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Comparison of Onset Times and Hemodynamic Changes of Bupivacaine and Levobupivacaine Used in Spinal Anesthesia

Spinal Anestezide Kullanılan Bupivakain ve Levobupivakainin Başlangıç Süreleri ve Hemodinamik Değişikliklerinin Karşılaştırılması

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Abstract

Objective: The present study compared the motor and sensory onset times and hemodynamic effects of bupivacaine and levobupivacaine used in spinal anesthesia. The aim was to assess whether levobupivacaine is a safer alternative.

Methods: The study included 50 patients who were classified as American Society of Anesthesiologists I-II and scheduled for inguinal hernia surgery. The patients were divided into two groups as bupivacaine (0.5%) and levobupivacaine (0.5%). In both groups, motor and sensory block onset times and hemodynamic parameters were evaluated following the administration of spinal anesthesia.

Results: In the levobupivacaine group, the motor block onset time was found as 8.99 minutes and the sensory block onset time as 8.47 minutes. In the bupivacaine group, these times were recorded as 3.54 minutes and 3.26 minutes, respectively ($p<0.001$). No significant difference was found between the groups in terms of hemodynamic parameters. Despite having longer motor and sensory block onset times compared to bupivacaine, levobupivacaine achieved adequate anesthesia, with no difference between the two groups in terms of hemodynamic changes.

Conclusion: Levobupivacaine has been shown to be an effective and safe alternative in spinal anesthesia. However, there is a need for larger-scale studies to generalize these findings.

Keywords: Bupivacaine, levobupivacaine, spinal anesthesia

Öz

Amaç: Bu çalışmada spinal anestezide kullanılan levobupivakain ve bupivakainin motor ve duysal blok başlangıç süreleri ile hemodinamik etkileri karşılaştırılmıştır. Amaç, levobupivakainin daha güvenli bir alternatif olup olmadığını değerlendirmektir.

Yöntem: Çalışmaya inguinal herni operasyonu planlanan, Amerikan Anestezistler Derneği I-II sınıflandırmasındaki 50 hasta dahil edilmiştir. Hastalar bupivakain (%0,5) ve levobupivakain (%0,5) olmak üzere iki gruba ayrılmıştır. Her iki grupta da spinal anestezi uygulandıktan sonra motor ve duysal blok başlangıç süreleri ile hemodinamik parametreler değerlendirilmiştir.

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Öz

Bulgular: Levobupivakain grubunda motor blok başlangıç süresi 8,99 dakika, duysal blok başlangıç süresi ise 8,47 dakika olarak tespit edilmiştir. Bupivakain grubunda bu süreler sırasıyla 3,54 ve 3,26 dakikadır (p<0,001). Gruplar arasında hemodinamik parametrelerde ise anlamlı bir fark bulunmamıştır. Levobupivakainin motor ve duysal blok başlangıç sürelerinin bupivakainin sürelerine göre daha uzun olmasına rağmen anestezi yeterliliği sağlamış, hemodinamik değişiklikler açısından her iki grup arasında fark gözlenmemiştir.

Sonuç: Levobupivakain, spinal anestezide etkili ve güvenli bir alternatif olarak değerlendirilmektedir. Ancak, bu bulguların genellenebilirliği için daha geniş ölçekli çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Bupivakain, levobupivakain, spinal anestezi

Introduction

Spinal anesthesia is a reliable regional anesthesia technique commonly preferred for lower abdominal and lower extremity surgeries, providing effective neural blockade and minimizing side effects when local anesthetics are administered in appropriate doses[1]. Bupivacaine is widely utilized in spinal anesthesia due to its prolonged duration of action and effectiveness as a local anesthetic. Levobupivacaine, the S(-) enantiomer of bupivacaine, exhibits similar pharmacokinetic and pharmacodynamic characteristics, but is suggested to offer a more favorable safety profile regarding adverse effects[2-4]. Despite all these advantages, it is not commonly used in routine spinal anesthesia practice[5]. This study aimed to evaluate the motor and sensory block onset times and hemodynamic effects of bupivacaine and levobupivacaine following intrathecal administration in order to determine the reliability of levobupivacaine as a potential alternative. In addition, we aimed to provide guidance for clinical practice by contributing to the limited number of comparative studies in the literature.

Materials and Methods

This study received approval from the Ethics Committee of University of Health Sciences Türkiye, İstanbul Haseki Training and Research Hospital and was carried out in compliance with the principles outlined in the Declaration of Helsinki (decision no: 12/07, date: 12.11.2007). All the patients were informed about the procedures to be performed and their written consent was obtained according to ethical standards. A total of 50 patients aged between 18 and 65 years, classified as American Society of Anesthesiologists (ASA) physical status I-II and scheduled for elective inguinal hernia repair without any contraindications to spinal anesthesia, were enrolled in the study. Patients who required intraoperative conversion to general anesthesia were excluded.

All the patients underwent preoperative anesthesia assessment one day before the surgery. Each patient was given 10 mL/kg of crystalloid solution over 30 minutes, one hour before being taken to the operating room. Once at the operating table, the patients were administered 0.03 mg/kg of midazolam intravenously for premedication.

Standard monitoring in general anesthesia (electrocardiogram, non-invasive blood pressure and pulse oximetry) was performed while demographic data [gender, age, height, weight, body mass index (BMI)] were recorded at the operating table. Prior to spinal anesthesia, patients' systolic, diastolic, and mean arterial pressures, as well as pulse rates, were measured and recorded using Petaş® KMA 800 monitors, which the company calibrates monthly. All preparations for a potential conversion to general anesthesia were prepared before initiating spinal anesthesia.

Spinal anesthesia was performed with the patient in the sitting position. While in this position on the operating table, the lumbar region was prepared using an antiseptic solution and then covered with a sterile drape. Later, a 22-gauge Quincke-Babcock type spinal needle (Spinocan®, Braun, Melsungen, Germany) was inserted at the L3-L4 interspace using the median approach, and cerebrospinal fluid flow was monitored. Following this, 3 mL (15 mg) of isobaric 0.5% bupivacaine (Marcaine®) was administered to the 25 patients in Group A and 3 mL (15 mg) of 0.5% levobupivacaine (Chirocaine®) was injected into the other 25 patients in Group B. Spinal anesthesia administration was performed on all patients by a single senior assistant.

Once the procedure was completed, patients were placed on the operating table in the supine position with a 30-degree tilt. Patients' sensory block levels were checked every 30 seconds using the pinprick test. The time from the intrathecal injection to the moment when pain sensation was completely lost was recorded as the sensory block onset time.

Similarly, patients' motor blocks were assessed every 30 seconds using the modified Bromage score. The time when they reached Bromage level 2-3, was defined as the motor block onset time (Table 1).

Postoperative systolic, diastolic, and mean arterial pressures, along with heart rates, were monitored and recorded at 1, 3, 5, 10, 15, 20, 30, 40, 50, 60, 75, 90, 105, and 120 minutes. In cases where hypotension developed during the operation (defined as a reduction in systolic arterial pressure exceeding 30% relative to baseline values), patients were immediately administered 200 mL of isotonic solution in 10 minutes. If the intervention failed to correct the condition, 5 mg of ephedrine was administered intravenously. Bradycardia (a condition where the heart rate is below 45 bpm) was treated with 0.5 mg of intravenous atropine administration.

Statistical Analysis

The analyses were conducted using the SPSS IBM Statistics 25 software. Statistical analyses were performed using the Student's t-test, paired t-test, Fisher's exact test, and chi-square test, where appropriate. A p-value less than 0.05 was considered indicative of statistical significance.

Results

Demographic data of the patients show that 38 of them were male (20 in the bupivacaine group, 18 in the levobupivacaine group), while 12 were female (5 in the bupivacaine group and 7 in the levobupivacaine group). The mean age of patients was 47.68±15.92 in the bupivacaine group and 38.76±15.65 in the levobupivacaine group. According to the ASA classification, in the bupivacaine group, 21 patients were classified as ASA I, 4 patients as ASA II; while 22 patients were classified as ASA I and 3 patients as ASA II in the levobupivacaine group. The distribution of the two groups was comparable with respect to age, sex, height, weight, BMI, and ASA classification (Table 2). Following the intrathecal administration, the mean motor block onset time in the levobupivacaine group was 8.99 minutes, and the mean sensory block onset time was 8.47 minutes. In the bupivacaine group, on the other hand, the mean motor block onset time was found to be 3.54 minutes, and the mean sensory block onset time was found to be 3.26 minutes. These results indicate that the mean onset times for both motor and sensory blocks were significantly longer in the levobupivacaine group compared to the bupivacaine group (p<0.001) (Table 3). At the 10th minute, 12% of the patients in the levobupivacaine group had a modified Bromage score of 3, while 76% of the patients in the bupivacaine group had a modified Bromage score of 3. At the end of 120 minutes, the modified Bromage score was still 2 in 20% of the patients in the levobupivacaine group, while 100% of the patients had a modified Bromage score of 3 in the bupivacaine group (Table 4). When the hemodynamic parameters were compared between the groups, no significant difference was found in their systolic, diastolic, mean arterial pressure, and heart rate values at any point (p>0.05) (Figures 1, 2). In the levobupivacaine group, a significant decrease in hemodynamic values compared to the pre-intrathecal application values was observed; systolic pressure, and mean arterial pressure decreased from the first minute onward and diastolic pressure decreased from the fifth minute onward. Heart rate showed a significant decrease during the first 5 minutes, but no significant difference was observed in the following time intervals.

A significant decrease in systolic pressure was observed throughout all time intervals after intrathecal administration in the bupivacaine group, compared to the pre-intrathecal application hemodynamic values. The mean arterial pressure and diastolic pressure showed a significant decrease from the first minute onward. A significant decrease was detected in the heart rate from the 10th minute onwards. There was no statistically significant difference between the groups

Table 1. Modified Bromage score

0	No paralysis, the patient can fully flex the knees and feet.
1	Can move only knees and feet, cannot lift the leg straight.
2	Cannot flex the knee, can only move the foot.
3	Cannot move the ankle or the big toe, complete paralysis.

Table 2. Patients' demographic characteristics

	Bupivacaine group	Levobupivacaine group	p
	Mean ± SD	Mean ± SD	
Age	47.68±15.92	38.76±15.65	0.051
Height	169.32±9.40	171.44±8.39	0.404
Weight	72.28±12.36	74.08±11.69	0.599
BMI	25.24±4.02	25.26±4.13	0.983

SD: Standard deviation, BMI: Body mass index

Table 3. Motor and sensory block onset times

	Bupivacaine group	Levobupivacaine group	p
	Mean ± SD	Mean ± SD	
Motor block onset time (min)	3.54±1.86	8.99±5.41	0.000
Sensory block onset time (min)	3.26±1.78	8.47±5.25	0.000

SD: Standard deviation, min: Minute

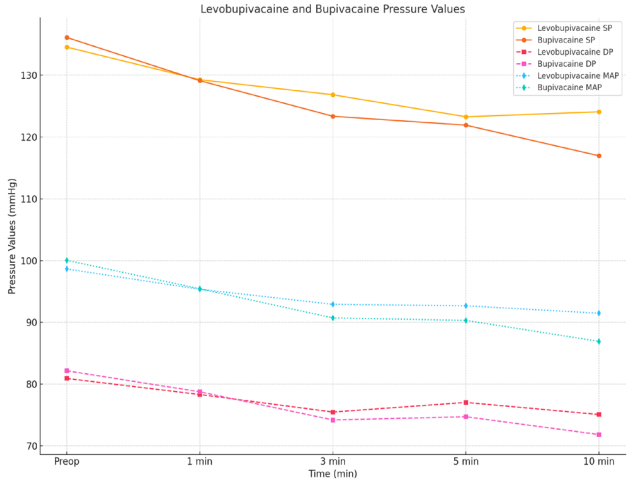

Figure 1: Levobupivacaine and bupivacaine pressure values

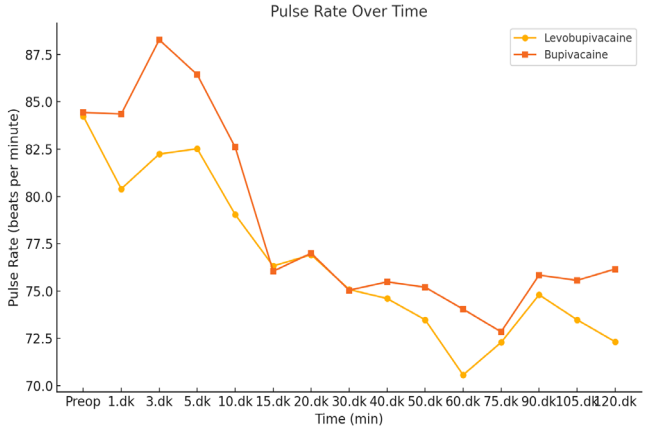

Figure 2: Pulse rate comparison between groups

regarding the requirement for additional medication (ephedrine hydrochloride) (p>0.05) (Table 5).

Discussion

Local anesthetics used for blockade in spinal anesthesia typically exhibit a low side-effect profile when administered in appropriate doses and with proper attention[6,7]. Bupivacaine local anesthetics, is one of the most preferred agents due to its ability to provide sufficient anesthesia and analgesia for medium to long-duration surgical procedures. Levobupivacaine, on the other hand, is the S(-) enantiomer of bupivacaine and shares similar pharmacokinetic properties with racemic bupivacaine. Nonetheless, evidence from *in vitro* studies, animal experiments, and clinical research suggests that levobupivacaine is associated with a reduced risk of cardiotoxicity and central nervous system toxicity when compared to bupivacaine[2-4,8,9]. Additionally, the median lethal dose of levobupivacaine (LD50) has been found to be approximately 50% higher than that of bupivacaine, and hemodynamic changes have been reported to be similar between the two agents after spinal anesthesia[4,5,10-13]. The results indicate that levobupivacaine may serve as a viable alternative, particularly in patients with elevated perioperative risk profiles.

Several randomized controlled trials have investigated the onset and duration of sensory and motor blockade, as well as the adequacy of anesthesia, with levobupivacaine and racemic bupivacaine[14-23]. Some of these studies have indicated that there is no statistically significant difference between levobupivacaine and bupivacaine regarding the onset times of sensory and motor block following intrathecal administration[14]. However, in our study, it was found

Table 4. Motor block status at the 10th and 120th minutes

		Bupivacaine group		Levobupivacaine group		p
		n	%	n	%	
Motor block at the 10th minute	Bromage 2	6	24	22	88	0.000
	Bromage 3	19	76	3	12	
Motor block at the 120th minute	Bromage 2	0	0	5	20	0.050
	Bromage 3	25	100	20	80	

Table 5. Additional medication needs

Vasopressor need	Bupivacaine group		Levobupivacaine group		p
	n	%	n	%	
Yes	20	84	21	80	0.050
No	5	16	4	20	

that the onset times of motor and sensory blockade for levobupivacaine were approximately twice as long as those for bupivacaine. This finding suggests that levobupivacaine could have different pharmacodynamic properties. The S(-) enantiomer configuration of levobupivacaine may alter receptor binding kinetics and agent efficacy, potentially explaining the difference in onset times. Since levobupivacaine provided sufficient anesthesia despite its longer onset time, we did not consider it to be a clinically significant issue.

Studies have indicated that both the initiation and resolution of spinal anesthesia are influenced by the administered dose of local anesthetics. While certain randomized controlled trials have found comparable durations of sensory and motor blockade, as well as overall anesthetic efficacy, between levobupivacaine and racemic bupivacaine, other investigations have reported that levobupivacaine may produce a more prolonged sensory block alongside a relatively shorter motor block[23-27]. In our study, there were no meaningful differences observed between the groups regarding the effectiveness of anesthesia or the length of sensory and motor blockade at 120 minutes. Although statistical significance was not reached, 88% of individuals receiving levobupivacaine exhibited a modified Bromage score of 2 at 10 minutes post-injection, and 20% maintained the score at 120 minutes. On the other hand, all patients in the bupivacaine group were observed to have a Bromage score of 3 at the 120th minute. While this does not affect anesthesia adequacy, it may suggest that levobupivacaine could offer an advantage for patients requiring early postoperative mobilization.

With respect to the hemodynamic impact of levobupivacaine, our results were consistent with existing literature, showing a comparable profile to that of racemic bupivacaine. In both groups, slight decreases in mean arterial pressure and heart rate were recorded following intrathecal administration, yet these fluctuations did not reach statistical significance regarding cardiovascular stability[17,18,21]. According to prior studies, the most frequently encountered adverse effects associated with spinal anesthesia include hypotension, bradycardia, shivering, nausea, and vomiting. However, the incidence rates of these effects did not differ meaningfully between patients receiving levobupivacaine and those administered bupivacaine. Particularly, hypotension has been reported to occur frequently in spinal anesthesia, and a randomized controlled study found that it developed in approximately 80% of the cases[28]. Thus, international guidelines recommend prophylactic use of intravenous fluid loading and vasopressors (ephedrine hydrochloride)[29]. In the present study, the requirement for vasopressor support was found to be comparable between the two groups.

Study Limitations

The research was conducted at a single institution and involved a relatively small number of participants. It covered only certain types of surgeries (elective surgeries) and excluded patients in the higher-risk group (e.g., ASA III and IV). Moreover, the potential effects of preoperative adjunct agents such as midazolam on the efficacy of local anesthetics were not investigated in the present study, which can be considered a significant limitation limiting the generalizability of the study findings.

Conclusion

Levobupivacaine and racemic bupivacaine are local anesthetics that can be used effectively and safely in spinal anesthesia. In our study, levobupivacaine was found to have a longer onset time for motor and sensory blockade compared to bupivacaine. However, this difference did not compromise anesthesia adequacy. Levobupivacaine may offer advantages for early postoperative mobilization. No meaningful statistical variation was observed between the groups in terms of cardiovascular response. Owing to its lower likelihood of inducing cardiac or central nervous system-related toxicity, levobupivacaine emerges as a promising option, especially for individuals with elevated perioperative risk. These findings support the effective and safe use of levobupivacaine in spinal anesthesia; however, there is a need for larger-scale studies involving various surgical indications.

Ethics

Ethics Committee Approval: It can be obtained from the relevant author upon request. This study received approval from the Ethics Committee of University of Health Sciences Türkiye, İstanbul Haseki Training and Research Hospital and was carried out in compliance with the principles outlined in the Declaration of Helsinki (decision no: 12/07, date: 12.11.2007).

Informed Consent: All the patients were informed about the procedures to be performed and their written consent was obtained according to ethical standards.

Footnotes

Authorship Contributions

Surgical and Medical Practices: U.U., K.İ., Concept: U.U., K.İ., Design: U.U., K.İ., Data Collection or Processing: U.U., K.İ., Analysis or Interpretation: U.U., K.İ., Literature Search: U.U., Writing: U.U.

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