaluation included a detailed patient history, clinical examination, and relevant investigations such as CBC, KFT, LFT, ECG, chest X-ray, echocardiography, INR, and serum electrolytes as required. Patients were kept nil per mouth (NPO) for at least six hours before surgery and were advised to take tablet Pantoprazole 40 mg along with tablet Alprazolam 0.25 mg for night sedation the evening before surgery. The procedure was thoroughly explained to the patients and their

relatives, and written informed consent was obtained. Patients were also instructed on the procedure and how to use the Visual Analog Scale (VAS) for pain assessment. On the day of surgery, NBM status was confirmed in the operating room. Standard monitors, including a blood pressure cuff, ECG leads, and SpO_2 probe, were attached, and baseline readings were recorded. Preloading was done with I/V Ringer Lactate 10 ml/kg. Premedication with Inj. Pantoprazole 40mg iv and Inj. Ondansetron 4mg iv was given. Under all the aseptic precautions lumbar puncture was done by the person having adequate exposure of spinal anesthesia technique. The person loading the syringes and giving the drug was different from the person recording the parameters. Thus, the person who observed the parameters and also the patients was not aware of the drug used intrathecally. The drug was given with 25 G spinal needle in L3-L4 intervertebral space in lateral position with table kept horizontal without any tilt. After conforming free flow of CSF, spinal anesthesia was given with drug as per group allotted as:

- **Group L+B**: intrathecal hyperbaric levobupivacaine 0.5% (heavy) 3.3 ml plus 60 mcg Inj. Buprenorphine (3.5 ml) - Study group
- **Group L** - intrathecal hyperbaric levobupivacaine 0.5% (heavy) 3.3ml plus 0.2 ml NS (3.5 ml) - Control Group

Time of injection of drug was noted and labeled as Time Zero. The patient was immediately made supine. Patient was supplemented with 02 by a hudson mask. After injection patient was turned supine slowly, following sensory and motor characteristics and hemodynamic parameters were monitored and noted. The parameters assessed included the onset of sensory and motor blockade, time to achieve the T10 sensory level, time to complete motor blockade, highest sensory level attained, time to reach the highest sensory level, total duration of surgery, and the duration of both sensory and motor blockade. Additionally, the quality of analgesia, vital parameters, intraoperative and postoperative side effects, and postoperative analgesia using the VAS were evaluated. The time of start of monitoring was taken from the time the drug was injected into the intrathecal space (t=0).

Statistical Analysis

The data are tabulated in Microsoft Excel and analysed with SPSS V.24 softwre. The continuous variables are presented with mean and standard deviation. The categorical variables are presented with frequency and percentage. Chi square test, independent t test are used for the statistical analysis. The p value ≤ 0.05 is considered statistically significant.

OBSERVATIONS AND RESULTS

Both groups were comparable, with no significant differences in demographic data and duration of surgery as shown in table 1.

Demographic data		**Group L**	**Group L+B**	**P value**
Age (Years)	Mean	43.06±11.23	42.64±9.40	0.840
Height (cm)	Mean	163.84±7.97	162.22±7.85	0.308
Duration of surgery (min)	Mean	49.40±15.90	52.50±27.37	0.490
Gender	Male	32 (64%)	25 (50%)	0.157
	Female	18 (36%)	25 (50%)	
ASA grade	I	44 (88%)	48 (96%)	0.140
	II	06 (12%)	02 (4%)	

Table 1: Demographic profileof patients and duration of surgery

The sensory and motor characteristics showed significant differences between the two groups, ($p<0.05$). The onset of sensory and motor block was significantly faster in the group receiving buprenorphine as an adjuvant. Similarly, the time to achieve the T10 sensory level and complete motor blockade was shorter in this group. The highest sensory level was also achieved more quickly

compared to the group receiving only levobupivacaine. Additionally, the duration of both sensory and motor blockade was significantly prolonged in the buprenorphine group, (Table 2).

Characteristics	Group L	Group L+B	P value
Onset of sensory block (min)	6.26±0.9	2.04±0.79	0.0001
Onset of motor block (min)	8.74±0.92	4.02±0.91	0.0001
Time to achieve T10 level (min)	10.7±1.18	5.4±0.81	0.0001
Time for complete motor block (min)	12.24±1	7.66±1	0.0001
Time to achieve highest sensory level (min)	14.08±1.18	8.42±0.99	0.0001
Duration of motor block (min)	175.92±8.63	214.42±18.18	0.0001
Duration of sensory block (min)	218.36±13.77	260.86±11.22	0.0001

Table 2: Sensory and motor characteristics

Group L showed significantly higher VAS scores at 1 and 2 hours compared to Group L+B, (p=0.0001). After that, Group L showed significantly lower VAS scores at 4 and 6 hours compared to Group L+B, (p=0.0001). At 8 hours, the VAS scores in the two groups were comparable, (p>0.05), (figure 1).

In Group L, 41 operating surgeons (82%) rated the anaesthesia as excellent, while in Group L+B, 46 operating surgeons (92%) gave this rating. The difference was not statistically significant (P=0.137).

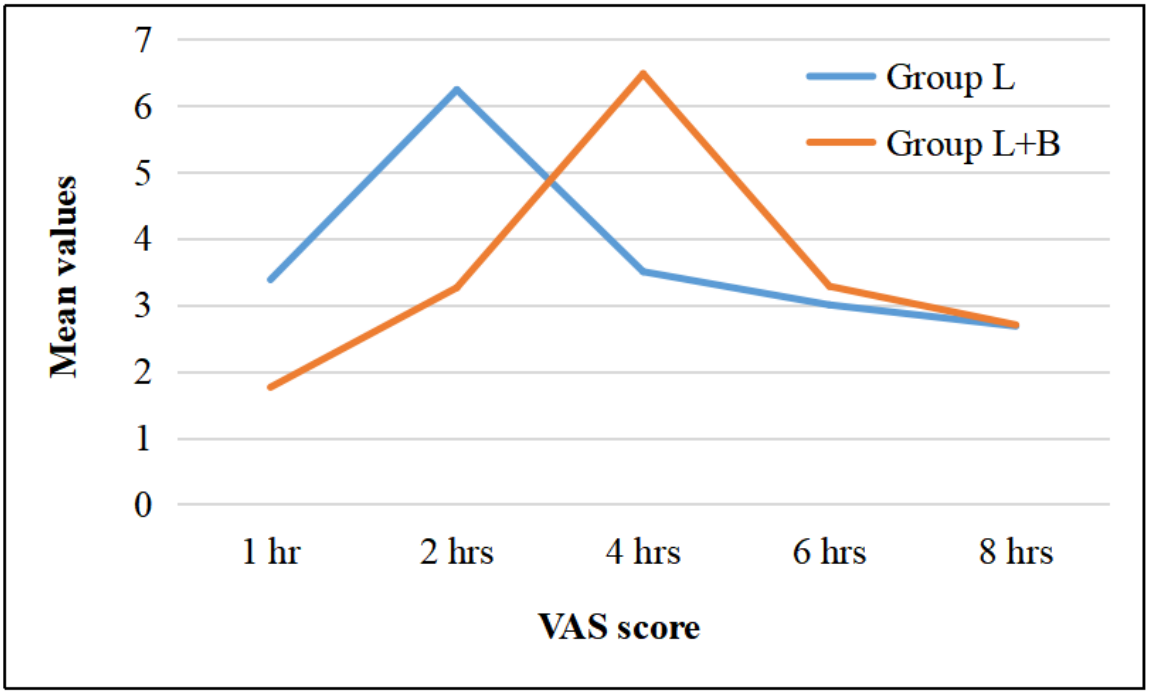

Figure 1: Distribution of VAS score

Preoperative and intraoperative hemodynamic parameters (pulse rate, SBP, DBP, MAP) were comparable between the two groups (p>0.05). Vasopressor was required in 6% of patients in Group L and 12% in Group L+B (P=0.294). Mild sedation was required in 10% of patients in Group L and 6% in Group L+B, with no cases of moderate sedation or conversion to general anesthesia (P=0.461). Nausea and vomiting were reported in 4% of patients in Group L and 6% in Group L+B, (P=0.646). The mean time for rescue analgesia was longer in Group L+B compared to Group L, showing a highly significant difference between the two groups, (P=0.0001) as depicted in figure 2.

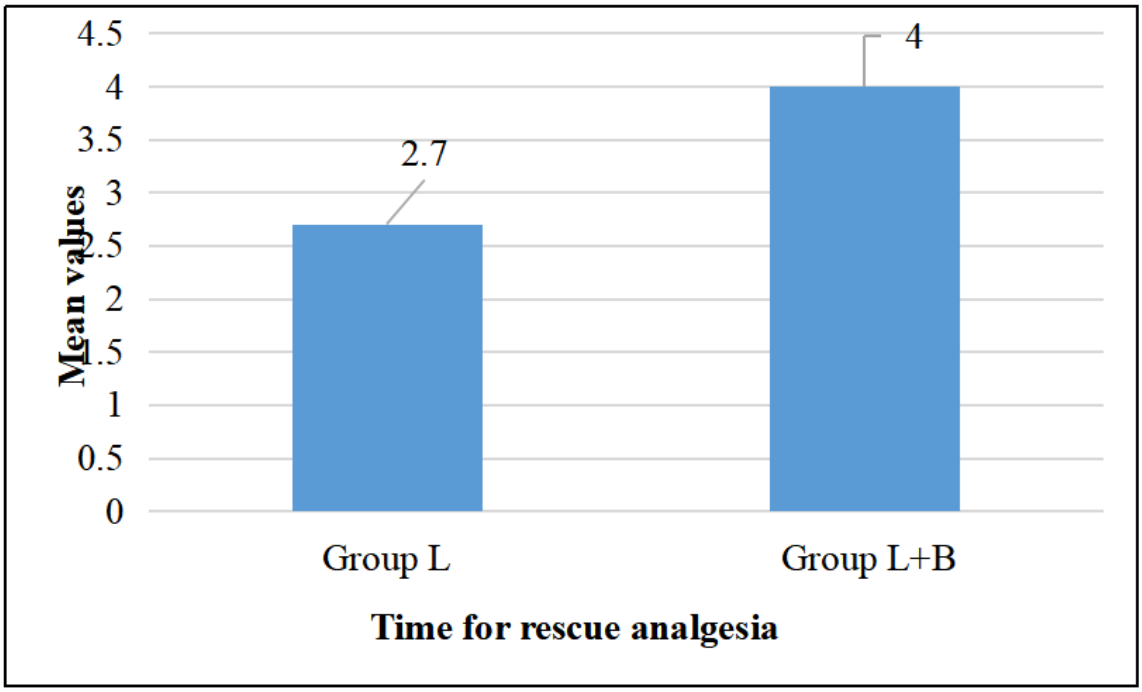

Figure 2: Distribution of Time for rescue analgesia

DISCUSSION

The dose of hyperbaric 0.5% Levobupivacaine (3.3 mL, 16.5 mg) used in our study was identical in both groups. As a general rule, intrathecal hyperbaric levobupivacaine at a 0.5% concentration blocks approximately one and a half spinal nerve segments per milligram in adults. Based on this, the recommended dose for lower abdominal surgeries ranges from 2.5 to 3.5 mL (12.5–17.5 mg).[10] Similar doses have been studied by Adate et al[11] and Furia et al[12]. In the present study, buprenorphine 60 mcg was used as an additive to 3.3 mL of hyperbaric 0.5% levobupivacaine. Intrathecal buprenorphine is commonly used in doses ranging from 30 to 150 µg. Identical doses of buprenorphine as an intrathecal additive have been evaluated by Adate et al[11], Furia et al[12], and Agarwal et al.[13]

In the present study, the onset of sensory block was significantly faster in Group L+B (2.04 ± 0.79 min) compared to Group L (6.26 ± 0.9 min) (p = 0.0001). Similarly, the onset of motor block was quicker in Group L+B (4.02 ± 0.91 min) than in Group L (8.74 ± 0.92 min) (p = 0.0001). The time to achieve the T10 sensory level was notably shorter in Group L+B (5.4 ± 0.81 min) compared to Group L (10.7 ± 1.18 min) (p = 0.0001). The time required for complete motor blockade was significantly less in Group L+B (7.66 ± 1 min) than in Group L (12.24 ± 1 min) (p = 0.0001). Furthermore, the time to achieve the highest sensory level was significantly shorter in Group L+B (8.42 ± 0.99 min) than in Group L (14.08 ± 1.18 min) (p = 0.0001). The duration of motor blockade was significantly prolonged in Group L+B (214.42 ± 18.18 min) compared to Group L (175.92 ± 8.63 min) (p = 0.0001). Similarly, the duration of sensory block was longer in Group L+B (260.86 ± 11.22 min) than in Group L (218.36 ± 13.77 min) (p = 0.0001). These results indicate that the addition of buprenorphine to intrathecal levobupivacaine significantly enhances the onset, depth, and duration of both sensory and motor blockade. Our results for Group L were comparable to the findings of Goyal et al,[14] Katariya et al,[15] Singh et al[16] and Patel et al[17] whereas For Group L+B, our results were consistent with those of Adate et al.[11] Furia et al[12] Agarwal et al[13] and Ture et al.[18]

VAS scores assessed at various time intervals were significantly higher in Group L compared to Group L+B, starting from 1 hour and continuing up to 8 hours. At 4 hours, the mean VAS score in Group L+B reached 6.48 ± 1.35, necessitating the administration of rescue analgesia, after which no further evaluation was conducted for this group. These findings align with those of Adate et al[11] and

Furia et al[12], who also reported lower pain scores and prolonged analgesia in groups receiving adjuvant medications along with local anesthetics.

In our study, duration of effective analgesia was defined as duration measured from the time of injection of study drug to the time of first rescue analgesic given to the patient (VAS ≥4) noted in minutes. The mean duration of effective analgesia in group L was noted to be 2.70±0.52 hours which is comparable with the previous studies.[15,17,19] The mean duration of effective analgesia in group L+B was noted to be 4.05±0.97 hours, these results are comparable to the study done by Agarwal et al[13] and Ture et al.[18]

In our study, 41 patients reported excellent quality of analgesia, and 9 patients reported good quality of analgesia in group L. In group L+B, 46 patients reported excellent quality of analgesia, and 4 patients reported good quality of analgesia Quality of analgesia was found to be comparable in both the groups (p= 0.137). Thus, addition of buprenorphine only marginally improved the quality of surgical analgesia in our study.

The average of mean pulse rate during the intraoperative period showed no significant differences between Group L+B and Group L, with P values all above 0.05. Authors of other studies did not record any significant variations in the pulse rate of the patients with either plain levobupivacaine group or levobupivacaine with buprenorphine group. In the current study, there were no significant differences in intraoperative SBP, DBP, or MAP between Group L+B and Group L ($P > 0.05$ for all comparisons). However, a greater fall in SBP was observed in Group L+B, with 6 patients (12%) developing hypotension compared to 3 patients (6%) in Group L, requiring IV fluids and Inj. Mephentermine 6 mg. Observations at other time points showed no significant differences in SBP between the groups. These findings are consistent with studies by Furia et al[12] Ture et al[18] and Fattorini et al.[20]

There were no adverse effects on respiratory function were evident in both the groups. The respiratory rate was within normal range as was the SpO2 levels which fluctuated between 98% to 100% during the intraoperative as well as postoperative period. 3 patients (6%) in Group L+B and 2 patients (4%) in Group L complained of nausea/ vomiting and were treated with Inj. Ondansetron 4mg IV. In group L+B, it can be attributed to higher level of spinal anaesthesia(T4). The incidence of nausea and vomiting following intrathecal and epidural opioids is approximately 30%, which is likely the result of cephalad migration of drug in cerebrospinal fluid and subsequent interaction in opioid receptors located in the area postrema.[21]

CONCLUSION

In the view of above observation, we are of the opinion that intrathecal buprenorphine 60µg acts synergistically to potentiate intrathecal local anaesthetic levobupivacaine with the result that there is rapid onset and prolongation of both sensory and motor block. It is worthwhile to note that prolongation of sensory block is beneficial to the patient in the sense that duration of effective analgesia is prolonged in the early postoperative period. We came to the conclusion that the quality of sensory and motor blockade was satisfactory, and the hemodynamic parameters were found to be stable in both the groups. No untoward perioperative complications were noted. Hence, we suggest intrathecal levobupivacaine + buprenorphine combination as a better alternative than levobupivacaine.

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