A Comparison of Spinal Isobaric Levobupivacaine and Racemic Bupivacaine for Lower Abdominal and Lower Extremity Surgery

Thepakorn Sathitkarnmanee MD*, Cattleya Thongrong MD*,
Sirirat Tribuddharat MD*, Maneerat Thananun BN*,
Khochakorn Palachewa BN*, Radda Kamhom BN*

** Department of Anesthesiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*

Background: *Levobupivacaine is a new long-acting local anesthetic, which is the isolated S-enantiomer of racemic bupivacaine with less cardiovascular and central nervous system toxicity than bupivacaine. Reports using levobupivacaine for epidural or brachial plexus anesthesia suggested equivalent clinical efficacy to bupivacaine. However, inadequate information for spinal anesthesia was found.*

Objective: *To study the onset of motor block and other anesthetic efficacy of intrathecally administered racemic bupivacaine compared with levobupivacaine.*

Material and Method: *A prospective randomized double blind study at Srinagarind Hospital included seventy patients aged 18-65 years, ASA I-II, scheduled for elective lower abdominal and lower extremity surgery under spinal anesthesia was done. Exclusion criteria were known hypersensitivity to amide local anesthetics, contraindication against spinal anesthesia, morbid obesity, or patient unable to understand the study protocol. The patients were divided into two groups. They received either 0.5% isobaric racemic bupivacaine 3 mL or 0.5% isobaric levobupivacaine 3 mL for spinal anesthesia. The measurement included vital signs, peak block height, motor and sensory blockade and side effects.*

Results: *There was no significant difference between the two groups in the quality of motor and sensory block (p-value > 0.05). The median of peak block height of racemic bupivacaine and levobupivacaine group was T9 (T6-T12) and T9 (T4-T12) respectively. A few adverse events were detected and treated carefully, with no clinically significant difference between groups.*

Conclusion: *The present study indicated that 15 mg of isobaric racemic bupivacaine and levobupivacaine for spinal anesthesia had equivalent peak block height and showed equally effective efficacy regarding to both the onset time and duration of motor and sensory blockade.*

Keywords: *Levobupivacaine, Racemic bupivacaine, Isobaric, Intrathecal, Spinal anesthesia, Motor block*

J Med Assoc Thai 2011; 94 (6): 716-20
Full text. e-Journal: *http://www.mat.or.th/journal*

Bupivacaine has been used for decades. For lower abdominal and lower extremity surgery, spinal anesthesia with racemic bupivacaine is a preferable choice of anesthesiologists. The duration of effect of 3-6 h can be assumed, but high relative cardiac toxicity of bupivacaine has been known since publications dating from the late 1970s, such as hypotension, atrioventricular block, idioventricular rhythms, ventricular tachycardia and fibrillation[1-3]. Levobupivacaine, an amide local anesthetic agent that is the isolated S-enantiomer of racemic bupivacaine, is a new long-acting local anesthetic agent that has recently been introduced for clinical use. It has less cardiovascular and central nervous system toxicity than bupivacaine[4-6]. Reports using levobupivacaine for epidural anesthesia or brachial plexus anesthesia suggested equivalent clinical efficacy to bupivacaine.

A few studies have investigated levobupivacaine and racemic bupivacaine for spinal anesthesia in hip replacement, urological surgery, inguinal herniorrhaphy, or knee arthroscopy[7-10]. However, some information is missing, especially for onset time of motor block, has been found. The present study aimed to investigate the onset of motor block of Intrathecal racemic bupivacaine compared with levobupivacaine in a prospective randomized double-blinded study.

Correspondence to:
Sathitkarnmanee T, Department of Anesthesiology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: 081-954-7622
E-mail: thepakorns@gmail.com

Material and Method

After approved by the Human Research Ethics Committee, Khon Kaen University and informed consent were obtained, 70 patients aged 18-65 years, American Society of Anesthesiologists (ASA) physical status I-II, scheduled for elective lower abdominal and lower extremity surgery under spinal anesthesia were enrolled. Exclusion criteria were known hypersensitivity to amide local anesthetics, general contraindication against spinal anesthesia, morbid obesity, or patients unable to understand the study protocol because of language problem or other reasons. The patients were randomly allocated to two groups receiving either 0.5% isobaric racemic bupivacaine 3 mL or 0.5% isobaric levobupivacaine 3 mL for spinal anesthesia, according to a computer-generated randomization list kept in sealed envelopes. After intravenous fluid preload of balanced salt solution (10 mL/kg), both drugs were administered intrathecally, under aseptic conditions with the patients in the lateral decubitus position, through a 25-gauge Quincke needle at L3-4. Immediately after drug administration, the patients were turned into a supine position. Vital signs, peak block height, motor and sensory blockade were recorded, using modified Bromage score (MBS, 0 = full flexion of knee and feet, 1 = just able to move knees, 2 = able to move feet only, 3 = unable to move feet and knees) and pinprick test respectively, every 2 minutes for up to 30 minutes after spinal anesthesia and every 15 minutes postoperatively until the sensory and motor variables were back to normal.

The anesthetic solution was prepared immediately before injection by an anesthesiologist who was not involved in patient care and assessment was performed by blinded nurse anesthetists.

The onset time of motor or sensory blockade started from time of drug administration to time of MBS equal to 1 or maximal spread of the sensory block. The duration of motor or sensory blockade was defined as the interval from drug administration to the point in which MBS was back to zero, or 2-segment sensory regression.

If inadequate or failed block occurred, the protocol was switched to general anesthesia. Decrease of blood pressure more than 20% from baseline or mean arterial pressure < 60 mmHg was defined as hypotension and would be treated with IV fluid or ephedrine bolus 6-12 mg. Heart rate < 50 bpm was defined as bradycardia and would be treated with atropine 0.02 mg/kg. Decrease in SpO_2 to < 92% was defined as hypoxemia and was treated with supplement oxygen via face mask. If nausea and vomiting occurred, ondansetron 0.1 mg/kg would be given intravenously.

Data were analyzed using SPSS version 11.0. The Student's t-test was used for continuous data, and Chi-square test or Fishers' exact test was used for categorical data. Results were considered statistically significant if $p < 0.05$.

Results

Seventy patients were enrolled in the present study. Demographic data is shown in Table 1. There was no significant difference between the two groups in onset time and duration of motor and sensory block ($p > 0.05$) as shown in Table 2. The median of peak block height of racemic bupivacaine and levobupivacaine group was T9 (T6-T12) and T9 (T4-T12) respectively. One patient in the levobupivacaine group required general anesthesia because of inadequate block. In the racemic bupivacaine group, one patient received supplemental sedative drug (midazolam 2 mg IV) during surgery because of anxiety and one patient required general anesthesia during operation because the operation was too long. A few adverse events, with no significant between groups, were detected and treated carefully (Table 3).

Discussion

The present study demonstrates that levobupivacaine, the pure S(-)-enantiomer of racemic bupivacaine, is increasingly popular because of its equipotency with lower cardiovascular and central nervous system side effect. The onset of motor block is one of the important qualities of local anesthetic agent used for spinal anesthesia, as delayed onset time will cause a delay in starting surgery, which may be too much time consuming.

The pharmacokinetic properties of spinal isobaric levobupivacaine in the present study are comparable to racemic bupivacaine, which is similar to other studies. Christian et al[4] reported that 0.5% spinal levobupivacaine and 0.5% isobaric racemic bupivacaine 3.5 mL for elective hip replacement achieved similar clinical effects, including sensory and motor block. This result was confirmed by Lee et al[10], who suggested that 0.5% levobupivacaine could be used as an alternative to 0.5% racemic bupivacaine in spinal anesthesia for urological surgery when a sensory block to at least T10 is required. Vanna et al[11] reported a study comparing 0.5% isobaric levobupivacaine and 0.5% hyperbaric bupivacaine for transurethral

Table 1. Demographic data

Variables	Racemic bupivacaine (n = 35)	Levobupivacaine (n = 35)
Age (year)	36.8 (12.67)	43.25 (14.22)
Sex (male:female)	27: 8 (77.1%:22.9%)	21: 14 (60%:40%)
Weight (kg)	56.94 (10)	57.07 (12.99)
Height (cm)	162.02 (9.82)	160.14 (8.32)
ASA (I:II)	27: 8 (77.1%:22.9%)	30: 5 (85.7%:14.3%)
Duration of surgery (min)	66.57 (34.35)	68.71 (45.92)
Type of surgery		
General	7 (20%)	7 (20%)
Gynecologic	6 (17.1%)	14 (40%)
Orthopedic	14 (40%)	12 (34.3%)
Urologic	7 (20%)	2 (5.7%)
Plastic	1 (2.9%)	0

Values are shown as mean (SD) and frequency (percentage)

Table 2. Anesthetic efficacy between racemic bupivacaine and levobupivacaine

Outcome (min)	Racemic bupivacaine	Levobupivacaine	p-value	Mean difference	95%CI of mean difference
Motor onset time	4.45 (3.25)	4.70 (4.56)	0.80	0.23	–2.13-1.66
Sensory onset time	17.37 (7.99)	15.35 (7.29)	0.28	1.94	–1.69-5.57
Duration of motor block	353.42 (82.41)	340.41 (80.61)	0.44	14.00	–23.08-51.08
Duration of sensory block	137.02 (40.01)	136.14 (45.32)	0.89	1.55	–25.01-21.89

Values are shown as mean (SD). No significant differences between groups

Table 3. Adverse events between racemic bupivacaine and levobupivacaine

Variable	Racemic bupivacaine (n = 35)	Levobupivacaine (n = 35)	p-value
Hypotension	1 (2.9%)	5 (14.3%)	0.19
Bradycardia	1 (2.9%)	2 (5.7%)	1.00
Hypoxia	1 (2.9%)	0 (0%)	1.00
Nausea/vomiting	2 (5.7%)	1 (2.9%)	1.00

Values are shown in frequency (percentage). No significant differences between groups

endoscopic surgery and found that onset time and duration of sensory and motor block, peak block height, and hemodynamic parameters are similar.

Incidence of hypotension in the levobupivacaine group is slightly higher than the racemic bupivacaine group (14.3% vs. 2.9%) but without significance (p = 0.19). Lee et al[9] found that the peak level of sensory block with 2.6 ml of spinal levobupivacaine ranged between T3-T10, causing side effects such as hypotension, bradycardia, hypoxemia, or shivering. Other side effects such as bradycardia, hypoxemia and nausea/vomiting are mild, few and comparable between the two group.

Conclusion

The results of the present study showed that 3 mL of 0.5% isobaric racemic bupivacaine and 0.5% isobaric levobupivacaine for spinal anesthesia had equivalent peak block height and showed equally effective efficacy regarding both the onset time and duration of motor and sensory blockade. Spinal levobupivacaine is an alternative to bupivacaine in

lower abdominal and lower extremity surgery, and no serious side effects occurred.

Potential conflicts of interest

This research was funded by Faculty of Medicine, Khon Kaen University.

References

1. Burke D, Kennedy S, Bannister J. Spinal anesthesia with 0.5% S(-)-bupivacaine for elective lower limb surgery. Reg Anesth Pain Med 1999; 24: 519-23.
2. Casati A, Putzu M. Bupivacaine, levobupivacaine and ropivacaine: are they clinically different? Best Pract Res Clin Anaesthesiol 2005; 19: 247-68.
3. Gristwood RW. Cardiac and CNS toxicity of levo-bupivacaine: strengths of evidence for advantage over bupivacaine. Drug Saf 2002; 25: 153-63.
4. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, et al. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesth Analg 2002; 94: 194-8.
5. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. Drugs 2000; 59: 551-79.
6. McClellan KJ, Spencer CM. Levobupivacaine. Drugs 1998; 56: 355-62; discussion 363-4.
7. Casati A, Moizo E, Marchetti C, Vinciguerra F. A prospective, randomized, double-blind comparison of unilateral spinal anesthesia with hyperbaric bupivacaine, ropivacaine, or levobupivacaine for inguinal herniorrhaphy. Anesth Analg 2004; 99: 1387-92.
8. Alley EA, Kopacz DJ, McDonald SB, Liu SS. Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. Anesth Analg 2002; 94: 188-93.
9. Cappelleri G, Aldegheri G, Danelli G, Marchetti C, Nuzzi M, Iannandrea G, et al. Spinal anesthesia with hyperbaric levobupivacaine and ropivacaine for outpatient knee arthroscopy: a prospective, randomized, double-blind study. Anesth Analg 2005; 101: 77-82.
10. Lee YY, Muchhal K, Chan CK. Levobupivacaine versus racemic bupivacaine in spinal anaesthesia for urological surgery. Anaesth Intensive Care 2003; 31: 637-41.
11. Vanna O, Chumsang L, Thongmee S. Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery. J Med Assoc Thai 2006; 89: 1133-9.

การศึกษาเปรียบเทียบผลของยาชา levobupivacaine และ racemic bupivacaine ในการฉีดยาเข้าช่องน้ำไขสันหลัง สำหรับการผ่าตัดตั้งแต่ช่องท้องส่วนล่างลงมาในโรงพยาบาลศรีนครินทร์

เทพกร สาธิตการมณี, คัทลียา ทองรอง, สิริรัตน์ ตรีพุทธรัตน์, มณีรัตน์ ธนานันต์, กชกร พลาชีวะ, รัดดา กำหอม

ภูมิหลัง: *Levobupivacaine เป็น isolated S-enantiomer ของ racemic bupivacaine ซึ่งมีคุณสมบัติคล้ายกัน แต่มีผลข้างเคียงต่อระบบหัวใจและหลอดเลือดและระบบประสาทที่รุนแรงน้อยกว่า ซึ่งนิยมใช้กับผู้ป่วยในกลุ่มสูติกรรม เช่น epidural block และการทำ brachial plexus block และ infiltration analgesia แต่สำหรับการทำ spinal block ยังไม่มีแพร่หลาย*

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบระยะเวลาในการเริ่มออกฤทธิ์ motor block และประสิทธิภาพอย่างอื่นของยา 0.5% isobaric racemic bupivacaine 15 มก. กับ 0.5% isobaric levobupivacaine 15 มก. สำหรับการผ่าตัดตั้งแต่ช่องท้องส่วนล่างลงมา*

รูปแบบงานวิจัย: *Prospective randomized double blind study*

วิธีการศึกษา: *ศึกษาในผู้ป่วย 70 ราย อายุ 18-65 ปี ที่มารับการผ่าตัดตั้งแต่ช่องท้องส่วนล่างลงมา ในโรงพยาบาลศรีนครินทร์โดยมี ASA status I-II ไม่มีประวัติแพ้ amide local anesthetics ไม่มีข้อห้ามในการระงับความรู้สึกโดยฉีดยาเข้าช่องน้ำไขสันหลัง และไม่มีภาวะ morbid obesity แบ่งผู้ป่วยออกเป็น 2 กลุ่ม ด้วยวิธีการสุ่มโดย computer และปิดผนึกซอง กลุ่มที่ 1 จำนวน 35 รายได้รับ 0.5% isobaric racemic bupivacaine 3 มล. กลุ่มที่ 2 จำนวน 35 ราย ได้รับ 0.5% isobaric levobupivacaine 3 มล. ซึ่งเตรียมโดยบุคคลที่ไม่ได้เป็นผู้ฉีดยา จัดท่านอนตะแคงซ้าย เลือกระดับ L3-4 ใช้ spinal needle No. 25 ทั้ง 2 กลุ่ม*

ผลการศึกษา: *ผู้ป่วย 2 กลุ่มที่ทำการศึกษาพบว่ามีความแตกต่างกันอย่างไม่มีนัยสำคัญทางสถิติ (p-value > 0.05) ทั้ง motor และ sensory ในด้านของ onset time และ duration โดยมีค่ามัธยฐานของระดับการชาสูงสุดในกลุ่ม isobaric racemic bupivacaine และ levobupivacaine อยู่ที่ระดับ T9 (T6-T12) และ T9 (T4-T12) ตามลำดับ ส่วนผลข้างเคียง จาก spinal block ทั้ง 2 กลุ่มพบเพียงเล็กน้อย ซึ่งทุกคนได้รับการรักษาและไม่มีอันตรายร้ายแรง*

สรุป: *การศึกษานี้แสดงให้ทราบว่า isobaric racemic bupivacaine และ isobaric levobupivacaine ขนาด 15 มก. สำหรับการฉีดยาเข้าทางช่องน้ำไขสันหลัง มีประสิทธิภาพในการระงับความรู้สึกที่ไม่แตกต่างกันทั้งระดับการชาสูงสุด onset time และ duration ของ motor และ sensory block รวมทั้งผลข้างเคียง*