

COVER PAGE

A Novel Application of Exparel for Postoperative Pain Management in Shoulder
Arthroplasty and Humerus Fracture Fixation

NCT02472314

4/14/2015

A Novel Application of Exparel for Postoperative Pain Management in Shoulder Arthroplasty

Shoulder arthroplasty is the fastest growing joint replacement surgery in the US, therefore effective pain management is critical and leads to early mobilization and rehabilitation, proven factors in patient satisfaction and clinical outcomes. This randomized controlled clinical trial is the first to establish the utility of liposomal bupivacaine-based multimodal analgesic regimen in patients undergoing shoulder arthroplasty. We will evaluate the potential promises of liposomal bupivacaine to address many of the shortcomings associated with interscalene blocks, including a favorable safety profile, decreased cost, increased duration of effect, and a potential improvement in functional outcomes and faster return to activities of daily living.

Shoulder arthroplasty patients have unique postoperative goals for mobilization and rehabilitation that are often limited by pain. Current pain management schemes are suboptimal. liposomal bupivacaine (Exparel) is a promising new agent, still untested in shoulder arthroplasty patients, and may improve outcomes such as opioid use, pain control, patient satisfaction, and shoulder function. This study aims to measure these outcomes in order to show that Exparel is superior to continuous interscalene block in reducing postoperative pain and healthcare cost and improving functional outcomes and patient satisfaction, which will hopefully lead to a widespread change in clinical practice for shoulder surgery.

With the mounting evidence that a liposomal bupivacaine-based multimodal analgesic regimen results in statistically significant and clinically meaningful reductions in opioid consumption, shorter length of stay and lower inpatient costs for general surgery procedures, it is important we examine its use in orthopaedics. The potential benefits of liposomal bupivacaine are significant enough to cause a widespread shift in clinical practice for postoperative pain management after total joint replacement. However, many providers are unconvinced regarding the potential utility and benefit of this agent due to current lack of evidence in orthopaedics. Results from this study may show that liposomal bupivacaine is superior to patient controlled continuous interscalene block for postoperative pain management in terms of decreased postoperative pain, decreased opioid use, less complications and improved patient satisfaction and shoulder function in shoulder arthroplasty patients. If the hypothesis is confirmed, this study will promote the use of liposomal bupivacaine-based multimodal analgesic regimen over continuous interscalene block as a method of postoperative pain control for shoulder arthroplasty patients.

HYPOTHESES& SPECIFIC AIM

Hypothesis – Liposomal Bupivacaine based multimodal analgesia will provide improved postoperative pain control, reduction in amount of opioid supplementation, decreased complications and quicker return to function compared to current standard of care pain management for patients undergoing shoulder arthroplasty surgery.

Specific Aim 1

To assess the impact of liposomal Bupivacaine compared to standard of care continuous peripheral nerve catheter in terms of postoperative pain control after shoulder arthroplasty surgery.

Specific Aim 2

To evaluate amount of supplemental opioid usage by patients after liposomal Bupivacaine as compared to that used by patients treated with controlled continuous peripheral nerve block (CPNB) after shoulder arthroplasty surgery.

Specific Aim 3

Test the safety of liposomal Bupivacaine compared to controlled continuous peripheral nerve block when used for postoperative pain management in patients undergoing shoulder arthroplasty.

Specific Aim 4

Compare functional recovery for patients treated with liposomal bupivacaine versus continuous peripheral catheter for postoperative pain management after shoulder arthroplasty surgery.

Study Design

Patients will be screened within 30 days prior to their scheduled surgical procedure. At the screening visit, eligibility criteria will be assessed, a complete history and physical exam and pregnancy test will be performed (for premenopausal women only), and concomitant medications and narcotic usage will be recorded. Training on self-assessment measures will also be conducted. Patients meeting inclusion criteria will be consented at prescreening visit for participation in this study by a study coordinator or PI.

At baseline (1 week prior to surgery) a physical examination, medical history, and pain assessment using a 11 point numeric rating scale at rest (NRS-R) and with activity (NRS-A) will be collected. Patients will then be enrolled and randomized into the study in one of two groups. All patients will receive standard of care preoperative analgesia. Preoperatively, the anesthesiologist will administer a 60mL single bolus brachial plexus nerve block with 0.5% bupivacaine to all patients. Patients in Group 1 will also undergo catheter placement at this time and continue to receive continuous peripheral nerve block (CISB) with 0.125% bupivacaine at a rate of 6 mL/hour postoperatively, allowing for the maximum dose to be administered over 100 hours. Patients in Group 2 will receive only the single shot peripheral nerve block preoperatively.

All patients will then receive standard of care general anesthesia with appropriate intraoperative doses of fentanyl or analogs equivalents. Patients in Group 2 will receive local tissue infiltration with liposomal bupivacaine intra-operatively in addition to the previously administered single shot peripheral nerve block to cover early postoperative pain. The study medication will be diluted to the recommended total volume of 60mL with 0.9% normal saline, and administered via recommended moving needle technique during the surgical procedure. The study drug administration will be done prior to prosthetic implantation (36ml) and after prosthetic implantation (12mL into the capsule and rotator cuff musculature) and wound during closure (12mL). The technique used has been validated and demonstrated success for total knee replacements as well as case series for total shoulder arthroplasty.

Post-operatively, the patients will be continued on oral acetaminophen and celecoxib for 96 hours after surgery when oral medications are tolerated. If postsurgical pain cannot be managed with nonnarcotic medications then patients will receive an appropriate rescue dose of intravenous morphine or 5 mg oral oxycodone on a request basis only for breakthrough pain.

Post-operatively all patients will be assessed for pain every 2 hours by the nurse using the Numeric Ranking Scale (NRS-A, and NRS-R) for pain (0=no pain, 10= worst pain) for the first 36 hours or until discharge, and scores will be recorded in the medical record and study log book. All doses and times of narcotics administered during the inpatient stay will be recorded in the medical record and study log book. All opioid doses will be converted to mg morphine equivalents. Following discharge, telephone evaluations will be conducted on postoperative days 2, 7 and 30 days by the research associate or PA. These interviews will collect data including

pain scales, narcotic usage, patient satisfaction with postoperative anesthesia/pain control, reason for not using medication, opioid related side effects, catheter related side effects, and use of other pain control methods from each consented participant prospectively, this data will be recorded using a standardized outcomes data collection form. Follow up postoperative assessments will include the above pain scores and narcotic usage logs as well as additional standard functional outcome assessments. These assessments will occur at 2 week, 6 week and 3 months post-operative clinic visits as per standard of care.

Primary outcomes measures will pertain to patient pain scores and narcotic usage until discharge and through day 30 postoperative. Secondary outcomes will include time to discharge, patient satisfaction with post-surgical anesthesia at discharge, and time to resumption of work or normal activities. Safety outcome measures will include, vital signs, wound healing status, neuropraxia, any adverse events (classified as being related to opioid, liposomal bupivacaine, or catheter), and patient responses regarding hospital readmissions, unplanned medical visits or health related problems. Short term functional assessments of shoulder function will also be measured at follow up clinic visits (2 weeks and 6 weeks post-operatively) and reported as secondary outcomes. These outcome measures are all well described and validated for use in outcomes following shoulder surgery. The scores all assess the patients' subjective quantification of pain and ability to complete functional activities. The Constant Score elaborates on this to include an objective physician assessment of shoulder range of motion and strength.

Statistical Analysis

Power calculations for this study are based on previous studies utilizing liposomal bupivacaine. These studies also utilized area under the curve of visual analogue scale and predicted that in order to detect a 30% difference with a power of >80% and a significance level of 0.05 a minimum of 25 patients would be needed in each treatment group. Continuous parameters will be summarized using descriptive statistics and categorical parameters will be summarized using number and percentage of subjects. The proportions of subject that require opioids versus those that do not will be compared using Fischer's exact test or chi-squared test as appropriate. All doses of opioids will be converted to morphine equivalents to allow for comparison. Total narcotic consumption and cumulative pain scores will be calculated as the area under the curve (AUC) using the trapezoidal method. The total narcotic consumption, cumulative pain scores, functional outcome scores, time to first rescue opioid dose, and length of hospital stay will be compared between groups using student t-test with treatment group as the main effect. All statistics will be performed using SPSS software (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp)