An Original Study

Total Knee Arthroplasty Performed With Long-Acting Liposomal Bupivacaine Versus Femoral Nerve Catheter

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Abstract

Inadequate pain management after total knee arthroplasty (TKA) can interfere with participation in and progression of physical rehabilitation, and thereby prolong hospital stay, and increase costs and overall dissatisfaction with the procedure. At our institution, TKA traditionally has been performed with femoral nerve catheters (FNCs) for postoperative pain control.

We conducted a retrospective, longitudinal, repeated-measures study to compare FNC and long-acting liposomal bupivacaine (LALB) with respect to pain control, range of motion, ability to ambulate, and hospital length of stay. Twenty-three patients underwent separately staged bilateral TKAs, the first with FNC and the second with periarticular injection of LALB.

Statistically significant differences favoring LALB over FNC were found for hospital length of stay ($P < .01$), per-attempt walking distance during hospitalization ($P < .01$), total range of motion (extension plus flexion) at 3-week follow-up ($P = .02$), and total morphine-equivalent dose during hospitalization ($P = .02$).

Our results showed that, compared with patients who received FNC, patients who received LALB had comparable pain control, improved knee range of motion, and shorter hospital stays. Additional clinical studies are needed to better determine the efficacy and cost-effectiveness of LALB and other long-acting local anesthetic formulations.

Almost 1 million total knee arthroplasties (TKAs) are performed in the United States each year, and the number continues to grow.[1,2] For patients about to undergo TKA, a significant concern is postoperative pain.[3] Fear of postoperative pain is often cited as a reason for delaying surgery.[3] Recent literature suggests that patients with poor pain management during the first 48 hours after surgery have a 50% chance of gaining satisfactory long-term pain relief.[4] In addition, inadequate postoperative pain management can interfere with participation in and progression of physical rehabilitation, prolong hospital stay, and increase patient dissatisfaction.[5] Poorly controlled pain results in decreased range of motion (ROM), strength, stability, and ambulation thereby prolongs hospital stays, and increases costs and overall dissatisfaction with the procedure.

Post-TKA pain management has received much attention in recent years. A multimodal pain management protocol is now a key component of clinical pathways in TKA. Appropriate postoperative pain control lowers postoperative complications and accelerates recovery.[6] Pain-caused loss of function makes surgical patients more susceptible to edema, deep vein thrombosis, and pulmonary embolism.[4] Various oral and intravenous medications are used to lessen the pain response during the perioperative period. In addition, regional or neuraxial anesthesia is often added to blunt the immediate surgical pain response.[7,8] At our institution, TKA traditionally has been performed with femoral nerve catheters (FNCs) for postoperative pain control. Although effective, this method often results in decreased quadriceps musculature function, which delays rehabilitation and increases the fall risk. Recently, there has been a shift toward using local anesthetic infusions about the

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knee to provide adequate pain relief and restore motor function, which is often sacrificed with use of regional nerve blocks and continuous catheter infusions.[9]

Many institutions have started using a new long-acting local anesthetic in their multimodal pain management pathways: Exparel (Pacira Pharmaceuticals), a liposomal membrane-bound bupivacaine with sustained release of approximately 72 hours. Several studies have verified the safety of this medication.[10] A systemic review of prospective studies revealed that, compared with bupivacaine, long-acting liposomal bupivacaine (LALB) in therapeutic doses had a higher safety margin and a favorable safety profile.[10] However, no study has compared the effectiveness of LALB and FNC in a matched TKA cohort with each patient serving as his or her own control.

We recently reviewed our multimodal pain management protocol for any areas in need of improvement and decided to compare the effects of the indwelling FNC protocol that was in use with the effects of injecting the local anesthetic LALB. We conducted a study to compare the 2 methods with respect to pain control, ROM, ability to ambulate, and hospital length of stay (LOS). We hypothesized that the longer acting local anesthetic would provide comparable post-TKA pain control and post-TKA opioid use but would accelerate post-TKA rehabilitation.

Materials and Methods

This retrospective, longitudinal, repeated-measures study was approved by the Greenville Hospital System Institutional Review Board and conducted at the Steadman Hawkins Clinic of the Carolinas, Greenville Health System.

Interventions

Twenty-three patients underwent separately staged bilateral TKAs between 2010 and 2013. For each TKA, a Genesis II implant (Smith & Nephew) was used, and the surgery was performed with the patient under spinal anesthesia. In each case, FNC was used for pain control after the first TKA, and periarticular injection (PAI) of LALB for pain control after the second TKA.

In the first TKAs, FNC-administered ropivacaine 0.2% (2 mg/mL) was maintained at a standard basal rate of 8 mL/h for 48 hours. In the second TKAs, LALB was administered along with bupivacaine/epinephrine. Twenty milliliters of LALB from a single-use vial was diluted in 40 mL of normal (0.9%) saline to obtain a 60-mL solution, and a 25-gauge needle was used to inject this solution into the periarticular soft tissues; another needle was used for PAI of 30 mL of bupivacaine 0.25% with epinephrine.

Continuous passive motion devices were not used. Most patients began therapy on day of surgery. Knee immobilizers were not used in the FNC group.

The same standardized multimodal pain management protocol was used for all TKAs. Nonnarcotic medications, including acetaminophen, ketorolac, and celecoxib, were given on a scheduled basis. Tramadol and opioid medications were administered as needed for pain. The attending physician based patient discharge timing on pain control, ability to safely ambulate, and absence of complications.

Outcome Measures

Outcome measures were LOS; extension and flexion at discharge and 3-week follow-up; total ROM (extension plus flexion) at discharge and 3-week follow-up; per-day and total hospital stay morphine -equivalent doses (MEDs); and per-attempt walking distance during gait training.

ROM was measured with a standard goniometer. Flexion was tested with the patient supine and the hip and knee in neutral rotation. The goniometer axis was along the lateral epicondyle of the femur with the proximal arm of the goniometer parallel to the long axis of the femur and pointing at the greater trochanter and with the distal arm parallel to the long axis of the fibula and pointing at the lateral malleolus. The patient was instructed to flex the hip and knee by moving the heel toward the buttock. Expected normal ROM is 135°. The same landmarks were used for extension. The patient was instructed to push the back of the knee toward the plinth/bed, for maximal active extension. The same ROM assessment strategy was used during the hospitalization and at the 3-week follow-up.

Several opioid medications (eg, hydrocodone, oxycodone, tramadol, hydromorphone, morphine) with different dosages were used

Take-Home Points

- At our institution, LALB has shortened our hospital stay.
- There is a trend towards decreased opioid consumption with LALB.
- With the opioid epidemic we face today, LALB can be one of many options in our toolbox towards a solution.
- As stated in prior publications, the effectiveness of LALB is definitely technique dependent.
- Additional clinical studies are warranted to better determine the efficacy and cost-effectiveness of LALB.

Table. **Comparison of Total Knee Arthroplasty Outcomes in the 2 Groups: Long-Acting Liposomal Bupivacaine and Femoral Nerve Catheter**

Outcome, mean (SD)	Group		*P*[a]
	Long-Acting Liposomal Bupivacaine	Femoral Nerve Catheter	
Length of stay, d	2.3 (0.55)	2.8 (0.38)	**<.01**
Range of motion, degrees			
Extension at discharge	–2.3 (3.9)	–1.7 (3.9)	.65
Flexion at discharge	84.0 (9.3)	78.7 (9.6)	.07
Extension at 3 wk	–0.24 (2.4)	1.0 (3.2)	.15
Flexion at 3 wk	115.5 (12.5)	109.8 (14.6)	.18
Total (extension plus flexion) at discharge	80.7 (10.4)	75.6 (9.8)	.10
Total (extension plus flexion) at 3 wk	116.3 (11.1)	107.2 (14.6)	**.02**
Morphine-equivalent doses			
Per-day (total/d in care)	66.18 (31.34)	76.65 (45.28)	.36
Total	145.47 (62.2)	214.30 (125.98)	**.02**
Walking distance, feet/d of inpatient stay	135.9 (56.7)	84.2 (31.0)	**<.01**

[a]Bold *P* values are significant.

during hospitalization. Opioid doses were converted to MEDs to permit FNC–LALB comparisons. For each patient, total MEDs were divided by LOS to determine MEDs per day.

Mean per-attempt walking distance was calculated by dividing the total distance walked during hospitalization—the sum of the number of feet walked during each and every attempt, as measured by the treating physical therapist—by the total number of walking attempts.

Data Analysis

A paired-samples *t* test was used to calculate differences between all outcome measures: LOS; extension and flexion at discharge and 3-month follow-up; per-day and total MEDs; and mean per-attempt walking distance. $P \leq .05$ was considered significant. We elected not to adjust our α for a potential familywise error.

Results

Of the 23 patients, 14 were female and 9 were male, and 19 were white and 4 were black. Mean (SD) age was 64.4 (6.4) years for the FNC group and 66.0 (6.0) years for the LALB group. The age difference was not statistically significant.

Statistically significant differences favoring LALB over FNC were found for mean LOS (LALB, 2.3 days; FNC, 2.8 days; $P < .01$), mean per-attempt walking distance (LALB, 135.9 feet; FNC, 84.2 feet; $P < .01$), and mean total ROM at 3-week follow-up (LALB, 116.3°; FNC, 107.2°; $P = .02$). Furthermore, a statistically significant difference was found for mean total MEDs during hospitalization (LALB, 145.47; FNC, 214.30; $P = .02$) (**Table**). In addition, there was a nonsignificant trend toward less drug administration.

Discussion

Poor pain control during the post-TKA period may have a significant impact on recovery rate, standard of living, psychological health, and postoperative complications.[10] Inadequate postoperative pain control increases postoperative morbidity, hinders physiotherapy, increases anxiety, disrupts sleep patterns, and decreases patient satisfaction.[9] There has been increased interest in PAIs. Local anesthetics are additional sources of pain control at surgical sites. However, the half-life of most local anesthetics is short. Soft-tissue infiltration of LALB into a surgical site extends the duration of active analgesia. Our study found that, compared with patients who received FNC, patients who received LALB had comparable pain control, improved knee ROM, and shorter hospital stays. In addition, the LALB group had no reports of quadriceps weakness or falls, both of which are associated with femoral nerve blocks. The FNC group had no reported falls, either. PAIs have the benefit of avoiding the invasiveness of femoral nerve blocks and possible neuritis.

Many complications are associated with or indirectly related to delayed rehabilitation and immobility during the acute post-TKA period. From prolonged hospitalization to need for manipulation, the consequences of inadequate pain control and decreased function can be numerous and costly for patients and the healthcare system. In the present study, LALB use led to a statistically significant overall decrease in mean LOS (LALB group, 2.3 days; FNC, 2.8 days). With LALB, there was a higher likelihood of discharge the day after surgery; 20% of patients in the LALB group and no patients in the FNC group went home that day.

The implication is that inadequate pain control led to decreased motion and decreased progression during postoperative rehabilitation. Local infiltration resulted in increased total ROM (extension plus flexion) at 3-week follow-up (LALB, 116.3°; FNC, 107.2°). In addition, there was an increase in walking distance per day of hospital stay (LALB, 135.9 feet; FNC, 84.2 feet). Furthermore, patients indicated LALB when asked which anesthetic they preferred. To our knowledge, this is the first study to compare LALB and FNC data in a matched TKA cohort with each patient serving as his or her own control.

Our study had several limitations. First was the retrospective design. Second was the small sample size, which made definitive conclusions difficult. However, the statistically significant differences we noted validated our conclusions. A statistically significant difference favoring LALB over FNC was found for total MEDs during hospitalization, but there was no significant difference in per-day MEDs. A possible reason for this difference is that LALB patients had shorter hospital stays, and therefore received fewer doses overall. Another possible reason is the small sample size; whereas a larger study using our protocol may find a statistically significant difference between LALB and FNC, we found only a trend. In the FNC group, anesthetic infiltration occurred with use of a computerized pump, which was removed on postoperative day 2; most of these patients were discharged home that day or the morning of postoperative day 3. As it is possible that some of these patients could have gone home sooner, our LOS data may have been affected. We do not consider this limitation significant, as one of our discharge criteria was 150 feet of ambulation, and most patients who received FNCs could not ambulate that far until after FNC removal. Furthermore, this study compared LALB only with FNC. It is possible that our improved outcomes could have resulted from the PAIs themselves, irrespective of LALB. In a recent TKA study by Bagsby and colleagues,[11] pain was controlled better with the less expensive traditional PAI of ropivacaine, epinephrine, and morphine than with the PAI of liposomal bupivacaine. Last, in our study, the experience of undergoing the first TKA may have increased patients' confidence going into the second TKA and then helped them make faster progress in rehabilitation. Regardless, the promising results of our study and the firsthand use of LALB at our institution led us to modify our intraoperative pain management protocol for surgeons who perform TKA.

As we continue to use LALB, our study numbers will increase, and we may discover other factors that, though now underpowered, will prove to be statistically significant. Additional clinical studies are needed to better determine the efficacy and cost-effectiveness of LALB and other long-acting local anesthetic formulations.

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This paper will be judged for the Resident Writer's Award.