



Abstract: 3229

Scientific Abstracts > Regional Anesthesia

Interscalene nerve block with liposomal bupivacaine versus bupivacaine with perineural dexamethasone: a noninferiority trial

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Introduction

Regional anesthetic techniques have long been recognized as potent, opioid-sparing modalities and are considered critical components of any multimodal pathway. In the context of shoulder surgery, the interscalene nerve block is the most commonly used regional anesthetic technique. Traditionally, it provides a significant analgesic benefit postoperatively. However, when used as a single shot approach it is limited by its duration, lasting no longer than 24 hours even when using the longer-acting local anesthetics, such as bupivacaine.

At our institution, we transitioned from using standard bupivacaine to adding perineural dexamethasone as an adjuvant to prolong peripheral nerve blockade up to 30 hours. There have been several meta-analyses and systematic reviews including a Cochrane review, supporting its safe and effective use for upper extremity blockade.

Liposomal bupivacaine is an extended-release formulation of bupivacaine approved by the FDA that theoretically sustains analgesia up to 72 hours via its multivesicular liposome formulation. Recently, the FDA approved its use in the interscalene nerve block. However, there has been a paucity of randomized controlled trials comparing liposomal bupivacaine limiting comparisons to a placebo (saline) or “standard” bupivacaine. It remains unclear if the liposomal bupivacaine can significantly prolong analgesia and demonstrate superiority over an active standard bupivacaine comparator.

This study represents the first randomized controlled trial comparing the two injectates. Our primary hypothesis was that the average numerical rating scale pain scores over 72 hours in patients given perineural liposomal bupivacaine would be noninferior to those patients given bupivacaine with perineural dexamethasone.

Materials and Methods

After obtaining IRB approval from our institution (Hospital for Special Surgery, New York, NY), this

study was conducted from August 2019 to March 2021. One-hundred twelve patients undergoing ambulatory shoulder surgery were randomized into two groups. Informed consent was obtained. The liposomal bupivacaine group received a mixture of 5 ml of 0.5% standard bupivacaine with 133 mg liposomal bupivacaine (n=56) while the dexamethasone group received a mixture of 15 ml of 0.5% standard bupivacaine with 4mg dexamethasone (n=55), respectively. The primary outcome was the average NRS pain scores at rest over 72 hours. The mean difference between the two groups was compared against a noninferiority margin of 1.3. Secondary outcomes were analgesic block duration, motor and sensory resolution, opioid consumption, NRS pain scores at rest and movement on POD1 to 4, as well as 7, patient satisfaction, readiness for PACU discharge, and adverse side effects related to the interscalene block. Of note, the use perineural dexamethasone adjuvant is considered an off-label use.

Results/Case Report

Liposomal bupivacaine group average numerical rating scale pain score over 72 hours was not inferior to the bupivacaine with dexamethasone group (mean (SD), 2.4 (1.9) versus 3.4 (1.9), mean difference (95%CI), -1.1 (-1.8, -0.4), $p < 0.001$ for noninferiority). There was no significant difference in duration of analgesia between the groups (25.5 (20.0, 42.0) hours versus 27.2(20.4,39.4) hours, $p = 0.851$). Motor and sensory resolutions were similar in both groups (26.9 (21.0, 48.2) hours versus 26.8 (19.2, 39.7) hours, $p = 0.436$) and (26.6 (20.9, 44.2) hours versus 30.9 (19.8, 41.8) hours, $p = 0.862$), respectively. There was no difference in opioid consumption, readiness for PACU discharge, or adverse events.

Discussion

Interscalene nerve blocks with perineural liposomal bupivacaine provided effective analgesia similar to perineural standard bupivacaine with dexamethasone. We conclude that bupivacaine with dexamethasone can be interchangeably used with liposomal bupivacaine for analgesia after shoulder surgery.

References

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Disclosures

Yes

Tables / Images

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Figure 1: LIPOSOMAL BUPIVACAINE CONSORT Flow

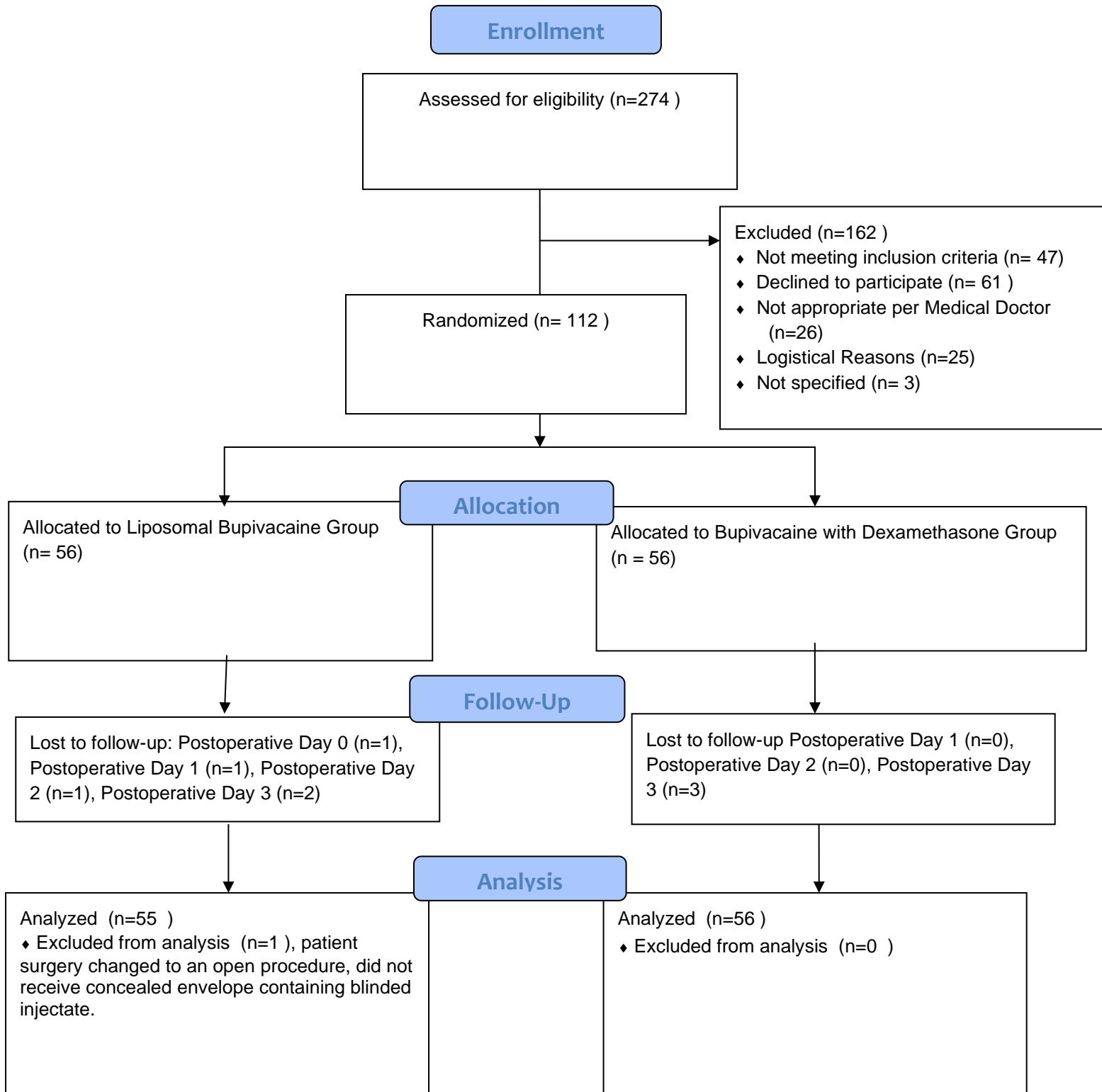


Table 2: NRS Pain Scores

Table 2a.	Liposomal Bupivacaine	Bupivacaine with Dexamethasone	Difference in Means [LB - BD] 95% CI	P-Value
Average NRS at Rest at POD1, POD2, and POD3. Mean (STD)*	2.4 (1.9)	3.4 (1.9)	-1.1 (-1.8, -0.4)	<0.001

*A non-inferiority t-test was conducted with non-inferiority margin of 1.3 points and an alpha level of 0.05. Missing values imputed with median. A sensitivity analysis without imputed values was run, and the results were consistent with the results from the imputed data

Table 2b. NRS Pain at Rest	LB Group	BD Group	Difference in Means [LB - BD] 95% CI	P-Value
PACU 60 Minutes Mean (STD)	1.3 (1.9)	0.9 (1.8)	0.4 (-0.4, 1.2)	0.351
POD1 Mean (STD)	2.1 (2.6)	3 (2.5)	-0.9 (-1.7, -0.1)	0.025
POD2 Mean (STD)	2.5 (2.3)	4.1 (2.7)	-1.5 (-2.3, -0.7)	<0.001
POD3 Mean (STD)	2.4 (2.2)	3.3 (2.4)	-0.9 (-1.7, -0.1)	0.028
POD4 Mean (STD)	2.5 (2.0)	3.0 (2.2)	-0.5 (-1.4, 0.4)	0.242
POD7 Mean (STD)	1.7 (2.0)	2.3 (2.2)	-0.5 (-1.4, 0.4)	0.245

Table 2c. NRS Pain with movement	Liposomal Bupivacaine	Bupivacaine with Dexamethasone	Difference in Means [LB - BD] 95% CI	P-Value
POD1 Mean (STD)	4(3.1)	4.3(3.1)	-0.3 (-1.6, 1.0)	0.676
POD2 Mean (STD)	4.1(2.9)	5.6(3.1)	-1.4 (-2.6, -0.2)	0.025
POD3 Mean (STD)	4(2.7)	5.3(2.3)	-1.2 (-2.4, -0.1)	0.041
POD4 Mean (STD)	4.0(2.8)	4.9(2.4)	-0.8 (-2.0, 0.4)	0.199

POD7
Mean (STD)

3.9(2.6)

4.7(2.5)

-0.7 (-2.0, 0.6)

0.272

Table 4. Opioid Consumption, Intraop Opioid Consumption

	Liposomal Bupivacaine	Bupivacaine With Dexamethasone	Difference in Means [LB - BD] 95% CI	P-Value
Opioid Consumption PACU. Mg OME. Mean (STD)	1.8(4.5)	1.7(4.6)	0.1 (-1.6, 1.8)	0.942
Opioid Consumption POD1. Mg OME. Mean (STD)	4.8(8.6)	8.1(10.4)	-3.0 (-6.7, 0.6)	0.102
Opioid Consumption POD2. Mg OME. Mean (STD)	12.3(15.6)	18.2(20.8)	-5.7 (-12.6, 1.2)	0.110
Opioid Consumption POD3. Mg OME. Mean (STD)	8.9(12.5)	13.2(14.0)	-4.0 (-9.0, 1.0)	0.116
Opioid Consumption POD4. Mg OME. Mean (STD)	6.9(13.8)	9.7(15.5)	-1.8 (-7.5, 4.0)	0.549
Opioid Consumption POD7. Mg OME. Mean (STD)	3.7(7.4)	3.3(7.2)	0.8 (-2.2, 3.8)	0.599

	Liposomal Bupivacaine	Bupivacaine With Dexamethasone	Wilcoxon Rank Sum Test P- Value
Intraoperative Opioid Consumption (Fentanyl and Dilaudid). Mg OME Median (Q1, Q3)	28.3 (15.0, 30.0)	23.2 (7.5, 30.0)	0.090

Table 5. Analgesic Block Duration, Sensory Resolution, Motor Block Resolution

	Liposomal Bupivacaine	Bupivacaine With Dexamethasone	Wilcoxon Rank Sum Test P-Value
When did your pain relief from the block completely wear off? (In terms of hours) Median (Q1, Q3)	25.5(20.0,42.0)	27.2(20.4, 39.4)	0.851
Sensory Resolution: When did your numbness completely resolbe and return to normal? Median (Q1, Q3)	26.6 (20.9, 44.2)	30.9 (19.8, 41.8)	0.862
Motor Block Resolution: When did your arm or hand weak resolve and return to normal? Median (Q1, Q3)	26.9(21.0, 48.2)	26.8 (19.2, 39.7)	0.436