**Name of journal: World Journal of Anesthesiology**

**ESPS Manuscript NO: 2680**

**Columns: BRIEF ARTICLE**

**Comparison between intrathecal hyperbaric bupivacaine and levobupivacaine for ambulatory knee arthroscopy**

Sagir O *et al*.Spinal anesthesia for knee arthroscopy

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**Received:** March 6, 2013 **Revised:** May 30, 2013

**Accepted:** June 18, 2013

**Published online:**

**Abstract**

**AIM**: To compare the effect of hyperbaric levobupivacaine and bupivacaine on the quality of the block, patient satisfaction, and discharge time in patients undergoing arthroscopic knee surgery under unilateral spinal anesthesia.

**METHODS:** One hundred and thirty-two patients, American Society of Anaesthesiologists (ASA) I or II, scheduled for elective ambulatory knee arthroscopy were randomly assigned to four double-blind groups. To achieve a unilateral spinal block, Group BF received 5 mg of hyperbaric bupivacaine plus 20 µg of fentanyl intrathecally, Group LF received 5 mg of hyperbaric levobupivacaine plus 20 µg of fentanyl intrathecally, Group B received 5 mg of hyperbaric bupivacaine intrathecally, and Group L received 5 mg of hyperbaric levobupivacaine intrathecally. The level and duration of the sensory block, the intensity and duration of the motor block, the time to first analgesic requirement, and the time elapsed until the patient’s discharge were recorded. Hemodynamic values and adverse effects were also recorded.

**RESULTS:** The duration of time needed to reach the T12 dermatome level was significantly longer in Group L [7 (3-20) min] than in Group B[6 (3-12) min] (*P =* 0.006). The maximum sensory level reached on the side undergoing the operation was significantly higher in Group BF than in Group B (*P <* 0.05). The intensity of the motor blockade was greater in Group BF than in Group LF and L. Complete recovery from motor blockade occurred earlier in Groups LF[75 (45-165) min] and L [63 (35-120) min] than in Group BF[115 (60-180) min] (*P <* 0.05). The length of time needed for the sensory block to regress to the level of S2 was shorter in Group L (154 ± 50) than in Group BF (192 ± 66) (*P <* 0.05). The quality of the block was significantly lower in Group L than in Groups BF, LF and B (*P =* 0.012, *P =* 0.003, and *P <* 0.001, respectively). The time elapsed until Visual Analog Scale (VAS) ≥ 4 was significantly shorter in Group L (110 ± 48) than in Groups BF (200 ± 60), LF (156 ± 61) and B (162 ± 52) (*P <* 0.05). The time elapsed until the patient’s discharge was shorter in Groups B (244 ± 54) and L (229 ± 55) than in Group BF (288 ± 64) (*P =* 0.021 and *P =* 0.001, respectively). There were no differences among the groups regarding hemodynamic parameters and adverse events, except for pruritus. The occurrence of pruritus was significantly more frequent in Groups BF and LF than in other groups.

**CONCLUSION:** In conclusion, 5 mg of hyperbaric bupivacaine and 5 mg of hyperbaric levobupivacaine plus 20 µg of fentanyl provided a better spinal anesthesia than 5 mg of hyperbaric levobupivacaine alone.

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**Key words:** Spinal anesthesia;Knee arthroscopy; Outpatient surgery; Bupivacaine; Levobupivacaine.

**Core tip:** Arthroscopic knee surgery is a common procedure performed in the ambulatory setting. The primary goals of the anesthetic techniques used in ambulatory surgery are to reduce anesthetic complications and to allow for early patient discharge. The aim of this study was to compare the effect of low dose hyperbaric bupivacaine and levobupivacaine, with and without fentanyl, on the quality of the block, patient satisfaction, and the time elapsed until discharge in patients undergoing arthroscopic knee surgery under unilateral spinal anesthesia.

Sagir O, Ozaslan S, Erduran M, Meric Y, Aslan I, Koroglu A. Comparison between intrathecal hyperbaric bupivacaine and levobupivacaine for ambulatory knee arthroscopy.

**Available from: URL:**

**DOI:**

**INTRODUCTION**

Arthroscopic knee surgery is one of the most frequently performed ambulatory orthopedic surgeries. The main goals of the anesthetic techniques used in ambulatory surgery are to reduce anesthetic complications, provide adequate postoperative analgesia and allow for early patient discharge[1].

Spinal anesthesia is often preferred for lower extremity surgery because of the procedure’s low level of difficulty, better postoperative analgesia and reduced incidences of nausea or vomiting[2]. Long-acting local anesthetics such as bupivacaine and levobupivacaine have been widely used in ambulatory surgery thanks to the development of the low-dose spinal anesthesia technique[3,4]. However, when small doses of local anesthetics are used, an adjuvant must be given to improve the quality of the block and decrease the risk of a failed block. Different adjuvants such as lipid soluble opioids can be added to the local anesthetics[5].

Levobupivacaine, the S-enantiomer of racemic bupivacaine, is approximately equipotent with bupivacaine when used in a similar concentration and dose. At the same time, levobupivacaine is a weaker cardiac and central depressant[6,7].Studies comparing the different doses and forms of levobupivacaine and bupivacaine for ambulatory arthroscopic surgery have been published[8,9]. However, there is no study comparing these two drugs in the context of arthroscopic knee surgery.

We hypothesized that levobupivacaine administered *via* spinal anesthesia for arthroscopic knee surgery would provide less motor blockade and earlier patient discharge compared to bupivacaine.

The primary outcome of this study was to compare the effect of low dose hyperbaric levobupivacaine and bupivacaine, with and without fentanyl, on the time elapsed until discharge in patients undergoing arthroscopic knee surgery under unilateral spinal anesthesia. The effect of these anesthetics on the quality of the block and patient satisfaction were also compared as a secondary outcome.

**MATERIALS AND METHODS**

With the approval of the Institutional Ethical Committee, written, informed consent was obtained from all patients. One hundred and thirty-two patients with ASA physical status I or II, aged 18-65 years, measuring 150-185 cm in height, and scheduled for elective ambulatory knee arthroscopy were included in this prospective, double-blind, randomized controlled study. The number of patients enrolled in this study was determined by considering the relevant literature[6,10]. Patients were excluded when they met one or more of the following criteria: history of a severe renal, hepatic, or cardiac disease; a neurologic or psychiatric condition; a coagulation defect; sepsis or a local infection at the site of the lumbar puncture; and/or any hypersensitivity to local anesthetics or opioids.

Patients were randomized to one of four groups to receive spinal hyperbaric bupivacaine or hyperbaric levobupivacaine, with or without fentanyl (Figure 1). Randomization was performed using a random number table. The local anesthetic solution was prepared aseptically by an anesthetist who was blinded to the study shortly before the spinal injection. Group BF received 5 mg (1 mL) of hyperbaric bupivacaine (Marcaine Heavy 0.5% AstraZeneca) with 20 µg of fentanyl (0.4 mL), Group LF received 5 mg (1 mL) of hyperbaric levobupivacaine with 20 µg of fentanyl (0.4 mL), Group B received 5 mg (1 mL) of hyperbaric bupivacaine with 0.4 mL of sterile water, and Group L received 5 mg (1 mL) of hyperbaric levobupivacaine with 0.4 mL of sterile water. The hyperbaric levobupivacaine solution was prepared by an anesthesiologist who was not involved in further patient care. This solution was composed of 2 mL of plain 0.75% levobupivacaine (Chirocaine: levobupivacaine hydrochloride, Abbott, United Kingdom), 0.8 mL of 30% dextrose, and 0.2 mL of normal saline solution, achieving a final concentration of 0.5% levobupivacaine with glucose. The total syringe volume was 1.4 mL in all four groups.

Patients received no premedication. Pulse oximetry (SPO2) values, non-invasive blood pressure (NIBP) measurements, and electrocardiogram (ECG) tracings were monitored in all patients. Heart rate, SPO2 and NIBP were recorded before spinal anesthesia, every 3 min during the first 15 min of the spinal anesthesia, and then every 5 min during the remainder of the surgery. After inserting a 20 gauge *iv* cannula in the dorsum of the hand, 0.5 mL kg-1 of0.9% normal saline was preloaded intravenously in all patients. The patients were placed in the lateral decubitus position, and their operated sides were positioned inferiorly. Spinal anesthesia was performed at the L4-5 intervertebral area using the mid-line approach with a 25 gauge Whitacre spinal needle. Correct needle positioning was confirmed with the free flow of cerebrospinal fluid, and the anesthetic solutions were injected slowly without barbotage. The lateral decubitus position was maintained for 10 min from the start of the injection to provide selective spinal anesthesia. Afterwards, patients were turned to supine position, and surgery was started as soon as the analgesic level reached T12. In the case of insufficient anesthesia during the procedure, fentanyl (1 µg kg-1), midazolam (0.05 mg kg-1) or both in *iv* formulations were used. If the pain was not controlled with an *iv* bolus of fentanyl and/or midazolam, general anesthesia was administered. Three liters of oxygen per minute was given *via* nasal cannula until the end of the surgical procedure. The anesthesiologist who performed the spinal anesthesia and evaluated the quality of the block was blinded to the study solution received by each group.

The quality of anesthesia was assessed by testing for sensory and motor blockade. Sensory blockade was evaluated by pinprick on each side of the mid-clavicular line, and motor blockade was evaluated *via* the 4-point modified Bromage scale (0 = no motor block, 1 = inability to raise extended legs, 2 = inability to flex the knees and 3 = inability to flex the ankle joints). These tests were performed bilaterally every 3 min up to 15minand then at 5 min intervals until the end of the operation. Postoperatively, these tests were done every 15 min until the sensory block regressed to the level of S2. The following lengths of time were recorded: achievement of a sensory block at the level of T12, maximum spread of the sensory block, highest dermatome level reached, regression to the level of S2, motor blockade levels, regression of the motor blockade, first analgesic requirement and discharge time. Postoperatively, patients who had a VAS score ≥ 4 were given 50 mg of *iv* dexketoprofen trometamol, and the time was recorded as the first analgesic requirement time. Home discharge criteria included stable vital signs, the absence of nausea or vomiting, minimal or no pain, the ability to tolerate liquids by mouth, and the ability to walk and void spontaneously. Complications such as hypotension, bradycardia, nausea, vomiting, shivering and pruritus were also noted.

Hypotension was defined as a decrease in systolic blood pressure > 30% from baseline and was initially treated with a rapid infusion of 250 mL of normal saline. In patients who did not respond to this treatment, 5 mg of *iv* ephedrine was given. Bradycardia was defined as a heart rate < 45 beat min-1 and was treated with 0.5 mg of *iv* atropine. Nausea and vomiting were treated with 10 mg of *iv* metoclopramide. Pruritus was assessed by a 4-point scale, where 0 = no pruritus, 1 = mild, 2 = moderate, 3 = severe pruritus. Moderate and severe pruritus was treated with *iv* naloxone. Shivering was treated by warming the skin surface. All patients underwent operations by the same experienced surgeon. The satisfaction of the patient and the surgeon regarding the anesthetic technique used was assessed with a 2-point scale, where 1= satisfied (*i.e.,* “I will accept to undergo the same procedure if it is required in the future”) and 2= unsatisfied (*i.e.,* “I would prefer the use of a different anesthetic technique in future operations”).

The quality of the spinal block was evaluated according to the need for additional *iv* analgesics and sedatives: adequate spinal block = neither sedatives nor analgesics were required to complete the surgery; inadequate spinal block = additional analgesia or sedation was required to complete the surgery (0.001 mg kg-1 bolus of *iv* fentanyl or 0.05 mg kg-1 bolus of *iv* midazolam); failed spinal block = general anesthesia was required to complete the surgery.

The day after surgery, the patients were contacted *via* telephone by a blinded research assistant and asked whether they had experienced headache, backache, or dysesthesia in the lower limbs or buttocks.

***Statistical analysis***

Statistical analysis was performed using SPSS (SPSS 15.0; SPSS, Inc., Chicago, IL, United States). The Kolmogorov Smirnov test was used to assess whether the data were normally distributed.Numerical results were expressed either as a mean ±SD or as a median and range, when appropriate. Nominal data were presented as frequencies. Categorical data in each study group were compared using a 2 test or Fisher’s exact test. The numerical data were compared between study groups with the Kruskall-Wallis test, followed by the Mann-Whitney *U* test, the Bonferroni correction test, and a One-way ANOVA with the Tukey HSD test. In the case of hemodynamic changes within the study groups, repeated measures analysis of variance was performed. In general, a p value of < 0.05 was considered statistically significant. However, the significance level of *P <* 0.008 was determined using a Bonferroni correction for multiple comparison test.

Post-analysis power calculation reached 93%, α = 0.05 (1-tailed), with the 33 patients included in group BF and LF (mean times elapsed until discharge were “288 ± 64” and “260 ± 61”, respectively), 32 patients included in group B (mean time elapsed until discharge was “244 ± 54”) and 28 patients included in group L (mean time elapsed until discharge was “229 ± 55”).

**RESULTS**

There was no statistically significant difference between the four study groups regarding demographic parameters, age, weight, height, sex, and ASA classification (Table 1). Spinal anesthesia was initially successfully performed in all patients. Six patients required conversion to general anesthesia due to an inadequate block level (one in group B and five in group L, *P <* 0.05) and were therefore excluded (Figure 1).

A significant difference was found among the study groups when comparing the lengths of time needed to reach the T12 dermatome level and to reach the maximum sensory level (*P =* 0.020, *P =* 0.041 respectively). Reaching the T12 dermatome level took significantly longer in Group L than in Group B (*P =* 0.006). The length of time needed to reach the maximum sensory blockade was significantly longer in Group L than in Group LF (*P =* 0.008). The maximum sensory level of the side undergoing the operation was higher in the Group BF compared to Group B (*P <* 0.05). The sensory block regressed to the level of S2 in a shorter amount of time in Group L than in Group BF (*P =* 0.049) (Table 2).

Although there was no statistical difference between the groups, the motor blockade was not observed in 3 patients from groups LF and L and 1 patient from group B. The intensity of the motor blockade was significantly higher in Group BF than in Groups LF and L and higher in Group B than in Group L (*P <* 0.05) (Figure 2). Complete recovery from the motor blockade occurred earlier in Groups LF and L than in Group BF and earlier in Group L than in Group B (*P <* 0.05) (Table 2).

A strictly unilateral sensory block (absence of detectable sensory block on the nonoperative side throughout the study period) was observed in 10 patients within Group BF (30%), 14 patients within Group LF (42%), 17 patients within Group B (53%) and 13 patients within Group L (46%) (*P =* 0.30). A strictly unilateral motor block (Bromage score = 0 on the nonoperative side throughout the study period) was observed in 20 patients within Group BF (60%), 24 patients within Group LF (72%), 23 patients within Group B (72%) and 23 patients within Group L (82%) (*P =* 0.32).

The time elapsed before micturition was significantly shorter in Group L than in Group BF (*P =* 0.006) (Table 2). Because of the inability to spontaneously void, four patients, one from each group, required urinary catheterization.

The time elapsed until VAS ≥ 4 was significantly longer in Group BF than in the other three groups and was significantly shorter in Group L than in Groups BF, LF, and B. There was no statistically significant difference between Groups LF and B (Table 2).

The time elapsed until the patient’s discharge was significantly shorter in Groups B and L than in Group BF (*P =* 0.021, *P =* 0.001, respectively) (Table 2).

The quality of the block was significantly lower in Group L than in Groups BF, LF, and B. (*P =* 0.012, *P =* 0.003, and *P <* 0.001, respectively). The requirement of additional sedation was greater in Group L than in the other groups. Patient satisfaction scores were significantly lower in Group L than on Groups BF and LF (*P =* 0.039). Surgeon satisfaction scores weresignificantly lower in Group L than in Groups BF, LF, and B (*P <* 0.001, *P <* 0.001, and *P =* 0.024, respectively) (Table 4).

Cardiovascular changes were unremarkable, and no statistically significant differences were found between the study groups regarding heart rate, mean arterial pressure, or hypotensive events. The occurrence of pruritus was significantly more frequent in patients receiving spinal fentanyl, and all cases resolved without treatment. Other side effects were not statistically different between the study groups (Table 2). None of the patients developed bradycardia or emesis in the postoperative period.

**DISCUSSION**

Our results suggest that 5 mg of hyperbaric bupivacaine and 5 mg of hyperbaric levobupivacaine plus 20 µg fentanyl provided spinal anesthesia of equivalent quality for patients undergoing outpatient arthroscopic knee surgery with unilateral positioning. However, the quality of the block was significantly lower in the group receiving 5 mg of levobupivacaine, and the time elapsed until discharge was significantly longer in the group receiving 5 mg of bupivacaine plus 20 µg of fentanyl.

The positioning of the patient during spinal anesthesia affects the distribution of the drug in the subarachnoid space and therefore affects recovery and discharge[11]. Patients who had received unilateral spinal anesthesia were ready to be discharged on average 42 min earlier than patients who received bilateral anesthesia[4]. Hyperbaric local anesthetic solutions have been often preferred over hypobaric and isobaric solutions in studies regarding unilateral spinal anesthesia. Hyperbaric bupivacaine is commercially available, but hyperbaric levobupivacaine requires the addition of dextrose to a commercially available plain solution[12]. In the present study, hyperbaric levobupivacaine was obtained by adding glucose to isobaric levobupivacaine to achieve a unilateral spinal block. A recent review article suggested that 4-5 mg of hyperbaric bupivacaine can provide effective spinal anesthesia for knee arthroscopy[4]. Therefore, we compared 5 mg of hyperbaric bupivacaine with 5 mg of hyperbaric levobupivacaine in our study.

There are several studies comparing the properties of sensory and motor blocks with hyperbaric bupivacaine and levobupivacaine. Luck *et al*[6] reported that spinal anesthesia with 15 mg of hyperbaric bupivacaine and 15 mg of levobupivacaine achieve similar sensory and motor block characteristics in patients undergoing elective surgery. A study conducted by Erdil *et al*[13] compared the effectiveness of 7.5 mg of plain levobupivacaine with bupivacaine plus 15 µg of fentanyl in elderly patients. It was emphasized that the peak sensory block level was found to be significantly higher for bupivacaine than for levobupivacaine and that the length of time needed to reach the T10 sensory level was significantly longer for levobupivacaine than for bupivacaine. The authors suggested that levobupivacaine may not be quite as potent as bupivacaine[13]. In our study, the peak sensory block level was found to be higher for bupivacaine plus fentanyl. Moreover, the length of time needed to reach the T12 sensory block level was longer when using 5 mg of hyperbaric levobupivacaine than when using bupivacaine. Cappelleri *et al*[3] reported that injecting 5 mg of 0.5% hyperbaric levobupivacaine unilaterally was sufficient for short-lasting spinal blocks in patients undergoing outpatient knee arthroscopy[3]. In their study, an inadequate spinal block was observed in one patient receiving 5 mg of hyperbaric levobupivacaine, and none of the spinal blocks failed. However, in our study, sedation was required in eleven patients receiving 5 mg of hyperbaric levobupivacaine, and five patient blocks failed. The length of time required for complete resolution of the sensory block and the time elapsed until the patient was ready to be discharged were slightly longer in the those receiving 5 mg of levobupivacaine in our study compared to the study described above. In our study, the use of 5 mg of hyperbaric levobupivacaine led to fewer motor blocks and a longer time needed to attain a sensory block at the level of T12. These findings could have led to the increased number of patients requiring sedation.

Camorcia *et al*[14] found that spinal levobupivacaine was 29% less potent than bupivacaine in producing motor blocks. In our study, motor block quality and motor block regression time were found to be lower in the levobupivacaine groups than in the bupivacaine groups. Dobrydnjov *et al*[15] studied a restricted spinal block using 6 mg of hyperbaric bupivacaine with or without clonidine for inguinal hernia repairs. In their study, the authors reported a strictly unilateral spinal block in 47% of the patients. Cappelleri *et al*[3] reported a strictly unilateral motor block in 83% of patients who had received 5 mg of hyperbaric levobupivacaine. In our study, there were similar rates of strictly unilateral sensory and motor blocks to these studies.

The use of low dose local anesthetics while limiting the dose of the spinal block may result in an inadequate sensory block. For this reason, the addition of opioids to the local anesthetics can enhance the analgesia and prolong the sensory block without affecting the motor block[16]. Ben-David *et al*[17] demonstrated that the use of a diluted, low-dose bupivacaine is insufficient to provide spinal anesthesia, but the addition of 10 µg of fentanyl provides reliable anesthesia. We observed inadequate sensory and motor blocks in the group receiving 5 mg of hyperbaric levobupivacaine. However, our findings suggest that the quality of sensory and motor blocks is better when using 5 mg of hyperbaric levobupivacaine plus 20 µg of fentanyl than when using 5 mg hyperbaric levobupivacaine alone.

Casati *et al*[18] reported that the unilateral technique with 8 mg of hyperbaric bupivacaine and 8 mg of hyperbaric levobupivacaine provided adequate spinal blocks for hernia repair procedures. Motor recovery was significantly faster after levobupivacaine, whereas the time elapsed until patient discharge was similar with both agents. Cappelleri *et al*[3] reported that the length of time required for the spinal block resolution and the time elapsed before discharge were shorter with 5 mg of levobupivacaine than with 7.5 mg of levobupivacaine. Although the time elapsed until the patient was discharged was slightly longer in the levobupivacaine group in our study compared to the study by Cappelleri *et al*[3], our results are not substantially clinically different.

Pruritus is a common complication arising from the use of intrathecal fentanyl[17].Itching arises in 30%-33% of patients receiving 20 µg of fentanyl, and they recover without any treatment. The incidence of side effects such as hypotension and bradycardia is lower with unilateral spinal anesthesia than with conventional bilateral spinal anesthesia[4]. In our study, hemodynamic parameters were within safe ranges during the intraoperative and postoperative periods, and these side effects were observed in less than 4%-6% of the patients. We believe that these side effects are due to the low-dose intrathecal drug and the unilateral spinal block.

A common side effect of spinal anesthesia is urinary retention, which could be due to the fluid therapy used in the treatment of spinal anesthesia-induced hypotension or bilateral blockade of the parasympathetic plexus, which innervates the detrusor muscle. However, urinary retention occurs rarely in unilateral spinal blocks, since hemodynamic stability is better maintained and the function of the detrusor muscle has not been totally blocked[19]. Casati *et al*[18] reported no urinary retention after unilateral spinal anesthesia for inguinal herniorrhaphy. In our study, one patient in each study group complained of urinary retention, and they resumed spontaneous micturition after one catheterization. Moreover, it has been reported that dose-dependent spinal opioids influence bladder function and may cause urinary retention[19,20]. Liu *et al*[2] reported that a 20 µg dose of fentanyl did not delay the ability to void. We also found no influence of the use of 20 µg of fentanyl in delaying the return of bladder function.

The main drawback associated with levobupivacaine is that the hyperbaric formulation is not available on the market. Diluting the hyperbaric formulation with dextrose for spinal anesthesia has a potential risk for infection. Furthermore, densities of solutions transformed into hyperbaric formulations can be different from the intended hyperbaric formulation. The density of the anesthetic solutions and the position of the patient are the most important factors affecting the intrathecal spread of the drug[4,12]. A limitation in our study is the fact that the density of levobupivacaine was not measured. However, in a laboratory investigation, McLeod showed that the density of levobupivacaine increases linearly with the addition of 8% dextrose[21].

In conclusion, both 5 mg of hyperbaric bupivacaine and 5 mg of hyperbaric levobupivacaine plus 20 µg of fentanyl provided adequate and reliable anesthesia for arthroscopic knee surgery in the ambulatory setting. Both solutions provided a high level of patient and surgeon satisfaction without affecting the time elapsed until patient discharge, compared to 5 mg of hyperbaric bupivacaine plus 20 µg of fentanyl. In our opinion, 5 mg of hyperbaric levobupivacaine does not provide sufficient anesthesia for unilateral arthroscopic knee surgery.

**COMMENTS**

***Background***

Arthroscopic knee surgery is one of the most frequently performed ambulatory orthopedic surgeries. Spinal anesthesia is often preferred for lower extremity surgery in the ambulatory setting. For decades, lidocaine was the local anesthetic of choice for spinal anesthesia in ambulatory surgeries. However, its use is limited due to the risk of a transient neurological syndrome and neurotoxicity. Therefore, lower doses of long-acting local anesthetics have been used in outpatient surgeries. The comparison of low-dose hyperbaric bupivacaine to levobupivacaine with respect to the quality of the block and the time elapsed until discharge in outpatient knee arthroscopy procedures has not been investigated in the literature.

***Innovations and breakthroughs***

There are several studies comparing the properties of sensory and motor blockade in hyperbaric bupivacaine and levobupivacaine. This is the first study to compare hyperbaric bupivacaine with hyperbaric levobupivacaine in arthroscopic knee surgeries in the ambulatory setting. In this study, the dose and concentration of levobupivacaine used resulted in an inadequate block and higher sedation requirement for a greater number of patients compared to studies using hyperbaric levobupivacaine.

***Applications***

The study results suggested that, in knee surgeries in the ambulatory setting, 5 mg of hyperbaric bupivacaine provides a better spinal anesthesia than 5 mg of hyperbaric levobupivacaine. Equivalent spinal anesthesia, postoperative analgesia and recovery were attained with 5 mg of hyperbaric levobupivacaine plus 20 µg of fentanyl without creating any adverse hemodynamic effects.

***Terminology***

Ambulatory surgery: Ambulatory surgery, also known as outpatient surgery, is surgery that does not require an overnight hospital stay. Unilateral spinal anesthesia: Unilateral spinal anesthesia consists of positioning the patient on the side that will undergo the operation for 10-15 min after the administration of the spinal anesthetic. Hyperbaric local anesthetic: Hyperbaric solutions are typically prepared by mixing the local anesthetic with 5 to 8% dextrose.

***Peer review***

The methodology of the investigation is sound and can support the outcome.

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**P-Reviewers** AjmalM, Amr YM  **S-Editor** Wen LL  **L-Editor**  **E-Editor**

Assessed for eligibility (n=132)

Enrollment

Randomized (n=132)

Excluded (n=0)

Allocated to Group BF

(n=33)

Allocated to Group LF

(n=33)

Allocated to Group B

(n=33)

Allocated to Group L

(n=33)

Failure (n=0)

Failure (n=0)

Failure (n=1)

Failure (n=5)

Analyzed (n=33)

Analyzed (n=33)

Analyzed (n=32)

Analyzed (n=28)

Allocation

Follow-up

Analysis

**Figure 1 Flowchart.** BF: Hyperbaric bupivacaine plus fentanyl; LF: Hyperbaric levobupivacaine plus fentanyl; B: Hyperbaric bupivacaine; L: Hyperbaric levobupivacaine.

11

3

1

2

1

6

3

4

11

10

23

18

5

28

**Figure 2** **Maximal intensity of motor blockade expressed as a percentage of the population with definite motor block grade.** 0 = No motor block; 1= Inability to raise extended legs; 2 = Inability to flex knees; and 3: Inability to flex ankle joints. BF: Hyperbaric bupivacaine plus fentanyl; LF: Hyperbaric levobupivacaine plus fentanyl; B: Hyperbaric bupivacaine; L: Hyperbaric levobupivacaine.

**Table 1** **Patient characteristics, duration of surgery and failed spinal blocks *n =* 33**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Group BF** | **Group LF** | **Group B** | **Group L**  | ***P* value** |
| Gender (M/F) | 16/17 | 13/20 | 12/21 | 14/19 | 0.779 |
| Age (yr) | 45 (11) | 46 (12) | 44(12) | 47 (11) | 0.863 |
| Height (cm) | 165(8) | 168 (9) | 165 (8) | 165 (9) | 0.664 |
| Weight (kg) | 79(12) | 77(11) | 76(12) | 80(11) | 0.253 |
| ASA (I/II) | 25/8 | 22/11 | 25/8 | 26/7 | 0.699 |
| Duration of surgery (min) | 50(40-60) | 60(35-60) | 50(30-60) | 55(40-60) | 0.621 |
| Failed spinal block | 0 | 0 | 1 | 51 | 0.0081 |

BF: Hyperbaric bupivacaine plus fentanyl; LF: Hyperbaric levobupivacaine plus fentanyl; B: Hyperbaric bupivacaine; L: Hyperbaric levobupivacaine; M: Male; F: Female. Data are presented as the median (min-max), SD, or frequencies. 1*P <* 0.05 compared with Group BF, Group LF and Group B.

**Table 2 Quality of sensory and motor blocks and post-anesthesia care unit variables per group**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Group BF****(*n =* 33)** | **Group LF****(*n =* 33)** | **Group B****(*n =* 32)** | **Group L****(*n =* 28)** |
| **Sensory block** |  |  |  |  |
| Onset to T12 (min) | 6(3-15) | 6(3-15) | 6(3-12) | 7(3-20)3 |
| Highest level of sensory block (dermatome) | T8(T12-T4) | T10(T12-T4) | T10(T12-T4)1 | T10(T12-T4) |
| Time to maximum sensory block (min) | 15(6-35) | 12(6-50) | 13(6-35) | 20(6-40) 2 |
| Sensory regression | 192 ± 66 | 173 ± 53 | 179 ± 47 | 154 ± 50 1 |
| **Motor block** |  |  |  |  |
| Time to maximum motor block (min) | 9(3-20) | 12(3-25) | 9(3-25) | 12 (3-35) |
| Motor block regression (min) | 115(60-180) | 75(45-165)1 | 95(40-150) | 63(35-120)1, 3 |
| Time to micturition (min) | 196 ± 57 | 174 ± 54 | 164 ± 45 | 151 ± 521 |
| Time to VAS ≥ 4 | 200 ± 60 | 156 ± 611 | 162 ± 521 | 110 ± 481, 2, 3 |
| Time to discharge | 288 ± 64  | 260 ± 61 | 244 ± 541 | 229 ± 551 |

BF: Hyperbaric bupivacaine plus fentanyl; LF: Hyperbaric levobupivacaine plus fentanyl; B: Hyperbaric bupivacaine; L: Hyperbaric levobupivacaine. Data are presented as the median (min-max) or mean ± SD.1*P* < 0.0*5* compared with Group BF; 2*P* < 0.05 compared with Group LF; 3*P* < 0.05compared with Group B.

**Table 3 Frequency of adverse events**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Adverse events *n* (%)** | **Group BF****(*n =* 33)** | **Group LF****(*n =* 33)** | **Group B****(*n =* 32)** | **Group L** **(*n =* 28)** | ***P* value** |
| Hypotension | 2 (6) | 2 (6) | 0 | 0 | 0.289 |
| Bradycardia | 0 | 0 | 0 | 1 (4) | 0.317 |
| Emesis/vomiting | 0 | 1 (3) | 0 | 0 | 0.417 |
| Shivering | 6 (18) | 5 (15) | 7 (21) | 6 (21) | 0.894 |
| Pruritus | 11 (33)1 | 10 (30)1 | 0 | 1 (4) | <0.001 |
| Headache | 4 (12) | 7 (31) | 6 (19) | 4 (14) | 0.754 |

BF: Hyperbaric bupivacaine plus fentanyl; LF: Hyperbaric levobupivacaine plus fentanyl; B: Hyperbaric bupivacaine; L: Hyperbaric levobupivacaine. 1*P <* 0.05 compared with Group L and Group B.

**Table 4 Intraoperative and postoperative outcomes**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Group BF****(*n =* 33)** | **Group LF****(*n =* 33)** | **Group B****(*n =* 32)** | **Group L** **(*n =* 28)** |
| Sedation | 0 | 2 | 3 | 112 |
| Patient satisfaction (satisfied/unsatisfied) | 33/0 | 33/0 | 28/4 | 24/41 |
| Surgeon satisfaction (satisfied/unsatisfied)  | 33/0 | 33/0 | 29/3 | 18/102 |

BF: Hyperbaric bupivacaine plus fentanyl; LF: Hyperbaric levobupivacaine plus fentanyl; B: Hyperbaric bupivacaine; L: Hyperbaric levobupivacaine. Data shown are the mean ± SD, median (range) or count. 1*P < 0.05* compared with Group BF and Group LF*;* 2*P <* 0.05 compared with Group BF, Group LF, and Group B.