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A Comparison of Levobupivacaine and Ropivacaine for Interscalene and Femoral Nerve Blocks: A Randomized, Double-Blind, Prospective Clinical Trial

Marie Hanna[1]* and Paul Sloan[2]

[1]Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland, USA

[2]Department of Anesthesiology, University of Kentucky, Lexington, Kentucky, USA

Abstract

Study Objective: To compare the quality of perioperative analgesia provided by levobupivacaine 0.5% and ropivacaine 0.5%.

Design: Randomized, double-blind, prospective clinical trial.

Setting: Operating room of a university medical center.

Patients: Thirty-five patients undergoing shoulder arthroscopy and thirty-six patients undergoing anterior cruciate ligament (ACL) reconstruction.

Interventions: Patients undergoing shoulder arthroscopy were administered interscalene blocks, and patients undergoing ACL reconstruction were administered femoral nerve blocks. Patients in each group were randomized to receive either levobupivacaine 0.5% or ropivacaine 0.5%.

Measurements: On postoperative days one and two, patients reported on the time of postoperative pain onset, the time when movement resumed in the operative limb, the time when pain medication was first required, and the amount of pain medication used. Patient satisfaction was measured 48 hours after the procedure on a 1–10 verbal numeric rating scale.

Main results: Time to onset of anesthesia, intraoperative and postoperative opioid requirements, duration of postoperative analgesia, and overall patient satisfaction were similar between patients who received levobupivacaine and those who received ropivacaine.

Conclusions: The study demonstrates that levobupivacaine and ropivacaine produce comparable postoperative analgesia when used for interscalene and femoral nerve blocks.

Keywords: Levobupivacaine; Ropivacaine; Interscalene block; Femoral block; Postoperative analgesia; Local anesthetics

Abbreviations: ACL: Anterior Cruciate Ligament; CNS: Central Nervous System; PACU: Post-Anesthesia Care Unit; VAS: Visual Analog Scale

Introduction

The use of regional anesthesia in arthroscopic orthopedic procedures has been shown to provide effective and comfortable intraoperative conditions. Regional anesthetic techniques can be used for prolonged procedures, offer quicker recovery than general anesthesia, and produce minimal side effects [1]. Historically, interscalene blocks have been used for arthroscopic rotator cuff repair [2], and femoral nerve blocks have been used for arthroscopic anterior cruciate ligament (ACL) reconstruction [3]. Such peripheral nerve blocks were generally performed with racemic bupivacaine; however, in recent years there has been a switch to ropivacaine owing to its more favorable clinical profile [4,5] and lower toxicity [6]. Levobupivacaine, an S-enantiomer of bupivacaine, has become the favored drug for various other types of regional anesthesia [7]. Clinical studies have shown that levobupivacaine and ropivacaine have fewer adverse affects on the cardiovascular system and central nervous system (CNS) than does bupivacaine [8-10], making them more advantageous in regional anesthetic techniques that require large volumes of local anesthetics. However, reports are conflicting in regard to the relative potencies of ropivacaine and bupivacaine for use in peripheral nerve blocks.

Animal studies on conduction blocks produced by bupivacaine, levobupivacaine, and ropivacaine in isolated nerves showed that the onset and duration of nerve block induced by equimolar doses of these three agents are similar [11]. Several studies comparing ropivacaine with levobupivacaine and racemic bupivacaine for different nerve blocks showed that nerve blocks produced by ropivacaine have a clinical profile similar to that obtained with bupivacaine and levobupivacaine when used at similar concentrations and doses [4,11,12]. Other studies, however, found prolongation of sensory analgesia with levobupivacaine compared to ropivacaine [13]. A recent clinical trial comparing levobupivacaine 0.5% with ropivacaine 0.5% for the management of postoperative ankle surgery pain found that levobupivacaine provided more long lasting postoperative analgesia compared with the same dose

***Corresponding author:** Marie N. Hanna, MD, Assistant Professor, Department of Anesthesiology, Johns Hopkins University, 600 N. Wolfe Street, Carnegie 280, Baltimore, MD 21287, USA, Tel: (410) 955-5608; Fax: (410) 614-1796; **E-mail**: mhanna9@jhmi.edu

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of ropivacaine [14]. In the obstetric literature, some studies of epidural analgesia for labor pain have shown that ropivacaine is 19% less potent than levobupivacaine and 30% less potent than bupivacaine [15,16].

The current literature has limited data comparing the clinical use of ropivacaine and levobupivacaine for single-dose femoral nerve blocks and interscalene blocks in the management of postoperative analgesia. The purpose of this prospective, randomized, double-blind study was to compare the perioperative analgesia of patients who received 30 mL of either levobupivacaine 0.5% with epinephrine 2.5 mcg/mL or ropivacaine 0.5% with epinephrine 2.5 mcg/mL when used in interscalene blocks for shoulder arthroscopy and in femoral nerve blocks for ACL reconstruction.

Methods

IRB approval was obtained from the institution before study recruitment began. We recruited patients 18–55 years old (ASA I, II) with a body weight of 60 to 100 kg who were undergoing shoulder arthroscopy or ACL reconstruction. Patients with severe bronchopulmonary disease, diabetes, neuropathy, or documented allergies to analgesics, or who were receiving chronic analgesic therapy were excluded from the study. Procedures that lasted for more than 3 hours and reoperations were also excluded. Thirty-five patients undergoing shoulder arthroscopy and thirty-six patients undergoing ACL reconstruction were enrolled. Each enrolled subject provided written informed consent before any procedure was performed.

Patients undergoing shoulder arthroscopy were administered interscalene blocks and were randomly allocated to receive either a 30 mL solution of levobupivacaine 0.5% (17 patients; Group 1A) or a 30 mL solution of ropivacaine 0.5% (18 patients; Group 2A). Patients undergoing ACL reconstruction were administered femoral nerve blocks and were randomly allocated to receive a 30 mL solution of levobupivacaine 0.5% (18 patients; Group 1B) or a 30 mL solution of ropivacaine 0.5% (18 patients; Group 2B). Randomization sequence was computer-generated and prepared in a double-blind manner. Local anesthetic solutions contained epinephrine (2.5 mcg/mL) and were prepared by the hospital central pharmacy and labeled with the patient's study number.

All peripheral nerve blocks were carried out in the preoperative area 30 minutes before surgery by a resident under the supervision of a regional anesthesiologist who was involved in the study. Both the residents and the anesthesiologists were blinded to the type of local anesthetic injected. Midazolam (0.02–0.05 mg/kg, IV) was given as premedication, standard monitors were placed, and oxygen was administered by nasal cannula. All blocks were completed using a nerve stimulation technique with a 22-gauge, 2-inch, Stimuplex needle (B. Braun, Bethlehem, PA). Local anesthetics were injected after the appropriate nerve stimulation response was obtained below 0.5 mA. Single shot interscalene block was performed after the appropriate anatomical landmark was identified (lateral border of sternocleidomastoid, groove between anterior and middle scalene muscles at the level of the 6th cricoid cartilage) and after motor stimulation of the pectoralis major or biceps muscle was obtained. Single shot femoral nerve block was performed after the anatomical landmark 1 to 1.5 inches lateral to the femoral artery at the inguinal groove was identified and after motor stimulation of the quadriceps muscle was obtained.

Date	_____		
Patient age	_____		
Patient weight	_____	PHONE ( ) _____-_____	
ASA status	_____	Appendix B received:	Y / N
Allergies	_____		
Randomization#	_____		
Surgery	_____		
Exclusion Criteria (Y / N)		Inclusion criteria (Y / N)	
DM/periph. Neuropathy	_____	Shoulder arthroscopy/ACL	_____
Chronic Analgesic Rx	_____	18-55 years old	_____
Local Anesth Allergy	_____	ASA I or II	_____
Mental/Psych Disorder	_____	Body weight 60 – 100 kg	_____
Respiratory dysfunction	_____		
Adverse event during INB/FNB	_____		
Surgery > 3 hours	_____	Consent signed	_____
INB/ FNB Procedure:			
30 cc + Epi given in increments Y / N	_____		
Zero time (completion of injection)	_____		
Five minute check (+/-)	sensory _____	motor _____	
Ten minute check	sensory _____	motor _____	
15 minute check	sensory _____	motor _____	
20 minute check	sensory _____	motor _____	
25 minute check	sensory _____	motor _____	
30 minute check	sensory _____	motor _____	
Surgical anesthesia began @	_____		
Surgery Start time	_____	End time _____	
Narcotic requirements	First hour	_____mcg fentanyl	
	Second hour	_____mcg fentanyl	
	Third hour	_____mcg fentanyl	
PACU			
Narcotic requirements	_____mg MSO4,	Other _____	
Pain scale on arrival		_____ (out of 10)	
Pain scale on departure		_____ (out of 10)	
Able to sense pinprick		_____(Y / N)	
Intra-articular pain pump		_____(Y / N)	

Figure 1: Peripheral nerve blocks follow-up sheet 1.

Introduce yourself to the study patient and remind them that this is a follow-up.
During the course of the conversation, ask the following questions:

First follow-up POD#1:

1. Did you wake up in the night in pain?
2. How would you rate your pain (0 -10)?
3. How often are you taking pain medication?
4. How many pills have you taken?
5. Can you move your arm? Elevate your leg?
6. When did you first notice you could move it?
7. Do you have any questions?

Second follow-up POD#2

1. How often have you been taking pain medication?
2. How many pills have you taken?
3. Has all of the sensation in the shoulder/ knee returned?
4. Are you able to move your shoulder? Your leg?
5. Are you experiencing any difficulties you are concerned may be related to the block?
6. Do you have any questions or concerns?
7. Would you have this procedure done again if you needed surgery again?
8. Are you satisfied with the overall experience?

Complications: _____

_____

_____.

Summary of home follow-up			
Time/date of first pain pill _____	Pain scale POD #1	_____ (out of 10)	Time _____
	Pain scale POD #2	_____ (out of 10)	Time _____
Time/date first noticed onset of movement	_____	Narcotics used 0-12 hr: _____	
Time/date first noticed return of sensation	_____		
	12-24 hr: _____		
Total analgesia time (sensory)	_____	24-36 hr: _____	
Total anesthesia time (motor)	_____	36-48 hr:	

Remind the patient that the Orthopedics team is in charge of their pain medication and would address these concerns if needed.
Thank them for participating in the study

Figure 2: Peripheral nerve blocks follow-up sheet 2.

Clinical Outcome Parameter	Levobupivacaine (Group 1A)	Ropivacaine (Group 2A)	*P* value
Onset of surgical anesthesia (min)	16.5 (1.2)	19.2 (1.1)	0.10
Intraoperative fentanyl requirement (mcg)	27.9 (10.5)	44.4 (15.1)	0.38
Morphine requirement in PACU (mg)	1.9 (0.9)	1.8 (0.8)	0.93
Initial VAS pain score in PACU	1.6 (0.7)	1.9 (0.7)	0.73
Time from block placement to first request for oral pain medication (hrs)	17.5 (2.0)	17.7 (2.0)	0.95
Number of (oxycodone 5 mg/acetaminophen 325 mg) tablets used in first 48 hrs	4.9 (0.6)	3.8 (0.4)	0.13
Amount of time to absence of motor block (hrs)	22 (1.6)	21 (1.5)	0.54
Sensory block time (hrs)	25 (1.7)	22 (1.5)	0.13
Patient satisfaction with postoperative analgesia (1 = very dissatisfied, 10 = very satisfied)	8.6 (0.2)	8.7 (0.2)	0.81

*Data = Mean (SEM). PACU, post-anesthesia care unit; VAS, visual analog scale

Table 1: Interscalene Blocks for Shoulder Arthroscopy with Levobupivacaine or Ropivacaine*.

An independent and experienced investigator blinded to anesthetic group recorded the onset of sensory and motor blocks for all four groups (Figure 1). In the interscalene groups, sensory block was defined by loss of pinprick sensation in the C4 to C7 distribution, and motor block was identified by the inability to abduct the shoulder against gravity. For the femoral nerve block groups, the onset of sensory block was defined by loss of pinprick sensation in the femoral nerve distribution and motor block by the inability to extend the leg from the flexed position. Time zero for clinical assessment for all of the groups was considered to be at the completion of local anesthetic injection.

After the block was established, all patients received standard general anesthesia with appropriate induction agents along with fentanyl (0.5–1.5 mcg/kg, IV) to aid in control of hemodynamic changes during airway manipulation. Intraoperative opioid requirements in the form of incremental doses of fentanyl were recorded after the airway was controlled. All operative procedures required less than 3 hours to complete. Intra-articular pain pumps are not used routinely in our institution and were not used in any of these cases. Once patients arrived in the post-anesthesia care unit (PACU), visual analog scale (VAS) pain scores and opioid (morphine, IV) requirements were recorded by a blinded investigator (Figure 1). All patients were discharged home on the day of surgery and given an opioid prescription (oxycodone 5 mg/acetaminophen 325 mg) postoperatively. Patients were discharged home per PACU protocol when pain was controlled, vital signs were stable, and perioperative complications were absent.

On postoperative days one and two, patients were contacted by a physician blinded to treatment group and asked a set of standard questions (Figure 2) regarding the time of postoperative pain onset, the time when movement resumed in the operative limb, the time when pain medication was first required, and the amount of oxycodone 5

mg/acetaminophen 325 mg used on postoperative days one and two. Patient satisfaction was measured 48 hours after the procedure by using a 1–10 verbal numeric rating scale (1 = very unsatisfactory; 10 = very satisfactory). The PACU VAS pain scores and amount of opioids used in the PACU were used to compare immediate postoperative pain relief. Oral pain medication used in the first 48 hours after surgery was used as a measurement of the quality of block achieved with each analgesic. The time between the block placement and the first request for oral pain medicine was used to compare the analgesic duration of the drugs. The time to onset of complete sensory and motor block was used to compare onset of action. The time to absence of motor block was used to differentiate the clinical properties of the two local anesthetics.

We determined sample size to be consistent with 80% power. A 3-hour difference in sensory or motor block duration was considered the no-difference limit. We determined that if no difference was present in sensory or motor block time duration (hours) between the local anesthetics, 50 subjects would be required in each group for the lower limit of a one-sided 95% confidence interval (or equivalently a 90% two-sided confidence interval) to be consistent with that difference. Outcome data were compared between the two groups by unpaired t-test with SigmaStat software (Systat Software Inc., Chicago, IL). A P-value < 0.05 was used to identify statistical significance.

Results

Thirty-five patients (18 male, 17 female) undergoing shoulder arthroscopy completed the study. The mean age was 33 years and the mean body weight was 75 kg. Thirty-six patients (22 male, 14 female) undergoing ACL reconstruction completed the study. The mean age was 28 years and the mean body weight was 78 kg.

Among subjects who underwent the interscalene nerve block, the data revealed no difference in outcome between those who received levobupivacaine and those who received ropivacaine. Mean block onset time was 16.5 minutes for Group 1A and 19.2 minutes for Group 2A (P=0.10; Table 1). Similarly, no difference was observed in patients who underwent femoral nerve block between those who received levobupivacaine and those who received ropivacaine. Mean onset time was 18.1 minutes for Group 1B and 16.1 minutes for Group 2B (P=0.15; Table 2). There were also no significant differences in intraoperative opioid requirements, PACU opioid requirements, or home opioid requirements between patients who received the two drugs (Tables 1 and 2).

Overall, the amount of opioid required intraoperatively was higher in patients who underwent the femoral nerve block (109 mcg fentanyl for Group 1B and 91.0 mcg fentanyl for group 2B) than for those who underwent interscalene nerve block (27.9 mcg fentanyl for Group 1A and 44.4 mcg fentanyl for Group 2A) because the sciatic component was not blocked for the ACL procedure. Likewise, in the PACU, morphine requirements were higher for those who underwent femoral nerve block than for those who underwent interscalene nerve block. In general, all patients in all treatment groups were very satisfied with the relief of postoperative pain. The satisfaction survey showed no difference in satisfaction level between the two groups.

No known complications occurred as a result of either procedure, and only one adverse event was reported among the 71 patients. One patient who underwent interscalene block for shoulder arthroscopy developed numbness around his ipsilateral ear. The patient's numbness resolved 24 hours after discharge, and he was included in the study.

Discussion

This prospective, randomized double-blind clinical trial demonstrates that levobupivacaine and ropivacaine produce comparable analgesic effects in interscalene and femoral nerve blocks for postoperative analgesia.

Clinical studies in various patient populations suggest that levobupivacaine is less potent than bupivacaine and more potent than ropivacaine when used for epidural analgesia [15-18]. It is believed that ropivacaine is less potent because of its lower lipid solubility but that it has the advantage of a stronger differentiation between sensory and motor blocks, a feature that is particularly useful when early mobilization is important to enhance recovery. Both levobupivacaine and ropivacaine are associated with lesser degree of motor block compared to bupivacaine when used for spinal anesthesia [19,20].

Clinical studies have shown that ropivacaine and levobupivacaine are effective in providing peripheral nerve analgesia when used for upper or lower limb surgery, but little information is available regarding their comparable clinical profile [21,22]. Few studies have compared the clinical profile of levobupivacaine and ropivacaine for brachial plexus block or femoral nerve block. Recent studies revealed a substantially similar clinical profile when equal volumes of levobupivacaine 0.5% and ropivacaine 0.5% were compared for use in combined psoas compartment-sciatic nerve block in patients undergoing total hip arthroplasty [23] and for ultrasound-guided popliteal sciatic nerve block in patients undergoing unilateral hallux valgus surgery [24]. At higher concentrations, levobupivacaine might be more potent than ropivacaine. Casati et al. [25] revealed different clinical profiles in the sciatic nerve block when levobupivacaine 0.75% was compared to

Clinical Outcome Parameter	Levobupivacaine (Group 1B)	Ropivacaine (Group 2B)	*P* value
Onset of surgical anesthesia (min)	18.1 (1.1)	16.1 (0.8)	0.15
Intraoperative fentanyl requirement (mcg)	109.7 (14.9)	91.0 (13.1)	0.35
Morphine requirement in PACU (mg)	4.0 (0.7)	4.6 (1.2)	0.68
Initial VAS pain score in PACU	4.6 (0.5)	4.7 (0.4)	0.94
Time from block placement to first request for oral pain medication (hrs)	15.5 (2.0)	14.7 (2.0)	0.76
Number of (oxycodone 5 mg/acetaminophen 325 mg) tablets used in first 48 hrs	5.4 (0.5)	4.8 (0.4)	0.36
Amount of time to absence of motor block (hrs)	26.5 (1.5)	23.5 (1.5)	0.16
Amount of time to absence of sensory block (hrs)	27.5 (1.5)	25.7 (1.5)	0.38
Patient satisfaction with postoperative analgesia (1 = very dissatisfied, 10 = very satisfied)	8.6 (0.2)	8.8 (0.1)	0.46

*Data =Mean (SEM). PACU, post-anesthesia care unit; VAS, visual analog scale

Table 2: Femoral Nerve Blocks for ACL Reconstruction with Levobupivacaine or Ropivacaine*.

ropivacaine 0.75% or levobupivacaine 0.5%. Levobupivacaine 0.75% provided a shorter onset time and longer duration of postoperative analgesia than the same volume of ropivacaine 0.75% and reduced the total use of rescue opioid consumption during the first 24 hours after surgery.

Our study showed that ropivacaine has a clinical profile that is similar to that of levobupivacaine when used for single-dose interscalene block or femoral nerve block at 0.5% concentration. The block onset time and the duration of motor and sensory block in the two groups of patients were similar. The intraoperative opioid requirements, PACU opioid requirements, and home opioid requirements were also similar. Morphine requirements were higher in patients who underwent femoral analgesia for ACL reconstruction than in patients who underwent interscalene block for shoulder arthroscopy due to lack of neural analgesia of the sciatic nerve in the ACL reconstruction group.

Our study had significant limitations. Specifically, there is no placebo group to truly assess outcome. In addition, we did not measure pain scores during both rest and movement. Furthermore, near the end of the study, the pharmaceutical company (Perdue, Cranbury, New Jersey) unexpectedly stopped manufacturing and supplying the hospital with levobupivacaine. As a result, the study was forced to end prematurely after recruiting only 71 patients rather than the 100 that had been anticipated. In addition to reducing the power of the study from 80% to 70%, the limited number of patients could have caused us to underestimate the incidence of rare serious adverse events. Another limitation of our study was that follow-up was only for 48 hours postoperatively. A more comprehensive study would have continued to evaluate the patients for a more extended period of time. Furthermore, the present findings apply only for single interscalene blocks and single femoral blocks. Additional studies should be done to evaluate the use of these analgesics in continuous peripheral nerve catheters. Finally, it would be advantageous to compare the clinical profile of the two local anesthetics in other peripheral nerve blocks.

Our study showed that peripheral nerve blocks with levobupivacaine 0.5% and ropivacaine 0.5% provide comparable postoperative analgesia for patients undergoing shoulder arthroscopy or ACL reconstruction surgery. The study also showed that both levobupivacaine and ropivacaine provide approximately 1 day of motor and sensory block postoperatively. Currently, levobupivacaine is not available in the USA, but it is still available in Europe and other parts of the world.

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