Continuous Femoral Perineural Infusion (CFPI) Using Ropivacaine after Total Knee Arthroplasty and its Effect on Postoperative Pain and Early Functional Outcomes

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Scientific abstract

Total Knee Arthroplasty(TKA) can involve an extremely painful recovery period with patients requiring narcotics and a hospital stay of 3 or more days. Recently, a relatively inexpensive disposable elastomeric pump that permits the provision of perineural infusions of local anesthetic for postoperative pain management has become available. The primary outcome in the proposed study is to determine if a continuous infusion of local anesthetic is effective in reducing postoperative pain after a TKA in a cost-effective manner; as well as define its effect in the perioperative period with respect to narcotic use, length of stay, patient satisfaction, postoperative blood loss, and early functional outcomes,as measured with Western Ontario and McMaster Universities Osteoarthritis Index(WOMAC) and the Knee Society Score(KSS).

Using a double-blind-randomized-placebo-controlled clinical trial with an FDA approved and commercially available system, the postoperative course of 40 patients will be assessed. Using a computer-generated randomization numbers table, half of the subjects will receive ropivacaine 0.2% through an indwelling femoral perineural catheter and the other half will receive saline 0.9%(placebo). Using a Visual Analog Scale(VAS), pain will be measured at baseline and postoperatively at 2, 4, 8, 24, 48, and 72 hours. At 2 weeks, 6 weeks, and 12 weeks postoperatively, patients will complete WOMAC and KSS questionnaires to assess their functional outcomes.

If this method proves to be effective at reducing postoperative TKA pain, patients may experience a lower incidence of opioid-related side effects, spend less time in the hospital, and have a more rapid recovery with better functional outcomes.

Lay abstract

Total Knee Arthroplasty (TKA) can involve an extremely painful recovery period with patients requiring narcotics and a hospital stay of 3 or more days. The following clinical study examines a popular method of pain control that reduces postoperative pain and possibly improves functional outcomes in patients receiving a TKA.

Study participants will receive a postoperative anesthetic via a continuous-infusion device placed alongside the femoral nerve on the operated leg which will remain in place for 2 days after their total knee arthroplasty. The device will supply a continuous infusion of either ropivacaine 0.2% (at 10 ml/hr) or saline 0.9% (at 10 ml/hr) (placebo). Pain control will be monitored via questionnaires after surgery to determine whether this technique will provide superior pain relief, and, if so, whether this will translate into additional benefits to the patient Eto help define its effect in the perioperative period with respect to narcotic use, length of stay, patient satisfaction, postoperative blood loss, and early functional outcomes, as measured with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Knee Society Score (KSS).

If this method proves to be effective at reducing postoperative TKA pain, patients may use less opioids via a PCA resulting in a lower incidence of opioid-related side effects, spend less time in the hospital, and have a more rapid recovery with better functional outcomes.

A. Study Description

Total Knee Arthroplasty (TKA) can result in severe postoperative pain. Commonly used pain management techniques include systemic opioids (intramuscular and intravenous), patient-controlled analgesia (PCA), and Non-Steroidal Anti-Inflamatory Drugs (NSAIDs); however, these modalities may not be the most effective and may be associated with side effects. Previous studies have

examined continuous infusions of local anesthetics for reduction of pain and analgesic requirements after shoulder surgery, and after foot and ankle surgery and concluded the safety and effectiveness of perineural infusions of local anesthetics including ropivacaine and bupivacaine. These studies have also shown that this FDA approved elastomeric pump is a safe and effective way to deliver postoperative pain control. (1, 2)

In the proposed study will examine the efficacy of a continuous femoral perineural infusion (CFPI) of ropivacaine 0.2% (at 10 ml/hr) compared with an infusion of saline 0.9% (placebo) in controlling postoperative pain following a TKA. The following information will be documented during the patient hospital stay: Visual Analog Scale (VAS) scores of pain, opioid use and incidence of related side effects, length of hospital stay, postoperative blood loss (as measured by a hemovac),and patient satisfaction with pain management.

A previous study showed that when a patient received a continuous femoral perineural infusion there was a decrease in blood loss postoperatively. (3) In the proposed study, all patients will receive a hemovac on the operated leg which will remain in place for 24 hours at which time the amount of blood loss will be recorded. Every patients hemoglobin and hematocrit levels will be measured daily postoperatively to see if there are any differences in both cohorts of patients.

In addition to short term variables measured during the hospital stay, we will also examine the effect of continuous femoral perineural infusion on early functional outcomes of patients undergoing TICA's. This information will be collected from patients using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Knee Society Score (KSS) (previously IRB approved). According to our extensive literature research, there have been no previous studies on functional outcomes over 5 days on patients who have undergone a TKA with CFPI. This information may help influence the recommendation or caution in use of such a method for acute postoperative pain control.

We hypothesize that patients who receive ropivacaine postoperatively will use the PCA pump less and have fewer opioid related side effects because of this reduced consumption. In previous studies, pain control has been shown to be more effective with a local perineural infusion as opposed to the standard of care which involves the use of a PCA pump. It is possible that if there is a more effective reduction of the pain immediately post surgery, sensitization may be blocked which can prevent the development of chronic pain. There may also be a reduced blood loss in patients who receive ropivacaine caused by a local anesthetic vasoactive property that has not yet been elucidated. One would expect that with better pain control, a patient will have better range of motion and be able to complete physical theray more effectively allowing for improved early functional outcomes. (see below for references)

B. Study Design and Statistical Procedures

Using a prospective, double-blinded, placebo-controlled, randomized clinical trial consisting of 40 patients undergoing TKA, the effectiveness of CFPI at reducing pain will be examined. Using a power analysis involving a previous study of single injection block of the femoral nerve in pain reduction after a TKA, pain without block using a VAS was shown to be 4.78, and pain with block was shown to be 3.67. If we assume an SD of 1, with an alpha of 0.05 and power of 0.8, then we need 17 patients in each group. In the stated study, 40 patients were treated and examined which allowed for significance to be determined in post operative VAS pain analysis and PCA use. (4, 5) In another study, an elastomeric pump (company - IFlow) similar to the one to be used in this study, a power analysis suggested that minimum group sizes of 9 would be required to detect a 60% reduction in the postoperative pain scores in the infusion group (assuming a mean pain score of 5 and an SD of 2 in the control group), with a power of 0.8 and an alpha of 0.05. (6) In the proposed study, we will enroll a total of 40 patients to ensure statistical significance is met.

On the basis of previous papers, statistical analysis will most likely include the following. Normally distributed continuous data will be analyzed with one-way analysis of variance, and continuous data not normally distributed will be analyzed by a Kruskal-Wallis analysis of variance. Pain scores will be measured by a repeated-measures analysis of variance. Other statistical measures may include Type III sum of squares analysis, Chi squared test, and Fishers exact test. A P value of less than 0.05 will be considered statistically significant. (6a)

The Center for Hip and Knee Replacement will collect prospective data on all total knee replacement surgeries at Columbia Presbyterian Medical Center. For each surgery performed, a preoperative Patient and Non-Patient survey will be completed. For each follow up point, a postoperative Patient and Non-Patient survey will be completed. This data collection will serve to improve surgical techniques and implants for future generations. The Patient survey includes items from the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Knee Society Score (KSS) outcome instruments. The Non-Patient survey, which includes surgical and patient information items as well as items from the above measures, will be answered by surgeons and/or residents. Surveys will be completed preoperatively, at 2 weeks, 6 weeks, and 12 weeks postoperatively. Once completed, all surveys will be scanned and imported into a database so that data will be available for future analysis. (See attached WOMAC and KSS forms with previous IRB approval)

Our study will utilize the WOMAC and KSS to assess functional outcomes in patients who receive continuous femoral perineural infusion (CFPI) of ropivacaine 0.2% (at 10 ml/hr) compared with an infusion of saline 0.9% after TKA.

C. Study Procedures

Prior to surgery, a femoral nerve catheter will be placed via the anesthesia team by means of the standard Winnie approach utilizing a Braun Contiplex system and a peripheral nerve stimulator. All patients in the study, regardless of group identity, will receive 30mL of bupivacaine 0.25%, at the time of catheter placement. Surgery will be performed under spinal anesthesia (isobaric 15mg of bupivacaine 0.5% and 25 micrograms of fentanyl). Prior to entering the operating room (OR), patients will be assigned to one of two study groups (ropivacaine or placebo) according to a computer-generated randomization number table. While the anesthesia team will know which infusion the patient receives, the surgeon will remain blinded to the identity of the system. Prior to the completion of surgery, the anesthesia team will attach a pump reservoir containing the fluid (either ropivacaine 0.2% or saline 0.9% depending on the patients study group) and continuous infusion will begin automatically and end when exhausted from the pump reservoir, 400mL, at 2 days. (7)

All other postoperative treatment regimens will be identical for both study cohorts. All patients will receive postoperative pain management using a PCA pump weaned to oral pain medications. Patients will receive identical physical therapy, hemovacs for 24 hours postoperatively, and out of bed (00B) mobilization protocols.

An office-based research assistant who is blinded to the infusion solution will carry out all data collection. The clinic team providing postoperative care will also be blinded to the infusion solution utilized. Randomization assignments will not be revealed until the completion of the study.

D. Study Drugs or Devices

This study will examine the efficacy of continuous femoral perineural infusion (CFPI) of ropivacaine 0.2%(at 10 ml/hr) compared with infusion of saline 0.9% (at 10 ml/hr)(placebo) using an FDA approved elastomeric pump in postoperative TKA patients. A Braun Contiplex catheter system and a disposable elastomeric pump, both of which are FDA approved and commercially available, will be used to insert a perineural catheter and provide perineural infusion of local anesthetic, respectively. (8) The proposed clinical trial will be a randomized placebo controlled phase IV trial using all products for their intended use.

Previous studies have demonstrated the safety of infusion of ropivacaine perineurally at a rate of 10m1/hr. Lierz et al. (9) reported success of infusion of 4-6mL/hr of ropivacaine 0.2% for a period of six days without any adverse events. In addition, Tuominen et al. (10) have demonstrated that by using 18.5 mg/hr of bupivacaine 0.25% for 48 hours (bupivacaine is a potentially more toxic local anesthetic), serum levels remained nontoxic. Klein et al used 10mL/hr of ropivacaine 0.2% in an interscalene brachial plexus block and after 24 hours found serum accumulation to be 1.04, only marginally larger than the concentration in the other group (0.34) who received a single injection block. All these levels remain well below any serum toxicity of ropivacaine. (11)

E. Study Questionnaires

Three 10cm Visual Analog Scale (VAS) will be used to collect information from the patient regarding pain management, nausea, and satisfaction. Pain control will be assessed at 2, 4, 8, 24, 48, and 72 hours after TKA. Along with the questionnaires, an office based research assistant or nurse will also record the patient PCA use, extra pain medications received, hemovac outputs, and hematocrit levels.

F. Study Subjects

Inclusion Criteria:
1. Primary TKA
2. Agreement to participate in study
3. ASA score I-III

4. Exclusion Criteria:
5. Revision TKA / Infected TKA
6. Age > 85
7. BMI > 35
8. Any contraindication to femoral nerve blockade
9. Peripheral neuropathy
10. Patients on long acting opioid therapy with less than 3 months since they have had to increase opioid requirements
11. Allergy to ropivacaine
12. Known adverse reaction or allergy to morphine and dilaudid and fentanyl preventing the use an opioid delivering PCA
13. Contraindicated to or refuses spinal anesthesia
14. Patient refuses to participate in study

G. Recruitment

All patients satisfying the inclusion criteria referred to and being treated at the Center for Hip and Knee Replacement at the Department of Orthopaedic Surgery at New York Presbyterian Hospital by Drs. W. Macaulay, H. Kiernan, 0. Nercessian, and J. Geller will be offered study participation. The surgeon will introduce the clinical trial to the patient. It will be explained to patient that he/she is not required to participate in the clinical research study and his/her decision will not affect his/her care at this hospital. If the patient decides not to participate in this study, they will receive the same preoperative care, perioperative protocol and attention to excellence, and postoperative care as if they agreed to participate. All of this will be explained to the patient when the clinical trial is introduced to them to ensure that they are not coerced involuntarily into participation.

H. Confidentiality of Study Data

Any information obtained during this study will remain confidential. A record of study data will be kept at the Center for Hip and Knee Replacement. Personal identifiers will not be listed on study data collected. Instead, study specific identifiers will be used (ie, CPIS 01 for patient #1, CPIS 02 for patient #2, CPIS 03 for patient #3, etc), and all links to these identifiers will be kept secure in a office cabinet that will remain locked and only be accessible to study personnel. Information obtained from this study and from subjects' medical records may be used for research purposes and published. No patient identification information will be released without separate consent, except as specifically required by law. Dr. W. Macaulay, the principal investigator, will maintain all patients identifiable information securely and will be solely responsible for its use as applies to the study.

I. Potential Risks

The risks associated with placement of perineural catheters is similar to that of single injection femoral nerve blockade and is extremely low. These include local anesthesia toxicity, peripheral nerve damage, and sepsis. In addition, there is a slight to small risk of block failure, early catheter dislodgement, and/or numbness or weakness of the leg due to the local anesthetic infusion which will resolve when the infusion is stopped.

J. Potential Benefits

The primary potential benefit of this investigation is to define a more effective strategy to manage severe postoperative pain encountered in the immediate to short term after TKA. Secondarily, patients may enjoy a reduced recovery time, less opioid use with a reduction of opioid-related side effects, a shorter hospital stay, reduced postoperative blood loss, and improved patient satisfaction.

K. Alternatives

If the patient decides not to participate in this study, he/she will still receive standard of care at this hospital which involves the use of a patient controlled analgesia (PCA) pump after surgery. The current standard of care involves using narcotics through the PCA pump in addition to other pain medications that may be taken by mouth (eg. NSAIDs) if the PCA pump is not effective at controlling postoperative pain.
Alternative procedures to the standard of care involve a variety of regional nerve blocks which involve single shot injections of local anesthetic at the femoral nerve or other nerves that control the sensation around the knee. At other hospitals, the standard of pain care may involve these alternative procedures in addition to PCA pumps.

L. References

1. Gottschalk et. al; Continuous Wound Infiltration with Ropivicaine Reduces Pain and Analgesic Requirement After Shoulder Sugery; Anesthesia Analgesia 2003;97:1086-91
2. White et. al; The Use of Continuous Popliteal Sciatic Nerve Block After Surgery Involving the Foot and Ankle: Does it Improve the Quality of Recovery?; Anesthesia Analgesia 2003;97:1303-9
3. Chelly et. al; Continuous Femoral Blocks Improve Recovery and Outcome of Patients Undergoing Total Knee Arthroplasty; Vol 16 No.4 2001: 436-45
4. Sczukowski et. al; Femoral Nerve Block for Total Knee Arthroplasty Patients; Journal of Arthroplasty 2004;19, 720-5.
5. Power Analysis by: http://ph1530.janak.org/gcrc/
6. (6,6a) White et al. The use of a continuous popliteal sciatic nerve block after surgery involving the foot and ankle: Does it improve the quality of recovery? Ambul Anesth 2003; 97:1303-09.
7. I-Flow Elastomeric Pump (C-Bloc) See attached Document for 510(k); IDE: K040337(traditional); Phone 949-206-2700; 20202 Windrow Dr., Lake Forest, CA 92630
8. Braun Contiplex (B. Braun Medical, Bethlehem, PA)
9. Lierz P. et al. Continuous interscalene blockade of both brachial plexus with ropivacaine in phantom pain. Pain 1998;78:135-137.
10. Tuominen, Met al. Continuous Interscalene brachial plexus block: clinical efficacy, technical problems and bupivacaine plasma concentrations. Acta Anaesthesiol Scand 1989;33:84-88.
11. Klein Set al. Interscalene Brachial Plexus block with a continuous isertion system and a disposable infusion pump; Anesth Analg 2000;91:1473-8