Title:

Do Intraoperative Topical Corticosteroids Aid in the Prevention of Postoperative Dysphagia Following Elective Anterior Cervical Discectomy and Fusion? A Randomized, Controlled, Double Blinded Clinical Trial

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Project Description:

This is a randomized, prospective trial with the primary aim of evaluating the effectiveness of intraoperative topical steroids in decreasing the severity of swallowing difficulty following anterior cervical fusion surgery.

Principal Investigator:

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Hypothesis:

The null hypothesis is that there will be no difference in swallowing difficulty between patients who do and patients who do not receive intraoperative topical steroids in the wound at the end of the surgical case.

Outcomes:

To determine if topical steroids placed intraoperatively in the wound of an anterior cervical discectomy and fusion surgery reduce the incidence of postoperative swallowing difficulty using the SWAL-QOL outcome measure. SWAL-QOL will be administered pre-operatively, on post-operative day one, post-operative day two, post-operative 4-6 weeks, post-operative 3 months, post-operative 6 months, and post-operative 12 months. Differences in SWAL-QOL scores will be stratified based on levels fused (2-, 3-, and 4-levels).

The Bazaz Dysphagia Score and the Eating assessment Tool 10 (EAT-10) will be administered at the same time points to provide additional data about swallowing difficulty

Additionally, questionnaires that assess how neck and arm related pain affects the patient's quality of life will be administered pre-operatively (NDI & VAS) , post-operatively day 1 and 2 (VAS) , week 4-6 (NDI & VAS), month 3 (NDI & VAS), month 6 (NDI & VAS), and at month 12 (NDI & VAS).

Background:

Swallowing difficulties are a major side effect of anterior neck fusion surgery. Steroids have the effect of reducing inflammation and swelling, factors considered likely to cause swallowing difficulties following anterior neck surgery. This study looks to determine if steroids placed into the wound at the end of an anterior neck fusion surgery decrease the severity of a patient having swallowing difficulty following the surgery.

Dysphagia is a serious post-operative concern in patients following anterior cervical surgery. Although many authors have acknowledged that dysphagia is often incompletely understood and defined, there is a significant amount of literature to support the significance of this clinical entity. Lee et al (The Spine Journal 2007) found the incidence of post-operative dysphagia at 1, 2, 6, and 12 months post-operatively to be 54.2%, 33.6%, 18.6%, 15.2%, and 13.6%, respectively. Rihn et al (CORR 2011) found the

incidence to be 71% at two weeks post-operatively. Bazaz et al (Spine 2002), found it to be 50.2%, 32.2%, 17.8%, and 12.5% at 1, 2 6, and 12 months post-operatively. Moreover, Lee et al (Spine 2010) performed a systematic review and found in 17 studies the average incidence of dysphagia to be 13-21% at one-year post-operatively.

This study will utilize a validated questionnaire, SWAL-QOL, to evaluate swallowing difficulty and dysphagia. In addition, the study will investigate these outcomes in 2-4 level ACDFs, which have not been examined previously.

If topical steroid use can be proven to be safe and effective, it is a relatively inexpensive, easy measure to institute to diminish the occurrence of a serious complication following anterior cervical surgery and improve patient-reported outcomes.

This is a randomized, prospective clinical trial.

Study Drug:

Depo-Medrol (Methylprednisolone acetate)

This drug is FDA-approved and being utilized in an "off-label" manner. We confirmed with clinical research administration that the use of this drug does not require notification to the FDA or filing of an IND.

Inclusion Criteria:

Any patient > 18 years undergoing a 2-4 level anterior cervical discectomy and fusion

Exclusion Criteria:

- Revision surgery
- Pediatric patients
- Patients with Cervical vertebra fracture(s)
- Patients with Cervical Spine Tumors
- Patients with active infection
- Patients with a known allergy to Depo-Medrol
- Patients who refuse to participate
- Non English speakers

Age Range:

>18 years

Target Enrollment:

128

Interventions and Observations:

We plan to observe the effect on SWAL-QOL scores in patients following ACDF in groups that either receive or do not receive intraoperative topical steroid. All individuals undergoing 2-4 level ACDF that meet the inclusion criteria will be randomized to either: 1) treatment arm or 2) control arm. Both arms will undergo their planned surgeries and will receive the exact same procedure and standard of care as if they were not enrolled in a study. The only difference is that the treatment arm will receive 40 mg of Depo-Medrol delivered with one SURGIFLO Hemostatic Matrix Kit (Ethicon, Somerville, NJ, USA) injectable delivery vehicle prior to closure in the prevertebral soft tissues. The control group will receive only SURGIFLO Hemostatic Matrix Kit prior to closure. The surgeon will inject the material directly in the pre-vertebral soft tissue.

Both groups will have the same standard evaluations both pre-operatively and post operatively. The SWAL-QOL questionnaire will be utilized as the primary instrument to measure outcome. Other questionnaires, the EAT-10 and Bazaz Dysphagia Score, which grades will be used to assess dysphagia and swallowing difficulty. Additionally, the Neck Disability Index and the Visual Analog Scale for neck and arm pain will be administered to assess how neck related pain impacts the patients' quality of life. The EAT-10, Bazaz, and Visual Analog scale will be utilized to assess secondary outcomes. These questionnaire will be given to the patients to complete pre-operatively, on post-operative day one, post-operative day two, at post-operative week 4-6, post-operative month 3, post-operative month 6, and post-operative month 12. The Neck Disability Index will be completed pre-operatively, at post-operative week 4-6, post-operative month 3, post-operative month 6, and post-operative month 12.

All test or images are standard of care. Administration of the EAT-10, SWAL-QOL survey, Neck Disability Index, VAS (Neck and Arm Pain), and Bazaz Dysphagia Score are not standard of care. Funds are not required for administration of these questionnaires.

Randomization:

The randomization will be done prior to surgery.

The randomization protocol will be stratified by procedure to ensure proper distribution of cases in the study. This will also ensure equivalent numbers of patients in each group over the course of the study in case early stopping is required as well as randomize any procedure effect that may contribute to the results. Randomization will be concealed using sealed opaque envelopes containing the randomization assignment for each enrolled patient. Randomization assignment will be made known only to the unblinded research assistant.

Statistical Plan:

Steroid and Control arms were compared in terms of demographics and surgical information using a student's independent t-test and chi square/fisher exact test for normally distributed data, and a Mann-Whitney U test otherwise. In terms of PROs, a Mann-Whitney U test was performed to compare the group medians for dysphagia scores at Baseline, Post-op Day 1, Post-op Day 2, post-operative week 4-6, post-operative month 3, post-operative month 6, and post-operative month 12. In addition, a pre-post op comparison was conducted by calculating the change in PRO from baseline to each post-operative time point for each patient. Statistical significance was determined for all results with $p<0.05$.

Enrollment

Assessed for eligibility (n= **277**)

Excluded (n= **149**)
- Not meeting inclusion criteria (n= **10**)
- Declined to participate (n= **90**)
- Identified for consent (n= **49**)

  Reason: *Missed Enrollment Period*

Randomized (n= **128**)

Allocation

Allocated to Steroid Group (n= **64**)
- Received allocated intervention (n= **63**)
- Did not receive allocated intervention (n= **1**)

  Reason: *Self-withdrawal prior to surgery.*

Allocated to Control Group (n= **64**)
- Received allocated intervention (n= **61**)
- Did not receive allocated intervention (n= **3**)

  Reasons: *Surgery was canceled by patient, self-withdrawal prior to surgery, Screen failure*

Follow-Up

Lost to follow-up (n= **1**)

Reason: *Withdrawn by investigator: Pt had a 1 level ACDF performed (exclusion).*

Discontinued intervention (n= N/A)

Lost to follow-up (n= **2**)

Reason: *Use of BMP (exclusion) and self-withdrawal after surgery.*

Discontinued intervention (n= N/A)

Analysis

Analysed (n= **56**)
- Excluded from analysis (n= **6**)

Reason: *Incomplete Dataset*

Analysed (n= **53**)
- Excluded from analysis (n= **6**)

Reason: *Incomplete Dataset*