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Prospective Randomized Trial comparing Narcotics vs NSAIDs for post-operative analgesia in outpatient Rhinoplasty

Purpose of the Study and Background

Hypothesis

That narcotic pain medication is not required to treat post-operative pain in outpatient rhinoplasty.

Purpose of the Study

The purpose of this study is to compare the efficacy and safety of oral opiate pain medication vs non-steroidal anti-inflammatory drugs (NSAIDs) in the treatment of postoperative rhinoplasty pain. This study will also evaluate potential contributing factors affecting the efficacy of these pain control methods.

Background

With the rise of opioid addiction within the United States and its adverse consequences, limiting or eliminating narcotic prescriptions after outpatient surgery should be a priority for all surgeons. In 2012, 4.2 billion prescriptions were written in the United States, 289 million (6.8%) for opioids[1], and of which hydrocodone was the number one most prescribed medication [2]. It is believed there are 3.8 million misusers of pain relievers[3], resulting in a prescription opioid abuse problem costing an estimated 55.7 billion dollars[4]. All physicians, including otolaryngologists, must find effective ways to combat this epidemic, while still providing appropriate postoperative care. As ambulatory procedures make up the majority of otolaryngologic surgeries performed in the United States, limiting or eliminating narcotic prescriptions for these cases should be a primary goal amongst otolaryngologists.

Rhinoplasty and septorhinoplasty are common procedures performed by Otolaryngologist and facial plastic surgeons with generally low complication rates. There is little data describing a patient's post-operative pain course. The majority of these procedures are performed at outpatient surgical centers or in an ambulatory hospital setting with immediate discharge home after recovery. Otolaryngologists routinely prescribe opioids for these procedures without an understanding of their patients' requirements for pain medications. This leads to overprescribing and eventual left-over narcotics. A recent study found 67% of patients had surplus narcotics from the initial prescription and 91% of those patients kept that medication at home following urological surgery[5]. Additionally, another study found that patients after upper extremity surgical procedures relating to soft tissue only required a mean 5.1 opioid pills after surgery and in general patients were being prescribed 3 times greater the amount of opioid medications than needed [4]. Currently at New York University Langone Hospital, it is standard practice to prescribe >12 narcotic pills to patients undergoing most procedures; however, there are no guidelines or criteria to assist in managing our patients' post-operative pain medications.

Study Design

The study is a prospective, randomized, clinical trial enrolling patients undergoing rhinoplasty or septorhinoplasty with Dr. Judy Lee, Dr. Jeffrey Markey or Dr. Matthew White in the Department of

Otolaryngology-Head and Neck Surgery at New York University. The length of the study participation will be approximately 1 week for each patient.

The randomization process will involve using Microsoft Excel rand() function, which generates and evenly distributed random decimal x between 0 and 1. If $0 < x < 0.5$, the patient will be randomized to the NSAID group. If $0.5 <= x < 1$, the patient will be randomized to the Norco group. This will be performed after a patient agrees and consents to participation in this study.

Patients will qualify for surgery if they require a septorhinoplasty for nasal airway obstruction or choose to undergo a rhinoplasty for cosmetic purposes. All patients who are recommended a rhinoplasty will be offered participation in this randomized clinical trial. After their surgery, all patients will be discharged home. Patients will be randomized into the opioid or NSAID arm of the trial. The control arm will be prescribed 20 tablets of Hydrocodone 5mg-Acetaminophen 325mg (Norco) and the test arm prescribed Ibuprofen 400mg for post-operative pain. Patients will be contacted via telephone on post-operative day 0 and post-operative day 1 and then seen in the office on post-operative day 7 to evaluate the patients. Each patient will be asked regarding their level of comfort or discomfort, and how effective they feel their pain regiment is. Outcome measure will be both objective and subjective. A pain scale from 0-10 will be utilized to assess a patient's pain objectively. Additionally, each patient will be asked if they felt their pain was subjectively controlled (yes/no). In each arm, a survey will be used to assess the frequency of usage, the dose, timing and amount of the specific analgesic consumed. Patients within the NSAID arm of the trial will have the ability to speak with their surgeon to escalate their level of analgesia if their pain is unable to be controlled on any post-operative day. This will be recorded in the results. Additional outcome measures will be recorded such as open vs closed rhinoplasty, use of osteotomies, concurrent septoplasty or turbinate reduction. Adverse effects, complications and demographics will also be examined.

Characteristics of the Research Population

Number of subjects (

We used similar previous studies to predict baseline pain scores as well as expected improvements after surgery[6,7]. With 30 subjects for each group, we can detect the difference between the intervention group with mean 1.6 and the control group with mean 2.6 (SD=1.3) by assuming a 80% power and 5% type-I error under a two-sided Two-Sample T-Test

Numeric Results for Two-Sample T-Test
Null Hypothesis: Mean1=Mean2. Alternative Hypothesis: Mean1<>Mean2
The standard deviations were assumed to be unknown and equal.

			Allocation						
Power	**N1**	**N2**	**Ratio**	**Alpha**	**Beta**	**Mean1**	**Mean2**	**S1**	**S2**
0.80000	25	25	1.000	0.05000	0.20000	2.6	1.5	1.3	1.3
0.80000	30	30	1.000	0.05000	0.20000	2.6	1.5	1.3	1.3
0.80000	35	35	1.000	0.05000	0.20000	2.6	1.7	1.3	1.3

Gender of subjects

The gender of subjects should be roughly equal within each treatment arm

Age of Subjects

Patients will be between the ages of 18-70.

Racial and Ethnic Origin

Patients should be a representative group across all racial and ethnic origins. There are no exclusion criteria based on race or ethnicity.

Inclusion Criteria

Patients 18-70 years old undergoing septorhinoplasty or rhinoplasty for either obstructive or aesthetic reasons. All approaches to rhinoplasty and surgical techniques utilized will be included. This will include patients that undergo additional procedures during the rhinoplasty including osteotomies, turbinate reduction, septoplasty, nasal valve repair and ear cartilage graft. These procedures are commonly performed as part of the rhinoplasty.

Exclusion Criteria

Patients who undergo a rhinoplasty requiring a rib cartilage graft for the procedure as this is known to cause significant pleuritic chest pain. Additionally, patients receiving functional endoscopic sinus surgery concurrently with the rhinoplasty will be excluded. Patients with known history of gastrointestinal bleeds, peptic ulcer disease or who have other comorbidities that prevent them from taking NSAIDs. Patients with a history of radiation, active head and neck malignancy or other pain disorders such as various rheumatologic diseases will be excluded to decrease confounding factors in the control of pain. Anyone who is allergic to either of the medications.

Vulnerable Subjects

There will be no vulnerable subjects enrolled in this study

Methods and Procedures

Methods and Procedures

The rhinoplasties and surgical techniques involved will be performed at the surgeons' discretion, utilizing either an open or closed approach. Incision types, cartilage grafts, techniques and correction methods will be determined by the surgeon for each individual patient and no patient will be excluded based on the techniques used. Nasal splints may be used in the patient's nose based on the procedures performed. All patients post operatively will have an aquaplast nasal splint placed over the bridge of their nose in the standard fashion. Patients will then be given and instructed on pain medication use depending on the treatment arm in which they were placed. The narcotic group will be given a prescription for twenty Norco tablets (5mg hydrocodone- 325mg acetaminophen) and be told to take for pain every 4-6 hours as needed. This is consistent with the standard of care within the department and follows the manufacturer labeling for pain management The NSAID treatment arm will be instructed to take 400mg Ibuprofen

every 4-6 hours for pain as needed consistent with the manufacturer labeling and the American Pain society use. All patients will be contacted on POD0 and POD1 to determine what their pain score is on a numerical scale and whether or not they believe their pain control has been effective. Patients within the NSAID treatment arm, at any point post operatively, will be able to request a prescription for narcotics if they feel that their pain is not well controlled. On POD7, the patients will be given a survey to document the total number of doses of pain medication taken (1 Norco tab vs 400mg Ibuprofen), number of days requiring pain medication, need to call for a prescription and side effects noted. The study for each patient will be concluded at that time point.

Data Analysis and Data Monitoring

Data analysis will be performed with the help of Binhuan Wang, a biostatician at NYU affiliated with the Department of Otolaryngology. He will not have any access to PHI, and will only be given de-identified patient data. The primary outcome to be compared will be the overall pain control based on the pain scale using a two-sample proportion test. We will also compare complication rates, necessity of a patient phone call, and subjective pain control.

Data Storage and Confidentiality

Data storage will be kept in a REDCAP database file. This ensures patient confidentiality. Any presentations or papers will not include any protected health information (PHI). Patient information entered into the database will include demographic information as well type of surgery performed, any complications, and survey results. Only Dr. Lee, Dr. Garber, Dr. White and Dr. Markey will be granted access to entering information into this database file. These individuals will have access to the linking key.

Risk/Benefit Assessment

Subject Safety

Patients will be monitored for safety by each specific surgeon performing their case. They will see their patients in the postoperative period based on current standard of care, and will address any complications that their patients may have. Complications will be treated with the current standard of care.

Any patient within the treatment arm requiring higher levels of pain control will be allowed to have a prescription called by their primary surgeon, as needed. These patients' data will be included and used as a secondary outcome measure to compare.

Risks

NSAIDs are known to cause an increased risk of gastrointestinal adverse events including bleeding, ulceration and perforation of the stomach or intestines. Additionally, other adverse reactions include heartburn, nausea, dyspepsia, vomiting.

Norco, as with all opioid medications have a risk associated with addiction, abuse and misuse. Additionally, they can cause respiratory depression. The acetaminophen within Norco has been associated with liver failure.

The risk of randomization exists in any randomized study. It is possible that one treatment is superior, or that one treatment poses additional risk compared to the other. These outcomes will be monitored at regular intervals throughout the study, as described in the data safety monitoring plan.

Protection against risks

Patients that enroll in this study are not subject to any additional risks than they would encounter if they underwent rhinoplasty without involvement in the study. For patients in the treatment group, they will have the option to increase their pain medication regiment, as needed. The primary surgeon will electronically prescribe pain medication for the patient if they feel at any point during their study that their pain is not managed appropriately. This will be explained to the patients prior to enrolling within the study. Additionally, all patients will be informed of the side effects and risk factors associated with narcotic and NSAID use prior to the surgery. Patients will be monitored on POD0, POD1 and POD7, and will have the ability to contact their physicians if they notice any side effects or problems related to the pain medications that are listed above.

Potential Benefits to the subjects

The patients benefit by potentially not requiring the use of narcotics and the known side effects related to narcotics. Decreasing narcotic use can lead to less addiction and abuse within society.

Data Safety monitoring plan

Data and adverse events will be monitored by the principal investigator, who has performed hundreds of rhinoplasty procedures. Adverse events will include post-operative bleeding, infection, significant gastrointestinal illness related to NSAIDs such as bleeding, ulceration or perforation or events of respiratory depression or liver failure related to Norco use. Any adverse events will be recorded in the patient's chart and within the REDCAP database. Safety information will be collected at the postoperative clinic visits (POD0, POD1, and POD7). Reportable Adverse events will be reported within 48 hours of their occurrence.

Interim analysis of the data will be conducted every 2 months to assess safety and/or identify whether a treatment arm demonstrates superiority in efficacy. The treatment outcomes, as well as complications, will be routinely analyzed at these intervals. If, after a minimum of 15 subjects in each arm, one treatment arm is statistically significant in pain control on the objective pain scale of 1-10 (based on a t-test comparing two means), the study will be closed early. Additionally, if it is determined that the risk of a major complication is significantly higher in one arm compared to the other (based on a Fisher's exact test), the study will be closed early. . A major complication would be respiratory depression requiring hospitalization, significant bleeding event, or a reaction related to the pain medications requiring hospitalization. The reason for the minimum number of subjects as stated above is to avoid statistical error due to sample size.

These interim analyses of data safety monitoring will be communicated to the IRB via email.

Subject Identification, Recruitment and Consent/Assent

Method of Subject Identification and Recruitment
Patients presenting to the offices of Dr. Judy Lee, Dr. Jeffrey Markey or Dr. Matthew White requiring a septorhinoplasty or rhinoplasty for nasal obstruction or cosmetic deformity, with or without septal deviation. Each clinician will be part of the recruitment process and will be the ones to explain the study to each patient.

Process of Consent
Each clinician will explain the study and both parts of the trial to each patient. The clinicians will explain the consent form to each patient. This will be done privately during their office visit. The patients will be scheduled for surgery after this office visit. If the patient is agreeable to the study, they will sign the consent form for the trial and surgery at a pre-operative visit

Subject Capacity
This study involves only patients who are capable of making their own medical decisions and are able to sign their own consent forms.

Subject/Representative Comprehension
Patients will only be eligible for study participation if they are able to demonstrate comprehension of the risks, benefits, and alternatives of surgery, as well as the risks, benefits, and alternatives of being involved in this study.

Debriefing Procedures
After the completion of the study, patients will be informed of the outcomes from the trial.

Consent Forms
Each patient will be required to understand and sign a consent form for enrollment in this study. In addition, they will sign another consent form for surgery.

Documentation of Consent
All study consent forms will be kept on file in Dr. Judy Lee's office

Costs to the Subject
There are no additional costs to the subject. The subject and/or their health insurance may be billed for the costs of medical care during this study if these expenses would have happened even if they were not in the study, or if their insurance agrees in advance to pay. These costs will be billed to their insurance company. If the subject's insurance does not cover these costs or they do not have insurance, these costs will be the subject's responsibility.

Payment for Participation
Patients will not be paid or incentivized for participation in this study.

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