Gavin Publishers
Journal of Orthopedic Research and Therapy
Volume 2016; Issue 2
Cole WW, et al.

Research Article

Hylan GF-20 Effectiveness in the Treatment of Compartmentalized Knee Osteoarthritis Using the KOOS Questionnaire

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Citation: Cole WW, Shields CL, Lerebours FR (2016) Hylan GF-20 Effectiveness in the Treatment of Compartmentalized Knee Osteoarthritis Using the KOOS Questionnaire. J Orthop Res Ther 2016: 34-37.

Received Date: 21 September, 2016; **Accepted Date:** 19 October, 2016; **Published Date:** 26 October, 2016

Abstract

Background: Osteoarthritis is the most common joint disorder in the world that will affect nearly half of all adults by age 85. The appropriate management in patients with mild to severe osteoarthritis still remains a challenging area where viscosupplementation (SYNVISC) can play an important role.

Hypothesis/Purpose: To analyze the efficacy of intra-articular injections of SYNVISC (Hylan G-F 20) for the treatment of Grade II-IV medial tibio-femoral, lateral tibio-femoral, and patellofemoral knee osteoarthritis using validated outcome scores (KOOS).

Study Design: This is a retrospective case series study including patients over a span of 6 years.

Methods: A convenience sample of 90 patients (107 injections) with Grade II-IV knee osteoarthritis participated in this study. Patients had an age range from 41-83 years of age with a mean age 60 years old. Patients were included if they completed a baseline KOOS survey and a 6-week follow-up KOOS survey after intra-articular injection of Hylan G-F 20.

Results: After Hylan G-F 20 injection, a clinically significant increase in the KOOS survey categories of pain,symptoms, and activities of daily life were seen in patients with grade III and grade IV lateral tibio-femoral osteoarthritis and a decrease in pain was seen in most patients.

Conclusions: The data from this study was statistically significant, and indicates that patients are satisfied and find it easier to perform daily activities with less knee pain after a viscosupplementation injection. Hylan G-F 20 injections provide good clinical benefits for the patient and are a safe treatment for knee osteoarthritis.

Introduction

Osteoarthritis (OA) of the knee can be characterized by focal and progressive loss of articular cartilage. Radiographic evidence of OA occurs in most people by age 65 and in about 80% of those aged over 75 years old [1]. Joint space narrowing, osteophytes, and bony sclerosis can be seen in patients diagnosed with painful knee osteoarthritis. The International Cartilage Repair Society rating scale classifies OA as the following: Grade I – Nearly Normal (soft indentation and/or superficial fissures and cracks), Grade II- Abnormal (lesions extending down to <50% of cartilage depth), Grade III- Severely Abnormal (Cartilage defects extending down >50% of cartilage depth as well down to calcified layer and down to but not through the subchondral bone, blisters included), Grade IV- Exposed subchondral bone [2]. Treatment of Grade II-IV OA can include exercising, bracing, NSAID's, narcotic pain relievers, topical pain solutions, physical therapy, and viscosupplementation.

Total knee arthroplasty is a surgical option for patients with severe grade IV OA [3].

Viscosupplementation injections are made from Hyaluronic acid, a polysaccharide chain made of repeating disaccharide units of N-acetylglucosamine and glucuronic acid extracted from rooster combs [4]. The healthy human knee contains about 2mL of synovial fluid, with a hyaluronic acid concentration of 2.5 to 4.0 mg/ml. In knees with OA the HA concentration decreases to about 1-2mg/ml [4]. HA injections are beneficial for the treatment of knee OA due to its viscoelastic properties as well as its anti-inflammatory, anabolic, and analgesic properties. HA's viscoelastic properties help the knee in shock absorption and is an effective knee lubricant [5]. HA with a high molecular weight has also been shown to elicit anti-inflammatory effects by inhibiting arachadonic acid release in inflamed joints [6]. Intra-articular HA modulates pain perception directly through inhibition of nocioreceptors or indirectly binding to substance P 4. HA injections have been shown to have a therapeutic effect at 4 weeks post-injection, with a peak at 8 weeks and extension to over 6 months [7-9].

HA products can differ in method of production, molecular weight, and dosing instructions.Synvisc (Hylan G-F 20) is an elastoviscous high molecular weight fluid containing cross-linked HylanA&Hylan B polymers. Hylan A (80%) is a soluble high MW molecule (6.000.000 DA), while Hylan B (20%) is an insoluble gel. The cross-linking of the two allows a longer residence time into the joint than that of linear HA products [10]. HA products that are cross-linked have been shown to be more effective and have less adverse effects than non cross-linked HA injections [11,5]. HA is cleared rapidly from the joint after injection (20 hrs), but in patients pain and function improvement can persist for months after treatment [12].

HA injection effectiveness can be measured using the Knee Injury and Osteoarthritis Outcome Score (KOOS). The KOOS is a self-reported score that covers five dimensions that are determined separately: pain, symptoms, activities of daily living, sport and recreation function, and knee related quality of life. The KOOS is organized to ensure content validity for older patients with osteoarthritis as well for younger or more physically active patients. Questions from the Western Ontario and MacMaster Universities (WOMAC) Osteoarthritis index (an outcome measure covering pain, stiffness, and function) are included in their original form in the KOOS questionnaire [13]. KOOS scores range from 0-100, with zero representing extreme knee problems and 100 representing no knee problems.

The objective of this study was to retrospectively analyze KOOS scores and perform an analysis of the efficacy of intra-articular injections of Synvisc® for the treatment of Grade II-IV lateral tibio-femoral, medial tibio-femoral, and patellofemoral knee OA in patients.

Methods

A convenience sample of 90 patients (107 injections) over a period of 6 years with unilateral of bilateral painful Grade II-IV knee OA were given a single or bilateral intra-articular injection of 6mL of Hylan G-F 20 by the senior author [14-17] patients received bilateral injections which accounts for the difference between the number of patients and the number of injections.The average age of subjects in our cohort was 60 years of age with a range of 41-83 years old and a standard deviation of 6 years. Patients were included if they completed a baseline KOOS survey and a 6 week follow up KOOS survey after intra-articular injection of Hylan G-F 20. Patients were excluded if there were no completed KOOS post-survey, knee MRI, or surgery reports to determine OA grade.

Grades and compartment of patient OA was determined by patient MRI reports and arthroscopic surgery reports. OA was identified as either mild (Grade II), moderate (Grade III), and severe (grade IV).OA grade was then classified by compartment; Patellofemoral (PF), MedialTibio-femoral weight bearing (M), and lateralTibio-femoral weight bearing (L). Patients had different OA grades for different compartments which was analyzed and compared.For comparisons of the quantitative measures between the pre and post KOOS survey scores, a paired t-test was used.

Results

In patients with grade II patellofemoral OA, KOOS symptom, pain, and ADL scores improved significantly from baseline to the 6 week follow-up ($p<.05$). No significant changes were seen with the other two scores for grade II PF OA. In patients with grade III PF OA underwent significant improvement in the KOOS scores of symptoms and pain ($p<.05$). No significant changes were seen in the other KOOS scores. In patients with grade IV PF OA a significant improvement in pain was seen among KOOS scores. No significant changes were seen in the other KOOS scores (Table 1).

In patients with grade II medial compartment knee OA no significant changes in KOOS scores were seen. In patients with grade III medial OA a significant improvement in pain was seen in KOOS score ($p<.05$). No significant changes were seen in the other KOOS scores. In patients with grade IV medial OA, a significant increase in the pain and knee-related quality of life KOOS scores were seen ($p<.05$). No significant changes were seen in the other categories (Table 2).

In patients with grade II lateral compartment knee OA significant changes in sports and recreation function were seen in KOOS score ($p<.05$). No significant changes were seen in the other KOOS scores. In patients with grade III lateral compartment OA significant improvement in the KOOS categories symptoms, pain, and activities of daily living were seen ($p<.05$). No significant changes were seen in the other categories. In patients with grade IV lateral OA, significant improvements in

symptoms, pain, and ADL were seen in KOOS scores (p<.05). Other scores showed no significant changes (Table3).

Table 1. Patellofemoral OA KOOS Scores			
Grade II (N=17)	**Baseline**	**6-Week post HA injection**	**P**
Symptoms	44+/- 10	55+/-11	<.05
Pain	51+/-13	65+/-18	<.05
ADL	53+/-24	72+/-18	<.05
Sports/Rec	23+/-26	15+/-20	0.28
QOL	21+/-14	29+/-20	0.2
Grade III (N=37)			
Symptoms	48+/-13	55+/-14	<.05
Pain	55+/-16	64+/-18	<.05
ADL	60+/-18	68+/-20	0.08
Sports/Rec	31+/-22	32+/-29	0.86
QOL	28+/-20	34+/-26	0.28
Grade IV (N=29)			
Symptoms	39+/-20	45+/-18	0.22
Pain	43+/-20	56+/-25	<.05
ADL	51+/-24	59+/-26	0.19
Sports/Rec	17+/-18	22+/-22	0.3
QOL	22+/-18	20+/-16	0.6

Table 1: Mean +/- SD baseline and 6 week follow-up KOOS scores of patients with grade II-IV patellofemoral OA.

Note: KOOS consists of five subscales: symptoms, pain, activities of daily living, sports and recreation function, and knee-related quality of life.

Table2. Medial Tibio-femoral Compartment OA KOOS Scores			
Grade II (N=13)	**Baseline**	**6-Week Follow-up**	**P**
Symptoms	57+/-15	62+/-13	0.42
Pain	59+/-14	63+/-21	0.52
ADL	58+/-22	69+/-21	0.2
Sports/Rec	30+/-17	36+/-23	0.52
QOL	31+/-18	34+/-18	0.7
Grade III (N=23)			
Symptoms	43+/-19	69+/-25	0.22
Pain	46+/-21	60+/-17	<.05
ADL	55+/-22	63+/-16	0.09
Sports/Rec	30+/-23	35+/-21	0.46
QOL	36+/-17	33+/-14	0.56
Grade IV (N=27)			
Symptoms	50+/-15	55+/-17	0.21
Pain	56+/-16	70+/-16	<.05
ADL	64+/-21	74+/-19	0.06
Sports/Rec	27+/-18	35+/-27	0.24
QOL	26+/-14	39+/-24	<.05

Table 2: Mean +/- SD baseline and 6 week follow-up KOOS scores of patients with grade II-IV medial compartment OA.

Note: KOOS consists of five subscales: symptoms, pain, activities of daily living, sports and recreation function, and knee-related quality of life.

Discussion

The purpose of this study was to compare the effects of Hylan G-F 20 injections on knee osteoarthritis, separated by knee compartment and grade. The main findings in the study included a significant reduction in pain and better function in the activities of daily life and symptoms in patients with grade III and grade IV lateral compartment knee osteoarthritis. Statistically significant increases in KOOS pain scores, meaning they experienced less pain, was seen in all patients except in patients with grade II lateral and medial compartment knee OA. An increase in scores in the KOOS category of symptoms category was also seen in patients with grade II and III patellofemoral OA.Similar improvements in knee pain, symptoms, and function have been documented in patients with OA treated with HA injections [14-16].

Table 3. Lateral Tibio-femoral Compartment OA KOOS Scores			
Grade II (N=5)	**Baseline**	**6-Week Follow up**	**P**
Symptoms	61+/-15	54+/-14	0.5
Pain	64+/-22	67+/-14	0.86
ADL	71+/-22	77+/-14	0.59
Sports/Rec	18+/-6	35+/-10	<.05
QOL	39+/-20	40+/-18	0.92
Grade III (N=22)			
Symptoms	50+/-11	57+/-16	<.05
Pain	52+/-14	66+/-18	<.05
ADL	59+/-16	70+/-19	<.05
Sports/Rec	33+/-24	33+/-24	0.99
QOL	31+/-17	35+/-21	0.46
Grade IV (N=38)			
Symptoms	49+/-16	56+/-18	<.05
Pain	55+/-15	65+/-22	<.05
ADL	60+/-17	69+/-22	<.05
Sports/Rec	30+/-19	35+/-29	0.37
QOL	30+/-13	37+/-21	0.09

Table 3: Mean +/- SD baseline and 6 week follow-up KOOS scores of patients with grade II-IV lateral compartment OA.

Note: KOOS consists of five subscales: symptoms, pain, activities of daily living, sports and recreation function, and knee-related quality of life.

The 2nd edition of the Academy of Orthopaedic Surgeons guideline on treatment of knee OA released a position statement claiming that "we cannot recommend using HA for patients with symptomatic knee OA", based on a lack of clinically important improvement [17]. The Osteoarthtitis Research Society International guideline for non-surgical management of knee OA also stated that the recommendation for HA injection was uncertain because of the inconsistent conclusions among the meta-analysis and conflicting results regarding the safety of HA [18]. In contrast, hylan G-F 20 has been shown to give greater improvement than placebo injection in patients [19]. HA injection has been shown to decrease knee pain from a time span of 6 month to a year and can also be used in combination with knee rehabilitation to reduce knee pain at night [16,20,21]. Viscosupplementation has also been proven effective in the treatment of not only knee OA, but shoulder gleno-humeral OA [22]. HA's effects can be due to its intrinsic anti-inflammatory characteristics and its increase in knee

viscosity [23,24]. Lower adverse effects are also seen in patients with HA injections [25].

There were a few limitations to this study. Many patients did not fill out post injection surveys and had to be excluded from this study. Since this is a retrospective study there may have also been some recall bias from the patients. We did not include parameters such as length of HA injection effect in this study or the amount of time it took for the patient to feel the effects of the injection. Also, many patients of our mean cohort age (60) do not engage in many rigorous sports activities and did not fully complete the sports and recreation or knee related quality of life portion of the KOOS survey.

Conclusion

This retrospective study showed that intra-articular injection of Hylan G-F 20 was most effective in providing statistically significant pain relief, and better knee function in everyday activities in patients with grade III and grade IV lateral compartment knee osteoarthritis.HA injection was also very effective in reducing the knee pain in the majority of patients.

References

1. Arden N, Nevitt MC (2006) Osteoarthritis: Epidemiology. Best Pract Res Clin Rheumatol 20: 3-25.
2. Ayhan E, Kesmezacar H, Akgun I (2014) Intraarticular injections (corticosteroid, hyaluronic acid, platelet rich plasma) for the knee osteoarthritis. World J Orthop 5: 351-361.
3. Baboolal TG, Mastbergen SC, Jones E, Calder SJ, Lafeber FPJG, et al. (2015) Synovial fluid hyaluronan mediates MSC attachment to cartilage, a potential novel mechanism contributing to cartilage repair in osteoarthritis using knee joint distraction. Ann Rheum Dis 1-8.
4. Bert JM, Waddell DD (2010) Viscosupplementation with hylan G-F 20 in patients with osteoarthrosis of the knee. Ther Adv Musculoskelet Dis 2: 127-132.
5. Boselli KJ, Ahmad CS, Levine WN (2010) Treatment of glenohumeral arthrosis. Am J Sports Med 18: 375-382.
6. Campbell DG, Angel KR, Dobson PJ, Lewis PL, Tandon S (2004) Experiences of viscosupplementation for knee osteoarthritis. Aust Fam Physician 33: 863-864.
7. Clinical A, Guideline P (2013) Treatment of Osteoarthritis of the Knee : Evidence-Based Guideline. J Am Acad Orthop Surg 21: 571-576.
8. Cohen M, Kam Z, Addadi L, Geiger B (2006) Dynamic study of the transition from hyaluronan- to integrin-mediated adhesion in chondrocytes. EMBO J 25: 302-311.
9. Evaniew N, Simunovic N, Karlsson J (2014) Cochrane in CORR®: Viscosupplementation for the treatment of osteoarthritis of the knee. Clin Orthop Relat Res 472: 2028-2034.
10. Feeley BT, Gallo RA, Sherman S, Williams RJ (2010) Management of osteoarthritis of the knee in the active patient. J Am Acad Orthop Surg 18: 406-416.
11. Jones G, Ding C (2010) Hylan G-F 20: Review of its Safety and Efficacy in the Management of Joint Pain and Osteoarthritis. Clin Med Insights Arthritis Musculoskelet Disord 3:55-68.
12. Kuroki H, Nakagawa Y, Mori K, et al. (2008) Ultrasound properties of articular cartilage in the tibio-femoral joint in knee osteoarthritis: relation to clinical assessment (International Cartilage Repair Society grade). Arthritis Res Ther 10: R78.
13. McAlindon TE, Bannuru RR, Sullivan MC, et al. (2015) OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthr Cartil 22: 363-388.
14. Palmieri B, Rottigni V, Iannitti T (2013) Preliminary study of highly cross-linked hyaluronic acid-based combination therapy for management of knee osteoarthritis-related pain. Drug Des Devel Ther 7:7-12.
15. Petrella RJ, Emans PJ, Alleyne J, Dellaert F, Gill DP, et al. (2015) Safety and performance of Hydros and Hydros-TA for knee osteoarthritis: a prospective, multicenter, randomized, double-blind feasibility trial. BMC Musculoskelet Disord 16: 57.
16. Press D (2015) Efficacy and safety of cross-linked hyaluronic acid single injection on osteoarthritis of the knee : a post-marketing phase IV study. Drug Des Devel Ther 9: 2063-2072.
17. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD (1998) Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. J Orthop Sports Phys Ther 28: 88-96.
18. Silvers HJ (2014) Viscosupplementation During Rehabilitation. Sport Heal A Multidiscip Approach 6: 422-426.
19. Smith GN, Myers SL, Brandt KD, Mickler EA (1998) Effect of intraarticular hyaluronan injection in experimental canine osteoarthritis. Arthritis Rheum 41: 976-985.
20. Tobetto K, Yasui T, Ando T (1992) Inhibitory Effects of Hyaluronan on [' 4CjArachidonic Acid Release from Labeled Human Synovial Fibroblasts. Japan J Pharmacol 60: 79-84.
21. Ulrich-Vinther M, Maloney MD, Schwarz EM, Rosier R, O'Keefe RJ (2003) Articular cartilage biology. J Am Acad Orthop Surg 11: 421-430.
22. Vincent HK, Percival SS, Conrad BP, Seay AN, Montero C, et al. (2013) Hyaluronic Acid (HA) Viscosupplementation on Synovial Fluid Inflammation in Knee Osteoarthritis: A Pilot Study. Open Orthop J 7: 378-384.
23. Watterson JR, Esdaile JM (2000) Viscosupplementation: therapeutic mechanisms and clinical potential in osteoarthritis of the knee. J Am Acad Orthop Surg 8: 277-284.
24. Yan C, Chan W, Yuen W, et al. (2015) Efficacy and safety of hylan G-F 20 injection in treatment of knee osteoarthritis in Chinese patients: results of a prospective, multicentre, longitudinal study. Hong Kong Med J 21: 327-332.
25. Zhang H, Zhang K, Zhang X, et al. (2014) Comparison of two hyaluronic acid formulations for safety and efficacy (chase) study of knee osteoarthritis: a multicenter, randomized, double-blind, 26 week non-inferiority trial comparing durolane® to artz®. Osteoarthr Cartil 22: S397.