# Does Liposomal Bupivacaine Injectable Suspension Peripheral Nerve Block Further Aid in Decreasing At-home Narcotic Utilization in Children and Adolescents After Anterior Cruciate Ligament Reconstruction

Halle R. Walls, BA,\*† Evelyn S. Thomas, DO,\*‡ Zeev N. Kain, MD, MBA,\*§ and John A. Schlechter, DO\*¶

**Background:** Opioid misuse and addiction among children and adolescents is an increasingly concerning problem. This study sought to determine whether liposomal bupivacaine injectable suspension admixture administered as a single-shot adductor canal peripheral nerve block (SPNB+BL) would decrease utilization of at-home opioid analgesics after anterior cruciate ligament reconstruction (ACLR) in adolescents compared with single-shot peripheral nerve block with bupivacaine (SPNB+B) alone.

**Methods:** Consecutive ACLR patients with or without meniscal surgery by a single surgeon were enrolled. All received a preoperative single-shot adductor canal peripheral nerve block with either admixture of liposomal bupivacaine injectable suspension with 0.25% bupivacaine (SPNB+BL) or 0.25% bupivacaine alone (SPNB+B). Postoperative pain management included cryotherapy, oral acetaminophen, and ibuprofen. A prescription for 10 doses of hydrocodone/acetaminophen (5/325 mg) was provided in a sealed envelope with instructions to only use in the case of uncontrolled pain. Pain using the visual analog scale; number of consumed narcotics, acetaminophen, ibuprofen, and pain treatment satisfaction for the first 3 postoperative days were recorded. Statistical analysis was performed.

**Results:** Fifty-eight patients were enrolled, the average age was  $15 \pm 1.5$  years (SPNB+B=32 patients, SPNB+BL=26 patients). Forty-seven patients (81%) did not require home opioids post-operatively. A significantly lower proportion of patients in the SPNB+BL group required opioids compared with control patients (7.7% vs. 28.1%, P=0.048). Average opioid use was 2 morphine milligram equivalents (MME), 0.4 pills (range, 0 to 20 MME). There were no differences in the visual analog scale or pain treatment satisfaction scores, other demographics, or other operative data. Inverse probability of treatment weighting

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analysis that was performed to account for any potential group differences revealed home opioid use between groups is significantly different (P < 0.001).

**Conclusions:** Liposomal bupivacaine injectable suspension admixture administered as an adductor canal nerve block in adolescents undergoing ACLR effectively reduces home opioid usage postoperatively compared with bupivacaine alone.

Level of Evidence: Level II—prospective comparative study.

**Key Words:** opioid, anterior cruciate ligament reconstruction, peripheral nerve blocks

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O pioid misuse and addiction among adolescents is an increasingly concerning problem and literature suggests that exposure to opioids before graduation from high school is associated with a 33% increase in risk for misuse or abuse of narcotics after high school.<sup>1</sup> Postsurgical opioid prescriptions for commonly performed surgeries such as anterior cruciate ligament reconstruction (ACLR) increase opioid exposure in young athletes.

Albeit in adults, many studies indicate other pain control modalities can be used in the postoperative period and successfully prevent the need for narcotics.<sup>2–4</sup> Singleshot peripheral nerve blocks are a pain control modality that has been noted as a viable option.<sup>5,6</sup> Liposomal bupivacaine injectable suspension has been used effectively in the adult population for postoperative pain management and is associated with lower rates of opioid utilization for pain control.<sup>7</sup> Liposomal bupivacaine is a liposomal formulation of bupivacaine, where the drug is encapsulated within liposomes to prolong its release and enhance its duration of action.<sup>8</sup> This liposomal encapsulation allows for a slow and controlled release of the medication over an extended period of up to 72 hours, as compared with plain bupivacaine, which typically provides local anesthesia for a duration of 9 to 12 hours, depending on the specific formulation used and concentration administered.<sup>8</sup>

Furthermore, although it has been previously identified that similar rates of opioid consumption occur with either a single-shot peripheral nerve block or a continuous peripheral

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From the \*Children's Hospital Orange County; ¶Pediatric Orthopaedic Specialists Orange County, Orange; †University of California San Diego School of Medicine, La Jolla; §Department of Anesthesia and Perioperative Care, University of California Irvine School of Medicine; ∥Center on Stress & Health, University of California, Irvine, CA; and ‡Kettering Health Dayton, Dayton, OH.

The authors declare no conflicts of interest.

Reprints: John A. Schlechter, DO, 1310 W Stewart Drive, Unit 508, Orange, CA 92868. E-mail: john\_schlechter@yahoo.com.

nerve block, it has also been shown that postoperative opioid use can be negated in 70% of children after ACLR.<sup>9</sup> With the findings of this prior study in mind, we designed a study that was aimed to analyze the efficacy of liposomal bupivacaine injectable suspension administered as a single-shot adductor canal peripheral nerve block (SPNB). This study thus sought to determine whether liposomal bupivacaine injectable suspension admixture administered as a single-shot adductor canal peripheral nerve block (SPNB+BL) would further decrease utilization of at-home opioid analgesics after ACLR in adolescents compared with single-shot adductor canal peripheral nerve block with bupivacaine (SPNB +B) alone.

### METHODS

A retrospective review of prospectively collected data of a consecutive cohort of patients undergoing arthroscopic ACL reconstruction with or without meniscal surgery by a single surgeon was approved by an Institutional Review Board. Surgeries on patients aged 12 to 18 years between June 2021 and February 2022 and performed at our inpatient hospital or outpatient surgery centers were included. Patients who received 0.25% bupivacaine alone as an SPNB were assigned to group 1 (SPNB+B), whereas patients who received an admixture of liposomal bupivacaine injectable suspension combined with 0.25% bupivacaine were assigned to group 2 (SPNB+BL). Liposomal bupivacaine and bupivacaine (without epinephrine) can be admixed in a single syringe. Up to 15 mL of 0.5% bupivacaine may be mixed with 10 mL liposomal bupivacaine. Because there is a lack of stability data to support expiration dating for admixture, the drug was mixed immediately before use. Thus, the purpose of the admixture of liposomal bupivacaine was to obtain a volume of 20 mL or an increased volume within weight-based dosing.<sup>10</sup> All blocks were placed in the operating room (OR) by the attending anesthesiologist with the patient anesthetized before the procedure. The same anesthesiologists/anesthesia group worked at both the hospital "inpatient" OR and at the outpatient surgery center OR. The decision to perform surgery at the outpatient center or at the hospital was determined by several factors, including OR/patient/surgeon availability and insurance type. Decisions regarding the type of SPNB used were based on whether the surgery occurred at the hospital or surgery centers as liposomal bupivacaine injectable suspension was only available at the surgery centers. All regional nerve blocks were administered at the adductor canal, which is a standard practice to avoid quadriceps weakness that can occur with femoral nerve blocks.<sup>5</sup> No patients required an extended or overnight hospital stay postoperatively.

Preoperative demographic data (sex, age, sports participation, insurance type of either government, or commercial) and operative data (procedure performed, ACLR graft, block type, tourniquet time, and surgery time) were collected. Surgery time was defined as the duration from procedure start time to procedure stop time. For postoperative analgesia, patients were instructed to use cryotherapy and to alternate the use of acetaminophen and ibuprofen. For cryotherapy, patients used a commercial cold therapy unit (DONJOY Iceman Clear or a similar product); if use of a cold therapy unit was not feasible, then ice packs were used. The prescribed use of cryotherapy was 20 minutes on, then 20 minutes off, several times per day, for at least the first 3 days postoperatively. A prescription for 10 pills or liquid equivalent of hydrocodone/acetaminophen (5/325 mg) was placed in a sealed business envelope and handed to the patient and/or caregivers with instruction to use the opioid only if the pain was uncontrolled by the previously described modalities.

Written and verbal education was provided on proper ibuprofen and acetaminophen dosing and patients were encouraged to fully utilize over-the-counter medications in keeping with weight-based dosing. All patients recorded their level of pain, as measured using the visual analog scale, pain treatment satisfaction score, and the amounts of ibuprofen, acetaminophen, and hydrocodone/acetaminophen taken during the 3 days after surgery in a written log. Those that reported not using narcotics were asked to return the unfilled prescription upon the first postoperative follow-up visit. Total and daily hydrocodone consumption was standardized through conversion to morphine milligram equivalents (MME), where 1 mg hydrocodone = 1 MME. In each case, an inquiry was run on the state Controlled Substance Utilization Review and Evaluation System (CURES), which is an electronic tracking program that reports all pharmacy dispensing of certain schedules of controlled drugs by drug name, quantity, prescriber, patient, and pharmacy. The inquiry was run as a control to ensure patients did not receive or fill prescriptions from other providers (ie, ER or primary care physician). Any patient who failed to return the written log was excluded from the study, as was any patient who reported not using narcotics but failed to provide the unfilled prescription.

Data were analyzed by an independent statistician. This study was adequately powered to detect a difference of 20% in the rate of narcotic consumption at 80% power and alpha  $\geq 0.05$ . Comparison of the proportion of patients who consumed narcotics (envelope open) versus those who did not between the 2 treatment groups was performed with  $\chi^2$  test. Further analysis of differences between the treatment groups was performed utilizing ANOVA or Mann-Whitney U nonparametric test for interval variables or  $\chi^2$  test for categorical variables. Multivariate binary logistic regression was performed to evaluate all variables found to be different between treatment groups at P < 0.10 on univariable analysis. In addition, an inverse probability of treatment weighting (IPTW) analysis was performed to account for treatment group differences in the comparison between treatment groups and narcotic use (envelope open).<sup>11</sup> Propensity scores were calculated utilizing all baseline differences between groups to estimate the average treatment effect. Inverse probabilities of the treatment group were calculated and utilized in a weighted  $\chi^2$  analysis. Alpha was set at P < 0.05 to declare significance and analyses were

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performed utilizing SPSS v. 27 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp.).

#### RESULTS

Baseline demographics are indicated in Table 1. Overall, 47 patients (81%) of the entire cohort did not consume any opioids at home after surgery. Eleven patients (19%) consumed opioids, of which 9 (28.1%) were in the SPNB+B group and 2 (7.7%) were in the SPNB+BL group (P=0.048). The average amount of reported opioids taken by the entire cohort was 2 MME, 0.4 pills, with an average reported 3.5 MME, 0.7 pills taken by the SPNB+B group and 0.29 MME, 0.058 pills taken by the SPNB+BL group (P=0.033).

There were no significant group differences in age, surgery time, visual analog scale scores, or pain treatment satisfaction scores on any postoperative day (Tables 1 and 2). All patients reported satisfaction with their postoperative pain control on a scale of 0 to 4 (0=unsatisfied, 4=completely satisfied) with an average score of 2.84 in the SPNB+B group and an average score of 2.96 in the SPNB+BL group (P=0.777). There were no differences in the characteristics of meniscal injury and treatment, graft type, and laterality between groups (Table 2). There was a statistically significant difference in total ibuprofen consumption between the groups (P=0.016); however, there was no difference in average

**TABLE 1.** Demographic Characteristics, Surgical Data, and Visual Analog Scale (VAS) Scores for Children and Adolescents Who Underwent ACLR With SPNB + B (Group 1) and Children and Adolescents Who Underwent ACLR With SPNB + BL (Group 2).

	Group 1 N=32, n (%)	Group 2 N = 26, n (%)	Р
Age (y) (mean $\pm$ SD)	15.5 ± 1	15.4 ± 2	0.614
Sex (male/female)	21/11	10/16	0.039
Insurance type	7/25	26/0	< 0.001
(commercial/government)			
Anesthesiologist years in practice			0.014
(y) 2 2 1			
<5	9 (30)	2 (8)	
5-10	2 (7)	8 (8)	
10-15	15 (50)	8 (32)	
15-20	2 (7)	11 (44)	
> 20	2 (7)	2 (8)	
Surgery time (min) (mean $\pm$ SD)	$101 \pm 21$	$114 \pm 30$	0.139
ACLR graft			0.058
Hamstring	16 (50)	6 (23)	
Hybrid auto/allograft hamstring tendon	1 (3)	0	_
Quadriceps	15 (47)	20 (77)	
Visual analog scale (mean $\pm$ SD)			
VAS day 1	6 ± 2	$6 \pm 2$	0.564
VAS day 2	6 ± 2	$5 \pm 2$	0.187
VAS day 3	$5 \pm 2$	4 ± 2	0.157

ACLR indicates anterior cruciate ligament reconstruction; VAS, visual analog scale.

daily or total acetaminophen taken during the 3-day postoperative period (Table 3).

There was a significant difference in the distribution private insurance versus government insurance of (P < 0.001), sex (P = 0.039), and anesthesiologist years in practice (P = 0.024) between the 2 groups. To account for these differences between treatment groups, further analysis was performed utilizing IPTW to compare narcotic use between treatment groups. Controlling for the above covariates of insurance type, sex, and anesthesiologist years in practice was done via IPTW. Utilization of IPTW creates a pseudo-population in which each patient is reweighted based on their initial likelihood of receiving the treatment to assess the effects of SPNB+BL on postoperative narcotic use in the event that SPNB+BL was offered to each patient in our study population. In this way, IPTW analysis can be used to assess the effects of treatment in a nonrandomized population.<sup>11</sup> Significant statistical difference was maintained for the use of at-home narcotics between the SPNB+B and SPNB+BL groups (*P* < 0.001).

## DISCUSSION

Under the conditions of this study, we found that liposomal bupivacaine injectable suspension admixture administered as an adductor canal nerve block in adolescents undergoing ACLR effectively reduces home opioid usage postoperatively compared with bupivacaine alone. Most notably, the results of this study uphold and increase upon the number of patients who do not require narcotics postoperatively as established by Schlechter et al.<sup>9</sup> Prior results indicated that 70% of patients, regardless of treatment group, did not consume narcotics postoperatively.<sup>9</sup> Of those patients who did consume narcotics, the average use was only 2 pills with no child using >10 pills.9 Comparatively, these current results maintain 72% of patients did not require postoperative opioids in the SPNB+B group, and 93% of patients did not consume narcotics in the SPNB+BL group. One study surveying the prescribing practices of opioids to pediatric patients after ACLR demonstrated that 48% of surgeons prescribed 11 to 19 opioid tablets and 25% prescribed 6 to 10 tablets.<sup>12</sup> Pain medication prescribing practices have also been demonstrated as undertreating pain in Black and Hispanic patients with White patients being more likely to receive opioid prescriptions than other racial and ethnic groups.<sup>13,14</sup> Beck et  $al^{15}$  found the median number of hydrocodone/acetaminophen 5/325 mg consumed by their adolescent patients after ALCR with or without meniscal treatment was less than half of what was prescribed (17/40 tablets). This study demonstrated pediatric patients with ACLR can tolerate the initial postoperative recovery period with an average of less than 1 pill per patient (0.29 MME) with the use of SPNB+BL statistically significantly decreasing the use of opioids compared with SPNB+B alone.

Regarding the safety of liposomal bupivacaine in the pediatric population, Tirotta and colleagues found mostly mild to moderate adverse effects associated with the use of the liposomal bupivacaine and maintained that peak

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<b>TABLE 2.</b> Meniscal Procedures Performed for Children and
Adolescents With ACLR With SPNB+B (Group 1) Versus SPNB
+BL (Group 2).

	Group 1, N = 32	Group 2, N = 26	Р
Medial meniscus repair (MMR)	4	8	0.378
Lateral meniscus repair (LMR)	4	3	
MMR + LMR	6	6	
Partial medial meniscectomy (PMM)	1	0	—
Partial lateral meniscectomy (PLM)	6	1	—
PMM + LMR	1	0	
PLM + MMR	3	1	
Any other procedure	7	7	

plasma concentrations of liposomal bupivacaine in children remained well below established cardiotoxicity and neurotoxicity levels.<sup>16,17</sup> In our study, patients were seen in the post-anesthesia care unit (PACU) for a distal motor exam postoperatively and within 5 to 7 days postoperatively for office exam. Patients were seen again at 3 weeks, 6 weeks, 12 weeks, 6 months, 9 months, 1 year, and 2 years for follow-up exams.

Although there was no statistical difference between groups regarding graft type used, Buescu et al<sup>18</sup> suggest patients who underwent ACLR with hamstring tendon graft experienced less postoperative pain as measured by the amount of analgesics consumed as compared with patients with free quadriceps tendon graft. With increasing rates of quadriceps graft utilization mirroring that of pediatric ACLR graft choices, the impact of graft choice

**TABLE 3.** Hydrocodone Reported as Morphine Milligram Equivalent (MME), Ibuprofen and Individual Acetaminophen Medication Consumption in Milligrams (mg) for Children and Adolescents Who Underwent ACLR With a SPNB + B (Group 1) and Children and Adolescents Who Underwent ACLR With a SPNB + BL (Group 2) Where 1 Dose Hydrocodone 5 mg = 5 MME, 1 Dose Ibuprofen = 200 mg, and 1 Dose Acetaminophen = 500 mg.

	Group 1, N = 32	Group 2, N = 26	Р
MME POD1	$1.1 \pm 3.04$	0	0.037
MME POD2	$1.3 \pm 2.5$	$0.095 \pm 0.49$	0.023
MME POD3	$1.1 \pm 3.30$	$0.2 \pm 0.98$	0.235
MME total	$3.52 \pm 6.44$	$0.29 \pm 1.08$	0.033
Ibuprofen (mg) POD1	$750 \pm 698$	$1076 \pm 677$	0.017
Ibuprofen (mg) POD2	$918 \pm 808$	1192 ± 626	0.065
Ibuprofen (mg) POD3	826 ± 694	$1200 \pm 792$	0.047
Ibuprofen (mg) total	$2494 \pm 2053$	3470 ± 1683	0.016
Acetaminophen (mg) POD1	$1640 \pm 1138$	$2115 \pm 1033$	0.067
Acetaminophen (mg) POD2	$1875 \pm 1283$	$2310 \pm 928$	0.077
Acetaminophen (mg) POD3	$1703 \pm 1190$	1971 ± 1103	0.381
Acetaminophen (mg) total	5219 ± 3312	6394 ± 2752	0.096

Bold indicates statistically significant value.

Measurements are reported as mean  $\pm$  SD.

MME indicates morphine milligram equivalents; POD, postoperative day.

on pain in the immediate postoperative period may be a topic of focus for future research.

The statistical difference in insurance type between the 2 treatment groups was attributed to insurance requirements that self-selected patients into their respective groupings. Patients with government insurance were required to receive their surgery at the children's hospital. Currently, the pediatric hospital does not provide liposomal bupivacaine injectable suspension; thus, patients of the pediatric hospital received SPNB with bupivacaine alone. Although liposomal bupivacaine is readily available across the United States and documented safety has been maintained, the lag in adoption by the children's hospital stems from concern over cost.<sup>16</sup> With any prescribed medication, there is an associated cost, in this case, \$214.75 for 10 mL. Conversely, patients with private insurance could opt for surgery at either the pediatric hospital or the surgery center, which provides liposomal bupivacaine injectable suspension, explaining the difference in distribution between groups. We recognize that the constraints of insurance determination of where a patient's operation is performed biases initial results and should be controlled for in future studies. However, further advanced statistical analysis maintained that patients who received SPNB with liposomal bupivacaine injectable suspension used significantly less narcotics than patients who received SPNB with bupivacaine alone.

The high rates of patients not requiring opioids after a minimally invasive, yet painful surgery, in this current study may be attributed to not only the peripheral nerve block administered preoperatively, but also in part by the extensive preoperative opioid counseling performed by the senior author and surgeon. Yet, although preoperative counseling may have impacted opioid usage, the full effect of preoperative counseling cannot be determined by the methodology of this study. Alongside counseling for the patient and parent, the opioid prescription was provided in a sealed envelope which serves as an extra barrier to fill the medication. Furthermore, the unfilled and returned prescription reduces the amount of unused narcotics that are left in the home that may be used for recreation or even accidental consumption. The advent of the electronic prescribing system for opioids being implemented throughout the United States is another barrier for opioid consumption by regulating the prescribing patterns of opioids by physicians. This system allows for more transparency of opioid prescribing and dispensing to patients by tracking the amount or duration of opioids prescribed to a patient. Although a federal or state regulation of limiting the ability to freely prescribe opioids may seem as an inconvenience to physicians due to increased complaints of uncontrolled pain from patients by phone calls at odd hours or increased visits to the office for pain medications, more studies are being published indicating pain can be managed with nonopioid medications or fewer opioids than believed to be necessary after painful procedures.7,19,20

This current study has several methodological limitations. The study did not quantify or control for type

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or frequency of cryotherapy nor were the perioperative narcotic administration records obtained as such decisions were left to the discretion of the attending anesthesiologist. Furthermore, preoperative consumption of over-the-counter pain medication was not recorded. Postoperative use of opioids during hospitalization before discharge was not recorded as the purpose of this study was to understand the need to prescribe opioid medication in an uncontrolled setting such as the home.

# CONCLUSIONS

The findings of this study demonstrate that liposomal bupivacaine injectable suspension, along with sufficient opioid counseling and barriers, may be used to effectively limit postoperative narcotic consumption while maintaining adequate pain control. Yet, larger multisite prospective randomized controlled studies are needed to further elucidate the role of liposomal bupivacaine injectable suspension as an admixture for regional blocks in children and adolescents undergoing ACL reconstruction.

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