

Study Design: Prospective observational study of cervical transforaminal epidural steroid injections 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 experience 50% or greater relief of index pain following cervical transforaminal epidural steroid injections (TFESI).

Specific Aims:

1. Determine the proportion of patients with an 80% or greater improvement in index pain following an initial cervical transforaminal epidural steroid injection (TFESI) at 3 weeks post-injection and the duration of response up to 12 months.
2. Determine the proportion of patients with a 50%-79% improvement in index pain following an initial cervical TFESI at 3 weeks post-injection and the duration of response up to 12 months.
3. Determine the proportion of patients with less than 50% improvement in index pain following an initial cervical TFESI at 3 weeks post-injection and the duration of response up to 12 months.
4. Determine the proportion of patients with an initial injection plus up to 3 additional injections that maintained 80% or greater improvement in their index pain for up to 12 months.
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, other specialty 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 and/or shoulder girdle/periscapular 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 spine 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. May consider using COMBI (Stojanovic *et al.* in *Pain Medicine*, 2015; 16: 513-519.). This may simplify outcome measures.
- Demographics
- Medical, surgical and psychiatric history
- BMI
- Radiologic details
 - o Location and morphology of the cervical disc herniation, disc osteophyte complex, or degenerative foraminal stenosis

Follow-up Only:

- Global perception of change. May consider using the Clinical Outcome Measurement Brief Instrument (COMBI) (Stojanovic *et al.* in *Pain Medicine*, 2015; 16: 513-519.)

Baseline & Follow-up:

- Numerical Pain Rating Scale (NPRS) for arm pain or shoulder girdle/ periscapular pain and for neck pain (3-day average) at baseline

- Patients will be given a daily pain diary chart to record NPRS and percentage improvement during the 1st month post-injection.
- Patients will be contacted in the 1st week post-injection with a standardized questionnaire about their symptoms and a reminder about the 3 week (+/- 1 week) post injection follow up.
- EQ-5D Health Related Quality of Life questionnaire
- Neck Disability Index (NDI)
- Personal goal achievement (COMBI)
- 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
- Neurological examination

Injection Treatment:

- Date
- Side and location of injection(s)
- Dexamethasone instilled into the cervical epidural space using the transforaminal technique described in the International Spine Intervention Society's 2nd Edition Practice Guidelines. The therapeutic 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 cervical TFESI. The baseline examination and all baseline questionnaires will be completed within 2 weeks before the first cervical TFESI.

Follow-up:

Patients will be given a daily pain diary chart to record NPRS and percentage improvement during the 1st month post-injection.

Patients will be contacted in the 1st week post-injection with a standardized questionnaire about their symptoms and a reminder about the 3 week (+/- 1 week) post-injection 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 cervical TFESI. The study start date and the outcome assessment timeline will begin from the date of the participant's first injection.

Study Protocol

Subjects who achieved 80% or more relief of their usual pain at the 3-week follow-up and who subsequently experience a recurrence of their usual index pain will be offered a repeat procedure. "Usual pain" is defined as their cervical radicular pain (upper extremity pain or shoulder girdle/ periscapular pain) which is greater than axial neck pain.

Patients with 50-79% relief should be offered a second injection (at 3 week follow-up) with the goal of achieving greater than 80% relief. Responders should be offered a repeat injection if pain returns to the extent that warrants consideration of an additional injection.

Duration of relief will be considered the time from the provision of the TFESI procedure until the subject reports a worsening of pain to the extent that warrants consideration of an additional injection. This may occur during an unscheduled follow-up, by phone correspondence, or as reported during scheduled follow-up or when a repeat TFESI is requested and performed.

All participants will be given a phone number to contact the research nurse or coordinator along with instructions to call if their pain has returned to the extent that warrants consideration of an additional injection. Consideration of an additional injection is warranted when pain exceed the "80% or greater improvement" threshold following a prior injection, or anytime participants think their situation warrants consideration of an additional injection. Immediate and early post-injection period, the PI and his/her representative will be available 24 hours to answer any urgent questions or concerns related to the procedure. In addition, the PI and his/her representative will be available to answer non-urgent questions during routine work hours.

Patients will be contacted in the 1st week with a standardized questionnaire about their symptoms and given a reminder about the 3 week (+/- 1 week) post-injection follow up. After the 3 week (+/- 1 week) follow up, patients will be followed up with once a month as a reminder to contact the physician's office when the pain returns.

Injection:

This study will investigate cervical transforaminal injections of steroid. The intervertebral level of the injection will be determined by the treating physician based on 1) clinical presentation (distribution) of their pain and 2) and the location of the patient's disc abnormality seen on the imaging study.

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:

1. 80% or greater improvement in index pain following an initial cervical transforaminal injection of steroid (TFESI) at 3 weeks post-injection, 3 months post-injection and response at 12 months.
2. 50%-79% improvement in index pain following an initial cervical TFESI at 3 weeks post-injection, 3 months post-injection, and response 12 months.
3. Less than 50% improvement in index pain following an initial cervical TFESI at 3 weeks post-injection, 3 months post-injection, and response at 12 months.

Secondary Outcomes:

1. Disability (Neck Disability Index)
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
10. Number or percentage of patients requiring more than 1 injection to reach the 80% improvement mark
11. Differences in long term outcome between the single injection group and the >1 injection group in
 - a. Need for surgery
 - b. Return to work
 - c. Personal goal achievement (COMBI)
 - d. Quality of life

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 by determining the proportion of participants with an 80% or greater relief of index pain at 3 weeks, 3 months, and at 12 months. 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 their “index pain” (upper extremity radicular pain or shoulder girdle/periscapular) (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.