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Original Research

Effectiveness of Amniotic Fluid Injection in the Treatment of Trigger Finger: A Pilot Study

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A R T I C L E I N F O

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Purpose: To assess the efficacy and safety of amniotic fluid therapy injections in patients with mild to moderate trigger finger.
Methods: All participants received 1 mL of amniotic fluid injected into the tendon sheath of the affected tendon. Pretreatment and posttreatment data were collected for triggering frequency, Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire scores, and numerical pain rating scale scores.
Results: Of 111 digits from 96 patients, 51% experienced clinically notable improvement and did not receive an alternative treatment. Average length of follow-up was 11 months. From baseline to end of follow-up, average pain score (0–10) decreased from 5.19 to 1.19 ($P < .001$), median triggering per day decreased from 5 to 0 ($P < .001$), and median DASH score (1–100) decreased from 20 to 6.03 ($P < .001$). There was a 50% success rate in patients with diabetes and a 52.6% success rate in digits diagnosed with concomitant Dupuytren contracture in the same hand.
Conclusions: Amniotic fluid therapy injections may offer a biologic alternative for conservative treatment of trigger finger, particularly for patients with diabetes. Decreased pain, decreased triggering, and improved DASH scores offer preliminary evidence supporting the use of amniotic injections for stenosing tenosynovitis.
Type of study/level of evidence: Therapeutic IV.

Stenosing tenosynovitis (trigger finger) is a common, idiopathic disease of the hand affecting the flexor pollicis longus or flexor digitorum tendons. It affects approximately 2.6% of the general population and 10% to 20% of people with diabetes.[1-3] Often involving entrapment at the first annular (A1) pulley, the disease is characterized by thickening of the tendon or narrowing of the tendon sheath.[4] With symptoms including pain and locking (triggering) of the metacarpophalangeal or proximal interphalangeal joints in the affected digits, trigger finger can negatively affect an individual's ability to work as well as his or her social life.[4,5] In severe cases, the finger cannot be straightened, even with assistance, which can result in permanent stiffness.

Evidence-based treatment for stenosing tenosynovitis is currently limited to 2 options: corticosteroid injection into the tendon sheath or surgical release of the tendon sheath. Conservative treatment with corticosteroid injections is inexpensive and easy to use in an outpatient setting. Current literature suggests that the success rate of corticosteroid injections is 60% to 80%.[6-8] Many patients fail corticosteroid steroid injections and ultimately require surgical intervention.[9]

There is an increased prevalence of stenosing tenosynovitis in people with diabetes, but corticosteroid injections can transiently raise glucose levels in these patients for up to a week, complicating treatment.[10,11] Although this increase in glucose levels does not necessarily contraindicate corticosteroid injections, it emphasizes the need to monitor glucose levels closely and adjust medications accordingly. Corticosteroid injections are also typically less

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Table 1
Mechanisms of Action in Amniotic Fluid in the Setting of Tendon Healing*

Growth Factors/Cytokines	Abbreviation	Function/Properties
Tissue inhibitor of metalloproteinases (1,2,3,4)	TIMP (1, 2, 3, 4)	Extracellular matrix breakdown inhibition[19]; cell growth regulation[19]; abnormal collagen structure/collagen degradation inhibition[20–23]
Hepatocyte growth factor	HGF	Anti-inflammatory[24]; tendon repair[25–27]; tendon cell growth[25]; abnormal collagen structure inhibition[25,26]; fibrogenic response enhancement[26,27]
Transforming growth factor (α, β1, β2)	TGF-(α, β1, β2)	Tendon cell proliferation[28]; fibroblast migration[29]; improved collagen structure and fibrogenesis[28,30]; upregulated during normal tendon healing[30,31]
Insulin-like growth factor (1, 2)	IGF (1, 2)	Fibroblast proliferation/migration[32]; cell proliferation[33]; extracellular matrix regulation[33]; collagen synthesis enhancement[33,34]; collagen degradation inhibition[34]; anti-inflammatory[35]
Interleukin 6	IL-6	Collagen synthesis[36,37]
Chemokine	GRO-α	Neovascularization[38]
Epidermal growth factor	EGF	Neovascularization[39]; collagen synthesis[39]; cell proliferation[39]; cell migration[39]
Tumor necrosis factor-α	TNF-α	Collagen synthesis[39]; cell proliferation[39]; fibroblast proliferation[39,41]
Interleukin 1-receptor agonist	IL1-RA	Anti-inflammatory[42]; collagen degradation inhibition[43,44]
Monocyte chemoattractant protein-1	MCP-1	Inflammation regulation[45,46]

* Table data from unpublished study (Smith TB, Raghavan M, Hamrick E, Shuler MS. Amniotic fluid therapy injection for tennis elbow: a pilot study).

effective in patients with diabetes, which limits their usefulness in this at-risk population.[12]

Surgical release is considered for severe cases that are refractory to conservative treatment. Reported success rates for surgical release in relieving symptoms of tenosynovitis are as high as 99%, but associated risks include digital nerve injury, infection, scarring, and tendon bowstringing.[13] Surgical release of the tendon sheath may also exacerbate the symptoms of Dupuytren contracture, which has been associated with trigger finger, particularly in populations of Northern European ancestry.[14] These drawbacks highlight an opportunity to expand the range and efficacy of conservative treatments for trigger finger.

Amniotic fluid therapy (AFT) injections have been studied and considered safe for various clinical applications.[15] They possesses low immunogenicity and are considered to have minimal risk in human use.[16–18] The growth factors and cytokines in amniotic fluid are naturally upregulated in healthy healing tissue and may be able to jump-start healing in disordered tissue (Table 1).[19-46] The purposes of this study were to evaluate the safety and potential benefits of AFT injections as a conservative treatment for trigger finger, as well as to build pilot data for a larger randomized clinical trial. We hypothesized that AFT injections would result in a clinically important reduction in pain and triggering frequency in patients with mild to moderate trigger finger, making AFT injections a safe conservative treatment for trigger finger.

Materials and Methods

This study was conducted under the supervision of the local university's institutional review board from February 2017 to December 2018. To be included, patients had a diagnosis of stenosing tenosynovitis with mild (able to be actively extended) to moderate (able to be passively extended) triggering and were aged 18 years or older. Exclusion criteria included pregnancy or previous surgical treatment for trigger finger in the affected digit. All patients presenting with trigger finger were screened, and all those who met inclusion criteria were offered treatment. Less than 10% of patients declined AFT injection. Before we administered the initial AFT injection, we recorded baseline triggering frequency, numerical pain rating scale scores (0–10), and Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire scores (1–100). The DASH score served as an indication of the patient's upper-extremity function. Triggering frequency was determined by asking about the frequency of triggering based on the number of times per day or per hour the subject experienced locking or catching. A day was assumed to be 16 hours, to compare frequencies described in terms of triggering per day versus triggering per hour.

All participants received 1 mL amniotic fluid mixed with 0.5 mL or 0.5% plain bupivacaine hydrochloride and 0.5 mL 1% plain lidocaine injected with a 27-g hubless needle. The 2-mL mixture was injected into the sheath of the affected tendon at the proximal aspect of the A1 pulley, with the needle angled at approximately 45° distally toward the fingertip. Passive finger flexion and extension was used to ensure the injection was not performed intratendinously. There were no immediate complications or pain. The amniotic fluid was stored at −30°C and thawed by submerging the frozen fluid within its storage vile in warm to hot tap water for approximately 2 minutes. A second injection was discussed and offered if patients received some benefit from the initial injection but symptoms persisted at 6 weeks. Patients who declined a second amniotic fluid injection were offered a steroid shot. Patients with no improvement were recommended to consider surgical intervention.

After the initial AFT injection, triggering frequency, pain score, and DASH score were collected by a follow-up phone call at 2 weeks and follow-up visits with the study physician at 6 weeks and 3 months and 5 or more months. For patients who did not attend their appointment at 5 or more months, an effort was made to collect outcome data over the phone. Aside from the 111 digits included in the analysis, 6 (from 5 participants) were lost to follow-up at an average of 68 days (range, 42–105 days).

In addition, all adverse events were recorded, with special attention given to signs and symptoms associated with tendon rupture, swelling, edema, erythema, or lymphedema. The presence of concomitant Dupuytren contracture was also recorded. The existence of contracted fascia over top of the A1 pulley may represent a specific variant in pathophysiology and may make the effected digit more resistant to conservative management. These patients also offer an increased challenge during surgical release and often have postoperative complications associated with increased contracture.

Failure was determined in 2 ways: (1) if a subject opted for an alternative treatment (corticosteroid injection and/or surgical release) after either the first or second amniotic fluid injection; or (2) if a subject did not experience clinically notable symptom relief. Clinically notable symptom relief was rigorously defined as a 50% decrease in triggering frequency combined with a 4-point reduction in pain score.[47] For patients with a baseline pain score of 5 or less, a 50% decrease in triggering frequency combined with a 50% reduction in pain score was considered clinically notable symptom relief. Only the baseline (pretreatment) and final (≥5-month) set of

Table 2
Characteristics of Study Population (n = 96)*

Characteristics	Values
Average age (SD)	65 (10)
Sex	
Male	48 (50)
Female	48 (50)
Race	
White	75 (78)
Black	9 (9)
Declined	12 (13)
Ethnicity	
Non-Hispanic	73 (76)
Hispanic	1 (1)
Declined	22 (23)
Comorbidity	
Diabetes	27 (28)
Dupuytren disease	50 (52)

* Data are shown as n (%).

Table 3
Total Change in Measurements of Interest

Outcome Measured	Baseline	End of Follow-Up	*P* Value
Pain (0–10)	5.19 ± 2.39	1.19 ± 2.03	<.001
DASH (0–100)	20 (15-37.1)	6.03 (1.67-15.8)	<.001
Triggering frequency per day	5 (3–24)	0 (0–0.14)	<.001

Table 4
Outcomes

Status	Count (%)
Success	57 (51.4)
Failure	
Steroid injection	2 (2)
Steroid injection plus surgery	10 (9)
Surgery	30 (27)
No alternative treatment	12 (10)
Lost to follow-up	6

Table 5
Changes in Pain and DASH Scores and Triggering per Day for Successes

Outcome Measured	Baseline	End of follow-up
Pain (0–10)	5.25 ± 2.35	0.60 ± 1.21
DASH (0–100)	20 (15–34.2)	5.1 (0.42–12.9)
Triggering frequency per day	5 (3–24)	0

Table 6
Changes in Pain and DASH Scores and Triggering per Day for Failures

Outcome Measured	Baseline	End of Follow-Up
Pain (0–10)	5.25 ± 2.46	4.43 ± 2.35
DASH (0–100)	25.8 (15.4–43.5)	30.8 (11.7–41.4)
Triggering frequency per day	10 (4–120)	4 (1–24)

Table 7
Second Injection Outcomes

Status	Count (%)
Success	17 (63)
Failure	
Alternative treatment	9 (33)
No alternative treatment	1 (3.7)

data points from each digit were used to determine success or failure based on symptoms (ie, for digits that did not definitively fail because they received an alternative treatment).

Paired 2-tailed *t* test was used to compare parametric data (pain scores), and Mann-Whitney U test was used to compare nonparametric data (DASH scores and triggering frequency). If a patient was categorized as a success before the end of the study but did not continue to follow-up, the last observed data were carried forward. Patients with failures who opted for another treatment method before the end of the study also had the last observed data carried forward. Results are presented as mean ± SD for parametric data and median (interquartile range) for nonparametric data.

Results

A total of 96 patients (48 men and 48 women, average age 65 ± 11 years) participated in the study (Table 2). A total of 111 digits received amniotic fluid injections. Pain scores, triggering per day, and DASH scores all decreased significantly from baseline to 5 or more months ($P < .001$) (Table 3). Average length of follow-up was 11 ± 4 months. Only 7 digits had a follow-up length of 5 months; all others were 6 or more months. No adverse events or complications were discovered based on the injection or amniotic fluid.

A total of 57 digits (51.4%) experienced clinically notable symptom relief and were categorized as successes, whereas 54 digits (48.7%) were categorized as failures (Table 4). As a group, those with successes experienced an 89% decrease in average pain score, a 75% decrease in median DASH score, and a 100% decrease in median triggering (Table 5).

Of the successfully treated digits, 41 (72%) had a final triggering frequency of 0. Five digits with pain scores that did not meet our criteria for clinically notable symptom relief were still categorized as successes based on a combination of drastic decreases in triggering frequency (−67%, −92%, −100%, −100%, and −100%), DASH scores, and self-reporting. All 5 subjects were specifically asked whether the injection provided benefit, and all responded affirmatively.

For failures, average length of time from initial injection until a patient opted for alternative treatment was 10 ± 7 weeks. Among the 54 digits that did not experience symptom relief and failed, average pain score decreased by 14%, median DASH score increased by 16%, and median triggering per day decreased by 60% (Table 6). The last reported data before failure were used to determine these differences.

Twenty-seven digits received a second amniotic fluid injection at an average of 8 ± 5 weeks (Table 7). Of these, 17 digits (63%) were successful at 5 or more months, 9 patients opted for an alternative treatment (33.3%), and one did not experience symptom relief but also forewent alternative treatment (3.7%). Of the 57 successfully treated digits, 30% had a second injection.

Thirty digits (27%) were from participants with diabetes. Of these, 15 experienced clinically notable symptom relief (50%). Five insulin-dependent digits (38.5%) and 10 non–insulin dependent digits (58.8%) were successful.

A total of 31 digits with coexisting Dupuytren disease (51.7%) and 26 without it (51%) were successful. Moreover, 57 digits were given a diagnosis of concomitant Dupuytren contracture in the same hand (51.4%); 30 of these (52.6%) experienced clinically notable symptom relief. Forty-four digits (39.6%) had a diagnosis of co-occurring Dupuytren (ie, triggering and Dupuytren disease in the same digit); 24 of these (54.6%) experienced clinically notable symptom relief. Of the 87 digits enrolled from Caucasian patients, 50 had a diagnosis of Dupuytren contracture (57.5%). In addition, 42 patients who were aged greater than 50 years and Caucasian had concomitant Dupuytren contracture (61%).

Discussion

Trigger finger pathophysiology has yet to be definitively determined; however, a common hypothesis is that consistent abrasion caused by friction between the tendon and sheath results in inflammation and an abnormal healing process.[1,4] Scar tissue from irregular collagen and matrix synthesis during healing then causes the tendon or sheath to thicken, further impeding tendon movement.[4,5] Amniotic fluid contains a variety of components that are upregulated during healing: hepatocyte growth factor, epidermal growth factor, tumor necrosis factor-α, GRO-α, monocyte chemoattractant protein-1, tissue inhibitor of metalloproteinases (1,2,3,4), insulin-like growth factor (1,2), interleukin 1-receptor agonist, transforming growth factor (α, β1, and β2), and interleukin 6 (Table 1). Introducing these components locally could promote normal healing and avoid abnormal collagen structure and fibrogenesis.[19–46] Amniotic fluid also has low immunogenicity, which makes it a lower-risk option for treating a disorder that is still being elucidated.[15,17] Further study is necessary to reach a consensus on the pathophysiology of trigger finger and the ways in which the specific components of amniotic fluid may work in this specific setting.

Based on our criteria for categorizing study digits as successes or failures, amniotic fluid injections successfully treated triggering and pain associated with stenosing tenosynovitis in about 51% of patients. A similar success rate was observed in the subset of patients with diabetes and in the subset with Dupuytren disease. We did not include DASH scores in our criteria for success and failure; however, improved scores seem to indicate that the treatment contributed to improved function. Many of the digits that were categorized as failures still experienced decreases in pain, triggering, and/or DASH scores even though those participants ultimately opted for alternative treatment or did not meet our threshold for clinically notable symptom relief.

The success rate of corticosteroid injections in treating trigger finger varies widely, but it has commonly been reported at around 60% to 80%. Success rates of corticosteroid injections are considerably lower for diabetic patients at roughly 30% to 60%, with insulin-dependent diabetic patients falling into the lower end of this range.[12,13,48,49] Among our participants, diabetic patients as a whole had a 50% success rate, which provides preliminary evidence that AFTs could be especially useful in this population.

Contrary to our initial belief that the presence of Dupuytren disease would result in resistance to conservative management, the success rate was just over 50% for both participants with Dupuytren disease in the same hand as the study digit and participants with Dupuytren disease co-occurring in the study digit. A total of 57% of participants who identified as white had a concomitant diagnosis of Dupuytren disease. Dupuytren contracture may increase the risk for developing trigger finger.[14] In these patients, the contracture may have a role in the A1 pulley pathology for stenosing tenosynovitis. Surgical intervention for trigger finger in the setting of Dupuytren contracture can lead to a Dupuytren flare and increased finger contracture after release. The high rate of Dupuytren disease in the participants of this study, specifically in the elderly Caucasian population, may constitute a poorly described risk or contributing factor to the development of trigger finger.

This study had several limitations. The small sample size precluded broad characterizations, such as the ability to determine differences in how digits, specifically thumb versus lesser digits, responded to treatment. In addition, follow-up was inconsistent across participants because encounters often varied in numbers and intervals. It was difficult to obtain follow-up for the entire duration of the study in subjects who were not experiencing continued symptoms. The last observed data were carried forward in this study, which could have led to short-term bias. A longer controlled study with enforced follow-up would be able to elucidate more clearly whether the effects of AFT injection hold true over the longer term. In addition, the pathophysiology of trigger finger, as well as the mechanism of action for corticosteroid injections, is poorly understood. Although this study presents plausible mechanisms of action for amniotic fluid, preinjection and postinjection histopathological studies are needed to identify these mechanisms with more certainty. The anti-inflammatory effects of amniotic fluid may act in a manner similar to that of typical steroidal injections.

The ability to differentiate success from failure in the conservative management of trigger finger sometimes offers a substantial challenge. We aimed to err on the side of a conservative estimate for success. Previous studies used surgical intervention only as a means to determine success versus failure. These criteria neglect to account for patients with limited improvement who opt to avoid surgical intervention. Simply using surgery or no surgery as a measure of success, AFT injections would have had a 64% success rate in this study.

Trigger fingers likely differ in etiology, and multiple contributing factors likely result in different successful response rates to either steroid or AFT injections. Conditions such as rheumatoid arthritis, diabetes, and Dupuytren contracture may contribute to the development of triggering.[14,50–52] A better understanding of the pathophysiology of trigger finger as well as the contributing conditions will assist in improved management of this common condition.

Based on these preliminary results, amniotic fluid injections constitute a promising alternative for conservatively treating stenosing tenosynovitis, particularly for patients who are diabetic or have not responded well to corticosteroid injections. Further studies, including a randomized, blinded study comparing corticosteroids and amniotic fluid, are needed to provide definitive Level I evidence for the efficacy of amniotic fluid in the setting of trigger fingers. The cost of AFT injections is also substantially higher than the cost of a typical steroid shot, so additional studies should seek to define subsets of trigger finger subjects better and identify which may benefit most from corticosteroids and/or amniotic fluid injections. This study provides pilot data to support further research and investigations into the potential benefits of amniotic fluid injections in managing mild to moderate stenosing tenosynovitis.

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