NCT01167907

WFUHS 00013823

PROTOCOL

Evaluation of Continuous Saphenous Nerve Block to Supplement a Continuous Sciatic Nerve Block After Ankle Surgery

September 30, 2010

Study Title: Evaluation of a Continuous Saphenous Nerve Block to Supplement a Continuous Sciatic Nerve Block for Postoperative Analgesia Following Ankle Surgery

Principal Investigator: Robert Weller MD
Co-investigator(s): Daryl Henshaw MD

Sponsor or funding source: Department of Anesthesiology at Wake Forest University Baptist Hospital. Pumps for saphenous infusion provided by I-Flow Corporation

Background, Rationale and Context

Orthopedic surgery of the lower extremity is particularly painful, and epidural analgesia or long-acting nerve blocks are commonly employed to reduce post-operative pain. Unilateral peripheral nerve blocks have advantages over epidural analgesia including: limited sympathetic blockade, no interference with bladder or contralateral limb function, and the ability to be discharged to home with a perineural catheter and pump for local anesthetic administration.[1] Patients undergoing ankle arthrodesis or bi/tri-malleolar fracture repairs are expected to have pain primarily in the sciatic nerve distribution, with a lesser component of their pain emanating from the medial side of the lower extremity innervated by the smaller, cutaneous saphenous nerve. At our institution, pain from this surgery is typically managed with a continuous sciatic nerve block maintained for 48-72h, and a single-shot saphenous or femoral nerve block with long-acting local anesthetic to provide 12-24h of saphenous analgesia. In spite of this aggressive regional analgesia approach, many patients still complain of significant pain in the postoperative period,and this study is designed to assess the analgesic effect of a continuous rather than single-shot saphenous block. We hypothesize that patients will have a clinically important reduction of pain score from a longer duration of saphenous nerve block provided by a continuous catheter, which would justify the added complexity of 2 perineural catheters

Ultrasound guidance to facilitate placement of peripheral nerve blocks has been shown to improve the onset time of analgesia, increase success of the block, reduce vascular puncture and increase patient satisfaction.[2-3] While various ultrasound-guided techniques for single-shot saphenous block have been described in the literature, currently no description of an ultrasound-guided continuous saphenous nerve block is available.[4-9] This study will employ an ultrasound-guided technique for continuous saphenous block and describe this technique.

Continuous femoral nerve block is a common practice and could also be used with sciatic block to provide analgesia of the medial ankle instead of a saphenous block. Continuous saphenous block, however, has potential advantages over an inguinal femoral nerve catheter including less bacterial colonization, and preservation of quadriceps motor function.[10] This study will assess the effect of continuous saphenous block on quadriceps function.

Objectives

This study will evaluate the effect of adding a continuous saphenous nerve catheter to a continuous sciatic nerve catheter in patients undergoing ankle surgeries. Specifically, patients undergoing ankle fusions or open reduction and internal fixation of bi- or tri-malleolar fractures will be evaluated. The primary endpoint of this study will be the verbal pain score at rest and with movement at 48h post-nerve blockade. At this point in time the primary saphenous nerve

block will have resolved, and any saphenous analgesia will be due to the infused solution. Secondary endpoints of opioid use, nausea and vomiting, sleep disturbance, and change in quadriceps strength will also be evaluated. Additionally, we will describe an ultrasound guided technique for placement of a continuous saphenous nerve catheter supported by cadaveric dissection.

Methods and Measures

Design

The study will be a randomized, double-blind, placebo-controlled trial. Patients will be recruited and have sciatic and saphenous perineural catheters placed as described below, and initial nerve blocks produced in the usual fashion. Patients will then be randomized to either an active drug (local anesthetic) or a placebo (saline) infusion group at the time of saphenous infusion preparation by Pharmacy personnel.

Setting

All patients in the study will be undergoing non-urgent surgery at Wake Forest University Baptist Medical Center. The interventions will be performed in the regional anesthesia area of the surgery center. Patients will remain in the hospital at least one night, and once discharged, all patients will have daily follow-up by phone with the regional anesthesia acute pain management team.

Subject selection criteria

Patients undergoing non-urgent unilateral ankle arthrodesis or open reduction and internal fixation of bi/tri malleolar fractures will be recruited for the study.

- **Inclusion Criteria**
  Patients will be eligible for inclusion in the study if they are between the ages of 18-75 and are scheduled to undergo unilateral ankle arthrodesis or open reduction and internal fixation of bi/tri malleolar fractures at Wake Forest University Baptist Medical Center. Patient must give written informed consent for anesthesia including continuous sciatic nerve block and saphenous block for postoperative analgesia prior to recruitment. Patients must be able to comprehend the use and care of the catheters and infusion pump systems both in the hospital, and at once discharged home with verbal and written instructions
- **Exclusion Criteria**
  Patients will be excluded if they have a contraindication to saphenous or sciatic nerve blockade (including significant coagulation abnormalities), history of opioid addiction, current chronic pain therapy with high-dose opioid (extended release opioids or > 40mg oxycodone equivalents per day), allergy to study medications, or failure to place a sciatic catheter. Failure to achieve successful sciatic analgesia or a successful primary saphenous block will also lead to exclusion.
- **Sample Size**
  74 patients will be recruited for the study and will be randomized into two groups of n = 37 patients each. This sample size provides power = 0.80 to allow reliable detection of group differences of d = 0.74 standard deviation units (approximately 1.5 points on a 0 -10 pain scale in our pilot data), assuming two-sided inferences held to the α =

0.025 level (see stats section for details on error control). Differences smaller than this magnitude are unlikely to be clinically meaningful.

Interventions and Interactions

Study participants will be asked to report a preoperative baseline pain score (Numeric Pain Scale (0-10)), and have quadriceps strength measured (see below) prior to any sedation being administered. Patients will undergo placement of a continuous subgluteal sciatic nerve catheter, and dosage with 25ml of 0.25% bupivacaine with epinephrine 1:200,000 and clonidine 25 mcg per usual technique after sedation. A perineural catheter will then be placed for primary saphenous nerve block and postoperative saphenous infusion. This continuous saphenous catheter will be placed using ultrasound guidance (Sonosite Turbo ™, Bothell, WA) (6-13MHz linear probe). The superficial femoral artery will be identified in short axis at approximately the midpoint or distal third of the femur as the artery lies deep to the sartorius muscle in the adductor canal. Using aseptic technique, an 18 gauge tuohy needle will be inserted in-plane from lateral to the transducer and advanced to a position anteromedial to the artery, between sartorius and vastus medialis muscles. Proper positioning will be confirmed by injection of saline, a 20g multiorifice catheter will be inserted 3-4 cm beyond the needle tip and the catheter will be tunneled and taped up the medial surface of the thigh. The catheter will be test dosed with 1.5% lidocaine with 1:200,000epinephrine to confirm position and rule out IV injection. The primary saphenous nerve block will be produced by incremental injection through the catheter of 10ml of 0.25% bupivacaine with epinephrine 1:200,000 and clonidine 15 mcg. Successful saphenous block will be defined as loss of sensation to pinprick in the mid, anteromedial leg measured at 15 and 30 minutes post-block. A 3-point scale will be used to define sensory block: 0=full sensation, 1= touch without sharp sensation, 2=absent sensation.

To determine the effect of saphenous block on quadriceps function, patients will have knee extension muscle strength tested pre-block and 30 min post-block using a Hoggan Health microFET 2 MT Digital Handheld Dynamometer. After placement of both the saphenous and sciatic nerve catheters, patients will receive either neuraxial or general anesthesia for surgical anesthesia at the discretion of the attending anesthesiologist medically directing their primary anesthetic technique.

Patients with evidence of sciatic and saphenous nerve block will be randomized to receive a postoperative continuous infusion of either saline (control) or 0.2% ropivacaine by elastomeric infusion pump at 5ml/h started within 6h of catheter placement. The randomization will occur by sealed envelope provided to the OR Pharmacy (block randomization in blocks of 10) and the OR pharmacy will prepare the 300 ml elastomeric pump with active or control solution. The On-Q C-Bloc™(300ml capacity) (I-Flow corporation) pump will be attached to the saphenous catheter in the PACU, or within 6h of primary block; the catheter will infuse for 60 hours.

The patients, physicians, nurses and investigators will be blinded to treatment group.

The sciatic infusion will be managed per usual practice: postoperatively all patients will receive 0.2% ropivacaine through their sciatic nerve catheter at a basal infusion rate of 10ml/h, . The sciatic pump will be an On-Q™ pump per usual practice. All patients will have oral and IV opioids prescribed while hospitalized, and oral opioids prescribed after hospital discharge. In the event of breakthrough pain, patients will be instructed to adjust the sciatic nerve pump, and/or to take oral opioids for the pain.

While patients are hospitalized, opioid administration and pain scores will be recorded by nursing staff on the patient care record. Side effects including nausea, vomiting, or itching will also be recorded. Patients will be seen on a daily basis while in the hospital by the acute pain service, and adjustment of their sciatic infusion performed if indicated. They will be questioned about sleep quality, pain score, opioid side effects, and sensory function in the sciatic and saphenous distributions. This information will be recorded by the acute pain management team. On postoperative day 1, all patients will again have their quadriceps muscle group strength assessed with the hand-held dynamometer, and the catheter sites will be inspected per standard protocol.

Patients will be generally discharged home with peripheral nerve catheters in place on POD #1, after receiving written and verbal instructions in perineural catheter management. These patients will be called at 24 and 48 hours post discharge to determine rest and incident numeric pain scores, opioid usage, sleep quality (as number of awakenings for pain), and the presence of nausea or vomiting. Patients will be given contact numbers and instructions to call with any questions or concerns per usual practice.

Outcome Measure(s)

The primary endpoint of this study will be a reduction of the rest and incident verbal pain scores 48hpost-nerve blockade when the primary saphenous single-shot block is expected to have resolved. Secondary endpoints of reduction of opioid use, nausea and vomiting, sleep disturbance (as number of awakenings), and reduction of quadriceps strength will also be evaluated. Additionally, we will describe an ultrasound guided technique for placement of a continuous saphenous nerve catheter supported by cadaveric dissection.

Analytical Plan

All analyses will be conducted with SAS 9.2 (SAS, Inc., Cary, NC). Prior to conducting the primary analysis, the distributional characteristics of all variables will be considered by examining histograms and descriptive statistics. Where possible, all analyses will be conducted using the general linear model (e.g., t-test), but where necessary nonparametric equivalents will be conducted for pairwise comparisons (e.g., Mann-Whitney U). As a result of random assignment, participant characteristics are expected to be similar, but treatment group characteristics will be compared using descriptive statistics. The primary analysis will consist of a direct comparison between treatment groups at 48 hours using an independent t-test. Because the primary analysis consists of two comparisons (i.e., pain with rest and pain with movement), each comparison will be evaluated at the $\alpha = 0.025$ level (i.e., holding the family to a conservative 5% type-I error rate). Secondary analyses will be conducted using tests appropriate for the level of measurement including t-tests, Mann-Whitney U (ordinal data such as number of awakenings), and χ^2 (categorical data such as presence of nausea). Statistical significance for all secondary comparisons will be interpreted at $p < 0.05$. No interim analyses will be conducted.

Human Subjects Protection

Informed Consent

Written informed consent will be obtained from each subject. Patients scheduled for elective ankle arthrodesis will be seen in the preoperative assessment clinic at North Carolina Baptist Hospital. Following preoperative assessment and consent for peripheral nerve block for analgesia, a research clinician will meet with the patient to discuss participation in the

study. They will be informed of the purpose of the study along with the risks, benefits, and alternatives. Questions will be answered and consent obtained. Patients not seen in our preoperative assessment clinic will be asked to participate in the study on the day of surgery when admitted to the Regional Anesthesia Holding Area. A copy of the signed informed consent will be placed in the patient's medical record. All subjects may decline participation in the study at any time. Informed consent and all necessary study data will be obtained prior to the administration of any sedative medication.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a separate master log. The master log will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed at the earliest opportunity, consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

References

1. Ilfeld B, Morey T, Wang R, Enneking K: Continuous Popliteal Sciatic Nerve Block for Postoperative Pain Control at Home. *Anesthesiology.* 2002; 97:959-965

2. Marhofer P, Greher M, Kapral S. Ultrasound Guidance in Regional Anesthesia. *Br J Anaesth.* 2005;94:7-17.

3. Perlas A, Brull R, Chan VW, McCartney CJ, Nuica A, Abbas S. Ultrasound Guidance Improves The Success Of Sciatic Nerve Block At The Popliteal Fossa. *Reg Anesth Pain Med*. 2008 May-June;33(3)259-65

4. Gray AT, Collins AB. Ultrasound-Guided Saphenous Nerve Block. *Reg Anesth Pain Med*. 2003;28:148.

5. Horn J, Pitsch T, Salinas F, Benninger B. Anatomic Basis to the Ultrasound-Guided Approach for Saphenous Nerve Blockade. *Reg Anesth Pain Med*. 2009 Sept-Oct;34(5)486-89

6. Lundblad M, Kapral S, Marhofer P, Lönnqvist P. Ultrasound-Guided Infrapatellar Nerve Block in Human Volunteers: Description of a Novel Technique. *B r J Anaesth*. 2006;97(5)710-14.

7. Tsui BC, Özelsel T. Ultrasound-Guided Transsartorial Perifemoral Artery Approach for Saphenous Nerve Block. *Reg Anesth Pain Med*. 2009;34:177-78.

8. Kirkpatrick J, Antonakakis J. Preliminary Experience With a New Approach to Performing an Ultrsound-Guided Saphenous Nerve Block in the mid to Proximal Femur. *Reg Anesth Pain Med*. 2010:35(2)222-223.

9. Manickam B, Perlas A, Duggan E, Brull R, Chan V, Ramlogan R. Ultrasound Guided Saphenous Nerve Block. *Reg Anesth Pain Med.* 2009;34(6)578-580.

10. López AM, Sala-Blanch X, Carrera A. Ultrasound Guided Perivascular Saphenous Nerve Block at the Midthigh for Ambulatory Surgery. *Anesthesiology*. 2008;109:A632.

Appendix

1. Data collection form
2. Consent form