Study Protocol with Statistical Analysis Plan

Study Ttitle: Post-operative Pain Control with Sphenopalatine Ganglion Nerve Block in Septorhinoplasty Patients

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IRB Protocol

1. **Project Title**: Post-operative pain control with sphenopalatine ganglion nerve block in septorhinoplasty patients

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3. Abstract:

Nasal septoplasty is a very common procedure performed by both otolaryngology and plastic surgery. This functional procedure is typically performed for nasal obstruction caused by septal deviation and may also be performed during aesthetic rhinoplasties or endoscopic sinus surgeries for greater exposure and access. Post-operative pain after septoplasty or septorhinoplasty, is generally mild with more moderate pain reported within the first 24-48 hours after surgery (1,2). Maxillary nerve blocks have been shown to significantly reduce post-operative pain within and analgesic intake during the 24-hour period following endoscopic sinus surgery (3, 4). This randomized, double-blinded, placebo-controlled study will investigate blocks of the pterygopalatine fossa bilaterally using a suprazygomatic approach. It is our hypothesis that this technique will result in decreased post-operative pain, post-operative opioid use, and the morbidity that is associated with it.

4. Background:

Nasal septoplasty is a very common procedure performed by both otolaryngology and plastic surgery (5). This procedure is commonly performed as a functional surgery to correct septal deviation and improve nasal obstruction but is also routinely performed along with aesthetic rhinoplasties. Notable post-operative complications include bleeding, septal hematomas, and septal perforations. Post-operative pain is generally mild following septoplasty or septorhinoplasty and is reported to be worse within the first 24-48 hours. Typical pain management following septoplasty or septorhinoplasty include narcotic and non-narcotic analgesics including oxycodone, hydrocodone, acetaminophen, and ibuprofen. Despite multimodal pain control, uncontrolled post-operative pain is reported and may be related to procedural complaints, delayed return to work and even hospital readmissions (4). The number of narcotic pain pills prescribed to patients can vary greatly. One study concluded that 11 opioid tablets were sufficient to control post-operative pain after septoplasty and rhinoplasty procedures (6), however, patients are typically prescribed a range of 20 – 30 pills post-operatively (7).

Maxillary nerve blocks have been shown to significantly reduce post-operative pain and analgesic use within the 24 hour period following endoscopic sinus surgery (3,4). It has also been described for pediatric cleft palate repair with excellent control of post-operative pain compared to systemic analgesics (8-11). The need for post-operative morphine was completely eradicated in one study (11) The effects of local anesthetic have been noted to have effects on pain for up to 10 days after injection, long after the local anesthetic wears off (8). The suprazygomatic approach to the pterygopalatine fossa is a technically easy procedure to perform with ultrasound guidance, with an average procedure time of 56 seconds (10). Suprazygomatic approaches to the pterygopalatine fossa have been associated with fewer complications than infrazygomatic approaches, which include orbital puncture, intracranial injection, maxillary artery puncture, or posterior pharyngeal wall injury (8). Using a suprazygomatic approach and ultrasound guidance, Sola et. al. experienced zero technical complications after 50 blocks (10).

Literature review produced no studies to date on the efficacy of suprazygomatic maxillary nerve blocks for the management of post-operative septorhinoplasty pain control. We currently perform SPG blocks in septorhinoplasty patients based on surgeon and anesthesiology discretion, as well as patients agreement on receiving block, but we currently do not have a standardized way of determining if pain is being controlled in a meaningful way, ie reducing the number the narcotics required post-operatively or reducing the PACU length of stay. Our aim is to conduct a prospective randomized controlled trial using bilateral suprazygomatic maxillary nerve blocks to control post-operative pain in adult patients undergoing septoplasty or septorhinoplasty. We hypothesize that using maxillary nerve blocks in adult patients is a safe and effective way to manage post-operative pain, decreasing complications, post-operative opioid use, and the morbidity that is associated with it.

5. Specific Aims:

The primary aims of this study are to demonstrate in a prospective, randomized, controlled trial, that the application of bilateral suprazygomatic maxillary nerve blockade can safely and effectively:

1) decrease the opioid requirement post-operatively

Secondary objectives are to demonstrate
1) a decrease in post-anesthesia care unit observation time
2) efficiency of SMS based survey for post-operative data collection

6. Research Plan:

PARTICIPANT SELECTION CRITERIA:

The PI and co-investigators already routinely do sphenopalatine ganglion nerve block in our septorhinoplasty patients. All patients undergoing septorhinoplasty who met the inclusion/exclusion criteria (see below) will be offered the opportunity to participate in the study. These patients will initially be approached at their pre-operative surgical visit by the surgical team about their potential interest in participating in the study. If they express interest, consent will be obtained by a surgeon involved in the study during the pre-operative clinic visit. If consent is unable to be obtained by the surgeon prior to surgery, it will be obtained on the day of surgery by a member of the Acute Pain Service to avoid the potential for perceived coercion – that somehow the performance of the operation will be dependent on their participation in the study.

Inclusion criteria shall be as follows:
1) Patient presenting for open or endoscopic septorhinoplasty
2) Age 18-80
3) Normal oral food and water intake before surgery
4) ASA physical classification 1-3

Exclusion criteria shall be as follows:
1) Refusal to consent
2) Patients without a cellular phone or who are unable to accept text messages
3) Allergy to opioid narcotics
4) ASA physical classification of 4 or higher
5) Patient requires other surgery in addition to septorhinoplasty
6) Age > 80 or <18
7) Any underlying chronic pain condition or ongoing opioid use over the preceding 3 months
8) Presence of any other factor which, at the discretion of any member of the study team, makes the patient a poor candidate for block placement.
9) Presence of any other factor which, at the discretion of any member of the study team, makes the patient a poor candidate for research participation.
10) Pregnant women

The ASA physical classification is a routine part of anesthesia per-operative evaluation. This information will be extracted from the anesthesia pre-operative evaluation note.

Nerve block injections will be performed as described below under 'study procedures' by either faculty or fellows in the division of Acute and Perioperative Pain Medicine, who are part of the study team, under the direction of one of the faculty members.

STUDY PROCEDURES:

Those that consent to participate will be randomized to either

Group 1: a single injection into the pterygopalatine fossa bilaterally of 0.5% ropivacaine at a dose of 20 mg (each side) in 4-mL solution plus 1 mL of 4 mg dexamethasone. This will be done after the conclusion of the operation but prior to emergence from anesthesia

or

Group 2: a single injection into the pterygopalatine fossa bilaterally of a balanced crystalloid intravenous solution (4 ml of normal saline) plus 4 mg dexamethasone (each side). This will be done after the conclusion of the operation but prior to emergence from anesthesia.

During the block placement the surgical team will be asked to leave the operating room briefly so that they can remain blinded to the group assignment of all patients as the surgical team will manage the subjects post-operative care and determine discharge readiness.

The group 1 injection procedure will be performed as follows: after preparation of the skin using appropriate skin preparation solution and using aseptic technique, a small-gauge spinal needle will be advanced into the pterygopalatine fossa under ultrasound guidance. Once the needle is properly positioned, 0.5% ropivacaine will be administered at a dose of 20 mg plus 4 mg dexamethasone and the needle will be removed. This procedure will be performed bilaterally.

In group 2 the same procedure will be performed, but the injectate will consist of 5 mL of a balanced crystalloid intravenous solution (4 ml of normal saline) plus 1 mL of 4 mg dexamethasone (each side). This procedure will be performed bilaterally.

Four mL of balanced crystalloid solution plus 1 mL dexamethasone 4mg/mL was chosen as placebo therapy for the control group to aid in blinding since its appearance is identical to ropivacaine plus dexamethasone, to administer the dexamethasone to all patients in the same fashion, and to ensure that effects attributed to the block are a result of the administration of local anesthetic rather than compression neuropraxia from the injection of any material into the pterygopalatine fossa.

Additionally, after induction with general anesthesia, both group 1 and 2 will receive 8 mg of dexamethasone intravenously to reduce PONV and post-operative edema at the surgical site. Dexamethasone when added to nerve blocks has been demonstrated to be neuroprotective, and patients randomized to the placebo arm should also benefit from the neuroprotective effects of the perineural dexamethasone. This is being done in both groups to keep everything as controlled as possible and as mentioned above, to reduce post-operative nausea and vomiting and edema, which would be given regardless of study participation.

Both active treatment and placebo groups will receive bilateral injections of a total volume of 5 mL into the pterygopalatine fossa.

No other changes to the subject's clinical care will be made. All patients will receive the standard of care for pain management for septorhinoplasty, which is 3 days of opioid narcotics (typically oxycodone or hydrocodone) plus over the counter analgesics including acetaminophen and ibuprofen. All opioids will be prescribed as PRN. PACU nursing staff will be informed of patient's participation in the study but will not be informed as to group assignment so that they can remain blinded.

There will be no procedure note by the anesthesiologist describing the placement of the block. The anesthesiologist will write a note describing the subject's participation in the study with accompanying contact information in the event that the blind must be broken. A sign will also be placed at the head of bed indicating that the subject is a study participant and may have received the bilateral suprazygomatic maxillary nerve blockade with the PIs contact information.
Data will be collected including, the time after leaving the operating room to first taking anything by mouth, at what time point did the patient first meet established readiness-for-discharge criteria (return to preoperative baseline oral food/liquid intake AND pain well-controlled with only oral medication) and at what time were they actually discharged. Additionally, information regarding pain scores and analgesic administration, both intraoperative and post-operative, will be gathered from the patient chart for the duration of their admission.

Patients will be sent a survey link via short message service (SMS) to their mobile device on POD 1, 3, and 5. Surveys will be created and distributed to participants using REDCap, a HIPAA compliant and secure platform, and distributed to participants through a third-party system Twilio. For security and privacy concerns, SMS transcriptions do not stay in Twilio's logs and are removed shortly after being completed. Surveys will be composed of 7 questions related to pain at its worst, pain at its least, average pain, current pain, as well as how many narcotic pain pills were consumed within the last 24 hours and what other pain medications were taken, ie acetaminophen, ibuprofen, etc. Relevant questions were adapted from the Brief Pain Inventory (short form) pain assessment. Data will be analyzed using the JMP statistical software package. Each survey will be the exact same set of questions. Patients will be advised to bring their opioid prescription bottle to their post-operative follow up visit and will be asked the same survey of questions during this visit. Additional data will be obtained through patient charting and may include any reported complications, PACU nurse notes, and phone calls to on call providers.

Outcome Measures:

The outcome measures for this study will be: decreased post-operative pain, reduced post anesthesia care unit recovery stays, and post-operative opioid use, as well as the morbidity that is associated with it, in patients undergoing septorhinoplasty surgery.

Table of Study Events

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Activity	Screening	Pre-Op	Intra-Op	Post-Op
Consent	X			
Randomization		X		
Group 1: Suprazygomatic maxillary nerve block			X	
Group 2: Placebo injection with normal saline			X	
Data Collection				X
Data Analysis				X

STATISTICAL METHODS, DATA ANALYSIS, AND INTERPRETATION:
Data will be collected from the patient record regarding the primary and secondary study aims, as well as demographic information including age, sex, height, weight, and BMI on a daily basis for the duration of the hospital admission. Data will be analyzed using ANOVA, ANCOVA and mixed-models repeated-measures ANOVA techniques using the JMP statistical software package from SAS Labs.

Given that these outcomes, to the best of the study team's knowledge, have not been studied previously, no preliminary data exist on which to base power or sample size calculations, and this study is designed to collect such preliminary data on which future studies could be built. That being the case, there is no sample size calculation here. We request permission to enroll 50 patients per group into this study as previous studies involving similar blocks of the maxillary nerve have used group sizes of 20-30.

DATA STORAGE AND DE-IDENTIFICATION PLANS:
Protected health information will be accessed by study team members until data collection is complete, at which point all patients will be de-identified. All retained records will be stored on password-secured data storage devices in accordance with UF policies. Patient contact information stored within REDCap will include participants mobile phone number and medical record numbers. No other patient identifier will be inputted in the REDCap system such as name, date of birth.

7. Possible Discomforts and Risks:

As with any needle puncture of the skin, there is always a minute risk of infection or bleeding. In this case, there is a very limited number of structures within the pterygopalatine fossa. Those include the nerves being targeted by the block, the maxillary artery, and a small amount of fat. In this case, infection risk is minimized with chlorhexidine skin prep as would be used for surgery and the entire procedure is performed using aseptic technique. The risk of bleeding is extremely low. There is only one named vessel in the pterygopalatine fossa: the maxillary artery. This vessel is so small that it cannot routinely be identified on ultrasound, so contacting it with a needle is extremely rare. An inadvertent arterial puncture is one of minimal to no consequence given that both the pterygopalatine fossa is not a contained space and the needle being used is so small that any injury seals almost instantly. This approach makes inadvertent placement of the needle anywhere other than where it is intended extremely unlikely as there is a very limited number of structures within the pterygopalatine fossa. The only tissue along the needle path is the superficial tissue layers (skin, muscle), the tissues of interest, and bone. Needle contact with bone indicates that the needle should be withdrawn approximately 2mm and guiding the needle to be properly positioned. There is a risk of feeling pressure in the area of the block due to the injection of the nerve block as well as feelings of facial numbness due to the nerve block. All nerve blocks will be performed using real-time ultrasound guidance for visualization of the pterygopalatine fossa and the spread of the local anesthetic in the fossa.

Placement of saline:
As with any needle puncture of the skin, there is always a minute risk of infection or bleeding. In this case, infection risk is minimized with chlorhexidine skin prep as would be used for surgery and the entire procedure is performed using aseptic technique. The risk of bleeding is extremely low. There is a risk of feeling pressure in the area of the saline injection.

There is a risk of patient contact information being breeched, ie mobile phone number and medical record number, though risk is minimal. The REDCap platform is HIPAA compliant with a secure server. Database access requires user authentication and password login. REDCap and Twilio are both IRB and UF Privacy Office approved for collection and storage of PHI including surveys.

Data Safety Monitoring Board:
The PI and lead co-investigators (Drs. Palomo and Smith) will meet at least once a month to review for any adverse events. A written report be generated.

8. Possible Benefits:

Participants randomized to the active nerve block arm can expect to experience less pain post-operatively. It is the hope of the investigators that this will also translate into decreased opioid consumption and a decrease in the number in opioid tablet prescriptions minimizing risk for potential abuse. If the findings are as expected, the investigators believe that this work may ultimately result in a change in the standard of care for patients undergoing septoplasty or septorhinoplasty, helping to improve patient comfort and safety.

9. Conflict of Interest:

No investigators have a conflict of interest.

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