

A Randomized Controlled Trial of Acetaminophen and Ibuprofen Versus Acetaminophen and Oxycodone for Postoperative Pain Control in Operative Pediatric Supracondylar Humerus Fracture

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Research Design and Methods: Describe in detail the design and methodology of the study.

This is a double-blinded, randomized controlled trial comparing the analgesic efficacy between acetaminophen and ibuprofen versus acetaminophen and oxycodone for postoperative pain control in patients following closed reduction and percutaneous pinning for isolated closed supracondylar humerus fractures. Each patient will be evaluated initially at our institution's pediatric urgent care center and placed in a long arm splint with instructions to elevate the affected arm. Patients will not be discharged with any prescriptions for narcotic pain medication and will be instructed to take weight-based doses of acetaminophen and/or ibuprofen for pain control as needed. All patients age 5-12 with closed Gartland type II supracondylar humerus fractures requiring fixation (e.g. satisfactory reduction not achieved with closed reduction and casting or medial column comminution) and Gartland type III supracondylar humerus fractures scheduled for surgery will be approached for participation in the study. Demographic data (age, gender, weight, height, ethnicity, primary language spoken at home, insurance type) will be obtained through chart review on each included patient. The exclusion criteria include open fractures, fractures with concomitant vascular or neurologic deficit, any fracture requiring open reduction, pathologic fractures, those presenting with concomitant injuries, swelling requiring post-operative hospitalization for monitoring, any known history of allergies to acetaminophen, ibuprofen or oxycodone, and patients with developmental delay that would preclude participation in the visual analog Faces Pain Scale-Revised. Informed consent will be obtained from all parents who wish to participate in the study, and assent will be obtained from patients when possible. If parents refuse participation in the study, the reason for refusal will be documented, and their child's care and post-operative protocol will be consistent with our typical protocol, which includes all 3 medications. All surgeries will be performed at our outpatient surgery center. The treating pediatric anesthesiologists will use a standardized anesthesia protocol. All patients will be under general anesthesia and will not receive any regional anesthetics or local anesthetics. All included patients will undergo closed reduction and percutaneous pinning using 2-3 pins placed either all laterally or medially and laterally by two pediatric orthopaedic surgeons (MS and RT). They will all be placed in posterior long arm splints thereafter and made non-weight bearing in that extremity. The patients will be transferred to our post-anesthesia care unit (PACU), where morphine IV 0.1mg/kg will be utilized as needed for before discharge home. Nursing staff will record the amount of pain medication provided in the PACU as well as the pre-discharge pain scores, as is our typical post-operative protocol. Prior to discharge, patients will be randomized to receiving acetaminophen for first-line medication (liquid oral medication, 15mg/kg/dose every 6 hours as needed, max 90mg/kg/day) with as needed ibuprofen for breakthrough pain (liquid oral medication, 10mg/kg/dose every 8 hours as needed, max dose 40mg/kg/day) or acetaminophen for first-line medication (liquid oral medication, 15mg/kg/dose every 6 hours as needed, max 90mg/kg/day) with as needed oxycodone for breakthrough pain (liquid oral medication, 0.1mg/kg/dose every 6 hours as needed). Each patient will receive 18 doses (3 days) of acetaminophen and the study medication. Pre-sealed, sequentially numbered randomization envelopes containing each subject's group will be delivered to the hospital pharmacy. Patients will be instructed to first take the labeled acetaminophen medication and to take the study medication (unlabeled) as needed for breakthrough pain as prescribed. Patients will be given both patient information for both study medications in order to keep the patients blinded to which study medication they received. They will be given patient information for both medications but told that they have been given only one of the two medications. Medication labels will be obscured by the pharmacist with a circumferential tape. Throughout the study, the investigators and the parents will be blinded as to which study medication

was given to each participant. Parents who contact the physician (a resident physician on-call for the pediatric orthopaedic surgery service who is not involved in the study) post-operatively for alternative pain medication will be provided the study medication not initially provided (i.e. those that were randomized to receive oxycodone primarily will be provided ibuprofen and vice versa), as confirmed by our pharmacy. Post-operatively, the parents of each participant will be asked to use the Faces Pain Scale-Revised (FPS-R)¹⁶ to rate the child's level of pain at 24 hours and 48 hours after surgery. A research team member will call each participant's guardian at 24 and 48 hours postoperatively to collect these responses. Parents will further be asked to complete the modified Total Quality Pain Management Instrument (TQPM)¹⁷ regarding their level of satisfaction with surgery and post-operative pain control. Parents will be asked to report any side effects (e.g. nausea, vomiting, lethargy, constipation) associated with the medications. A take-home medication log will be utilized by the parents to record the type and amount of medication given to each participant and to record any associated side effects. For breakthrough pain experienced during pharmacy hours the patient will have the option to return to our pharmacy to obtain the medication they were not originally prescribed. Though we believe this will be unlikely, if they are unable to get to the pharmacy for the other medication (e.g. oxycodone if they were in the ibuprofen group or ibuprofen if they were in the oxycodone group), parents can go to the ER for IM/IV medication for pain relief and they can get a prescription for oxycodone or ibuprofen from the ER if necessary, once they contact the resident on call. There will always be a resident on call 24/7 to advise patients if they are unable to achieve adequate pain control with medications received. Again, we believe this will be an unlikely/rare event. The resident on call will have access to the study medication that the patient received. At this point, the resident on call can reveal what medication they were getting (in case they need a new prescription from the ER) so they do not get oxycodone if they were already prescribed oxycodone (and can get something different) or they have the option to obtain ibuprofen over-the-counter if they wish. Patients who need to get the other medication would be considered a "failure in treatment" and would not be analyzed together from the original group.

Statistics and Data Analysis: Describe the proposed statistical procedures or descriptive analyses for the study. If applicable, indicate how the sample size was determined.

Sample size was based on the self-reported pain scale (FPS-R, FACES Pain Scale-Revised) which is a 0 to 10 scale. A standard deviation of approximately 1.6 was assumed. With a sample size of 45 patients in each group, given a power of 80% and an alpha of 0.05, the study will be able to detect differences of 1 or larger (on the scale 0 to 10). Based on this previous study, this is a sufficiently large sample to detect clinically significant differences.

Baseline characteristics of the study groups will be summarized using descriptive statistics. Spearman rank correlation will be used to determine whether numerical data points were non-parametric. For non-parametric continuous variables, Mann-Whitney-U test will be used. Student's T-tests will be utilized to analyze parametric variables. For categorical variables, comparisons will be completed using the Fischer's Exact Test for non-parametric data and Chi-Squared Test for parametric data.

Patients who fail the treatment drug (e.g. requires another medication in addition to the medications initially prescribed) will not be included in the original group for analysis. They will be accounted for with

Kaplan-Meier analysis comparing the number of failures in each group (which will also account for the time at which they required the "rescue" medication).