Official Title: Efficacy of a Peri-Operative Surgical-Site, Multimodal Drug Injection in Pediatric Patients with Cerebral Palsy Undergoing Hip Surgery: A Randomized Controlled Trial.

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Study Title:

Efficacy of a Peri-Operative Surgical-Site, Multimodal Drug Injection in Pediatric Patients with Cerebral Palsy Undergoing Hip Surgery: A Randomized Controlled Trial.

Study Design:

This study is a prospective, randomized controlled trial with 2 parallel arms. Patients will be randomly assigned to the 2 treatment groups: surgical-site injection with ropivacaine, ketorolac, and epinephrine, or surgical-site injection with normal saline. Randomization will be performed via random number generator and will be carried out by a research associate who will not participate in study recruitment or outcomes assessment. Allocations will be concealed on a password-protected database accessible only to the research associate. Patients, surgeons, and nursing staff who perform post-operative assessments will be blinded to treatment allocation.

Participants:

Patients will be eligible to be included in this study if they are under the age of 18 years, have a known diagnosis of cerebral palsy, and are scheduled to undergo surgery of the proximal femur (specifically, unilateral or bilateral proximal femoral osteotomy for hip dysplasia). Patients will be recruited from both UCLA/Orthopaedic Institute for Children and Lurie Children's Hospital of Chicago. Patients and parents/guardians will be asked at their pre-operative clinic visit if they would like to participate in the study. They will be provided with the informed consent form at their pre-operative visit in order to allow them time to review the information prior to signing consent. Informed consent for the study will then be obtained in the pre-operative holding area prior to surgery. Patients will be excluded from the study if they have ongoing pre-operative opioid use, or a history of an allergic reaction to any of the components of the pain injection.

Surgical Procedure:

Patients undergoing unilateral or bilateral hip proximal femoral osteotomies will be included in the study. All patients will be treated with standard-of-care techniques chosen by the treating surgeon. The addition of pelvic osteotomies and/or soft tissue procedures will be at the discretion of the treating surgeon and will not exclude the patient from the study. Written consent will be obtained for all patients prior to the surgical procedure. Parental consent will be obtained, in addition to patient assent for all patients of appropriate age and intellectual capability. All patients will have a general anesthetic with a lumbar epidural. No preemptive scheduled analgesic regimen will be employed. All medications administered during induction and maintenance of anesthesia will be managed by the anesthesiologist and titrated at their discretion.

The local anesthetic group will be injected with ropivacaine 2mg/mL (3mg/kg), epinephrine 1mg/mL (0.5mg), and ketorolac 30mg/mL (0.5mg/kg). If bilateral hips are involved, the total amount will be split evenly between the two sides. The control group will receive equivalent volumes of 0.9% sodium chloride solution (these volumes will be calculated based on the volumes of medication the patient would have received had they been assigned to the cocktail group). The injections will be performed while the patient is still under general anesthesia,

following wound closure, and medications will be injected evenly between the deep and superficial tissues in an extra-articular pattern (no injection of the synovium or capsule). All injections will be performed using a 20-gauge needle. The injection medications will be placed in a sterile cup. The surgical technician will fill syringes from the labeled cup, which will be handed to the surgeon for immediate administration.

Post-Operative Protocol:

The epidural anesthesia will be started at the discretion of the attending anesthesiologist either before or on-arrival to the post-anesthesia care unit. Any additional medications administered during the immediate post-operative period in the post-anesthesia care unit will be prescribed by the attending anesthesiologist and will not be standardized. Beginning when the patient leaves the post-anesthesia care unit, all patients will be given the following pain regimen: acetaminophen (15mg/kg PO or per g-tube every 6 hours around the clock), ketorolac (0.5mg/kg IV every 8 hours for 3 doses) followed by ibuprofen (10mg/kg PO or per g-tube every 8 hours as needed for mild pain (pain score 1-3)), diazepam (0.1mg/kg PO or per g-tube every 6 hours around the clock for 36 hours followed by every 6 hours as needed for muscle spasms), and oxycodone (0.1mg/kg PO or per g-tube every 6 hours as needed for severe pain (pain score 7-10)). Nurses will be instructed to offer this as-needed medication to patients at standardized intervals every 4 hours when performing pain assessments. Additional medication for pain may be administered if the protocol does not result in adequate pain relief, at the discretion of the treating physician. The epidural will be titrated by the acute pain anesthesiology team for inadequate pain control, and all epidurals will be discontinued the morning of post-operative day two. All patients will be discharged on a standardized medication regimen as follows: diazepam (0.1mg/kg PO or per g-tube every 6 hours for 14 days), oxycodone (0.1mg/kg PO or per g-tube every 6 hours as needed for severe pain, 20 doses), acetaminophen (15mg/kg PO or per g-tube every 6 hours for 14 days), and ibuprofen (10mg/kg PO or per g-tube every 8 hours for 14 days). Inpatient and outpatient narcotic consumption will be recorded as morphine equivalents.

All other aspects of post-operative care, including (but not limited to) physical therapy, weight bearing status, mobilization, and bracing will be decided on a case-by-case basis by the treating surgeon.

Data Collection and Protection:

Data will be collected by IRB-approved research personnel via access to the medical record. Personal identifying information collected will include name, date of birth, medical record number, and telephone number. All data will be labeled with a code that can be linked to this personal identifying information. Data will be collected only from the hospitalization following the surgical procedure and from the first post-operative visit. This data will include: narcotic consumption, pain scores, complications or adverse events, and re-admission in the immediate post-operative period (first two weeks post-operatively). All data will be stored on a secure, encrypted data storage device or password protected and encrypted internet-based storage device.

Outcome Measures:

The primary outcome measure will be total narcotic consumption in the first 48 hours after surgery. Narcotic consumption will be recorded in the medical record while in the post-anesthesia care unit and while inpatient and will be converted into morphine equivalents according to a conversion table. The secondary outcome will be pain scores during inpatient hospitalization following the surgical procedure. Pain score assessments will be completed in the post-anesthesia care unit, and every 4 hours following the surgical procedure. Scores will be collected by nursing staff on the inpatient ward who are blinded to treatment allocation and recorded in the electronic medical record. The type of pain score collection will vary based on patient age and level of intellectual disability. In verbal children, either the VAS or FACES pain scale will be employed. In non-verbal children, the FLACC scale will be employed.

Additional secondary outcome measures will include total narcotic consumption following hospital discharge, length of stay, parent satisfaction scores, and complications. Patients will be instructed to bring their medications with them to their first post-operative visit, and outpatient narcotic use will be recorded based on amount of medication remaining. This will also be converted into morphine equivalents according to the same conversion table. Parent satisfaction scores will be based on a standardized questionnaire taken by parents in person at the first post-operative clinic visit aimed to assess their satisfaction with their child's pain management peri-operatively.

Statistical Analysis Plan

Outcome measures will be analyzed using a two-tailed t-test or a non-parametric Mann-Whitney test for quantitative variables; a Fischer exact test was used for categorical variables. Further, while a t-test will be utilized to demonstrate differences in narcotic consumption and average pain scores during *discrete, comparable, clinically-relevant measures of time*, mixed effects modeling will be utilized to further analyze narcotic consumption and pain scores *over time*. Statistical significance will be defined as $p<0.05$.