Efficacy of Ketorolac for Postoperative Pain Management in Hip Arthroscopy: A Prospective Randomized Controlled Trial

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1. STUDY AIM, BACKGROUND, AND DESIGN ABSTRACT

The purpose of this study is to investigate the use of alternative pain management protocols for controlling post-operative pain in patients undergoing hip arthroscopy. Hip arthroscopy (HA) is commonly used to treat patients with femoroacetabular impingement (FAI), trochanteric pain syndrome, snapping hip disorders, and young adult hip disorders [1]. Previous protocols for perioperative pain management of hip arthroscopy have included opioids for pain management, however, with the increasing severity of the opioid epidemic in the United States, it is important to find other means for treating pain post-operation. The use of opioids have been shown to subject patients to a greater chance of addiction, depression, and anxiety and it has been found that patients who required one refill on their post-operative opioid medication were likely to have a lower baseline patient recorded outcomes and achieved patient acceptable symptomatic state (PASS) at lower rates compared to those who did not. [2]It is important to find alternatives to opioid pain treatment for pre/post-operative hip arthroscopy to improve patient outcomes.

Current alternative pain treatments for HA include multimodal strategies combining NSAIDs with opioids. [3] Kahlenburg et al found that patients who were administered 400mg of celecoxib (NSAID) 1 hour before surgery had significantly lower VAS pain scores after surgery as well as reduced opioid consumption and hospital stay compared to those who were not. Gabapentin and acetaminophen have also been found to reduce opioid consumption post-surgery [4]. There has been success with entirely non-opioid pain protocols for arthroscopic surgeries. [5] Jildeh et al found that a multimodal non-opioid pain protocol post-operatively was better or equivalent at pain control than the traditional opioid protocol which used oxycodone for arthroscopic rotator cuff surgery. [6] Moutzouros et al also found that a multimodal pain protocol without opioids was equivalent to or better than an opioid-only postoperative pain plan in anterior cruciate ligament (ACL) reconstruction. Previous studies have assessed the impact of ketorolac on rotator cuff repair and ACL reconstruction and found improved pain scores postoperatively[4, 5,6,7.]

We propose testing the efficacy of ketorolac-based multimodal pain management protocol in patients at one institution undergoing hip arthroscopy and comparing the results to the current facility protocols. Variables for comparison will be a 5-day pain journal assessment, VAS, PROMIS scores collected at follow-up appointments, and postoperative opioid consumption. Subjects will be randomly assigned to a control group and a non-opioid pain group. The control group will be given the typical regimen of hydrocodone-acetaminophen and diazepam while the study cohort will receive ketorolac in addition. We hypothesize that the ketorolac pain management protocol will be just as effective as or better than the current standard of care in reducing immediate post-operative pain and opioid consumption. Finding an alternative to opioid pain relief is vital to providing the best patient care and outcomes post hip arthroscopy.

2. SUBJECT POPULATION AND ELIGIBILITY

Subject Population

The participants will be selected from those who are undergoing hip arthroscopy at Henry Ford Health System in Detroit, Michigan. Participants will include males and females over the age of 18.

Exclusion Criteria	Inclusion Criteria
Patients with inability to consent and/or do not speak English	Patients undergoing hip arthroscopy over the age of 18 with Dr. T. Sean Lynch

Patients with conditions contraindicated with NSAIDs (medication allergy, peptic ulcer disease, bleeding diathesis, and renal disease)	
Patients with history of drug and alcohol use disorder	
Patients with chronic analgesia (filled two opioid prescriptions within 6 months of the surgery)	
Patients with psychotropic medication usage	
Patients who take pentoxifylline, probonecid, aspirin, and/or NSAIDs who cannot stop taking it for the study	
Patients who are not discharged same day after surgery	

Enrollment and/or Screening

- Consecutive patients on Dr. T. Sean Lynch's clinic schedule will be reviewed for qualifying patients as well as potential study participant medical records to ensure inclusion and exclusion criteria are met. This will be performed by study personnel only.
- In order to ensure criteria is met and potential participants have no contraindications to ketorolac their medical history and medical chart will need to be reviewed
- Criteria will be reviewed beforehand for prospective patients and then with the patient to ensure they are appropriate for the study.
- Only patients from Dr. T Sean Lynch's clinic will be included
- If patients were to fail screening they will not be eligible for the study and will not be enrolled. They will continue with the standard of care medications. If the patient decides not to have surgery or are not discharged home POD0 after surgery will be removed from the study.

3. STUDY PROCEDURES

A prospective randomized controlled trial to study the effects of ketorolac as an adjunct for postoperative pain management after hip arthroscopy. Eligible participants will be randomly assigned to two groups. At discharge, the control group will receive the standard of care pain protocol at our institution. The ketorolac group (experimental group) will receive the standard of care pain protocol along with an intraoperative loading dose of IV ketorolac, a prescription of ketorolac (10mg by mouth every 6 hours for 3 days, and omeprazole (20 mg by mouth once daily for 3 days) for gastrointestinal prophylaxis on discharge. The standard of care pain protocol is hydrocodone-acetaminophen 5mg/325mg and diazepam 5mg. On POD0 both groups will be given a journal to record their pain levels during the 5 days after surgery as well as adverse effects to medication such as nausea, abdominal pain, allergic reaction, dark stool, dry mouth, fever, headaches, cough, gastritis, drowsiness, and insomnia. VAS and narcotic consumption will be measured for 5 days via the journal as well as 2 and 6 weeks post-operative. PROMIS PF and PI scores will be recorded preoperatively, 2 weeks, 6 weeks, and 3 months post-operatively.

Our primary outcome is VAS at POD4. Based on previous studies using visual analog scale pain scores for hip arthroscopy, a difference of 1-3 was considered significant for most patients[3,7]. Therefore, we determined via a priori analysis that we needed to enroll 80 patients (40 patients in each cohort) to detect a VAS difference of 2 assuming standard deviation of 3, alpha of 0.05, power of 0.8, and drop out of 10%.

Randomization after consent will be performed by a research assistant with a 1:1 allocation ratio using

adaptive randomization computer software (Adaptive Randomization; MD Anderson Cancer Center). At 1 week before surgery, appropriate surgeon, physician assistant, anesthesiologist, and/or resident physician will be notified by secure email of the patient's group designation.

Summary statistics using mean and standard deviation for continuous variables and frequency (percentage) for categorical variables. Mann-Whitney U tests will be used to correct for any non-normality. Statistical differences in patients' characteristics will be examined with univariate analysis. Chi square tests for categorical variables and Student t-tests for continuous variables will be used to compare the control and experimental cohort. Statistical significance will be defined with a P value of 0.05, and all tests will be two-sided tests using statistical software SPSS.

Control	hydrocodone-acetaminophen 5mg/325mg 1 tablet q6hrs PRN to start on POD0 30 tablets	indomethacin 75mg 1 tablet QD to start on POD0 10 tablets	diazepam 5mg 1-2 tablets q8hrs PRN to start on POD0 15 tablets		
Experimental	hydrocodone-acetaminophen 5mg/325mg 1 tablet q6hrs PRN to start on POD0 30 tablets	indomethacin 75mg 1 tablet QD to start on POD4 after completion of ketorolac 10 tablets	diazepam 5mg 1-2 tablets q8hrs PRN to start on POD0 15 tablets	IV ketorolac intraoperative loading dose Ketorolac 10mg 1 tablet q6hrs to start on POD0 12 tablets	Omeprazole 20 mg qd 3 tablets

4. ANTICIPATED RISKS

A known risk to participants could be the side effects of the postoperative pain management medications and specifically ketorolac. Patients will be monitored post operatively and will be kept in contact with once they have returned home. Patients are also given the typical standard of care pain medications to ensure appropriate postoperative pain management. If an adverse side effect occurs, the medication will be discontinued, a new course of pain management will be explored for these individuals, and the patient will be removed from the study.

Another known risk that is part of any study is a breach of confidentiality. All actions will be taken to minimize the risk of breach of confidentiality. More information on how patient data will be protected and stored can be read in the Privacy and Confidentiality section and the Data and Safety Monitoring Plan section of the document.

There is also the risk of patients becoming uncomfortable or tired of answering the survey or pain journal questions. These questions were minimized to take only up to 10 minutes daily for 5 days during the post-operative period.

5. ANTICIPATED BENEFITS

Participants of the study could receive adequate or improved pain management with less risk of adverse effects and potential abuse of narcotics if ketorolac provides similar or better pain relief to narcotics alone. Future patients and society could benefit from these results as addiction to opioids is a global health concern and an alternative could reduce the prevalence of opioid drug abuse after hip arthroscopy.

6. RENUMERATION/COMPENSATION

There is no compensation offered for taking part in this study.

7. COSTS

Ketorolac is a commonly-used and affordable postoperative pain medication, commonly covered by insurance and it is unlikely to incur additional cost to the patient. However, potential for increased cost will be disclosed to the patient in the consent process.

8. ALTERNATIVES

An alternative treatment to the one discussed in this study is to adhere to the current postoperative pain management protocol for hip arthroscopy set by Dr. Lynch. The patient will be provided all standard of care medications in addition to the study treatment if he/she chooses to drop out of the study.

9. CONSENT PROCESS AND DOCUMENTATION

Subjects will be screened for eligibility by a research assistant or other research personnel at a routine clinic appointment during which they are scheduled for a hip arthroscopy. Following consent for surgery, a member of the research team will approach the potential subject and asses their interest. Informed consent will be thoroughly reviewed with the patient.

Consents will be kept in a locked area, only accessible to study personnel. This will be kept in folders so there is no visible identifying information. The information pulled from the EMR will be kept on a password protected HF computer and there will be no identifying information aside from MRN kept on these forms. All data will be destroyed following publication of this study or after six months of inactivity.

10. WITHDRAWAL OF SUBJECTS

Patients who opt out from the study will have their information deleted. Additionally, subjects who do not undergo hip arthroscopy will be excluded. Patients who do not attend their postoperative follow-up appointments with their surgeon and/or deviate from study protocol will also be withdrawn.

11. PRIVACY AND CONFIDENTIALITY

Confidentiality Agreements: All users of the data will sign confidentiality agreements and receive training on proper procedures for how to handle patient level data.

System Controls to Limit Data Access: Only authorized personal will be given permission to access study data.

Computer System Security Plan: A security plan exists within the organization to provide protection for patient level data.

Virus Protection Software: A virus protection software is in place within the organization to protect patient level data.

Firewall: The organization's network system is protected by a firewall. The computer systems in place will have the operating system firewall in place.

Computer Locking: The computer(s) have automatic locking after 20 minutes of inactivity. Computer System are password protected with duo activation.

Physical Security: Physical access to servers and computers are restricted to only authorized personnel. The computer system is in a room which is inaccessible to the public.

Secure Electronic Copies: All electronic copies of patient level data will be secured to a room for authorized personnel only.

Secure Paper Copies: All paper copies of patient data will be kept under lock and key in a room accessible to only authorized individuals.

HIPAA authorization will be obtained for all patients.

12. DATA AND SAFETY MONITORING PLAN

All electronic data will be stored on a secure, encrypted server with a second secure document decoding the unique patient identity number associated with this study to their medical record number. Patient data will be kept in a locked spreadsheet that contains no patient identification aside from a unique patient ID associated with their MRN. This will only be accessible to the investigators. Patients will be de-identified following data collection. Data will be destroyed following publication or six months of inactivity, whichever occurs first. All non-electronic documents will be kept in the PI's office in a locked drawer that only members of the research team will have access to.

Unanticipated Problems and Adverse Events
The PI or research coordinator will report any problems or adverse events to the IRB via email

13. QUALIFICATIONS OF THE INVESTIGATOR(S)

Briefly summarize investigators prior experience and/or history relevant to the research. Student qualifications should include any relevant work, volunteer or research experience. Sometimes the addition of investigator qualifications makes the difference in getting approval for participant contact that may otherwise be too risky, for either the subjects or the student investigator. Staff qualifications should be stated concisely and clearly.

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14. REFERENCES

Be sure that any sources cited in the Study Aim, Background and Design section are included in your bibliography. Conversely, make sure that you have included references in this section that support your hypothesis or research purpose.

1. Jamil M, Dandachli W, Noordin S, Witt J. Hip arthroscopy: Indications, outcomes and complications. *International Journal of Surgery*. 2018;54:341-344. doi:10.1016/j.ijsu.2017.08.557

2. Beck EC, Nwachukwu BU, Jan K, et al. The Effect of Postoperative Opioid Prescription Refills on Achieving Meaningful Clinical Outcomes After Hip Arthroscopy for Femoroacetabular Impingement Syndrome. *Arthroscopy - Journal of Arthroscopic and Related Surgery*. 2020;36(6):1599-1607. doi:10.1016/j.arthro.2020.02.007

3. Kahlenberg CA, Patel RM, Knesek M, Tjong VK, Sonn K, Terry MA. Efficacy of Celecoxib for Early Postoperative Pain Management in Hip Arthroscopy: A Prospective Randomized Placebo-Controlled Study. *Arthroscopy - Journal of Arthroscopic and Related Surgery*. 2017;33(6):1180-1185. doi:10.1016/j.arthro.2017.01.016

4. LaPorte C, Rahl MD, Ayeni OR, Menge TJ. Postoperative Pain Management Strategies in Hip Arthroscopy. *Curr Rev Musculoskelet Med*. 2019;12(4):479-485. doi:10.1007/s12178-019-09579-x

5. Jildeh TR, Abbas MJ, Hasan L, Moutzouros V, Okoroha KR. Multimodal Nonopioid Pain Protocol Provides Better or Equivalent Pain Control Compared to Opioid Analgesia Following Arthroscopic Rotator Cuff Surgery: A Prospective Randomized Controlled Trial. *Arthroscopy - Journal of Arthroscopic and Related Surgery*. 2022;38(4):1077-1085. doi:10.1016/j.arthro.2021.11.028

6. Moutzouros V, Jildeh TR, Tramer JS, et al. Can We Eliminate Opioids After Anterior Cruciate Ligament Reconstruction? A Prospective, Randomized Controlled Trial. *American Journal of Sports Medicine*. 2021;49(14):3794-3801. doi:10.1177/03635465211045394

7. Bloom DA, Kirby DJ, Thompson K, Baron SL, Chee C, Youm T. Effect of Acetaminophen on Postoperative Percocet Use In Hip Arthroscopy: A Randomized Controlled Trial. *Arthroscopy - Journal of Arthroscopic and Related Surgery*. 2021;37(2):530-536. doi:10.1016/j.arthro.2020.09.046