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SCIENTIFIC ARTICLE

Addition of lidocaine to levobupivacaine reduces intrathecal block duration: randomized controlled trial

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KEYWORDS

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Abstract

Background: The duration of the spinal block is a concern for anesthetists. Low dose intrathecal lidocaine has vasodilatory effects and increases the local anesthetic clearance from the intrathecal space. The aim was to investigate whether this effect of lidocaine can be used to increase the resolution of levobupivacaine spinal anesthesia.

Method: After obtaining ethical approval and informed patient consent, 40 patients underwent transurethral prostate resection were studied. Patients were randomized into two groups and patients received either levobupivacaine 6.75 mg + 0.3 mL 2% lidocaine (Group L) or levobupivacaine 6.75 mg + saline (Group C). The main outcome measures were the difference between groups regarding the duration of the spinal block and PACU stay. Secondary outcome measures were the difference between groups in onset and resolution of the spinal block, adverse events and treatments were also investigated.

Results: Spinal block resolved faster in Group L than Group C; 162.43 ± 39.4 min vs 219.73 ± 37.3 min ($p=0.000$). PACU time was shorter in Group L (109 ± 49.9 min in Group L vs 148 ± 56.8 min in Group C) ($p=0.036$). There was no difference between groups with respect to the incidence of adverse events and treatments. Groups were also similar regarding complications. PDPH and TNS were not observed in any group.

Conclusion: Addition of low dose lidocaine to hyperbaric levobupivacaine reduces the duration of the intrathecal block provided by hyperbaric levobupivacaine. This technique can be used to reduce the spinal block duration for relatively short procedures like TUR-P.

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Introduction

The duration of the spinal block in short or medium duration procedures is a concern for anesthetists and is studied widely. Lower doses of long acting local anesthetics compromise the efficacy of anesthesia.¹ Adding opioids

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to low dose local anesthetics for outpatient procedures caused urinary retention, unpredictable onset and extension of the spinal block.^{2,3} Low dose lidocaine has vasodilatory effects and increases the local anesthetic clearance from the intrathecal space as shown with a microdialysis technique in animals.⁴ The clinical studies reported controversial results regarding the use of lidocaine to shorten the spinal block resolution.^{5,6} It was hypothesized that the duration of the levobupivacaine intrathecal block could change when performed with hyperbaric levobupivacaine mixed with lidocaine.

Methods

Patients and procedures

It was planned to enroll 40 patients requiring elective transurethral resection of the prostate (TUR-P) with a prospective protocol. All patients signed an informed consent before the operation. The study was conducted in the Yildirim Beyazit Teaching and Research Hospital. Ethical approval for this study was provided by the Yildirim Beyazit EAH Ethical Committee, Ankara, Turkey Ch. Prof I Sencan on 30 June 2009 (Clinical trials Identifier NCT01675895).

Patients with contraindications for spinal anesthesia, known sensitivity to the study drugs, emergency cases, and patients who refused spinal anesthesia were excluded. The following parameters were recorded: gender, age, body mass index (BMI), concomitant diseases, American Society of Anesthesiologists (ASA) physiologic state, and the duration of surgery. Monitoring included electrocardiogram (lead II), heart rate, noninvasive blood pressure and peripheral oxygen saturation. It was ensured that every patient was hydrated 10 mL kg⁻¹ Ringer's lactate solution before the spinal block was commenced. Patients were not premedicated. Patients were randomized by a nurse anesthetist in one of two groups by using computer generated sequence of numbers and sealed envelopes were used for allocation (Fig. 1).

Hyperbaric levobupivacaine was aseptically prepared just before the injection using 30% dextrose (%30 Dekstroz, Turktipsan, Ankara, Turkey) and plain levobupivacaine (Chirocaine 5 mg mL⁻¹ Abbott Laboratories Elverium, Norway). The prepared hyperbaric levobupivacaine was containing 30 mg mL⁻¹ dextrose.⁷ Lidocaine group (Group L) (*n*=20) received 1.5 mL hyperbaric levobupivacaine (Chirocaine® 5 mg mL⁻¹ Abbott Laboratories Elverium, Norway) (6.75 mg) + 0.3 mL 2% lidocaine (6 mg) (%2 Lidokain®, Adeka Ilac Sanayi, Samsun, Turkey) in total 1.8 mL and Control Group (Group C) (*n*=20), hyperbaric levobupivacaine 0.5% (6.75 mg) + saline (100 mL 0.9% Izotonik Sodium Klorur® Turktipsan, Ankara, Turkey) in the same volume. The pH of the mixtures was 5.16 and 5.15 (Corning Phmeter 450, Thermoscientific, 8157 pH electrode). Spinal anesthesia was performed at the L4–5 intervertebral spaces, with the patient placed in the lateral decubitus position: a midline approach was used with a 25 G Quincke needle. After verifying free flow of clear cerebrospinal fluid the prepared solution was injected into the intrathecal space in 30 sec. The patients were placed supine after the injection. Heart rate, blood pressures and peripheral oxygen saturation were

measured and recorded every 5 min. Hypotension (defined as a >30% decrease in the systolic blood pressure in comparison with the baseline values or a systolic blood pressure less than 80 mmHg) was treated with 5 mg i.v. ephedrine or 250 mL crystalloid fluid boluses. Bradycardia (defined as a heart rate ≤50 beats/min) was treated with 0.5 mg i.v. atropine.

Assessment of onset and recovery of the block

The onset and recovery of the block was assessed by an anesthetist who was blind to group allocation. Sensorial block was measured with pinprick test via a 22 gauge hypodermic needle. Assessment was done with 1 min intervals until the maximum block was achieved and with 15 min intervals thereafter until the block resolved to S1 dermatome. Motor block was measured when the sensorial block reached maximum dermatomal spread and when the block resolved to S1. The modified Bromage scale was used (0: no motor loss, full movement; 1: inability to flex the hip; 2: inability to flex the hip and knee; 3: inability to flex the hip, knee and ankle). Time of subarachnoid injection, onset of sensorial block (block at L1 dermatome), time to readiness for surgery (block at T10 dermatome), maximum level of sensorial block, time to reach maximum level of sensorial block was recorded. Resolution was determined with the two segments, T10, L1 and S1 regression of the sensorial block. Time between subarachnoid injection and the regression of the sensorial block to S1 was defined as block duration. The S1 resolution of the sensorial block was chosen for the determination of block duration considering patient comfort during the assessment and since all the patients had an urinary catheter after surgery further assessment was unnecessary. Perirectal sensory evaluation was not done. Surgery started when the block reached the T10 dermatome. A head-down tilt for 5 min was used as a rescue maneuver when the sensorial block did not reach T10. Intra operative use of fentanyl as a rescue analgesic and midazolam for sedation were recorded.

At the end of the surgery the patients were transferred to the post anesthesia care unit (PACU). After the block was resolved to S1 dermatome and fulfilling an Aldrete score ≥9, patients were transferred to the surgical ward. Pain was measured with a visual analog scale (VAS) (0: no pain and 10: worst pain ever). Postoperative analgesia was provided with acetaminophen (Parol 10 mg/mL, Atabay Kimya, Istanbul, Turkey) 1000 mg i.v. three times a day with the first dose administered when the block resolved to T12 or earlier when the pain score was >3. Rescue analgesia consisted of peroral 50 mg tramadol (Contramal tb 50 mg Abdi Ibrahim Ilac, Istanbul, Turkey) when the pain score still was >3. The patients were assessed for postdural puncture headache (PDPH) and transient neurologic symptoms (TNS, defined as pain and/or dyesthesia in the buttocks and lower extremities) at the day of surgery and following 3 days. TNS assessments were made with a standardized questionnaire by daily visits during hospitalization and by telephone calls after discharge.

Statistical analysis

Data were expressed as mean (standard deviation) or median (minimum–maximum), where applicable. Shapiro–Wilk test

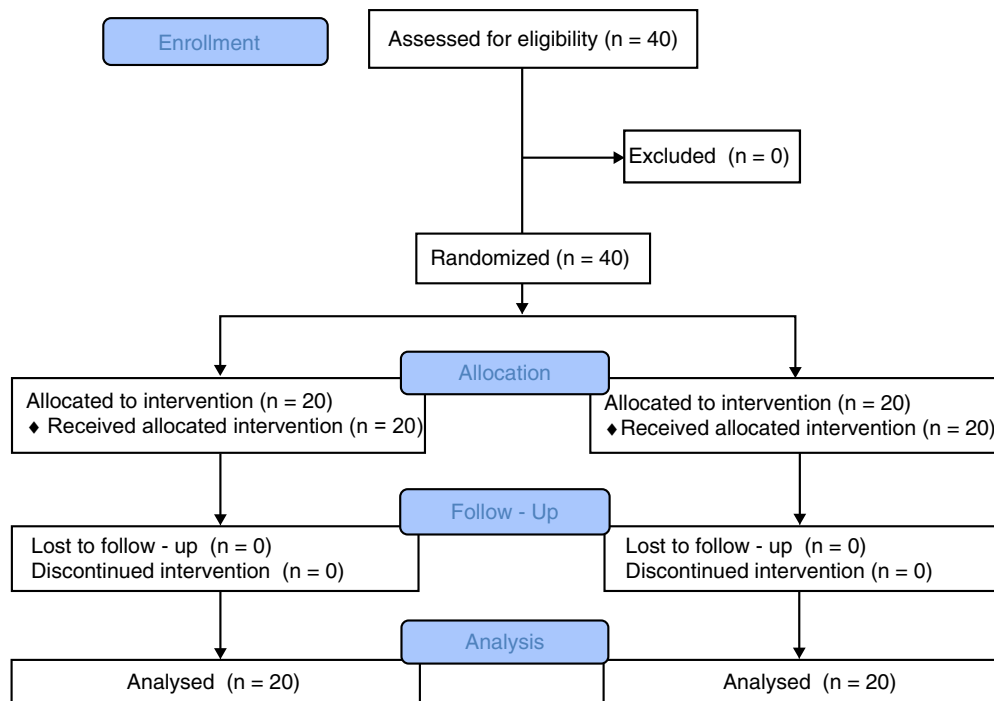


Figure 1 Consort flow diagram of the study.

was used to test the normality of distribution for continuous variables. While the mean differences were compared by unpaired *t* test, Mann–Whitney *U* tests was used for the comparison of median values. Hemodynamic parameters (i.e. systolic, diastolic and mean blood pressures, pulse rate and oxygen saturation) were evaluated by Repeated Measures of ANOVA. The Greenhouse–Geisser test statistics was applied for testing the significance of interaction term (i.e. Time \times Group). Nominal data were analyzed by Fisher's exact test. A *p* value less than 0.05 was considered statistically significant.

A sample size of 19 patients in each group was calculated from a pilot study of 16 subjects which achieved 95% power with a $\alpha = 0.05$ (Group C mean 228.3 ± 50.0 min and Group L mean 172.5 ± 52.3 min for S1 regression times). We included 20 patients in each group for possible dropouts.

The primary endpoint was the difference between groups regarding the duration of the spinal block (S1 regression of the block). Secondary end points were onset of sensorial block (block at L1 dermatome), time to block at T10 dermatome, maximum block level, time to maximum block, the intensity of the motor block at maximum block and the times to two segments regression, T10 regression, L1 regression of the block and postoperative care unit (PACU) stay.

Results

The study was completed with 40 patients. There was no difference between groups regarding age, weight, height and BMI. The duration of surgery was also similar (Table 1). Duration of the spinal block (sensorial block regression to S1) was significantly shorter in Group L (162.43 ± 39.34 min in Group L versus 219.73 ± 37.3 min in Group C; $p = 0.000$). PACU time was also significantly shorter in Group L compared

to Group C (109 ± 49.9 min versus 148.15 ± 56.7 min; $p = 0.036$). Time to T10 blockade was longer in Group L mean 6.55 ± 2.13 min versus 4.55 ± 1.76 min ($p = 0.04$). The block did not reach T10 in 3 patients in Group L a head down rescue maneuver was used for these patients. The time to two segment regression and L1 regression were also significantly shorter in Group L ($p = 0.02$ and $p = 0.02$). Time to T10 regression was not different between groups (Table 2). The onset times of sensory block and the degrees of motor block at the time of maximum blockade were not different. In Group C 9 patients and in Group L 10 patients experienced motor block. The highest Bromage score was 2. The motor block resolved in both groups by the time the block resolved to S1 dermatome. The maximum blocked sensorial level was T8 dermatome (Group C, min T10, max T4 and Group L min T10 max T4). Blood pressures and heart rates of the patients were similar. The mean MAP's were similar at the time that the blocks reached maximum sensory level. There was no difference between groups with respect to the incidence of adverse events complication and treatments. One patient in each group experienced hypotension that needed treatment with intravascular volume expansion and ephedrine and 3 patients in the control group needed treatment with

Table 1 Demographic data.

	Group C (n = 20)	Group L (n = 20)
Age (yr)	68 ± 8.6	68 ± 8.9
Weight (kg)	79.5 ± 11.6	76.4 ± 11.2
Height (m)	1.69 ± 0.06	1.71 ± 0.05
BMI (kg m^{-2})	27.6 ± 4.4	25.8 ± 3.6
Duration of surgery (min)	61.9 ± 32.2	57.5 ± 25.9

Values are mean \pm SD (standard deviation).

Table 2 Onset and recovery profiles of sensory and motor block, and PACU time.

	Group C (n: 20)	Group L (n: 20)	P
<i>Onset profile</i>			
Max sensory block level (median)	T8 (T8 – T6)	T8 (T10 – T4)	0.863
Time to L1 block (onset time) (min)	1.9 (1.07)	1.9 (0.82)	1.000
Time to T10 block (min)*	4.5 (1.76)	6.5 (2.13)	0.004
Motor block (n, max density)	9, Bromage2	10, Bromage2	0.465
Duration (min)*	160.2 (40.1)	131.8 (32.4)	0.003
<i>Recovery profile</i>			
Time to 2-level regression (min)*	97.9 (±38.9)	55.2 (±38.7)	0.002
Time to T10 regression (min)*	97.3 (±45.5)	60.7 (±39.7)	0.019
Time to L1 regression (min)*	160.7 (±44.3)	101 (±64.3)	0.001
Time to S1 regression (min)*	219.73 (±37.3)	162.43 (±39.4)	0.000
PACU time (min)*	148 (±56.8)	109 (±49.9)	0.036

Values are mean ± SD or numbers, except the peak sensory block levels described with median (range).

* There were statistically significant differences between L and C groups regarding the times to sensorial block onset at T10, block regression at T10, L1 and S1, and post anesthesia care unit (PACU) stay.

atropine. Two patients in each group needed additional intraoperative sedation. The total midazolam dose was 5 mg in both groups. The use of postoperative rescue analgesia was also similar. Tramadol 50 mg peroral was used in one patient in both groups at the postoperative sixth hour. Groups were also similar regarding complications (Table 3). PDPH and TNS were not observed in both groups at 3 days follow up.

Discussion

The results showed that 6 mg of 2% lidocaine shortens the duration of the levobupivacaine spinal block approximately 50 min and the PACU stay 45 min. This is an important finding because decreasing the PACU time by at least 10% makes it possible to decrease the number of patients in PACU by 20% this enables PACU's to lower the costs, increase the number of patients admitted, increase the quality of care delivered and reduce the risks after anesthesia.⁸

Evidence concerning duration of the spinal block with levobupivacaine reflects variations. These variations can

be related to dose differences of the local anesthetics administered. Time to S1 sensation recovery from intrathecal administered 2.5 mL 0.5% isobaric levobupivacaine was mean 256.2 min in a previous study.⁹ The same dose isobaric levobupivacaine was also investigated by Cuvas and coworkers. They observed mean 355.2 min for time to regression of the sensory block to S1 dermatome.¹⁰ This was almost twofold the dose used in this study. These studies were conducted with plain levobupivacaine.

Studies with similar doses of hyperbaric levobupivacaine as in this study also reported longer recovery times. Alley et al. assessed the duration of blockade, with spinal hyperbaric levobupivacaine 8 mg 0.5% in volunteers. In their study time to L1 regression was mean 147 min.¹¹ In the present study, time to L1 regression was mean 101 min in the lidocaine added group.

In a previous study Lee and coworkers reported that the addition of lidocaine to bupivacaine provided an increase in the resolution of the spinal block.⁵ On the contrary in a recent report the authors did not confirm this shortening effect of lidocaine. This difference in outcome can be related to differences in methodology. The bupivacaine dose was higher and the patients stayed in the lateral decubitus position after the intrathecal injection.⁶

Although it is expected that adding a short acting local anesthetic to a mixture would speed up the onset of the block we did not observe any difference between groups regarding onset of the block. The dose of lidocaine used was too low to produce local anesthetic action and the pH of both study drugs were similar and asidotic.

In the lidocaine group time to T10 block was longer than the control group. Particularly the block did not reach T10 in 3 patients at the 9th, 10th and 11th min. When administering small doses (3–6 mg) of levobupivacaine, the effect of the posture of the vertebral column can be crucial due to the hyperbaric character of the drug.¹² The results of this study do not explain why the slow onset blocks were only in the lidocaine added group and not in the control group despite the same low dose hyperbaric levobupivacaine. The delay in T10 sensorial block may be important in outpatient

Table 3 Adverse events, complications and treatments during surgery and 3 days follow-up.

	Group C (n=20)	Group L (n=20)
Hypotension	1	1
Bradycardia	3	0
Additional fluids	3	0
Atropine	3	0
Ephedrine	1	0
Nausea/vomiting	1/0	0/0
Additional sedation	2	2
Additional analgesia	1	1
PDPH	0	0
TNS	0	0

Data are presented as counts of frequencies.

There was no statistically significant differences between the groups.

anesthesia by effecting readiness for surgery and thus prolonging operation room time. The hyperbaric levobupivacaine solution with 30 mg mL⁻¹ dextrose has a density of 1.00945 (0.00016) at 37°C.¹³ The baricity of sodium chloride 0.9% 0.99951 (0.00001) and lidocaine 2% 0.99994 (0.00000) are very close.¹⁴ It was reasonable to accept that there was no clinically relevant difference between the study drugs concerning baricity even if the density of the study drugs were not measured. Consequently, the highest dermatomal spread and maximum block levels were not different.

The resolution of motor block can be a problem in recovery from spinal anesthesia. Adding lidocaine to levobupivacaine did neither affect the incidence nor the density of the motor block.

The overall incidence of adverse events (hypotension, bradycardia, nausea) was low in both groups. TNS after spinal anesthesia have been reported most commonly in association with lidocaine, but have been observed with other local anesthetics. After spinal anesthesia with levobupivacaine, the incidence of TNS is much less than after lidocaine. However, it appears that TNS may occur in association with levobupivacaine.¹⁵ The patients were meticulously questioned for such symptoms during the whole study period. We did not observe any TNS.

Levobupivacaine 0.5% mixed with lidocaine 2% is previously used in sub-tenon's anesthesia and infraclavicular block with success.^{16,17} To our knowledge this is the first study using levobupivacaine 5% and lidocaine 1% together in the intrathecal route.

We conclude that spinal anesthesia performed with the levobupivacaine–lidocaine mixture has shorter block duration and provides a shorter PACU stay compared to levobupivacaine alone. This method can be used to reduce the levobupivacaine spinal block duration in TUR-P and operations with similar duration. The validity of this effect of lidocaine on other local anesthetic agents still needs further research.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Arzola C, Wiczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. *Br J Anaesth*. 2011;107:308–18.
2. Bachmann M, Pere P, Kairaluoma PH, et al. Randomised comparison of hyperbaric articaïne and hyperbaric low-dose bupivacaine along with fentanyl in spinal anaesthesia for day-case inguinal herniorrhaphy. *Eur J Anaesthesiol*. 2012;29:22–7.
3. Gupta A, Axelsson K, Thörn SE, et al. Low-dose bupivacaine plus fentanyl for spinal anesthesia during ambulatory inguinal herniorrhaphy: a comparison between 6 mg and 7.5 mg of bupivacaine. *Acta Anaesthesiol Scand*. 2003;47:13–9.
4. Clement R, Malinovsky JM, Corre P, et al. Spinal biopharmaceutics of bupivacaine and lidocaine by microdialysis after their simultaneous administration in rabbits. *Int J Pharm*. 2000;203:227–34.
5. Lee SJ, Bai SJ, Lee JS, et al. The duration of intrathecal bupivacaine mixed with lidocaine. *Anesth Analg*. 2008;107:824–7.
6. Jacobsen J, Husum B, Staffeldt H, et al. The addition of lidocaine to bupivacaine does not shorten the duration of spinal anesthesia: a randomized, double-blinded study of patients undergoing knee arthroscopy. *Anesth Analg*. 2011;113:1272–5.
7. Luck JF, Fettes PD, Wildsmith JA. Spinal anesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. *Br J Anaesth*. 2008;101:705–10.
8. Dexter F, Tinker JH. Analysis of strategies to decrease postanesthesia care unit costs. *Anesthesiology*. 1995;82:94–101.
9. Vana O, Chumsang L, Thongmee S. Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery. *J Med Assoc Thai*. 2006;89:1133–9.
10. Cuvas O, Ongen E, Basar H. Spinal anesthesia for transurethral resection operations: bupivacaine versus levobupivacaine. *Miner Anesthesiol*. 2008;74:697–701.
11. Alley EA, Kopacz DJ, McDonald SB, et al. Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. *Anesth Analg*. 2002;94:188–93.
12. Korhonen AM, Valanne JV, Jokela RM, et al. Influence of the injection site (L2/3 or L3/4) and the posture of the vertebral column selective spinal anesthesia for ambulatory knee arthroscopy. *Acta Anaesthesiol Scand*. 2005;49:72–7.
13. McLeod GA. Density of spinal anesthetic solutions of bupivacaine, levobupivacaine and ropivacaine with and without dextrose. *Br J Anaesth*. 2004;92:547–51.
14. Horlocker TT, Wedel DJ. Density, specific gravity and baricity of spinal anesthetic solutions at body temperature. *Anesth Analg*. 1993;76:1015–8.
15. Eberhart LH, Morin AM, Kranke P, et al. Transient neurologic symptoms after spinal anesthesia. A quantitative systematic overview (meta-analysis) of randomized controlled studies. *Anaesthesist*. 2002;51:539–46.
16. Raman SV, Barry JS, Murjane S, et al. Comparison of 4% articaïne and 0.5% levobupivacaine/2% lidocaine mixture for sub-Tenon's anesthesia in phacoemulsification cataract surgery: a randomised controlled trial. *Br J Ophthalmol*. 2008;92:496–9.
17. Kuş A, Gürkan Y, Gök CN, et al. Infraclavicular block with ultrasound at amputated upper extremity. *Agri*. 2010;22:134–6.