Multimodal Analgesia with Acetaminophen vs. Narcotics Alone After Hip Arthroscopy

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I. PURPOSE OF THE STUDY AND BACKGROUND

Purpose

The purpose of this proposed study is to evaluate the efficacy of a multimodal approach to analgesia for patient's pain after hip arthroscopy and to also assess if this new approach will result in a reduction in post-operative narcotic use.

We hypothesize that the majority of patients, following hip arthroscopy, forego their prescribed narcotic medication and, instead, are able to adequately control their post-operative pain with acetaminophen.

Rationale

Many studies have highlighted the impact of physicians' propensity to over-prescribe opioid analgesics in the United States.[1-5] While orthopaedic surgeons prescribe opioid analgesics at the third highest rate in the U.S.,[6] some believe these mostly go unused and end up being improperly stored in patients' homes[1]. This data encourages us to critically evaluate the necessity of these prescriptions for common outpatient procedures such as hip arthroscopy.

The current standard post-operative medications for patients after hip arthroscopy consists of a narcotic analgesic such as oxycodone/acetaminophen (Percocet) for pain along with two non-steroidal anti-inflammatory drugs (NSAIDs) – aspirin for DVT prophylaxis and celecoxib for heterotopic ossification prophylaxis. It is known that NSAIDs have the ability to reduce the inflammatory processes associated with the body's physiological response to surgical trauma, specifically the cyclooxygenase (COX) inflammatory pathway.

If surgeons can reduce the amount of narcotic analgesics prescribed after hip arthroscopy while effectively managing post-operative pain with acetaminophen, aspirin and celecoxib, this can reduce overall narcotic use and, therefore, reduce the incidence of adverse events and addiction commonly associated with narcotics.

Study Design

This will be a single-center, randomized prospective study. The study will compare post-operative pain scores and narcotic consumption between two cohorts – one cohort will receive acetaminophen along with a reduced quantity of Percocet (to be used as needed for breakthrough pain) and the other cohort will receive Percocet only. Both pain management options are considered to be standard of care. Both cohorts will receive aspirin for DVT prophylaxis and celecoxib for heterotopic ossification prophylaxis.

Primary Objective

The primary objectives of the study are to compare patients' narcotic consumption and reported pain following arthroscopic hip surgery, and determine if acetaminophen can provide adequate pain relief compared to a narcotic medication.

II. CHARACTERISTICS OF THE RESEARCH POPULATION

Number of Subjects

We will aim to enroll a total of 100 subjects (50 per cohort).

Gender of Subjects
Men and women will be included in this study.

Age of Subjects
Subjects included study will be at least 18 years of age, but less than 65.

Racial and Ethnic Origin
There are no enrollment restrictions based on race or ethnic origin.

Inclusion Criteria
All study subjects must meet the following inclusion criteria:

- Must be at least 18 years of age
- ASA class I-II
- Patients indicated and scheduled for arthroscopic hip surgery

Exclusion Criteria
Patients meeting the following criteria will be excluded from participation in this study:

- Contraindication to acetaminophen or oxycodone/acetaminophen (e.g. hypersensitivity, history of GI or bleeding disorder)
- Legally incompetent or mentally impaired (e.g. minors, Alzheimer's subjects, dementia, etc.)
- Younger than 18 years of age or older than 65
- Any patient considered a vulnerable subject
- Patients on pain medication prior to surgery

Vulnerable Subjects
We do not intend to enroll vulnerable subjects.

Subject withdrawal criteria.
Patients are free to withdraw at any time from the study.

III. METHODS AND PROCEDURES

Methods and Procedures
Patients indicated and scheduled for hip arthroscopy will be identified by participating orthopaedic surgeons at NYU Langone Orthopedic Hospital. After informed consent is obtained, a chart review of patients' medications and past medical histories will be performed based on their electronic medical records to identify any current pain medications or exclusion criteria. Patients will then be randomized to one of two cohorts based on patients' medical record number (MRN):

- MRN ending in an EVEN #: will receive acetaminophen 600 mg to be taken every 8 hours (TID) and oxycodone/acetaminophen (Percocet) 5 mg/325 mg as needed for breakthrough pain. These patients should only take 3 Tylenol within a 24 hour period and 2 Percocet within 24 hours..

- MRN ending in an ODD #: will receive the current standard of care postoperative pain management, which is Percocet 5 mg/325 mg every 6 hours PRN.

Both pain management options are considered to be standard of care and the patient would be able to receive either option regardless of study participation. Immediate post-operative management will not be affected by this study. All patients will receive a standardized regimen of aspirin for DVT prophylaxis and celecoxib for heterotopic ossification prophylaxis, which is standard of care post-operative treatment. As the study focuses on the first week post-operatively, both cohorts will equally experience limitations in mobility. The Acetaminophen cohort should not have more mobility or recovery issues than the Percocet cohort.

Information to be recorded pre-operatively includes age, sex, height, weight, BMI, and American Society of Anesthesiology (ASA) classification. Intra-operative information will also be recorded, including operative time, and intraoperative morphine-equivalent doses. Pain severity scores at rest will be assessed by use of a visual analog scale (VAS; 0 = no pain, 10 = worst pain imaginable) at 0.5, 1, 1.5, 2, 4, 6, 24, and 48 hours as well as 7 days after surgery. Morphine-equivalent consumption will be recorded immediately after surgery, during phase II recovery, and at 24 hours, 2 days and 7 days after surgery. Incidence of narcotic-related side effects (nausea/vomiting, itching, constipation) in the first 24 hours will be noted. Time to discharge from the post-anesthesia care unit (PACU) and time to discharge from the hospital will be recorded.

Patients will be given a journal to record their pain scores throughout their first week after surgery. They will record whether they used any Percocet and, if so, the daily amounts. Patients in the Acetaminophen cohort will be advised to take Percocet if they are experiencing distressing pain, a 5 on the VAS scale. Distressing pain is defined as pain that is not alleviated with Acetaminophen and cannot be ignored. This journal will be collected during the patient's standard 1-week post-operative checkup along with their bottle of prescription medication, which will also be recorded. Patients will be advised to seek medical attention if they experience any adverse events, including nausea, vomiting, dizziness, drowsiness, and stomach disturbances, or continue to have uncontrolled pain.

Data Analysis and Statistical Plan

In order to determine sample size an a priori power analysis was conducted to estimate the minimum sample size needed to achieve 80% power (1 – b) at the .05 significance level for the primary outcome measure, VAS score. Variables used in the power calculation were taken from the literature including an assumed effect size of 2.5 and standard deviation (SD) of 2. This analysis suggested that a minimum of 28 patients per group would suffice. To allow room for potential loss to follow-up and to ensure a robust data set, we will aim to enroll a total of 100 subjects (50 per cohort). We will use patient subjective pain and narcotic consumption data as statistical endpoints.

Statistical analysis will be performed using t-tests for continuous variables, and chi-square tests for categorical ones. If the data is not normally distributed, Mann-Whitney tests will be used. All protected health information will be removed prior to statistical analysis.

Data and Safety Monitoring Plan

Data monitoring will be done by Dr. Thomas Youm, the principal investigator and individual medical monitor.. They will review the following points quarterly.
They will monitor whether or not:

1. Collection and storage of patient data was performed in a sensitive and secure manner, as defined in the informed consent form and protocol
2. All study activities were conducted with primary emphasis on patient care and wellbeing
3. If there were any adverse events, and if so were addressed appropriately and per protocol
4. The risk/benefit to patients has remained the same throughout the course of the study

The study will be stopped if there are unexpected severe AE's in more than one patient. Adverse events will be defined as negative reactions to the NSAIDs or Percocet including a hypersensitivity reaction or drug dermatological eruption. We will submit summaries of data and safety monitoring bi-annually.

Data Storage and Confidentiality

Data recorded from this study will be organized in REDCap. Participant medical information will only be available to the principal investigator and research staff as necessary for data analysis. All patient health information will be de-identified and assigned a code. Information linking participants' names, social security numbers and medical record numbers will be stored in a secure location separate from the medical information. No data will be shared to anyone outside of the study team.

Adverse Event Reporting

Information about any breach of confidentiality will be documented in the electronic data collection system and/or on the paper CRFs, as appropriate. It will be the responsibility of the Principal Investigator to report any Serious Adverse Event (SAE) that occurs during the course of the retrospective data collection to the Institutional Review Board (IRB) within the timeframe specified by NYU SoM.

Adverse events will be defined as negative reactions to the NSAIDs or Percocet including a hypersensitivity reaction or drug dermatological eruption. Patients will be instructed to call immediately if they have an issue. Additionally, they will be coming to the hospital the day after taking the drug when they will be further evaluated. Subjects will be evaluated by the operating physician prior to the procedure. After the procedure, patients will have post-operative visits (standard of care) when they may be further evaluated for AEs. Given the immediacy of AEs in this case, the timeframe will be limited to the first post-op visit (10-14 days after initial medication ingestion).

IV. RISK/BENEFIT ASSESSMENT

Risk

Because this study involves the standard of care for post-operative hip arthroscopy pain management, the risks are minimal and include a risk of breach of confidentiality. Together, acetaminophen and Percocet have not shown to have an adverse drug interaction. However, each medication carries its' own side effects. Acetaminophen may cause an allergic reaction. Symptoms may include: itching or hives, swelling or tingling in your mouth or throat, swelling

of your face or hands, tightness of the chest, trouble breathing. Other serious side effects of acetaminophen may include: nausea, vomiting, loss of appetite, or severe stomach pain, trouble passing urine or change in the amount of urine, light-headedness, sweating, fainting, or weakness, unusual bruising or bleeding, yellowing of the skin or whites of your eyes. Percocet may cause side effects such as constipation, nausea, vomiting, upset stomach, sleepiness, drowsiness, dizziness, lightheadedness, itching, headache, blurred vision, dry mouth, and sweating. Percocet contains oxycodone, which is an opioid. There is a less than 5% chance patients who take opioids for a short period of time (<2 weeks) have a risk of developing a physical dependence or of becoming addicted.

These side effects are more likely if Acetaminophen or Percocet are if taken with alcohol or grapefruit juice. The risks and side effects of the medications will be discussed with the patients prior to surgery and the standard post-operative follow up visits.

Protection against Risks

Patients will be screened for any contraindication to acetaminophen or Percocet use.

Additionally, all patients will be de-identified and given a code. Information linking the patient codes to the participants' names and medical record numbers will be stored in a secure location separate from the medical information. Access to the information linking the linkage codes with participant identifiers shall be restricted.

Potential Benefits to the Subjects

Patients may experience less pain post-operatively, and may require less narcotics use, which has a steeper side-effect profile. However, these benefits cannot be guaranteed.

Additionally, it is the hope of the research team that results of this study will benefit future patients and their physicians by providing more information regarding the use of acetaminophen after surgery. This will allow for a more open and informed dialogue, and possibly a change in treatment.

V. INVESTIGATOR'S QUALIFICATIONS AND EXPERIENCE

The CV, medical license, and human subjects' tutorial completion report are attached for all investigators who are participating in this study. All research personnel have medical research experience and are qualified to participate in this quality study. Most importantly, staff have been properly educated and certified with CITI training to conduct research in a matter that will maintain full patient confidentiality. The research coordinator for this study is trained in GCP principles and practices and will be responsible for compliance with GCP guidelines for all study investigators and research assistants.

VI. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT

Method of Subject Identification and Recruitment

Appropriate patients, who meet all of the inclusion criteria and none of the exclusion criteria, who require a hip arthroscopy, will be identified from the clinical offices of the investigator surgeons.

Process of Consent

Written consent will be obtained from subjects who are eligible candidates for hip arthroscopy based upon their medical condition (as determined by their physician). The consent process will take place during the office visit when it is determined necessary to perform the procedure—at which time the investigator has determined subject's voluntary participation has been upheld. Subjects will be informed about the study and the intended purpose. They will be given the opportunity to ask questions and receive thorough explanations. They will be made aware of the possible risks and anticipated benefits. They will also be informed of alternative procedures. Subjects will then be given another opportunity to ask questions and agree or disagree to consent.

Subject Capacity

All subjects enrolled in this study will have capacity to provide informed consent.

Consent Forms

Written consent will be obtained from the patient.

Documentation of Consent

Signed consent forms will be kept in a binder and stored in a locked file cabinet.

Costs to the Subject

Subjects will not incur any additional financial costs as a participant in this study.

Payment for Participation

No payments/reimbursements will be provided to subjects for their participation in this study.

Clinical Trial

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

VII. References

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