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Single Hyaluronate Injection in the Management of Insertional Achilles Tendinopathy in Comparison to Corticosteroid Injections and Non-invasive Conservative Treatments

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Abstract: The Achilles tendon is the strongest and thickest tendon in the body and plays an important role in the biomechanics of the lower extremity. It can withstand high forces during sporting exercises and excessive torsion and stretching. Achilles Tendinopathy (AT) has no pathophysiological theory and no clear understanding of the pathological process. Rest and specific exercises, NSAIDs, steroid injections and surgical treatments are currently used to treat AT. Not one of them has a dominant efficacy for any length of time. Lately, hyaluronate injections have increasingly been used for the treatment of different degenerative processes of joints and soft tissues. The authors reviewed 56 patients with insertional AT treated between 2007 and 2012. All patients were followed up for one year. Patients were divided into three groups: the first group treated by the corticosteroid injection, the second group treated by single hyaluronate injection and the third group treated by rest, splint, NSAIDs, and physiotherapy. Most patients that treated by a single hyaluronate injection showed good to excellent results for a long time in comparison with corticosteroids injections and the conservatively treated patients, according to FADI and VAS scores. In conclusion, it seems that hyaluronate injection therapy is superior to steroid therapy and non-invasive conservative treatment for insertional AT.
Keywords: Achilles tendon, Achilles insertional tendinopathy, corticosteroid injection, hyaluronate injection

INTRODUCTION

Achilles tendinopathy (AT) is becoming a more common complaint due to increased medical awareness and greater physical activities of the general population. It can be the reason for substantial pain and loss of function of the affected limb for a long time. AT is considered an overload injury at the point of attachment at the calcaneus and two to six cm. proximally of that point at the region of maximum torsion. Chronic stress can lead to a defective arrangement of collagen fibers in the AT and result in pain and limited function. At this time, there is no pathophysiologic theory with a clear understanding of the pathological process of this entity. There first appears the evidence of the existence of the TNF-α system in the human AT. Findings are confirmed by mRNA and protein levels as well as biochemically. The TNF-α system was in principle confined to the tenocytes. The connection between tenocyte morphology and the expression pattern of TNF-α, TNFR1, and TNFR2 suggests that the TNF-α system may be involved in tenocyte activation in Achilles tendinosis [1]. AT disorders are multifactorial and include tendinosis, tendinosis with partial rupture, insertional tendinitis, paratenonitis, retrocalcaneal bursitis, and subcutaneous Achilles tendon bursitis. It occurs in combinations of the above in most cases.

The wide spectrum of nonsurgical treatment modalities (the rest, activity modification, specific exercises, use of a brace, NSAIDs, steroid injections, shockwave therapy) indicate that not one of them is strongly effective. AT, therefore, is difficult to manage and up to 29% of AT patients may require surgery [2]. Specific exercises show the most evidence of effectiveness in the treatment of AT [3]. Injection of corticosteroids have strong potential for pain relief for a short period but is problematic because of potentially severe adverse effects [4]. Rupture of the Achilles' tendon following intratendinous injections has been reported. There is evidence supporting the use of hyaluronate injections in patients with ankle sprain, adhesive capsulitis of the shoulder, patients after flexor tendon injury, trochanteric bursitis, and rotator cuff disorder, although the mechanism of the effect has not yet been clarified [5-10]. There is some evidence in experimental laboratory studies that hyaluronate increases proliferation of vascular endothelial growth factor (VEGF) and collagen type 4 during the six weeks after

injection, and decrease the amount of adhesion tissue [11]. Hyaluronic acid dose-dependently inhibited cell proliferation and decreased the expression level of mRNA for adhesion-related procollagens and cytokines [6, 9]. In another study, Hylan G-F 20 has shown a promising curative effect on the tendon and paratenon in an experimental study in rats, and Hylan-injected tendons and paratenons demonstrated significant improvement in comparison to saline injection especially after 75 days [12]. A single hyaluronate injection resulted in similar improvements in pain in each of the four enthesopathies - lateral epicondylitis, patellar tendinopathy, insertional AT, and plantar fasciitis [13]. No published studies have been found that have followed patients who were administered hyaluronate in AT in comparison to other kinds of conservative treatments. Corticosteroid injection is beneficial in the short term for the treatment of tendinopathy but may be worse than other treatments in the intermediate and long term[14].

The use of hyaluronate injections for different kinds of tendinopathy has been routine in this author's practice for the last seven years. This study evaluates of three groups of patients treated with Hyaluronate and compared with corticosteroid injection and non-invasive therapy.

METHODS

Patients

This study evaluates of a consecutive series of 56 patients treated for Achilles insertional tendinopathy. M/W ratio was 21/35. The average age was 54 (range 20-85 years). 17 patients treated by rest, splint, NSAIDs, and physiotherapy. 19 patients treated with corticosteroid injection (betamethasone dipropionate five mg. and betamethasone sodium phosphate two mg.). 20 patients of the third group treated with a standard single sodium hyaluronate 2% (40 mg/2.0 ml) injection (Ostenil Tendon, TRB Chemedica International S.A., 1211 Geneva, Switzerland).

Achilles tendinopathy diagnosis.

Insertional AT is characterized by "deep pain at the tendon-bone junction of the posterior calcaneus point over a bony prominence or spurs located at the posterior superior aspect of the calcaneus" [15]. High-resolution sonography made of all patients for diagnosis of AT as a relatively reliable diagnostic method in Achillodynia [16].

Inclusion Criteria.

All patients were newly diagnosed with insertional AT without any previous treatment before being included in the study.

Exclusion Criteria.

- All patients treated in the past and having received any intervention due to insertional AT.
- Patients who operated on in the same area.
- Patients that had a systemic or rheumatological disease, tarsal tunnel syndrome, moderate to severe osteoarthritis of the ankle and foot, lumbar stenosis or disc disease, and instability of the ankle.
- Patients who were unable to understand the questionnaires.

Treatment Effect Assessment

Patients were assessed using a back-translated FADI (Foot and Ankle Disability Index) version (Hebrew, Russian and Arabic). The questionnaire was self -filled by the patients, and a research assistant verified questionnaire filling. Also, a standardized VAS (Visual Analogue Scale) score was filled out in answer to the question:"What number would you give your pain right now?"

Statistical Analysis

Statistical analysis was performed using the SPSS statistical program. ANOVA with post-hoc analysis was used. Between-group differences in the primary outcome analyzed based on the intention-to-treat principle. Between-group differences in continuous outcome measure analyzed with repeated measures for general linear models. A difference at the 0.05 level is termed significant.

RESULTS

FADI Score

The FADI score evaluated for the entire cohort. The FADI score increased from 26.3 to 67. 91 after six months and 75.179 after a year. The pre-treatment average score was similar in the three groups. A significant difference was found between the groups (ANOVA, $p < 0.05$). The average score of patients treated by corticosteroid injection was 55.39 as compared with 64.77 for the hyaluronate injected group and 48.96 for the conservative treatment group. There was a time interaction with inter-group difference in time. In the corticosteroid group, the average score significantly improved from 26.95 to 73.95 at six months but decreased at 12 months (65.26). The time-related behavior was different in the hyaluronate group with a pre-injection average of 24.90 increasing to 72.85 at six months, and to 96.55 at 12 months. The conservative treatment group had a time-related behavior similar to the corticosteroid group at the one-year follow-up (Figure 1).

VAS Scale

VAS scale declined over time for the entire cohort from 10 to 2.68 after a year. There was a significant inter-group difference of the VAS scores with average VAS of the conservative treatment group higher (5.46) than the corticosteroids treated group (4.74) and the hyaluronate group (3.88). There is a time-dependent intergroup difference with a steep decline from pre-treatment to the six weeks mark, and an insignificant decrease in conservatively treated group at later time points of three months, six months and one year. There

is an insignificant increase of the VAS scale in the corticosteroids treated group at three months and a significant increase at six and twelve months (Figure 2). The time dependence of the hyaluronate groups is different with a continuing significant drop during the one year of follow-up.

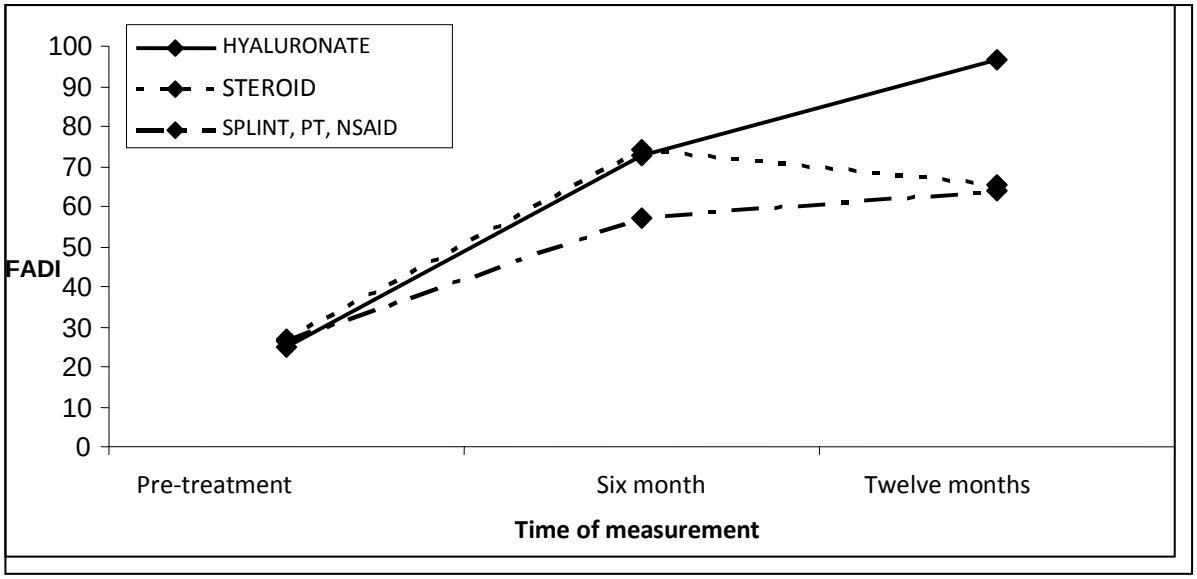

Figure 1: The FADI score is similarly affected by injection therapy in the hyaluronate and steroid at six months, while the ameliorative effect of steroids appears to be short-lived. No difference between steroid and non-invasive treated groups at long time follow-up.

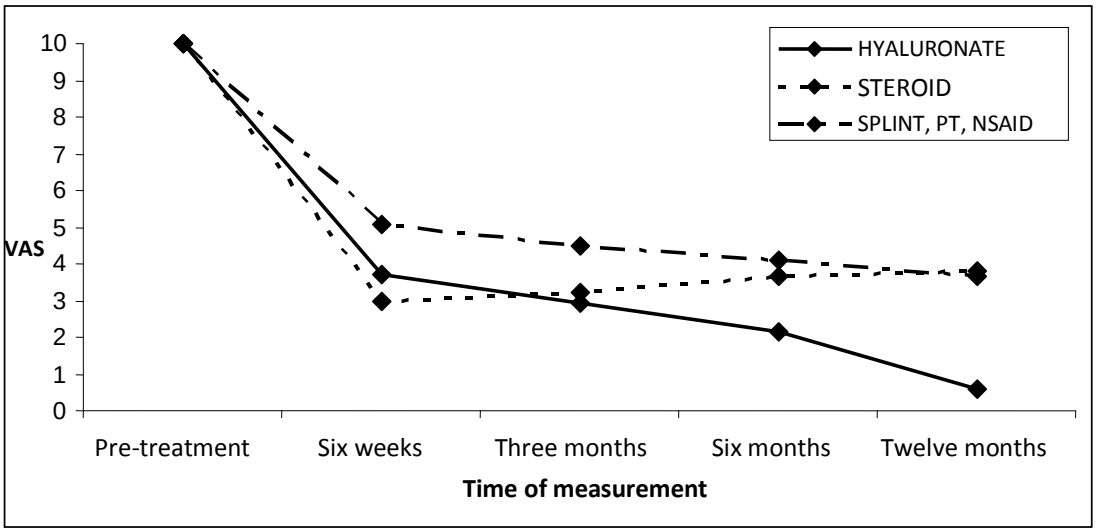

Figure- 2: The VAS score response to injection therapy is similar to that of the FADI score but in decreased direction. Note the similar effects of steroids and non-invasive therapy at twelve months of the follow-up.

DISCUSSION

The mechanism of action of hyaluronate in Achilles tendinopathy appears to be complicated. The basic pathology underlying the symptoms is not yet fully understood. The disorder is apparently complex as a spectrum of diseases ranging from inflammation of the paratendinous tissue to structural degeneration of the tendon. Hyaluronate plays a significant role during wound healing and regeneration. It has anti-inflammatory effects as well as the possibility that its presence will restore normal tissue function. It enhances muscle progenitor cell recruitment and inhibits premature myotube fusion, implicating a role for these glycosaminoglycans in functional repair[17].

The current study appears to demonstrate that there is an ameliorative effect of hyaluronate injections in AT. The pain relief appears to be significant with a large effect size for the hyaluronate group. The effect of steroids appears to be short lived, and this observation concurs with the findings comparing effects of steroids and hyaluronic acid in knee osteoarthritis [18].

Corticosteroid injection may be worse than other treatments in the intermediate and long term. There is no consensus as to whether local steroid injections have a therapeutic role in the treatment of AT. However, they may incur a risk of tendon damage [19].

The current study appears to indicate that hyaluronate injection is an acceptable alternative to steroid injections for the treatment of AT. This alternative treatment may be more useful in a diabetic patient without any complications and side effects of steroids [20].

CONCLUSION

The current study appears to indicate that single hyaluronate injection is efficacious for the treatment of insertional AT. The effect size is larger with hyaluronate injections and lasts longer. Limitations of the current study were the small size of the groups and the fact that the patient were not randomized. A further prospective randomized clinical trial should be done prior to making a clear- cut recommendation that hyaluronate injections are superior to other conservative modalities and may provide an alternative for clinicians

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