

Prospective Assessment of Perioperative Intra-Articular Morphine Injection in Hip Arthroscopy on Postoperative Pain Management

PROTOCOL TITLE: Prospective Assessment of Perioperative Intra-Articular Morphine Injection in Hip Arthroscopy on Postoperative Pain Management

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1.0 Objectives

The goal of this study will be to measure:

- 1) Total narcotic consumption
- 2) VAS pain scores
- 3) Length of stay in the post anesthesia care unit (PACU)

following total hip arthroscopy in two groups of patients, one that receives intra-articular (IA) morphine and clonidine in addition to the standard pre and postoperative analgesia and the other group that receives normal saline in addition to the standard pre and postoperative analgesics.

The primary goal of this study will be to determine if perioperative intra-articular morphine and clonidine injections will reduce the postoperative narcotic consumption, pain scores, and time to recovery for patients undergoing hip arthroscopy.

The primary outcome of this study will be narcotic consumption during PACU recovery duration, which will be measured by total opioid consumption in units of morphine equivalents. PACU opioid consumption will be calculated from the medications list, which is regularly recorded in the electronic medical record.

2.0 Background

Since January 2015 many of Dr. Terry's patients have been receiving IA morphine and clonidine injections as prophylaxis for postoperative pain control after hip arthroscopy. However, prior to January 2015 IA morphine and clonidine were not administered as standard of care.

Because there is so little published about the efficacy of such injections in hip arthroscopy, the purpose of this study is to further explore this gap in knowledge.

A retrospective pilot study at Northwestern Memorial Hospital (under IRB STU00200639) has shown the proposed intervention to be successful in decreasing postoperative narcotic consumption. The control group receiving only the current standard of care had a 40 mEq narcotic consumption, while the interventional group receiving the additional IA morphine and clonidine had only a 23 mEq narcotic consumption ($p=.0259$).

Over the last few decades, the use and safety of arthroscopic hip surgery has considerably improved though the evolution and development of arthroscopic imaging and instrumentation¹. There is still a considerable amount of room for growth and research in comparison to arthroscopic knee and shoulder surgery, which have been around much longer. One area which needs attention is postoperative pain management for patients undergoing hip arthroscopy. The benefits to controlling postoperative pain are multifocal and range from improved patient comfort and decreased

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time of recovery to decreased narcotic consumption and reduced cost of care².

Many studies on the use of intra-articular morphine (IA) injections in arthroscopic knee surgery have demonstrated effectiveness in reducing both patient reported pain and narcotic consumption post-operatively³⁻⁵. Furthermore, studies have shown that intra-articular clonidine, an α_2 agonist, potentiates the analgesic effect of morphine when the two are used in combination⁶. While there is considerable evidence supporting the use of IA morphine for knee surgery, very little has been cited for such use in hip arthroscopy⁷. The purpose of our study is to expand upon the retrospective data that we have already analyzed to better assess the effectiveness of IA morphine and clonidine injections in reducing patient reported pain and narcotic consumption.

3.0 Inclusion and Exclusion Criteria

All patients who are undergoing a hip arthroscopy procedure by the senior surgeon (Dr. Michael Terry) will be approached to participate in the study, with the exception of pregnant women, adults unable to consent, prisoners, and any patient under the age of 18 years.

Any patient with a medical contraindication to morphine or clonidine will not be included in either the therapeutic or control group. Additionally, for the final analysis, the data for all subjects in our data set will be analyzed using a random study number as the key identifier. In some cases, if there is substantial data missing for a subject, which would be otherwise essential for analysis, the subject's information for that particular analysis will be excluded. To the best extent possible, data that can be interpolated will be utilized.

4.0 Study-Wide Number of Subjects:

N/A

5.0 Study-Wide Recruitment Methods:

N/A

6.0 Multi-Site Research:

N/A

7.0 Study Timelines

- Each individual subject who consents to the study will be participating from the day of their surgery until their two week postoperative appointment. Their coded data will remain in use until the study is complete, upon which all data will be destroyed electronically or physically.
- The duration of this study is anticipated to be 18 months for collection of 100 participants, 50 for the therapeutic group and 50 for the control group.

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- The estimated date of completion for primary analysis will be 18 months from the beginning of the study (October 2016).

8.0 Study Endpoints

The primary endpoint is patient narcotic consumption in the PACU after hip arthroscopy. Narcotic consumption will be measured by converting the patient's opioid consumption during their PACU recovery duration into morphine equivalents. This conversion is necessary to standardize different types of narcotics that can be administered in the PACU. We will also be determining the utility of IA morphine and clonidine in decreasing the patient reported pain in the PACU and during the first postoperative week, time until discharge from the PACU, and the quality of patient recovery using the QoR-15 survey.

9.0 Procedures Involved

100 patients will be consented for this study. 50 for the "control group" injection and 50 for the "therapeutic group" injection. For patients who are consented and enrolled in this study, prior to surgery, Dr. Terry will place a written order to the OR pharmacy for the randomized injection. Each order placed will be associated with a sequential study number (1-100) to keep track of each patient and the intervention that they received. The OR pharmacy will randomize the injection into the control or therapeutic group, so as to keep the team involved in patient care blinded to the intervention.

In the preoperative holding area prior to surgery, all patients will be asked to fill out the QoR-15 questionnaire (see Appendix), rate their current level of pain on the Visual Analog Scale (0-10), and be asked if they have taken any pain medication in the past 24 hours. Those in the control group will receive a 11 mL injection of .9% normal saline, and the therapeutic group will receive a 11 mL injection of 10 mg morphine and 100 mcg of clonidine in .9% NaCl solution. Both injections will occur at the conclusion of the hip arthroscopy procedure. All other pre, peri, and postoperative procedures will follow the standard of care.

Postoperatively, pain scores, amount of narcotics used, and discharge times, which are recorded in the patient's medical record as part of standard of care, will be collected. The control group will be compared to the therapeutic group. All postoperative pain management will follow the normal standard of care procedures for hip arthroscopy patients.

Additionally, patients will be sent home with a short "diary" for logging their pain and narcotic consumption in the first week following surgery. They will be rating their pain and logging narcotic consumption at 6, 18, 24, 48 hours, and 7 days postoperatively. This diary will be collected from the patient at their two week follow-up appointment.

The research procedures required for this protocol include the intra-articular injection at the conclusion of the hip arthroscopy procedure. At

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the conclusion of the hip arthroscopy, before closing the incision with sutures, an intra-articular injection of both morphine and clonidine, for the therapeutic group, or normal saline, for the control group, will be performed. All other operative procedures will occur as standard of care to ensure optimal patient safety.

- All standard of care procedures will take place for a hip arthroscopy procedure. No additional procedures are needed to reduce the magnitude of risk, as patients with a contraindication to morphine or clonidine will not be enrolled in the study, and patients will be under the watch of nurses, physician assistants, and doctors while in the postoperative recovery room.
- The only drugs used in this study that are beyond the standard of care for hip arthroscopy are intra-articular morphine and clonidine. In the context of this study, morphine and clonidine are FDA approved drugs for non-approved use. The control group will receive intra-articular normal saline, which is FDA approved.
- Northwestern's Powerchart electronic medical record system will be used to access patient medical records for those who consent to the study. Basic patient demographics, pre and post-op VAS pain scores, discharge times, and narcotic/analgesic consumption will be recorded from data in the medical records. The QoR-15 survey will also be used to assess patient quality of recovery. All data will be coded and stored in the attached Excel spreadsheet, which will be on a database in Dr. Terry's locked office, only accessible to research personnel of the project via an encrypted password. All paper based documents will be kept in a locked cabinet in Dr. Terry's office.

All data collected for this study can be found in the attached MS Excel spreadsheet and sample QoR-15 survey. Data points include age, sex, height, weight, tobacco use, VAS pain scores, discharge times, duration of surgery, discharge criteria score, medication use, and the following quality of recovery scores (as seen in the QoR-15): comfort, independence, and support. The postoperative diary will be asking patients for VAS pain scores, narcotic consumption, and potential complications at 6, 18, 24, 48 hours, and 7 days postoperative.

10.0 Data and Specimen Banking

To maintain patient confidentiality, the study coordinator will assign an arbitrarily generated identification number to each patient. This patient identifier list will be kept separately from the study database on an encrypted computer in Dr. Terry's office. All study data will be entered into an MS Excel Database created by Dr. Terry. The data will be entered into the database in Dr. Terry's office by the research coordinators—no personal information containing identifiers will be used. The consent forms and QoR-15 surveys will be kept in a locked file in Dr. Terry's

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office until the completion of the research project. Only the PI and co-investigators will have access to the coded database. The OR pharmacy will have a numbered list that connects each patient to the intervention that they received via randomization.

In summary, all information that includes personally identifying information, such as name or medical record number, is not entered into the database with the medical information. Identifying information is only entered into a separate database that links the patient to an arbitrary study number. This identifying list will be kept only in Dr. Terry's office, under his control. A separate list will be kept by the OR pharmacy to track which patients received the control or study group intervention. The plan to destroy the identifiers will be accomplished by a program designed to permanently erase "destroy" all subject identifiers after the completion of the study. The paper based data will be placed in a locked bin which will be permanently destroyed by Citadel Management.

No data will be shared with anyone other than the co-investigators of this study.

11.0 Data and Specimen Management

All analyses will use the database with a coded study number as the patient indicator. The data will be analyzed with a Student's T-Test, non-parametric Mann Whitney test, and chi-square test.

All analyses will use the database with a coded study number as the patient indicator. Additionally, all information will be stored in a locked room on a password protected computer. As aforementioned, patient identifiers will be kept separately from medical data. Only the PI will have access to the patient identifier list, and only the PI and co-investigators will have access to the coded database. All non-electronic information, including consent forms, QoR-15 surveys, and patient postoperative diaries will be kept in a locked file cabinet in Dr. Terry's office.

- The data extracted from the chart review will be maintained in a computer that is located in a secure area accessible only by research personnel of the project via an encrypted password. The computer is password protected and logs out the current user if no activity is detected for five minutes. The electronic data storing patient identifying information will be stored on a single password protected computer in Dr. Terry's office in the Department of Orthopedics (676 N. Saint Clair, Suite 1350, Chicago, IL 60611).
- Data will be stored until the completion of the study, whereupon all data with personally identifying health information will be destroyed. All paper based data will be placed in a locked bin to be destroyed by Citadel Management once the study is complete.

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- Only the PI will have access to the patient identifier list, and only the PI and co-investigators will have access to the database for analysis.
- The PI and co-investigators will be the only ones handling data.
- The patient identifier list will never leave the password protected computer in Dr. Terry's locked office. Any electronic transmission of the coded data will occur over Northwestern's secure Microsoft Outlook email service and will only be accessed through Northwestern's secure remote database, FSMFiles.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

12.1 Morphine and clonidine are drugs frequently prescribed for pain management, and as such pose no more than minimal risk to the patient beyond their assumed risks from hip arthroscopy. Both morphine and clonidine are FDA approved drugs for pain management, but they are being injected for a non-approved use (intra-articular injection).

13.0 Withdrawal of Subjects*

13.1 Patients with unforeseen complications due to the standard protocol of hip arthroscopy procedure, which lead to treatment beyond the standard of care, will be removed from the study. Additionally, any patients for whom insufficient data is entered in Powerchart will not be considered for that particular aspect of analysis.

13.2 Any patient who wishes to withdraw from the study may do so at any time. If the patient wishes to withdraw after the procedure has taken place, they must do so in writing to Dr. Terry to prevent use of their coded health information in the study.

13.3 Any patient who wishes to withdraw from the study may do so at any time. If a patient revokes consent after the procedure has already taken place, any data that has already been collected is eligible for use. If the patient wishes to have all of their data removed from the study after revoking consent, they must notify Dr. Terry in writing.

14.0 Risks to Subjects*

IA morphine and clonidine are currently administered as a standard practice to most of Dr. Terry's patients undergoing hip arthroscopy. Prior to January 2015, IA morphine and clonidine were not administered as standard practice. No clear scientific evidence supports or opposes the use of IA morphine and clonidine in hip arthroscopy for postoperative pain management. No patient who has a contraindication to either of these medications will receive it.

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While the potential benefits of pain control are believed to outweigh the mild to moderate side effects, morphine is a narcotic, and related side effects include nausea, vomiting, itching, respiratory depression, low blood pressure, and addiction⁸. Potential side effects of clonidine are less common and include sedation, dizziness, slowed heartbeat, and dry mouth⁹. All aforementioned side effects are temporary until the drug wears off.

In addition, while we have worked hard to protect patient privacy, there is a small risk of potential loss of confidentiality and privacy. The database will be password protected and the computer will be locked. Personal identifying information will not be input into the database with the study data. Study data will be linked to patient name through a separate database using a randomly generated number.

15.0 Potential Benefits to Subjects

A patient is not likely to have any direct benefit from participating in this study. However, the information obtained from the results may aid in understanding and will benefit the future patients as we learn more about hip arthroscopy pain management. The potential benefits of this study outweigh the risks. We believe that the knowledge gained from this study will allow us to better care for our patients and to improve pain management following hip arthroscopy.

16.0 Vulnerable Populations:

N/A

17.0 Community-Based Participatory Research:

N/A

18.0 Sharing of Results with Subjects

18.1 No information regarding the potential therapeutic involvement will be explicitly shared with the patient beyond what is normally shared as per standard postoperative protocol.

19.0 Setting

- All subject identification and recruitment will occur in the preoperative waiting area of the Orthopedic Surgical Center at the 259 E. Erie building associated with Northwestern Medicine.
- All procedures will occur in the operating rooms on the 12th floor of the Orthopedic Surgical Center at the 259 E. Erie building associated with Northwestern Medicine.

20.0 Resources Available

The research team is comprised of board certified orthopedic surgeons, physician assistants, and medical students who all have research experience and knowledge of the facility (259 E. Erie Orthopedic Surgical

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Center) and programs (Powerchart, MS Excel) involved in the study. Additionally, the team is led by a PI with over ten years of experience in orthopedic surgery and patient care. All members of the team are HIPAA trained and certified.

- Due to Dr. Terry's high volume of hip arthroscopy patients (around 100 per six months), it is entirely feasible to recruit 100 patients in the estimated one year period.
- The consenting process and respective statistical analysis should be feasible within an 18 month time frame.
- All procedures will be carried out at Northwestern Medicine's brand new Orthopedic Surgical Center at 259 E. Erie, Chicago, IL. The surgical team has been performing surgeries at this facility since it opened in October 2014.
- All subjects will be under constant watch of trained medical professionals including multiple doctors and nurses while participating in this study. All staff members are trained to deal with adverse events following surgical procedures, and if needed, all patients will be right next door to Northwestern Memorial Hospital for whatever further medical support they may need. Complications with hip arthroscopy are rare.
- All involved investigators and pertinent surgical staff will meet prior to the initiation of the project in order to walk through all phases of the study, including consent, drug administration, and postoperative data collection and patient management. Additionally, the study protocol will be printed out and handed to each member of the team for future reference.

21.0 Prior Approvals

21.1 The process for approval of this randomized controlled trial with clinicaltrials.gov has begun. Completion of the clinicaltrials.gov application is contingent upon IRB approval, and the application is ready for submission upon IRB approval of this clinical trial. Approval for research and funding will be obtained from Northwestern's Orthopaedic Department. The only funding required for this project is the modest price of the morphine and clonidine injection.

22.0 Recruitment Methods

22.1 Patients will be approached on the day of surgery by Dr. Terry or one of the co-investigators and informed about the study. If the patient would like to participate in the study, a written consent will be obtained. Consent cannot be obtained prior to this day because some surgeries are scheduled tentatively or scheduled over the phone. Additionally, the co-investigators obtaining consent are not always present in the office visit prior to surgery.

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- 22.2 All subjects approached to participate in this study will be among Dr. Terry's patient population undergoing hip arthroscopy (as defined in section 3).
- 22.3 All subjects will be identified from the list of patients undergoing hip arthroscopy under Dr. Terry for a particular day.
- 22.4 No payment will be provided to subjects for participating.

23.0 Local Number of Subjects

100. 50 subjects in the therapeutic group. 50 subjects in the control group

24.0 Confidentiality:

N/A, single-center study

25.0 Provisions to Protect the Privacy Interests of Subjects

No information will be asked of patients beyond what is standard of care for hip arthroscopy and the questions in the QoR-15 survey, results of which will only be accessible to the research team. Furthermore, data for this study will only be accessible to the research team through the aforementioned confidentiality procedures.

All patients will be properly informed about the procedure prior to consent and given the opportunity to ask whatever questions they may have to the research investigator asking for consent. Subjects will also be allowed to ask any questions they may have throughout the remainder of their participation in the study. The only question that may not be answered is whether or not the patient was assigned to the control or therapeutic group for internal validity of the study.

All research members are HIPAA certified affiliates of Northwestern (either students or staff) and have personal access to Powerchart and the surgical facility.

26.0 Compensation for Research-Related Injury:

N/A

27.0 Economic Burden to Subjects:

N/A

28.0 Consent Process

- All consent will be obtained in a written format in the preoperative waiting area at 259 E. Erie Chicago, IL.
- "SOP: Informed Consent Process for Research (HRP-090)." will be followed
- Only English speaking subjects will be eligible for consent.
- Cognitively impaired adults will not be eligible for consent

29.0 Process to Document Consent in Writing

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29.1 “SOP: Written Documentation of Consent (HRP-091).” will be followed

30.0 Drugs or Devices

30.1 All storage, handling, and administration of the morphine and clonidine will occur on site at the surgical center of 259 E. Erie Chicago, IL. The on-site operating room (OR) pharmacy follows all USP 797 protocol for sterile compounding and storage. All orders for the randomized injection will be placed prior in the OR pharmacy computer system by Dr. Terry. The on-site pharmacist will then compound the correct dosage (10 mg morphine and 100 mcg clonidine in 11 mL .9% NaCl solution or 11 mL .9% NaCl solution). The OR nurse for the particular patient’s procedure will then bring the injection directly from the pharmacy to the patient’s OR. Administration of the injection will then be done by Dr. Terry. Morphine and clonidine are FDA approved drugs for non-approved use in this study.

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