Postoperative Pain Management Following Total Knee Arthroplasty: A Randomized Comparison of Continuous Epidural Versus Femoral Nerve Infusion

William T. Long, MD
Samuel R. Ward, PT, PhD
Lawrence D. Dorr, MD
Julio Raya, MD
Myriam Boutary, BS
Leigh Ellen Sirianni, OPAC

INTRODUCTION

Intravenous (IV) opioids are the mainstay of effective pain relief immediately following total knee arthroplasty (TKA), however, the common side effects (nausea and lethargy) often are disabling. Both continuous infusion and continuous epidural infusion have been shown to reduce opioid consumption and the associated complications when used to control pain following TKA.[1] In a prospective randomized fashion, this study compared the use of epidural versus femoral nerve catheter infusion analgesia and the concomitant use of a multimodal approach. The regimen is designed to disrupt pathways for painful stimuli at the peripheral (close to the site of injury) and central (spinal cord and brain) receptors. The administration of preemptive oral analgesics prevents the establishment of central sensitization and the amplification of postoperative pain.[16] Blocking of neurogenic afferent pain signals decreases the inflammatory impact of released cytokines and prostaglandins.[6] This study was designed to determine the effectiveness of continuous femoral infusion and continuous epidural infusion in controlling disabling pain and preventing common opioid side effects when used with a multimodal pain management protocol.

Drs Long, Dorr, and Raya and Mss Boutary and Sirianni are from The Arthritis Institute, Inglewood; and Dr Ward is from the Department of Radiology, University of California and VA Medical Center San Diego, La Jolla, Calif.

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Reprint requests: William T. Long, MD, The Arthritis Institute, 501 E Hardy St, Ste 300, Inglewood, CA 90301.

MATERIALS AND METHODS

Patients undergoing unilateral TKA provided informed consent to participate in this prospective randomized study; and the study was approved by the Institutional Review Board of our institution.

Of 208 eligible patients, 80 were enrolled in the study from January 2004 to August 2005. Of the 80 enrolled patients, 10 were eliminated from the study because of catheter failures.

Average patient age at the time of the operation was 69±1.4 years (range: 41-85 years). There were 30 men and 40 women. Patient exclusions were systemic arthritis, history of substance abuse, chronic pain syndrome, diabetes with peripheral neuropathy, and allergy to study medications.

Patients had the same postoperative pain management plan, with the exception of random assignment to either continuous epidural catheter or continuous femoral nerve catheter infusion for 36 hours postoperatively (Table).

One to two hours prior to surgery, each patient received oral oxycodone 10 mg, acetaminophen 1000 mg, and a Cox-II inhibitor (valdecoxib and celecoxib). Thirty patients in the epidural group used valdecoxib and 5 used celecoxib. Thirty-two patients in the femoral catheter group used valdecoxib and 3 used celecoxib. Valdecoxib was removed from the market in April of 2005 and celecoxib has been used since that time without changes to the postoperative course. Lansoprazole 30 mg orally and metoclopramide 10 mg IV was given to each patient to prevent gastrointestinal upset.

The anesthesia was epidural with ropivacaine 1% 60-80 mg and 1.5%-2% lidocaine with epinephrine at 80 mg. Sedation was achieved with a continuous intravenous in-

TABLE

ARTHRITIS INSTITUTE ANESTHESIA PAIN MANAGEMENT PROTOCOL

Preoperative

1. Oxycodone hydrochloride 10 mg orally x 1 dose (if aged <65 years)
2. Acetaminophen 500 mg 2 tablets orally (if aged =65 years)
3. Celecoxib 400 mg orally x 1 dose (unless sulfa allergy or abnormal CREATINE)
4. Lansoprazole 30 mg orally x 1 dose
5. Metoclopramide 10 mg IV
6. Epidural placement and test with 75 mg of lidocaine 1.5% with epinephrine

Operating Room

1. Epidural activated with ropivacaine 1% at 80-100 mg
2. IV sedation with continuous infusion propofol at 10 mg/kg/hr initially
3. Maintain airway with oral airway or laryngeal mask
4. Dolasetron mesylate 12.5 mg IV
5. Intra-articular injection total volume of 60 mL (1/2 concentration if bilateral joints) for all patients except those TKA research patients only receiving an epidural
   a. Ropivacaine 100 mg
   b. Methylprednisolone acetate 40 mg
   c. Morphine 4 mg

Postoperative

1. Indwelling femoral nerve catheter for TKA
   a. Placement at end of surgery with 21 gauge stimyntex insulated needle
   b. Activated with ropivacaine 100 mg in 20 mL of normal saline (1/2 concentration if bilateral joints)
   c. Maintained by continuous infusion of ropivacaine 0.2% at 5 mL/hr via Infusor system (Baxter) for 48 hours
2. Continuous epidural
   a. Infusion of ropivacaine 0.2% at 5-8 mL/hr initiated in recovery room after a positive neurological examination has been obtained
3. In post anesthesia care unit
   a. Epidural catheter removed for all primary THA and TKA
   b. Toradol 30 mg IV (if aged <65 years) or 15 mg IV (if aged =65 years) for pain
   c. Oxycodone 5 mg orally as needed moderate to severe pain (if aged <65 years)
4. On floor
   a. Celecoxib 200 mg orally daily (start postoperative day #1 for THA and postoperative day #3 for TKA with femoral nerve catheters)
   b. Norco 10 mg orally alternating with acetaminophen 500 mg every 4 hours from 6 PM to 6 AM for 2 days (if aged <65 years)
   c. Darvon 65 mg orally alternating with acetaminophen 500 mg every 4 hrs from 6 PM to 6 AM for 2 days (if aged =65 years)
   d. If femoral nerve catheter, keterolac tromethamine 30 mg IV every 6 hours x 48 hours (if aged <65 years) and 15 mg IV every 6 hours x 48 hours (if aged =65 years)
   e. Cap femoral nerve catheter at 6 AM postoperative day #2, then pull on rounds
   f. Metoclopramide 10 mg IV every 6 hours x 48 hours
   g. Ecotesil coated aspirin 325 mg po twice a day

Abbreviations: IV=intravenous, THA=total hip arthroplasty, and TKA=total knee arthroplasty.

fusion of propofol 10 mg per kg/per hr. The patient was not intubated and the airway was controlled with laryngeal mask anesthesia. No intravenous narcotics were given during the operation. Ondansetron hydrochloride 4 mg or metoclopramide 10 mg was given during the operation. A pericapsular injection (with emphasis on the posterior capsule) and injection into the extensor mechanism was administered with a mixture of morphine 4 mg, ropivacaine 100 mg, and methylprednisolone sodium succinate 40 mg diluted in a total volume of 60 mL of normal saline. This provided blockade to the peripheral mechanical and inflammatory receptors.

In the recovery room, oxycodone hydrochloride immediate release 5 mg, which is a rapid acting oral oxycodone was given. Intravenous ketorolac 15 mg and intravenous ydromorphone 2-5 mg was available for breakthrough pain. Ondanesetron hydrochloride 4 mg, metoclopramide 10 mg, or dolasetron mesylate 12.5 mg was given intravenously if needed for nausea.

Group 1 patients had a femoral nerve catheter placed immediately after surgery, while still in the operating room. The catheter was placed using a sheath needle and accurate confirmation of placement was confirmed with a nerve stimulator. Obvious muscle twitch of the quadriceps that occurred at <0.4 mA was considered indicative of accurate needle placement. The femoral regional analgesia was loaded with a bolus of ropivacaine 0.2% using 100 mg and 20 mL of normal saline, then maintained by continuous infusion at 5 mL per hour for 36 hours.

Group 2 patients had continuous epidural infusion for management of postoperative pain using the catheter that was inserted preoperatively for use during the TKA operation. Ropivacaine 0.2% was infused at 5 mL per hour for 36 hours. The femoral nerve catheter and epidural catheter were discontinued at 6 AM on postoperative day 2.

Oral opioid analgesics used were hydrocodone or hydrocodone bitartrate and acetaminophen. Oxycodone 10 mg was given at 6 PM on the day of surgery unless the patient was comfortable. Patients who had minimal discomfort and patients who reported stomach discomfort or nausea, were given xanodyne, tramadol hydrochloride, or acetaminophen. During the first postoperative night, oral analgesics were ordered for patients every four hours. These medications were given on request for the remainder of the hospitalization. Ketorolac 30 mg IV was given every 6 hours for the first 24 hours. For the second 24 hours, ketorolac was given as needed for breakthrough pain. Cox-II inhibitors were given to each patient each morning of the hospitalization (Table).

If the patient was aged ≥75 years the protocol substituted propoxyphen napsylate or acetaminophen for the opiate analgesics, no other postoperative oxycodone was used, and IV ketorolac 15 mg was given every 6 hours.

Aspirin 325 mg daily was used for deep venous thrombosis (DVT) prophylaxis, combined with thromboembolic disease hose for a total of four weeks. Patients were discharged home with the COX-II inhibitor to be taken each morning for two weeks and with the oral pain medication that was best tolerated during the hospitalization.

For statistical comparison of the amount of medication used for each patient and for the two groups of patients (epidural infusion and femoral nerve catheter infusion) the pain medications were all converted to equianalgesic dose of morphine. The conversion rates were obtained from conversion tables.[7,13,14]

Pain assessment was obtained using the visual analog scale of patient scoring from 0-10 (0=no pain and 10=severe) every four hours. Pain scores were obtained by the nursing staff 30 minutes after the administration of any pain medication.

The patient's function in the hospital was graded daily by a physical therapist. Ambulation, quadriceps strength as measured by the ability to do an independent straight-leg raise, the assistive device required for safety and balance was listed, as was the range of motion of the knee. The patient ambulated the day of surgery if the patient returned to the floor before 2 PM. Patients who returned after 2 PM ambulated the next morning. Therefore, the assessment of ambulation according to the postoperative day was adjusted depending on the time the patients returned to the floor. Patients ambulated twice a day during physical therapy on postoperative day 1 and thereafter. When it was judged to be safe, patients were permitted to ambulate as they wished for bathroom privileges and within the confines of the hospital floor. The assistive device needed for ambulation and for safety and balance at the time of discharge also was recorded. The ability of the patient to perform a straight-leg raise, both lifting the entire leg and then independently extending the leg below the knee was recorded daily. Range of motion, both extension and flexion, also was recorded.

The data was statistically analyzed using SPSS 11.5 software (SPSS Inc, Chicago, Ill). Activity level and straight-leg raises were analyzed using the Pearson's Chi-square test. Student two-tailed *t* tests were used to compare pain scores, equianalgesic morphine, extension, flexion, and walking distance for normally distributed data. Otherwise, the Mann-Whitney Test was applied. To more precisely compare femoral catheter group pain scores with epidural group pain scores, one-way analysis of variance was used with pain scores adjusted by the volume of pain medication intake. A 95% confidence interval was used for each statistical analysis.

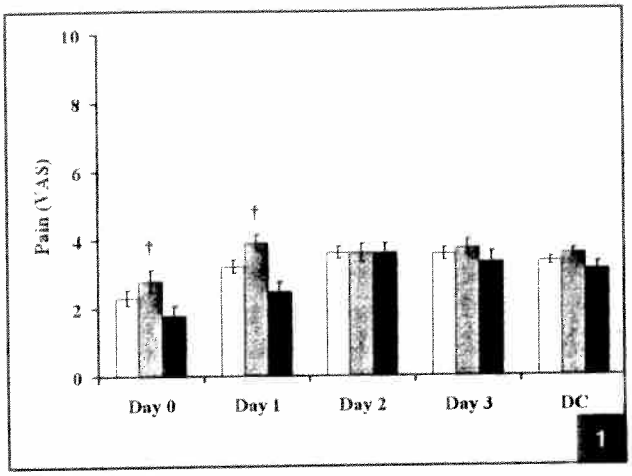

Figure 1. Pain (visual analog scale) is plotted as a function of day in the hospital. The femoral catheter group (black bars) had less pain on day 0 and on day 1 compared to the epidural group (gray bars). These data are shown relative to all patients (white bars). † indicates statistical significance ($P<.05$).

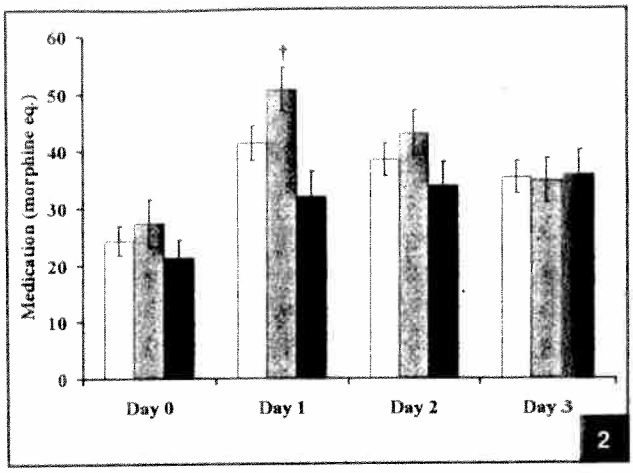

Figure 2. Medication (morphine equivalent units) is plotted as a function of day in the hospital. The femoral catheter group (black bars) consumed less medication on day 1 compared to the epidural group (gray bars). These data are shown relative to all patients (white bars). † indicates statistical significance ($P<.05$).

RESULTS

The mean pain scores for all 70 patients for each postoperative day were postoperative day 0, 2.29±1.9; day 1, 3.2±1.7; day 2, 3.6±1.4; and day 3, 3.5±1.4; and at the time of discharge was 3.3±1.0 (Figure 1). Equianalgesic milligrams of morphine for all 70 knees on postoperative day 0 was 24.3±21.8 mg; day 1 was 41.3±25.9 mg; day 2 was 38.3±23.4 mg; and day 3 was 35.2±21.2 mg (Figure 2).

The average pain scores for patients with epidural infusion versus patients with femoral nerve catheter infusion on the day of surgery were 2.9±2.0 versus 1.7±1.7 ($P=.002$) and on day 1 were 3.9±1.4 versus 2.5±1.7 ($P=.02$). The statistical comparison in these pain scores was done after the effect of medications was eliminated. There was no statistical difference of pain scores between the two groups of patients on day 2, (3.7±1.4 versus 3.6±1.5) nor on day 3 (3.7±1.3 versus 3.4±1.6); and no difference at the time of discharge, 3.58±0.8 versus 3.1±1.24 (Figure 1).

The average oral medication intake in equianalgesic units of morphine for patients with epidural catheter infusion versus patients with femoral nerve catheter infusion on the day of surgery was 27.4±24.5 versus 21.2±18.4 ($P=0.241$) and on day 1 was 50.7±22.8 mg versus 31.9±25.7 mg ($P=.0002$). There was no statistical difference on any other postoperative day with day 2, 43±21.1 versus 33.9±24 and day 3 was 34.7±20.8 mg versus 35.8±22.1 mg (Figure 2).

Three patients (all with epidural catheters) used hydromorphone hydrochloride in the recovery room with the mean dose being 9.6 equianalgesic milligrams of morphine. Pain medications were ordered for all patients every four hours during postoperative night 1; on postoperative night 1, 59 patients (28 patients with an epidural and 31 with a femoral nerve catheter) refused medication at least once. Pain medications were offered to patients every four hours on postoperative night 2; on postoperative night 2, 60 patients refused pain medications. Patients no longer had any infusion catheter pain medications and were treated solely with oral pain medications. No patient used IV narcotics once they had returned to the patient floor.

There was no statistical difference in self-reported preoperative activity level (scale 1-6, 1=unlimited by symptoms) of patients in the femoral catheter and epidural catheter groups (3.7±1.3 versus 3.8±1.0, $P=.676$). Initially patients with the epidural catheter had superior walking distance. The walking distance on postoperative day 0 was statistically better for patients with epidural infusion (41±48.4 versus 28±43.3 feet, $P=.022$).

On postoperative day 1, patients with epidural infusion also had statistically better walking distance (165±99.7 versus 111±95.4 feet, $P=.024$). There was no statistical difference on day 2 (212±140 versus 243±156 feet) nor on day 3 (252±134.5 versus 266±204 feet). Patients with the femoral nerve catheter infusion walked wearing a knee immobilizer when the femoral catheter was activated to avoid buckling of the knee from quadriceps weakness. All patients walked 250-275 feet at the time of discharge.

There was statistically better extension on days 2, 3,

and at discharge for patients who had the epidural infusion. On day 2, the mean extension was 7°±3.3° for epidural patients versus 12°±8.3° (P=.009) for patients with the femoral nerve catheter. Both groups of patients had a mean flexion of 74°. On day 3, the mean extension for the epidural group was 7°±4.4° and for the femoral nerve catheter patients, 12°±9.2° (P=.011). Both groups had mean flexion of 76°. At discharge, extension was 6°±3.5° for the epidural patients and 12°±8.8° for the femoral nerve catheter patients (P=.01), and the epidural patients had 84°±10.9° flexion while the femoral nerve catheter patients had 80°±13.3° flexion. The improved extension was a result of improved quadriceps strength in patients with the epidural catheter. On the day of surgery, 8 (23.5%) of 35 patients with the epidural infusion could perform a straight-leg raise, whereas only 1 (2.8%) of 35 femoral nerve catheter infusion patients could perform a straight-leg raise (P=.006); on day 1, 31 (88.2%) patients versus 5 (14.2%) (P=.001); day 2, 29 (90.6%) patients versus 18 patients (20.5%) (P=.001); day 3, 29 (100%) of 29 patients versus 18 (69%) of 26 patients (P=.003); and at the time of discharge, 35 (100%) of 35 epidural patients versus 30 (85%) of 35 of femoral nerve catheter patients could straight-leg raise (P=.020) (Figure 3).

There was no difference on any postoperative day in the use of assistive devices. Forty patients were discharged with a single assistive device (one crutch or cane) and 30 patients were discharged with a bilateral assistive device (two crutches or walker).

Six months postoperatively, the patients scored their results as 21 excellent, 39 very good, 7 good, and 3 fair. Sixty-seven patients used no assistive device, 1 used two crutches due to back pain, 1 a walker due to ataxia, and 1 a wheelchair for multiple medical comorbidities. Strength against manual resistance was grade 5 in 63 patients, 4 in 6 patients, and 3 in the patient with ataxia.[11] The flexion range of motion did not differ between epidural patients (114°±13.7°) or femoral nerve catheter patients (111°±12.2°) nor extension (1.7°±4.0° versus 1.8°±4.2°).

Only 1 (1.4%) of 70 patients had emesis on day 1 and day 2. No other patient had emesis during this study. Fifteen (21%) of 70 patients had nausea in the recovery room and were treated with metoclopramide 10 mg or dolasetron mesylate 12.5 mg IV and none had emesis. On postoperative day 1, 8 (11%) patients had nausea, most after physical therapy, and were treated with dolasetron mesylate 10 mg intravenously without emesis.

One patient had a deep infection that was successfully treated with two-stage reimplantation. Two patients with femoral nerve catheter infusion required closed manipulation and one fell at home with dehiscence of the surgical wound that required reoperation. One patient in the epidural group had bladder inflammation caused by reaction to latex of the foley catheter. No patient had a hematoma formation in the knee or drainage that required prolonged hospitalization. All patients had a Doppler ultrasound prior to discharge from the hospital and no patient had a positive study for DVT, and there were no clinical thrombolic events. Two patients were treated postoperatively with warfarin and one with enoxaparin for medical conditions unrelated to surgery.

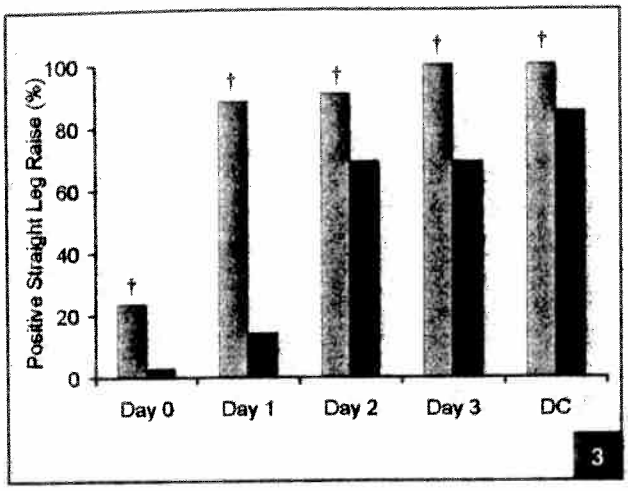

Figure 3. The percentage of patients with a positive straight leg raise is plotted as a function of day in the hospital. The femoral catheter group (black bars) had fewer patient with sufficient quadriceps strength to perform this task compared to the epidural group (gray bars). † indicates statistical significance (P<.05).

DISCUSSION

In our experience, TKA is more painful than total hip arthroplasty and rehabilitation is more difficult. Uncontrolled pain can make the TKA surgical experience unpleasant or miserable for the patient and health-care providers. Vomiting, dizziness, constipation, pruritus, and behavioral changes associated with parenteral opioid use interrupts postoperative rehabilitation. Animal studies have shown that brief noxious stimuli can result in prolonged behavioral and psychological sequelae that are prevented by preemptive opioids and local anesthetics.[2,3,17] These findings suggest that chronic pain syndromes, in some patients, may result from pain experienced immediately after TKA. The use of preemptive oral analgesics, local injection of anesthetics, and ropivacaine delivered by catheter is intended to reduce these complications and improve outcome after TKA.[4,12]

Continuous femoral infusion and continuous epidural infusion have consistently been shown to reduce pain, while at the same time, decreasing morphine consumption

after TKA. Chelly et al[1] observed that continuous femoral infusion and continuous epidural infusion decreased morphine requirements by 74% and 35% respectively, compared to patient controlled analgesia without a catheter. The decrease in morphine use was associated with a 90% decrease in serious cardiovascular and pulmonary complications with the continuous femoral infusion and a 55% decrease using continuous epidural infusion. Morphine-related postoperative complications were dramatically reduced using either catheter, with the exception of nausea and vomiting, which occurred in nearly 50% of patients who used the epidural catheter or the patient controlled analgesia and <20% of patients who used continuous femoral infusion. Only 1 patient in the current study had an episode of vomiting. However, the study by Chelly et al[1] is not comparable to the current study because the patients in that study were administered morphine in the recovery room and all study patients had free access to parenteral opiates by patient-controlled analgesia. Similar to our study, Chelly et al[1] found superior pain relief using the femoral nerve infusion catheter. Our use of infusion catheters in combination with a multimodal regimen is the only study, of which we are aware, that did not use patient controlled analgesia as the control.

Quadriceps weakness has not been reported as a complication in reports using continuous femoral infusion after TKA, and other investigators have reported better rehabilitation with increased ability to tolerate continuous passive motion, earlier ambulation, and shortened length of hospital stay.[9,10] Quadriceps weakness may have been overlooked because none of the patients in those studies ambulated on the day of surgery and the authors did not report quadriceps function. In each of the studies, the benefits of shorter hospital stay or improved rehabilitation with use of continuous femoral infusion was attributed to reduced incidence of opioid side effects.

Despite the obvious advantages of infusion catheter techniques, several deterrents have discouraged wider application following TKA. Anesthesiologists are not equally proficient with catheter placement techniques and catheter placement is more difficult in obese patients. Six failed femoral catheters and four failed epidural catheters in 80 enrolled patients were related to inaccurate catheter placement. Because we use only acetaminophen, intermittent compression devices and thromboembolic disease [illegible] for DVT prophylaxis, we were able to study continuous epidural infusion. Unfortunately, use of the epidural catheter with low-molecular-weight heparin for the prevention of venous thrombotic embolism has been shown to increase the risk of epidural hematoma and irreversible nerve damage by as much as 50 times.[5,8,14] Therefore, continuous epidural infusion is contraindicated when low-molecular-weight heparin is used for postoperative DVT prophylaxis. In addition, femoral nerve catheter infusion in patients with bilateral TKA can prevent effective ambulation because of bilateral quadriceps weakness. Early ambulation was not interrupted in patients with unilateral TKA because the use of a knee immobilizer successfully compensated for quadriceps weakness. With the current trend toward earlier hospital discharge, poor quadriceps function is a severe deterrent because patients are not able to ambulate safely while the femoral nerve infusion catheter is activated.

The pain management protocol described in this article is indicated for use in all TKA patients. The continuous femoral infusion and the continuous epidural infusion techniques require that the patient remain hospitalized. While both catheter techniques can provide excellent pain relief after minimally invasive techniques, they do not facilitate discharge earlier than 48 hours according to the findings of this study. The limitations of this study are the exclusion of groups of patients, not testing this protocol in combination with chemical prophylaxis for DVT, and lack of control group that had no infusion technique.

Based on the findings presented in this study, both patients and care providers, including the nurses and physical therapists, prefer the superior pain relief provided by the continuous femoral catheter over the continuous epidural infusion. Although infusion with ropivacaine has the theoretical advantages of preferential sensory block and decreased toxicity compared to bupivacaine, the motor impairment with continuous infusion of ropivacaine was prevalent. Patients did not perceive the temporary quadriceps weakness as a significant problem and walking without pain was more important than walking without a knee immobilizer.

After this study was completed we began a trial using single injection femoral nerve blocks in an attempt to avoid quadriceps weakness. Several patients in that study developed severe pain on the night of surgery when the single injection wore off. Based on the findings of this study, TKA using this multimodal approach with the continuous femoral infusion minimizes the complications of parenteral opioids while providing safe and effective postoperative relief. Further research is indicated to determine if all of the advantages of pain relief can be achieved while maintaining normal motor function.

REFERENCES

1. Chelly JE, Greger J, Gebhard R, et al. Continuous femoral blocks improve recovery and outcome of patients undergoing total knee arthroplasty. *J Arthroplasty*. 2001;16:436-445.
2. Coderre TJ, Vaccarino AL, Melzack R. Central nervous system plasticity in the tonic pain response to subcutaneous formalin injection. *Brain Res*. 1990;535:155-158.
3. Dickenson AH, Sullivan AF. Subcutaneous formalin-in-

duced activity of dorsal horn neurones in the rat: differential response to an intrathecal opiate administered pre or post formalin. *Pain.* 1987;30:349-360.
4. Flory DA, Fankhauser RA, McShane MA. Postoperative pain control in total joint arthroplasty: a prospective, randomized study of a fixed-dose, around-the-clock, oral regimen. *Orthopedics.* 2001;24:243-246.
5. Heit JA. Low-molecular-weight-heparin: biochemistry, pharmacology, and concurrent drug precautions. *Reg Anesth Pain Med.* 1998;23(6 suppl 2):135-139.
6. Kehlet, H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatments. *Anesth and Analg.* 1993;77:1048-1056.
7. Kim MH, Hahm TS. Plasma levels of interleukin-6 and interleukin-10 are affected by ketorolac as an adjunct to patient-controlled morphine after abdominal hysterectomy. *Clin J Pain.* 2001;17:72-77.
8. Leclerc JR, Geerts WH, Desjardins L, et al. Prevention of venous thromboembolism after knee arthroplasty. A randomized, double-blind trial comparing enoxaparin with warfarin. *Ann Intern Med.* 1996;124:619-626.
9. Lee VC, Kendrick WD, Brown NW, Harman AM, Grove GW. Ketorolac given prior to arthroscopic knee surgery decreases postop pain scores and narcotic doses. *Anesth and Analg.* 1992;74:351-355.
10. Lombardi AV, Berend KR, Mallory TH, Dodds KL, Adams JB. Soft tissue and intra-articular injection of bupivacaine, epinephrine, and morphine has a beneficial effect after total knee arthroplasty. *Clin Orthop.* 2004;428:125-130.
11. Magee DJ. Principles and Concepts. In: Saunders, ed. *Muscle Test Grading: Orthopedic Physical Assessment.* 4th ed. Philadelphia, Pa: Elsevier Science. 2002:30-31.
12. Mallory TH, Lombardi AV Jr, Fada RA, Dodds KL, Adams JB. Pain management for joint arthroplasty: preemptive analgesia. *J Arthroplasty.* 2002;17(4 suppl 1):129-133.
13. Max MB, Payne R, Edwards WT, et al. *Massachusetts General Hospital: Equianalgesic Doses of Opioid Analgesics.* 4th ed. Chicago, Ill: American Pain Society, 1999.
14. Schroeder DR. Statistics: detecting a rare adverse drug reaction using spontaneous reports. *Reg Anesth Pain Med.* 1998;23:183-189.
15. Veterans Affairs and Department of Defense. Quality Tools. Tool summary: Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain Medications Pocket Guide [QualityTools Web site]. Available at: http://www.oqp.med.va.gov/cpg/cpg.htm. Accessed June 2003.
16. Wall PD. The prevention of postoperative pain. *Pain.* 1988;33:289-290.
17. Woolf CJ, Wall, PD. Morphine-sensitive and morphine-insensitive actions of C-fibre input on the rat spinal cord. *Neurosci Lett.* 1986;64:221-225.