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Original Research Article

Comparison of Intrathecal Isobaric Levobupivacaine with or without Fentanyl in Infraumbilical Surgeries: A Prospective Randomized Study

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Abstract:

Background: The subarachnoid block is the preferred anaesthetic technique for operations performed below the belly button due to its cost-effectiveness, ability to effectively relax muscles, and improved post-operative pain management. Levobupivacaine is superior to bupivacaine due to its shortened period of motor blockage, longer duration of sensory blockade, and lower risk of cardiotoxicity. When used with intrathecal local anaesthetics, opioids enhance the efficiency of anaesthesia and pain management during and after surgery.

Aim and objectives: This study set intended to evaluate the effects of levobupivacaine in spinal anaesthesia with and without fentanyl.

Material and methods: Eighty patients who met the Physical Status I and II criteria for the American Society of Anesthesiologists were divided into two groups at random for this study. The way the study was carried out meant that neither the researchers nor the patients knew which group they belonged to. The study's goal was to look at the consequences of abdominal surgery. Two groups were randomly assigned to the subjects. A combination of 0.5 ml of normal saline and 2.5 ml of isobaric levobupivacaine 0.5% was given to the Levobupivacaine group (n = 40). A combination of 25 µg (0.5 ml) of fentanyl and 2.5 ml of isobaric levobupivacaine 0.5% was administered to the Levobupivacaine + fentanyl group (n = 40). The duration of the sensory and motor block was noted in the research, along with its onset time. The study also recorded their adverse outcomes in groups, blood pressure and heart rate variations, the duration of analgesia, and their Visual Analogue Scale score.

Results: Group LF experienced a significantly faster onset of both sensory and motor block ($P < 0.05$). Group LF experienced a significantly longer average duration of sensory blockage ($P < 0.05$). Both groups had steady hemodynamics as well as no sedation all throughout the perioperative phase, and the average length of motor block was found to be similar ($P > 0.05$). With a p-value of less than 0.001, the analgesic effect persisted significantly longer in Group LF (336.5 ± 31.3 min) than in Group L (223.65 ± 32.17 min).

Conclusion: When administering isobaric 0.5% levobupivacaine in conjunction with intrathecal fentanyl (25 µg), patients having surgeries below the umbilicus can experience significantly superior block characteristics and minimal side effects.

Keywords: Fentanyl; Infraumbilical surgeries; Levobupivacaine; Spinal anesthesia.

Introduction

Since spinal anaesthesia has a high level of credibility, is reasonably priced, and can effectively relax muscles and relieve pain both before and after surgery, it is the recommended anaesthetic technique for non-traumatic operations. There is a current trend in which more and more surgeries are being performed as outpatient procedures. [1] Spinal anaesthesia for non-traumatic treatments usually entails the injection of 0.5% hyperbaric bupivacaine. However, bupivacaine may cause cardiac toxicity, a protracted loss in motor function, and hemodynamic instability. The S-enantiomer of bupivacaine is levobupivacaine, a local anaesthetic that functions as an amino amide. It acts on the

nerves in a particular way by causing a differential neuraxial blockage. When it comes to both motor and sensory block, levobupivacaine has a faster onset than other medications in its class. It also has a lower risk of cardiotoxicity and a more prolonged period of sensory blockade. [2]

Postoperative pain management is still a major issue despite advances in our understanding of the physiology of acute pain, the development of new opioid and non-opioid painkillers, the use of multiple drug delivery mechanisms and routes, and the growing popularity of minimally invasive surgical procedures. [3] Various intrathecal adjuvants have been utilized to increase the effectiveness of analgesia and anaesthesia while concurrently reducing the side effects associated with high doses of local anaesthetic administered alone. [4] It has been shown that the intrathecal injection of local anaesthetics and opioids at the same time has a synergistic effect that prolongs the duration of sensory block and analgesia without prolonging motor block further. [5] Therefore, in order to extend the sensory block without escalating the motor block, additional additives like fentanyl and sufentanil have been used with local anaesthetics.

The purpose of this study was to determine whether intrathecal fentanyl combined with isobaric levobupivacaine could prolong the duration of sensory block and pain alleviation while leaving motor block intact. In patients having infraumbilical surgeries, we investigated the effects of administering a comparable dosage of local anaesthetic without fentanyl against 25 µg fentanyl with 0.5% isobaric levobupivacaine (12.5 mg). We examined the subarachnoid block's properties, the total amount of rescue analgesics required, and any alterations in hemodynamics.

Aim and Objectives:

The primary objective of the current study was to determine how long analgesia would last. The secondary objectives included perioperative sedation score, perioperative as well as postoperative hemodynamic changes, the onset and duration of sensory and motor blockade, and any adverse consequences or complications.

Material and Methods:

Eighty patients, ages 18 to 65, who were scheduled for infraumbilical surgeries and had Physical Status I or II according to the American Society of Anesthesiologists, participated in this prospective, randomized, double-blind study. The Institutional Ethics Committee gave its clearance before the study could be carried out. This trial did not include patients with known allergies to the study medications, which included opioids and local anesthetics, nor those who were ineligible for subarachnoid block.

The patients were randomly assigned using the sealed envelope approach, in which each preparation was placed within its own envelope and then shuffled. The experimental drug was diluted to a final volume of 3.0 ml. Levobupivacaine (12.5 mg) or a combination of 12.5 mg levobupivacaine and 25 µg fentanyl was given to the subjects. A resident anesthesiologist who was not further involved in the study designed the study solutions to ensure the prevention of bias.

The day before surgery, each patient underwent a preanesthetic evaluation and was instructed to refrain from oral intake in accordance with institute protocol. The first vital signs, which included heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (SpO2), and respiratory rate (RR), were taken as soon as the patient entered the operation room. After that, the patient was given a 10 ml/kg preload of ringer's lactate. The patient was given spinal anaesthesia while sitting, taking great care to maintain sterility. The L2–L3 or L3–L4 interspace was needled with a 25G Quincke needle. Patients in Group A received a 0.5 ml injection of normal saline in addition to a 2.5 ml (12.5 mg) injection of 0.5% isobaric levobupivacaine. In contrast, patients in Group B received a 0.5 ml injection of fentanyl (25 µg) and a 2.5 ml (12.5 mg) injection of 0.5% isobaric levobupivacaine.

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation (SpO2), and respiratory rate (RR) were among the vital physiological measurements that were continuously tracked for the first ten minutes at 2-minute intervals. After that, they were monitored every five minutes until the thirty-minute mark, and lastly, every fifteen minutes until the procedure was completed. When the heart rate (HR) went below 60 beats per minute and the mean arterial pressure (MAP) fell below 60 mmHg, respectively, an intravenous (IV) bolus of atropine 0.6 mg and ephedrine 6 mg with IV fluids was given to treat bradycardia and hypotension. An intravenous injection of ondansetron (4 mg) was used to treat the symptoms of nausea and vomiting. The Modified Bromage score, sometimes referred to as the Modified Bromage scale, was used to evaluate motor block. The following is the paralysis grading scale: A score of 0 denotes no paralysis and the capacity to move the hips, knees, and ankles; a score of 1 denotes the ability to move the knees but not the extended legs; a score of 2 denotes the ability to move the ankles but not the knees; and a score of 3 denotes complete paralysis and the inability to move any part of the limb. The beginning of the motor block is defined as the point

at which the Modified Bromage Score approaches 2. The amount of time needed to return to Modified Bromage 0 was measured as the duration of the motor block. Using a blunt 23G hypodermic needle, the sensory block was assessed in the dermatomal areas from T8 to S2. A 0 scale denoted normal feeling, 1 denoted loss of prick sensation (analgesia), and 2 denoted loss of touch sensation (anaesthesia) in the evaluation. The time interval between injecting a drug into the spinal canal and when the drug reaches the T8 dermatomal level is referred to as the onset of sensory block. The amount of time it takes for a sensory block to retreat from its highest level to the S1 dermatome in the heel is known as the duration of the block. The amount of time that passed between the intrathecal injection and the patient's request for more pain medication was used to calculate the duration of analgesia. A 10-point Visual Analogue Scale (VAS) was used to measure postoperative pain; a score of "0" denoted no pain at all, while a score of "10" denoted the presence of the most severe pain. When a patient's VAS (Visual Analogue Scale) score was ≥4, rescue analgesia was administered via intramuscular injection of 75 mg of diclofenac sodium. The total duration of analgesia was defined as the period of time from the injection's administration till the pain subsided.

The Ramsay Sedation Score (RSS) was used to evaluate sedation throughout the perioperative phase. The following was RSS's grade: A light tap on the glabella or a loud auditory stimulus will cause the patient to react quickly; a light tap on the glabella or a loud auditory stimulus will cause the patient to respond slowly; a light tap on the glabella or a loud auditory stimulus will cause the patient to respond slowly; and a nod will indicate that the patient is not responding at all. Vital signs such as heart rate (HR), oxygen saturation (SpO2), diastolic blood pressure (DBP), systolic blood pressure (SBP), mean arterial pressure (MAP), and respiratory rate (RR) were recorded following the procedure. For a total of 12 hours, adverse responses (such as nausea, vomiting, low blood pressure, a sluggish heartbeat, and itching) were recorded every two hours.

Statistical analysis:

A recent study by Bidikar et al. [6] found that 36 patients were the appropriate sample size for each group. The computation used in this study was based on an alpha error of 0.05 and a power of 80% to identify a projected difference in the 8.6±13 minute motor block duration. The sample size in each group was increased to 40 after a 10% dropout rate was taken into consideration. Using the duration of analgesia as the major end measure, the sample size for each group was found to be 1. The central limit theorem states that in order to detect a substantial difference in the outcomes, each group must have a minimum of thirty people. As a result, we have calculated the sample size by taking into account all pertinent factors. In particular, we have decided to base the final sample size calculation on the motor block time. As the statistical analysis explains, this choice was used to improve the study's power and external validity.

The statistical tool Epi Info version 7.2.1.0, created by the US CDC (Centres for Disease Control and Prevention), was used to analyze the data. The median value, range, and number of patients were provided together with the mean value±standard deviation of the data. The nominal or categorical variables were expressed as percentages and numbers, and depending on the situation, Fischer's exact test or the Chi-square test were used for analysis. The Student's t-test was used to compare the two groups and analyze the continuous scale parameters. Statistical significance was defined as a p-value of less than 0.05.

Results:

Both groups had similar demographics, baseline hemodynamic parameters, and the total duration of the surgery. [Table 1]

Table 1: Demographic variables

Variables		Group L (Mean±SD) (N=40)	Group LF (Mean±SD) (N=40)	P value
Mean age (in years)		47.84 ± 10.43	46.39 ± 14.58	0.211 (NS)
Gender (M:F) (%)		30:10 (75:25)	31:9 (77.5:22.5)	0.793 (NS)
Weight (in kg)		66.39 ± 8.2	66.64 ± 8.05	0.891 (NS)
ASA grade (%)	Grade I	37 (92.5)	32 (80)	0.195 (NS)
	Grade II	03 (7.5)	08 (20)	
Mean duration of surgery (min)		47.44 ± 7.99	49.09 ± 7.88	0.356 (NS)
Baseline HR (bpm)		81. 86 ± 11.29	84. 44 ± 11.24	0.308 (NS)
Baseline mean BP (mmHg)		94.02 ± 9.74	96. 21 ± 9.37	0.306 (NS)
Baseline RR (per min)		13.81 ± 1.33	14.14 ± 1.15	0.301 (NS)
Baseline SpO2 (%)		99.41 ± 0.72	99.21 ± 0.81	0.303 (NS)

NS- Not Significant (p>0.05)

The Levobupivacaine group required an average of 5.61 ± 1.54 min longer than the Levobupivacaine + fentanyl group (4.71 ± 1.71 min) for the sensory block to start (particularly in the T8 dermatome). This difference was determined to be statistically significant (P = 0.016). Based on the median, the highest degree of sensory blockage reached in Groups L and LF was T8 and T6, respectively. Group L required an average of 9.26 ± 1.65 minutes to achieve Bromage 2 motor block, while Group LF required 7.46 ± 1.75 minutes, with a statistically significant difference (P < 0.001). Group LF had a significantly longer sensory block (336.51 ± 31.31 min) in comparison to Group L (223.66 ± 32.18 min) (P < 0.001). The two groups' motor block lengths, however, were comparable (144.25 ± 13.83 min for Group L and 139.89 ± 31.84 min for Group LF) (P = 0.429). [Table 2]

Table 2: Block characteristics in both groups

Parameters (min)	Group L (Mean±SD) (N=40)	Group LF (Mean±SD) (N=40)	P value
Onset of sensory block to T8 dermatome	5.61 ± 1.54	4.71 ± 1.71	0.016 (S)
Total duration of sensory block	198.71 ± 17.82	268.89 ± 21.06	<0.001 (S)
Onset of motor block to achieve ≥2	9.26 ± 1.65	7.46 ± 1.75	<0.001 (S)
Total duration of motor block	144.25 ± 13.83	139.89 ± 31.84	0.429 (NS)
Duration of analgesia	223.66 ± 32.18	336.51 ± 31.31	<0.001 (S)
Total number of doses of rescue analgesia	2.01 ± 0.962	1.09 ± 0.28	<0.0001 (S)

The Visual Analogue Scale (VAS) score was used to assess pain following surgery. There was a statistically significant difference in the VAS score between 0 and 6 hours (P < 0.05) and between 10 and 12 hours (P < 0.05). [Table 3] About 4 hours later, patients in Group L asked for the first dosage of rescue analgesia; whereas, about 6 hours later, patients in Group LF need rescue analgesia. Group LF experienced a significantly longer duration of analgesic effect (336.51 ± 31.31 min) in comparison to Group L (223.66 ± 32.18 min) (P < 0.001). Group LF required significantly fewer rescue analgesia doses overall in a 24-hour period than Group L (P < 0.0001). [Table 2]

Table 3: VAS scores between groups

Time point (hour)	Median VAS Score (IQR)		P value
	Group L (N=40)	Group LF (N=40)	
0	0 (0-0)	0 (0-0)	0.022 (S)
2	2 (1-2)	0 (0-2)	<0.001 (S)
4	5 (3-6)	2 (2-3)	<0.001 (S)
6	4 (0-5)	5 (3-5)	0.006 (S)
8	0 (0-3)	0 (0-0)	0.404 (NS)
10	0 (0-3)	0 (0-0)	<0.001 (S)
12	0 (0-4)	0 (0-0)	0.028 (S)

The hemodynamic measurements (HR, SBP, DBP, MAP, RR, and SpO2) did not significantly change between the two groups when compared across groups (P > 0.05). Across the range of hemodynamic measurements, both groups' heart rates (HR) stayed steady and close to starting points during the study. Two of the patients (5%) in Group LF along with one patient (2.5%) within Group L experienced bradycardia during the procedure. Intravenous atropine was used to treat this disease satisfactorily.

There was no discernible difference among the two groups, according to the statistical analysis (P = 1.00). Hypotension was reported by one patient (2.5%) within Group L but not by any patients in Group LF. Throughout the study, the mean arterial pressure (MAP), diastolic blood pressure (DBP), and systolic blood pressure (SBP) were constant with their initial levels. For every patient in both groups, there was no instance of respiratory depression. During the postoperative phase in both groups of patients, no adverse symptoms were noted, including headache, backache, nausea, vomiting, pruritus, drowsiness, or sedation.

Discussion

The current study shows that for the surgeries performed below the umbilicus, 12.5 mg of intrathecal 0.5% levobupivacaine and 25 µg fentanyl results in a longer duration of pain alleviation than 12.5 mg of levobupivacaine alone. There was not only an extended period of analgesia but also a more rapid onset of movement and loss of sensations. A shorter duration of immobility and a reduction in the quantity of additional painkillers required were other advantages.

Patients often describe experiencing excruciating agony following surgery. It prolongs hospital stay, interferes with early walking, and intensifies the stress response following surgery. In order to

minimize problems and patient discomfort, the best anaesthetic approach should place a high priority on pain management during the recovery period. An important breakthrough in the management of postoperative pain occurred with the understanding of the neurobiology of pain and the pharmacology of currently available drugs. Over time, a variety of organizations have used and created intrathecal adjuvants with a range of mechanisms of action. Various opioids, including morphine, fentanyl, sufentanil, hydromorphone, buprenorphine, and tramadol, have been used in addition to local anaesthetics with varying degrees of success. [7] It has been discovered that levobupivacaine, an amino-amide drug used as a local anaesthetic, affects the nerve system differently. It specifically causes a shorter length of muscular paralysis and a lower likelihood of adverse effects connected to the heart, along with a speedier start and longer-lasting numbing impact on sensory neurons. [8] By selectively binding to both μ1 and μ2 receptors found in the spinal cord's dorsal horn, fentanyl enhances the suppression of peripheral nerve sensory impulses. This results in a nociceptive action. By acting as an adjuvant, fentanyl improves the effects of local anaesthetics, leading to greater anaesthesia and pain relief both during and after surgery. There are no obvious adverse consequences from this.

This study demonstrated that, in comparison to Group L, Group LF reached maximum sensory and motor block at a much faster rate and began sensory block at a faster rate. Compared to the plain levobupivacaine group, the fentanyl and levobupivacaine groups showed a significant lengthening in the duration of sensory block and postoperative analgesia, without prolonging the motor block. The greatest level of sensory response attained in Group LF was T6, while in Group L it was T8. But the greatest motor block of Bromage 2 was present in both groups. Compared to Group L, Group LF took longer to achieve a VAS score of more than three throughout the postoperative phase. Furthermore, during the course of a 24-hour period, Group LF consumed fewer doses of rescue analgesics.

A research by Bozdogan Ozyilkan et al. [9] assessed the effects of several levobupivacaine combinations. Levobupivacaine 0.5% (2.2 ± 0.2 ml), Levobupivacaine 0.5% (2.2 ± 0.2 ml) in addition with 2.5 mg sufentanyl, and Levobupivacaine 0.5% (2.2 ± 0.2 ml) in addition with 10 μg of fentanyl were the combinations that were tested. Researchers found that compared to the control group, the groups receiving fentanyl and sufentanyl had a quicker onset of sensory blocking. Comparable results were found in our experiment about the mean duration of the sensory block in the fentanyl group. Fentanyl may act more quickly because of the interaction between opioids and local anaesthetic medications. The motor block started in Group LF more quickly. The combined effect of opioids and local anaesthetics may explain why motor block occurred earlier in Group LF compared to Group L in our investigation. The results obtained from this investigation are in line with those of Attri et al. [10], who compared levobupivacaine 0.5% 10 mg and levobupivacaine 0.5% 10 mg + fentanyl 25 μg for intraoperative procedures. They found that the start of motor block occurred much sooner in the fentanyl group. Levobupivacaine 15 mg + normal saline 0.5 ml and levobupivacaine 15 mg + fentanyl 25 μg were compared by Agrawal and colleagues [11]. The fentanyl group had a longer duration of sensory block, according to the research. In a similar vein, Attri and colleagues' [10] research showed that the fentanyl group's sensory blackout lasted considerably longer than that of the control group. The duration of the sensory blackout was also significantly prolonged in this study. Levobupivacaine 5 mg in combination with 25 μg of fentanyl and levobupivacaine 7.5 mg on its own were compared by Maniyar and colleagues [12]. They found that both groups had motor block for the same amount of time. Our conclusion is in line with our investigation's findings as well as the findings of a number of other researches that have been published in the literature. [13, 14, 15, 16] The prolonged motor block does not seem to be beneficial in terms of patient satisfaction because it might be uncomfortable throughout the recovery phase.

Levobupivacaine 10 mg and a combination of levobupivacaine 7.5 mg and fentanyl 12.5 μg were compared by Bidikar and colleagues [6]. According to the study, the group that got fentanyl had analgesia for a significantly longer period of time than the group that just received levobupivacaine. A study comparing the effects of levobupivacaine 10 mg + normal saline 0.3 ml and levobupivacaine 10 mg + fentanyl 15 μg was conducted on women giving delivery by Rajsekaran and colleagues [17]. In contrast to the levobupivacaine group, the fentanyl group had much prolonged pain alleviation, according to the research. This investigation's findings are similar to those of another study. The longer duration of pain alleviation seen in this study might be ascribed to the higher dosage of fentanyl and local anaesthetic administered. Analogously, Attri et al. [10] found similar results for the duration of pain alleviation. The results of this investigation are consistent with those of studies by Attri et al. [10] and Gadkari et al. [18], which showed no appreciable changes in hemodynamic parameters.

According to the study, Group LF's VAS score was much lower than Group L's. Over the course of the

whole postoperative period, there were significant fluctuations in the Visual Analogue Scale (VAS) ratings. Compared to Group L, Group LF required a much less total dose of rescue analgesic following the procedure. Most patients (37) in Group L only needed one dose of the rescue analgesic. In this experiment, hypotension was observed in one patient (2.5%) in Group L and not in any of the patients in Group LF. Two patients (5%) in Group LF and one patient (2.5%) in Group L both had bradycardia.

Between the two groups, there was no statistically significant difference in the amount of sedation used during surgery or in the incidence of postoperative complications such low blood pressure, a sluggish heartbeat, itching, nausea, and vomiting. The results of Bozdogan Ozyilkan et al. [9] and Koppal et al. are corroborated by this investigation. [19]

The main focus of this investigation was the effect of intrathecal injection of fentanyl in addition to levobupivacaine. Evaluating the impact of this combination on subarachnoid block's efficacy was the goal. It is essential to recognize that this study has several limitations. Since there was no premedication given to the patient, their participation was necessary. Intrathecal fentanyl (25 µg) was used as an adjuvant in a single dose; the drug's dosage was not altered in response to the patient's weight or height.

The therapeutic relevance of the shorter duration of motor block brought on by the combination of fentanyl and levobupivacaine would be early ambulation. The pharmacological properties of levobupivacaine indicate a low incidence of cardiotoxicity. To evaluate and improve the safety and efficacy of different fentanyl doses when used in conjunction with isobaric levobupivacaine as a supportive drug, further research is needed.

Conclusion

According to our research, intrathecal fentanyl (25 µg) combined with isobaric 0.5% levobupivacaine can significantly extend the duration of analgesia, decrease the requirement for further analgesics, and hasten the onset of both motor and sensory block. Additionally, this combination shows little side effects in patients having infraumbilical surgeries and sustains consistent hemodynamics without prolonging the motor block.

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