Comparison of the effectiveness of intrathecal bupivacaine and levobupivacaine in hip surgery

Primerjava učinkovitosti intratekalne aplikacije bupivakaina in levobupivakaina pri operacijah kolka

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Abstract

Purpose: We aimed to compare the anesthetic and hemodynamic effects of intrathecally administered levobupivacaine and bupivacaine in combination with fentanyl in hip surgery.

Subjects and methods: Sixty patients categorized as class 1 or 2 according to the American Society of Anesthesiologists (ASA) Physical Status classification, aged between 18 and 65 years and scheduled for hip surgery were randomly assigned to two groups. Patients in Group I received spinal anesthesia with 0.5 % bupivacaine 12.5 mg + fentanyl 10 µg (total 2.6 ml), and patients in Group II received 0.5 % levobupivacaine 12.5 mg + fentanyl 10 µg (total 2.6 ml) intrathecally. The level of sensory block and motor block was evaluated, and hemodynamic data were recorded.

Results: The onset of sensory block and the time to two-segment regression were similar between the two groups. In the levobupivacaine group, the time to motor block onset was longer and the motor block regression time was shorter than that of bupivacaine group. The groups were similar with respect to hemodynamic data.

Conclusion: We consider that levobupivacaine may be a good alternative to bupivacaine, particularly in surgical procedures where less motor block development is desired.

Izvleček

Namen: Naš namen je bil primerjati anestezijske in hemodinamične učinke intratekalne aplikacije levobupivakaina in bupivakaina v kombinaciji s fentanilom pri operacijah kolka.

Preiskovanci in metode: Šestdeset bolnikov, razvrščenih glede na fizično stanje po klasifikaciji Ameriškega združenja anestezologov (ASA) v razred 1 ali 2, starih med 18 in 65 let, pri katerih je bila načrtovana operacija kolka, je bilo randomiziranih v dve skupini. Bolniki v 1. skupini so prejeli spinalno anestezijo z 12,5 mg 0,5 % bupivakaina + 10 µg fentanila (skupaj 2,6 ml), bolniki v 2. skupini pa 12,5 mg 0,5 % levobupivakaina + 10 µg fentanila (skupaj 2,6 ml), intratekalno. Ocenjevali smo senzorično in motorično blokado in beležili hemodinamične podatke.

Rezultati: Nastop senzoričnega bloka in čas do dvosegmentne regresije sta bila pri obeh skupinah podobna. V skupini z levobupivakainom je bil čas do nastopa motorične blokade daljši, regresija motoričnega bloka pa krajša kot pri skupini z bupivakainom. Hemodinamični podatki so bili pri obeh skupinah podobni.

Zaključek: Menimo, da je lahko levobupivakain dobra alternativa bupivakainu, posebej še pri kirurških posegih, kjer želimo doseči manj motorične blokade.

Introduction

Stereoisomers of local anesthetic drugs used in regional anesthesia procedures have been developed to avoid toxicity and negative effects on hemodynamic parameters.[1] Levobupivacaine – the S(-)-enantiomer of bupivacaine – is a local anesthetic with lower plasma clearance and a shorter elimination half-life. Although bupivacaine is a frequently used and highly safe local anesthetic used in regional anesthesia procedures, its erroneous intravenous injection may result in fatal cardiotoxicity.[2,3]

In many studies of levobupivacaine and bupivacaine, levobupivacaine has been suggested to display less cardiovascular and central nervous system adverse effects compared to bupivacaine, although the onset and duration of their effects are identical; thus levobupivacaine has been suggested to be a new alternative for patients with cardiovascular pathologies.[4]

Levobupivacaine has been used in epidural and peripheral nerve blocks, and information on its intrathecal use is limited.[5]

We aimed to compare the effects of intrathecally administered levobupivacaine and bupivacaine in combination with fentanyl on the hemodynamic parameters, sensory and motor block times and systemic and neurological side effects in adult patients undergoing hip surgery.

Subjects and methods

A total of 60 ASA I-II patients aged between 18 and 65 years were included in the study after approval had been obtained from the ethics committee of the Research Hospital, Dicle University, and written informed consents from the patients were obtained. Patients who had cardiovascular diseases, neuromuscular or neuropsychiatric diseases and peripheral neuropathy, alcohol and/or drug addiction, a history of operations on the lumbar spine, contraindications for regional anesthesia, and a history of allergy to local anesthetics, who were shorter than 155 cm or taller than 190 cm, and had a body mass index > 30, were excluded from the study.

At the preoperative visit, all patients were informed about the anesthesia method and the verbal rating scale (VRS) that would be used for postoperative pain assessment.

All patients underwent standard monitoring using electrocardiography, pulse-oximetry and non-invasive blood pressure measurements. All patients were administered 0.05 mg/kg midazolam intravenously to the dorsum of the hand through a 20-gauge needle. Next, 5 ml/kg hydroxyacetyl starch and 5 ml/kg 0.9 % NaCl were administered within approximately 30 min. An infusion of 5 ml/kg/hour 0.9 % NaCl was administered during the operation. Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), and heart rates (HRs) of the patients were recorded.

Spinal anesthesia was performed in the sitting position in all patients. The puncture site was disinfected using 10 % povidone-iodine (IsoSol®), and the L_{3-4} lumbar space was accessed through a 26-gauge spinal needle following local anesthesia. After free cerebrospinal fluid flow had been observed, Group I patients received 0.5 % bupivacaine 12.5 mg + fentanyl 10 µg (total 2.6 ml) and Group II patients received 0.5 % levobupivacaine 12.5 mg + fentanyl 10 µg (total 2.6 ml) intrathecally. Patients were laid in the supine position and SAP, DAP, MAP, HR and SpO_2 values were recorded at 2, 5, and 10 min, and at every 5 min thereafter. The level of sensory block was assessed using the pin-prick

Table 1: Demographic data and duration of surgery.

	Group I (n = 30)	Group II (n = 30)	p
Age (year)	58 ± 13.8	56 ± 15.3	0.58
Height (cm)	167 ± 7.5	165 ± 8.0	0.32
Weight (kg)	71 ± 12.3	76 ± 11.9	0.19
Male/Female	20/10	17/13	0.42
ASA I/II/III	10/18 /2	13/15/2	0.30
Duration of surgery (min)	59 ± 10	61 ± 10	0.06

Values are given as mean ± standart deviation.
ASA, American Society of Anesthesiologists

test, and surgery was initiated when the level of sensory block reached T_6. Patients were administered 3 L/min oxygen via a facial mask during the operation.

A more than 20 % reduction in basal SAP was accepted as hypotension, and 5–10 mg of ephedrine were applied if hypotension developed. An HR of less than 50 beats per min was accepted as bradycardia, and 0.5 mg of Atropine IV was administered if bradycardia developed.

The degree of motor block was assessed using a four-point modified Bromage scale by asking the patient to flex the hip, knee, and ankle joints (0: full flexion of the knees and feet; 1: just able to flex knees, full flexion of feet; 2: unable to flex knees, flexion of feet; 3: unable to move legs or feet, full motor block) after the patient was placed into the supine position at 5, 10, and 15 min after spinal anesthesia.

The sensory block level was measured using pin-prick testing and was recorded. Time to two-segment regression of the sensory block and side effects, such as hypotension, bradycardia, nausea and vomiting, were recorded. Postoperative pain was assessed using the VRS (0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain, 4: intolerable pain).

Patients were observed for ~1 h in the post-anesthesia care unit after the end of the operation, and motor and sensory block regression times, hemodynamic parameters, and time to first postoperative analgesic requirement were recorded.

All intraoperative and postoperative assessments were evaluated by an unbiased observer who was blinded to the study groups.

Analysis

Statistical analyses were performed using the SPSS 15.0 for Windows software package (SPSS Inc., Chicago, IL, USA). The mean and standard deviation were calculated for descriptive statistics of constant variables. Compatibility of groups to a normal distribution was determined using the Kolmogorov–Smirnov test. Student's *t*-test was used for comparison of the mean values between two groups. Yates correction and chi-squared test were used for analysis of cross-tabs. A p value less than 0.05 was deemed to indicate statistical significance.

Results

Demographic data and operative times were similar between the two groups (Table 1). No statistically significant difference was found between the groups in terms of time to the start of the operation, sensory block elevation time to T_{10}, time to two-segment regression of the sensory block (T_{10}-T_{12}), intraoperatively used fluids, amount of ephedrine used, and time to first postoperative analgesic requirement (Table 2). No

Table 2: Data of groups related to spinal anesthesia

	Group I (n = 30)	Group II (n = 30)	*p*
Time up to T_{10} level of sensorial block.	9 ± 2	10 ± 3	0.54
Surgery onset time (min)	10 ± 1.8	9.83 ± 1.7	0.36
Time up to 2 segment regression (min)	63 ± 7	62 ± 8	0.56
Crystalloid (ml)	706 ± 218	700 ± 218	0.90
Colloid (ml)	133 ± 224	100 ± 203	0.54
Ephedrine (mg)	1.8 ± 3.8	1 ± 2.4	0.31
First postoperative analgesic time (min)	233 ± 23	242 ± 16	0.10
Time up to motor block regression (min)	182.06 ± 14,12	132.26 ± 9.78	0.001

Values are given as mean ± standart deviation.

Table 3: Bromage Scale of Both Groups (0-3 Score)

Bromage scale	G I (n = 30)	G II (n = 30)			G I (n = 30)	G II (n = 30)	
ASA				30.min			
0 score	25	30	$X^2 = 3.49$ P = 0.06	0 score	0	0	$X^2 = 0.218$ P = 0.640
1 score	5	0		1 score	0	0	
2 score	0	0		2 score	3	2	
3 score	0	0		3 score	27	28	
5 min				40 min			
0 score	1	11	X2 = 13.91 P = 0.001*	0 score	0	0	$X^2 = 0.315$ P = 0.554
1 score	24	19		1 score	0	0	
2 score	5	0		2 score	2	1	
3 score	0	0		3 score	28	29	
8 min				50 min			
0 score	0	2	$X^2 = 13.67$ P = 0.001*	0 score	0	0	$X^2 = 0.315$ P = 0.554
1 score	8	20		1 score	0	0	
2score	22	8		2score	1	1	
3 score	0	0		3 score	28	29	
10 min				60 min			
0 score	0	0	$X^2 = 4.87$ P = 0.087	0 score	0	0	$X^2 = 0.315$ P = 0.554
1 score	1	6		1 score	0	0	
2 score	28	24		2 score	1	1	
3 score	1	0		3 score	28	29	
15 min				PO 5 min			
0 score	0	0	$X^2 = 9.40$ P = 0.009*	0 score	0	0	$X^2 = 0.000$ P = 1.000
1 score	0	4		1 score	0	0	
2 score	17	22		2 score	2	2	
3 score	13	4		3 score	28	28	
20 min				PO 15 min			
0 score	0	0	$X^2 = 9.40$ P = 0.611	0 score	0	0	$X^2 = 2.308$ P = 0.128
1 score	0	0		1 score	0	0	
2 score	9	9		2 score	2	6	
3 score	21	21		3 score	28	24	
25 min				PO 30 min			
0 score	0	0	$X^2 = 1.176$ P = 0.278	0 score	0	0	$X^2 = 10.817$ P=0.000
1 score	0	0		1 score	0	0	
2 score	3	6		2 score	9	26	
3 score	27	24		3 score	21	4	

ASA: After Spinal Anesthesia; X^2: chi-squared test

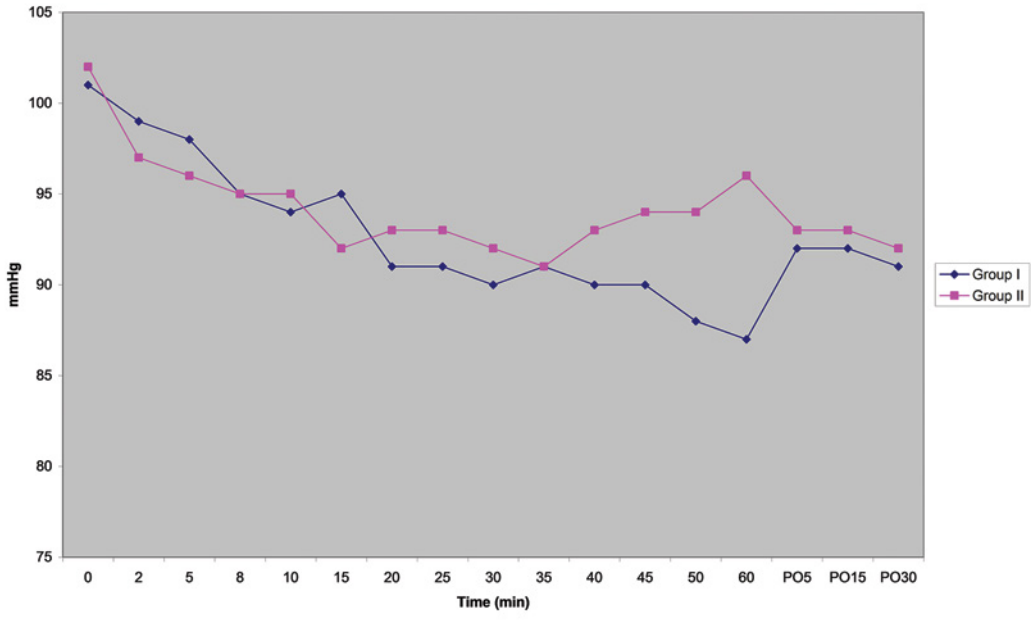

Figure 1: Mean arterial pressure values of groups.
PO: post-operative period.

significant difference was found between the groups in terms of the mean arterial pressure and heart rate values measured at all times (Figures 1 and 2).

The times to motor block development at 5, 10, and 15 min following spinal anesthesia were significantly shorter in Group I. (p values at 5, 10, and 15 min were 0.001, 0.007, and 0.009, respectively).

Motor block was observed in 29 patients in the bupivacaine group and 19 patients in the bupivacaine group at 5 min following spinal anesthesia (Bromage 1–2) ($p < 0.01$). Motor block developed in all patients in the bupivacaine group and 28 patients in the levobupivacaine group at 8 min following spinal anesthesia (Bromage 1–2) ($p = 0.42$). At 15 min following spinal anesthesia, full motor block developed in all patients of the bupivacaine group but in only four patients of the levobupivacaine group (Bromage 3) ($p < 0.001$) (Table 3).

The motor block regression time was 182.06 ± 14.12 in the bupivacaine group and 132.26 ± 9.78 min in the levobupivacaine group ($p = 0.001$) (Table 2).

The groups were similar in terms of post-operative pain levels ($p > 0.05$).

Discussion

In many studies of levobupivacaine and bupivacaine, levobupivacaine has been suggested to result in fewer cardiovascular and central nervous system adverse effects than bupivacaine, although the onset and duration of the effects are identical, and so levobupivacaine has been suggested to be a new alternative for patients with cardiovascular pathologies.[4] However, studies regarding these adverse effects are ongoing, and few have evaluated levobupivacaine in patients with cardiovascular pathologies.

Clinical studies using levobupivacaine and bupivacaine demonstrated similar effects when the drugs were used at a 0.5 % concentration.[4,5] In our study, we used these drugs at the same volume and concentration by adding 10 µg of fentanyl to both local anesthetic agents.

In our study, the local anesthetic and hemodynamic effects of intrathecally administered fentanyl with levobupivacaine or bupivacaine were found to be similar. This result is consistent with previous reports.[4-6]

In spinal anesthesia, use of lipophilic opioids in combination with local anesthetics improves the quality of local anesthesia without prolonging the duration of motor block. The recovery time of motor block also improves.[3] Opioid addition in spinal anesthesia has been shown to improve blood pressure stability and the quality of anesthesia by reducing the required local anesthetic dose due to its synergistic effect with local

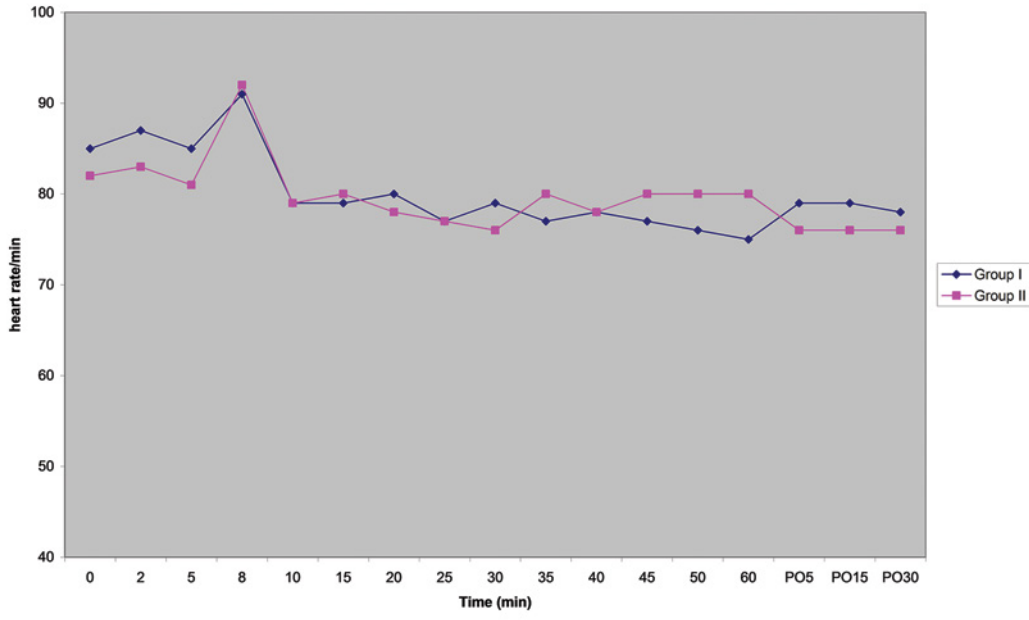

Figure 2: Heart rate values of groups *PO: post-operative period.*

anesthetics without causing sympathetic blockade.[7,8,9] In our study, we considered that the stability of the hemodynamic parameters and the lack of difference observed between the two groups was likely due to adequate hydration prior to spinal anesthesia.

In the study by Glaser *et al.*[4], the anesthetic and hemodynamic efficacy of intrathecally administered 0.5 % levobupivacaine (3.5 ml) and 0.5 % bupivacaine (3.5 ml) were compared in 80 patients who underwent hip surgery; the onset and duration of sensory and motor blocks were similar in both groups. In the study of Lee *et al.*[6], the anesthetic and hemodynamic efficacy of intrathecally administered 0.5 % levobupivacaine (2.6 ml) and 0.5 % bupivacaine (2.6 ml) were compared in 50 patients who underwent urological operations; the onset and duration of sensory and motor blocks were similar in both groups. In our study, no significant difference was found between the sensory block times of both local anesthetics; this result is consistent with previous reports.[4-6] The drug doses used in the above trials are different from our study. Moreover, fentanil was not used. This could explain why these results were different from our study.

Liao *et al.*[10] found the onset of motor block to be longer, and the motor block regression time to be shorter, with levobupivacaine than with bupivacaine. Erbay *et al.*[11] used intrathecal bupivacaine and levobupivacaine in 50 patients who underwent transurethral surgery and found the motor block regression time to be shorter in the levobupivacaine group. Lee *et al.*[6] did not find a difference between the onset and duration of motor block between bupivacaine and levobupivacaine. In our study, the motor block onset time was found to be longer, and the motor block regression time was found to be shorter in the levobupivacaine group (levobupivacaine: 132.26 ± 9.78 min; bupivacaine: 182.06 ± 14.12 min) ($p = 0.001$). Our study is similar to Liao and Erbay's study in term of the dose of drug and adjuvant agent used. This could explain why our results were similar to both the above mentioned studies.

These studies of levobupivacaine reported different results with respect to motor block timing. More detailed studies of the factors underlying the differences in the results and choosing drugs according to the characteristics and duration of surgical intervention are therefore important.[13]

Recovery of motor block after spinal anesthesia is important for early mobilization. Thus, it may also be effective for reducing the postoperative complications (*e.g.*, thromboembolic events and pulmonary complications) that can occur in the elderly.

The incidence of adverse effects associated with the two local anesthetics, levobupivacaine and bupivacaine, has been reported to be similar.[4-6,10,11] Our results are consistent with previous reports.

The effects of drugs may vary among studies due to differences in patients' characteristics, patients' emotional status, position of the body, adjuvant drugs, local anesthetic baricity, the spinal level of intrathecal injection, surgical procedures, surgical stimulation, and tolerance of side effects.[13,14] Because of this, we believe that it is possible to expect different results to be obtained in various experiments even when using levobupivacaine in identical doses. For this reason, an optimal dose which we did not calculate for levobupivacaine in our experiment could be a limitation in our experiment.

In conclusion, we consider that levobupivacaine, which has similar sensory block properties to bupivacaine, may be a good alternative anesthetic to bupivacaine, particularly during procedures in which less motor block development is desired, such as hip surgery.

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