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Research Article

Comparison of Levobupivacaine and Levobupivacaine with Fentanyl for Infra Umbilical Surgeries under Sub-Arachnoid Block

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ABSTRACT

Background: Levobupivacaine's superior clinical profile and shorter block duration make it an intriguing substitute for other local anesthetics. In order to intensify block and offer postoperative analgesia, intrathecal opioids have been employed as additives. This study compares the effectiveness of levobupivacaine alone and in combination with fentanyl. The effect on hemodynamics, duration of postoperative analgesia, and complications were also compared.
Methods: Fifty patients in the age group of 18-65 years with ASA grade I or II posted for elective surgery under subarachnoid block were enrolled in this prospective double-blind study and randomly allocated into two groups. Group 1 (n=25) patients received 3.0 ml (15 mg) of 0.5% levobupivacaine plus 0.5 ml of normal saline, and Group 2 (n=25) patients received 3.0 ml (15 mg) of 0.5% levobupivacaine plus 0.5 ml (25 mcg) of fentanyl intrathecally. Hemodynamics, features of sensory and motor block, postoperative need for rescue analgesia within 24 hours, and adverse events were documented.
Results: Sensory block onset was earlier in group 2 (4.31±0.58) minutes than in group 1 (6.51±0.62). Likewise, group 2 experienced the onset of motor block earlier (2.91±0.39) than group 1 (5.62±0.50), and group 2 saw a faster regression of the motor block (153.00±13.23) than group 1 (186.00±20.82). Hemodynamic and side effects were comparable in both groups. Group 2 required considerably fewer postoperative rescue analgesics in the first 24 hours ($p < 0.05$).
Conclusion: Fentanyl added to levobupivacaine provides a relatively faster initiation of block and earlier recovery of motor power, improving the chances of early patient mobilization.

Introduction

Subarachnoid block (SAB) is opted for in infra-umbilical and lower limb surgeries for outpatient procedures for its ease of performance, lesser risk of adverse events in patients with co-morbidities, avoidance of polypharmacy, and better pain management postoperatively. However, the principal limiting factor to its more widespread use is the secondary effect of the residual block, which delays ambulation, voiding, and thus hospital discharge. These shortcomings are known to depend upon the drug characteristics. An ideal intrathecal agent for ambulatory surgery should have a rapid onset of sensory and motor block, provide adequate duration of operative time, have a predictable regression within an acceptable time frame, and have a low incidence of adverse effects [1-2].

Over the years, various local anesthetics (LA) have evolved. Presently, bupivacaine is the most commonly

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used LA for SAB, which has a good safety profile but is associated with a long duration of action, limiting its use in the ambulatory setting [3]. Levobupivacaine, the pure S (-) enantiomer, was recently introduced as an alternative to bupivacaine, providing similar surgical conditions with faster recovery, which may potentially facilitate early mobilization and shorter hospital stays [4-5].

Good postoperative analgesia also plays a pivotal role in early patient discharge. Opioids are often used in conjunction with LA to provide effective pain relief as a component of multimodal analgesia and have a dose-sparing effect. They are known to cause pruritus, urinary retention, nausea, vomiting, and respiratory depression, which may lead to prolonged hospitalization [6-7]. However, recent evidence suggests no increased risk of respiratory depression with lipophilic opioids such as fentanyl when used intrathecally [8-9].

The findings for the use of levobupivacaine with opioids are inconsistent in the current literature [10-12]. Thus, we planned this study to compare the efficacy of intrathecal hyperbaric levobupivacaine with and without fentanyl in infra-umbilical and lower limb surgeries and its possible role in promoting early ambulation after surgery.

Methods

After approval from the Institutional Ethical Committee dated 30/04/2023 (project number 2571), this prospective randomized controlled trial was conducted in accordance with the Helsinki Declaration at the Department of Anesthesiology at MMIMSR, Mullana, Ambala. Patients of ASA-PS 1 and 2 of either gender and age group between 18 and 65 years requiring surgery for non-traumatic causes under SAB were enrolled. Patients with pre-existing local infection at the site of needle insertion, contraindication or allergy to study drug, coagulopathy and bleeding disorders, neurological deficits, chronic pain patients, redo surgeries, patients with hemodynamic instability, failed SAB, and pregnant and lactating women were excluded.

Enrolled patients were randomly allocated to two groups using a computer-generated random number table, and the allotted numbers were secured in coded, opaque, sealed envelopes. Fifty patients were divided into Group 1 (n=25), who received levobupivacaine 0.5% 15mg + normal saline (NS) 0.5ml, and Group 2 (n=25), who received levobupivacaine 0.5% 15mg + Inj Fentanyl 25mcg. The total volume of drug was kept constant to avoid bias.

Patients were evaluated for fitness a day prior to surgery, and routine investigations were done. The visual analogue scale (VAS) for pain management was explained, with 0 for no pain and 10 for the worst imaginable pain [13]. Fasting was ensured as per standard ASA guidelines, and pre-medication with alprazolam 0.25 mg and pantoprazole 40 mg orally was given a night prior and two hours before surgery [14]. On the day of surgery, informed consent was taken, intravenous (IV) access was established, and infusion of 7 ml/kg of Ringer's solution was started in both groups. Monitoring was started as per ASA standards prior to the procedure using a Philips IntelliVue MX800 multichannel monitor. The technique of spinal block involved maintaining a sitting position, palpating the spine, and performing a lumbar puncture under all aseptic precautions in the L3-4 space with a 25G Quincke spinal needle. The final volume of intrathecal injection was prepared in a 5 ml syringe by an anesthetist not involved in the study. The drug was administered at a rate of 0.25 ml/second according to the group allocation, and patients were made supine after the procedure [15]. Observations were recorded in a pro forma at 0, 1, 3, 5, 10, 15, and 30 minutes and thereafter every 30 minutes till the end of surgery. Postoperatively, patients were monitored in the post-anesthesia care unit for two hours. Any adverse effects, including bradycardia, defined as heart rate (HR) <50 bpm, were treated with Inj. Atropine 0.6mg IV, and hypotension, defined as a fall in blood pressure (BP) of 30% from baseline, was treated with Inj. Mephentermine 6mg IV incrementally. Block parameters recorded were the onset and duration of sensory and motor block, time to peak block height, 2-segment regression, and complete regression time. Sensory block was determined by a cold cotton swab and pinprick, and motor block was determined by the Modified Bromage Scale [16]. In the postoperative period, patients were evaluated for pain using the VAS score, and rescue analgesia was given with Inj. diclofenac 75mg in 100 ml of saline if the VAS score was greater than 4.

Statistical Analysis

Data were described in terms of range, mean ± standard deviation (±SD), median (IQR), frequencies (number of cases), and relative frequencies (percentages), as appropriate. To determine whether the data were normally distributed, a Kolmogorov-Smirnov test was used. A comparison of quantitative variables between the study group was done using the Mann-Whitney U test for non-parametric data. For comparing categorical data, the chi-square (x^2) test was performed, and Fisher's exact test was used when the expected frequency was less than 5. A probability value (P value) less than 0.05 was considered statistically significant. The statistical software SPSS 21.0 (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) for Microsoft Windows was used for all statistical computations.

Results

Fifty-eight patients were enrolled for the study, out of which 6 did not meet the inclusion criteria, 1 patient refused to participate, and 1 patient's surgery was postponed (Figure 1). The remaining 50 patients were randomized into 2 groups of 25 each. Group 1 patients were given 0.5% levobupivacaine 15 mg + normal saline 0.5 ml, and group 2 patients were given 0.5% levobupivacaine 15 mg + Inj. Fentanyl 25 mcg. Age, gender, and ASA-PS were found to be comparable between the two groups ($p > 0.05$). Baseline values of HR, systolic (SBP), and diastolic (DBP) blood pressure were statistically insignificant between the two groups, as shown in (Table 1) ($p > 0.05$).

After administration of the study drug intrathecally, both groups experienced a decrease in HR, SBP, and DBP when compared to baseline, but none of the patients required any intervention for the same, and the difference was statistically insignificant, as shown in Figures 2 and 3). (Table 2) shows that group 2 had onset of sensory block to the T10 dermatome in 4.31±0.58 minutes, while group 1 patients took 6.51±0.62 minutes. This difference was statistically significant ($p=0.001$). The maximum sensory block attained was T6, and the maximum motor block achieved in both groups was Modified Bromage 3, both of which were significantly faster in group 2 compared to group 1 ($p=0.001$). While the duration of regression of motor block was significantly longer in group 1 (186±20.82 minutes), the two-segment regression of block was statistically insignificant.

As shown in (Table 3), the modified bromage score postoperatively was significantly lower in group 2 ($p=0.001$). VAS was used to monitor the patients for postoperative pain, and the VAS score as well as analgesic requirement was significantly lower in group 2 as compared to group 1. The total number of rescue analgesic doses required in 24 hours was 3.36±0.95 in group 1 and 1.96±0.61 in group 2. Patients were monitored for side effects and complications. 2 patients in both groups experienced nausea each, 1 patient in group 2 had pruritus, and 1 had shivering in the postoperative period. There were no statistically significant differences.

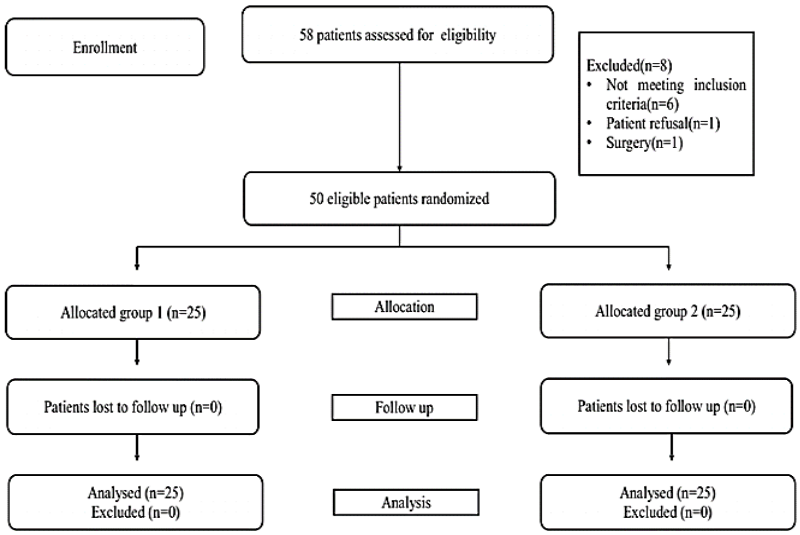

Figure 1- Consort diagram

Table 1- Patient demographics and baseline data.

Parameters	Group 1 (n=25) Mean±SD	Group 2 (n=25) Mean±SD	P value
Age (years)	42.28±10.71	42.20±9.50	0.823
Gender F	7	12	0.145
M	18	13	
ASA-PS I	19	18	0.747
II	16	7	
Duration of surgery (minutes)	77.60±20.21	82.68±26.31	0.448
Baseline HR (beats/min)	77.20±9.33	75.08±8.32	0.351
Baseline SBP (mmHg)	129.36±7.35	130.24±11.85	0.754
Baseline DBP (mmHg)	73.80±5.86	74.72±7.07	0.619

Data is presented as n=number and mean±standard deviation (SD).

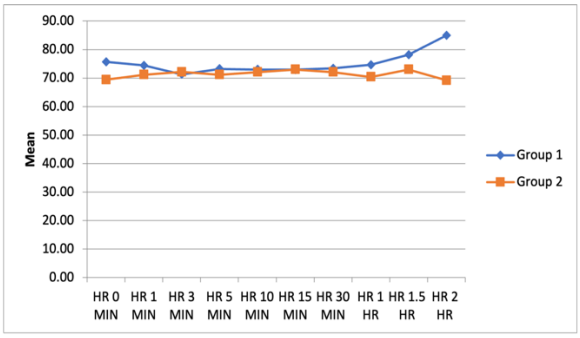

Figure 2- Heart rate at various time intervals in group 1 and group 2 intraoperatively.

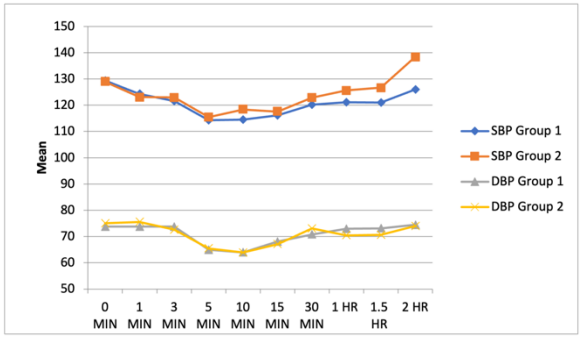

Figure 3- SBP and DBP at various time intervals in group 1 and group 2 intraoperatively.

Table 2- Intraoperative block characteristics (minutes)

Parameters	Group 1 (n=25) Mean±SD	Group 2 (n=25) Mean±SD	P value
Onset of sensory block	6.51±0.62	4.31±0.58	0.001
Onset of motor block	5.62±0.50	2.91±0.39	0.001
Time to achieve T6	14.35±1.87	8.35±0.81	0.001
Time to achieve complete motor block	10.19±0.95	7.27±1.03	0.001
Time to two segment regression	128.84±7.30	125.48±9.16	0.158
Time to complete regression	186.00±20.82	153±13.23	0.001

Data is presented as n=number and mean±standard deviation (SD).

Table 3- Follow up parameters

Parameters at various time points	Group 1 (n=25) Mean±SD	Group 2 (n=25) Mean±SD	P value
VAS			
0 min	0.00±0.00	0.00±0.00	1.000
30 min	1.24±1.05	0.00±0.00	0.001
1 hour	3.20±0.71	1.00±0.82	0.001
2 hours	4.48±1.08	2.28±0.98	0.001
Modified bromage score			
0 min	3.00±0.00	2.04±0.20	0.001
30 min	2.44±0.71	1.28±0.54	0.001
1 hour	1.40±0.71	0.68±0.63	0.001
2 hours	0.28±0.46	0.16±0.37	0.311
24-hour analgesic requirement	3.36±0.95	1.96±0.61	0.001

Data is presented as n=number and mean±standard deviation (SD).

Discussion

Early ambulation places high demands on the anesthetic technique. Concerns about prolonged motor block and urinary retention have limited the use of SAB in such settings until recently.

Levobupivacaine is proposed to be advantageous over bupivacaine due to its lesser impact on motor blockade, possibly minimizing the psychological discomfort of being immobile for a prolonged period [4]. While a shorter motor block is desirable, it may also be associated with higher pain scores, for which additional analgesics may be required. Contrary to the previous literature, there is emerging evidence that fentanyl may be used intrathecally without undue increased risk of respiratory depression [8-9].

According to our study, when fentanyl 25 mcg is added to hyperbaric levobupivacaine 0.5% (total volume = 3.5 ml), it provides good surgical anesthesia with a noticeably quicker onset of both sensory and motor block. The maximum sensory level attained was T6, and motor was modified bromage score 3, and the mean duration to achieve maximum block levels was also significantly faster. The duration of sensory block was similar in both groups; however, the duration of motor block was shortened in the combination group. Postoperative VAS was lower with fentanyl than with levobupivacaine alone.

It is well known that the addition of opioids to intrathecal LA has a synergistic effect. Gupta P. et al.

recently examined the effects of 15 mg hyperbaric levobupivacaine with 25 mcg fentanyl versus 15 mg levobupivacaine with 10 mcg dexmedetomidine on characteristics of the block in patients undergoing lower abdominal surgeries. They discovered that adding fentanyl greatly increased the onset of both sensory and motor block [17]. Akan B et al. also demonstrated that the onset of sensory block and duration of motor block were significantly shortened with the use of fentanyl 25 mcg and sufentanil 2.5 mcg with 7.5mg levobupivacaine as compared to levobupivacaine alone. They also found a longer analgesia time in the fentanyl and sufentanil groups [18]. Cuvas O. et al. demonstrated a similar onset time of block but a shorter duration of motor block when 15 mcg fentanyl was added to 2.3 ml levobupivacaine [19]. In our study, time taken for maximum sensory and motor block was substantially less with the addition of fentanyl. This variation could be attributed to the difference in the dose of levobupivacaine used.

Kulkarni A. et al., Bidikar M. et al., and Rajasekaran S. et al. noted observations similar to our study, with the addition of fentanyl resulting in earlier onset of block as well as earlier regression of motor block and better postoperative analgesia [11, 20-21]. The density of the final drug is known to influence block characteristics, with higher density also prolonging sensory and motor block. Solutions of LA in normal saline are less hypobaric than the opioid combination, thus explaining the early onset of block and regression of motor block in our study [22-23].

The patients in the levobupivacaine group reported a higher VAS score and hence required more analgesics postoperatively compared to those given intrathecal fentanyl as an adjuvant. This is explained by the synergistic interaction between spinal opioids and LAs, without effect on degree or level of LA-induced sympathetic or motor blockade. Similar findings were observed by Attri J.P. et al. [24].

Our study was not short of limitations. We included patients with ASA grades I and II only. Hence the results cannot be extrapolated to ASA III and IV patients. The study would have given a better correlation if a larger sample size having more groups being provided with varied doses of each medication were also recruited. The speed of injection of the drug could not be maintained uniformly in all the cases. No sedation assessment and total days of hospital stay were done in the study.

Conclusion

Thus, to conclude, fentanyl combined with levobupivacaine provides the benefit of quicker initiation of sensory and motor block, as well as a shorter period of motor block in comparison to levobupivacaine alone. This could potentially assist in enabling early ambulation after surgery. However, both regimens were adequate in providing optimal operating conditions with similar quality of block and no significant alterations in hemodynamic profiles. The benefits of intrathecal fentanyl administration also extend into the postoperative phase by enhancing analgesia and reducing the need for rescue pain management.

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