Dysphagia Following Anterior Cervical Spine Surgery; Single Dose Steroid Vs Saline (DysDexVSSal)

NCT03711474

04DEC2019

Human Subject Research

Does the protocol meet the federal definition of research? For help determining the type of research you are conducting, see the DHHR Human Subject Regulations Decision Charts at http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html.
Yes

Does the research involve living person(s)?
Yes

Will information from individual person(s) be collected as part of this research?
Yes

Funding Source

Is there a secured funding source?
No

Locations of Research

Select the location(s) where the research will be conducted. At least one location must be selected.
Ruby Memorial Hospital or Other WVU Healthcare Site

Select the location(s) where the research will be conducted. At least one location must be selected.
WVU Campus

Will the research take place at an off campus location?
No

Will this study require an Inter-Institutional Authorization Agreement (IAA)?
No

Design

Please provide a lay summary (written at 6th grade level) that includes a statement about the purpose and the general aims of the research.
Dysphagia (difficulty swallowing) is common following anterior cervical spine surgery. Studies have documented persistent swallowing difficulty up to two years postoperatively. The long term objective is to change the treatment paradigm for cervical spine surgery to minimize dysphagia and associated complications. The specific aims are to identify the effect of a single dose of perioperative steroid on dysphagia and to develop a treatment protocol for the frequency of perioperative steroids needed to reduce dysphagia. This is a prospective, randomized, placebo-controlled study. Patients will be given a single dose of dexamethasone or normal saline intratoperatively and then assessed at multiple time points up to one year. The research question is what is the effect of a single dose of perioperative steroid on dysphagia after anterior cervical spine surgery? The survey instruments used to determine difficulty swallowing include the Bazaz, Dysphagia Short Questionnaire, and EAT 10. To administer the Bazaz instrument, the study coordinator will ask the subject if he/she has difficulty swallowing liquid food and give the options 'none', 'rare', 'present all the time'. The options for solid food with are 'none', 'rare', 'occasional only with specific foods', or 'frequent majority of solids'. The options on the left side of the questionnaire determine the level of difficulty. If a subject has no difficulty swallowing both liquid and solid food, 'none' will be chosen. The level of difficulty swallowing is determined by the highest difficulty, e.g. if a subject had no difficulty swallowing liquid food and has rare difficulty swallowing solid food, 'mild' will be chosen. If the subject has no difficulty swallowing liquid food but has frequent difficulty swallowing solid food, 'severe' will be chosen.

Fully describe all procedures to be performed, from start to finish, numbering your procedures 1,2,3 or A, B, C (e.g., 1. Recruiting, 2. Consent, 3. Collecting data, 4. How findings will be shared, etc.).
1.Potential subjects will see Drs. Daffner, France, Cui, Sedney or Emery at their visit prior to elective anterior cervical spine surgery at the Spine or Neurosurgery Clinic. 2. Subjects will be told about the study at this visit, all questions will be answered by the surgeons and the research coordinator, all surveys that need to be completed will be shown to the potential subjects and they will be given the opportunity to consent. 3. If consented, the subject will be asked to complete baseline surveys (Bazaz, EAT-10, and Dysphagia Short Questionnaire) at this visit. The subject will also complete Standard of Care Patient Reported Outcome Measures (PROMS) at this visit. 4. The subject will be randomized to receive either single dose steroid (dexamethasone) or saline (placebo) prior to surgery. The dose is calculated based on body weight group will receive 0.3 mg/kg of intravenous dexamethasone (experimental group) 0.3 mg/kg saline (control group). The subject will not be charged for dexamethasone or saline. 5. The subject will undergo anterior cervical spine surgery per standard of care. 6. After administration of the antibiotics in the operating room, the single dose of steroid or saline will be given by the anesthesia team, who are blinded to the group assignment, via an intravenous bag (study drug) prepared by the investigational pharmacist, the only person who knows the group assignment. 7. The surgeon, patient, and research team are blinded to the group assignment. 8. The subject will be administered the surveys by phone call or in the hospital by the research coordinator on Day 1. 9. On Day 2, if the subject is still hospitalized, surveys will be administered by the research coordinator in the hospital or via phone call. 10. Following Day one surveys, and if the subject has been discharged, the subject will be called to complete the answers to the surveys via phone call at Day 2, Week 1, Week 2, Month 1, Month 3, Month 6 and Month 12. At Month 12, the subject will be asked to also complete standard of care PROMS. If the subject is in the clinic for follow up at the designated time frame for survey administration, the surveys will be completed in the clinic. If the subject is not in clinic at Month 12, the PROMS will be completed via phone call. 10. At the end of the study, all subjects will be called or mailed a letter indicating the group assignment they had been in. 11. Study Results will not be shared with the subjects.

Please describe the investigational procedures that will be performed throughout the duration of the study.
Randomization to steroids or no steroids for anterior spinal fusion subjects and completion of the Bazaz, Short Dysphagia Questionnaire and EAT-10 survey.

Please describe the standard of care procedures that will be performed throughout the duration of the study.

Everything outside of the randomization.

Will you be assigning or randomizing participants to groups or conditions (e.g., control, placebo)?
Yes

Describe the group assignment.
Random assignment to receive either one dose of steroid or one dose of saline (Placebo) during the first hour of surgery.

Does the research involve surveys/interviews/questionnaires? If so, attach a copy of the interview/survey questions on the Notes & Attachments page.
Yes

Will you be asking any questions that are likely to distress your subjects (e.g., questions about abuse, trauma, or suicide ideation)? If so, attach counseling services referral list on the Notes & Attachments page.
No

Describe what is known about this topic and why this study is needed. Please include at least two reference citations to support your rationale.
See lit review and scientific rationale under Notes and Attachments.

What method are you going to use to analyze the data?
Swallowing symptoms will be measured using the patient reported Bazaz Dysphagia Scale, EAT-10 survey, and the Dysphagia Short Questionnaire. Swallowing data will be obtained pre-operatively, one and two days post-operatively and then one week, two weeks, four weeks, three months, six months, and one year post-operatively. Scores from the Bazaz Dysphagia Scale and the Dysphagia Short Questionnaire from the two groups will be compared at the various time points using the Mann-Whitney U test. Power and sample size calculations are based on the presence or absence of dysphagia at two weeks. Based on a literature review, we postulated that 50% of the patients in the control group would experience mild, moderate, or severe dysphagia. If that figure can be improved to the point where just 20% of the patients are similarly affected then that, in our opinion, would represent clinical success. Under the above scenario, 32 patients in each group would give us 81% power to reject the null hypothesis. Assuming a dropout rate of 20% our total sample size for the study is 80. Statistical significance is set at $p<0.05$. We plan to analyze the data in three ways. First, we will look at the time-to-event where the event is "no dysphagia" in a discrete time survival model. Second, we will use a repeated measures ordinal categorical model to assess the effect of steroid/control in a generalized linear model. Lastly, we will compare the data from this study with that of our previous three-dose model to assess any difference in the degree of impact of the two dosing regimens.

Full Board Review Risk Assessment

Is this study more than minimal risk? (If NO, then this study should be submitted as an expedited protocol)
Yes

Does the study involve intervention and/or manipulation of the subjects or the subjects' environment (e.g., educational intervention or training, experimental or quasi-experimental design)?
Yes

Is the research categorized as interventional medical research?
Yes

Will monitoring for harms occur?
Yes

Describe monitoring for harm.
Please see the Data Safety Monitoring Plan under Notes and Attachments

Is there a Data and Safety Monitoring Plan (DSMP) for this study?
Yes

Is there a Data and Safety Monitoring Board (DSMB) for this study?
Yes

Is the DSMB independent?
No

Who will monitor the data?
The research team and Dr. Balcik, who is outside the department but serving on the DSMB.

What data will be monitored?
Adverse reaction to dexamethasone.

How frequently will data be monitored?
The board will meet after the first five subjects have had surgery. If no unexpected harms have been found, the board will meet every 3 months. Should an unexpected AE occur during the study, the board will be notified immediately and a decision will be made regarding continuing or discontinuing the study.

Describe how information relevant to the protection of participants will be managed addressing unanticipated problems involving risk to participants or others, interim results, and protocol modifications.
Should an unexpected AE occur during the study that is related to the research, the board will be notified immediately and a decision will be made regarding continuing or discontinuing the study.

Describe how the monitoring of data may ensure the safety of participants (e.g., a drastic blood pressure increase).
Dexamethasone may increase blood sugar in subjects with diabetes. All subjects with diabetes are carefully monitored for any rise in blood sugar per standard of care.

List all the standard medical, behavioral, and/or educational procedures that will be utilized.
The surgeries are standard of care as well as completion of patient reported outcomes at the time frames listed.

List the investigational interventions that will be utilized, above and beyond the standard of care.
Randomization to steroid or placebo; completion of Bazaz and the Short Dysphagia Questionnaire.

What decision rules (e.g., stopping rules) will be considered?
The board will meet after the first five subjects have had surgery. If no unexpected harms have been found, the board will meet every 3 months. Should an unexpected AE occur during the study, the board will be notified immediately and a decision will be made regarding continuing or discontinuing the study.

Will the protocol be stopped once harms are proven to outweigh benefits?
Yes

Will clinical findings be shared with the subjects?
Yes

Describe how findings will be shared with the subjects.
At the completion of the study all patients will be notified by phone call or letter their group assignment and results of the study.

Will incidental findings be shared with the subjects?
Yes

Will WVU's procedures on incidental findings be followed?
Yes

Describe how and where researchers will interact with participants, explaining how these interactions will be kept private.
Researchers will interact with participants in private rooms of the spine clinic and neurosurgery clinic at the participant's history and physical visit prior to elective anterior spine surgery. They will see participants in their hospital room Day 1 after surgery and possibly Day 2 if the participant remains in the hospital past day 1. They will ask participants to complete the Bazaz, EAT-10, and Dysphagia Short Questionnaire on Day 1 and Day 2. They will call participants from a private room to complete questionnaires should the subject not return for regularly scheduled follow up visits. They will interact with participants at their standard of care follow up visits in the clinic.

Describe any possibilities for risk or harm to the subjects as a result of their participation in the research (e.g., discomforts or hazards to the subjects). Please assess the severity of these risks.
The only inconvenience is answering questions on the surveys face to face or via a phone call. The subjects will have a full understanding of the time frames by which they will be contacted to anser questions before consenting. Subjects will not be recruited if they don't want to answer the survey questions during the time frames. There should be no discomfort with administration of the study drug.

Will subjects intentionally be deceived as to the purpose of the study?
No

HIPAA

Does the research involve protected health information (PHI)?
Yes

Will the HIPAA and consent forms be combined? If not, attach a separate HIPAA Authorization to the Notes & Attachments page.
Yes

Are you requesting a HIPAA waiver? If yes, attach a HIPAA Waiver Form on the Notes & Attachments page.
No

Will the research being conducted at a covered entity require authorization from the subject? If yes, attach a HIPAA Form on the Notes & Attachments page - only if a combined consent with HIPAA is not used.
No

Are you transferring identifiable data to or from another institution? If yes, attach a signed and WVU Legal Counsel approved HIPAA Data Use Agreement Form on the Notes & Attachments page.
No

Will the research being conducted at a covered entity involve data that is de-identified? If yes, attach a HIPAA De-Identification Certification Form on the Notes & Attachments page. You can find the form here (this is only for NHSR studies).
No

Will the study include deceased individuals? If yes, attach a HIPAA Decedents Form on the Notes & Attachments page.
No

Will data/samples with identifiers be received from another entity? If yes, attach a signed, Legal Counsel approved HIPAA Data Use Agreement Form on the Notes & Attachments page.
No

Subjects

Indicate the maximum number of subjects to be enrolled or medical records to be reviewed at all sites by the WVU or VAMC research team.
80

Provide a rationale for choosing your sample size.
Scores from the Bazaz scale, the EAT-10, and the Dysphagia Short Questionnaire from the two groups will be compared at the various time points using the Mann-Whitney U test. Statistical significance is set at $p<0.05$. With a power of 0.80 and a clinical meaningful difference of 30% in scores, an estimated 32 patients per group is needed. However, based on a recent unpublished study at our institution, we expect a dropout rate of approximately 20%, and therefore plan for a total sample size for this study of 80 patients.

State the requirement(s) to become a participant in the study (e.g., age range, sex, language spoken, class enrollment/ranking).
Ages 18-80; undergoing elective ACDF, hybrid constructs, corpectomies, disc arthroplasty surgery

Explain why selection of participants will be equitable addressing gender, ethnicity, and/or race of subjects.
No one will be excluded based on gender, ethnicity or race. Exclusion criteria include: < 18 years of age; major trauma or neoplastic or infectious conditions requiring surgery. Also excluded will be patients undergoing anterior-posterior operations, those with a history of previous anterior cervical spine surgery, any patient requiring a halo vest, patients on chronic steroids, and patients remaining intubated post-operatively, and women who are pregnant.

In outline format and chronological order, describe what will be done to identify and recruit participants (e.g., A, B, C or 1, 2, 3).
1. Potential subjects will see Drs. Daffner, France, Cui, Emery or Sedney at their History and Physical visit prior to elective anterior cervical spine surgery at the Spine Center. 2. Subjects will be told about the study at this visit, all questions will be answered by the surgeons and the research coordinator, all surveys that need to be completed will be shown to the potential subjects and they will be given the opportunity to consent. 3. If consented, the subject will be asked to complete baseline surveys (Bazaz, EAT-10 and Dysphagia Short Questionnaire) at this visit. 4. The subject will be randomized to receive either single dose steroid (dexamethasone) or saline (placebo) prior to surgery.

Will any of the subjects be less than 18 years old?
No

Will your study target populations such as pregnant women, fetuses, neonates, or any groups likely to be vulnerable to coercion or undue influence such as children, prisoners, individuals with impaired decision-making capability or economically or educationally disadvantaged persons?
No

Does this research involve participants who could be coerced or unduly influenced, such as current students/employees of research team members?
No

Does the protocol deal with cancer prevention, treatment, or diagnosis (including surveys)?
No

Has this protocol been reviewed by Clinical Trials Working Group (CTWG)? If yes, please attach the CTWG's correspondence on the Notes & Attachments page.
No

Consent Procedures

Will SIGNED informed consent be obtained from subjects (all or in part)?
Yes

Will the informed consent form be translated into any other language(s)?
No

Is a waiver of informed consent being requested (i.e., there will be no consent process at all)?
No

Is a waiver of the requirement to obtain written documentation of the consent process being requested (if yes, attach the information to be provided to the participants)?
No

Are you requesting an alteration of consent (e.g., short form, braille consent or witnessed verbal consent)?
No

Describe the consent process (using 1, 2, 3 or A, B, C), addressing when, where, and how participants will be informed.
Potential participants will be told of the study in the Spine or Neurosurgery Clinic in a private room during their History and Physical visit prior to surgery. A research team member will inform the subject about the study, answer all their questions, show them the surveys and the subject will be given the opportunity to consent.

Indicate who will be consenting subjects and describe the process of training all personnel who will be obtaining consent.

Research team members including research coordinators who have been consenting patients for years.

Potential Benefits

Is there any known benefit to the individual subject as a result of participating in the research? Payments to subjects should not be included in this section, but addressed in the Payments/Reimbursements section.
Potential benefit is less difficulty swallowing if the subject is assigned to the steroid group.

Describe the potential benefit(s) to society and/or scientific / medical knowledge of the planned work.
The results of this study will provide evidence for the use of steroids as a treatment for reducing the incidence and severity of dysphagia among patients undergoing anterior cervical spine surgery. A recently performed study at our institution has promising results from a three-dose regimen of steroids. Similarly, two recent clinical studies have also shown decreased dysphagia with a multi-dose steroid regimen. If the hypothesis of this proposal is supported, the use of a single dose of perioperative steroid specifically lends itself well to application in patients undergoing these procedures in outpatient surgery centers, improving the safety of such procedures.

Confidentiality

At any point during this study, will identifiable data be viewed or recorded?
Yes

Data must be kept for a minimum of three (3) years after study completion. In addition to the required 3 years, how much longer will the data be kept?
Three years after study completion.

Where will data be securely located?
In REDCAP, on the password protected computer of a research team member in the Department of Orthopaedics.

How will data be destroyed?
It will be erased from the password protected computer.

Will anyone other than the PI, research team members, or IRB have access to the identifiable data (e.g., sponsor/funding source, other collaborators)?
No

Describe the steps that will be taken to maintain the privacy of subjects (e.g., where interaction takes place) and the confidentiality of data (e.g., master code).
1.Potential subjects will see Drs. Daffner, France, Cui, Emery or Sedney at their History and Physical visit prior to elective anterior cervical spine surgery in a private room at the Spine Center. 2. Subjects will be told about the study at this visit, all questions will be answered by the surgeons and the research coordinator, all surveys that need to be completed will be shown to the potential subjects and they will be given the opportunity to consent. 3. If consented, the subject will be asked to complete baseline surveys (Bazaz, EAT-10 and Dysphagia Short Questionnaire) at this visit. 4. The subject will be randomized to receive either single dose steroid (dexamethasone) or saline (placebo) prior to surgery. 5. The subject will be seen post-op day one by the research coordinator (and post op Day 2 if the subject is still hospitalized) who will administer the surveys in the hospital room. 6. Following Day one surveys, and after discharge, the subject will be called from a private room of a research coordinator to complete the answers to the surveys via phone call at Day 2, Week 1, Week 2, Month 1, Month 3, Month 6 and Month 7. If the subject is in the clinic for follow up at the designated time frame for survey administration, the surveys will be completed in a private room in the clinic.

Does this study have a Federal Certificate of Confidentiality? If yes, attach the certificate on the Notes & Attachments page.
No

Financial Considerations

Will the subjects incur any costs to participate in this project (e.g., travel, physician fees, study procedures, study drugs)?
No

Will the subject be paid (money, gift certificates, coupons, etc.) to participate in this research project?
No

Will WVU students receive extra credit for participating in this research project?
No

Advertisements

Will there be advertisements for this study?
No

Drug/Substance/Nutrient/Biologic

Are there any drugs/substances/nutrients/biologics being used in this research study for investigational/research purposes ONLY?
Yes

Enter the name of the first drug being used for investigational/research purposes ONLY.
dexamethasone

Is this an Investigational New Drug (IND) (if so, please attach the investigator brochure or applicable documentation)?
No

Is this drug/substance/nutrient/biologic being used off-label (if so, please attach the package insert or applicable documentation)?
No

Does this drug/substance/nutrient/biologic meet the requirements of an IND exemption? The clinical investigation of a marketed drug or biologic does not require submission of an IND if all six (6) exemption conditions are met.
No

Is there a second drug/substance/nutrient/biologic used in this research study for investigational/research purposes ONLY?
No

Provide any other information regarding the drugs/substances/nutrients/biologics being used in this study that is relevant to the IRB review.
Dexamethasone is a commonly used drug administered by anesthesiologists when patients are having difficulty swallowing after surgery or to reduce nausea and vomiting.

Will all drugs/substances/nutrients/biologics being used in this study be provided free of charge?
Yes

Will all drugs/substances/nutrients/biologics being used in this study be stored at the WVU Healthcare Pharmacy (WVUHP)? All drug storage must be approved by the WVUHP.
Yes

Will there be any drugs/substances/nutrients/biologics used in this study NOT for investigational/research purposes?
No

Device Information

Are there investigational devices that will be used in this study?
No

Sample Collection

Will sample(s) be used?
No

Radiation Safety

Will there be any radioactive materials or ionizing radiation used solely for research in this study?
No

Biological Safety

Does the study involve the handling of any infectious and/or non-infectious agents or recombinant DNA?
No

Data Protection for IRB

Does the project have data protection requirements?
No

Protocol Notes

DATE	AUTHOR	TOPIC	NOTE
06/25/2019 03:48 PM	Sherri Davis	A003	Removing Hanna Jiles from study personnel, and adding Olivia Hill and Skylar Braga to study personnel to assist with data entry.
06/19/2019 11:43 AM	Sherri Davis	Response to Spec Min Rev R001	*Please include clinicaltrials.gov language in the consent form. Please find the requested language in the consent form on page three, the last paragraph of the confidentiality section.
		Renewal 001	Renewing protocol with 17 subjects to date. DSMB reports filed. No SAEs to report.

06/05/2019 03:55 PM	Sherri Davis		