The Journal of Arthroplasty 29 (2014) 1687–1690

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Liposomal Bupivacaine Versus Traditional Periarticular Injection for Pain Control After Total Knee Arthroplasty

Deren T. Bagsby, MD, Phillip H. Ireland, MD, R. Michael Meneghini, MD

Department of Orthopaedic Surgery, Indiana University Health Physicians, Indiana University School of Medicine, Indianapolis, Indiana

ARTICLE INFO

Article history:
Received 10 January 2014
Accepted 29 March 2014

Keywords:
knee arthroplasty
knee arthroplasty
periarticular injection
pain control
bupivacaine
liposomal

ABSTRACT

The purpose of this study was to compare a novel liposomal bupivacaine to traditional peri-articular injection (PAI) in a multi-modal pain protocol for total knee arthroplasty (TKA). A retrospective cohort study compared 85 consecutive patients undergoing TKA with a traditional PAI of ropivacaine, epinephrine and morphine to 65 patients with a liposomal bupivacaine PAI. After the initial 24 h, inpatient self-reported pain scores were higher in the liposomal bupivacaine group compared to the traditional PAI group ($P = 0.04$) and a smaller percentage (16.9%) of patients in the liposomal bupivacaine group rated their pain as "mild" compared to the traditional group (47.6%). Liposomal bupivacaine PAI provided inferior pain control compared to the less expensive traditional PAI in a multi-modal pain control program in patients undergoing TKA.

A substantial number of patients experience severe pain after total knee arthroplasty (TKA). Appropriate postsurgical pain management promotes healing and recovery, faster patient mobilization, shortened hospital stays, and reduced healthcare costs. Other potential benefits of optimal pain control in surgical patients include improving cardiac, respiratory, and gastrointestinal function; minimizing thromboembolic complications; reducing chronic post surgical pain; reducing mortality in high-risk patients; improving patient participation in physical therapy and reducing healthcare costs [1].

While parenteral narcotics were the mainstay in pain management strategies of the past, utility as the sole analgesic technique was limited by side effects and inconsistent pain relief [2]. Multimodal pain control programs, which utilize lower doses of multiple drugs that work via different mechanisms, have recently been popularized to maximize pain control while minimizing side effects [1–9]; however, the optimal components of such programs remain unknown. One modality that is frequently used in the multi-modal pain protocols is a periarticular injection of local anesthetic.

Liposomal bupivacaine had recently emerged for periarticular injection with proposed benefits of longer acting pain control in TKA [10]. Liposomes are lipid-based multi-vesicular particles that function as drug carriers and offer a controlled delivery of drugs, such as bupivacaine, with a resultant longer term effect [11]. However, there is no study to date that examines the effectiveness of this modality on postoperative pain levels or outcomes in TKA. The purpose of this study is to assess the efficacy of liposomal bupivacaine versus a traditional periarticular injection in minimizing opiate consumption and postoperative pain levels following primary total knee arthroplasty.

Methods

IRB approval was obtained to retrospectively review the inpatient hospital medical records of all patients who underwent unilateral primary TKA by two joint arthroplasty specialists at a single hospital from January through September 2013. A multimodal pain protocol consisting of pre-emptive oral pain medications preoperatively and throughout the hospital stay until discharge, a preoperative single-shot spinal, and an intraoperative periarticular anesthetic injection was employed in all patients. All patients received pre-emptive and postoperative oral analgesia in the form of acetaminophen and celecoxib unless contraindicated. If the patients were 65 years old or younger, all received oral sustained release oxycodone and pregabalin preoperatively and postoperatively. Patients greater than 65 years old were given tramadol preoperatively and postoperatively. A single shot spinal consisting of intrathecal morphine was administered in all patients, along with light general anesthesia per the discretion of the anesthesiologist. Hydroxyzine and famotidine were administered in all patients to counteract the side effects of the intrathecal morphine. Postoperatively, all patients were managed with oral acetaminophen, celecoxib, pregabalin and narcotics. Intravenous narcotics and patient-controlled analgesia were avoided and only administered when necessary for breakthrough pain. Intra-operatively, all patients received a periarticular injection consisting of ropivacaine, morphine

The Conflict of Interest statement associated with this article can be found at http://dx.doi.org/10.1016/j.arth.2014.03.034.

Reprint requests: R. Michael Meneghini, MD, Department of Orthopaedic Surgery, Indiana University School of Medicine, 13100 136th Street, Suite 2000, Fishers, IN 46037.

http://dx.doi.org/10.1016/j.arth.2014.03.034
0883-5403/

and epinephrine or liposomal bupivacaine (Exparel, Pacira Pharmaceuticals, Parsipanny, NJ).

During the entire study period, the only modification in the perioperative multi-modal pain protocol was the two different periarticular injections, which minimized confounding variables and isolated the outcome effects of the single variable change. From January through June the periarticular injection consisted of 400 mg ropivacaine, 5 mg morphine and 0.4 mg epinephrine in 100 cc solution. From July 1st, 2013 through September 30th, 2013, the periarticular injection consisted of liposomal bupivacaine per the instruction of use by the liposomal bupivacaine manufacturer. An initial syringe of 30 cc of 0.5% marcaine with 1:200,000 epinephrine was injected into the periarticular tissues to provide initial pain control during the immediate postoperative period due to the delayed onset of action of the liposomal bupivacaine. Subsequently 20 cc of 1.3% liposomal bupivacaine (1 vial; 266 mg) added to 30 cc normal saline to a total of 50 cc solution was injected into the periarticular tissues at the conclusion of the surgical procedure.

All patients completed perioperative patient education specifically to address pain control, physical therapy and discharge expectations. All patients were encouraged to ambulate the afternoon day of surgery and discharge home on postoperative day two. A standard rehabilitation protocol was followed for all patients. Patients were deemed ready for discharge when medically stable, they satisfied physical therapy requirements and demonstrated adequate pain control.

During the hospital stay, patient self-rated pain scores were taken during regular nursing rounds per the protocol established on the orthopaedic surgery inpatient floor. Pain scores were recorded in the EMR approximately every 2–4 h, unless the patient was asleep. The pain scores were averaged during two time periods, the first 24 h and during the remainder of hospital stay. The self-reported pain score at the time of discharge was also recorded. Pain scores were evaluated on the visual analog scale of 0 to 10, with 0 indicating no pain and 10 indicating the worst possible pain. In order to further characterize pain levels, categorical pain scores were defined as: none 0; mild 0.01–3.99; moderate 4.00–6.99; severe 7.00–10.0. Oral narcotics were given to patients per standardized protocols developed and implemented by a perioperative medical specialist and utilized hydrocodone at various dosages depending on the pain level of the patient. In order to accurately and comparatively assess the total opioid usage by the patients during their hospital stay, the oral narcotics and intravenous opioids were converted to intravenous equivalents of morphine through the following formula: 0.33 [PO hydrocodone] + 0.57 [mg PO oxycodone] + 0.33 [mg PO morphine] + 0.05 [mg PO codeine 3] + [mg IV morphine] + 0.1 [mcg IV fentanyl] + 6.67 [mg IV hydromorphone] + 1.8 [mcg fentanyl patch/24 h].

Standard statistical Student's t-tests were utilized to compare the mean outcome variables between groups. Mean pain scores at the different time periods and the mean morphine equivalents of narcotic usage between the two groups were compared. Statistically significant difference was considered at a P value less than or equal to 0.05 between groups.

Results

150 consecutive patients underwent total knee arthroplasty. There were 85 patients in the traditional periarticular injection group and 65 patients in the liposomal bupivacaine group. All patient demographic data are found in Table 1. The mean age of the traditional group was 65.2 (±9.2) years comprised of 71% female, and the mean age of the liposomal bupivacaine group was 63.1 years (±0.3) with 72% female. The mean body mass index in the traditional injection group was 35.4 (±8.5) compared to 34.6 (±7.8) in the liposomal bupivacaine group ($P = 0.6$). There were no statistically significant differences between comparison groups demographically with the numbers available.

Table 1
Patient Variables.

	Liposomal Bupivicaine (n = 65)	Ropivicaine Injection (n = 85)	P Value
Age (years)	63.13 ± 10.32	65.19 ± 9.21	0.20
BMI	34.64 ± 7.81	35.25 ± 8.49	0.60
Length of Stay	2.32 ± 0.53	2.31 ± 0.93	0.93
Gender:			
Male	18 (27.7%)	25 (29.1%)	
Female	47 (72.3%)	61 (70.9%)	
Side:			
Left	34 (52.3%)	49 (57.0%)	
Right	31 (47.7%)	37 (43.0%)	

With respect to the outcome variables, there was no statistical difference between groups in mean postoperative opiate usage in morphine equivalents between groups at any time frame, mean anti-emetic doses, or mean naloxone doses (Table 2). With regard to postoperative patient-reported pain scores, during the first 24 h after surgery there was no statistical difference between the 1.94 (±2.1) in the traditional group compared to the 1.93 (±2.1) in the liposomal bupivacaine group ($P = 1.0$), likely due to the spinal anesthetic. At the time of discharge, the mean pain scores in the traditional injection group were 3.6 (±2.1) compared 4.1 (±1.9) in the liposomal bupivacaine injection group and this difference did not reach statistical significance ($P = 0.14$). Most notably, the mean patient reported pain scores during the remaining hospitalization after the first 24 h until discharge were lower in the traditional injection group at 4.4 (±1.6) compared to 4.9 (±1.4) in the liposomal bupivacaine, which reached statistical significance ($P = 0.04$) (Fig. 1).

Categorical pain scores demonstrate similar findings as the mean numerical pain scores (Table 3). There was no substantial difference in the percentage of patients who rated their pain as either mild or moderate between the traditional and liposomal bupivacaine groups during the first 24 h after surgery or at the time of discharge. However, during the time interval after the initial 24 h, 81.5% of patients in the liposomal bupivacaine rated their pain an average of "moderate", compared with only 46.4% in the traditional injection group. Conversely, during the same time period only 16.9% of patients in the liposomal bupivacaine rated their pain as mild, compared to 47.6% of patients in the traditional injection group (Table 3).

In the traditional injection group, there were no cases of reoperation or revision during the follow up period. However, in the

Table 2
Patient Drug Outcome Measures.

		Liposomal Bupivacaine	Ropivicaine Injection	P Value
Time until 1st opiod (min)		505 ± 417	486 ± 447	0.79
Self-Rated Pain				
	First 24 h	1.94 ± 2.10	1.93 ± 2.14	0.97
	Remaining Stay	4.89 ± 1.35	4.38 ± 1.60	0.04
	Final	4.11 ± 1.86	3.62 ± 2.09	0.14
Opiate Usage (Meq)				
	First 24 h	6.21 ± 18.30	13.75 ± 13.42	0.34
	Remaining Stay	79.40 ± 62.97	65.53 ± 65.00	0.19
Anti-Emetic Doses				
	First 24 h	0.72 ± 1.14	0.47 ± 0.85	0.12
	Remaining Stay	1.03 ± 1.85	0.81 ± 1.55	0.43
Naloxone Doses				
	First 24 h	0.03 ± 0.25	0.00 ± 0.00	0.25
	Remaining Stay	0.00 ± 0.00	0.02 ± 0.15	0.22

Meq = Intravenous Morphine Equivalents.