

AKRON CHILDREN'S HOSPITAL

**Ultrasound Guided Single Shot Adductor Canal Block (ACB)
Versus Single Shot Femoral Nerve Block (FNB) for Postoperative
Analgesia after Arthroscopic Anterior Cruciate Ligament (ACL)
Reconstruction in Pediatrics**

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+Ultrasound Guided Single Shot Adductor Canal Block (ACB) Versus Single Shot Femoral Nerve Block (FNB) for Postoperative Analgesia after Arthroscopic Anterior Cruciate Ligament (ACL) Reconstruction in Pediatrics

ABBREVIATIONS

ACL *Anterior Cruciate ligament*

ACB *Adductor Canal Block*

ACH *Akron Children's Hospital*

AE *Adverse Event*

ASA *American Society of Anesthesiologist*

FNB *Femoral Nerve Block*

GE *General Electric*

HIPPA *Health Insurance Portability and Accountability Act*

IRB *Institutional Review Board*

Kgf *Kilogram-force*

NS *Numeric Scale*

PACU *Post Anesthesia Care Unit*

PHI *Protected Health Information*

PI *Principal Investigator*

POD *Post-operative Day*

PONV *Post- Operative Nausea and Vomiting*

PNB *Peripheral Nerve Block*

SAE *Serious Adverse Event*

SRF *Study Report Form*

1.0 INTRODUCTION

Motor preservation with adequate analgesia has become the optimal postoperative goal in orthopedic surgeries, and in particular, knee surgeries. This enables earlier physical therapy, faster recovery and shorter hospital stays. Both ultrasound guided ACB and FNB have been used to provide postoperative analgesia for knee surgeries including anterior knee reconstruction (1,2,12). To our knowledge, no comparison has been made between these blocks in relation to postoperative quadriceps muscle strength, or duration and quality of postoperative analgesia for arthroscopic ACL reconstruction in pediatrics. ACB predominantly blocks the sensory component of the femoral nerve without much effect on the motor component. Hence, it may lead to less quadriceps muscle weakness, early postoperative mobilization and a decrease in the incidence of postoperative fall (3, 4). With the advent of ultrasonography, the adductor canal can be easily visualized at the mid-thigh level, allowing performance of adductor canal block (ACB) with a high success rate (5). In recent years, ACB has been successfully used for postoperative pain control after knee surgery (5-7). Anatomical study demonstrated that the adductor canal may serve as a conduit for more than just the saphenous nerve, possibly including the vastus medialis nerve, medial femoral cutaneous nerve, articular branches from the obturator nerve, as well as the medial retinacular nerve (8, 9). Thus, the sensory change is not limited to the distribution of the saphenous nerve (8) but includes the medial and anterior aspects of the knee from the superior pole of the patella to the proximal tibia. In addition, recent evidence demonstrating of persistent strength deficits in patients receiving FNB further underscores the need for

effective alternatives(10)This prospective, double-blinded, randomized, controlled study will test the hypothesis that ACB would be associated with less quadriceps motor weakness than FNB at 4 hour post block. We also hypothesize that ACB will provide analgesia to the anterior knee that is not inferior to FNB and not different in opioid requirement at 4 and 24 hours after Peripheral Nerve Block (PNB) .

2.0 STUDY OBJECTIVES

2.1 Hypothesis

ACB would be associated with less quadriceps motor weakness than FNB and provide analgesia that is not inferior to FNB in quality or duration as determined by Numeric Scale (NS) pain scores and opioid use at 4 and 24 hours post PNB.

2.2 Objectives

To compare FNB and ACB regarding:

- 1-Quadriceps muscle strength on both sides (surgical and non –surgical) in the immediate pre-operative period) and at 4 hours after PNB.

2-Pain scores at anterior knee at 4 hours and 24 hours after PNB as assessed by Numeric Scale (NS) pain scoring system. Also pain site other than the anterior knee will be recorded and specified (posterior knee, calf, leg)

3- Total opioid consumption at 4 and 24 hours after PNB.

3.0 STUDY DESIGN

3.1 Randomized, double blinded, single center clinical trial. A total of 52 pediatric patients (ASA 1 or 2), aged between 8 to 18 years, for elective ACL reconstruction at Akron Children's Hospital (ACH) will be enrolled in the study. Patients will be randomly assigned to one of two groups, A (26 patients) or B (26 patients). Group A patients will have ultrasound guided ACB and group B will have ultrasound guided FNB after induction of anesthesia. Quadriceps strength of both legs will be assessed by placing the dynamometer on the anterior of the ankle, between the malleoli. Patients will be instructed to extend their legs three times each, with a 30 seconds pause between each attempt as described by Maffiuletti (11). The assessment will be performed in the pre-operative period and will be repeated postoperatively at 4 hours after PNB. Intraoperative, all patients will receive fentanyl 1-2 mcg/kg and/or morphine 0.05 mg/kg. All patients will receive adjuvant analgesic medications in the form of IV Tylenol 10-12.5 mg/kg (maximum 1 gm) after the induction of anesthesia. Also, with start of skin closure, patients will receive IV Ketorolac 0.2-0.3 mg/kg, maximum of 15 mg, unless contraindicated. After emergence from anesthesia, all patients will be observed in the post-operative period by an observer unaware of the technique of analgesia used. Pain will be assessed using the NS. Postoperatively, PCA morphine pumps will be attached to patients. A loading dose of 0.05 mg/kg to a maximum of 5 mg will be administered in the Post Anesthesia Care unit (PACU) as needed, followed by demand interval dosing of 0.015 mg/kg every 10 minutes as demanded by the patient. Four-hours limits for morphine will be set at 0.35 mg/kg. No continuous infusion and no adjuvant NSAIDs or acetaminophen will be administered in PACU. Rescue morphine dosing will be ordered via PCA pump at 0.05 mg/kg (repeated once as needed) and will be available every two hours as needed by pain assessment (for a NS ≥ 4) or patient request. Diazepam 0.03 mg/kg IV will be available every 4 to 6 hours as needed for muscle spasm or anxiety. Patients will be considered ready for discharge from hospital when all the following criteria are met: Child is alert, oriented, stable vital signs, and can tolerate clear liquids, with no nausea or vomiting, and good pain control (no to mild pain). The evaluation for meeting the discharge criteria will be done after one hour from arrival in PACU and every 30 minutes thereafter until the patient meets all the discharge criteria. After discharge, parents will be instructed to give the patient oxycodone 0.1 mg/kg PO q 4 hours as needed for pain. Acetaminophen 10 mg/kg q 4 hours and/or ibuprofen 10 mg/kg q 4 hours may be

administered as needed for residual pain, not exceed 2400 mg in 24 hours. The total dose of oxycodone, ibuprofen and acetaminophen will be recorded per parents for a total of 24 hours after PNB. Pain scores and pain site will be also recorded by parent at 24 hours post -block. The data for total opioids used in the first 24 hours after PNB and pain score at 24 hours will be collected from parents by phone call.

3.2 Study Endpoints

1-Quadriceps muscle strength on both sides (surgical and non-surgical) pre-operatively and at 4 after PNB

2- Total morphine/morphine equivalent at 4 and 24 hours after PNB.

3-Pain scores at anterior knee via NS at 4 and 24 hours after PNB.

3.3 Primary Safety Endpoints

Adverse events related to both procedures (ACB and FNB) will be recorded (Please refer to section 8). Known possible adverse events and complications are those associated with peripheral nerve blocks in general and includes potential for bleeding (hematoma) , infection, nerve injury , allergy to the local anesthetics (ropivacaine) or adjuvant medication (methylprednisolone) used to achieve the block.

4.0 SUBJECT SELECTION AND WITHDRAWAL

4.1 Inclusion criteria:

1-ASA I or II

2- Age 8 to 18 years

3-All research subjects must have an acceptable legally authorized representative capable of giving consent on the subject's behalf if under 18 years old.

4.2 Exclusion criteria:

Those who were unable to use a standard 0-10 NS., those with infection at the site of the block; those with bleeding disorders; those with allergy to the drugs used to perform the block (ropivacaine , methylprednisolone); and those who refused a nerve block or enrollment in the study.

4.3 Subject recruitment:

The surgical schedule will be reviewed for potential research subjects. Potential subjects will be seen in the orthopedic office prior to the scheduled surgery. If they are found to be eligible to participate in the study, the authorized legal representative(s) will be given the choice to participate in the study. The study will be explained to the authorized legal representative(s). An informed consent will be provided for review by the authorized legal representative (s). They will be given a phone number to contact in case they have any questions regarding the study. If they agree to participate in the study, the authorized legal representative (s) will be requested to sign and date the informed consent prior to the scheduled surgery. Patient ascent to the study may be also requested if needed.

4.4 Patient withdrawal:

Patient and/or authorized legal representative may withdraw from the trial at any time and for any reason. Some possible reasons for withdrawal include:

- 1- Patient and/or authorized legal representative withdraws consent to continued participation in the trial
- 2- Patient develops a complication related to anesthesia and/or surgery

4.5 Data Collection and Follow Up for Withdrawn Subjects:

All subjects that withdraw from the study after randomization and/or performance of the block will be asked if they will allow for the collection of data. This will keep the subjects in their already assigned group thereby allowing for the collection and analysis of data with the **intention to treat principle**. However, if the subject does not want to allow collection of data, all follow-up must stop. At that time the subject will be considered as drop out.

5.0 STUDY TREATMENT

5.1 Description:

The patient will be randomly assigned to one of two groups, A or B. Group A patients will have ultrasound guided ACB performed at mid-thigh level and group B will have ultrasound guided FNB, with nerve stimulator confirmation with the type of motor response (e.g., quadriceps, patellar) and the minimum current needed to be recorded. Both blocks will be performed under general anesthesia. Both group will have ropivacaine 0.2 % (0.5 ml/kg, maximum of 30 ml and methylprednisolone acetate 1 mg/kg , maximum of 40 mg).Both blocks will be performed using a 22-gauge 2-inch Stimuplex A needle; ; B. Braun Medical Inc., Melsungen, Germany).Both blocks will be

performed using linear ultrasound transducer, General Electric (GE). Ultrasound pictures will be obtained to Verify proper local anesthetic placement. Unfortunately, surgeons are not able to determine the type of procedure needed to correct ACL injury, until after knee arthroscopy is performed under general anesthesia ACL reconstruction using a hamstring graft, which is the surgical procedure used in this study may not always be possible to perform by the surgeon. The surgical alternative of ACL reconstruction is ACL repair, which seldom is done by our surgeon. Patient undergoing ACL reconstruction can experience pain in the posterior aspect of the knee, in the distribution of the sciatic nerve. This is due to the hamstring graft. In contrast to the anterior knee pain covered by both ACB and FNB, posterior knee pain is controlled with IV/oral analgesic. This is why recording the site of the knee pain is important to determine the PNB success. Due to the inability to determine beforehand, the type of procedure to be performed, we decided therefore to continue the study procedures and data collection on both ACL reconstruction and ACL repair. The statistical analysis will include only patients that undergo ACL reconstruction. For the other patients that undergo ACL repair, data will be collected but not included in the statistical analysis. The data from these patients may be used as a pilot for future research.

5.2 Method for Assigning Subjects to Treatment Regimen

Random allocation for one of the two treatments will be achieved using sealed envelope assigned by an external third party not involved in the study to ensure allocation concealment.

5.3 Blinding of Study Procedure:

Both the observer and the patient (and the legally authorized representative) will be blinded to the type of block performed.

6.0 STUDY PROCEDURES

Following emergence from anesthesia, all the patients will be observed in the post-operative period by an observer unaware of the technique of analgesia used. Children will be evaluated in the PACU every 10 minutes. Pain will be assessed using the NS. PCA morphine pumps will be attached to patients' IV. A loading dose of 0.05 mg/kg to a maximum of 5 mg will be administered in the PACU as needed, followed by demand interval dosing of 0.015 mg/kg

every 10 minutes, as demanded by the patient. Four-hour limits for morphine will be set at 0.35 mg/kg. No continuous infusion and no adjuvant NSAIDs or acetaminophen will be administered. Rescue morphine dosing will be ordered via PCA pump at 0.05 mg/kg (repeated once as needed) and will be available every two hours as needed by pain assessment (for a NS ≥ 4) or patient request. Diazepam 0.03 mg/kg IV will be available every 4 to 6 hours as needed for muscle spasm or anxiety. Patients will be considered ready for discharge from hospital when all the following criteria are met (but actual discharge will not be allowed before 4 hours after PNB for the purpose of the study):

Child is alert, oriented, stable vital signs and would tolerate clear liquid, with no nausea or vomiting and with good pain control.

After discharge, parents will be instructed to give the child oxycodone tablets/elixir 0.1 mg/kg PO q 3 hours as needed for pain. In addition, acetaminophen 10mg/kg q 4 hours PRN and/or ibuprofen 10 mg/kg q 6 hours PRN may be administered for any residual pain.

Quadriceps muscle strength will be recorded at 4 hours after PNB in the PACU.

Pain scores using the NS and total opioids consumption will be recorded at 4 and 24 hours post-block. The assessment at 4 hours will be done in the PACU and the assessment at 24 hours will be done via phone call.

7.0 ANALYTICAL PLAN

7.1 Summary Statistics will be provided for all variables. Examination of continuous data will include normality testing as well as assessment of potential outliers. Statistical testing will be based upon distributional shape, but for purpose of analytical planning and sample size analysis normality of distributions will be assumed.

To examine for potential differences in quadriceps motor strength (QMS) between the two groups (ACB, FNB), two change scores will be created and analyzed via T-Test for Equal and Unequal Variances with appropriate Bonferroni adjusted alpha testing paired difference at two distinctive time points. Assuming no statistically significant baseline differences between the two groups the QMS Change scores will be a) Baseline to 4 hours. Sample size analysis will be based upon testing of the QMS Change scores. Non-inferiority of ACB to FNB in analgesia provided will be assessed by examination of pain scores. Non-inferiority of ACB compared with FNB is defined as the mean ACB - NRS pain score not higher than the mean FNB - NRS pain score by an amount of 1.6. (Kim, 2014) Pain scores and pain site will be individually examined at the 4 hour and 24 hour post-operative time points with appropriate Bonferroni adjusted alpha. In addition, a change in pain score from 4 to 24 hours will be created and evaluated for potential difference between groups.

Total opioid consumption as measured in morphine equivalents will be assessed at the 24 hour post-operative time point to determine whether a difference exists. Opioid consumption will also be examined by creating a change score from 4 to 24 hour consumption and comparing between the groups.

Examination of subjects who undergo reconstruction will include descriptive statistics.

Any other testing done will be exploratory in nature based upon examination of data and results of testing described above.

All testing will be completed utilizing SAS 9.4 © software and evaluated at the Type I Error Rate of $\alpha = 0.05$ level for statistical significance unless otherwise noted.

7.2 POWER AND SAMPLE SIZE ANALYSIS

Sample size analysis is based upon utilization of the T-Test to analyze for potential differences in QMS Change Scores between the two groups. Calculated effect size = 1.1 based upon reported quadriceps strength mean (SD) as 7.3 (5.4) for ACB and 2.2 (3.8) for FNB utilizing information from study by Kim et al. (13). To account for analysis of paired differences at two time points the α = Type I Error Rate of 0.05 is adjusted using Bonferroni's method to 0.025. Power set at 80%.

Population differences from cited study limit the ability to calculate sample size requirements accurately. Considerations must also be taken into account for potential departures from normality, non-evaluable subjects / drop outs and potential effect size smaller than calculated. Therefore the **minimum recommended sample size** for this study is 50 subjects (25 in each arm). Refer to tables below for more information regarding power and sample size.

Minimum sample size required for given effect sizes

Effect Size	n_1	n_2	N
0.7	40	40	80
0.9	25	25	50
1.1	18	18	36

Power approximations for varying effect sizes and sample sizes

Effect Size	Alpha	N	Approximate Power
1.1	0.025	36	80%
1.1	0.025	30	74%
1.1	0.025	24	62%
0.9	0.025	50	80%
0.9	0.025	40	69%
0.9	0.025	30	54%
0.7	0.025	80	80%

0.7	0.025	70	74%
0.7	0.025	60	66%

Sample size analysis was completed utilizing the “pwr” package in R 3.1.2 ©.

7.3 Randomization Table

A randomization table for up to 60 patients will be provided to the person responsible for blinding the study. Randomization table completed using utilizing SAS 9.4 © software.

8 SAFETY AND ADVERSE EVENTS

8.1 Definitions

Adverse events related to both procedures (ACB and FNB) will be recorded. Known possible adverse events and complications are those associated with peripheral nerve blocks in general, and includes potential for bleeding (hematoma) , infection, nerve injury , allergy to the local anesthetics or adjuvant medications used to achieve the block.

Also, any unexpected side effects suspected to be related to the study will be reported.

8.2 Recording of Adverse Events

The investigator will seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events will be recorded immediately in the source document, and also in the appropriate adverse event section of the Study Report Form (SRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results will also be recorded in the source document.

The clinical course of each event will be followed until resolution, stabilization, or until it has been determined that the study treatment is not the cause. Serious adverse events that are still ongoing at the end of the study period will be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study treatment or study participation will be recorded and reported immediately.

8.3 Reporting of Serious Adverse Events

IRB Notification by Investigator(s)

The following four types of events will be reported to IRB:

1. Adverse events which are serious, unexpected, and related or possibly related to participation in the research.
2. Other unexpected adverse events, regardless of severity, that may alter IRB analysis of the risk versus potential benefit of the research and, as a result, warrant

consideration of substantive changes in the research protocol or informed consent process/document.

3. Unanticipated Problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB.”

9 DATA HANDLING AND RECORD KEEPING

9.1 Confidentiality and Privacy

- Protected health information (PHI) that will be collected from subjects in this study will be **name, birth date** and **medical record number**.
- Only the PI and the Co-investigator(s) on the study will have an access to this information. This information will be kept in a locked box in the anesthesia control office.
- None of these PHI will be published or disclosed to any other parties other than the investigators participating in the study.
- All Informed consents /assents will be also kept in a locked box in the anesthesia office and will be kept for reviews for at least 2 years after the publication of the study.
- Legal authorized representative of the patient will also be requested to sign **“Authorization for Release of Information for research”** to address Health Insurance Portability and Accountability Act (HIPPA) requirements.

9.2 Source Documents:

Source documents will include PACU nurse assessment flow sheets, pain score flow sheets and medications flow sheets. Dynamometer measurements for each patient will be also collected pre-operatively; and at 4 hours postop-

10 STUDY MONITORING, AUDITING AND INSPECTING

10.1 Study Monitoring Plan

This study will be monitored through a **data monitoring committee**.

This is a relatively short study that will be performed over a period of 9-12 months. This study offers minimal risk to the patient. The data monitoring committee will include the PI, at least one of the co-investigators, the principal statistician, and the principal research nurse.

The data monitoring committee will meet when approximately 25%, 50%, 75% and 100% of the primary outcomes are observed. The priority of the data monitoring

committee will be to ensure the safety of the participants in the trial and to ensure the integrity of the trial. Also, these meetings will monitor the quality of the collected data to assess for weaknesses and errors. If any weakness and/or errors are identified, feedback will be provided during these meetings. The investigator(s) will allocate adequate time for such monitoring activities. The investigator(s) will also ensure that the monitor or other compliance or quality assurance reviewer is given access to all the above noted study-related documents.

10.2 Auditing and Inspecting

The investigator(s) will permit study-related monitoring, audits, and inspections by the IRB, Institutional compliance and quality assurance groups of all study related documents (for example, source documents, regulatory documents, data collection instruments, study data etc.). Participation as an investigator(s) in this study implies acceptance of potential inspection by government regulatory authorities and applicable Institutional compliance and quality assurance offices.

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