Are NSAIDs effective enough for postoperative pain control after functional endoscopic sinus surgery and septoplasty?

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Protocol Title:	Are NSAIDs effective enough for postoperative pain control after functional endoscopic sinus surgery and septoplasty?
Principal Investigator:	Martin Citardi MD
Co-Investigators:	Alok Saini MD, William Yao MD, Amber Luong MD PhD, Zi Yang Jiang, MD
Study Coordinator:	None
Population:	100 adult patients undergoing functional endoscopic sinus surgery and/or septoplasty with Drs. Citardi, Luong, or Yao at Memorial Hermann-Texas Medical Center and the Plaza Ambulatory Surgery Center will be included
Number of Sites:	Single site / UTHEALTH
Study Duration:	We anticipate recruitment will take 9 months.
Subject Duration:	Each subject will be followed for 5 days after surgery.

General Information

- Endoscopic sinus surgery (ESS) is a common procedure performed in the US with roughly 500,000 cases occurring annually. Many surgeons prescribe opioid pain medications for pain control in the postoperative period. Given the current opioid epidemic, studies ought to determine the true necessity of their use to prevent unnecessary narcotic usage.

Background Information

- Endoscopic sinus surgery is an extraordinarily common procedure performed in the US. Currently, there is no standardized postoperative pain regimen. Generally, most surgeons prescribe opioids for postoperative pain control in patients undergoing functional endoscopic sinus surgery. Traditionally, rhinologists have avoided the use of non-steroidal anti-inflammatory drugs (NSAIDs) due to fear of increased bleeding risks in the postoperative period. However, opioids have their own side effects, including respiratory depression, constipation, addiction, and nausea/vomiting. Recently, our group has found the use of NSAIDs to be safe and effective in the postoperative period. There is now equipoise regarding the medication of choice for pain control after FESS. No definitive study has compared the level of pain control in patients receiving NSAIDs to those receiving opioids in the postoperative period after ESS. In fact, there is a significant paucity of data regarding postoperative pain scores in patients undergoing ESS.
- Our hypothesis is that NSAIDs, specifically diclofenac, are safe and effective in the postoperative period after ESS. We believe that NSAIDs will provide pain relief that is non-inferior to opioids in the days following ESS. To our knowledge, no studies have compared the use of NSAIDs to opioids in the postoperative period following ESS. If our hypothesis is true, this study will provide the basis for a significant shift in prescribing patterns following ESS and obviate the need of opioid usage in the roughly 500,000 patients undergoing ESS annually.

Objectives

- Our primary objective is to compare overall pain score (10 cm visual analog scale) at 24 hours post-surgery between patients receiving diclofenac sodium to those receiving acetaminophen-hydrocodone following ESS and/or septoplasty.
- Secondary objectives will be to compare average, most severe, and least severe 24 hour pain score at 48 hours, 72 hours, and 120 hours post-surgery between patients receiving diclofenac sodium to those receiving acetaminophen-hydrocodone following ESS. Additional secondary objectives will be to determine the rate of bleeding complications in patients receiving diclofenac sodium to those receiving acetaminophen-hydrocodone following ESS as well as noting the rates of constipation and nausea/vomiting in each group.

Study Design

- We propose to perform a randomized, controlled study to compare the safety and efficacy of diclofenac sodium when compared to the acetaminophen-hydrocodone following ESS. Patients will be randomized by computer-generated sequencing in conjunction with a standard envelope system.
- Our primary outcome will be the overall pain score on a 100 mm visual analog scale at 24 hours following ESS.
- Secondary outcome measures will be the overall pain scores, most severe pain score experienced in the 100 mm VAS, and least severe pain score experienced at 48 hours, 72 hours, and 120 hours following ESS. An additional secondary outcome will be the number of bleeding complications as defined as those requiring a trip to the emergency room or requiring intervention or epistaxis as well as rates of constipation and nausea/vomiting among participants in each group.

Study Population

- Inclusion criteria will be English speaking adults (age >18) who are candidates for endoscopic sinus surgery as determined by medical necessity by the treating rhinologist.
- Exclusion criteria will be allergy to either NSAIDs or opioids, contraindication to NSAIDs (ex. gastritis, chronic kidney disease), surgical plan exceeding basic endoscopic sinus surgery, use of anti-coagulation, the presence of any pain disorder, the current usage of any analgesic medication, history of opioid addiction, pregnancy, history of chronic pain or fibromyalgia, current daily use of NSAIDs, acetaminophen, opioids or other analgesics (pregabalin, tramadol, etc).
- All patients scheduled for surgery will be offered inclusion in the study.

Study Procedures

- This study will require no additional study visits beyond the routine clinical postoperative visits.
- An electronic REDCap database will be created and postoperative pain surveys will be emailed to each patient at 24 hours, 48 hours, 72 hours, and 120 hours post-ESS.
- Background information including age, sex, history of migraines, temporomandibular joint disorder, fibromyalgia, pain disorders and the current use of pain medication or NSAIDs will be input into the REDCap database prior to surgery.

Data and Safety Monitoring

- No adverse events are expected. Epistaxis after ESS is not uncommon and patients receive instructions regarding postoperative epistaxis as standard procedure.
- Any unexpected events (including adverse events, protocol deviations, other problems) will be reported directly to the principal investigator at the time of the incident.

- On the first day of every month after study initiation, information regarding bleeding events experienced postoperatively will be reviewed. In the event of a >5% increase in bleeding rate in the group receiving diclofenac, the study will be halted.

Statistics

- Based off of a small pilot series of 9 patients, the means score 24 hours after FESS was 30 with a range of 10-75 and standard deviation of 22.8.
- Sample calculations were performed for a non-inferiority limit of 15mm on the 100mm VAS score, 90% power, alpha of 0.025, with an estimated standard deviation of 22.8.
- 41 patients are calculated to be required in each group for a total patient count of 82
- Due to roughly an anticipated 10% dropout (failure to complete survey at 24 hours), we plan to recruite 100 patients
- Interim analysis for safety purposes will only be performed via the proportionality test for epistaxis requiring unplanned visits to the emergency room or physician's office. The anticipated baseline rate for this complication is 1% each month of the trial. The trial will be terminated if a significant number of epistaxis beyond the baseline is found in the NSAID group.
- Analysis for primary and secondary outcomes will be performed via a t-test for two independent means for pain scores at 24, 48, 72, and 120 hours after FESS
- Analysis of other secondary outcomes of patients' experiences with epistaxis, constipation, and nausea/vomiting is to be done via the proportionality test
- All randomized subjects with returned questionnaires will be included in the statistical analysis.
- Analysis is performed with STATA 14 (College Station, TX)

Ethics

- IRB approval will be sought from CPHS.
- Patients will be offered inclusion in the clinic and will be consented at that time if they elect to participate.

Data handling and record keeping

- All data will be maintained in the UTHEALTH REDCap database. Data will only be accessible by the principal investigator and co-investigator Saini.
- The only identifying information that will be stored in the REDCap database will be the patient's Allscripts MRN and email address. Once all information is collected, medical record numbers and email addresses will be removed from the dataset so that the information is no longer identifiable.

Quality control and assurance

- Co-investigator Saini will aggregate data directly from Allscripts for input into the REDCap database. This will ensure that data is accurate, consistent, complete and reliable.
- There are no plans to have ongoing third party monitoring.

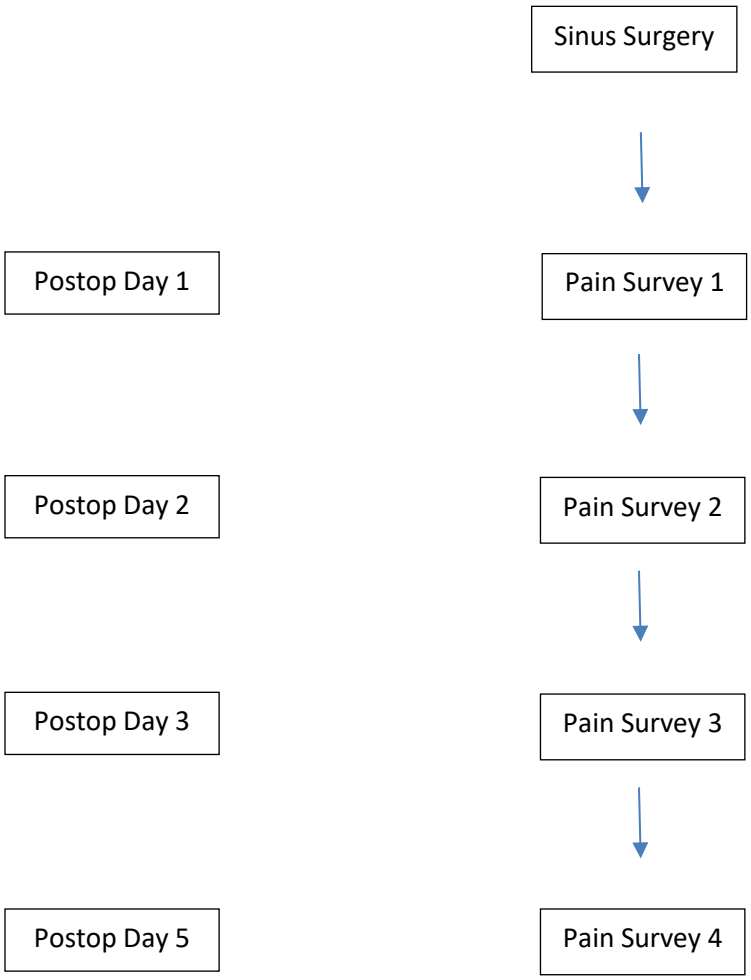
Publication Plan

- The study results will be submitted to the American Rhinologic Society for oral presentation for the Spring 2019 meeting.
- The results will not be directly returned to the study participants.

ATTACHMENTS

1. Schematic of Study Design
2. Study Schedule
3. Consent Document
4. Case Report Form

Schematic Design of Study



Study Schedule

1. Study Initiates: April 1, 2018
2. Data Collection Concludes January 1, 2018
3. Data Analysis Complete February 1, 2018
4. Submission for Publication March 1, 2018