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Original Article

Effect of Viscosupplementation with Hylan in Patients Undergoing Treatment for Osteoarthritis

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ABSTRACT:

Background: Osteoarthritis is the most common joint disorder in the aging population. Osteoarthritis is also a clinically significant cause of disability. Hence; we planned the present study to assess the effect of viscosupplementation with Hylan in patients undergoing treatment for osteoarthritis. **Materials and methods:** The study was conducted in the Department of Orthopedics of the Medical institute. Patients for study were selected from the OPD of the department. Inclusion criteria consisted of symptomatic knee OA and radiologically confirmed disease on standard weight bearing knee radiographic views. All patients included had confirmed arthritic symptoms following clinical evaluation in the knee clinic. A total of 40 patients were included in the study and received treatment. Baseline characteristics and diagnostic data were recorded at the initial visit and patients were entered into a prospectively collected database for evaluation of clinical outcomes at one year and at two years after the initial injection. **Results:** A total of 40 patients were included in the study. 22 patients were females and 18 patients were males. The mean age of the patients was 41.21 years. We observed that 35 patients responded to the treatment, 3 patients were put into waiting list arthroplasty, 1 patient had to undergo arthroscopic procedure due to persistent symptoms. {Fig 1} Table 2 shows the frequency of patients with different outcomes at 2 years of treatment. **Conclusion:** We conclude that about 50% of osteoarthritic patients treated with viscosupplementation with hylan had improvement in symptoms; however, about 20% of patients had to undergo arthroplasty due to persistent symptoms. This treatment of choice can be beneficial in patients who are not indicated to undergo surgery.

Keywords: Hylan, Osteoarthritis, Viscosupplementation.

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INTRODUCTION:

Osteoarthritis is the most common joint disorder in the aging population. Osteoarthritis is also a clinically significant cause of disability.[1,2] Although surgical treatment of osteoarthritis can reduce pain and improve joint mobility and function, the operative management of osteoarthritis is associated with significant cost and potential morbidity. Furthermore, not all patients are candidates for surgical intervention, and they may wish to delay or avoid it if possible.[3] There are several nonsurgical treatment options for symptomatic osteoarthritis including weight loss, exercise, activity modification, physical therapy, bracing, wedged shoe insoles, walking aids, nonsteroidal anti-inflammatory drugs (NSAIDS), and intra-articular injections of corticosteroids.[4] In September 2000, the American College of Rheumatology guidelines for the treatment of osteoarthritis of the knee recommended that one treatment option to be considered is the use of intra-articular injections of hyaluronic acid for the relief of osteoarthritic pain.[5] Since then, hyaluronic acid viscosupplementation has become one of the more popular nonoperative treatment options for symptomatic osteoarthritis.[6–8] Hence, we planned the study to assess the effect of viscosupplementation with Hylan in patients undergoing treatment for osteoarthritis.

MATERIALS AND METHODS:

The study was conducted in the Department of Orthopedics of the our institute. Patients for study were selected from the OPD of the Orthopedics department. Inclusion criteria consisted of symptomatic knee OA and radiologically confirmed disease on standard weight bearing knee radiographic views. All patients included had confirmed arthritic symptoms following clinical evaluation in the clinic. In addition to those having radiographs confirming tibiofemoral compartment location of disease, patients not medically fit for surgery, considered too young for arthroplasty, or patients whose occupation would have precluded them from having an arthroplasty were included in the intervention protocol. A total of 40 patients were included in the study and received treatment. Baseline characteristics and diagnostic data were recorded at the initial visit and patients were entered into a prospectively collected database for evaluation of clinical outcomes at one year and at two years after the initial injection.

The statistical analysis of the data was done using SPSS version 20.0 for windows. The Student's t-test and Chi-square test were used to check the significance of the data. The p-value less than 0.05 was predetermined as statistically significant.

RESULTS:

A total of 40 patients were included in the study. 22 patients were females and 18 patients were males. The mean age of the patients was 41.21 years.

Table 1: Frequency of patients with various outcomes at 1 year

Outcomes of treatment at 1 year	
Parameters	**Number of patients (%)**
Responders of treatment	35
Waiting list arthroplasty	3
Arthroscopic procedure	1
Reviewed and Symptomatic	1

Fig 1: Frequency of patients with various outcomes at 1 year

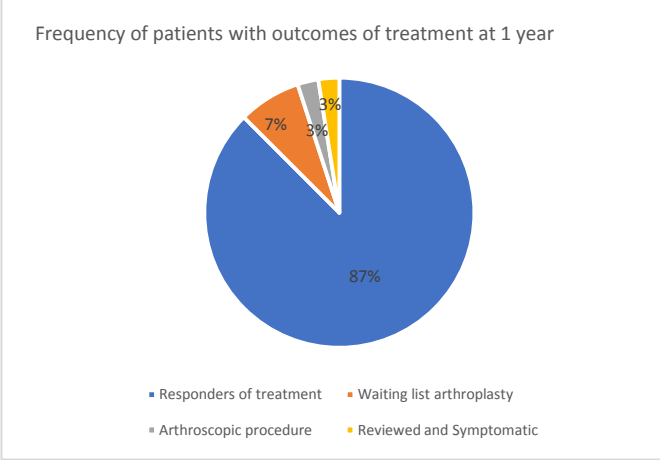
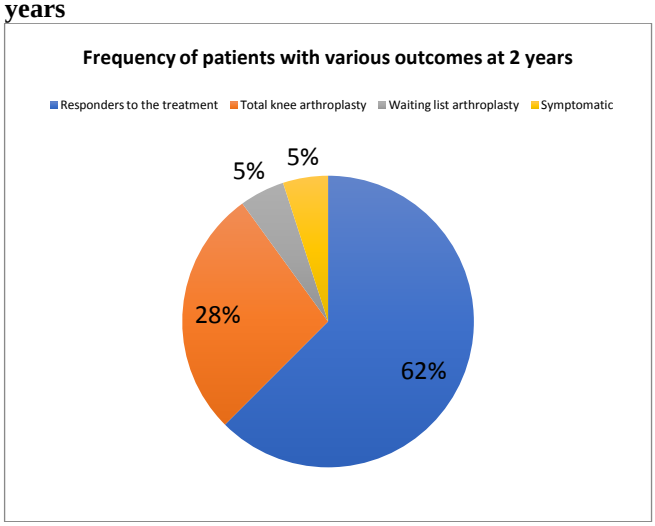


Table 1 shows the frequency of patients with different outcomes at 1 year of treatment. We observed that 35 patients responded to the treatment, 3 patients were put into waiting list arthroplasty, 1 patient had to undergo arthroscopic procedure due to persistent symptoms. {Fig 1} Table 2 shows the frequency of patients with different outcomes at 2 years of treatment. We observed that 25 patients responded to the treatment, 11 patients underwent total knee arthroscopy, 2 patients were put into waiting list arthroplasty, 1 patient was still symptomatic. The results were statistically non-significant (p>0.05). {Fig 2}

Table 2: Frequency of patients with various outcomes at 2 years

Outcomes at 2 years	
Parameters	**No. of patients**
Responders to the treatment	25
Total knee arthroplasty	11
Waiting list arthroplasty	2
Symptomatic	2

Fig 2: Frequency of patients with various outcomes at 2 years



DISCUSSION:

In the present study we assessed the effect of viscosupplementation with Hylan in patients undergoing treatment for osteoarthritis. We observed that about 60% of patients responded well to the treatment. But the results were statistically non-significant. The results were compared with previous studies and results were consistent with previous studies. Lussier A et al evaluated viscosupplementation with intraarticularhylan G-F 20 in current clinical practice. A retrospective study of all patients with osteoarthritis of the knee treated with hylan by 5 Canadian clinicians over a period of 2.5 years. A total of 1537 injections were performed in 336 patients involving 458 knees. The overall response and the change of activity level were judged better or much better for 77 and 76% of

the treated knees after the first course of treatment (3 weekly injections), and 87 and 84% after a 2nd course. The mean time elapsing between the first and 2nd course, 8.2 +/- 0.5 months, is an evaluation of the duration of benefits. Local adverse events were observed in 28 patients (32 knees), with an overall rate of 2.7% adverse events per injection, 7.0% per joint, and 8.3% per patient. No systemic adverse events were noted in any patient. The adverse events were characterized by pain and/or transient swelling of the injected joint, mostly mild or moderate in intensity, and 72% of the adverse events were considered to be possibly or probably related to the injection. The incidence of adverse events is significantly influenced by the injection technique: 5.2% adverse events per injection with a medial approach to a partially bent knee, and 2.4% (straight medial) and 1.5% (straight lateral). After an adverse event, clinical improvement still occurred in 69% of the affected knees. It was concluded that Hylan G-F 20 provided good clinical benefits and an acceptable safety profile in current clinical practice. The occurrence of adverse events after an intraarticular hylan injection is infrequent and unpredictable and is not necessarily hylan related, although injection related. Wobig M et al conducted a 12-week, double-masked, randomized, multicenter study to compare the elastoviscous properties of a high-molecular-weight viscosupplement, hylan G-F 20 (polymer concentration, 0.8%), with those of a lower-molecular-weight hyaluronan (LMW HA) product (polymer concentration, 1%) and to determine the relationship of elastoviscosity to efficacy in the treatment of patients with osteoarthritis (OA) of the knee. Patients had radiographically confirmed primary idiopathic OA of the knee (Larsen grades I to V) with pain despite other treatments. After a 2-week washout period, 70 patients (73 knees) received three 2-mL intra-articular injections of test solution at 1-week intervals. Thirty-eight patients (38 knees) received hylan G-F 20, and 32 patients (35 knees) received LMW HA. During the 12-week follow-up period, the primary outcome measures assessed by patients (using a visual analogue scale) were weight-bearing pain, most painful knee movement, and overall treatment response; the primary outcome measures assessed by study evaluators were weight-bearing pain and overall assessment of treatment. The dynamic elastoviscous properties of the test solutions were measured on an oscillating Couette-type rheometer. Hylan G-F 20 was more elastoviscous than the LMW HA at all frequencies measured (0.001 to 10 Hz). At the final evaluation, patients who received hylan G-F 20 had significantly better results on all primary outcome measures compared with those who received LMW HA. No systemic adverse events were reported. Local adverse events consisted of pain or swelling, noted in 2 of 38 knees injected with hylan G-F 20, and pain, noted in 1 of 35 knees injected with LMW HA (adverse event rates per injection, 1.8% and 0.9%, respectively). The difference in the incidence of adverse events between groups was not statistically significant. The higher-molecular-weight, more elastoviscoushylan G-F 20 had significantly greater pain-relieving effects than did the lower-molecular-weight, less elastoviscous hyaluronan.[9, 10]

Adams ME et al determined the safety and efficacy of viscosupplementation with hylan G-F 20, a cross-linked hyaluronan preparation, used either alone or in combination with continuous non-steroidal anti-inflammatory drug (NSAID) therapy, a randomized, controlled, multicenter clinical trial, assessed by a blinded assessor, was conducted in 102 patients with osteoarthritis (OA) of the knee. All patients were on continuous NSAID therapy for at least 30 days prior to entering the study. Patients were randomized into three parallel groups: (1) NSAID continuation plus three control arthrocenteses at weekly intervals; (2) NSAID discontinuation but with three weekly intra-articular injections of hylan G-F 20; and (3) NSAID continuation plus three injections, one every week, intra-articular injections of hylan G-F 20. Outcome measures of pain and joint function were evaluated by both the patients and an evaluator at baseline and weeks 1, 2, 3, 7 and 12, with a follow-up telephone evaluation at 26 weeks. At 12 weeks all groups showed statistically significant improvements from baseline, but did not differ from each other. A statistical test for the equivalence, the q-statistic, demonstrated that viscosupplementation with hylan G-F 20 was at least as good or better than continuous NSAID therapy for all outcome measurements except activity restriction. At 26 weeks both groups receiving hylan G-F 20 were significantly better than the group receiving NSAIDs alone. A transient local reaction was observed in three patients after hylan G-F 20 injection; only one patient withdrew from the study as a result and all recovered without any sequela. Hylan G-F 20 is a safe and effective treatment for OA of the knee and can be used either as a replacement for or an adjunct to NSAID therapy. Conrozier T et al assessed different dosing regimens of hylan G-F 20, a high molecular-weight cross-linked derivative of HA, in the treatment of pain due to knee OA. Pilot, prospective, multi-centre, open-label, randomised trial in 100 patients with unilateral, symptomatic, tibio-femoral OA (Kellgren-Lawrence grade II or III), aged > or =40 years. Patients were randomised to receive varying dosing regimens of hylan G-F 20 (1 x 6 mL, 1 x 4 mL, 2 x 4 mL 2 weeks apart, 3 x 4 mL 1 week apart, or 3 x 2 mL 1 week apart). Adverse events (AE's) were monitored throughout the study. The primary efficacy endpoint was the change from baseline in the patient-rated knee OA pain assessment (100 mm visual analogue scale (VAS)) at 24 weeks. The secondary efficacy criteria included the WOMAC index, patient and physician global assessments using a 100 mm VAS, and knee OA pain assessment at all other visits. Concomitant use of permitted rescue medications (paracetamol) was also assessed. The treatment was well tolerated overall. Patients in the 3 x 4 mL group reported the highest percentage of device-related local AE's (30%) while patients in the 1 x 6 mL and 3 x 2 mL groups reported only 10%. There were no serious

device-related AEs. There was a statistically significant improvement from baseline at week 24 in all efficacy endpoints for all treatment regimens. The 1 x 6 and 3 x 4 and 3 x 2 mL treatment groups showed the greatest mean improvements (-34.9, -32.6 and -36.7 mm respectively) in the patient-rated knee OA pain assessment VAS. This study suggested that a single 6 mL injection of hylan G-F 20 may be as efficacious, and as well tolerated, as 3 x 2 mL one week apart. A double-blind, controlled trial is needed to confirm these data.[11, 12]

CONCLUSION:

Within the limitations of the study we conclude that about 50% of osteoarthritic patients treated with viscosupplementation with hylan had improvement in symptoms; however, about 20% of patients had to undergo arthroplasty due to persistent symptoms. This treatment of choice can be beneficial in patients who are not indicated to undergo surgery.

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