

RESULTS OF TREATMENT OF GREATER TROCHANTERIC PAIN SYNDROME IN DIABETIC PATIENTS BY SINGLE HYALURONIC ACID INJECTION

LAUREN GORELICK M. D.¹, AYALA ROZANO-GORELICK, M. D, MHA²,
ANWAR SAAB, M. D, MHA³ & EDWARD RAM, M. D.⁴

¹Orthopaedic and Hand Surgeon, Assuta Medical Center, Haifa, Israel

²Clalalit Health Services- Bar Ilan Medicine Faculty, Zefat, Israel

³Clalalit Health Services- Bar Ilan Medicine Faculty, Zefat, Israel

⁴Division of General Surgery, Rabin Medical Center- Campus Golda, Sackler School of
Medicine, Tel Aviv University, Israel

ABSTRACT

Backgrounds: Typically presenting with pain and a reproducible tenderness in the region of the greater trochanter or lateral thigh, Greater Trochanteric Pain Syndrome (GTPS) is relatively common, reported to affect more than 10% of the general population. Previously, the etiology of GTPS was thought to be caused by inflammation. In that time the results of histologic study, along with recent MRI and ultrasound studies strongly suggest that there is no etiologic role of inflammation in the trochanteric pain syndrome. Treatment of GTPS includes physical therapy measures, activity modification, analgesics, NSAID, shock wave therapy and local glucocorticosteroid injection. The current study performed in order to assess the efficacy of single hyaluronic acid trochanteric injections in diabetic patients.

Methods: 92 diabetic patients (74 female/18 male) treated for GTPS by single injection of hyaluronate.

Results: Pre-injection average HOOS score were 23 ± 3 . Following injections, the HOOS score increased from 23 to 62 after six months and 72 after year. The average VAS score of patients treated by hyaluronate fall from 10 before the treatment to 2.25 at one year. This data are similar to results of treatment GTPS by hyaluronate injection in the general population.

Discussion: It appears that hyaluronate injections are highly safe and efficacious for treating trochanteric bursitis in diabetic patients as in the general population.

KEYWORDS: Greater Trochanteric Pain Syndrome, Trochanteric Bursitis, Hyaluronic Acid, Diabetes

INTRODUCTION

Greater trochanteric pain syndrome (GTPS) that affect more than 10% of the population in industrial countries is a condition resulting in pain over a greater trochanter and once described as trochanteric bursitis or tendinitis. In most cases, it is often idiopathic and prevalence in women and adults (1). The incidence of trochanteric bursitis peaks between the fourth and sixth decades of life, but cases reported in all age-groups (2). At that time, the precise nature of the lesion in this syndrome has not been clearly defined. Previously, the etiology of the trochanteric pain syndrome was thought to be caused by inflammation. In that time the results of histologic study, along with recent MRI and ultrasound studies strongly suggest that there is no etiologic role of inflammation in the trochanteric pain syndrome (3). GTPS associates with pain and limitation of function for a long period in most patients that underrecognized and not treated. Trochanteric bursitis should distinguish from sciatica and irradiating pain of pelvic and spinal origin, osteoarthritis of hip and local nerve pathology.

Treatment includes physical therapy measures, activity modification, analgesics, NSAID, shock wave therapy and local glucocorticosteroid injection. Most patients respond to conservative treatment. Injection therapy is considered quiet efficient with over 60 percent pain alleviation (4). A clinically relevant effect is shown at a 3-month follow-up visit for recovery and pain at rest and with activity. At a 12-month follow-up visit, the differences in outcome were no longer present (5). There are inherent dangers to injection steroids anywhere in the body (6). It may be especially problematic in patient with diabetes that may have systemic effects of local glucocorticoid injections. It notes in a clinical study that administration of three local corticosteroid injections followed by suppression of the corticotropic axis that persisted beyond 21 days after epidural injection and recovered more rapidly after intraarticular injection. Systolic blood pressure increased transiently. Elevations in postprandial glucose levels lasted longer in diabetic than non-diabetic patients (7). An alternative injectable medication is hyaluronate.

It was found highly effective for the treatment of GTPS in the general population and appears to be longer lasting than that of steroid alone (8). Hyaluronate significantly and dose-dependently inhibited cell proliferation, decreased the expression levels of mRNA for adhesion-related procollagens and cytokines. There is a growing body of evidence supporting the use of hyaluronate injections in patient with an ankle sprain, adhesive capsulitis of the shoulder, patients after flexor tendon injury, trochanteric bursitis, rotator cuff disorder although the mechanism of the effect has not yet been clarified (8, 9, 10, 11, 12). In the experimental laboratory study hyaluronate increase proliferation of vascular endothelial growth factor (VEGF) and collagen type 4 during six weeks after injection and decrease amount of adhesion tissue. Hyaluronic acid dose-dependently inhibited cell proliferation and decreased the expression level of mRNA for adhesion related procollagens and cytokines (10, 12, 13). In another study, Hylan G-F 20 has a promising curative effect on the tendon and paratenon an experimental study in rats and Hylan-injected tendons and paratenons demonstrated significantly improvement to comparison saline injection especially after 75 days (14). Although it found that HA preferentially binds to elastic fibers, it remains to be shown that such attachment prevents damage to the fibers (15). It is thus possible that a similar therapeutic effect be achieved using hyaluronate injections in the trochanteric bursa. The use of hyaluronate injections in diabetic patients has been routine in author's practice for the last nine years.

METHODS

Patients

There is a retrospective evaluation of a 92 diabetic patients that treated for GTPS (74 female/18 male). The average age was 61 (range 41-80 years). All 92 patients treated with single hyaluronate injection (Ostenil Plus, TRB Chemedica International S.A., 1211 Geneva, Switzerland).

Trochanteric Bursitis Diagnosis

The diagnosis was made as suggested by Brinks et al: "Trochanteric Bursitis was diagnosed when the patient complained of pain persisting for more than one week in the lateral region of the hip, and tenderness to palpation of the greater trochanter, reproducing the patient's pain, was found on physical examination" (16). All patients underwent at least one month of conservative treatment consisting of standard physiotherapy regimen of physical strengthening of the gluteus medius and electrotherapy of the affected region. Treatment with NSAID agents was given to some of the patients as per family physician decision.

Inclusion Criteria

1) Diagnosis of GTPS in diabetic patients as described above; 2) Failure of one month of conservative therapy; 3) Agreement to injection therapy.

Exclusion Criteria

1) Patients who were unable to understand the questionnaires; 2) Patients who had consulted their general practitioner with the same symptoms in the previous year and had received any intervention except the conservative therapy described above; 3) Patients who were operated on in the same region, or who had a systemic neurological or rheumatologic disorder; 4) Patients suffering from chronic low back pain or sciatica as per medical records; 5) Non-diabetic patients diagnosed as GTPS.

Treatment Effect Assessment

Patients were assessed using a back-translated HOOS (www.koos.nu/HOOSEng.pdf) version (Hebrew, Russian and Arabic). The questionnaires were self-filled by the patients, and a research assistant verified questionnaire filling. In addition, a standardized VAS score was filled out in answer to the question: "What number would you give your pain right now?"

RESULTS

HOOS Score

The pre-injection average HOOS score was 23 ± 3 . The average HOOS score increased in all patients from 23 to 72 after a year (Figure 1). The time-related behavior was different into the group. Seven from 92 patients (8%) showed increase HOOS score at six months but a slight decrease at one year. 85 patients (92%) had increased HOOS score at all points of measurement.

VAS Scale

Average VAS scale declined over time for the entire cohort from 10 to 2.25 after a year (Figure 2). There is a time-dependent difference in changes of VAS score into the group with a steep decline from pre-treatment to the six weeks, insignificant increase at three and six months and marked significant decrease at the points of one year.

DISCUSSIONS

The current study performed in order to assess the efficacy of single hyaluronic acid trochanteric injections in diabetic patients. According to accepted data, there is a significant improvement of pain and function after injection of hyaluronic acid in diabetic patients with GTPS. These effects are long lasting and without any complications and side effects. A possible mechanism of action of hyaluronate in GTPS based on its anti-inflammatory and restore tissue regeneration and function effects (17). Steroid injection particularly in diabetics is likely to raise glucose levels and may be worse than other treatments in the intermediate and long terms (7, 18). The disorder is apparently non-inflammatory, and there is no evidence that local steroid injections have a therapeutic role in the treatment of GTPS. No clear evidence of benefit of other injections was shown, except for sodium hyaluronate in the long term (8, 18). Analogical single hyaluronate injection results in similar improvements of pain in each of the four enthesopathies as lateral epicondylitis, patellar tendinopathy, insertional Achilles tendinitis and plantar fasciitis according preliminary results of the study from Japan (19).

CONCLUSIONS

The current study appears to indicate that hyaluronate injection is an acceptable alternative to steroid injections for the treatment of trochanteric bursitis in diabetic patients. The HOOS and VAS scores of the recent study compatible with HOOS and VAS scores of hyaluronate treated group with GTPS from the general population. Limitations of the

current study include its design being not randomized and retrospective. A further prospective randomized clinical trial should be done prior to making a clear-cut recommendation that hyaluronate injections are superior to steroid injections in the treatment of this syndrome in diabetic patients.

Disclosure

No author who contributed to this article has any conflict of interests to declare. The study conducted in compliance with the current laws applying in the country of the authors.

REFERENCES

1. Strauss EJ, Nho SJ, Kelly BT. Greater trochanteric pain syndrome. Sports Med Arthrosc. 2010 Jun; 18(2):113-9. doi: 10.1097/JSA.0b013e3181e0b2ff
2. Shbeeb MI, Matteson EL. Trochanteric bursitis (greater trochanter pain syndrome). Mayo Clin Proc 1996; 71: 565–9.
3. Silva, Fernando MD; Adams, Thomas MD; Feinstein, Jeffery MD; Arroyo, Ramon A. MD. Trochanteric Bursitis: Refuting the Myth of Inflammation. JCR: Journal of Clinical Rheumatology. April 2008 - Volume 14 - Issue 2 - pp 82-86 doi: 10.1097/RHU.0b013e31816b4471
4. P. Walker, S. Kannagara, W. J. Bruce, D. Michael and H. Van der Wall, “Lateral Hip Pain: Does Imaging Predict Response to Localized Injection?” Clinical Orthopedics and Related Research, Vol. 457, 2007, pp. 144-149.
5. Brinks A, van Rijn RM, Willemsen SP, Bohnen AM, Verhaar JA, Koes BW, Bierma-Zeinstra SM. Corticosteroid injections for greater trochanteric pain syndrome: a randomized controlled trial in primary care. Ann Fam Med. 2011 May-Jun; 9(3): 226-34. doi: 10.1370/afm.1232
6. M. B. Stephens, A. I. Beutler and F. G. O’Connor, “Musculoskeletal Injections: A Review of the Evidence,” American Family Physician, Vol. 78, No. 8, 2008, pp.
7. Younes M, Neffati F, Touzi M, et al. Systemic effects of epidural and intraarticular glucocorticoid injections in diabetic and non-diabetic patients. Joint Bone Spine. 2007;74(5):472–476
8. L. Gorelick, A. Rozano-Gorelick, D. Robinson, O. Marcus, S. Joubran, E. Ram, "Treatment of Hip Trochanteric Bursitis Using Hyaluronate Injections," Open Journal of Rheumatology and Autoimmune Diseases, Vol. 3 No. 2, 2013, pp. 125-129. doi: 10.4236/ojra.2013.32019.
9. Petrella RJ, Petrella MJ, Cogliano A. Periarticular hyaluronic acid in acute ankle sprain. Clinical Journal of Sports Medicine. 2007; 17(4):251–257. doi: 10.1097/JSM.0b013e3180f6169f. [[PubMed](#)] [[Cross Ref](#)]
10. M. Nago, Y. Mitsui, M. Gotoh, K. Nakama, I. Shirachi, F. Higuchi and K. Nagata, “Hyaluronan Modulates Cell Proliferation and mRNA Expression of Adhesion-Related Procollagens and Cytokines in Glenohumeral Synovial/Capsular Fibroblasts in Adhesive Capsulitis,” Journal of Orthopaedic Research, Vol. 28, No. 6, 2010, pp. 726-731.
11. Ozgenel GY, Etöz A. Effects of repetitive injections of hyaluronic acid on peritendinous adhesions after flexor tendon repair: a preliminary randomized, placebo-controlled clinical trial. Ulus Travma Acil Cerrahi Derg. 2012 Jan; 18(1): 11-7. doi: 10.5505/tjtes.2011.95530

12. Mitsui Y, Gotoh M, Nakama K, Yamada T, Higuchi F, Nagata K. Hyaluronic acid inhibits mRNA expression of proinflammatory cytokines and cyclooxygenase-2/prostaglandin E(2) production via CD44 in interleukin-1-stimulated subacromial synovial fibroblasts from patients with rotator cuff disease. *J Orthop Res.* 2008 Jul;26(7):1032-7. doi: 10.1002/jor.20558.
13. Halici M, Karaoglu S, Canoz O, Kabak S, Baktir A. Sodium hyaluronate regulating angiogenesis during Achilles tendon healing. *Knee Surg Sports Traumatol Arthrosc.* 2004 Nov;12(6):562-7. Epub 2004 Jul 27
14. Tatari H, Skiak E, Destan H, Ulukuş C, Ozer E, Satoğlu S. Effect of hylan G-F 20 in Achilles' tendonitis: an experimental study in rats. *Arch Phys Med Rehabil.* 2004 Sep;85(9):1470-4.
15. Cantor JO, Shteyngart B, Cerreta JM, Liu M, Armand G, Turino GM. The effect of hyaluronan on elastic fiber injury in vitro and elastase-induced airspace enlargement in vivo. *Proc Soc Exp Biol Med.* 2000 Oct;225(1):65-71
16. A. Brinks, R. M. van Rijn, A. M. Bohnen, G. L. Slee, J. A. Verhaar, B. W. Koes and S. M. Bierma-Zeinstra, "Effect of Corticosteroid Injection for Trochanter Pain Syndrome: Design of a Randomised Clinical Trial in General Practice," *BMC Musculoskeletal Disorders*, Vol. 8, 2007, pp. 95-99. doi:10.1186/1471-2474-8-95
17. S. Calve, J. Isaac, J. P. Gumucio and C. L. Mendias, "Hyaluronic Acid, HAS1 and HAS2 Are Significantly Upregulated during Muscle Hypertrophy," *American Journal of Physiology: Cell Physiology*, Vol. 303, No. 5, 2012, pp. C577-C588. doi:10.1152/ajpcell.00057.2012
18. Hart L. Corticosteroid and other injections in the management of tendinopathies: a review. *Clin J Sport Med.* 2011 Nov;21(6):540-1. doi: 10.1097/01.jsm.0000407929.35973.b9.
19. Kumai T, Muneta T, Tsuchiya A, Shiraishi M, Ishizaki Y, Sugimoto K, Samoto N, Isomoto S, Tanaka Y, Takakura Y. "The short-term effect after a single injection of high-molecular-weight hyaluronic acid in patients with enthesopathies (lateral epicondylitis, patellar tendinopathy, insertional Achilles tendinopathy, and plantar fasciitis): a preliminary study." *J Orthop Sci.* 2014 Jul;19(4):603-11. doi: 10.1007/s00776-014-0579-2. Epub 2014 May 10.

APPENDICES

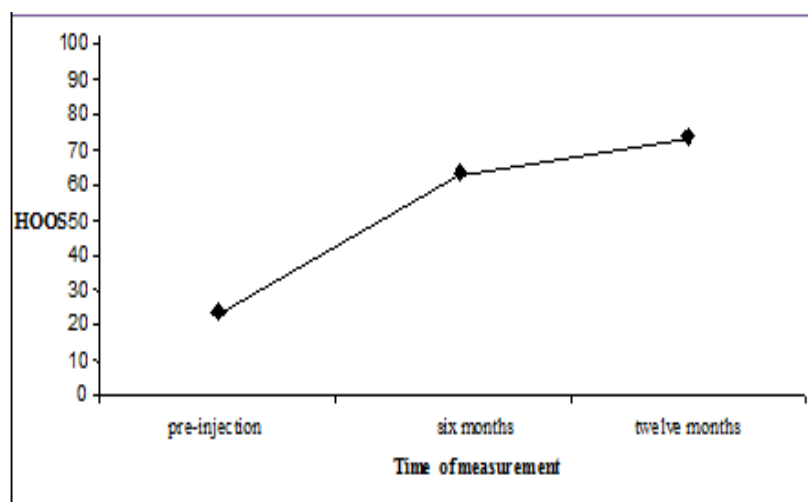


Figure 1: Changes in HOOS Score Following Single Hyaluronic Acid Injection with Significant Increase at One Year Follow-Up

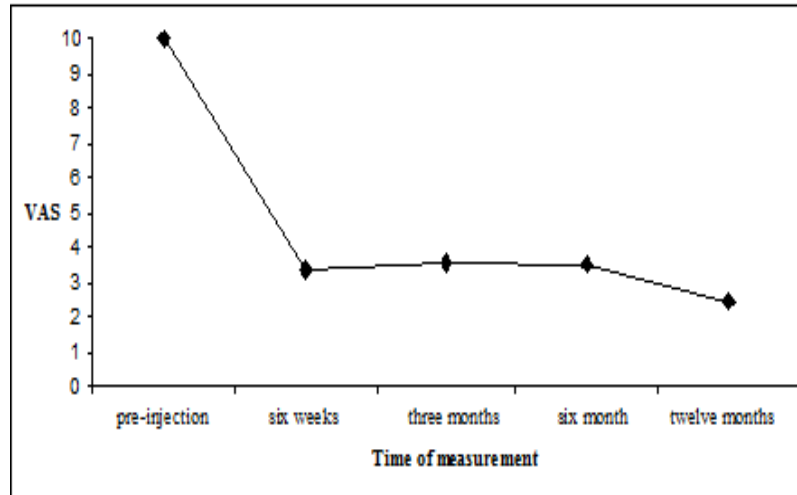


Figure 2: The Graph Show Significant Decrease of Pain According to VAS Scale from the Point of Pre-Injection to the Point of One Year Follow-Up



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