Corticosteroid Injections for the Treatment of Common Upper Extremity Pathologies, With or Without Lidocaine: A Randomized Control Trial

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Project Summary

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Lay Summary: A tendon is a type of tissue that connects your muscles to your bones. These tissues help control actions such as running, jumping, grasping, and lifting. Without tendons, you wouldn't be able to control the movement of your body. A protective layer known as synovium covers tendons. This sheath produces fluid, which keeps the tendon lubricated and moving properly. Inflammation or swelling of the sheath is known as tendon sheath inflammation or tenosynovitis. This condition is often treated with an injection into or around the sheath. This injection often consists of a corticosteroid with or without lidocaine. Corticosteroid are drugs that decrease inflammation and are given for a number of orthopaedic conditions to decrease symptoms of the underlying disease. Lidocaine is also a drug that blocks the pain response, although it only blocks it momentarily. Our study aims to determine if corticosteroid injection alone is as effective as corticosteroid combined with lidocaine for the relief of tenosynovitis of the upper extremity.

Precis/Abstract:

This will be a randomized control trial to study the efficacy of a combined lidocaine and corticosteroid injection on pain, range of motion, and patient reported outcomes versus a corticosteroid injection alone for the treatment of common upper extremity tendinopathies and nerve entrapments that are often treated with a combination of these injectates. Patients will be assigned randomly to a control group (corticosteroid injection alone) or the treatment group (lidocaine plus corticosteroid injection). At the initial injection a 10-point likert scale prior to and after the injection will be administered. The patients will be followed up at 6 weeks after the injection, at which time the Visual Analog Scale for pain (VAS-pain), range of motion (ROM), and patient reported outcome data will be collected and any complications will be noted. Patients will also utilize a pain journal to track VAS-pain over the first 7 post-injection days. We hypothesize that those who receive lidocaine plus corticosteroid injection will be non-inferior in regards to pain, range of motion (ROM), failure of injection requiring surgery, and patient reported outcome scores compared with patients who received corticosteroid injection alone.

Background and Significance:

Tenosynovitis is a common ailment of the upper extremity resulting in pain around the affected joint due to injury to the tendon sheath. One of the most common manifestations of tenosynovitis is trigger finger. Trigger finger is an extremely common pathology encountered by primary care providers and hand surgeons. Reported incidence of 28 cases per 100,000 has been documented [1]. This entity occurs when the contents of the flexor tendon sheath do not fit cleanly

within the sheath, causing friction on movement of the fingers. Progression from a clicking or locking sensation to complete inability to flex or extend the finger (hence the designation "trigger finger") occurs over the course of the disease. Therefore, triggering may not be initially noted on exam. Pain from this pathology can be experienced at the proximal interphalangeal joint, the metacarpophalangeal joint, or even the palm [2]. Reported increases in rates have been documented in diabetics, cases of repetitive trauma, those with renal and thyroid disease, and individuals with inflammatory conditions [3].

The cause of trigger finger is poorly understood, with early studies identifying the condition as a form of tenosynovitis on histologic analysis. More recent studies have identified a lack of inflammatory cells, suggesting an abnormality in proliferation of fibrocartilage rather than a primary inflammatory condition [4]. Treatment of trigger finger has been studied extensively, but few evidence based guidelines exist for the treatment of this disease process [1]. Current treatment modalities are diverse and numerous, including non-operative management (splinting, stretching techniques, heat therapy, electric stimulation therapy, acupuncture, corticosteroid injection, and high-intensity focused ultrasound aimed at degrading the fibrosis surrounding the tendon sheath) and operative management (with open, percutaneous, and endoscopic methodology all having been described) [1, 5]. In 2017, Amirfeyz *et al*. proposed an evidenced based treatment guideline for trigger finger, with the first line treatment listed as "steroid and local anesthetic injection" followed by open operative management upon either failure of corticosteroid injection or patient refusal of corticosteroid injection [1].

This treatment algorithm reflects existing research regarding treatment of trigger finger: corticosteroid injection for trigger finger has been studied extensively [6-25]. However, few well, randomized control trials have been undertaken comparing corticosteroid injection to placebo. Of the trials that have been done, both studies indicated improved outcomes with a combined injectate of corticosteroid with lidocaine versus just lidocaine alone [26, 27]. The long term efficacy of steroid injection is reasonable, with success rates as high as 69% [8]. That said, many patients will experience return of their symptoms and will go on to need open surgical treatment for recurrent trigger finger [3].

While several studies have compared corticosteroid injection with lidocaine to lidocaine injection alone, to date, no study has evaluated the effectiveness of a corticosteroid injection either with or without lidocaine. Our study aims to evaluate whether or not lidocaine in the injectate combined with corticosteroid improves patient reported outcomes and recurrence of pain and morbidity from trigger finger as compared with corticosteroid injection alone.

In addition, similar pathologies exist where the role of lidocaine remains vague. One such pathology is de Quervain tenosynovitis. de Quervain tendinopathy affects the abductor pollicis longus (APL) and extensor pollicis brevis (EPB) tendons in the first extensor compartment at the styloid process of the radius. It is characterized by pain or tenderness at the radial side of the wrist. Although de Quervain tendinopathy is often attributed to overuse or repetitive movements of the wrist or thumb, the cause is generally unknown. It most commonly affects woman between the ages of 30-50 years old [28].

A small randomized trial found that glucocorticoid injections resulted in significantly better symptom improvement compared with placebo one week after injection [29]. Among those who responded to glucocorticoid injections, the beneficial effects were maintained during the 12-month follow-up period. Another randomized trial also found that splinting plus glucocorticoid injection was better than splinting alone [30]. Most patients experience pain relief after a single glucocorticoid injection [30, 31] In patients with recurrent symptoms after initial relief with the

first glucocorticoid injection, a second injection may provide benefit. However, limited evidence is available about the role of lidocaine during these injections. We further aim to elucidate the role of corticosteroid and lidocaine versus corticosteroid alone in the treatment of de Quervain tenosynovitis.

Furthermore, the role of lidocaine with corticosteroid in the treatment of a number of other tenosynovitides remains ambiguous. These include tenosynovitis of the shoulder, biceps, elbow, wrist, thumb, carpometacarpal, midcarpal, elbow, and small joints of the hand (PIP, DIP, MP). We aim to ascertain whether the corticosteroid and lidocaine injectate together is as effective as corticosteroid in the treatment of these tenosynovitides. For all these pathologies corticosteroid with or without lidocaine is standard of care for orthopaedic hand and shoulder surgeons and the use of either treatment regimen is based on personal preference by the surgeon.

Objectives:

1. Determine differences in pain scores / likert scale at the time of injection and during follow up in the corticosteroid plus lidocaine group as compared to the corticosteroid alone group.
2. Determine differences in range of motion of the affected joint in the corticosteroid plus lidocaine group as compared to the corticosteroid alone group.
3. Determine differences in patient-reported outcome scores (VAS-pain, qDASH, PRWE, ASES, SF12, EQOL) in the corticosteroid plus lidocaine group as compared to the corticosteroid alone group.
4. Report patient characteristics associated with efficacy of addition of lidocaine to corticosteroid injectate for pain and ROM resolution (type of injury, affected joint, age, BMI, comorbidities, etc.).

Hypotheses:

Hypothesis^{0}: Corticosteroid injectate alone will result in statistically significant reduced pain scores as compared to corticosteroid with lidocaine for the treatment of tenosynovitis.
Hypothesis^{1}: Lidocaine plus corticosteroid injectate will result in equivalent requirements for repeat injection or conversion to surgery as compared with corticosteroid injectate alone for the treatment of tenosynovitis.
Hypothesis^{2}: Lidocaine plus corticosteroid injectate will result in equivalent patient reported outcomes scores as compared to corticosteroid alone for the treatment of tenosynovitis.
Hypothesis^{3}: Lidocaine plus corticosteroid injectate will result in equivocal patient-reported outcome scores, ROM, and pain reduction as compared to corticosteroid alone for the treatment of tenosynovitis.

Study Design

This will be a randomized control trial of a group of patients with upper extremity tenosynovitides treated with either lidocaine plus corticosteroid or corticosteroid injection alone by upper extremity fellowship trained surgeons at Emory University. Patients will be randomly assigned to one of two groups at the time of treatment: 1. Lidocaine Plus Corticosteroid and 2. Corticosteroid Alone. A random allocation sequence, concealed in consecutively numbered, opaque, sealed envelopes, determining active treatment or placebo, will be computer generated. Written-informed consent will be obtained from patients prior to injection.

Patients in the Corticosteroid group will be treated with a 40 mg/mL injection of corticosteroid following sterile preparation. The volume of injectate differs for each tenosynovitis being treated. For example, trigger finger patients in the corticosteroid alone group will receive a 1mL of injectate total (consisting of 1 mL of 40mg/mL triamcinolone).

Patients in the Corticosteroid and Lidocaine group will be treated with a 40 mg/mL injection of corticosteroid combined with 1% lidocaine. The volume of injectate differs for each tenosynovitis being treated. For example, patients being treated for trigger finger will receive 0.5 mL of 1% lidocaine and 1 mL of 40mg/mL triamcinolone.

Needle size and insertion site of needle differs for each tenosynovitis being treated. For trigger finger specifically, needle injections will be performed with an appropriately sized needle inserted over the A1 pulley at a 45-degree angle. The injection will be done with the same technique for both groups by the attending physician. The medication will be injected extra-synovially in order to make the treatment more reproducible. This method of injection has been supported in previous studies.

Outcome Measures:

- Likert Scale: A 10-point likert scale will be asked before and after injection which has been previously validated in other studies looking at efficacy and pain surrounding injections of the upper extermity.

- Pain Assessment: A pain assessment will be assessed before performing the injection, at the time of injection, and at each subsequent follow up visit. Pain scores will be obtained via the Visual Analog Pain Scale (VAS-pain), which is ranked from 0 (no pain) to 10 (highest amount of pain). Pain will be assessed at rest and active movement of the affected joint. Patient will also be asked to fill out the VAS-pain score twice daily in a pain journal (once in the morning and once at night) each day until post-injection day 7.

- qDASH/PRWE/ASES/SF12/EQOL score: These scores will be administered at each clinic follow up. They will also be administered 6 week after the injectate has been performed.

- Need for subsequent reinjection and surgical operation will be recorded.

These scores, specifically the 10-point likert, will also be assessed before performing the injection, immediately after the injection, and again at the various follow up appointments. During clinic follow up we will monitor for complications.

Inclusion Criteria:
- All adult clinical patients of Emory upper extremity surgeons undergoing injection for treatment of the following who are willing to participate in the study will be included in the study: Tenosynovitis of the upper extremity, including but not limited to, the shoulder, biceps, elbow, wrist, thumb, carpometacarpal, midcarpal, elbow, and small joints of the hand (PIP, DIP, MP).
- Between the ages of 18 years and 95 years.

- For trigger finger: patients with a diagnosis of stenosing tenosynovitis based on a history of triggering and the presence of tenderness over the A1 pulley upon clinical examination. All patients, based on the Quinnell grading of trigger finger see in the figure below, will be included.

Grade	Clinical findings (during flexion and extension)
0	Normal movement
I	Uneven movement
II	Actively correctable
III	Passively correctable
IV	Fixed deformity

Exclusion Criteria:
- Patients who are minors, vulnerable subjects, or who are not willing to consent to participate in the study.
- Allergies to glucocorticoids, current daily use of glucocorticoids or strong opioids (morphine, fentanyl, hydromorphone, ketobemidone, methadone, nicomorphine, oxycodone, and meperidine), severe diabetic neuropathy of the hand influencing pain perception, rheumatoid arthritis, and neurological or psychiatric diseases, potentially influencing pain perception.
- Subjects who, in the opinion of the investigator, may be non-compliant with study schedules or procedures.

Statistical Analysis:

Data will be stored on an excel spreadsheet. We will collect the name, medical record number, age at time of surgery, ethnicity, gender, BMI, presence of diabetes, Quinnell grading of trigger finger, smoking status, pre-injection VAS-pain, post-injection VAS-pain, 10 point likert scale, complications, and need for repeat injection or surgical release. It is possible that other variables may be added depending on analysis. Each variable will be used as a nominal variable when possible (e.g. smoking status) or a continuous variable if needed (e.g. VAS-pain, patient related outcome scores). For some statistical calculations we may break up the continuous variables in to ranges (e.g. Ages 15-20, 25-30). We will perform statistical analysis using unpaired, 2-tailed Student t test to compare means for normally distributed data, Kruskal-Wallis test to compare medians of non-normally distributed data, and chi-square test to compare proportions. Statistical significance will be interpreted as $P < .05$. Confidence intervals will be calculated with a confidence level of 95%.

Specifically, the 2 groups will be compared using the Mann-Whitney U test to analyze the difference between the post-injection VAS scores. The Wilcoxon sign-rank test will be used to test the difference between the treatment and control group for pain and patient related outcomes.

The minimally clinically important difference (MCID) varies for each outcome measure. Therefore, for the purposes of a power analysis, we will use the VAS-pain at the time of injection as the primary outcome. A similar study was published in 2017 from Earp *et al*. comparing needle-free jet lidocaine for pre-corticosteroid injection anesthesia with simultaneous lidocaine and corticosteroid injection. Using the results of this study as a metric, for the purposes of our study, to determine a 1-point change in VAS (4.5 to 3.5) with the reported standard deviation of 2 (SEM

was 0.4, with 30 subjects in each group) in the Earp *et al*. study, the number needed to treat to detect a difference between the treatment and placebo group would be 63 [32]. Therefore, we aim for a sample size of 63 patients for each possible tenosynovitis described in the inclusion criteria.

In total, **we plan to enroll 1000 patients total into this study** when combining all possible tenosynovitides encountered at Emory. These outcomes will be feasible to obtain in a reasonable time frame given the high volume of patients treated for tenosynovitis of all types at Emory. Patients will be grouped together for analysis and also broken into subgroups for sub-analysis based on primary diagnosis for injection.

JMP Pro Software or SPSS will be used to analyze the data and perform the statistics.

Risks to participation

Risks to participation include breach of confidentiality from PHI used to conduct the study. Every effort will be used to scrub data when possible and to use subject numbers/unique identifiers when possible.

As stated above, the first line treatment for trigger finger is corticosteroid injection with lidocaine, although there are a significant proportion of hand surgeons who inject corticosteroid alone. As no study has evaluated the efficacy of lidocaine mixed with the injectate versus corticosteroid alone, our study does not constitute deviation from current status quo of best medical practice for the treatment of trigger finger. **Both treatment options are considered standard of care and it is solely based on physician preference for which regimen is chosen as an injectate.** Patients will be notified of any potential risks with signed written consent as they would before any standard corticosteroid injection for the treatment of trigger finger. They will also be asked to sign an additional consent form agreeing to participate in our study outlining the nature of the study and the fact that no deviation from current best medical practice will occur throughout the course of the study.

Benefits to future subjects or science

By identifying whether or not lidocaine combined with corticosteroid injectate leads to improved patient outcomes as compared with corticosteroid injection alone, we will be able to educate physicians and patients on best medical practice for treatment of trigger finger. Additionally, as lidocaine has been reported to cause significant burning during injection, if there is no additional benefit to addition of lidocaine to corticosteroid injection, we will be able to spare future patients the discomfort of combining the injectate with lidocaine.

Data safety and monitoring plan:

Patients will be followed up closely in clinic at 2 weeks and 6 weeks post-injection to ensure patients did not experience side effects from the injection and to assess for efficacy of the injection. A low dose of corticosteroid and lidocaine is being utilized and we do not anticipate adverse effects.

Patients will have the ability to remove themselves from this study either completely or partially, and these options will be elucidated on the written consent form.

Every effort will be made to keep data confidential. All data will be kept in encrypted files on password protected devices and when possible on Emory Box and accessible only by Institutional Review Board (IRB) approved study personnel. Each file and folder is password encrypted and personnel must login via passwords to gain access to the folders. When data collection is complete, all identifiers will be removed from the data set prior to analysis. If there is a data breach the study personnel will report this immediately to the IRB.

Government agencies and Emory employees overseeing proper study conduct may access study records. These may include personnel from the Office for Human Research Protections, the Emory Institutional Review Board, the Emory Office of Research Compliance, the Office for Clinical Research, and the Clinical Trials Audit & Compliance Office.

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