Comparison Between Ipack Block And Periarticular Infiltration In Total Knee Arthroplasty - A Randomised Controlled Trial
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Mount Sinai	Protocol Name:	COMPARISON BETWEEN IPACK BLOCK AND PERIARTICULAR INFILTRATION IN TOTAL KNEE ARTHROPLASTY - A RANDOMISED CONTROLLED TRIAL
	Principal Investigator:	YAN LAI MD,MPH.
	Primary Contact Name/Contact Info:	POONAM PAI B.H MD. [redacted]
	Date Revised:	7/22/2017
	Study Number:	IF# 2087568 , GCO#17-04304

HRP-503 PROTOCOL TEMPLATE

- *Note that, depending on the nature of your research, certain questions, directions, or entire sections below may not be applicable. Provide information if and when applicable, and in cases where an entire section is not applicable, indicate this by marking the section "N/A". Do not delete any sections.*
- ***For any items below that are already described in the sponsor's protocol, the investigator's protocol, the grant application, or other source documents, you may simply reference the title and page numbers of these documents in the sections below, rather than cutting and pasting into this document. Do not refer to the Sample Consent document, or information on the application form in this document..***
- *Keep an electronic copy of this version of the document. You will need to modify this copy when making changes.*

Brief Summary of Research (250-400 words):

Total knee arthroplasty (TKA) is an effective modality for the treatment of advanced osteoarthritis of the knee joint with excellent outcomes. With 719,000 cases being performed as of 2010, the incidence is expected to increase up to 3.48 million procedures annually by 2030. Multimodal analgesia is the cornerstone intervention in TKA that is utilized to minimize postoperative pain and improve functional outcomes in patients. Pain management in perioperative period enhances recovery and rehabilitation that improves length of stay and facilitates faster discharge with improvements in patient satisfaction scores. Numerous strategies devised as a part of multimodal analgesia after TKA are epidural anesthesia, femoral nerve block, adductor canal block, intra articular epidural catheter (Caledonian protocol), intra articular cocktail, intra venous patient control analgesia along with IV analgesics and combinations. The goal to minimize narcotics has been based on several studies demonstrating opioid related adverse events, increased length of stay as well as hospitalization costs.

Local infiltrative analgesia administered by the surgeon around the joint capsule has been an emerging adjunct to multimodal analgesia advocated by surgeons claiming improved rehabilitation by reducing venous stasis and maximizing motor strength. Periarticular analgesia (PAI) primarily targets the mechanoreceptors and the free nerve endings in the intra articular area.

IPACK block is a novel technique gaining popularity where one injects local anesthesia safely under ultrasound guidance in the interspace between the popliteal artery and capsule of the knee. It primarily targets genicular nerves innervating the knee joint. It does not affect the sciatic nerve hence motor blockade is avoided promising enhanced recovery.

There have been no studies till date comparing the efficacy between IPACK block and PAI.

The purpose of our study is to evaluate the difference in quality of analgesia between efficacy of IPACK block and PAI performed by surgeon as measured by patient's opioid consumption and pain scores.

1)Objectives

Research Question*:* Does IPACK block provide superior analgesia in comparison with surgeon performed periarticular infiltrate (PAI) in TKA patients?

Primary outcome: The amount of opioid consumption (in mg IV morphine equivalents) postoperatively during the first 24 hours after the procedure. VAS pain scores on arrival and departure from PACU.

Secondary outcome:

The degree of postoperative pain in terms of VAS scores from arrival to the floors to the first 24 hours after surgery.

Time to first dose of narcotic administration, PACU length of stay, location of pain, ambulation distance with assistance on POD 1 as assessed by PT and activities of daily living(ADL's) on POD 1 as assessed by OT.

2)Background

See above. There have been several studies regarding efficacy of peri-articular infiltration. IPACK block is a novel technique gaining popularity where one injects

local anesthesia safely under ultrasound guidance in the interspace between the popliteal artery and capsule of the knee.

There have been no studies till date comparing the efficacy between IPACK block and PAI.

3)Setting of the Human Research

Prospective triple blinded randomized control trial undergoing total knee arthroplasty surgeries. The research study will take place at Mount Sinai West hospital and Mount Sinai St. Luke's hospitals. The site PI is Yan Lai, MD, MPH.

4)Resources Available to Conduct the Human Research

For n=200, the feasibility of recruitment is manageable. Recruitment will be done through a coordination of the operating schedule and the surgeon's office. Patients presenting for preoperative visits at the preoperative joint clinic will be approached. Patients routinely are seen by anesthesiologists at the pre operative testing clinic as part of pre operative anesthetic evaluation. Patients will be approached by research personnel and details of the study will be explained. The consent will be obtained in the pre operative testing clinic after all questions are thoroughly answered. After confirmation on the operating schedule, patients will be provided detailed instructions the day before surgery. The staff members on this protocol are all employees of Mount Sinai and will either be a resident or attending physicians that are included on the IRB protocol. There are two primary members of the research personnel:

a)Yan Lai, MD, MPH – Roles for Dr. Lai in this study include serving as primary investigator responsible for study design and planning, data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. He is certified in PPHS/IRB protocols, all Citi/IRB required training in human subject protection, and has prior clinical research experience. He is also a board certified anesthesiologist and assistant professor of anesthesiology with the Icahn School of Medicine and the Mount Sinai Health System.

b) Poonam Pai. B.H MD – Roles for Dr. Pai include serving as primary research coordinator involved in data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. She has completed all of her required CITI training to be IRB certified and has experience in clinical research. In addition she has been a resident physician in anesthesiology with the Icahn School of Medicine in good standing for the previous three years going on her fourth.

There are institutional processes to ensure that all persons assisting with the protocol will be well informed. The research personnel will conduct regular meetings and department email updates to review the results and safety data of the study. The research personnel will initiate the formation of a safety monitoring board for adverse effects, complications, or complaints from patient subjects.

5) Study Design

Prospective triple blinded randomized control trial. Recruitment will be done through a coordination of the operating schedule and the surgeon's office. Patients presenting for preoperative visits at the preoperative joint clinic will be approached. Patients routinely are seen by anesthesiologists at the pre operative testing clinic as part of pre operative anesthetic evaluation. Patients who meet the inclusion criteria will be approached by research personnel and details of the study will be explained. The consent will be obtained in the pre operative testing clinic after all questions are thoroughly answered. The team will finalize participation and ask the subject to sign study consent forms. All patients will be provided with copies of the IRB protocol and consent if they wish to have it. Copy of the consent form will be sent in a secured email to the potential subject. The email will be secured by entering in [SECURE] in the e-mail subject line. Once recruited blinding assessments will be done by the study team.

Patients will be assigned randomly using a computer- generated table of numbers to either IPACK block (IPACK group) or Periarticular infiltration (PAI group). Block team will perform all blocks. Resident anesthesiologist will know the group allocation but will not be involved in the study. Patients assigned to IPACK block group will receive 20cc 0.25% bupivacaine under USG guidance on the side of

surgery. At the conclusion of the surgery prior to skin closure, all patients in the PAI group will receive 100cc of joint cocktail infiltrated by the surgeon. Patients in both groups will receive a post operative adductor canal catheter in the PACU, with Bupivacaine 0.1% 8-12 cc/hr with demand dose of 3-5 cc q20 min. Otherwise, the patient, surgeon, and anesthesiologist in the case will be blinded.

a) Recruitment methods: Patients will be recruited and consented in pre operative testing/Joint clinic.

b) Inclusion and Exclusion Criteria

Inclusion criteria: ASA (American Society of Anesthesiology) class I-IV, age 18-75.

Exclusion criteria: ASA class V, morbid obesity, patient refusal, patients with chronic pain or on pain medications, allergy to LA, patients receiving any additional regional techniques, coagulopathy, patients receiving systemic anticoagulation, local infection, and procedures anticipated to last more than 5 hours.

c)Number of Subjects

We intend to recruit 200 patients.

Based on a confidence level of 99% with a Z score of 2.58, standard deviation of .5 and a confidence interval of 10% our sample size should be 166. For ease of statistical calculations we rounded up to 200 patients. Based on previous literature pertaining to local articular infiltration in total knee arthroplasty and postoperative femoral nerve block, we found studies included anywhere from 40 to 100 patients. We intend to use a higher sample size to see any statistical significance.

$$ss = \frac{Z^2 * (p) * (1-p)}{c^2}$$

Where:

Z = Z value (2.58 for 99% confidence level)
p = percentage picking a choice, expressed as decimal (.5 used for sample size needed)
c = confidence interval, expressed as decimal (e.g., .01= ±1)

Sample size= [(2.58^2)(.5)(.5)]/(.1^2)=166 subjects
For effect size, we expect a Cos d medium effect of 0.5. The estimate for sample sizes was obtained by using the first set of pain scores obtained in the PACU. A previous study of 45 patients undergoing knee arthroplasty treated with a femoral nerve block reported a mean visual analog scale score of 3.6 (SD 1.1) upon movement, at 24 h (Singelyn et al. 1998). In an earlier study on total knee arthroplasties (Axelsson et al. 2005), the mean morphine consumption over 48 hours postoperatively was 64.6 (SD 36.3) mg in the placebo group.

The aim of this study was to investigate whether the IPACK technique could reduce the morphine consumption. The Mann-Whitney U test will be used for the analysis of the primary endpoint (morphine consumption). Mann-Whitney U test will be used to assess pain scores and the Bonferroni-Holm method was used to correct for multiple measures. Hospital stay, time to fulfill discharge criteria, knee function scores, and patient satisfaction scores will be analyzed using the Mann-Whitney U test. Dichotomous data will be analyzed using the chi-squared test or Fisher's exact test, as appropriate. Values of $p < 0.05$ were considered to be statistically significant.

d)Study Timelines

2017-2018 and subsequent data analysis. The subject's participation will be from time of enrollment in the pre-operative period until first 24 hours after surgery. Estimated date of enrollment completion will be when 200 eligible subjects are enrolled in final data analysis. Estimate date for study completion will be June 2018.

e)Endpoints

The primary endpoints will be the amount of opioid consumption (in mg IV morphine equivalents) postoperatively up to 24 hours after the surgery.

f)Procedures Involved in the Human Research

Prospective randomized controlled trial and data analysis only. IPACK block and PAI. Intraoperative care of the patient will be provided by an anesthesia team member who is a part of the Mount Sinai System. The anesthesia provider will not be aware of the randomization of the patient. Standard post-operative orders will be written for patients during their time in the PACU.

g)Specimen Banking

N/A

h)Data Management and Confidentiality

Data collected in excel file to be de-identified after initial collection. Excel file be subsequently encrypted and shared only between the above listed investigators via secure Mt. Sinai (chpnet) electronic mail. The information included in the data will be medical record number, age, gender, ASA class, type of surgery, pain score assessments, and time to first narcotic, total narcotic use and satisfaction/pain scores during the first 24 hours after surgery. Pain scores on arrival and discharge from PACU, PACU length of stay, location of pain, and ambulation distance with assistance on POD 1 as assessed by PT and activities of daily living (ADL's) on POD 1 as assessed by OT will be other data collected.

Only the research personnel will have access to the data. The data will be stored as a hard copy files and on a secure spreadsheet. The research personnel is responsible for the receipt of the data. The PI will keep the hard copies secure and any electronic data will be encrypted. No personal identifiers will be used. The data will undergo statistical analysis

i)Provisions to Monitor the Data to Ensure the Safety of Subjects

Part I: Elements of Data and Safety Monitoring Plan

MSSM Principal Monitor:

Last Name: Lai
First Name: Yan
Academic Title: Attending Physician, Assistant Professor
Department: Anesthesiology
Mailing Address: Mount Sinai West 1000 10th Avenue, New York, NY 10019
Phone: 212-523-6915
Fax:
E-mail: ylai@chpnet.org

MSSM Additional Monitor:

Last Name: Pai B.H
First Name: Poonam
Academic Title: Research Personnel, Physician
Department: Anesthesiology
Mailing Address: Mount Sinai West 1000 10th Avenue, New York, NY 10019
Phone: 212-523-6915
Fax:
E-mail: phebbalasankatte@chpnet.org

The principal monitor is a board certified anesthesiologist thus minimizing the risk to the subjects and further optimizing their health and wellbeing. Adverse events will be monitored as a standard of care everyone receives regardless of participation in the study. The safety and data information will be reviewed on a daily basis until the desired sample size is achieved. All temporary and/or permanent suspensions will be reported.

Poonam Pai B.H MD – Roles for Dr. Pai include serving as primary research coordinator involved in data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. She has completed all of her required CITI training to be IRB certified and has experience in clinical research. In addition she has been a resident physician in anesthesiology with the Icahn School of Medicine in good standing for the previous three years going on her fourth.

j)Withdrawal of Subjects

Patients may withdraw from the study at any given time by contacting any member of the research study group. Data will not be collected on patients who wish to withdraw. Patient do not need to withdraw consent in writing.

6)Risks to Subjects

If patients are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to the patient or their insurance in the ordinary manner and the patient will be responsible for all treatment costs not covered insurance, including deductibles, co-payments and coinsurance. This does not prevent the patient from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

As with any medication, there is a possibility of an allergic reaction. Although rare, possible complications include LA toxicity, hypersensitivity reaction, bleeding or local site infection, chance of pneumothorax. All anesthesiologists involved in patient care will be prepared for the prevention and rescue for any complications involving local anesthetic injections.

7)Provisions for Research Related Harm/Injury

If patients are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to the patient or their insurance in the ordinary manner and the patient will be responsible for all treatment costs not covered insurance, including deductibles, co-payments and coinsurance. This does not prevent the patient from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

8)Potential Benefits to Subjects

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be improved knowledge about how the different forms of analgesia affect pain control in knee surgery. There is potential for better pain control after the surgery.

9)Provisions to Protect the Privacy Interests of Subjects

Patients will be appropriately educated about the research study. Any questions or concerns they have will be adequately addressed and patients will have the option to decline participation. Patients will be given as much time as they need to review the consent form. The study personnel will be approaching the subjects. Privacy will be maintained by not including any identifiers such as names or addresses in the data collected.

The identities of human subjects whose data is being studied will be de-identified as per HIPAA Privacy Rule.

10)Economic Impact on Subjects

Patients will not incur any additional cost for participating in the study. The medications used are part of a standard anesthetic regimen that will be billed to subject's insurance as bundled standard of anesthesia care. The cost of the procedure is overall unaffected.

11)Payments to Subjects

Patients will not be reimbursed for their participation.

12)Consent Process

Informed consent will be obtained prior to the procedure. Both the HRP-090 (SOP) Informed Consent Process for Research and the HRP-091 (SOP) Written Documentation of Consent will be followed by the study team. These documents are both available at http://icahn.mssm.edu/research/resources/program-for-the-protection-of-human-subjects/irb-members-palette.

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13.Process to Document Consent in Writing

The patients will receive a paper copy of the IRB approved consent packet and will sign in the designated areas to confirm consent of participation. They will have the option of have a copy of the consent and may ask for a personal copy of the consent.

14.Vulnerable Populations

Indicate specifically whether you will include (target) or exclude each of the following populations:

Include	*Exclude*	*Vulnerable Population Type*
	X	*Adults unable to consent*
	X	*Individuals who are not yet adults (e.g. infants, children, teenagers)*
	X	*Wards of the State (e.g. foster children)*
	X	*Pregnant women*
	X	*Prisoners*

15.Multi-Site Human Research (Coordinating Center)

This study will be performed within the Mount Sinai West and St. Luke's Hospitals. No additional centers will be involved.

16.Community-Based Participatory Research

This does not apply to our study.

17.Sharing of Results with Subjects

Results will not be shared with the patients since the study will take time to complete. Patients can request results if they contact the PI by writing.

18.External IRB Review History

This does not apply to our study.

19.Control of Drugs, Biologics, or Device

Not applicable. Local anesthetic are routinely used in this setting.