Femoral Nerve Block Versus Long-Acting Wound Infiltration in Total Knee Arthroplasty

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abstract

Multimodal wound infiltration analgesic techniques have attracted growing interest for applications in total knee arthroplasty (TKA). A benefit of using wound infiltration instead of femoral nerve block (FNB) in a multimodal pain control regimen is the limitation of muscle strength impairment to the surgical area, which will focus the pain control effort and may provide the opportunity for easier rehabilitation and earlier discharge from the hospital. The current study directly compares patients undergoing TKA who are given a continuous FNB with those who were administered an injection of liposomal bupivacaine infiltration. The study cohort included 36 patients with osteoarthritis who were treated with a continuous FNB (OnQ pump; I-Flow, Lake Forest, California), and 36 patients who were administered an injection for liposome bupivacaine infiltration (EXPAREL; Pacira Pharmaceuticals, Inc, Parsippany, New Jersey) for postoperative pain analgesia. The average number of narcotic doses and the total number of narcotics consumed was greater in the FNB group ($P<.001$). Average visual analog scale pain scores trended higher for patients in the FNB group (2.29 vs 1.93) overall and for each day postoperatively up to day 5, although the overall difference was not significant in this study sample ($P=.115$). The results of the current study support the conclusion that long-acting liposome bupivacaine infiltration gives comparable postoperative analgesia compared with a continuous FNB, but with significantly less narcotic medication. [Orthopedics. 2016; 39(3):e449-e455.]

The introduction of less invasive surgical techniques to the practice of total joint replacement has led to a new focus on pain management. Effective pain control improves satisfaction, promotes earlier mobility and physiotherapy, results in fewer cardiac and pulmonary complications, enhances recovery,
improves quality of life, and reduces the likelihood of developing chronic pain syndromes. Given the importance of the pain experience, the Agency for Healthcare Quality and Research and the Joint Commission recommend that adequacy of pain management and patient satisfaction serve as metrics for hospital performance.

To date, there are no prevailing best practices for pain management following total knee arthroplasty (TKA). Common pain management techniques for TKA are still heavily opioid dependent, despite the observance that opiate analgesics on their own are a suboptimal modality. Opioid-related adverse events, including constipation, nausea, vomiting, and ileus, are common early complications that, along with difficulties in pain control, may delay patient rehabilitation and discharge. Multimodal analgesia regimens have been designed to combine oral medications (eg, nonopiate analgesics, opiate analgesics, anti-inflammatory medication) with regional techniques, either wound infiltration with local anesthetics or femoral nerve block (FNB), to decrease opiate consumption. Femoral nerve blocking is a commonly used regional technique and has been shown to be highly effective for pain relief after TKA. However, quadriceps weakness due to the block can delay rehabilitation and is a known contributing factor for patient falls inside and outside of the hospital. It is estimated that quadriceps strength can be reduced by at least 50% of baseline with nerve blocks, even with low infusion rates. Given the muscle strength impairment inherent in femoral nerve blocking, the dosage must be balanced to allow early physical therapy, and thus more opioids may be necessary to supplement pain control.

Wound infiltration analgesic techniques have attracted growing interest for applications in large joint arthroplasty. In relation to FNB, a major benefit of using wound infiltration in a multimodal pain control regimen is the limitation of muscle strength impairment to the surgical area, which will focus the pain control effort and may provide the opportunity for easier rehabilitation and earlier discharge from the hospital. In terms of pain control, there is no current consensus on the effectiveness of local infiltration compared with peripheral nerve blocks. Traditionally, the effectiveness of local wound infiltration with bupivacaine-based injections has been limited by the duration of its effectiveness, having a half-life of 2.7 hours. Recently, a single-dose local analgesic was introduced that uses bupivacaine in combination with a liposomal time-released product delivery platform (EXPAREL; Pacira Pharmaceuticals, Inc, Parsippany, New Jersey). It has been proposed that the time release mechanism can improve the duration of effectiveness for wound infiltration analgesia, and thus could potentially reduce the amount of opioid medications required for effective pain control.

The current study directly compared patients undergoing TKA who were given a continuous FNB supplementing local surgical-site bupivacaine hydrochloride infiltration with those who were administered liposomal bupivacaine infiltration supplementing the same local surgical-site bupivacaine hydrochloride infiltration. The purpose of this study was to compare the pain scores and opiate consumption for patients undergoing primary TKA with these differing pain management techniques. The hypothesis was that the liposomal bupivacaine could provide equivalent pain relief to a continuous FNB while requiring a lower supplemental opioid dosage.

**Materials and Methods**

The study cohort included 72 patients with osteoarthritis treated with primary TKA by a single surgeon (R.H.E.) between December 2011 and August 2013. The treatment course for all patients was identical aside from the analgesic regimen. Anesthesia for all patients included preemptive medications (75 mg of pregabalin, 10 mg of oxycodone, and 200 mg of nonsteroidal anti-inflammatory drugs [NSAIDs]), along with general anesthesia. In addition, all patients received local infiltration with 0.5% bupivacaine hydrochloride with epinephrine and ketorolac (30 mg) if medical status permitted. For postoperative pain analgesia, 36 patients (from December 2011 to September 2012) were treated with a continuous FNB using 0.5% bupivacaine administered with a pump device (OnQ pump; I-Flow, Lake Forest, California) to achieve longer effectiveness, and 36 patients (from October 2012 to August 2013) were administered liposome bupivacaine infiltration (EXPAREL) to achieve similar extended analgesia. For all analgesic infiltration, the posterior injections were done just prior to placing the implant components, and all other anatomic layers were injected while the cement was setting up prior to closure at the end of the surgery. Additional medications were administered on a scheduled basis as shown in Table 1. Opiate medications were available on a scheduled basis and for rescue at the discretion of the patient. The number of opiate doses given and requested and the total amount of opiates (converted to hydrocodeine equivalents) were tabulated. Patients from each group were selected randomly from a prospectively collected database to minimize unforeseen biases.

The wound infiltration for both groups was done with a 21-gauge, 1.5-inch needle. A moving injection technique was used on all tissue layers, inserting the needle and injecting on the way out to prevent a large volume of medication placed into one location. The back of the knee was injected prior to placing the components due to ease of access, aspirating before injecting and avoiding the midline vascular structures. The synovium, suprapatellar pouch, medial and lateral capsule, and subcutaneous layers were injected while the cement was setting. A total volume of injected solution was adjusted with normal saline to be between 60 and 100 cc, depending on...
the size of the incision. Liposomal bupivacaine was injected separately and diluted with normal saline as needed. EXPAREL has been approved by the US Food and Drug Administration (FDA).

Outcomes collected for each patient included the 10-point visual analog scale (VAS) pain score, total opiates converted into hydrocodone equivalents, and the number of opiate rescues administered postoperatively. Each outcome was quantified for each postoperative day (up to 5 days) and over the entire postoperative period. With assistance of the hospital information technology department, the authors created a pain management report as part of the hospital electronic medical record that tracked the patients’ VAS pain scores and the medications used postoperatively. Data were gathered prospectively in the course of the postoperative management of the patients. All information was tracked after the patient left the post-anesthesia care unit until discharge.

Inclusion criteria included a knee osteoarthritis diagnosis, treatment by a single surgeon (R.H.E.), and a primary TKA procedure. Sample size was determined using a power analysis to estimate the sample size based on determining a difference in VAS pain scores between the 2 groups. The analysis assumed a 95% confidence level with α=0.05, 5% chance of committing a type I error (false positive), and 20% likelihood of a type II error (false negative). Ranges and relative treatment effects were estimated from pilot research studies and the literature. The power analysis determined a sample size of 36 patients for each group.

Statistical analysis was performed with SAS version 9.4 statistical software (SAS Institute Inc, Cary, North Carolina) comparing demographics, pain scores, and opiate administration. The study sample size was large enough that 2 sample Student’s t tests were implemented to test for differences in the means between FNB and EXPAREL groups for age, body mass index (BMI), and hospital length of stay, even as the variables were not normally distributed. Chi-square tests were used for categorical variables, including sex. Differences in pain scores, average number of opiate doses, and total hydrocodone equivalents were tested using 2-sample t tests to compare differences between group means. In addition, regression analyses were used to investigate associations between patient demographics, surgery, or treatment groups with average pain scores overall and by day. Variables in the regression analysis included race, ethnicity, BMI, sex, hospital length of stay, unilateral/bilateral TKA, and patient age at surgery. For all tests, statistical significance was adjusted for multiple comparisons (P=.003).

This study was approved by the institutional review board of the authors’ institution.

### RESULTS

Demographics, including sex, age, and BMI, were similar between the EXPAREL and FNB groups (P>.193) (Table 2). The distribution in procedures was not statistically different, although there were 3 more bilateral TKAs in the EXPAREL group (Figure 1). Average hospital length of stay was 2.92 days in the EXPAREL group and 3.14 days in the FNB group (P=.213).

Average VAS pain scores trended higher for patients in the FNB group (2.29 vs 1.93) overall and for each day postoperatively up to day 5 (Figure 2), although the overall difference was not significant in this study sample (P=.115). When excluding patients undergoing bilateral TKA, average pain scores decreased to 2.17 for the FNB group and 1.81 for the EXPAREL group, a difference that was still not significant for this sample.

### Table 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Continuous Femoral Nerve Block</th>
<th>Liposome Bupivacaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain pump, ropivacaine hydrochloride for injection</td>
<td>EXPAREL® 20 cc, 266 mg</td>
<td></td>
</tr>
<tr>
<td>0.2% bolus, 0.15% infusion</td>
<td></td>
<td></td>
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<tr>
<td>Dose adjusted by nursing, physical therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivacaine 0.5% 30 cc, diluted total volume 60 cc</td>
<td>Bupivacaine 0.5% 30 cc, diluted total volume 60 cc</td>
<td></td>
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<tr>
<td>Morphine sulfate 10 mg</td>
<td>Morphine sulfate 10 mg</td>
<td></td>
</tr>
<tr>
<td>Oxycodone sustained release 10 mg every 12 h</td>
<td>Tramadol 50 mg every 6 h</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone 10/325 every 6 h as needed</td>
<td>Tylenol® 1000 mg by mouth every 8 h</td>
<td></td>
</tr>
<tr>
<td>Gabapentin 300 mg twice daily</td>
<td>Gabapentin 300 mg every 12 h</td>
<td></td>
</tr>
<tr>
<td>Ketorolac 15 mg IV every 6 h as needed</td>
<td>Meloxicam 7.5 mg every 12 h</td>
<td></td>
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<tr>
<td>Rescue opiates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-controlled Dilaudid® 24 h</td>
<td>Hydrocodone 10/325 every 6 h as needed</td>
<td></td>
</tr>
<tr>
<td>Dilaudid by mouth, IV as needed</td>
<td>Dilaudid by mouth, IV</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: IV, intravenous.

*Purdue Pharma LP, Stamford, Connecticut.*


*Pacira Pharmaceuticals, Inc, Parsippany, New Jersey.*
A similar pattern was observed in the distribution of VAS scores of 0, which was higher in the EXPAREL group, although the difference was not significant ($P = .308$) (Figure 3).

Average number of requested or scheduled opiate doses was 14.92 in the FNB group and 7.47 in the EXPAREL group ($P < .001$). There was a clear trend for increased opiate doses in the FNB group up to postoperative day 5 (Figure 4). The total amount of opiates consumed, measured as the total hydrocodone equivalents, was also greater in the FNB group (161.66 vs 89.53; $P < .001$) (Figure 5). Multivariate regression analysis also found the FNB group to have a greater number of total rescue doses ($P = .0018$) and an increase in total hydrocodone equivalents consumed ($P = .0188$) (Table 3).

**DISCUSSION**

This study found that patients undergoing TKA who were treated with a local injection of liposomal bupivacaine as part of a multimodal pain program consumed less opiates overall and required fewer rescue opiate doses (requested opiates) when compared with patients whose postoperative pain was primarily managed with FNB. Pain scores also trended lower for the liposomal bupivacaine group, although the differences were not significant. The observed mean difference was smaller than the expected difference based on previous pilot studies. A larger patient sample may elucidate whether these differences are significant.

Optimized analgesic regimens aim to control pain during early and frequent physical therapy but are also balanced to allow adequate lower limb motor function for safe early ambulation. It is well recognized that failure to adequately control pain after TKA induces pathophysiological responses that increase postoperative morbidity, hinder physical therapy, increase anxiety, disrupt sleep patterns, and decrease patient satisfaction. Opioid analgesics, including intravenous patient-controlled and oral, have been a standard modality for postoperative pain management but are associated with the risk of nausea, pruritus, vomiting, respiratory depression, prolonged ileus, cognitive dysfunction, and addiction. As a result, opioid-related adverse events are associated with a marked increase in costs, hospital length of stay, and need for readmission.

Surgeons are attracted to the benefits of a continuous FNB as part of a multimodal pain program due to the ability to adjust dosing and its flexible duration of action and generally good pain relief. Known risks and drawbacks of FNB are prolonged quadriceps weakness.
tra time and tools needed in the operating room to place a catheter, and the other resources necessary to monitor the block and pump. Motor block complications are observed in approximately 2% of patients and may include accidental falls, fractures, or a delay in ambulation and physical therapy.1 All patients receiving FNB in the current study were ambulated with a knee immobilizer, whereas a knee immobilizer was not used with the liposome bupivacaine group. The authors found that the physical therapist would frequently reduce the dosage on the pump before therapy sessions to allow safer ambulation. In many cases, this diminished pain relief hindered range of motion exercises and necessitated opiate rescue medication.

Despite the difficulty in comparing studies with nonstandardized treatment groups, trends from the literature support the findings of the current study. Crowley et al12 conducted a review of studies comparing local anesthetic techniques with placebo injections and patient-controlled intravenous morphine; most of the studies (5 of 6) showed that local anesthetic techniques significantly reduced opioid requirements or lowered VAS scores. Parvataneni et al13 reported that local infusion of bupivacaine, morphine, and epinephrine in combination with FNB results in better pain relief and patient satisfaction than FNB alone. Perlas et al16 compared patients undergoing TKA who received a 48-hour continuous FNB with patients who received either a local infiltration analgesia or local infiltration analgesia (LIA) plus an adductor nerve block. They found that the LIA groups walked more on the first day, had lower Numeric Rating Scale pain scores, used 30% to 50% less opioid analgesics during the first 3 postoperative days, and required fewer intravenous opioid rescue doses. Affas et al7 compared femoral nerve block with LIA (mixture of ropivacaine, ketorolac, and epinephrine) and found less pain in the LIA group at rest, but not during movement, in the first 24 hours after TKA. They also found the total morphine (per kg) to be similar among groups. They concluded that despite the lack of parity between groups, LIA should be considered the preferred option because it was less expensive and easier to perform vs FNB.7 Toftdahl et al14 reported that LIA with ropivacaine, ketorolac, and epinephrine results in better early analgesia and mobilization after TKA, as indicated by being able to walk more on postoperative day 1 as compared with FNB.

Liposomal bupivacaine is a 72-hour local anesthetic formulation that was FDA approved in 2011 for surgical-site soft tissue injection. This formulation uses a novel delivery system to combine the well-established benefits of bupivacaine with time-released delivery and prolonged duration of effect. The efficacy and safety of liposomal bupivacaine have been established in more than 21 clinical trials, including 10 double-blind, randomized, controlled trials that collectively involved 823 patients undergoing a range of surgical procedures, including TKA.15-24

Figure 3: Percentage of 0 visual analog scale (VAS) pain scores in the femoral nerve block (FNB) and EXPAREL (Pacira Pharmaceuticals, Inc, Parsippany, New Jersey) treatment groups is shown over the entire hospital stay (left) and at each day postoperatively until day 5 (right). Abbreviation: CI, confidence interval.

Figure 4: Average number of rescue doses for the femoral nerve block (FNB) and EXPAREL (Pacira Pharmaceuticals, Inc, Parsippany, New Jersey) treatment groups is shown for the entire hospital stay (left) and at each day postoperatively until day 5 (right). The asterisk indicates statistical significance after adjusting for multiple comparisons. Abbreviation: CI, confidence interval.
bupivacaine act as a substitute for traditional methods of pain control, primarily patient-controlled morphine or other opioids. By reducing opiate consumption, there is a great potential to reduce nausea and vomiting and hospital length of stay, improve patient satisfaction, and increase physical therapy participation.25 Future studies should evaluate the combination of liposomal bupivacaine with regional blocking techniques, primarily FNB. Although no additional regional blocks were included in the treatment of any patients in the current study, an alternate technique includes the addition of a sciatic nerve block in conjunction with an FNB, which is favored when complete anesthesia to the posterior aspect of the knee is desirable.1

A major strength of the current study is the prospective pain report, which allows for randomized patient selection and records the patient’s pain score multiple times during the day. Although classified as a retrospective study, the data presented in this study were collected as part of a prospective data-gathering system, improving the consistency and completeness of relevant data relative to a traditional retrospective chart review. The high frequency of VAS score time points (a typical knee patient will have pain recorded up to 40 times during hospital stay) reduces the risk for inaccuracy due to sampling errors.

The primary limitations of this study are its nonrandomized design and small sample size. There were also differences between groups in scheduled medications. Opiates in each group were taken as needed at the discretion of the patients, and neither group was limited in the amount of opioids they could consume. The analysis quantified both scheduled and requested doses of opioids. Also, despite the sufficiency of the sample size to show effects in recorded opiate use, the nonsignificant differences in pain scores would likely be clarified with a larger patient sample. Finally, this study sample was not powered to evaluate complications, and mobilization rates were not tracked.

**CONCLUSION**

The results of this study support the conclusion that long-acting liposome bupivacaine infiltration, as part of a multimodal program after TKA, gives similar postoperative analgesia compared with a continuous FNB, but with significantly less opiate medication. The authors have ceased to use a continuous FNB for primary TKA in favor of the long-acting liposome bupivacaine.

**REFERENCES**


5. Ganapathy S. Wound/intra-articular infiltration or peripheral nerve blocks for orthopedic joint surgery: efficacy and safety issues. *Curr


