

Journal of
Shoulder and
Elbow
Surgery

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### **SHOULDER**

# Liposomal bupivacaine provides superior pain control compared to bupivacaine with adjuvants in interscalene block for total shoulder replacement: a prospective double-blinded, randomized controlled trial



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**Introduction:** Optimal pain control methods after total shoulder arthroplasty (TSA) achieve reduced opioid consumption, shortened hospital stay, and improved patient satisfaction in addition to adequate analgesia. Interscalene brachial plexus block is the gold standard for TSA, yet it typically does not provide pain relief lasting beyond 24 hours. Liposomal bupivacaine (LB) purportedly provides prolonged analgesia, yet it has been minimally explored for interscalene block, and it is significantly more expensive than standard bupivacaine.

**Methods:** This is a prospective, 2-arm, double-blinded randomized controlled trial. Subjects presenting for anatomic or reverse TSA were randomized in a 1:1 ratio to receive interscalene brachial plexus block with either LB plus bupivacaine (LBB group) or bupivacaine plus dexamethasone and epinephrine (BDE group). The primary outcome was 120-hour postoperative opioid consumption. Secondary outcomes were pain scores up to 96 hours postoperatively, pain control satisfaction, complications, level of distress from block numbness, and hospital stay.

**Results:** Ninety patients, 45 per group, were included in the intention-to-treat analysis and randomized. Because of withdrawal of consent and loss to follow-up, 40 in each group completed enrollment through postoperative day 60. Total 120-hour postoperative opioid consumption was similar between groups (P = .127), with no differences within 24- or 48-hour time intervals. Postoperative pain scores at 24-48 hours, 48-72 hours, 72-96 hours, and day 60 were significantly lower for the LBB group.

**Discussion:** LB interscalene brachial plexus block before total shoulder arthroplasty did not reduce 120-hour postoperative opioid consumption but significantly reduced postoperative pain between 24 and 96 hours and at postoperative day 60.

Hartford HealthCare institutional review board approved this study (HHC-2018-0231).

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1058-2746/\$ - see front matter © 2024 Journal of Shoulder and Elbow Surgery Board of Trustees. All rights reserved. https://doi.org/10.1016/j.jse.2023.12.014

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Keywords: Liposomal bupivacaine; interscalene nerve block; postoperative analgesia; perioperative pain management; regional anesthesia: local anesthesia

It is critical that techniques of pain control after total shoulder arthroplasty (TSA) also reduce opioid consumption, shorten hospital stay, and improve patient satisfaction. Interscalene brachial plexus block is considered the gold standard for TSA, but pain relief typically does not last beyond 24 hours. Various techniques are used to prolong block duration, such as interscalene catheters and adjuvants. However, catheters are difficult to place, may become dislodged, and require routine follow-up. Furthermore, adjuvants like dexamethasone and epinephrine typically cannot prolong analgesia for more than 6 to 8 hours. <sup>15-17,21</sup>

Liposomal bupivacaine (LB; EXPAREL; Pacira Bio-Sciences, Inc., Tampa, FL, USA) purportedly provides analgesia up to 72 hours after surgery.<sup>2</sup> Although this is based on clinical evidence with substantial support from the drug manufacturer,9 and despite being substantially more expensive than standard bupivacaine, LB has not been shown convincingly to be superior to local anesthetics for pain or opioid control. 1,6,12,13,18-20,22 However, LB was just recently approved for use in interscalene block and, thus, its effectiveness in this setting has yet to be determined. Findings from recent clinical trials suggest LB interscalene block may lead to significant improvements in pain and opioid control, but it is still not known conclusively whether these improvements warrant the drug's high cost.3,5,7,11 Furthermore, just one such trial has included a more comparable long-acting formulation of local anesthetics plus adjuvants vs. LB. 11 Therefore, more randomized trials, free from manufacturer pressure, are needed to determine whether LB can provide improvements in pain and opioid consumption that justify its cost in interscalene block for shoulder surgery.

Our study compared LB vs. bupivacaine plus dexamethasone and epinephrine adjuvants in interscalene brachial plexus block for patients undergoing TSA. The primary outcome was postoperative opioid consumption, with secondary outcomes of postoperative pain, perceived block duration, and hospital stay. We hypothesized that LB would lead to reduced postoperative opioid consumption and prolonged time until first opioid use.

# **Methods**

This prospective, 2-arm, double-blinded randomized controlled trial was a collaboration between the Anesthesiology and Orthopedic Surgery departments at Hartford Hospital. It was registered

on January 14, 2021 with clinicaltrials.gov (https://clinicaltrials.gov/study/NCT03887650). The study followed CONSORT guidelines and was conducted at the Bone & Joint Institute at Hartford Hospital from January 2019 until January 2021 when it achieved the desired number of participants.

Adult patients 18 years of age or older presenting for anatomic or reverse primary TSA with American Society of Anesthesiologists physical status of III or less were approached for study inclusion. Patients with history of any of the following were excluded: allergies to local anesthetics, contraindications to multimodal pain management, chronic pain syndrome, opioid use greater than 50 morphine milliequivalents (MME) per day, use of marijuana or cannabinoid products, substance abuse within 3 months, peripheral neuropathy of the brachial plexus, severe chronic obstructive pulmonary disease, respiratory disease that increases the risk for respiratory arrest from phrenic nerve palsy, revision arthroplasty, or pertinent anatomic abnormalities. Patients who weighed less than 45 kg or were pregnant, nursing, or planning to become pregnant during the study or within 1 month of surgery were also excluded. A list of reasons for each of the patients who were excluded is available on request.

Patients who provided written informed consent to join the study were enrolled. The study research coordinator used an online randomizer (https://randomizer.org) to randomize subjects 1:1 to receive preoperative interscalene brachial plexus block with either liposomal bupivacaine plus bupivacaine (LBB group) or bupivacaine plus dexamethasone and epinephrine (BDE group). Study subjects, surgeons, all health care providers but the anesthesiologists, and research staff who collected data were blinded. Because of the different appearance of the interventional drugs, the anesthesiologist performing the block could not be blinded, but they did not participate in any other study-related activities involving the patient. Despite the difference in cost of interventions, an internal grant allowed patients to be billed identically and remain blinded.

## **Block placement**

A preoperative assessment of the operative extremity was performed to confirm adequate sensory and motor function. Motor function was assessed by shoulder abduction and elbow flexion using the Oxford Scale of muscle strength grading. Sensory function of the shoulder was measured by assessing sensation to a pin prick on the shoulder in the axillary nerve distribution and was graded by the anesthesiologist using a 4-point scale: 0 = no sensation, 1 = sensation to pressure only, 2 = paresthesia, and 3 = full sensation. A peripheral intravenous (IV) catheter was then inserted, and standard monitors including a pulse oximeter, blood pressure monitor, and 3-lead electrocardiograph were applied. Nasal cannula oxygen at 2 L/min was administered. Patients were positioned in a 45-degree semiupright position with the head turned contralateral to the surgical site.

Each single-injection interscalene block was performed by one of 3 regional anesthesiologists. A high-frequency linear ultrasound transducer was used to locate the brachial plexus at the level of the nerve roots in the neck. Ultrasonographic guidance was used to monitor the distribution of local anesthetic deposited perineurally via a 22-G short bevel needle using an in-plane approach. In the BDE group, the local anesthetic solution totaled 20 mL and consisted of 5 mg preservative-free dexamethasone plus 5 µg epinephrine with 0.5% bupivacaine. In the LBB group, the solution totaled 20 mL and consisted of 10 mL of 133 mg LB and 10 mL of 0.5% bupivacaine. The anesthetic was injected using a 10-mL syringe under low pressure with frequent aspiration to minimize risk of intravascular injection. During block placement, patients were mildly sedated with IV midazolam or propofol yet were kept adequately alert to indicate paresthesias. The syringe was held under an opaque towel to maintain patient blinding. Prior to induction of general anesthesia and at least 15 minutes after block placement, patients were evaluated for block failure by a different, blinded anesthesiologist through assessment of motor and sensory function as detailed previously.

# Operative procedures

In the operating room, a standardized multimodal analgesic regimen was followed that included preoperative oral acetaminophen 975 mg and celecoxib 200 mg unless contraindicated. Induction of general anesthesia was achieved using propofol 1 to 2 mg/kg, fentanyl 1 to 3  $\mu$ g/kg, and lidocaine 0.5 to 1 mg/kg followed by paralysis with rocuronium 0.5 to 1 mg/kg prior to securing the trachea with the endotracheal tube. IV fentanyl was given as needed. IV dexamethasone was not given for prophylaxis of postoperative nausea and vomiting. Postoperative analgesia in the postanesthesia care unit (PACU) consisted of IV hydromorphone and/or fentanyl as needed. Analgesia after PACU discharge on the hospital floor consisted of scheduled acetaminophen, scheduled celecoxib or ibuprofen, and as-needed opioid medication.

### Outcomes and data collection

The primary outcome was 120-hour postoperative opioid consumption. Secondary outcomes included maximum, minimum, and average pain scores in the PACU and up to 96 postoperative hours, pain score on postoperative day 60, perceived block duration, distress from block numbness, pain control satisfaction, and complications, including postoperative nausea and vomiting and postoperative neurologic symptoms.

Baseline demographic data and comorbidities as well as preoperative and intraoperative medication use were collected from electronic medical records. Postoperative opioid consumption in the PACU and on the hospital floor in MME was collected from electronic medical records. Pain on postoperative day 1 (ie, the day after surgery) was assessed in-person in the PACU and on the morning of postoperative day 1 using a questionnaire sourced from the Modified Brief Pain Inventory. Postoperative opioid consumption and pain on postoperative days 2 and 4 were assessed by phone call with a medication diary used as backup. Perceived block duration was assessed by phone call on postoperative day 4. Postoperative pain up to day 60 and complications, including the need to visit the emergency department, were determined by phone call on postoperative day 60. Level of distress from block numbness was assessed using a scale adapted from the Overall Benefit of Analgesia Score (OBAS) from 0 = not at all to  $10 = \text{very much.}^{16}$  Level of satisfaction with pain relief was assessed using an 11-point numeric rating scale from 0 = very dissatisfied to 10 = very satisfied. Sensation was assessed using methods described previously in the PACU and patient room at 24 hours postoperatively.

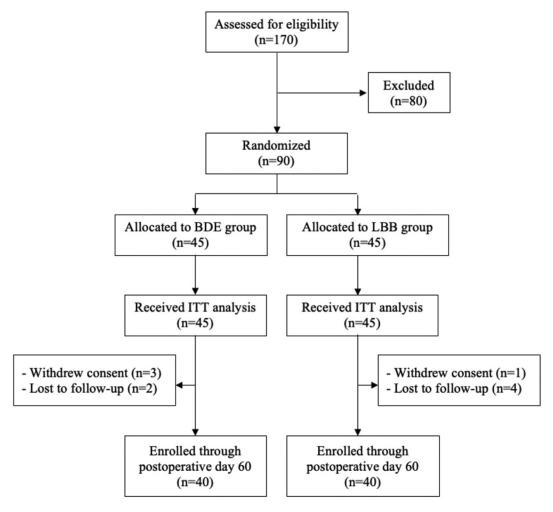
### Statistical analysis

An a priori power calculation was done based on the primary outcome. Observed effect sizes and calculated sample size targets were obtained from a study of intraoperative LB infiltration vs. interscalene ropivacaine nerve block, given the recent FDA approval of LB for interscalene block, which resulted in an initial target of 40 per group. This was supplemented by an interim analysis of the primary outcome conducted when half the target sample size completed postoperative day 3. To maintain the type I error rate of P = .05, the O'Brien-Fleming method for alpha sharing was used, establishing a significance level of .0054 for the interim analysis. Interim findings were suggestive but not conclusive, so the decision was made to continue the study. A power calculation was done to determine the sample size necessary to detect differences at least equal to those seen in the interim analysis at 80% power and estimated 10% attrition rate, which resulted in a target of 45 per group. Full details of the interim analysis are available on request.

All continuous data were first tested for adherence to normal distributions. As none of the continuous variables were determined to meet normality assumptions, median and interquartile range were used for descriptive data and the Wilcoxon rank sum test was used for group differences and ordinal variables (eg, American Society of Anesthesiologists class). Categorical variables were analyzed using the chi-square test of proportion or Fisher exact test. An overall significance level of .05 was chosen for the study analysis. For analysis of opioid consumption, the O'Brien Fleming data share was applied, resulting in a significance criterion of .0492. For self-reported pain data, the same pain assessment scores were analyzed 3 times, with minimum pain, average pain, and maximum pain calculated and analyzed separately; to counteract any resulting increase in likelihood of false positive results, a Bonferroni correction was applied, resulting in a significance level of .016 for analyses of these data.

### Results

One hundred seventy patients were assessed for eligibility as shown in the CONSORT flow diagram (Fig. 1). Eighty patients were excluded according to inclusion and exclusion criteria. Ninety patients met inclusion criteria, provided consent, and were included in the intention-to-treat analysis, with 45 randomized to the BDE or LBB group. However, because of loss to follow-up and withdrawal of consent, 40 in each group completed enrollment to post-operative day 60 as detailed in the CONSORT diagram. Demographic and preoperative characteristics as well as



**Figure 1** CONSORT diagram. *BDE*, bupivacaine plus dexamethasone and epinephrine group; *LBB*, liposomal bupivacaine plus bupivacaine group.

nonopioid analgesic use up to 96 hours after surgery were similar between groups (Table I).

### Postoperative opioid consumption

Postoperative opioid consumption, although reduced in the LBB group, was not significantly different between groups within 120 hours overall or for measured 24- and 48-hour intervals (Table II). Duration of opioid treatment according to first and final opioid use was also not significantly different between groups.

### Postoperative pain

Pain in the PACU and in the first 24 hours were not significantly different between groups as expected (Table III). However, the LBB group showed significantly lower minimum, maximum, and average pain scores at 24-48 hours and 48-72 hours as well as lower maximum

and average pain at 72-96 hours and lower maximum pain at postoperative day 60 (Fig. 2).

### Block and hospital outcomes

Perceived block duration did not differ between groups (P=.681). The proportion of patients who reported 10/10 satisfaction with pain control on postoperative day 4 was higher in the LBB group than in the BDE group (32 of 41 vs. 24 of 41, respectively; P=.048), with no differences on postoperative day 60 (28 of 41 vs. 27 of 39, respectively; P=.560). The proportion of patients who reported distress greater than zero was similar between LBB and BDE groups in the PACU (14 of 45 vs. 14 of 45, respectively; P=.590) and on postoperative day 2 (12 of 43 vs. 12 of 44, respectively; P=.569). Length of stay was similar between groups at a median of 1 day (P=.179). Reports of complications on postoperative days 2, 4, and 60 totaled 11, 9, and 3 in the BDE group compared with 8, 4, and 0 in the

Parameter	BDE $(n = 45)$	LBB (n $=$ 45)	<i>P</i> value
Demographic data			
Age, years, median (IQR)	73 (66.5, 78.0)	72 (66.5, 77.0)	.747
Gender, n (%)	· · ·	· · ·	
Male	22 (48.9)	23 (51.1)	.751
Female	23 (51.1)	22 (48.9)	.751
Race, n (%)			
White	42 (93.3)	44 (97.8)	.471
Black/African American	2 (4.4)	0 (0.0)	
Other Other	1 (2.2)	1 (2.2)	
Ethnicity, n (%)			
Hispanic/Latino	1 (2.2)	1 (2.2)	
Non-Hispanic/Latino	44 (97.8)	44 (97.8)	
BMI, median (IQR)	31.6 (27.0, 35.9)	31.3 (27.3, 33.7)	.862
ASA Physical status, median (IQR)	2 (2, 3)	2 (2, 3)	.529
Comorbidities, n (%)			
Diabetes mellitus	9 (20)	6 (13.3)	.399
Hyperlipidemia	25 (55.6)	26 (57.8)	.832
Hypertension	25 (55.6)	29 (64.4)	.392
Chronic obstructive pulmonary disease	2 (4.4)	0 (0.0)	.155
Rheumatoid arthritis	3 (6.7)	0 (0.0)	.080
Home opioid use	6 (13.3)	3 (6.7)	.295
Preoperative shoulder pain, median (IQR)	3.0 (0.5, 4.5)	2 (0.0, 5.0)	.698
Presence of full sensation, n (%)			
Pre-block	42 (93.3)	42 (93.3)	.662
Return of full sensation time, n (%)			
PACU	2 (4.4)	0 (0.0)	.441
Postoperative day 1	9 (20.0)	11 (24.4)	
Postoperative day 2-60	27 (60.0)	27 (60.0)	
After postoperative day 60	2 (4.4)	0 (0.0)	
Unknown	5 (11.1)	7 (15.6)	

BDE, bupivacaine plus dexamethasone and epinephrine group; LBB, liposomal bupivacaine plus bupivacaine group; IQR, interquartile range; BMI, body mass index; ASA, American Society of Anesthesiologists.

LBB group, respectively, which were not significantly different. None of these complications were determined to be related to either study intervention. An emergency department visit for pulmonary embolism unrelated to the block 1 month after surgery was reported in the LBB group. Details of each reported event are included as a supplement.

# **Discussion**

This study adds to the limited research of LB in interscalene brachial plexus block for TSA and is the first to compare it to bupivacaine plus dexamethasone and epinephrine. It is also one of few studies of LB without industry sponsorship or manufacturer conflicts of interest. LB did not lead to reductions in 120-hour postoperative opioid consumption but led to reductions in pain between 24 and 96 hours and at postoperative day 60. Furthermore, patients who received LB reported greater satisfaction yet did not experience detrimental effects regarding hospital

stay, distress from the block, or complications. Evidence from our study, therefore, in addition to our clinical experience supports that LB can safely improve pain control, but clinicians and hospitals must consider our findings along-side current evidence as well as the drug's high cost to determine whether LB should be considered standard practice for interscalene brachial plexus block for shoulder surgeries.

Clinical trial evidence of LB for pain management in shoulder surgery has been aggregated by meta-analyses in 2019 and again in 2022, which found LB to be similar to non-LB agents for pain and opioid control. The vast majority of trials in these analyses, however, studied LB used in infiltration rather than in interscalene block. The only study included that compared interscalene block between LB and non-LB agents was funded by the manufacturer of LB, Pacira Pharmaceuticals, Inc. Several studies of interscalene block have since compared LB to non-LB anesthetics, with one even comparing against bupivacaine plus dexamethasone. 3,5,7,11 These trials show

Table II Postoperative opioid consumption and non-opioid analgesic use					
Parameter	BDE (n = 45)	LBB (n = 45)	P value		
Total opioid consumption, MME, median (IQR) Opioid consumption, MME, median (IQR)*	90.3 (57.4, 133.4)	71.3 (43.0, 120.0)	.127		
0-24 h	25.0 (25.0, 38.0)	25.0 (25.0, 39.0)	.648		
24-48 h	24.0 (11.5, 42.5)	16.0 (0.0, 38.8)	.285		
48-72 h	5.0 (0.0, 15.0)	2.0 (0.0, 8.0)	.122		
72-120 h	15 (0.0, 37.5)	10 (0.0, 27.0)	.367		
Time to first opioid use, days, median $(IQR)^{\dagger}$	0.40 (0.07, 0.78)	0.36 (0.12, 0.81)	.755		
Day of final opioid use, days, median (IQR)	4.0 (1.0, 4.0)	4.0 (1.5, 4.0)	.876		
Non-opioid analgesics used, n (%) <sup>§</sup>					
PACU	2 (4.4)	1 (2.2)	>.999		
PACU-24 h	43 (95.6)	45 (100.0)	.494		
24-48 h	24 (54.5)	26 (59.1)	.669		
48-72 h	28 (66.7)	26 (59.1)	.470		
72-96 h	28 (66.7)	24 (54.5)	.253		

BDE, bupivacaine plus dexamethasone and epinephrine group; LBB, liposomal bupivacaine plus bupivacaine group; MME, morphine milliequivalents; IQR, interquartile range.PACU, post-anesthesia care unit.

Table III Postoperative pain					
Parameter	BDE (n = 45)	LBB (n = 45)	P value		
Reported pain in operative shoulder, MBPI, median (IQR)*					
PACU	0.0 (0.0, 1.5)	0.0 (0.0, 1.0)	.852		
PACU-24 h					
Minimum	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	.661		
Maximum	1.0 (0.0, 4.5)	2.0 (0.0, 4.5)	.747		
Average	0.0 (0.0, 3.5)	1.0 (0.0, 2.0)	.604		
24-48 h					
Minimum	2.0 (0.0, 3.8)	0.0 (0.0, 2.0)	.002		
Maximum	7.0 (5.0, 8.0)	4.5 (1.0, 6.0)	<.001		
Average	4.0 (3.0, 5.0)	2.0 (0.0, 3.8)	<.001		
48-72 h					
Minimum	2.0 (1.0, 3.0)	1.0 (0.0, 2.0)	.011		
Maximum	6.0 (4.5, 7.0)	4.0 (1.8, 6.0)	.001		
Average	3.0 (2.0, 5.0)	2.0 (1.0, 3.3)	.003		
72-96 h					
Minimum	2.0 (0.0, 2.0)	0.5 (0.0, 2.0)	.230		
Maximum	5.0 (4.0, 7.0)	4.0 (1.8, 5.3)	.007		
Average	3.0 (2.0, 4.0)	2.0 (1.0, 3.0)	.011		
Postoperative day 60					
Minimum	0.0 (0.0, 1.0)	0.0 (0.0, 0.8)	.378		
Maximum	6.0 (4.3, 8.0)	5.0 (2.0, 6.0)	.001		
Average	2.0 (1.0, 3.0)	1.0 (0.3, 3.0)	.403		

BDE, bupivacaine plus dexamethasone and epinephrine group; LBB, liposomal bupivacaine plus bupivacaine group; MBPI, Modified Brief Pain Inventory; IQR, interquartile range; PACU, post-anesthesia care unit.

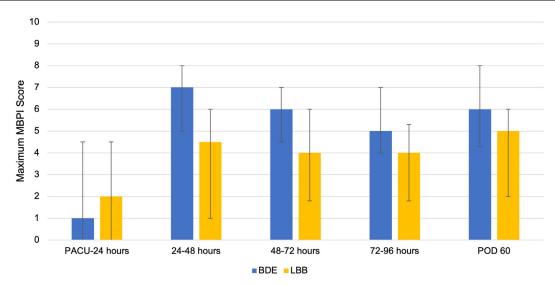
<sup>\*</sup> Sample sizes: 0-24 hours, 45 for both groups; 24-48 hours, 44 for both groups; 48-72 hours, 42 for both groups; 72-96 hours, 42 for both groups.

<sup>†</sup> Sample sizes: 42 for the BDE group and 43 for the LBB group.

<sup>&</sup>lt;sup>‡</sup> Sample sizes: 42 for the BDE group and 45 for the LBB group.

<sup>§</sup> Sample sizes: PACU and PACU-24 hours, 45 for each group; 24-48 hours, 44 for each group; 48-72 and 72-96 hours, 42 for the BDE group and 44 for the LBB group.

<sup>\*</sup> Sample sizes: PACU and PACU-24 hours, 45 in each group; 24-48 hours, 44 in each group; 48-72 and 72-96 hours, 41 in the BDE group and 42 in the LBB group; day 60, 40 in each group.



**Figure 2** Postoperative pain from PACU to postoperative day 60 measured using the Modified Brief Pain Inventory. *BDE*, bupivacaine plus dexamethasone and epinephrine group; *LBB*, liposomal bupivacaine plus bupivacaine group; *MBPI*, Modified Brief Pain Inventory; *PACU*, post-anesthesia care unit; *POD*, postoperative day.

reduced postoperative opioid consumption in LB groups,<sup>3</sup> but each ultimately concluded that these improvements from adding LB to interscalene block are not clinically significant, and the trial of LB vs. bupivacaine plus dexamethasone concluded that the 2 formulations can be used interchangeably.<sup>11</sup> Thus, a large body of evidence finds LB in infiltration to be comparable to techniques using non-LB agents, and recent evidence suggests this is no different when LB is used in interscalene block. We similarly found that LB interscalene block provides no added benefit for postoperative opioid consumption.

Our finding that LB significantly improves pain control from 24 to 96 hours compared with bupivacaine is consistent with our experience in clinical practice. Furthermore, the lack of difference between groups up to 24 hours suggests that the bupivacaine was effective up to 24 hours as expected and that the improved pain scores in the LB group beyond 24 hours was in fact due to LB and its prolonged efficacy. Our additional finding that LB improves pain even at 60 days postsurgery is notable and should be investigated further because this long-term pain reduction could significantly improve patient quality of life and satisfaction. These findings contradict current evidence that LB is not clinically different from bupivacaine, particularly when bupivacaine is admixed with dexamethasone. 3,5,7,11,13 Because current evidence is based on just a handful of trials, however, our findings support that future studies should aim to determine whether LB is indeed superior to traditionally used anesthetics for interscalene block and, if so, whether its benefits justify its higher cost.

Several studies found differences in block duration, recovery, and complications between LB and non-LB block.<sup>3,5,7</sup> Elmer et al<sup>3</sup> reported longer perceived block duration with LB interscalene block (39.9  $\pm$  0.6 vs.

 $24.3 \pm 0.9$  hours; P < .001), and Hattrup et al<sup>7</sup> found that LB blocks improved quality of recovery at 72 hours, though not at 15 days after surgery. Conversely, Flaherty et al<sup>5</sup> found LB block to be associated with an increased number of complications vs. bupivacaine block (9 of 35 vs. 2 of 35; P = .05). Our study found no differences between groups for hospital stay, perceived block duration, distress from block numbness, and adverse events. However, we did find that the proportion of patients reporting 10/10 satisfaction was greater in the LB group. Although evidence finds LB to be similar overall to non-LB agents in regional anesthesia, evidence for LB in shoulder surgery remains sparse and requires expansion from additional randomized trials.  $^{8,12,13}$ 

The strengths of our study include that it was the first to compare LB with the more comparable long-acting formulation of bupivacaine plus dexamethasone and epinephrine adjuvants when used in interscalene block for shoulder surgery. Our study also did not receive any funding or support from industry, and its results are, therefore, not at risk for bias due to industrial pressure, financial or otherwise, considering the potential for drug manufacturers to influence product research particularly in the anesthetic drug industry. A recent Cochrane review found that compared with nonmanufacturer sponsorship, industry-sponsorship of drug trials were more likely to lead to favorable efficacy results (relative risk 1.3, 95% confidence interval 1.2-1.4) and conclusions (relative risk 1.3, 95% confidence interval 1.2-1.5).

Our study does have limitations. First, it was not possible to blind the regional anesthesiologist who delivered the block because of the difference in physical appearance of the 2 interventional drug formulations. However, this anesthesiologist was not involved in any

other study procedures, including assessment of block effectiveness or measurement of opioid consumption or pain. Second, measurements of opioid consumption and pain recorded outside of the hospital relied on patient recall, which may have led to recall bias and inaccuracies. Third, sensation and movement were not able to be measured on postoperative days 2 or 3 because of short hospital stay, and thus, whether LB was associated with longer block duration as advertised could not be determined based on these measures. Finally, block duration was not measured directly through assessment of sensation but indirectly by using opioid consumption and pain scores as proxies.

### Conclusion

LB used in interscalene brachial plexus block for total shoulder arthroplasty did not reduce 120-hour post-operative opioid consumption but reduced postoperative pain between 24 and 96 hours and at day 60 compared with bupivacaine plus dexamethasone and epinephrine. LB should continue to be compared against more cost-effective formulations that also achieve prolonged analgesia, such as those including standard anesthetics with adjuvants like dexamethasone, to determine whether its benefits justify its cost and standard use in interscalene block for shoulder surgery.

### **Disclaimers:**

Funding: No funding was disclosed by the authors. Conflicts of interest: The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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