1. STUDY AIM, BACKGROUND, AND DESIGN ABSTRACT

Open reduction and internal fixation (ORIF) is a common procedure performed by orthopedic surgeons for a variety of indications.[5] Narcotics are widely used for pain control post ORIF. Traditionally, opioid analgesia has been the gold standard for postoperative pain control. However, given the harmful side effect profile and opioid epidemic in the United States, it is advantageous to use alternate forms of analgesia[3]. Multimodal pain control captures the effectiveness of different analgesic modalities and maximizes analgesia while minimizing side effects. The theory behind their use is that agents with different mechanisms of action work synergistically in preventing acute pain. Multimodal pain modalities have been used in orthopaedic trauma in the context of fracture care, as well as with knee and hip arthroplasty[2].

The purpose of the study is to investigate a potentially superior pain control modality in ORIF and its cost saving benefits[1]. Currently methods are effective, but have complication. This could potentially identify a pain control regimen that provides the same or better relief without the risk of complications and with decreased cost. This has the potential to improve patient reported outcomes, patients overall experience with ORIF of the clavicle, and decrease their hospital expenses.

This project aims to compare postoperative pain control in patients in two treatment arms of ORIF of the clavicle: a treatment group given a nonopioid pain control regimen, and a standard of care control group given standard opioid pain control regimen.

1) We aim to compare postoperative pain control following the use of traditional narcotic intervention and a novel nonopioid pain regimen.

2) We aim to review the operative time, blood loss, complications, and operative details of all patients undergoing ORIF following traumatic fractures at our hospital.

3) We aim to compare postoperative pain control interventions by looking at the amount of pain medication required post-op, patient reported pain scores post operatively, and take home patient diaries.

4) We hope to compare the type of pain regimen with amount of opiate use, patients pain score, and speed of rehabilitation and overall cost difference to the health care system.

2. SUBJECT POPULATION AND ELIGIBILITY

Subject Population

All adult patients over age eighteen and scheduled for primary open reduction internal fixation following a traumatic fracture at Henry Ford Hospital (Detroit, Michigan, United States), and Henry Ford West Bloomfield Hospital (West Bloomfield, Michigan, United States) will be eligible for inclusion in this study. All patients will be met in our abulatory orthopedic clinics. All surgeries will be performed by a fellowship trained truama surgeons. Exclusion criteria will include patients with a medical history of known allergies or intolerance to allergies or intolerance to Motrin, Lyrica, Tylenol, tramadol, Zanaflex, substantial alcohol or drug abuse, and pregnancy, history of narcotics within 6 months of surgery, renal impairment, peptic ulcer disease, GI bleeding.

Controls will be chosen from the above inclusion and exclusion criteria and these patients are assigned randomly to the control group of postoperative opioid pain control. Their pain, opioid consumption, and

complication rate will be compared to the treatment arm. This will provide the only scientifically rigorous method by which to assess the effects of nonopioid postoperative pain control regimen.

3. STUDY PROCEDURES

This is a randomized, single blinded, standard of care-controlled clinical trial. All adult patients over eighteen desiring an ORIF following a traumatic fracture will be eligible. Nonnarcotic postoperative pain control regimen described below were chosen based on previous studies in nonopioid postopeartaive management follow common orthopedic procedures[4].

Patients will be consented and recruited according to the inclusion and exclusion criteria described above at their preoperative visit 1-2 weeks prior to their scheduled surgical date. Once participation has been determined and consent obtained, the names of participating patients will be provided to the research pharmacy. Patients will be randomized with a computer-generated table in 2 patient blocks by the research team.

Patients will be divided into one of the following 2 treatment arms: Non-narcotic and Narcotic

Pre-operative pain protocol for all patients: Celebrex 400mg PO, Lyrica 75mg x1 dose pre-op, Tramadol 50mg x 1. All patients will be given the following intraoperative pain injection: Epinephrine 1mg (1mL), 0.5% ropivacaine (60mL), Acetaminophen 1000mg IV, Toradol (30mg) 1cc,

Postoperative day 1:
Mortin – also known as ibuprofen
800 mg every 6 hours; not to exceed 3200 mg/day
Lyrica – also known as pregabalin
75mg q12hr
Tylenol – also known as acetaminophen
1000mg PO q8hr PRN pain
Zanaflex – also know as tizanidine
4mg PO q6hr

Non-Narcotic Group discharge medication:
Weeks 1 and 2:
Motrin - also known as Ibuprofen (for 2 weeks)
800 mg every 6 hours; not to exceed 3200 mg/day
Lyrica (also known as pregabalin) 75mg twice per day for 5 days then wean off as described below
Dispense: 30 tablets at discharge (75mg/tablet)
Days 6-7: morning-75mg; evening- 75mg
Days 8-9: morning-75mg
Days 10: No more Lyrica
Tylenol (also known as acetaminophen) 1000 mg three times per day
Do not exceed a total of 4 grams of Acetaminophen per day.
Zanaflex (also known as tizanidine) 4 mg every 6-12 hours for 2 weeks

Weeks 2 – 4:
Tylenol (also known as acetaminophen) 1000 mg three times per day
Do Not exceed a total of 4 grams of Acetaminophen per day.
Motrin (14 days)

Narcotic Group: Will be given 60 pills of Norco 5-325 q4 hours PRN.

Primary endpoints is reduction in pain as measured by NRS.

If pain is uncontrolled, patients will also be sent home with a prescription with 10 pills of 5 mg of Oxycodone for breakthrough pain. The amount of oxycodone taken will be recorded. Patients can call the resident on call, available 24-hours per day, if additional pain control is needed.

Incisions will be closed in typical fashion and the wound dressed. Following the procedure pain will be accessed subjectively through patient pain journals, nurse recorded pain scores and objectively through narcotic pain requirement. A blind observer will also access outcomes.

Data Analysis and Statistical Considerations

Data analysis will consist of summary statistics between the two patient groups. Intention to treat analysis will be employed when comparing the two arms. Potential confounders will be identified including demographic and functional data). Weighted means will be used with standard deviations and 95% confidence intervals for qualitative data. Categorical variables will be compared using a 2x2 Chi-square test and a p value of <0.05 for statistical signficance.

4. ANTICIPATED RISKS

All patients will be included by informed consent detailing the risks and benefits of multimodal pain regimen administration. The potential loss of privacy is addressed in Section 11 as it pertains to securing confidential information in a locked file and password-encrypted files available only to the investigators. The aforementioned regimen has been used in a similar protocol with no statistically significant increase in side effects.

5. ANTICIPATED BENEFITS

Direct benefits of non-narcotic regimen may include decreased postoperative pain and oral narcotic requirement, as well as a decreased potential for narcotic addiction.

6. RENUMERATION/COMPENSATION

There is no compensation offered

7. COSTS

No increased cost incurred by the patient. All costs outside of standard care will be incurred by departmental research funds.

8. ALTERNATIVES

The alternative to study inclusion (no randomized treatment) will be presented as a perfectly reasonable course of action. There are no other known alternatives for achieving appropriate post-operative pain control following a total shoulder arthroplasty. Patients may not participate in the study if they do not wish to participate.

9. CONSENT PROCESS AND DOCUMENTATION

Patients will be presented with consent for the clinical trial at the time of surgical consent, always performed during the final preoperative office visit 1-2 weeks prior to the surgical date. The subject will have the duration of the office visit to decide on participation. Understanding will be ascertained using the teach-back method of informed surgical consent. Language used in the surgical consent will mimic a sixth grade reading level. The patient must be able to verbally state their diagnosis and planned intervention. The risks and benefits of the proposed treatment will be detailed and the patient must repeat these back to the person obtaining consent. Voluntary withdrawal at any point will be stressed. The alternative to study inclusion (no randomized treatment) will be presented as a perfectly reasonable course of action. Patients will be allowed unlimited time to ask and have their questions answered by an M.D. involved in the study. Non-English speaking persons will be consented according to IRB guidelines in the following manner: A certified non-family member fluent in the patient's native language and English will be present to review the English patient consent form with the patient and a Short Form Consent from the IRB website in the patient's native language. If freely consenting non-English speaking patients represent more than 5 enrolled patients at any point in the study conduction, the full IRB consent form will be translated into the native language of those represented languages and this new consent will be submitted as a "request for planned changes" to the Henry Ford IRB Committee before any further non-English speaking patients are enrolled.

10. WITHDRAWAL OF SUBJECTS

Subjects will be withdrawn from the study if they are unable to tolerate any of the medication prescribed.
Data collection on patients who were withdrawn will be terminated and data destroyed.
Patients may withdraw from the study at any time for any reason without affecting the quality of their care.

11. PRIVACY AND CONFIDENTIALITY

Data will be stored on a password protected HFH computer. Patient data will either be located in the chart or 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. Data will be destroyed following publication or after six months of inactivity. We will also obtain HIPAA authorization in order to access the medical record.

12. DATA AND SAFETY MONITORING PLAN

The principal investigator will perform safety monitoring. Our study does not include mortality as a major endpoint, purport to provide definitive information about efficacy of each nonnarcotic intervention, nor does prior data suggest unacceptable toxicity with the intervention. Previously published data suggests that 75 patients are needed at minimum for determination of statistical significance between two such treatment arms. The principal investigator will be responsible for premature cessation of the study if unacceptably high risks are

incurred (uncontrolled pain, higher rates of cardiovascular or neurological events beyond hospital averages, or any other life-threatening outcomes,). This is consistent with federal guidelines 21 CFR 50.24 and 45 CFR 46.111

Unanticipated Problems and Adverse Events
We will report any problems or adverse events to the IRB via email

13. QUALIFICATIONS OF THE INVESTIGATOR(S)

William Hakeos, MD Medical Education: University of Michigan, Ann Arbor, MI, Residency: Henry Ford Hospital, Detroit, MI, Orthopedic Surgery, Fellowship: Vanderbilt Orthopedic Institute, TN, Truama. Additionally he has conducted and published multiple clinical trials and has extensive experience in the academic arena. The co-investigators are all medical school graduates and current orthopedic residents at HFH. Each has experience with conducting medical research and has multiple recent publications in medical literature.

14. REFERENCES

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4. Moutzouros V, Jildeh T, Khalil L, et al. A Multimodal Protocol to Diminish Pain Following Common Orthopedic Sports Procedures: Can We Eliminate Postoperative Opioids? *Arthroscopy.* 2020.
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