NCT: NCT04553913
DATE: 10/13/20

Study Title: Proof-of-Concept: A Device to Determine Return of Sensation After a Regional Anesthetic Block.

Principal Investigator, Co-investigator(s): Seiha Kim DO; Wessley McKnight, MD; Robert S. Weller MD

Sponsor or funding source: Department of Anesthesiology, Wake Forest School of Medicine

Background, Rationale and Context

Regional anesthesia investigators have always shown interest in measuring the specific duration of neuraxial or peripheral nerve blocks, and how variations in block technique or medications affect that duration. Although ostensibly a simple concept, there are many sensory modalities available for block testing (light touch, cold or hot temperature, pain, pressure, etc.) and there is no consensus in the anesthesia literature on how best to measure the duration of nerve block (1). Sensory testing is repetitive, and must be practical and consistent. Pinprick and cold sensation are commonly employed, and these modalities share the same afferent fibers (C-delta) so there is close overlap in the sensory loss mapping after regional block (2). With respect to pinprick sensation (3 , 4) there can be variability in the sharpness, pressure, and reproducibility of a pinprick test. Testing for cold sensation may be more consistent, using a controlled stimulus temperature and duration, and there are different methods of testing such as a cooled glass vial (4) (5℃) or Rolltemp (5) (25℃).

Cold therapy is a commonly applied modality following strenuous exercise or during recovery from extremity surgery, and is expected to reduce tissue damage and relieve pain. There is some evidence of benefit but little consensus on the optimum interval and duration of therapy (6), and there are many approved medical devices available for use.

This investigation proposes an adaptation of an approved cold therapy device to administer automated, periodic cold stimuli at a location made insensate by regional block. When the patient perceives cold at that site, they will press a stop switch to discontinue cooling which will also stop a timer and give an accurate duration of the time to sensory recovery at that site.

The concept will be tested by comparing the duration measured by this device to the standard measurement of recovery from spinal block employed by post-anesthesia care unit (PACU) nurses who will use pinprick (toothpick) testing of lumbar dermatomes every thirty minutes.

Objectives

Main objective: To test the agreement of standard pinprick (toothpick) sensory recovery testing after spinal anesthesia with the duration of sensory block as determined by the modified device.

.

Methods and Measures

Design

This is an observational series to determine the agreement of an experimental application of an approved medical device designed to test recovery of sensation from spinal anesthesia, with the customary clinical method of testing recovery from spinal anesthesia.

Subjects selection criteria

- **Inclusion Criteria**
  - Patients 18-75 y/o and scheduled to undergo unilateral primary knee or hip arthroplasty under spinal anesthesia with bupivacaine, ropivacaine or tetracaine will be eligible The study will be conducted at Wake Forest Baptist Hospital and Davie Medical Center
- .**Exclusion Criteria**
  - Exclusions to cold therapy due to medical disease such as Raynaud's disease, Buerger's disease, sickle cell disease, significant peripheral vascular disease (history of limb vascular stents or bypass), hypercoagulable clotting disorders, cold agglutinin disease, history of frostbite of the legs, and neuropathy in the lumbar dermatomes under investigation.
  - Subjects will be excluded if pre-block sensation is abnormal in the L3 dermatome of the non-operative leg , or if spinal anesthesia is not performed or is unsuccessful.
  - Subjects will be excluded if sensation has already returned in the L3 dermatome of the non-operative leg upon arrival to the PACU.
- **Sample Size**
  - Sample size calculations (see analysis below) predict 9 subjects will be sufficient to show equivalence. We will recruit 15 subjects for the study to account for drop-out after enrollment.

Interventions and Interactions

Subjects will be recruited before their surgical date in one of two ways. They may be approached at the conclusion of their preoperative assessment clinic (PAC) appointment to

review the study and provide written consent if willing to participate. If not approached at the PAC visit, they may be contacted by phone prior to the surgical date using a telephone script to introduce the study, review exclusion criteria and determine interest. If interested, subjects will have questions answered and later complete a written informed consent in the preoperative holding area on the day of surgery. The subject's ability to perceive cold (ice) and pain (toothpick) will be assessed in the L3 dermatome on the non-operative thigh, and they will be excluded if pre-block sensation is abnormal in the L3 dermatome, They will also be excluded if decision to use general rather than spinal anesthesia is chosen at this time. If eligibility is confirmed, a skin location on the non-operative thigh will be marked with a circled "X" using marking pen after this assessment to show the location for the device pad to be applied in PACU. Subjects will be shown the cooling device and instructed on how and when to press the "stop" button when they feel cold at the application site.

The patient will then undergo usual anesthesia care with preoperative analgesic and sedative medications, peripheral blocks if indicated, spinal anesthesia and intraoperative sedation. The time of spinal injection and medication and dose will be recorded. Subjects will be excluded at this point if spinal anesthesia is unsuccessful.

After surgery and upon arrival in PACU, if the subject has already recovered sensation at the L3 dermatome (at the "X"), they will be excluded from the study at that time. If they have not recovered sensation, the device pad will be wrapped to the non-operative thigh at the "X" location by a study team member, and an elastic bandage used to secure the cooling pad to the patient. Cycling will begin with 15 min of cold circulation, then 15 minutes off. A PACU nurse who is not aware of the cooling pump activity will test the patient in the lumbar dermatomes (L1 to L4) every 30 minutes per usual practice (the L3 dermatome will be tested adjacent to the cooling pad). The most cephalad level of prick sensation with toothpick stimulus will be recorded on the PACU flowsheet in WakeOne. Cooling pad temperature during pump cycling will be measured with a wireless sensor, and expected to reach approximately 40-50 degrees Fahrenheit when cooling (based on in vitro testing), and return toward body temperature when not cooling; the range will be recorded on the data sheet. Usual PACU discharge criteria will be employed, but it is expected the testing will end when regression of spinal block to L3 is achieved. Study participation will continue until the subject stops the pump cycling, and is expected to continue up to 4 hours.

Outcome Measure(s)

- **Primary Outcome Measure**
  Block Recovery Time: Time to resolution of spinal anesthetic (minutes from injection) will be measured in minutes for (i) the device and (ii) standard nursing pinprick testing on the same (non-operative) thigh.

Analytical Plan

Time to resolution of spinal anesthetic will be measured in minutes for (i) our device and (ii) standard nursing pinprick testing on the same (non-operative) thigh. We will test the equivalence of (i) and (ii), where the equivalence region is defined as the difference in (i) and (ii) falling in the interval [-29, 29] minutes. In the sample size calculation, it is assumed that time to spinal resolution has a mean of 140 minutes (standard deviation 29 minutes) such that we are targeting an equivalence region of [-1, 1] standardized units. With type 1 error set to 0.05, we need 9 pairs of observations to achieve 80% power. Calculations were performed using the R package 'TOSTER '.
To test equivalence of the measurements in real data, the same procedure of "two one-sided tests" will be employed, with t-tests of the one-sided hypotheses that the null difference is less than -29 minutes or that the null difference is greater than 29 minutes.

Human Subjects Protection

Subject Recruitment Methods

Study team members (Anesthesiology Faculty) will be providing the anesthesia care for patients undergoing hip and knee arthroplasty and routinely review clinical information in the days before surgery to prepare for this care. They will identify eligible patients as a part of this review and let the clinical research staff know of potential subject recruitment. Patients meeting eligibility requirements will be recruited before their surgical date in one of two ways. They may be approached at the conclusion of their preoperative assessment clinic (PAC) appointment to review the study and consent form. If not approached at the PAC visit, they may be contacted by phone prior to the surgical date as described above in "interactions" using a telephone script to introduce the study, review exclusion criteria and determine interest. If interested, patients will have questions answered and later complete a written informed consent in the preoperative holding area on the day of surgery. Patients will NOT be recruited on the day of surgery if they have not already been contacted by phone or seen in person prior to their day of surgery.

Informed Consent

Signed informed consent will be obtained from each subject.

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 linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection

subject identifying information will be destroyed by shredding 3 years after study completion 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. Ode K., et al Monitoring regional blockade. Anaesthesia 2017, 72 (Suppl. 1), 70–75
2. M. Nersesjan , et al Sensory distribution of the lateral femoral cutaneous nerve block – a randomised, blinded trial Acta Anaesthesiologica Scandinavica 62 (2018) 863–873
3. Turner JD, et al. Single-Injection Adductor Canal Block With Multiple Adjuvants Provides Equivalent Analgesia When Compared With Continuous Adductor Canal Blockade for Primary Total Knee Arthroplasty: A Double-Blinded, Randomized, Controlled, Equivalency Trial. J Arthroplasty. 2018 Oct; 33(10): 3160-3166.
4. Nader A, et al. A dose-ranging study of 0.5% bupivacaine or ropivacaine on the success and duration of the ultrasound-guided, nerve-stimulator-assisted sciatic nerve block: a double-blind, randomized clinical trial. Reg Anesth Pain Med. 2013 Nov-Dec; 38(6): 492-502.
5. Madsen MH, et al. Local Anesthetic Injection Speed and Common Peroneal Nerve Block Duration: A Randomized Controlled Trial in Healthy Volunteers Reg Anesth Pain Med. 2018 Jul; 43(5): 467-473.
6. Bleakley C, et al The Use of Ice in the Treatment of Acute Soft-Tissue Injury A Systematic Review of Randomized Controlled Trials. The American Journal of Sports Medicine, 2004: 32(1):251-261

Appendix

1. Data collection form

2. Consent form
3. Device information, modification, clinical engineering testing
4. Telephone “script”