

Comparison of the Effects of Epidural 0.5% Bupivacaine and 0.5% Levobupivacaine Administration Without Adjuvant Medication on Anaesthesia Quality, Side Effect Incidence and Analgesia Requirement Times in Electively Operated Cases on Hip and Lower Extremity

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Abstract

The study was carried to compare the anesthetic effectiveness of epidural levobupivacaine and bupivacaine without adjuvant medication in cases who were electively operated on lower extremity and hip. This study was conducted in total of 50 ASA I-II patients aged between 20 and 60 years, who underwent elective hip and lower extremity surgery. The cases who received bupivacaine were assigned into Group B (n:25) and those received levobupivacaine into Group L (n:25). Statistically no significant difference was found between the groups in terms of the onset and regression times of the sensory and motor blockade, time to reach dermatomes, initial analgesic requirement time, resolution time of the motor block, patient and surgeon satisfaction, heart rate (HR), noninvasive systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP) and peripheral oxygen saturation (SpO₂) values ($P > 0.05$). levobupivacaine could be a good alternative to bupivacaine in the patients whom we administered epidural anesthesia in elective hip and lower extremity surgeries, in terms of hemodynamic parameters, quality of anesthesia and analgesia, patient and surgeon satisfaction and complications.

Key Words

Epidural Anesthesia, Bupivacaine, Levobupivacaine, Lower Extremity Hip Surgery

Introduction

Spinal and epidural anesthesia techniques are regional anesthesia methods widely used especially in lower abdominal and lower extremity surgeries (1,2). Epidural anesthesia is a versatile technique widely used in anesthetic practice. Its potential to decrease postoperative morbidity and mortality has been demonstrated by numerous studies(3).

Stereoisomers of the local anesthetic agents are being developed in order to avoid the toxic effects of local anesthetic agents as much as possible. S forms of the isomers are less toxic and provide longer-lasting analgesia (4,5). We aimed to compare anesthetic effectiveness of epidural levobupivacaine and bupivacaine without adjuvant medication in the cases who were electively operated on lower extremity and hip.

Material and Methods

This study was a prospective, randomized double-blind study conducted with approval of the hospital Ethical Committee, after informed written consent from the patients was taken, in Post Graduate Department of Anesthesiology and Intensive Care. Total of 50 ASA I-II patients aged between 20 and 60 years, who underwent elective hip and lower extremity surgery were included in the study. The patients were assigned randomly by a computer randomization program to receive either 25ml of isobaric bupivacaine in Group B (n= 25) or received 25ml isobaric levobupivacaine in Group L (n = 25).

The patients who accepted the regional anesthesia and had not any contraindication for regional anesthesia, with a height of 150 to 180 cms were included in the study. The patients who refused the regional anesthesia, substance and alcohol addicts and those who had an

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allergy to any drugs in the study protocol were excluded from the study. All the patients were premedicated before the surgery with 2 mg of midazolam IV stat. The patients were hydrated with 10 ml/kg of Ringer's lactate before the epidural analgesia. Systolic, diastolic and mean blood pressures (SBP, DBP, MBP), heart rate (HR) were monitored and peripheral oxygen saturation (SpO₂) was measured with pulse oximetry in all the cases taken to the operating room. Demographic data, heart rate, systolic, diastolic and mean blood pressure values were recorded for all the cases before the blockade.

Under all aseptic precautions, epidural needle (18 Gauge Touhy Needle) was inserted from L3-L4 or L4-L5 space in the sitting position using loss of resistance technique. After aspiration of the blood was defined as negative, Group B received 0.5% isobaric bupivacaine of 5 ml initially in the epidural space and after 2 minutes rest of the drug was given as to be 25 ml. Similarly in Group L 25ml of 0.5% isobaric levobupivacaine was given.

Systolic, diastolic, mean arterial pressure, heart rate, peripheral oxygen saturation were measured and recorded after patient were taken on the operating table (T1), following injection of epidural solution after 5.(T2), 10.(T3), 20.(T4),30.(T5) and 60.minutes (T6) of the solution administered and at postoperative 1st (T7) and 2nd (T8) hours.

The sensory block was tested with 2-minute intervals by pinprick into the region corresponding to each dermatome of both anterior axillary lines. Absence of pain in T10 (umbilicus) level with pinprick was recorded as the onset time of sensory block. The last dermatome in which the patient did not feel pain was accepted as the maximal level of sensory block. Times of onset, reaching T6 (xyphoid level), regression of two segment and termination were recorded during this monitoring. Sensory block to reach to thoracal (T6) level was accepted sufficient to start the surgery. The duration between epidural injection and sensory block to regress to L1 (inguinal region) level was accepted as the epidural analgesia duration. Degree of motor block of the lower extremity was evaluated using the Modified Bromage Scale every two minutes.

Bromage score as well as onset, termination and recovery times of the motor block were recorded. Recovery time of motor block was considered as the time of maximal Bromage scores to drop one point.

Postoperative pain of the cases was evaluated with VAS (Visual Analog Scale) scores. The patients were asked to mark a position indicating the pain severity on a continuous horizontal line (measuring in cms) between 0 (no pain) at one end and 10 (the most severe pain) at the other end.

When VAS scores of the patients were 4 or higher; 1.5 mg/kg of diclofenac sodium I/M was given for postoperative analgesia. In addition, initial analgesia requirement time, side effects such as nausea-vomiting, hypotension, bradycardia, patient-surgeon satisfaction and analgesia quality were recorded in all the patients. Initial analgesia requirement time was accepted as the time when the cases have a postoperative VAS score of 4 or higher.

The patients were stabilized with 0.5 mg atropine when their heart rates dropped under 50 beats/minute and with mepenteramine in 6 mg doses when their mean arterial pressures decreased by 30% of the preoperative value.

Analgesia quality was evaluated in three stages as excellent (no pain, patient comfortable), good with sedation (required mild analgesia) and poor (discomfort with moderate pain and required general anesthesia).

The patients were taken to the recovery room at the end of the surgery were monitored for 60 minutes. Following hemodynamic findings (basal systolic and diastolic blood pressures, heart rates) to be stable, the patients were sent to the separate wards. In addition, termination time of motor block (when to be able to move his/her feet) was recorded. The patients were questioned by another anesthesiologist for the head and back pain, motor and any neurological problem after after surgery.

Data were expressed as number, percentage, mean and standard deviation. Analysis of the data was performed with SPSS 18.0 statistical software. Mann-Whitney U test was used in analysis of the continuous variables and Chi-square test for the analysis of categorical variables. $P < 0.05$ values were considered statistically significant.

Results

Demographic features of the cases such as age, weight and height were 55.91 vs 56.77; 167.26 vs 168.03; 69.11 vs 69.69; respectively, in Group L and Group B and no significant difference was found between the groups.

No significant difference was found in terms of onset and regression times of sensory block, onset and regression times of motor block, time of sensory block to reach T6, initial analgesic requirement time and surgery duration (*Table 1*).

When values of the groups were compared; sensory block was seen to reach T6 earlier, to terminate later and to last longer in Group B; however, this was not statistically significant ($P > 0.05$). Maximum motor levels of the patients in Group B and Group L were compared according to the case number. There was not a significant difference between the groups (*Table 2*).

When mean SAP values of the groups were compared; no significant difference was seen between Group B and Group L in SAP values at 5, 10, 20, 30, 60 minutes of the

Table 1. Comparison Sensory-Motor Blockade Onset And Regression Times, Initial Analgesic Requirement Time And Surgery Durations Of The Patients.

	Group L	Group B	T	P
Sensory block onset time (min)	6.86±1.94	6.80±1.812	-0.143	0.886
Time of sensory block to reach T6 (min)	24.54±2.27	23.97± 1.485	-1.221	0.222
Motor block onset time (min)	15.37± 1.46	15.60±1.288	-0.727	0.467
Sensory block regression time (min)	180.54± 9.34	183.17±7.48	-1.291	0.197
Motor block Initial analgesic requirement time (min)	207.86±45.96	223.29±40.76	-1.358	0.175
Surgery duration(min)	140.29±22.94	140.57±23.51	-0.172	0.863
Time of motor block to reach maximum level (min)	26.80 ± 1.96	26.54± 1.88	-0.548	0.574

Table 2. Bromage Scale of the patients in Group B and Group L.

Bromage Scale	Group L		Group B		P values
0					
1	13	45%	16	55%	0.550
2	22	53%	19	47%	0.430
3					

Table 3. SAP (Systolic Arterial Pressure) Values of The Groups

SAP (mmHg)	Group L (mean±SD)	Group B (mean± SD)	T	P
Basal (T1)	125.20 ±11.15	123.86± 11.64	-0.722	0.470
5 min (T2)	123.14 ±10.67	122.31± 10.15	-0.365	0.715
10 min (T3)	122.34 ± 11.01	123.63± 10.61	-0.768	0.442
20 min (T4)	122.09 ± 10.07	122.40± 10.11	-0.238	0.812
30 min (T5)	119.14 ± 8.34	117.49± 9.78	-0.628	0.430
60 min (T6)	119.60 ± 7.94	118.69± 7.92	-0.580	0.562
Post op. 1. hour(T7)	121.54 ± 9.86	121.18± 8.10	-0.329	0.742
Post op. 2. hour(T8)	124.43 ± 8.20	127.29± 7.89	-1.546	0.122

epidural block, at the end of the surgery and 1. and 2. hours of the surgery, compared to the preoperative SAP values (Table 3).

When DAP and MAP values of the groups were compared; no significant difference was seen between Group B and Group L in DAP values at 5, 10, 20, 30, 60 minutes of the epidural block, at the end of the surgery and 1. and 2. hours of the surgery, compared to the

preoperative DAP values ($P > 0.05$). When heart rate values of the groups were compared; no significant difference was found between Group B and Group L in HR values at 5, 10, 20, 30 minutes of the epidural block, at the end of the surgery and 1st. and 2nd. hours at the postoperative time, compared to the preoperative HR values. However, borderline difference was found at 60. minute of the epidural block between groups ($P = 0.049$)

Table 4. HR (Heart rate) Values of the Groups

HR (beats/minute)	Group L (mean ± SD)	Group B (mean ± SD)	T	P
Basal (T1)	89.20 ± 10.363	89.49 ± 6.793	-0.497	0.619
5 min (T2)	87.66 ± 7.174	89.51 ± 7.056	-0.809	0.419
10 min (T3)	87.77 ± 11.149	89.71 ± 10.366	-1.023	0.306
20 min (T4)	87.57 ± 8.012	87.34 ± 7.227	-0.077	0.939
30 min (T5)	86.11 ± 8.953	87.83 ± 7.342	-0.619	0.536
60 min (T6)	84.20 ± 8.781	88.06 ± 6.553	-1.970	0.049*
Post op. 1. Hour (T7)	84.83 ± 8.266	87.83 ± 7.286	-1.943	0.052
Post op. 2. Hour (T8)	86.17 ± 7.015	88.31 ± 6.101	-1.677	0.093

Table 5. Comparison of The Side Effects Seen In The Groups During The Surgery

Side Effect	Group L	Group B	P
Hypotension	4	5	0.50
Bradycardia	1	3	0.30
Nausea- Tremor	1	2	0.50
Coughing	0	0	-

Table 6. Comparison of the Analgesia Quality in the Groups

		Group L	Group B	P value
Analgesia Quality	Excellent	32	31	1.00
	Good with sedation	3	4	

(Table 4). When SpO₂ values of the groups were compared, no significant difference was found between Group B and Group L in SpO₂ values at 5, 10, 20, 30 minutes of the epidural block, at the end of the surgery and 1. and 2. hours of the surgery, compared to the preoperative SpO₂ values. When side effect rates of the groups were compared; hypotension and nausea-vomiting were seen in a higher rate in Group B, while Group L had fewer side effects. In Group B; hypotension was found in 5 patients, bradycardia in 3 patients, nausea-vomiting in 3 patients and tremor in 2 patients; while in Group L hypotension was found in 4 patients, bradycardia in 1 patient, nausea-vomiting in 1 patient and tremor in 1 patient. Postoperative side effects were found similar in both groups. No significant side effect was seen in none of the patients after the surgery (Table 5).

In our study, analgesia quality was found as excellent in 31 patients, good with sedation in 4 patients in the Group B, while it was found as excellent in 32 patients and good with sedation in 3 patients in the Group L (Table 6). Patient and surgeon satisfaction, analgesia quality and VAS values were compared in all the patients, and no significant difference was defined between the groups.

Discussion

Advantages of the regional anesthesia include conscious patients, early awareness of the complications owing to the cooperation of the patient, protection of the airway reflexes, thromboembolism to be encountered less and no or fewer motor blocks, while it has the disadvantages of late onset of the effects and motor block that may develop (6). This method is preferred by anesthesia physicians, especially in the patients who suffer from respiratory diseases (7). Also for high-risk cardiac patient, epidural anesthesia followed by epidural postoperative analgesia should be preferred (8).

Bupivacaine is a long acting local anesthetic from the amino-amide subgroup, which is frequently used in local infiltration, epidural and spinal anesthesia. Although it has been safely used in all types of the regional anesthesia for many years, fatal cardiotoxic effects may be seen following its accidental intravascular injection (9,10). Important cause of cardiovascular side effects is that bupivacaine leave sodium channels slowly. Therefore, local anesthetics with similar action to bupivacaine, but fewer effects on cardiovascular system is needed for regional anesthesia. Levobupivacaine, is S (-) enantiomer

of racemic bupivacaine. Affinity of S (-) isomer to cardiac sodium channel in the inactive state is lower than R (+) isomer (11-13). In the various studies; levobupivacaine has been demonstrated to present similar pharmacokinetic characteristics to bupivacaine and to be less cardiotoxic and neurotoxic. Levobupivacaine is considered as a good alternative to bupivacaine, because of its lower side effects on cardiovascular and central nervous system (14-17).

In their study with 88 patients, Cox *et al.* (18) found that 0.5% bupivacaine and 0.75% levobupivacaine administered for epidural anesthesia was tolerated by the patients as well as those who received bupivacaine and there was not a significant difference in producing sensory block, maximal diffusion and onset time of motor block. They defined the time of sensory block as about 460 minutes for 0.75% levobupivacaine and about 377 minutes for 0.5% bupivacaine. They reported that the time of sensory block was 32 or 45 minutes longer compared to equal doses of bupivacaine (about 345 minutes) and motor block did not occur in 14 of 29 patients received levobupivacaine, whereas only in 9 of 29 patients who received bupivacaine.

Kopacz and Allen (19) reported that sensory block onset time may be between 5 and 15 minutes after 0.5% levobupivacaine injection, and this was similar to onset time of the effect of 0.5% bupivacaine.

In our study, 25 ml of 0.5% isobaric bupivacaine and 25ml of 0.5% isobaric levobupivacaine injected epidurally were compared in two groups (25 patients in each) that underwent elective hip and lower extremity surgery, in terms of anesthetic and hemodynamic parameters.

In our study, no difference was found between the times to reach the sensory block sufficient for the surgical intervention (23.97 min. in Group B and 24.54 min. in Group L). Motor block onset time was found as 15.60 min. in group B and 15.37 min. in group L, while times of the sensory block to regress to two segments were found as 183.17 and 180.54 min. in the Group B and Group L; respectively. Regression time of the motor block in the lower extremities was found as 195.60 min. in group B and 191.60 min. in group L. According to these results, statistically no difference was found between the groups in terms of the sensory block onset and regression times, motor block onset and regression times, time of sensory block to reach T6, initial analgesic requirement time and mean surgery durations. No toxicity signs were found in any patient. We attributed this to the fact that patients were selected from the low-risk group (ASA Grade-I & II), and the doses of the drugs were not high.

Kopacz and Allen (19) found in the patients, they administered bupivacaine and levobupivacaine from epidural that motor block time was about 1 minute shorter

in the group receiving levobupivacaine. They reported extremity block occurred within 30 minutes in only 14% of the patients who received levobupivacaine compared to 71% of the patients received bupivacaine. In our study, when the degrees of motor block over time were compared, no difference was found between the groups ($P > 0.05$). In Group B and Group L, the degree of motor block reached to the peak level within 30 minutes, remained in the same level at 60. minute and then decreased by time, completely resolving in 350 minute.

Our study indicates that epidurally administered bupivacaine produced an analgesia duration of 363 min. and levobupivacaine a duration of 347 min. which means both medications caused almost similar analgesic effect. Maximum sensory block height was at T4 level and maximum motor block diffusion were occurred after 30 minutes of the administration, and complete motor block was not seen in any patients.

In their studies, Cox *et al.* (18), Bader *et al.* (20) and Kopacz and Allen'in (19) evaluated SAP, DAP, MAP, HR and SpO2 parameters and did not find a significant difference between the two groups. Similarly, we compared the same parameters in our study. No statistically significant difference was found in these parameters after epidural block compared to the baseline values.

In their study with patients to undergo caesarean section, Bader *et al.* (20) epidurally administered 30 ml of 0.5% levobupivacaine in the first group and 30 ml of 0.5% bupivacaine in the second group, and they found that incidence of hypotension was lower in the levobupivacaine group. We also obtained the same result in our study. When Kopacz and Allen (19) compared levobupivacaine and bupivacaine in terms of the side effects, they found a similar tolerability profile. In their study where levobupivacaine was epidurally administered, they reported that cardiac depression or central nervous system (CNS) toxicity was not encountered following vascular absorption or direct intravascular injection with the exception of minimal CNS symptoms (transient agitation and disorientation) seen in one patient who incidentally received intravascular injection, and they did not find signs of cardiovascular system (CVS) toxicity. In our study, no significant difference was defined between the groups in terms of the side effects that may be encountered in the perioperative period.

In animal studies, CNS symptoms and convulsions have been shown to occur in lower doses of bupivacaine than in levobupivacaine. In a double-blind, randomized study by Van *et al.* (16) with 12 voluntary patients, iv administered 40 mg of levobupivacaine was found, on EEG, to produce less CNS depression compared to 40 mg of bupivacaine. Bhatt *et al.* (21) reported that side

effects of levobupivacaine compared with bupivacaine and other local anesthetics of the amide groups were the same. The most common side effects are nausea, hypotension, fever, headache, and vomiting were reported. Similar to the safety profile and lower incidence of adverse effects of these drugs. There was statistically no significant difference in side effects. In our study, statistically no significant difference in term of side effects was seen. No significant difference in the quality of analgesia was recorded between these local agents and all of them provided efficient clinical anesthesia (18,22). In our study too, statistically no significant difference in quality of analgesia was observed.

After epidural blockade there was a statistical significant difference in term of heart rates at 60th minute. However this difference of heart rate is not significant clinically.

Conclusion

We conclude from the study that, there was no difference between 0.5% bupivacaine and 0.5% levobupivacaine received epidurally in hip and lower extremity surgery, in terms of motor and sensory blockade, onset and regression times, time of sensory block to reach T6 and visual analog scale. Levobupivacaine also decreases the cardiovascular and central nervous system toxicity to some extent (p value insignificant) which makes levobupivacaine an interesting alternative to bupivacaine. Thus, it can be used with equal efficacy and slightly better safety than as bupivacaine in similar dose when injected epidurally.

References

1. Kleinman W: Regional Anesthesia and Pain Management: Spinal, Epidural and Caudal Blocks. Clinical Anesthesiology. Morgan GE, Mikhail MS, Murray MJ (ed). 3rd edition Appleton & Lange Los Angeles 2002. pp. 253-82.
2. Longo S. Postdural puncture: implications and complications. *Curr Opin Anaesth* 1999;12: 271-75.
3. Maria B, George J.E, Seif J, Farag E. Recent Advances in Epidural Analgesia. *Anesthesiol Res Pract* 2012; 2012:309219. .
4. Apan A, Sar F, Ekmekçi AB. Single shot "3-in-1" femoral nerve blockade with 0.25% or 0.375% levobupivacaine provides similar postoperative analgesia for total knee replacement. *Turk J Med Sci* 2010; 40: 77-82
5. Yurtlu B.S, Hanc? V, Ege A, Bostankolu S.E, Ayolu H, Ozkoçak turan I. Tramadol as an adjunct for levobupivacaine in axillary plexus blockade: a prospective, randomized, double-blind study. *Turk J Med Sci* 2012; 42: 55-62
6. Ouellette SM, Ouelette R. Regional anesthesia : is it safer? *CRNA* 1995; 6: 70-8
7. Burke D, Kenndy S, Bannister J. Spinal anaesthesia with 0.5% S (-) -bupivacaine for elective lower limb surgery. *Region Anaesth Pain Med* 1999; 24: 519-523.
8. Atalay C, Da C, Bayram E, Alici HA, Erdem AF. Effects of three different methods of anesthesia on the release of brain natriuretic peptid in patients with cardiac risk undergoing lower extremity surgery. *Turk J Med Sci* 2010; 40 (3): 405-14
9. Reiz S, Nath S. Cardiotoxicity of local anaesthetic agents. *Br J Anaesth* 1986; 58: 736-746.
10. Marx GF. Cardiotoxicity of local anesthetics-the plot thickens. *Anesthesiology* 1984; 60: 3-5.
11. Huang YF, Pryor ME, Mather LE, Veering BT. Cardiovascular and central nervous system effects of intravenous levobupivacaine in sheep. *Anesth Analg* 1998; 86: 797-804.
12. Aberg G. Toxicological and local anaesthetic effects of optically active isomers of two local anaesthetic compounds. *Acta Pharmacologica Toxicologica* 1972; 31: 273-286.
13. Luduena FP, Bogado EF, Tullar BF. Optical Isomers of Mepivacaine and Bupivacaine. *Archives of Int Pharmacodynamics* 1972; 200: 359-69.
14. McClellan KJ, Spencer CM. Levobupivacaine. *Drugs* 1998; 56: 355-62.
15. Foster RH, Markham A. Levobupivacaine: A review of its pharmacology and use as a local anaesthetic. *Drugs* 2000; 59: 531-79.
16. Van F, Rolan PE, Brennan N, Gennery B. Differential effects of levo and racemic bupivacaine on the EEG in volunteers (abstract). *Regional Anesth Pain Med* 1998; 23:48.
17. Valenzuela C, Snyders DJ, Bennett PB, et al. Stereoselective block of cardiac sodium channels by bupivacaine in guinea pig ventricular myocytes. *Circulation* 1995; 92: 3014-24.
18. Cox CR, Faccenda KA, Gilhooly C, et al. Extradural S (-) -bupivacaine: comparison with racemic RS-bupivacaine. *Br J Anaesth* 1998; 80: 289-93.
19. Kopacz DJ, Allen HW. Accidental intravascular injection of 0.75% levobupivacaine during lumbar epidural anaesthesia. *Anesth Analg* 1999; 89: 1027-29.
20. Bader AM, Tsen LC, Camann WR, Nephew E, Datta S. Clinical effects and maternal and fetal plasma concentrations of 0.5% epidural levobupivacaine versus bupivacaine for cesarean delivery. *Anesthesiology* 1999; 90: 1596-1601.
21. Bhatt SH. Levobupivacaine. A stereo - selective amide local anaesthetic. *J Pharm Soc Wiscon* 2001;3:28-34
22. Cox CR, Faccende KA, Gilhooly C, Bannister J, Scott NB, Morrison LM. Extradural S(-)- bupivacaine: comparison with racemic RS - bupivacaine. *Br J Anaesth* 1998; 80(3): 289-93.