Pre vs. postoperative adductor canal block for total knee arthroplasty: prospective randomized trial

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PI: Victor Hugo Hernandez MD

NCT#: 05974501

1) Protocol Title

Pre vs. postoperative adductor canal block for total knee arthroplasty: prospective randomized trial

2) Objectives*

The purpose of this project is to determine if a change in patient reported pain, nausea and vomiting after total knee arthroplasty can be observed with the substitution of post operative adductor canal block for a preoperative adductor canal block in the current established peri-operative pain protocol and if these changes lead to a decrease in opioid consumption (in morphine equivalents).

3) Background*

Levels of postoperative surgical pain are often high, particularly in orthopedic procedures such as total joint replacement [1, 2]. Increases in postoperative pain not only present discomfort to the patient, but can increase length of postoperative hospitalization and affect overall quality of life [3]. Furthermore, increases in postoperative pain have previously been associated with increased use of opioid pain medications which can later lead to addiction [4].

Due to these implications, there has been interest in exploring more effective options in pain management after total joint replacement including various types of multimodal pain management strategies. Currently, guidelines widely suggest that opioid usage should be minimized with a larger focus on options such as multimodal pain management, though the optimal multimodal protocol has yet to be established. [5-6]

Adductor canal blocks have been demonstrated to be effective in reducing post-operative pain, reducing the amount of opioid medication required, thus reducing the adverse effects related to opioids, as well as improving the recovery time required [7-9].

Whether the adductor canal block must be performed preoperatively versus immediately postoperatively, however, has yet to be investigated. While preoperative blocks are effective in reducing the postoperative pain, by performing the adductor canal block immediately postoperatively, the analgesic benefits to the patient will potentially last longer into their postoperative recovery as the administration will be held until the end of the procedure.

4) Inclusion and Exclusion Criteria*

<u>Inclusion criteria-</u>
1- Patients over the age of 18,
2- Patients undergoing primary total knee replacement at the University of Miami Hospital,

3- Patients that have capacity to provide medical consent

Exclusion criteria-
1- All patients under the age of 18
2-Prisoners, diabetics, increased risk of bleeding, pregnant women, women planning on becoming pregnant in the next year, and women who think they might be pregnant.
3- Patients with prior surgery or history of infection on the joint of interest.
4- Patients on steroid preoperatively.
5-Inability to provide medical consent.
6- Patients with a history of significant unmitigated pain in parts of their body not including the knee the procedure is to be performed or a history of pain catastrophizing (the tendency to magnify the threat value of the pain stimulus and to feel helpless in the context of pain, and by a relative inability to inhibit pain-related thoughts in anticipation of, during or following a painful event) regarding pain anywhere in the body.
7-Any condition that, in the opinion of the investigator, would compromise the well-being of the patient or the study or prevent the patient from meeting or performing study requirements will exclude the participant.
8-Allergy to local anesthetic or any medication used in the standard protocol for joint replacement.

5) **Procedures Involved***

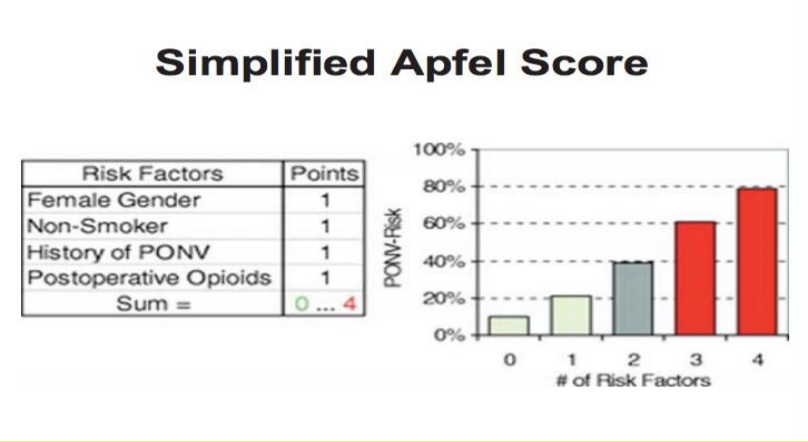
Study design: All patients who fulfill inclusion criteria, including undergoing a pregnancy test if a woman of childbearing age, undergoing total knee arthroplasty will be randomized to one of two groups to be given the standard orthopaedic joint replacement protocol including general anesthesia with the preoperative adductor canal block **or** the standard orthopaedic joint replacement protocol including general anesthesia except the adductor canal block will be given at the end of the procedure instead of the beginning. General anesthesia for the groups will be standardized, and no intraoperative analgesics given. Nerve blocks will be placed for both groups by anesthesiologists as is the standard protocol. All nerve blocks will be placed following the same procedural protocol with the same supplies under ultrasound guidance to ensure consistency and minimize variation. Nerve blocks in both groups will include the standard 20mL Ropivacaine 0.2% (local anesthetic) injected in the same manner. PACU orders will not differ between the groups and will be the standard procedure for total joint arthroplasty at the facility. Cases will be assigned randomly in a 1:1 fashion. A computer program such as Microsoft Excel will be employed for the randomization process.

Standard orthopaedic joint replacement protocol at our institution includes all of the following:

1. ***Dexamethasone 10mg IV once postoperatively within 24 hours for pain and swelling***
2. ***Tylenol 1,000mg every 8 hours for pain during the first 1-2 weeks postop***
3. ***Lyrica 75mg nightly for pain during the first 1-2 weeks postop***
4. ***Celebrex 200mg twice a day for pain and swelling during the first 1-2 weeks postop***
5. ***Meloxicam 30mg IV once postoperatively within 24 hours for pain and swelling***

6-Oxycodone 5mg every 4 hours as needed for pain during the first 1-2 weeks postop

After surgery, patients will be evaluated for the primary outcome of pain status at time points 2 hours and 24 hours using the numeric rating pain scale (0-10). Patient's nausea and vomiting will be evaluated by using a binary "yes" or "no" for nausea and recording the number of episodes of vomiting. The Apfel score will be used during statistical analysis to explore possible causes for differences in nausea and vomiting (0-4). Opioid consumption will also be recorded during the first 24 hours and converted to morphine milliequivalents using patient medical records. Patient data will then be compiled for statistical analysis.
Patients will be assessed routinely once every hour by the circulating nurse for the duration of their care in the hospital. Should a patient receive ambulatory care and depart from the hospital before 24 hours have elapsed, they will be contacted via telephone for assessment using the numeric rating pain scale (1-10) and post-op nausea and vomiting.



6) Study Timelines*

- *Participants will be active in the study for the 24 hours after the index knee replacement surgery.*
- *It will take about 6 months from the start of the study to recruit the total anticipated participants.*
- *We will allot 1 month after the final participant has completed the study for analysis and write up.*

7) Study Design

- The primary purpose of this project is in the treatment of pain around the immediate post-operative time after total knee replacement surgery. As a parallel experimental/ interventional study design, patients will be randomized to either the control group (institution specific joint replacement pain protocol) or the intervention group (receiving the postoperative adductor canal block). Patients and those collecting the postoperative data will be blinded to eliminate bias in a 1:1 randomization process matching intervention group patients with control group patients. The surgeon will not be informed

ahead of time regarding which cohort a patient belongs to in an effort to reduce bias, though during the procedure may become privy to the group due to when the anesthesiologist places the block. The anesthesiologist will be informed the night before the respective procedure as to which group the patient was randomized into by one of the other non-primary surgeon members of the team. The randomization will be done using a random number generator. We aim to enroll 84 patients. If interested, the subject will be allowed to find out their group assignment when the study is over.

- Power Analysis:

Study Group Design: Two independent study groups
Primary Endpoint: Continuous
Data normally distributed
Alpha: 0.05
Power: 0.80

Total number of patients enrolled: 84

Based on similar study design [10], the standard deviation for pain scores was 3. Assuming a reasonable clinically significant difference of 2 on VAS score, this calculates to sample size of 35 in each group. Assuming attrition rate of 20%, 42 samples in each group will be obtained

8) **Study Endpoints***

- *Primary endpoint – change in pain score at time points 2 hours and 24 hours after primary total knee arthroplasty for each group. The numeric pain rating scale will be used- a higher pain score would indicate higher pain levels. It is scaled from 0-10.*
- *Secondary endpoint - (1) Total opioid consumption in the immediate post-operative period (preoperative block versus postoperative block) (2) change in patient nausea scores and vomiting scores at time points 2 hours, and 24 hours (3) duration of hospital stay.*

9) **Data Management***

We will perform a superiority test and examine the mean pain score differences at time points 2 hours and 24 hours after surgery as our primary outcome. A t test or Mann Whitney U will be performed to compare the means depending on the distribution of the data with confidence intervals. Secondary outcomes include postop nausea and vomiting scores and morphine equivalents received. We will compare these scores between groups similarly using t test or Mann Whitney U with confidence intervals.

INTERIM ANALYSIS:
We plan to analyze this trial for futility by employing the O'Brien and Fleming method of interim analysis. Specifically, we will analyze our groups at interims n = 21 (total 42) for futility using

appropriate boundaries for the mean difference. Should the mean difference exceed the boundary, the trial will conclude concluding significance between the groups; conversely, should the mean difference be below the boundary, the trial will terminate with futility.

10) **Risks/Benefits**

This study is a prospective cohort study that will collect private, identifiable information about human subjects. The main risk is to subjects' confidentiality should an individual outside of the study team access the study data.

There may be no direct benefit to subjects.
The group receiving the postoperative nerve block may have better pain control and less opioid use.
This research might lead to the benefit of others should the analysis of the data lead to better selection of surgical candidates and possible interventions to reduce adverse outcomes.

11) **Adverse Events / Serious Adverse Events**

Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research will be recorded for the first 24 hours post-operatively.

12) **Setting**

Single center study - University of Miami Hospital

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