Liposomal Bupivacaine has Superior Pain Control to Bupivacaine with Adjuncts In Interscalene Blocks for Total Shoulder Replacement

21st Annual Pain Medicine Meeting
November 17-19, 2022 | #ASRAFALL22
ASRA PAIN MEDICINE

INTEGRATED ANESTHESIA ASSOCIATES
DEPARTMENT OF ANESTHESIA RESEARCH & DEVELOPMENT
Hartford HealthCare Bone & Joint Institute at Hartford Hospital

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Introduction

Pain control after total shoulder arthroplasty can be challenging, and use of a multimodal analgesic approach that includes peripheral nerve blockade is commonly used to reduce pain and opioid consumption.

Interscalene nerve blocks are common analgesic techniques for these surgeries but are typically limited by duration of action. Efforts to prolong the analgesic effects of blocks include using adjunctive additives (1) to traditional local anesthetics, as well as the use of liposomal bupivacaine, which has been suggested to have a duration of up to 72 hours (2). Much of the literature comparing similar interventions with bupivacaine to liposomal bupivacaine has been contradictory and received financial support from the manufacturer of liposomal bupivacaine (3).

Thus, we conducted a randomized controlled trial, free from manufacturer financial support, in which patients undergoing total shoulder arthroplasty received interscalene blocks with either mixtures of liposomal bupivacaine with bupivacaine or bupivacaine with dexamethasone and epinephrine. Opioid consumption (expressed as morphine milliequivalents), pain scores, perceived duration of the block, and satisfaction were compared for the two groups.

Methods and Material

- Randomized controlled, double-blinded (patient and surgeon) trial as a collaboration between the Depts. of Anesthesiology and Orthopedic Surgery at Hartford Hospital and the Bone and Joint Institute.
- Approved by Hartford HealthCare IRB (IRB # HHC-2018-0321) and registered with the National Clinical Trials (NCT# 03887650) starting in March 2019 and completed within 2.5 years as planned.
- Patients having anatomic or reverse total shoulder arthroplasty randomized to receive a preop interscalene nerve block with either **10ml of 1.3% liposomal bupivacaine + 10ml of 0.5% bupivacaine (LB/B group)** or **20ml of 0.5% bupivacaine + 5mg dexamethasone + 5mcg epinephrine (B/D/E group).**
- **Primary outcome was opioid consumption in morphine milligram equivalents (MME) on postoperative days, up to 120 postoperative hours. Secondary outcomes were maximum, minimum, and average pain scores using the Modified Brief Pain Inventory in the PACU and up to 96 postoperative hours, pain recalled at the 60th postoperative day, perceived block duration, and pain control satisfaction. Patient satisfaction was assessed with a numeric scale from 0 to 10.**
- **Categorical variables were analyzed using chi-square tests of proportion or Fisher's Exact tests; continuous variables were analyzed using Wilcoxon Ranked Sum tests, as none met the assumption of normal distribution required for parametric analysis.**

Results

90 patients were randomized to the two groups, 45 to each of LB/B or B/D/E. Four patients withdrew their consent, 1 in the LB/B group and 3 in B/D/E, resulting in incomplete data for the primary and secondary outcomes. The analysis presented here includes the 86 per-protocol patients (44 LB/B and 42 B/D/E). An intent to treat analysis performed adding additional available data showed no differences in findings. Among the 86 patients, there were no differences for demographics, comorbidities, baseline preoperative pain scores, and opioid consumption prior to surgery between the groups.

- **LB/B group reported significantly lower maximum, minimum, and average pain scores 24 -48 and 48-72 post-op hours than the B/D/E group. (Table 1.)**
- **LB/B group reported significantly lower maximum and average pain scores on 72-96 postoperative hours than the B/D/E group. (Table 1.)**
- **LB/B group reported significantly lower maximum pain scores than B/D/E group for the 2-month period recalled on post-operative day 60 there were no significant differences for average and minimum pain. (Figure 1. and Table 1.)**
- **There were no differences in opioid consumption between the LB/B and B/D/E groups at any time point. (Figure 2.)**
- **There was no difference in the perceived block duration between the LB/B and B/D/E group. [(LB/B median (IQR) hours 23.1 (18.0, 45.4); B/D/E median (IQR) hours 21.5 (18.8, 30.7) P=.533].**
- **There was no difference in reported satisfaction of pain control at 60 days between the LB/B and the B/D/E groups [(LB/B median (IQR) 10.0 (9.0, 10.0); B/D/E median (IQR) 10.0 (9.0, 10.0) P=.888].**

Figure 1. Reported Maximum Postoperative Pain Scores

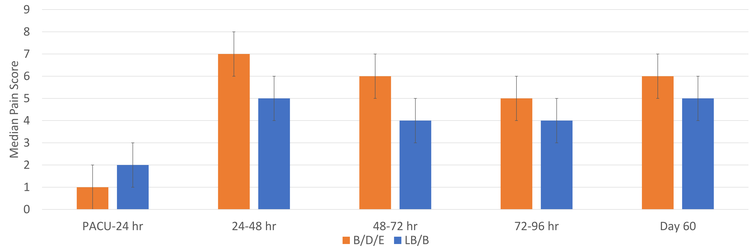
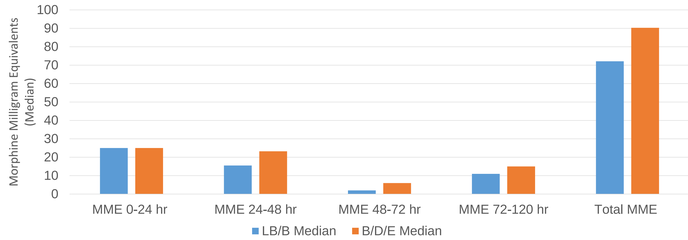


Table 1. Reported Maximum, Average, and Minimum Postoperative Pain Scores

	Maximum Pain (Median, IQR)			Average Pain (Median, IQR)			Minimum Pain (Median, IQR)		
Measure	Liposomal Bupivacaine/ Bupivacaine Median , IQR	Bupivacaine/ Dexamethasone/ Epinephrine Median , IQR	p	Liposomal Bupivacaine/ Bupivacaine Median , IQR	Bupivacaine/ Dexamethasone/ Epinephrine Median ,IQR	p	Liposomal Bupivacaine/ Bupivacaine Median ,IQR	Bupivacaine/ Dexamethasone/ Epinephrine Median ,IQR	p
Pre Op pain				2.5 (0.25, 5.0)	3.0 (.075, 5.0)	.713			
Post Op pain PACU				0.0 (0.0, 1.0)	0.0 (0.0, 2.0)	.97			
Post Op pain PACU-24	2.0 (0.0, 4.75)	1.0 (0.0, 4.0)	.618	1.0 (0.0, 2.0)	0.0 (0.0, 2.25)	.473	0.0 (0.0, 1.0)	0.0 (0.0, 0.0)	.534
Post Op pain 24-48	5.0 (1.0, 6.0)	7.0 (5.0, 8.25)	**< .001**	2.0 (0.0, 4.0)	4.0 (3.0, 5.25)	**< .001**	0.0 (0.0, 2.0)	2.0 (0.0, 4.0)	**.002**
Post Op pain 48-72	4.0 (1.5, 6.0)	6.0 (4.5, 7.0)	**< .001**	2.0 (1.0, 3.0)	3.0 (2.0, 5.0)	**.002**	1.0 (0.0, 2.0)	2.0 (1.0, 3.0)	**.009**
Post Op pain 72-96	4.0 (1.5, 5.5)	5.0 (4.0, 7.0)	**.008**	2.0 (1.0, 3.0)	3.0 (2.0, 4.0)	**.008**	0.0 (0.0, 2.0)	2.0 (0.0, 2.0)	**.169**
Post Op pain 60 days	5.0 (2.0, 6.0)	6.0 (4.25, 8.0)	**.001**	1.0 (0.25, 3.0)	2.0 (1.0, 3.0)	.403	0.0 (0.0 0.75)	0.0 (0.0, 1.0)	**.378**

Figure 2. Daily and Total Morphine Milligram Equivalents



Discussion

Interscalene blocks with **liposomal bupivacaine** resulted in superior pain control starting at 24 postoperative hours through 96, and for maximum pain at 60 days after total shoulder arthroplasty compared to blocks done with **bupivacaine with dexamethasone and epinephrine**. Pain control was similar between groups on the day of surgery.

These findings suggest that **liposomal bupivacaine** provides a superior and possibly longer duration of pain control in a study free from manufacturer support. The difference in the maximum pain scores at 60 postoperative days suggests that liposomal bupivacaine may have an analgesic effect beyond the medication's typical duration of action. However, the improved pain control was not associated with a reduction in opioid consumption.

The lack of association between pain scores, opioid consumption, and block duration may be multifactorial and requires further investigation.

References

1. Vieira PA, Pulai I, Tsao GC, Manikantan P, Keller B, Connelly NR: Dexamethasone with bupivacaine increases duration of analgesia in ultrasound-guided interscalene brachial plexus blockade. Eur J Anaesthesiol 2010; 27:285–8
2. Candiotti K: Liposomal bupivacaine: an innovative nonopioid local analgesic for the management of postsurgical pain. Pharmacotherapy 2012; 32:19S – 26S
3. Finkel K, Takata E, Maffeo-Mitchell C, Neal J, Nankin M, Braffett B, Perillo L, Gammerman S, Stuart W, Walker A. Manufacturer financial conflicts of interest are associated with favourable outcomes in randomized controlled trials of liposomal bupivacaine. British Journal of Anaesthesia, Epub 2022 Aug 16.