IPACK (interspace between the popliteal artery and the capsule of the knee)

The Analgesic Efficacy of Adding the IPACK block to a multimodal analgesia protocol for primary total knee arthroplasty

Taras Grosh, MD

Nabil Elkassabany, MD MSCE

Ignacio Badiola, MD

Craig Israelite, MD

IRB # 828618

Clinical Trials.gov #: NCT03703206

Date: October 15, 2018

Contents

Title: The Analgesic Efficacy of Adding the IPACK block to a multimodal analgesia protocol for primary total knee arthroplasty

1. Background

Regional anesthesia plays a pivotal role in pain control after total knee replacement. A combination of a femoral and sciatic nerve blocks provides anesthesia to the knee circumferentially. Unfortunately, blocking the common femoral and sciatic nerve trunks comes at the expense of quadriceps weakness resulting in possibly delayed patient involvement in their postoperative physical therapy and possibly increased risk of falls. Anesthesiologists have moved to blocking the saphenous nerve in the adductor canal to preserve muscle motor strength. The adductor canal block (ACB) has been shown to have similar analgesic efficacy to the femoral nerve block in the context of administration of a multimodal analgesia protocol. Recently, a novel ultrasound guided Injection of local anesthetic between the Popliteal Artery and the Capsule of the Knee (iPACK) was described (1,2,3, 4). Target nerves are the terminal genicular branches of the sciatic nerve that supply the posterior knee capsule. Potentially, this block can be an alternative for the sciatic nerve block as it may block the pain signals from areas supplied by the terminal branches of the sciatic nerve, namely the posterior capsule of the knee. Similar to the ACB, it should not have any effect on the motor power of the muscles of the lower extremity, allowing patient to actively participate in their physical therapy while providing analgesia in this nerve block sensory distribution. Our hypothesis is that adding the IPACK to the current multimodal protocol and the ACB should cover the pain generated from the posterior capsule of the knee and improve pain control after surgery. This prospective, randomized controlled trial aims to assess the analgesic efficacy of adding the IPACK (for the purpose of this study iPACK is considered investigational although it is FDA approved and standard of care) to a multimodal analgesia protocol in patients undergoing primary total knee arthroplasty.

2. Study Objectives

The Overall Objectives of this study are:

1. Assessment of the analgesic efficacy of adding IPACK to our current multimodal pain protocol.

   This will be achieved by comparing percentage of patient presenting with pain in the sensory distribution of the sciatic nerve (back of the knee) 6 hours after surgery, pain scores, and opioid requirements between the two study groups.

   2- Compare the quality of recovery questionnaire in 24, 48 hours and one week between two groups, one with ACB alone and the other is with ACB+ I-PACK

   3-Compare discharge times between ACB alone vs ACB + iPACK after primary knee arthroplasty

IPACK (interspace between the popliteal artery and the capsule of the knee)

4-Assessment of functional outcomes and patient performance during physical therapy sessions between the two groups

2.1 Primary outcome

The primary outcome variable is the percentage of patients presenting with pain in the distribution of the sciatic nerve (back of the knee) 6 hours after surgery.

2.2 Secondary outcome

The secondary outcome variables are: pain scores at different time intervals (every 12 hours after surgery), opioid consumption first 48 hours postop, PACU discharge times, and results of the QOR scores. Additionally we will collect the ambulation distance, time to up and go (TUG) test and manual muscle testing (MMT) from the physical therapy notes every day while patients are in the hospital

2.3 Methods

1- Measure visual analogue scores at the end of each nursing shift for the first 48 hours every 6 hours using the numeric rating scale for pain assessment
Additionally, each patient will be provided with a chart representing a drawing of different areas of the knee to point any specific areas where pain is mostly generated
2- Measure opioid requirement at the end of each 12 hour period x 48 hours
3- Assess independent ability to stand and sit down (evaluated with the Timed Up and Go test), unassisted ambulation of at least other physical therapy endpoints that will be measured include; Manual muscle testing (MMT) of the quadriceps and the Tinetti scale for gait and balance. These measurements will be done in the morning of POD#1 and POD#2, and POD#3
4- Asses the QOR-15 at 24 hours, 48 hours, and 1 week

3 Study design

This is a prospective, randomized, blinded study with a parallel design and an allocation ratio of 1 to 1 for the treatment groups**.**

3.1 Inclusion Criteria

Patients scheduled for total knee arthroplasty with American Society Anesthesiologists (ASA) physical status I- III, mentally competent and able to give consent for enrollment in the study.

3.2 Exclusion criteria

Patient refusal, allergy to local anesthetics, systemic opioids (fentanyl, morphine, hydromorphone, and any of the drugs included in the multimodal perioperative pain protocol (MP3). Revision surgery will be excluded. Impaired kidney functions and patient with coagulopathy will be also excluded. Chronic pain

syndromes and patients with chronic opioid use in excess of a daily morphine equivalent dose (MED) of 40mg or greater for the past 3 months prior to the surgery. BMI of 45 or more

4 Recruitment

Patients will be identified from the surgical schedule the day before surgery and will be contacted by one of the study investigators and/or research coordinators to scan for eligibility for enrollment. Study aims and procedures will be explained to patients over the phone. Patients will be consented the morning of their surgery by one of the study investigator and/or the research coordinator.

50 patients undergoing unilateral total knee arthroplasty will be enrolled in each study group with a total of ***100*** patients. Patients will be randomized to one of two study groups. Additionally, we plan to enroll 20 pairs of bilateral and/or staged bilateral knee arthroplasty. The total number of patients enrolled will be 140 patients

5 Randomization

A computer generated randomization table will be used for patient allocation to one of the two study groups: ACB + iPACK or ACB w/o iPACK. Patients' assignments will be written in a sealed envelope that is only open after patient consent for the study. Staged and Bilateral knee arthroplasty: patients will follow a different randomization scheme in which the patient serves as his or her own control for the iPACK block. For example, patient's will be randomized to either receive the ACB + iPACK for knee #1 or for knee #2.

The nurses on the floor and the physical therapist will also be blinded and not aware of the nature of group assignment.

6 Study procedures

The choice of anesthetic technique will be at the discretion of the anesthesiologist. In our institution we usually advocate for spinal anesthesia for total knee arthroplasty with an adductor canal block and infusion catheter placed for postoperative analgesia. All Patients will receive their MP3 medication as per protocol in the patient receiving area (300 mg of gabapentin, 200 mg of Celecoxib, and 1gm of acetaminophen). Patients will be approached and consented for the study by one of the study investigators.

Once consented their group assignment will be revealed to the anesthesiologist on the acute pain service who will be performing the block.

6.1 Surgical Standard of Care

Unilateral knees: Patient's will either receive the iPACK block or not.

IPACK (interspace between the popliteal artery and the capsule of the knee)

Bilateral/staged knees: Patient's will also be randomized to receive iPACK block in addition to the ACB for one knee. Once the block has been performed, they will be excluded from future randomization (staged knees). If they are randomized to not receive the block for their first knee (staged knees) they will automatically receive the iPACK block for the second knee.

Patients will be monitored during block performance with standard ASA monitors. All patients will be receiving 2 L of oxygen via a nasal cannula. Sedatives will be titrated to effect. Midazolam 1-2 mg, and fentanyl 50-100 mcg will be used for sedation.

Block time out will be performed according to standard operating procedure.

All blocks will be done under ultrasound guidance. Sonosite S nerve machine will be used with either a high frequency linear (HFL) US probe with 6-13 MHZ frequency or high frequency curvilinear US probe with 2-5 MHZ. The iPACK block will be performed according to the standard operating procedures (SOP) in our department which includes a bed side procedure time out, sterile preparation and draping of the block site and strict adherence to sterile techniques.

Procedure: The patient will be placed in the supine position with their knee flexed and abducted. Ultrasound survey will be performed at the posterior aspect of the knee, slightly superior to the popliteal fossa proximal to the crease to identify the femoral condyle. Scan proximally to identify the medial femoral condyle of the femur and popliteal artery in a short axis view. The needle will be introduced in-plane and advance from medial to lateral until it is between the popliteal artery and the femur. A bolus of total volume of 20 ml of ropivicaine 0.5% will be injected through the needle.

The attending assigned to the regional anesthesia and acute pain service for that given day will perform the block. Qualifications of the anesthesia staff on the service include board certification in anesthesiology and subspecialty training in regional anesthesia and acute pain medicine. No need for additional training for performance of this block.

The endpoint for injection will be defined by visualizing the spread of the local in a fascial plane between the popliteal artery and the femur. Coupled with a change in cutaneous sensation to touch with an alcohol pad in the saphenous nerve distribution over the medial leg within 30 min after injection. Subjects with successful catheter placement per protocol and nerve block onset were retained in the study. Subjects with a failed catheter insertion or misplaced catheter indicated by a lack of sensory changes had their catheter replaced or were withdrawn from the study.

Postoperative analgesia will follow the standard MP3 protocol for total knee arthroplasty at our institution. Drugs that are used for the multimodal analgesia protocol include acetaminophen (1 gm every 8 hours for 72 hours), celecoxib (200 mg every 8 hours for 72 hours), Gabapentin (300 mg every 8 hours for one week if the patient is opioid naïve and for two weeks if patients are opioid tolerant), and oxycodone (5-10-15 mg oral as needed every 4 hours for pain based on patient reported pain score).

IPACK (interspace between the popliteal artery and the capsule of the knee)

All patients will receive prophylaxis for postoperative nausea and vomiting (PONV) during surgery. The protocol for prophylaxis against PONV include administration of 4 mg of dexamethasone after induction of anesthesia and 4 mg of ondansetron 20 minutes before recovery from anesthesia. Dexamethasone is withheld if the patient has poorly controlled diabetes mellitus. Uncontrolled DM will be defined as random blood glucose above 250 mg/dl.

6.2 Measurements

1- Pain scores will be collected from the nursing documentation every 6 hours for the first 48 hours or until discharge, whichever is closer.
2- Opioid consumption for the first 48 hours after surgery or until discharge, whichever is closer
3- R-APR-POQ and Quality of recovery-15 (QOR-15) questionnaires at 24, 48 hours and one week after surgery
4- MMT at 24 hours and 48 hours
5- TUG (time to up and go) at 24 hours and 48 hours. (TUG) is a simple test used to assess a person's mobility and requires both static and dynamic balance. It uses the time that a person takes to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down.
6- patients will be shown a chart with each pain score assessment to mark the site of the knee where they are feeling most of the pain, the chart is included

7. Study duration

We plan to begin enrollment once IRB approval is finalized (tentatively June 2018). The enrollment of all subjects is projected to be completed in June 2019 with data analysis to follow. The study is expected to be completed by June 2020. The length of participation for each subject will be about one week for screening, day of surgery and 48 hours during their regular hospital stay. Follow will be by telephone interview in the event that their length of stay is shorter than 48 hours.

8. Risks

There are known risk for Ropiviacaine used for both ACB and iPACK blocks and the most common are:

- Feeling very tired or weak
- Fast or slow heartbeat
- Nausea and sometimes vomiting

Less common side effects include:

- Burning or prickling sensation
- Fever
- Itching
- Seizures
- Specifically, for the I-PACK block, risks may include injection into adjacent blood vessels in the

neighboring area (popliteal artery and vein). That should be rare as these injections take place under ultrasound guidance. Additionally, frequent intermittent aspiration before injection take place to make sure we are not inside a blood vessel

- Specific risk to the IPACK block may also include unintended extension of local anesthetic to the common peroneal or to the posterior tibial nerve which may result in motor weakness and foot drop in case of extension of local anesthetic to the common peritoneal. In the event it happens, it should be temporary and should resolve as the effect of local anesthetic wear off. Neuro examination will follow the block procedure to determine if involvement of any other nerves occur

Allergic Reaction: Subjects will be screened prior to enrollment to determine if they have any allergies to any medications, especially local anesthetics.

Risks of Surgery: The most common risk of TKA blocks are neurovascular complications such as bleeding and increased pain.

Adverse Events and Serious Adverse Events will be recorded and reported according to standard research protocol. The PI and Sub-PIs will monitor the subjects throughout the trial.

9. Statistical Analysis

Statistical analyses will be performed using STATA 13 statistical software, Dallas, TX. Demographic data will be analyzed using student's T test or fisher's exact test as appropriate. Repeated measurements (pain scores, nausea scores) will be analyzed by repeated measures ANOVA or ANOVA on ranks, with further paired comparisons at each time interval performed using the t-test or Mann-Whitney U-test as appropriate. Categorical data will be analyzed using X2 analysis or Fisher's exact test where applicable. Normally distributed data will be presented as means ± SE of the mean (SEM), non normally distributed data are presented as medians ± quartiles (interquartile range) and categorical data will be presented as raw data and as frequencies. The α level for all analyses was set as $P<0.05$.

Sample size: Based on pilot data collected from 30 patients prior to the start of the study, 60% of patients complain of pain in the back of the knee 4-6 hours after surgery. For the I-PACK block to be clinically effective, we assumed that this percentage would be reduced to 30% . Also assuming a power of 0.8 and an alpha error of 0.05 and running a one sided test for comparison with an allocation of 1:1, we will need to enroll 33 patients per group. To account for drop out and loss to follow up, we ill inflate the sample size to 50 patients per group. We also plan to enroll additional 20 pairs of bilateral and/or staged knees so that each patient in the bilateral knee cohort can serve as her/his own control.

IPACK (interspace between the popliteal artery and the capsule of the knee)

References:

1- Sinha SK, Abrams JH, Arumugam S, et al. Femoral nerve block with selective tibial nerve block provides effective analgesia without foot drop after total knee arthroplasty: a prospective, randomized, observer-blinded study. *Anesth Analg*. 2012. July; 115 1: 202- 206. doi: 10.1213/ANE.0b013e3182536193.

2-Thobhani S, Scalercio L, Elliott CE, Nossaman BD, Thomas LC, Yuratich D, Bland K, Osteen K, Patterson ME. Novel Regional Techniques for Total Knee Arthroplasty Promote Reduced Hospital Length of Stay: An Analysis of 106 Patients. Ochsner J. 2017 Fall;17(3):233-238

3- Vlessides M. New regional technique controls post-TKA pain. *Anesthesiology News*. 2012. December; 38(12). https://issuu.com/mcmahongroup/docs/mman0012_2012_tab. Accessed July 12, 2017

4- Kim D, Lin Y, Beathe J, Goytizolo E, Oxendine J, YaDeau J, Maalouf D, Garnett C, Ranawat A, Su E, Mayman D, Westrich G, Alexiades M, Memtsoudis S. The Addition of ACB and IPACK to PAI Enhances Postoperative Pain Control in TKA: a Randomized Controlled Trial.*Hospital for Special Surgery, New York, NY. Found at : https://www.asra.com/content/documents/4886_the-addition-of-acb-and-ipack_1802040321.pdf. Last accessed 3/21/2018*