Continuous Bupivacaine Infusion versus Liposomal Bupivacaine in Adductor Canal Block for Total Knee Arthroplasty

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Abstract

Multimodal pain management for total knee arthroplasty (TKA) is essential to enhance functional recovery. Regional anesthesia became a vital component to decrease pain after TKA. Several studies compared femoral versus adductor canal blocks, including evaluating medications that can prolong adductor canal blocks. Liposomal bupivacaine (LB) and continuous local infusion (OnQ) both extend local anesthetic delivery beyond 24 hours. This superiority study compared the use of OnQ versus LB in adductor canal blocks. A retrospective study was conducted between two cohorts of consecutive patients who received adductor canal blocks with either LB or a continuous ropivacaine infusion catheter. Morphine equivalent dose (MED), pain scores, and length of stay (LOS) were compared between the two groups by using the analysis of covariance test. There were 106 patients in the OnQ group and 146 in the LB group. The OnQ group consumed significantly fewer opioids compared with the LB group in the recovery room (5.7 MED vs. 11.7 MED, $p = 0.002$) and over the entire hospitalization (the recovery room plus on the floor; 33.3 MED vs. 42.8 MED, $p = 0.009$). Opioid use between the OnQ and LB group did not reach statistical significance ($p = 0.21$). The average pain scores at rest and with activity were similar in both groups ($p = 0.894$, $p = 0.882$). The LOS between the OnQ and LB groups was not statistically significant (1.2 vs. 1.3, $p = 0.462$). OnQ and LB were equally effective in decreasing opioid consumption on the floor over the averaged 1.3 days of hospitalization; however, the OnQ group significantly reduced opioid use in the recovery room. There was no difference in pain scores or LOS between the two groups. OnQ comparatively prolonged infusion of local anesthetic is a potential edge over LB. This advantage may offset the inconvenience of catheter management and infrequent catheter complications.

Keywords

- total knee arthroplasty
- continuous local infusion
- liposomal bupivacaine
- continuous infusion of ropivacaine
- Exparel

Total knee arthroplasty (TKA) is an effective procedure to decrease pain, improve function, and enhance the quality of life for patients with severe osteoarthritis and end-stage knee disease.[1] Providing optimal postoperative pain control proves challenging. Insufficient management of postoperative knee pain may result in prolonged opioid use, poor sleep, and curtailed functional status and range of motion.[2,3]

The current multimodal regimen used to manage pain include acetaminophen, gabapentin, narcotics, periarticular injections, and peripheral nerve blocks, such as femoral and

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adductor canal blocks. The adductor canal block selectively anesthetizes the saphenous nerve and posterior branch of the obturator nerve. It serves as an effective modality to manage anterior and medial knee pain while minimizing quadriceps weakness that is commonly associated with femoral nerve blocks.[4–6]

Single-shot adductor canal block with either ropivacaine or bupivacaine is active for 7 to 15 hours.[7] In 2011, the U.S. Food and Drug Administration (FDA)-approved liposome-encapsulated bupivacaine (Exparel; Pacira Pharmaceuticals Inc., Parsippany, NJ), a long-acting analgesic for single-dose infiltration. As the liposome degrades and slowly releases bupivacaine, pain relief may be achieved for up to 72 hours.[8] Following a prospective randomized controlled trial, the U.S. FDA approved the use of LB for peripheral nerve block in interscalene brachial plexus in 2018.[9] Meanwhile, many centers assessed off-label use of LB for adductor canal blocks with mixed results.[10,11]

The OnQ pain relief system consists of an elastomeric pump that continuously delivers local anesthetic through a catheter system.[8] Ultrasound guided-adductor canal block with continuous delivery of 0.2% ropivacaine significantly decreased cumulative IV morphine consumption for 48 hours after surgery as compared with a sham catheter.[12] In addition, continuous adductor canal block exhibited lower pain scores, decreased rescue analgesia, and offered better ambulation and functional recovery compared with a single-shot adductor canal block after TKA.[13] Moreover, continuous adductor canal block, as opposed to local infiltration alone, improved analgesia without motor weakness after medial unicondylar knee arthroplasty at 48 hours; pain scores at rest and with activity were lower at 24 and 48 hours.[14] However, a conflicting study demonstrated no superiority in morphine consumption, pain score, or ambulation after postoperative day (POD) 1 and 2 with continuous adductor canal block added to local infiltration analgesia.[15]

Several studies examined the effectiveness of LB or OnQ in adductor canal blocks to other methodologies. Wang et al performed a retrospective matched cohort study comparing adductor canal blocks using LB versus ropivacaine pain ball for total knee replacement surgery. Their findings showed that LB had lower pain scores than 0.1% ropivacaine pain ball within the first 36 hours, and pain scores were comparable 37 to 72 hours.[16] Unfortunately, standard dosing for ropivacaine pain ball is 0.2%, which diminishes the impact of their conclusion.

This study may be the first superiority analysis comparing LB versus OnQ in adductor canal blocks using standard dosing. A retrospective review and analysis were conducted to evaluate the efficacy between LB and OnQ during patients' hospitalization in terms of opioid usage, pain level, and length of stay (LOS). With OnQ's continuous infusion of ropivacaine as opposed to LB's tapering effect after 12 to 36 hours peak, the hypothesis was that OnQ would be a better vehicle to reduce pain with the added advantage of increasing duration.

Methods

This study was approved by our institutional review board (IRB ID: STUDY2020000343). Between January and April 2019, consecutive patient data were collected for the LB cohort; between July and November 2019, consecutive patient data were collected for the OnQ cohort. Patients who had placement of the OnQ catheter for continuous infusion of ropivacaine were categorized as the OnQ group. Patients who received a single injection of LB were classified as the LB group. Patient data were retrieved from one surgeon with over 18 years of knee arthroplasty experience and 13 anesthesiologists. All patients underwent primary TKA with a cemented, fixed bearing design. Analysis of data was performed retrospectively. Exclusion criteria included incomplete charting, nontotal knee cases, revision knee arthroplasty, use of intrathecal narcotics, and use of nonstandard anticholinergic cognitive burden medication. Chronic pain patients were not explicitly sought or excluded from this study.

Adductor canal blocks were performed in the preoperative suite immediately before patients entered the operating room. Ultrasound guidance with Sonosite 15–6 Mhz linear probe (Sonosite Inc, Bothell, WA) was used to identify the sartorius muscle, femoral artery, and saphenous nerve over the mid-upper thigh on the operative side.[17] Prior to introducing the needle into the adductor canal, the skin was infiltrated with 2 to 3 mL of lidocaine. In the OnQ group, 18 g Touhy was inserted into the adductor canal, and a (20 g and 61 cm) SPIROL catheter was inserted through the Touhy to the adductor canal space prior to removing the Touhy. The type and volume of local anesthetic administered were at the discretion of individual anesthesiologists. Precisely, 29 ± 3 mL of 0.25% bupivacaine, 20 ± 3 mL 0.2% ropivacaine, or 17 ± 4 mL 0.5% ropivacaine of the volume was initially injected through the Touhy, followed by completing the injection through the catheter. In the LB group, 80 or 100 mm echogenic needle was inserted into the adductor canal space and then 10 mL of LB with 14 ± 5 mL 0.25% bupivacaine was injected through the needle.

Preoperatively, patients received 650 mg acetaminophen and 40 mg pantoprazole PO. Either spinal or general anesthesia was performed intraoperatively, depending on patients' preferences. About 4 mg dexamethasone and up to 30 mg ketorolac IV were administered based on the renal function. Subcutaneous infiltration of 20 mL of 0.25% bupivacaine with 1:200,000 epinephrine was given to both groups. All patients received a periarticular injection. Specifically, in the OnQ group, a mixture of 20 mL 0.5% bupivacaine with 60 mL saline was injected into the periarticular soft tissue space. In the LB group, a mixture of 10 mL (133 mg) LB, 10 mL 0.5% bupivacaine, and 60 mL saline was administered. At the end of the surgery, the elastomeric pump with a select-a-flow variable rate controller was connected to the SPIROL catheter in the OnQ group, infusing 0.2% ropivacaine at an average rate of 6 mL/h. Unless contraindicated, patients in both groups received ketorolac every 6 hours for 24 hours postoperatively. Opioids were given on an as-needed basis.

Nurses and anesthesiologists charted the data in the Epic electronic medical record system; later, the data were collated by a pain management pharmacist. Information collected included LOS, total opioid use in the recovery room and on the floor, expressed in morphine equivalent dose (MED) in

Table 1 Demographics of patients in the continuous local infusion and liposomal bupivacaine group

	OnQ ($n = 106$)	LB ($n = 146$)	p-Value
Age (y)	71.3 ± 8.1	70.8 ± 8.1	0.59
Gender (n)	Female (57)	Female (81)	0.79
	Male (49)	Male (65)	
Weight (kg)	84.3 ± 21.5	77.9 ± 16.1	0.01
Type of anesthesia (n)	Spinal (80)	Spinal (105)	0.53
	General (26)	General (41)	

Abbreviations: LB liposomal bupivacaine; OnQ, continuous local infusion.

milligrams, and average pain scores at rest and with activities based on a 0 to 10 scale with 10 being the worst pain ever experienced. Physical therapy started on the first POD. Discharge criteria included adequate pain control on oral pain medication, independent transfer, minimum ambulation of 200 feet, and stair climbing if patients had stairs at home. All patients stayed at the hospital for at least one night.

Statistical Analysis

A normality test was performed among each of the independent categories. Pearson's Chi-square test was used to calculate p-values comparing gender and type of anesthesia between OnQ and LB groups. Independent sample t-tests were applied to calculate p-values for age, weight, and MED/kg in recovery room (RR) on the floor and total between OnQ and LB groups. Analysis of variance (ANCOVA) was used to calculate p-values for the LOS, MED in RR on the floor, and total and average pain scores at rest and with activities. Statistical significance was set at a p-value of less than 0.05 with a two-tailed hypothesis testing. All statistical analyses were performed by using IBM SPSS Statistics, version 25.

Results

Overall, 197 patients in the OnQ cohort and 198 patients in the LB cohort were collected for analysis. About 91 were excluded from the OnQ group, and 52 were excluded from the LB group, leaving 106 in the OnQ group and 146 in the LB group. There were 46% females in the OnQ group and 55% in the LB group. Nearly, 75% of the patients in the OnQ group received spinal anesthesia, and 72% of the patients in the LB group received spinal anesthesia. No statistical differences were found in the demographics between the two groups, except for weight, where patients in the OnQ group was 6.4 ± 5.4 kg heavier ($p = 0.007$; ►**Table 1**).

Statistical difference was detected in the recovery room ($p = 0.002$). Opioid use on the floor in the OnQ group was 27.7 MED as compared with the LB group of 31.2 MED, but that difference by itself did not reach statistical significance. Total opioid use between the two group was lower in the OnQ group ($p = 0.009$; ►**Table 2**). Similar statistical results were achieved when comparing opioid use per kilogram weight in the OnQ group and LB group (►**Table 2**). Average pain scores at rest and with activity, and LOS between OnQ and LB groups did not test statistically significant (►**Table 2**).

Of the 106 OnQ patients, 87 patients had documented follow-up in the chart. Twenty-two percent of the followed patients had complications ranging from mild catheter leakage to possible infection (►**Table 3**). A total of 9 of the 87 patients did not complete the OnQ infusion. The causes were early dislodgment, possible catheter migration, premature removal, and one catheter leak. One patient had failed catheter placement where he was admitted to the ER for severe pain on

Table 2 Comparison of narcotic consumption, average pain scores, and length of stay

	OnQ ($n = 106$)	LB ($n = 146$)	p-Value
MED in RR (mg)	5.7 ± 11.1	11.7 ± 18.3	0.002
MED/kg in RR (mg)	0.07 ± 0.13	0.15 ± 0.25	0.003
MED on floor (mg)	27.7 ± 24.7	31.2 ± 27.3	0.210
MED/kg on floor (mg)	0.35 ± 0.34	0.41 ± 0.36	0.180
MED total (mg)	33.3 ± 27.6	42.8 ± 33.5	0.009
MED/kg total (mg)	0.41 ± 0.37	0.56 ± 0.43	0.004
Average pain score at rest	2.3 ± 1.3	2.3 ± 1.4	0.890
Average pain score with activity	3.6 ± 1.7	3.5 ± 1.5	0.880
Length of stay (d)	1.2 ± 0.5	1.3 ± 0.5	0.460

Abbreviations: LB, liposomal bupivacaine; MED, morphine equivalent dose; OnQ, continuous local infusion; RR, recovery room; total, recovery room plus the floor.

Table 3 Continuous local infusion catheter complications

	OnQ patients followed ($n = 87$)	Comments
Failed placement	1	Replaced catheter in ER
Dislodgment	3	Accidental removal by patients
Possible migration	2	Pain not well controlled
Premature removal	3	Patient decision
Catheter leak	7	Mild completed treatment × 6
Allergic reaction	2	Blistering and/or erythema
Possible infection	1	Resolved with antibiotics
Total (*n*)	19	

Abbreviations: ER, emergency department; OnQ, continuous local infusion.

POD 1. A new OnQ catheter was subsequently placed without any complication. The reasons for premature removal of the catheters by patients were as follows: OnQ ball did not shrink on POD 1, balance concern with carrying the OnQ on POD 4, and undocumented reason on POD 2. Six of the catheter leaks were mild, and treatments were completed. Two patients noticed erythema, with one having a blister after dressing removal on POD 5. One patient was admitted to Lomita Acute Care Facility for possible infection with erythema between the knee and catheter site. She was treated with antibiotics with complete resolution of symptom.

Local anesthetic toxicity or motor weakness resulting in falls was absent in both groups. There was no significant adverse outcome in the Exparel group.

Discussion

Total knee arthroplasty is an effective procedure for patients with severe osteoarthritis who have exhausted less invasive modalities. Pain control is key to optimal functional recovery in these patients. Periarticular infiltration and adductor canal blocks are particularly efficacious in managing pain after TKA. Smith et al conducted a randomized, controlled, and double-blinded study finding no difference in opioid consumption in periarticular LB injection versus intra-articular bupivacaine infusion catheter after TKA.[18] This retrospective study may be the first to compare continuous bupivacaine infusion versus LB in the adductor canal using standard dosing.

Applying descriptive analysis of the data, similar histograms between the two groups were obtained but did not follow a normal distribution. Despite weight as a covariate, a sample size of over 100 allowed us to use the parametric test ANCOVA to test significance.[19] When the covariate was not considered, similar statistical results were obtained with Student's *t*-test, which yielded an increased effect size. To further determine whether differences in mean weight between the two groups affected the outcome, we divided opioid consumption by patient weight and obtained an identical conclusion.

Interestingly, the results demonstrated a statistically significant difference between the OnQ and LB group in RR but not on the floor. A plausible explanation could be that the OnQ group had a higher volume of active medication (average 21 mL of bupivacaine hydrochloride) as opposed to the LB group, where most of the active drug was bound to the liposome and only around 10 mL was extra-liposomal. If similar bupivacaine HCL volume was used with LB, the increased opioid consumption in the recovery room by the LB group might be obviated.

The significant difference in total MED during hospitalization between the two groups was primarily attributed to a reduction in opioid use in RR. MED decrease on the floor in the OnQ group as opposed to the LB group was small and not statistically significant. There was no statistical difference between the OnQ and LB group with pain scores at rest or with activity on the floor.

Several factors may have accounted for the above results. LB exhibited biphasic peaks: a small peak in the first hour and a larger peak at 12 to 36 hours.[20] This model could be replicated whether LB was used alone or in combination with bupivacaine HCL as long as the 2:1 LB to bupivacaine HCL was maintained.[21] The average LOS for LB patients was 1.3 ± 0.5 days. The analgesic effect of LB usually subsides after 1 to 2 days.

Another explanation rendering no difference between LB and OnQ on the floor may be the presence of extended-release bupivacaine in the periarticular tissues and in the posterior capsule in the LB group as opposed to the OnQ group that only received bupivacaine HCL. After 7 to 15 hours when bupivacaine HCL was metabolized, patients may have required pain medication for lateral and posterior aspects of the knee in the OnQ group.

LB offered the simplicity of a single injection, providing pain relief on the floor comparable to that of OnQ for at least 30 hours based on our study. The OnQ system's clear advantage was the duration. A 750 mL OnQ reservoir with a pump set at 6 mL/h provided analgesia for 5 days. Local toxicity was not a concern for continuous ropivacaine infusion in this system.[22] However, this reservoir may have been cumbersome for patients to carry and shower. Moreover, challenging catheter placement, catheter leakage, inadvertent catheter removal, catheter breakage and retention, pump failure, and infection were potential disadvantages of the OnQ system that required deliberation.

There was no direct comparison of patient satisfaction between OnQ and LB; however, the OnQ patients received regular phone calls to monitor the pump over 5 days, which boosted patient satisfaction. Four patients in the OnQ group who also had LB in a previous knee surgery by the same surgeon stated better pain control, improved physical therapy, and decrease narcotic use with OnQ. Another limitation in this study is that pain scores and MED were not recorded beyond hospitalization. While we may infer that pain control for the OnQ would remain stable for up to 5 days as long as the medication reservoir is not depleted, we cannot prove that in this series. Future studies examining pain relief after discharge are warranted.

This retrospective study showed that LB was as efficacious as OnQ after the recovery room for at least 30 hours. OnQ theoretically offers pain control for 5 days at an effective rate of 6 mL/h, as opposed to LB, which is purported to last 2 to 3 days. The simplicity of a single injection with LB for patients and providers could not be overstated. However, the prolonged infusion of local anesthetic by the OnQ system, allowing for an extended period of pain control for functional recovery of patients, is a definite advantage. At our institution, we switched from LB to the OnQ system because of the positive feedbacks from home physical therapy, and the longer infusion time of local anesthetic to the adductor canal space despite the minor cost difference (~$100 more marginal cost for the OnQ system). On the other hand, LB was the preferred choice for patients with specific conditions, such as bleeding disorders or inability to manage the OnQ pain pump.

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Conflict of Interest
None declared.

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