Study Design: Prospective observational study of cervical interlaminar injection of steroid in patients with cervical radicular pain

Background and Significance

To be completed by the project's Principal Investigator (PI) and include rationale for the selected prospective observational design.

Hypothesis

At least 50% of patients with cervical radicular pain will achieve a moderate or good response to interlaminar injection of steroids (ILIS) as determined by improvement in pain.

Specific Aims:

1. Determine the proportion of patients with a good response (80% or greater improvement in index pain) to their initial ILIS at 3 weeks who have no need for repeat injection(s) at 1-year follow-up.
2. In patients with a good response (80% or greater improvement in index pain) who undergo repeat injection(s) during the following year, determine the short-term (6-week) and long-term (12-month) success following the repeat injection(s).
3. In patients with moderate response to their initial ILIS (50%-79% improvement in index pain at 3 weeks), determine the short-term (6-week) and long-term (12-month) success of repeat "booster" injections.
4. In patients with poor response to their initial ILIS (less than 50% improvement in index pain at 3 weeks), determine the short-term (6-week) and long-term (12-month) success of repeat "booster" injections.
5. Compare patient characteristics between response groups.
6. Report adverse effects.

Recruitment Process

Preferred: Identification of potential study participants from the research center's interventional and surgical clinics, and the interventional treatment room's schedule.

Allowed: Response to marketing in local primary care physician clinics and local media.

Enrollment Process

Presentation of study and interview by physician or research assistant for study eligibility; determination (screening evaluation) based on inclusion and exclusion criteria; and, informed consent of qualifying volunteers. A power analysis to determine target enrollment numbers will be performed by the project PI.

Inclusion Criteria:

- Adult patients aged >18 capable of understanding and providing consent in English and capable of complying with the outcome instruments used.
- Arm pain or shoulder girdle pain/periscapular pain with or without neck pain with duration less than or equal to 6 months.
- 3-day average numeric pain rating score (NPRS) for arm pain or shoulder girdle/periscapular pain of at least 4/10 at baseline evaluation, with neck pain score not exceeding arm pain score.
- MRI (or CT if MRI not available) shows either a one level cervical disc herniation, disc osteophyte complex or degenerative foraminal stenosis, corresponding in side and location with predominately unilateral radicular pain, with or without neurological deficits. MRI may show degenerative changes at other levels.
- Patient consents to treatment with epidural injection in a shared decision-making process with the treating physician.
- Pain duration of at least 6 weeks or more.

Exclusion Criteria:

- Those receiving remuneration for their pain treatment (e.g., disability, worker's compensation).
- Those involved in active litigation relevant to their pain.
- The patient is incarcerated.
- Neck pain is greater than arm pain or shoulder girdle/periscapular pain.
- Bilateral radicular signs/symptoms (< 90% laterality of pain intensity, or bilateral neurological signs).
- BMI>35.
- Prior epidural steroid injections for treatment of current episode or within the prior 6 months in any location within the spine.
- Those unable to read English and complete the assessment instruments.
- Spondylolisthesis at the involved or adjacent segments.
- Systemic inflammatory arthritis (e.g., rheumatoid, lupus).
- Addictive behavior, severe clinical depression, or psychotic features.
- Possible pregnancy or other reason that precludes the use of fluoroscopy.
- Treatment of infection with antibiotics within the past 7 days.
- Progressive motor deficit, and/or clinical signs of myelopathy.
- History of prior cervical surgery.
- Medical conditions causing significant functional disability (e.g., stroke, COPD)

Outcome Instruments

Baseline Only:

- At initial visit: patient's description of pain (characteristics of pain e.g., burning, electric) and location of pain symptoms.
- Demographics
- BMI
- Radiologic details

    - Location and morphology of the cervical disc herniation, disc osteophyte complex or degenerative foraminal stenosis

Follow-up Only:

- Global perception of change

Baseline & Follow-up:

- Numerical Pain Rating Scale (NPRS) for arm pain or shoulder girdle/ periscapular pain and for neck pain (3-day average)
- EQ-5D Health Related Quality of Life questionnaire
- Neck Disability Index (NDI)
- Personal goal achievement
- Work history and current status
- Analgesic use log
- Ancillary treatment log, of any treatment related to the underlying condition other than analgesic use (e.g., physical therapy, chiropractic care, acupuncture, ice or heat, home cervical traction)
- Physical examination

Injection Treatment:

- Date
- Side and location of injection(s)
- Medications (normal Saline and steroid or local anesthetic, physician's choice) instilled into the epidural space using interlaminar technique described in the International Spine Intervention Society's Practice Guidelines. The therapeutic medication(s), dose(s), and volume(s) must be standardized and specified by the investigator. It is suggested that the investigator comply with information provided in the latest Society guidelines.

Power Analysis

To be completed by the project's Principal Investigator (PI) to demonstrate the size of the study is sufficient to provide acceptable confidence intervals for the anticipated success rates in the different groups.

Study Timeline

Baseline:

Participants who meet inclusion and exclusion criteria will be enrolled into the study after consenting to and before receiving a first ILIS. The baseline examination and all baseline questionnaires will be completed within 2 weeks before the first ILIS.

Follow-up:

Routine scheduled follow-up will occur at 3 weeks (+/- 1 week), 6 weeks (+/- 2 weeks), 3 months (+/- 2 weeks), 6 months (+/- 1 month), and 12 months (+/- 1 month), at which times all

follow-up measures will be obtained.

This study is intended to monitor outcomes for 1 year following an initial ILIS. The study start date and the outcome assessment timeline will begin from the date of the participant's first injection. During the first year from this start date, a participant may receive up to 3 ILIS per protocol. After every ILIS, the follow-up schedule will revert back to the beginning, starting with the 3-week timepoint and continuing up to the final 12-month follow-up.

Study Protocol

Group Assignments:

Patients are divided into 3 groups based on outcomes obtained at their initial 3-week follow-up after their first ILIS.

A. Good response: 80% or greater improvement in index pain

B. Moderate response: 50% - 79% improvement in index pain

C. Poor response: Less than 50% improvement in index pain

Repeat Injection Criteria:

At the 3-week follow-up, any participant with <80% improvement in their usual pain relative to the baseline measure, will be offered a repeat "booster" ILIS. Any participant with 80% or greater improvement in index pain at the 3-week follow-up, or anytime thereafter, who experiences a recurrence of pain such that their usual pain is now less than 80% improved relative to the baseline measure, will be offered a repeat ILIS.

"Usual pain" is defined as the pain that matches their cervical radicular pain. Arm pain or shoulder girdle/ periscapular pain is greater than neck pain.

To this end, all participants will be given a phone number to contact the research nurse or coordinator along with instructions to call anytime their pain has returned to exceed the "80% or greater improvement" threshold, or anytime they think their situation warrants consideration of an additional injection. A live person will be available to field calls in the late afternoon and early evening (4:00 PM to 8:00 PM). If a repeat injection is provided, the follow-up schedule will revert back to the beginning as described above.

"Booster" injections are defined as the repeat ILIS that are deemed necessary before the 6-week follow-up, based on the above criteria. "Repeat" injections are defined as ILIS that are deemed necessary, based on the above criteria, at or anytime after the 6-week follow-up.

A participant who receives an injection outside of this criterion, if deemed necessary by the treating physician, will be identified as a protocol deviation with follow-ups timed to the most recent injection received. Injections may be repeated twice, as per this protocol, for a total of 3 ILIS during the first year from the study start date and inclusive of the injection received on the start date. Any injection received after the third injection, or after the first anniversary of the

study start date, will result in the participant being classified as a treatment failure.

Injection:

This study will investigate interlaminar injections of steroid. The intervertebral level of the injection will be determined by the treating physician based on the location of the patient's disc herniation and corresponding clinical findings and MRI findings but will be done at one of three levels: C7-T1, C6-C7 or T1-T2.

Co-interventions:

Patients are allowed to receive usual care, including co-interventions, as deemed necessary by the patient and the treating physician. Any treatments related to the participant's spine condition will be reported on the ancillary treatment log.

Primary Outcomes:

The primary outcome is "treatment response" as defined by classification into one of the three following categories, with "success" defined as meeting criteria for category 1 or 2:

1. Initial injection success (short-term and long-term): defined as 80% or greater improvement in index pain at the 6-week and 12-month follow-up, and no need for repeat injection during this time.
2. Booster and repeat injection success (short-term and long-term): defined as 80% or greater improvement in index pain maintained at the 6-week and 12-month follow-up after a repeat injection or two (performed anytime before the first anniversary of the study start date).
3. Booster and repeat injection failure: defined as less than 80% improvement in index pain at the 6-week or 12-month follow-up from the last injection (performed anytime before the first anniversary of the study start date), or surgery at anytime during the 12-month follow-up, or any injection received after the third injection, or any injection after the first anniversary of the study start date
4. Decay curves: Calculate the half-life of the initial injection response, booster response, and repeat injection response. Calculate how many injections are required to maintain relief during the first 12 months of the study, and how many participants sustain relief for 12 months after their final injection in the study.

Secondary Outcomes:

1. Disability (NDI)
2. Health-related quality of life (EQ-5D)
3. Surgery
4. Personal goal achievement
5. Work status
6. Analgesic use
7. Quantity of type of ancillary treatment
8. Predictors of repeat injections from baseline physical and radiologic findings

9. Predictors of overall response with injection treatment from baseline exam and radiologic findings

Data Management

Data will be collected on standardized case report forms and entered into a HIPPA-compliant electronic database (e.g. Microsoft Access) that provides an appropriate interface with a robust statistical package (e.g. SPSS). All study-related hard copy materials will be stored in locked file cabinets.

Analysis

Overall success will be calculated for the entire cohort and separately for each of the three groups (A, B, and C). To analyze the impact of repeat injections, patients in Group A who do not have a repeat injection (patients classified as "initial injection success") will be removed from the following analyses. The proportion of the remaining patients in groups A, B, and C who are classified as "repeat injection success" or "repeat injection failures" will be calculated and compared. Success of "booster" injections will also be compared to the success of "repeat" injections. Secondary outcomes will be determined by measuring and comparing interval change in group mean scores for both short-term (6-week) and long-term (12-month) follow-up. For short-term and long-term changes in arm pain or shoulder girdle/ periscapular pain (NPRS) and for all secondary outcomes with a defined minimal clinically important difference (MCID), the outcomes will also be dichotomized into responders (those exceeding the MCID) and non-responders (those not exceeding the MCID) to allow comparison of categorical outcomes. Correlations between the primary (and secondary) outcomes and baseline exam findings and radiologic variables will be calculated.