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**Comparison of the effects of epidural 0.5% bupivacaine and 0.5% levobupivacaine administration on anesthesia quality, side effect incidence, and analgesia requirement times in hip and lower extremity surgery**

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## Comparison of the effects of epidural 0.5% bupivacaine and 0.5% levobupivacaine administration on anesthesia quality, side effect incidence, and analgesia requirement times in hip and lower extremity surgery

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**Aim:** To compare the anesthetic effectiveness of epidural levobupivacaine and bupivacaine without adjuvant medication in patients who were to have elective operations on the lower extremities and hips.

**Materials and methods:** This study was conducted on a total of 70 ASA I-II patients aged between 30 and 70 years, who underwent elective hip and lower extremity operations. The patients that received bupivacaine were assigned to Group B (n = 35) and those that received levobupivacaine to Group L (n = 35).

**Results:** No statistically 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, noninvasive systolic artery pressure, diastolic artery pressure, mean artery pressure, and peripheral oxygen saturation values ( $P > 0.05$ ).

**Conclusion:** Levobupivacaine could be a good alternative to bupivacaine in patients administered epidural anesthesia in elective hip and lower extremity operations in terms of hemodynamic parameters, quality of anesthesia and analgesia, patient and surgeon satisfaction, and complications.

**Key words:** Epidural anesthesia, bupivacaine, levobupivacaine, lower extremity and hip operation

### 1. Introduction

Spinal and epidural anesthesia techniques are regional anesthesia methods that are widely used, especially in lower abdominal and lower extremity operations (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 agents are being developed for use instead of the isomers, 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 patients who had elective lower extremity and hip operations.

### 2. Materials and methods

This study was designed and conducted with the approval of the faculty's ethics committee and written consents

were obtained from patients in the Atatürk University Faculty of Medicine, with a total of 70 American Society of Anesthesiology classification (ASA) I-II patients, aged between 30 and 70 years, who underwent elective hip and lower extremity operations enrolled in a prospective, randomized double-blind study.

The patients were assigned randomly by a computer randomization program to receive either isobaric bupivacaine (Marcaine 0.5%, Astra Zeneca, UK) as Group B (n = 35) or to receive isobaric levobupivacaine (Chirocaine 0.5%, Abbott, Norway) as Group L (n = 35).

The patients that accepted the regional anesthesia and did not have any contraindication for this, with a height of between 150 and 180 cm, were included in the study. Patients who rejected the regional anesthesia, were substance abusers or alcohol addicts, or had an allergy to any drugs in the study protocol were excluded from the study. All the patients were premedicated before the operation with 2 mg of midazolam (Dormicum, Roche, France).

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The patients were hydrated with 10 mL/kg of Ringer's lactate before the epidural analgesia. Electrocardiography with standard DII-derivation and monitoring (CAMS II Comprehensive Anesthesia Monitor) of basal systolic, diastolic, and mean blood pressures, and heart rate (HR) was performed, and peripheral oxygen saturation (SpO<sub>2</sub>) was measured with pulse oximetry for all patients taken to the operating room. Demographic data, HRs, and systolic, diastolic, and mean blood pressure values were recorded for all patients before the blockade.

In all patients, the region in which the epidural catheter (Braun, Melsungen, Germany) was inserted was widely cleaned with an antiseptic solution (10% povidone-iodine) and covered with a sterile drape. An epidural catheter was inserted from the L3-L4 or L4-L5 space, with the patient in the sitting position, using the hanging drop technique with an 18-gauge Tuohy needle. The catheter was left at 4 cm in the epidural space and fixed to be protected. After aspiration of the blood, and when blood and oxidative stress was defined as negative, Group B received 5 mL of 0.5% isobaric bupivacaine in the epidural space with 2-min intervals to a total of 15 mL, and Group L received 5 mL of 0.5% isobaric levobupivacaine with 2-min intervals to a total of 15 mL.

Systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), HR, and SpO<sub>2</sub> were measured and recorded after patients were taken to the operating table, following injection of the epidural solution (T1), at 5 (T2), 10 (T3), 20 (T4), 30 (T5) and 60 (T6) min after the solution was administered, and postoperatively in the first (T7) and second (T8) hours.

The sensory block was tested at 2-min intervals by pinprick into the region corresponding to each dermatome of both anterior axillary lines. Absence of pain from a pinprick at the T10 (umbilicus) level 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 of T6 (xiphoid level), regression of 2 segments, and termination were recorded during this monitoring.

The duration between the epidural injection and when sensory block regressed to the L1 (inguinal region) level was accepted as the epidural analgesia duration. When the sensory block reached the thoracic (T6) level, it was accepted as sufficient to start the operation. The degree of motor block of the lower extremity was evaluated using the modified Bromage scale every 2 min.

The Bromage score and onset, termination, and recovery times of the motor block were recorded. Recovery time of motor block was considered as the time when the maximal Bromage score dropped to 1 point.

Postoperative pain of the patients was evaluated with visual analog scale (VAS) scores. The patients were

asked to mark a position indicating the pain severity on a continuous horizontal line between 0 (no pain) at one end and 10 (the most severe pain) at the other end, measured in centimeters.

When VAS scores of the patients were 4 or higher, 3 mg of morphine diluted with 50 µg of fentanyl and 11 mL of isotonic solution was administered as a total of 15 mL of epidural fluid from the epidural space for postoperative analgesia. In addition, initial analgesia requirement time, side effects such as nausea and vomiting or hypotension and bradycardia, patient–surgeon satisfaction, and analgesia quality were recorded for all the patients. Initial analgesia requirement time was accepted as the time when the patients had a postoperative VAS score of 4 or higher.

The patients were stabilized with 1 mg of atropine (Galen, İstanbul, Turkey) when their HRs dropped under 50 beats/min and with ephedrine in 10-mg doses when their MAPs decreased by a rate of 30% of the preoperative value (OSEL, İstanbul, Turkey).

Analgesia quality was evaluated in 3 stages as excellent (no pain, patient comfortable), good with sedation (required mild analgesia), and poor (discomfort with moderate pain or required general anesthesia).

We planned to use propofol if agitation and discomfort were observed in patients. If required, a 30-mg I.V. bolus or 1–2 mg kg<sup>-1</sup> h<sup>-1</sup> propofol infusion (propofol 1%, Fresenius, Germany) was administered.

Surgical satisfaction was recorded as good or poor by asking the surgeons 15 min after the beginning of operation.

The patients taken to the recovery room at the end of the operation were monitored for 60 min. Following stable hemodynamic findings (basal systolic and diastolic blood pressures, HRs), the patients were sent to the clinical wards.

The patients were questioned by another anesthetist about head and back pain and motor and neurological deficit the day after surgery. In addition, the termination time of motor block was asked (when they were able to move their feet) and recorded.

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

### 3. Results

Mean demographic features of the patients such as age, weight, and height were 55.91 vs. 56.77 years, 75.87 vs. 76.22 kg, and 1.76 vs. 1.77 m, 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 for sensory block to reach T6, initial analgesic requirement time, and operation 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 no 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, or 60 min of the epidural block; at the end of the operation; or at the first and second hours after the operation, as 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, and 60 min of the epidural block; at the end of the operation; or at the first and second hours after the operation, as compared to the preoperative DAP values ( $P > 0.05$ ).

When pulse values of the groups were compared, no significant difference was found between Group B and Group L in HR values at 5, 10, 20, or 30 min of the epidural block; at the end of the operation; or at the first and second hours of postoperative time, as compared to the preoperative HR values. However, a borderline difference was found at 60 min of epidural block between groups ( $P = 0.049$ ) (Table 4).

When SpO<sub>2</sub> values of the groups were compared, no significant difference was found between Group B and Group L in SpO<sub>2</sub> values at 5, 10, 20, or 30 min of epidural block; at the end of the operation; or at the first and second hours after the operation, as compared to the preoperative SpO<sub>2</sub> values.

When side effect rates of the groups were compared, hypotension and nausea-vomiting were seen at 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 tremors in 2 patients. In Group L hypotension was found in 4 patients, bradycardia in 1 patient, nausea-vomiting in 1 patient, and tremors in 1 patient. Postoperative side effects were found to be similar in both groups. No significant side effect was seen in any of the patients after the operation (Table 5).

In our study, analgesia quality was found as excellent in 31 patients and good with sedation in 4 patients in Group B, while it was found as excellent in 32 patients and good with sedation in 3 patients in Group L (Table 6).

Patient and surgeon satisfaction, analgesia quality, and VAS values were compared in all the patients, and no significant difference was found between the groups.

#### 4. Discussion

Advantages of regional anesthesia include consciousness of the patient, early awareness of complications owing to the ongoing cooperation with the patient, protection of the airway reflexes, less thromboembolism, a better hemodynamic stability compared to general anesthesia, and no or fewer motor blocks, while it has

**Table 1.** Comparison of sensory-motor blockade onset and regression times, initial analgesic requirement time, and operation 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 regression time (min)	191.60 ± 9.51	195.60 ± 6.40	-1.801	0.72
Initial analgesic requirement time (min)	207.86 ± 45.96	223.29 ± 40.76	-1.358	0.175
Operation 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					

the disadvantages of late onset of its effects and possible development of motor block (6). This method is preferred by anesthesia physicians, especially in patients who suffer from respiratory system problems (7). Epidural anesthesia followed by epidural postoperative analgesia is also preferred for high-risk cardiac patients (8).

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

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

In their study of 88 patients, Cox et al. (18) found that 0.5% and 0.75% levobupivacaine, administered for

epidural anesthesia, was tolerated by patients as well as bupivacaine was, 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 min for 0.75% levobupivacaine and about 377 min for 0.55% bupivacaine. They reported that the time of sensory block was 32 or 45 min longer compared to equal doses of bupivacaine (about 345 min) and motor block did not occur in 14 of 29 patients who received levobupivacaine, whereas this was the case in only 9 of 29 patients who received bupivacaine.

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

In our study, 75 mg of 0.5% isobaric bupivacaine and 0.5% isobaric levobupivacaine of similar doses were compared in 2 groups, including 35 patients in each that underwent elective hip and lower extremity surgery, in terms of anesthetic and hemodynamic parameters. No toxicity signs were found in any patient. We attributed this to the fact that patients were selected from low-risk groups, and the doses were not at high limits.

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 the times for the sensory block to regress to 2 segments were found as 183.17 and 180.54 min in 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, no statistically significant 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 operation durations.

**Table 3.** SAP 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
Postop. first hour (T7)	121.54 ± 9.86	121.18 ± 8.10	-0.329	0.742
Postop. second hour (T8)	124.43 ± 8.20	127.29 ± 7.89	-1.546	0.122



**Table 4.** HR values of the groups. \*: P < 0.05.

HR (beats/min)	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*
Postop. first h (T7)	84.83 ± 8.266	87.83 ± 7.286	-1.943	0.052
Postop. second h (T8)	86.17 ± 7.015	88.31 ± 6.101	-1.677	0.093

Kopacz and Allen (19) found in the patients to which they administered epidural bupivacaine and levobupivacaine that motor block time was about 1 min shorter in the group that received levobupivacaine. They reported that extremity block occurred within 30 min in only 14% of the patients that received levobupivacaine, compared to 71% of the patients that 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 its peak level within 30 min, remained at the same level at 60 min, and then decreased over time, completely resolving in 350 min.

Our study indicates that epidurally administered bupivacaine produced an analgesia duration of 363 min and levobupivacaine a duration of 347 min, which means that both medications caused a similar analgesic effect. Maximum sensory block height was at the T4 level and maximum motor block diffusion occurred 30 min after 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 (19) evaluated SAP, DAP, MAP, HR, and SpO<sub>2</sub> parameters and did not find a significant difference between the 2 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 undergoing 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 this study.

When Kopacz and Allen (19) compared levobupivacaine and bupivacaine in terms of side effects, they found a similar tolerability profile and, in their study in which levobupivacaine was epidurally administered,

they reported that cardiac depression or central nervous system (CNS) toxicity were not encountered following vascular absorption or direct intravascular injection, with the exception of minimal CNS symptoms (transient agitation and disorientation), which was seen in one patient who incidentally received intravascular injection, and they did not find any signs of cardiovascular system toxicity. In our study, no significant difference was found between the groups in terms of the side effects that were encountered in the perioperative period.

In animal studies, CNS symptoms and convulsions have been shown to occur at lower doses of bupivacaine than levobupivacaine. In a double-blind, randomized study by Van et al. (16) with 12 voluntary patients, 40 mg of intravenously administered levobupivacaine was found, on electroencephalogram, to produce less CNS depression compared to 40 mg of bupivacaine.

Bhatt et al. (21) reported that side effects of levobupivacaine with bupivacaine and other local anesthetics of the amide groups were the same. The most common reported side effects are nausea, postoperative pain, hypotension, fever, headache, and vomiting. These drugs all had a similar safety profile and a low incidence of adverse effects. There was no statistically significant difference in side effects. In our study, as well, there was no statistically significant difference in term of side effects.

**Table 5.** Comparison of the side effects seen in the groups during the operation.

Side effect	Group L	Group B	P
Hypotension	4	5	0.50
Bradycardia	1	3	0.30
Nausea-vomiting	1	3	0.30
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	

No significant difference of the quality of analgesia was recorded between these local agents and all of them provided efficient clinical anesthesia (18,22). In our study, no statistically significant difference was found in the quality of analgesia.

After epidural blockade there was a statistically significant difference in terms of HRs at 60 min. However, this difference of HR is not significant clinically.

Finally, we concluded from this study that there was no difference between 0.5% bupivacaine and 0.5% levobupivacaine in patients receiving epidural anesthesia for hip and lower extremity operations, in terms of motor and sensory blockade onset and regression times, time of sensory block to reach T6, VAS scores, hemodynamic parameters, patient and surgeon satisfaction, side effects, and postoperative analgesia requirement times and that levobupivacaine may be a good alternative to bupivacaine.

## References

- Kleinman W. Regional anesthesia and pain management: spinal, epidural and caudal blocks. In: Morgan GE, Mikhail MS, Murray MJ, editors. *Clinical Anesthesiology*. 3rd ed. Los Angeles: Appleton & Lange; 2002. p.253–82.
- Longo S. Postdural puncture: implications and complications. *Curr Opin Anaesth* 1999; 12: 271–5.
- Bauer M, George JE 3rd, Seif J, Farag E. Recent advances in epidural analgesia. *Anesthesiol Res Pract* 2012; 2012: 309219.
- Apan A, Sarı 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.
- Yurtlu BS, Hancı V, Ege A, Bostankolu SE, Ayoğlu H, Özkoçak 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.
- Ouellette SM, Ouelette R. Regional anesthesia: is it safer? *CRNA* 1995; 6: 70–8.
- Burke D, Kennedy S, Bannister J. Spinal anaesthesia with 0.5% S(-)-bupivacaine for elective lower limb surgery. *Region Anaesth Pain Med* 1999; 24: 519–23.
- Atalay C, Dağlı C, Bayram E, Alici HA, Erdem AF, Keleş MS et al. 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: 405–14.
- Reiz S, Nath S. Cardiotoxicity of local anaesthetic agents. *Br J Anaesth* 1986; 58: 736–46.
- Marx GF. Cardiotoxicity of local anesthetics - the plot thickens. *Anesthesiology* 1984; 60: 3–5.
- 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.
- Aberg G. Toxicological and local anaesthetic effects of optically active isomers of two local anaesthetic compounds. *Acta Pharmacol Toxicol* 1972; 31: 273–86.
- Luduena FP, Bogado EF, Tullar BF. Optical isomers of mepivacaine and bupivacaine. *Arch Int Pharmacodyn Ther* 1972; 200: 359–69.
- McClellan KJ, Spencer CM. Levobupivacaine. *Drugs* 1998; 56: 355–62.
- Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. *Drugs* 2000; 59: 531–79.
- 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 Suppl* 1998; 23: 48.
- Valenzuela C, Snyders DJ, Bennett PB, Tamargo J, Hondeghem LM. Stereoselective block of cardiac sodium channels by bupivacaine in guinea pig ventricular myocytes. *Circulation* 1995; 92: 3014–24.
- Cox CR, Faccenda KA, Gilhooly C, Bannister J, Scott NB, Morrison LM C et al. Extradural S(-)-bupivacaine: comparison with racemic RS-bupivacaine. *Br J Anaesth* 1998; 80: 289–93.
- Kopacz DJ, Allen HW. Accidental intravascular injection of 0.75% levobupivacaine during lumbar epidural anaesthesia. *Anaesth Analg* 1999; 89: 1027–9.
- 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: 1596–601.
- Bhatt SH. Levobupivacaine. A stereo-selective amide local anesthetic. *J Pharm Soc Wiscon* 2001; 3: 28–34.
- 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: 289–93.