

Can Hylan G-F 20 With Corticosteroid Meet the Expectations of Osteoarthritis Patients?

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Abstract

The purpose of this study was to document expectations and outcomes of active adults suffering from knee osteoarthritis (OA) who underwent treatment protocol of hyaluronic acid injection series with single injection of corticosteroid at initial injection. Our hypothesis was that patients would have functional improvement and pain relief following treatment, and that this treatment protocol will meet patients' expectations of treatment for knee OA. Forty-seven knees (range, 42-80 years) with a diagnosis of knee OA completed a self-administered questionnaire before and post injection series. Prior to injections, patients completed a validated expectation questionnaire and activity level questions. Following treatment, patients expected pain relief, to walk longer distances, and to increase activity level. Patients showed significant improvement in WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain subscale, comparing pre-injection and 6 months post-injection scores ($P = .003$) and overall WOMAC score ($P = .038$). SF-12 physical component significantly improved. Patients in this study expected to return to high levels of activity. Results showed significant improvement in pain relief and function. Our results supported that Hylan G-F 20 and corticosteroid are able to meet expectations of older patients with OA who desire to return to an active lifestyle. This study showed patient expectations do influence patient outcome scores and patient satisfaction.

According to "A National Public Health Agenda for Osteoarthritis 2010," 46 million Americans suffer from arthritis and 27 million suffer from osteoarthritis (OA).¹ The prevalence of OA is expected to increase as the "baby boomers" reach

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retirement age. Early onset OA is also expected to become a more prevalent problem. As individuals suffer major knee injuries at younger ages, OA may develop earlier. People with knee OA have difficulty walking and performing normal daily activities. Hip and knee OA are the third leading causes of years lived with disability in the United States.² This disability may lead to inactivity, which complicates many other adult diseases such as diabetes and heart disease. The physical inactivity following OA plays a major role in aggravating pain, function, and disability.³

As more and more people are affected by knee OA, demand for more treatment options increases. Although some surgical treatments have been developed for knee OA, many patients do not wish to undergo surgery for various reasons. While nonsteroidal anti-inflammatories have shown to decrease pain, the effects of long-term use remain unclear.⁴

Intra-articular knee injections have been shown to be effective in some patients with knee OA. Two types of intra-articular injections are commonly used in the osteoarthritic knee; corticosteroid and hyaluronic acid (HA). The lasting effects of each type of injection have shown varied results. While corticosteroid injections have shown the most pain relief at 1 to 3 weeks following injection, HA injections were shown to provide superior symptomatic relief between weeks 4 and 13, and up to 6 months.⁵⁻⁷ Multiple studies have reported intra-articular injections to improve pain and function in patients with OA.^{8,9} However, there is little research on results following the injections with corticosteroid and HA.

Healthcare in the United States is rapidly changing to a consumer driven industry. Now, more patients research doctors as well as treatments. Treatments are chosen based on how the patient feels the treatment will meet their needs. Measurement of patient expectations is relatively new in orthopedics. A patient-derived patient expectation of knee surgery questionnaire was developed.¹⁰ This survey gathered information from patients regarding their expectations of their treatment. The survey included symptoms and function. This survey provides important information when determining treatment algorithms in orthopedics.¹⁰ With the cost of treating OA greater than \$22 billion, it is critical to identify treatment protocols that meet the patients' expectations and reduce the burden of OA.¹

The purpose of this study was to document expectations and outcomes of adults suffering from knee OA

Table I. Average Outcome Scores at Study Time Points With Range (Minimum-Maximum)

	Pre-injection	3 weeks	6 weeks	12 weeks	6 months
WOMAC Pain	7 (0-12)	3 (0-10)	4 (0-11)	5 (0-12)	5 (0-13)
WOMAC Stiffness	3 (0-3)	2 (0-8)	2 (0-5)	2 (0-5)	5 (0-44)
WOMAC Function	18 (0-41)	11 (0-25)	13 (0-39)	15 (0-36)	15 (0-44)
Total Womac	28 (2-56)	16 (0-38)	19 (0-55)	22 (0-53)	22 (0-63)
Patient Satisfaction With Outcome Median*	–	8	8	7	7

*Patient satisfaction with outcome.

who underwent a treatment protocol of an HA injection series in addition to a single injection of corticosteroid at the initial injection. Our hypothesis was that patients would have functional improvement and pain relief following treatment, and that this treatment protocol will meet patients' expectations of treatment for knee OA.

MATERIALS AND METHODS

Patients were enrolled in a prospective cohort study. The study was Institutional Review Board approved and informed consent was obtained from all patients. Patients who met the inclusion criteria were enrolled. The inclusion criteria were men or women aged 40 to 80 years old with a diagnosis of OA of the knee. Diagnosis was based on radiographic examination (Kellgren-Lawrence Grade 3 or 4).¹¹ Patients with prior synovectomy of the knee to be injected were excluded. Patients were excluded if they had rheumatoid disease or any other serious systemic disease, acute synovitis or excessive effusion, allergy to avian products/hyaluronan-based injection components/corticosteroid injection, pregnant, previ-

ous arthroscopic surgery within the last 6 months, or had a joint infection within the previous 3 months. Patients were given the standard course of 3 (2 mL) weekly injections. At the first injection, in addition to the standard Hylan G-F 20 injection, corticosteroid was added. Prior to injection of the HA, 2 mL of Kenalog-10, 3 mL of Marcaine, and 3 mL of Lidocaine were injected. HA was then injected. The second and third injection did not include corticosteroid. Patients did not receive any other corticosteroid injections during the 6 months of the study period.

Injections were completed in 47 patients (27 females, 20 males). The average age was 65 years (range, 42 to 80 years).

Prior to injection, patients completed the Hospital for Special Surgery Patient Expectation Survey.¹⁰ This is a self-administered questionnaire with 20 items measuring patient expectations. The survey covers pain and function. The responses to the questions range from "very important" to "I do not expect this." There is also a response for "this does not apply to me." This survey

Table II. Patient Expectations

	Very Important	Somewhat Important	A Little Important	I Do Not Expect This
Relieve pain	69%	14%	11%	6%
Improve ability to walk	78%	11%	–	11%
Increase knee stability	70%	11%	3%	16%
Increase knee mobility	68%	16%	–	16%
Improve ability to go up and down stairs	71%	16%	5%	8%
Improve ability to squat	43%	24%	5%	27%
Improve ability to kneel	49%	19%	11%	21%
Stop knee from catching or bucking	53%	22%	9%	16%
Stop knee from giving way when coming to a quick stop	23%	11%	14%	51%
Stop knee stiffness or swelling	54%	24%	16%	5%
Be employed for monetary reimbursement	–	–	–	–
Improve ability to run (ie, across the street, to catch the bus)	19%	35%	8%	38%
Improve ability to perform daily activities	51%	38%	–	11%
Improve ability to participate in sports	72%	11%	3%	14%
Have confidence in knee	90%	8%	–	2%
Avoid future degeneration of knee	95%	2.5%	–	2.5%
Improve ability to maintain general health	95%	2.5%	–	2.5%
Improve ability to interact with others	65%	12%	6%	18%
Improve psychological well-being	56%	21%	3%	21%
For knee to be back the way it was before this problem	61%	16%	3%	21%

was designed to provide patients with a way to state what they expect from their treatment.

Before the injection series, and at 3 weeks, 6 weeks, 12 weeks, and 6 months following the completed series of injections, patients completed a self-administered questionnaire that included the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score¹² and a 10 point patient satisfaction question as a visual analog scale (0 = unsatisfied and 10 = highly satisfied). In addition, the Short Form 12 (SF-12) was completed prior to injection and at 6 months following injection. The Tegner activity scale^{13,14} was collected pre-injection to determine patient activity level at time of injection and the patients' desired activity level following treatment.

Statistical Analysis

Comparisons between scores at pre-injection and final follow-up (6 months) were performed using the paired t-test. Comparisons between independent groups were performed using the independent t-test. The patient satisfaction was ordinal 0-10, so the median was reported for these scores. We used repeated-measures analysis to report pre-injection, 3 weeks, 6 weeks, 12 weeks, and 6 months for WOMAC pain and function scores. As the WOMAC scores were assessed on the same patient over time, we used repeated-measures analysis to adjust for the within-patient factors.

RESULTS

The average pre-injection scores are listed in Table I. No patients were on sick leave or disability pension due to their knee. Twenty-seven patients (57%) reported a pre-injection Tegner activity scale of 1 or 2. This corresponds to light labor or walking, but not hiking. Twenty patients (43%) had a pre-injection Tegner activity scale of 3 to 6. This corresponds to moderate to heavy work and recreational sports activity. All patients had a desired Tegner activity scale of 3 or greater. Thirty-eight patients (81%) had a desired Tegner activity scale of recreational sport activity (Tegner = 6), while 9 patients (19%) had a Tegner activity scale of competitive sports (Tegner = 9).

Patient expectations are listed in Table II. Three expectations were considered very important in 90% of patients. These questions were regarding the knee in general (confidence in knee, degeneration in knee, maintain general health) and not specific symptoms or activities. The expectations based on symptoms and function were very important to somewhat important in more than 80% of patients. These included pain, walking, knee stability, knee mobility, stairs, and sports. Knee giving way when coming to a stop and ability to run had the lowest percentage of patients who considered these to be very important.

Patients who considered pain relief a very important expectation had significantly lower pre-injection SF-12

physical component scores (36 vs 48; $P = .002$). Patients who considered improvement in ability to participate in recreational sports an important expectation had more disability documented by WOMAC function scores (12 vs 19; $P = .048$).

Outcomes

Of patients who considered the ability to maintain general health important, 79% ($n = 37$) saw an improvement in the SF-12 physical component and 83% ($n = 39$) saw an improvement in the SF-12 overall score. In all patients, the physical component of the SF-12 improved from 41 pre-injection to 46 at 6 months ($P = .015$). The mental component of SF-12 showed no significant improvements ($P = .795$). The expectation of maintaining general health was met in most patients.

Patients showed improvement in both symptoms and function. A significant improvement was observed in disability, as measured by the WOMAC score in the initial weeks following completion of the injection series (Figure 1). Patients showed significant improvement in the WOMAC pain subscale when compared to pre-injection scores and 6 months post-injection scores ($P = .003$) and overall WOMAC score ($P = .038$). All patients had improvement in WOMAC pain subscale at 3 weeks. Based on repeated measures analysis of variance, there was a significant association between WOMAC pain and time (Wilks' λ , 0.305; $P < .001$). There was also a significant association between WOMAC function and time (Wilks' λ , 0.354; $P < .001$). There was a significant association between total WOMAC score and time (Wilks' λ , 0.271; $P < .001$).

On a scale of 1 to 10, with 10 being very satisfied with outcome of treatment, patients showed the highest level of satisfaction at the 3 week time point (median, 8) and 6 week time point (median, 8). The level of patient satisfaction with outcome of treatment remained steady for the remainder of the time points (12 week median, 7; 6 month median, 7).

DISCUSSION

This study showed that patients who desire to be active in recreational sports and seek treatment for OA have expectations for maintaining their health and reducing their symptoms and disability. The patients' expectations were met following a series of Hylan G-F 20 knee injections with the addition of corticosteroid in the first injection. Our results showed significant improvements in function and pain in the initial weeks following completion of the injection series and 6 months post-injection series.

In this study, all patients expected pain relief. The majority of patients also expected to be able to walk more than 1 mile. Previous studies have documented expectations of patients who underwent total knee arthroplasty (TKA),¹⁰ which are similar to patients' expectations in our study. This may be due to the fact

that our patient population consisted of older patients (>40 years old) suffering from OA, which is comparable to patients indicated for TKA. Although patients vary in degree of OA, this study demonstrates the similarities in expectations of patients suffering from severe knee OA, who underwent conservative and surgical procedures. While there were similarities in expectations for patients undergoing viscosupplementation and TKA, there were some differences as well. In our study, patients reported expectations to return to recreational sports. This difference in desired activity level may be what differentiates patients indicated for viscosupplementation instead of arthroplasty. Since this cohort of patients wanted to remain active and participate in recreational sports, arthroplasty was not a suitable option. Viscosupplementation may be a more appropriate initial treatment for patients who wish to return to recreational sports.

Many studies have looked at the effect of Hylan G-F 20.¹⁵⁻²⁰ In 2005, Yavuzer and colleagues¹⁸ showed that not only can intra-articular injections of Hylan G-F 20 decrease pain in patients suffering from knee OA, but that this treatment can also alter the natural history of OA by decreasing excessive knee loads. This study showed a 10% improvement in WOMAC score at 1 week, while our study showed a 43% improvement at 3 weeks. The Yavuzer study also showed a 47% reduction in pain at 1 week and our study demonstrated a 58% reduction at 3 weeks.¹⁸ Other studies have shown significant pain relief as early as 3 weeks post-injection,^{21,22} but these studies did not address early functional improvement. Our study did demonstrate that with Hylan G-F 20 and corticosteroid, significant pain reduction and functional improvement were seen at early time points and up to 6 months, with greater reduction than what has been seen with HA injections or corticosteroids alone.

Limitations of this study include patients from a referral practice. Also, many of the patients in this study had a low pre-injection WOMAC score, which may not have allowed for as much improvement. Most of these patients were active patients who were receiving treatment in order to remain active. In a recent study in active patients,²³ Hylan G-F 20 injections allowed patients to improve activity level at 3 months. The author suggested that injections may be more beneficial in patients who want to increase their activity.²³ Most patients in our study had a desired Tegner activity level that indicated a desire to return to recreational sports. This may be why our patient group saw more improvement than other groups.

CONCLUSION

In this study, patients expected improvement in function and a decrease in pain. Patients also had a desire to return to high level recreational activities. This study also documented that patient expectations were met with this treatment protocol. Our results showed sig-

nificant improvement in pain relief and function in the initial weeks following the injections series, and that these improvements were maintained at 6 months. Our results supported that Hylan G-F 20 and corticosteroid were able to meet the expectations of older patients suffering from OA who expected pain relief and an improvement in function, including a desire to return to an active lifestyle.

AUTHORS' DISCLOSURE STATEMENT

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REFERENCES

- Centers for Disease Control and Prevention and the Arthritis Foundation. A National Public Health Agenda for Osteoarthritis 2010. <http://www.cdc.gov/arthritis/docs/oaagenda.pdf>. Published February 2010. Accessed June 2011.
- Michaud CM, McKenna MT, Begg S, et al. The burden of disease and injury in the United States 1996. *Popul Health Metr*. 2006 Oct 18;4:11.
- Dunlop DD, Semanik P, Song J, Manheim LM, Shih V, Chang RW. Risk factors for functional decline in older adults with arthritis. *Arthritis Rheum*. 2005;52(4):1274-1282.
- O'Connor JP, Lysz T. Celecoxib, NSAIDs and the skeleton. *Drugs Today (Barc)*. 2008;44(9):693-709.
- Adams ME, Atkinson MH, Lussier AJ, et al. The role of viscosupplementation with Hylan G-F 20 (Synvisc) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing Hylan G-F 20 alone, Hylan G-F 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone. *Osteoarthritis Cartilage*. 1995;3(4):213-225.
- Waddell DD, Bricker DC. Total knee replacement delayed with Hylan G-F 20 use in patients with grade IV osteoarthritis. *J Manag Care Pharm*. 2007;13(2):113-121.
- Habib GS, Saliba W, Nashashibi M. Local effects of intra-articular corticosteroids. *Clin Rheumatol*. 2010;29(4):347-356.
- Raman R, Dutta A, Day N, Sharma HK, Shaw CJ, Johnson GV. Efficacy of Hylan G-F 20 and Sodium Hyaluronate in the treatment of osteoarthritis of the knee -- a prospective randomized clinical trial. *Knee*. 2008;15(4):318-324.
- Huskin JP, Vandekerckhove B, Delincé P et al. Multicentre, prospective, open study to evaluate the safety and efficacy of Hylan G-F 20 in knee osteoarthritis subjects presenting with pain following arthroscopic meniscectomy. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(8):747-752.
- Mancuso CA, Sculco TP, Wickiewicz TL, et al. Patients' expectations of knee surgery. *J Bone Joint Surg Am*. 2001;83-A(7):1005-1012.
- Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis*. 1957;16(4):494-502.
- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15(12):1833-1840.
- Lysholm J, Gillquist J. Evaluation of knee ligament surgery results with special emphasis on use of a scoring scale. *Am J Sports Med*. 1982;10(3):150-154.
- Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. *Clin Orthop Relat Res*. 1985;(198):43-49.
- Goorman SD, Watanabe TK, Miller EH, Perry C. Functional outcome in knee osteoarthritis after treatment with Hylan G-F 20: a prospective study. *Arch Phys Med Rehabil*. 2000;81(4):479-483.
- Waddell DD, Bricker DC. Clinical experience with the effectiveness and tolerability of Hylan G-F 20 in 1047 patients with osteoarthritis of the knee. *J Knee Surg*. 2006;19(1):19-27.

17. Lee S, Park D, Chmell SJ. Viscosupplementation with Hylan G-F 20 (Synvisc): pain and mobility observations from 74 consecutive patients. *J Knee Surg.* 2004;17(2):73-77.
18. Yavuzer G, Sonel B, Süldür N, Ergin S. Effects of intra-articular Hylan G-F 20 injections on clinical and biomechanical characteristics of the knee in osteoarthritis. *Int J Rehabil Res.* 2005;28(4):371-374.
19. Raynauld JP, Torrance GW, Band PA, et al. Canadian Knee OA Study Group. A prospective, randomized, pragmatic, health outcomes trial evaluating the incorporation of Hylan G-F 20 into the treatment paradigm for patients with knee osteoarthritis (Part 1 of 2): clinical results. *Osteoarthritis Cartilage.* 2002;10(7):506-517.
20. Leopold SS, Redd BB, Warme WJ, Wehrle PA, Pettis PD, Shott S. Corticosteroid compared with hyaluronic acid injections for the treatment of osteoarthritis of the knee. A prospective, randomized trial. *J Bone Joint Surg Am.* 2003;85-A(7):1197-1203.
21. Kemper F, Gebhardt U, Meng T, Murray C. Tolerability and short-term effectiveness of Hylan G-F 20 in 4253 patients with osteoarthritis of the knee in clinical practice. *Curr Med Res Opin.* 2005;21(8):1261-1269.
22. Cubukçu D, Ardiç F, Karabulut N, Topuz O. Hylan G-F 20 efficacy on articular cartilage quality in patients with knee osteoarthritis: clinical and MRI assessment. *Clin Rheumatol.* 2005;24(4):336-341.
23. Zietz PM, Selesnick H. The use of Hylan G-F 20 after knee arthroscopy in an active patient population with knee osteoarthritis. *Arthroscopy.* 2008;24(4):416-422.

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