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Postoperative Pain After Primary Total Knee Arthroplasty: Comparison of Local Injection Analgesic Cocktails and the Role of Demographic and Surgical Factors



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ABSTRACT

Background: It has been reported that pain-related outcomes after total knee arthroplasty (TKA) may vary with different analgesic techniques and with patient demographics. The purposes of this study were to compare local infiltration of regular bupivacaine (periarticular infiltration [PAI] group) vs liposomal bupivacaine (LBUP group) and to examine the effect of patient characteristics on postoperative pain after TKA.

Methods: The study sample included 665 consecutive TKA cases performed between December 2011 and August 2013. The primary outcome measures were the average visual analog scale (VAS) pain score and the percent of VAS pain scores that indicated no pain. Multivariable regression analyses investigated the effect of age, race, ethnicity, body mass index, gender, surgeon, and analgesic protocol on outcomes. For the analgesic groups, the “PAI” group received injections of a cocktail including bupivacaine, ketorolac, and morphine, whereas the “LBUP” group received injections of LBUP.

Results: The regression analysis demonstrated that postoperative pain was higher in females ($P < .001$) and younger patients ($P < .001$). Although overall average VAS pain scores were not significantly different, when specific postoperative days were evaluated, the LBUP group had lower pain scores from day 1 to 5 ($P < .014$). There were no differences in VAS scores based on patient body mass index ($P = .250$), race ($P = .205$), or ethnicity ($P = .961$) in this sample.

Conclusion: This multivariate regression analysis study showed that in patients undergoing primary TKA, postoperative pain was lower in males, older patients, and those treated with LBUP. Awareness of these factors may assist in developing patient-specific multimodal postoperative pain and education protocols that reduce opioid reliance and related adverse events.

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Immediate postoperative pain resulting from total knee arthroplasty (TKA) can be severe and difficult to manage [1]. Despite the success of TKA in alleviating daily pain and improving the quality of life of patients suffering from osteoarthritis, early postoperative pain may result in an increased risk of complications, including a delay in normal functioning, rehabilitation delay, progression to persistent pain states, prolonged hospital stay, elevated readmission rate, and an elevated cost of care [2-15]. Effectively controlling perioperative pain can improve patient satisfaction, promote earlier mobility and physiotherapy, result in fewer cardiac and pulmonary complications, enhance recovery, improve quality of life, and reduce the likelihood of developing chronic pain syndromes [16-18].

A recent study by the authors found improved pain control in a large sample of TKA and total hip arthroplasty (THA) (revision and primary) patients after switching a standard periarticular injection cocktail with an injection of a cocktail including liposomal bupivacaine (LBUP) [19]. However, the use of LBUP specifically for TKA patients has been presented with varying results [20]. In addition, most studies evaluating local injection techniques for TKA neglect evaluating the role of patient demographics on pain-related outcomes after TKA, despite evidence to support consideration [21]. Previous studies have hypothesized that patient demographics may be associated with lower expectations before surgery, potential surgical delays, and worse preoperative osteoarthritis status [22]. In addition, for better evaluation of treatment techniques, placing more emphasis on patient demographics as a contributing factor to outcomes may help surgeons identify high-risk patients and better counsel and treat them [23]. With any emerging treatment, it is necessary to evaluate how effectiveness may vary over differing patient populations.

The purposes of this study were to compare local infiltration of regular bupivacaine (periarticular infiltration [PAI] group) vs LBUP group and to examine the effect of patient characteristics on postoperative pain after TKA. We hypothesized that the patients treated with LBUP will have reduced pain within the first 3 postoperative days relative to control patients treated with a standard periarticular injection technique. In addition, we expect to observe associations in pain according to patient factors, including gender, age, and patient body mass index (BMI).

Materials and Methods

The study sample included 665 consecutive TKA cases in the time period between December 2011 and August 2013. Four surgeons in a dedicated arthroplasty practice provided cases for this study. All patient information was deidentified, and this is an institutional review board-approved study via exemption.

The primary outcome measures were the average visual analog scale (VAS) pain score for each patient and the percent of VAS pain scores during hospitalization that were 0, which is a result of a patient answering that they had “no pain.” The average pain score was calculated for each patient for the entire stay and for each individual day of stay. VAS pain data were collected at every instance in which nursing personnel had contact with the patient, resulting in multiple VAS scores for each day of hospital stay. The collection of VAS pain scores was implemented through a robust prospective data gathering system. VAS data and other relevant medical parameters are collected routinely on every case that passes through the study center.

There were 2 differing multimodal analgesia treatment protocols utilized over the study period. In the period of time between December 2011 and October 2012, 349 consecutive TKA cases were performed using a well-established multimodal analgesia (including PAI with bupivacaine, ketorolac, and morphine) and therapy protocols (referred to as the “PAI” group). For the period which immediately followed (October 2012 through August 2013), 316 consecutive TKA cases were performed with similar therapy protocols, but substituting the established PAI for an Food and Drug Administration-approved LBUP surgical-site soft tissue injection technique (EXPAREL, Pacira Pharmaceuticals, Parsippany, NJ), as part of their multimodal analgesia protocol (“LBUP” group). The procedures covered during both periods were performed by the same 4 surgeons. For both groups, the periarticular injection technique used a small volume (0.5–1.0 mL), small needle (22 gauge, 1 5/8 in. length), multisite moving needle technique. The range for total volume of anesthetic was between 50 and 90 mL.

Low-dose (<8 mg) bupivacaine spinal (or combined spinal/epidural) plus general endotracheal anesthesia was the preferred

anesthetic for 3 surgeons. Straight general anesthesia was the preferred anesthetic for 1 surgeon but was also used for all patients with prior lower lumbar spine procedures. A femoral block was the preferred adjunct in the PAI group for one of the 4 surgeons, though was not used by any surgeons in the LBUP group. No adductor canal blocks were used for any patients. The preferred approach was through a medial parapatellar approach. The total knee systems utilized were primarily cruciate retaining and fixed bearing types.

As >300 patients were recruited for each group, this study has >80% power at an alpha level of 0.05 to detect an effect size of 0.30 in the average VAS pain score based on post hoc power calculations. This was the smallest effect size detectable at these levels. The study sample size was large enough that 2-sample Student *t* tests were implemented to test for differences in the means between PAI and LBUP groups for patient characteristics, such as age and BMI, even as the variables were not normally distributed. Chi-square tests were used to test for a difference in the rates of LBUP and PAI groups for categorical variables. Multivariable regression analyses were implemented to investigate associations between patient demographics, surgery, or treatment group with average pain scores overall and percent of zero pain scores. Variables in the regression analysis included race (white, black, Asian, Native American, unknown), ethnicity (Hispanic, non-Hispanic, unknown), BMI, gender, length of stay (LOS), surgeon, PAI/LBUP, and patient age at surgery. Statistical significance was assessed at an alpha level of 0.05. Statistical analysis was performed with SAS software (SAS Institute Inc, Cary, NC), version 9.4.

Results

There were no differences in age ($P = .644$), BMI ($P = .472$), gender breakdown ($P = .523$), or race ($P = .059$) between groups (Table 1). The LBUP group had more patients identifying as Hispanic (4.4% of LBUP group vs 2.6% of PAI group) or unknown ethnicity (7.3% of LBUP group vs 1.4% of PAI group) ($P < .001$) and had a shorter hospital LOS (2.7 vs 2.9 days, $P = .003$).

The regression analysis demonstrated that VAS pain scores were affected by patient gender ($P = .001$), age ($P < .001$), LOS ($P < .001$), and the surgeon administering the treatment ($P < .001$; Table 2). Postoperative pain was generally higher in females and younger patients if other variables are constant. There were no differences in VAS scores based on patient BMI ($P = .250$), race ($P = .205$), or ethnicity ($P = .961$) in this sample. The LBUP group showed lower overall average VAS pain scores than the PAI group, though this difference was not significant ($P = .233$). When specific postoperative days were evaluated, the LBUP group had lower pain scores from day 1 to 5 ($P < .014$; Fig. 1). Patients treated by surgeons 1 and 4 experienced lower overall postoperative pain scores ($P < .001$) relative to patients treated by surgeons 2 and 3.

The trends observed for average pain scores were similar for the average percentage of VAS zero scores per patient across their stay (Table 3). Patient gender ($P = .029$), age ($P < .001$), and hospital LOS ($P < .001$) were all found to have significant associations with the rate of zero VAS scores. If all other variables are controlled for, a higher percentage of patients reporting no pain were associated with males, older patients, and patients with a shorter hospital stay. When specific postoperative days were evaluated, more patients in the LBUP group reported zero pain on postoperative days 1–5 ($P < .007$).

Discussion

Pain control has a critical role in encouraging earlier ambulation and initiation of physiotherapy after TKA [18]. Effective pain control improves satisfaction, promotes earlier mobility and physiotherapy,

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