Study Protocol and Statistical Analysis Plan

The Effect of IV NSAID's and Corticosteroids on Dysphasia and Dysphonia Following ASDF

NCT04650893

Recent Date of Approval : 1/19/2023

Study Protocol

Background & Rationale

Dysphagia and dysphonia are the most common postoperative complications following anterior cervical discectomy and fusion (ACDF). While most postoperative dysphagia and dysphonia is transient, severe cases place the patient at risk for malnutrition, aspiration, pneumonia, airway obstruction, persistent cough, and death. The reported prevalence of dysphagia varies from 3% to 67% and dysphonia from 1% to 51%. The variability is a result of the different ways in which dysphagia and dysphonia are measured and defined. There are many different classification systems for dysphagia, the Eating Assessment Tool-10 (EAT-10) has proven to be reliable, valid, treatment-responsive, and multiculturally versatile. Scores of 3 or greater qualify as clinically relevant dysphagia and scores of 15 or greater qualify as severe dysphagia, which is associated with a higher risk of aspiration. The Voice Handicap Index-10 (VHI-10) has proven to be reliable, valid, and expedient tool to evaluate for dysphonia. Scores greater than 11 are indicative of clinically significant dysphonia. Recent research suggests that these are appropriate patient reported outcome measures (PROMs) to evaluate for dysphagia and dysphonia after cervical spine surgery. Local and intravenous (IV) steroids have been shown to reduce dysphagia and prevertebral soft-tissue swelling following ACDF. A recent study compared the efficacy of local versus intravenous steroids on the likelihood of developing dysphagia and dysphonia after ACDF. It found that both yielded better PROMs for dysphagia compared the control group, with a reduced number of patients reporting severe dysphagia with local steroid application within the first 2 weeks post-op. Local corticosteroids have been associated with impaired wound healing, esophageal complications, and pseudoarthrosis, particularly when administered in the retropharyngeal space. In the study mentioned above, 2 patients in the local corticosteroid group (out of 29 total) developed pseudoarthrosis. Perioperative ketorolac has been shown to have no adverse effect on spinal fusion when administered for < 2 days, or for >2 days at a dose of < 120 mg/day. Current standard of care processes include both IV or local steroid use as well as no steroid use in decreasing the risks of dysphagia or dysphonia post operatively. There are no current specific or routinely used methods in using steroid or no steroidal treatments to those receiving this surgical procedure.

Objectives

The purpose of this study is to assess the efficacy of intraoperative intravenous nonsteroidal anti-inflammatory drug (ketorolac) versus intravenous (dexamethasone) administration on dysphagia and dysphonia after ACDF. Primary measures for dysphagia include the classification of the Bazaz and EAT-10 outcome results. The primary measures for Dysphonia will be analyzed by the Voice Handicap Index (VHI-10). Secondary measurements include result classification utilizing results from the Neck Disability Index(NDI) and Visual Analogue Pain Scale (VAS) for neck pain. Additional measurements to be analyzed are comparisons in complication factors in surgical site infection, need for re-operation and pseudoarthrosis.

Design

An on-line randomization generator will be used www.researchrandomizer.org.

Randomization will be an equal split between the three groups with no predictable pattern. The subject has a one in three chance of being randomized to any of the three different groups.

Subjects are blinded to the randomization assignment. This is a single blinded study. The treating physician and study personnel will know which group the subject is randomized into.

The lead study coordinator will track the randomization assignments, withdrawals and study completions. Once 25 from each of the 3 groups have completed the study, the study will cease enrollment.

Methods

Each study participant will have equal chance of being assigned to one of the three study groups. The subjects medical record will be reviewed and the data collected/documented will include: gender, age, diagnosis or reason for surgery, co-morbidities, medications, BMI pre-operative and post-operatively. All clinic follow-up progress notes will be reviewed to specifically collect any findings documented as complications from surgery.

Subjects who elect to consent into the study will be assigned a random study number and randomized into three cohorts: control (no steroid or NSAID), IV NSAID (1-time dose of 30 mg of IV ketorolac at the time of closure), and IV steroid (1-time dose of 10 mg of IV dexamethasone at the time of closure). Randomization schedule will be performed in a 1:1:1 fashion. Patients will be blinded with regard to which treatment they received until at least 1 year after surgery.Those subjects whom willingly volunteer to be part of the study will be notified promptly if they are found to not meet trial criteria and advised that they will be automatically withdrawn from the study.

Patient outcomes (patient completed questionnaires to evaluate for dysphagia and dysphonia) will be collected preoperatively and at 1 day (post-surgical day to day 3 post-op), 3 weeks (+/- one week), 6 weeks (+/- two weeks), 3 months (+/- three weeks), 6 months (+/- one month), and 1 year (+/- three months) postoperatively and will include: The Eating Assessment Tool (EAT-10), The Voice Handicap Index (VHI-10), Neck Disability Index (NDI), and Visual Analogue Pain Scale (VAS), Bazaz classification for dysphagia.

Post operative questionnaire collection will occur at time of outpatient clinic follow-up or subject may be called by phone and data collected over the phone or questionnaires mailed if patient preference. (Clinic visit follow up per the usual standard of medical care is per the above data collection timeline points, however, many times patients are feeling better and do not return for all suggested follow-up).

Eligibility

Inclusion

>/= 19 years of age
Undergoing ACDF for radiculopathy or myelopathy
No known allergies or sensitivities to steroid or non-steroidal medications
This is not an ACDF revision procedure or surgery related to treatment of trauma, infection or tumor.

Exclusion

Procedure is being done for revision, trauma, infection or tumor.
Patients with known diagnosed metabolic diseases (diabetes, pancreatitis, gout, electrolyte imbalances, hypertension, hematological abnormalities including gastrointestinal bleeding...)
Patients with known kidney disease or a creatinine level above the upper limit of normal > 1.27) (BMet labs are completed pre-operatively as standard of care on all patients unless there is documentation of normal labs completed within the past 6 months of surgery).
Patients with known allergy or sensitivities to steroid or non-steroidal medications

Statistical Analysis Plan

For dysphagia, primary outcome measures will be the Bazaz classification and the EAT-10. For dysphonia, primary outcomes will be measured by the VHI-10. Secondary outcomes will be measured with Neck Disability Index (NDI), Visual Analogue Pain Scale (VAS) for neck pain. Complications will also be documented for comparison to include: surgical site infection, need for reoperation and pseudoarthrosis.

Descriptive statistics (specifically counts and percentages) will be computed for all variables to ensure data quality and to evaluate the assumptions of statistical tests. Fisher's exact test will be used to evaluate associations between treatment groups and categorical measures at each time point. Analysis of variance (ANOVA) or the Kruskal-Wallis test, depending on the distribution of the data, will be utilized to compare continuous variables between the groups. If the overall p-value from ANOVA is statistically significant, pairwise comparisons will be performed and adjusted using Tukey's method. Mixed effect models also will be explored, with time, treatment group, and time x treatment group interaction terms as fixed effects and with a random intercept term to account for repeated measures All tests will be 2-sided and a p-value < 0.05 will be considered statistically significant.

No analysis was ultimately completed due to poor follow-up and lack of data.