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An evaluation of role of intraarticular hyaluronic acid in treatment of osteoarthritis of knee

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Abstract

Objective: To evaluate the role of intraarticular hyaluronic acid in treatment of osteoarthritis of knee among the patients admitted in a north Indian hospital.

Methods: This was a prospective study conducted on 80 patients attending the out patient department of the hospital with a diagnosis of osteoarthritis of one or both knees were enrolled in this study. All the patients were symptomatic for osteoarthritis of knee and did not respond adequately to conservative treatment for osteoarthritis. 3 patients were lost to follow-up. The results are finally presented on 96 knees of 77 patients who underwent series of 5 intraarticular injections of hyaluronic acid at weekly interval.

Results: The mean age of patients was 59.13 ± 2.3 years. Duration of symptom ranged from 6 months to 5 years. Most of the knees (55.2%) had moderate grade of osteoarthritis. The pain at rest and joint tenderness were significantly ($p=0.0001$) lower among mild grade of osteoarthritis as compared to moderate and severe. There was significant effect of intraarticular myaluronic acid in decreasing VAS and joint tenderness from baseline to 6 month.

Conclusion: Visco-supplementation with hyaluronic acid may be considered an alternative option to major surgical procedure in developing countries provided the injections are given before mechanical changes take place and patient complies with regular exercise, weight control and postural habits.

Keywords: Osteoarthritis, intraarticular, hyaluronic acid

Introduction

Global statistics reveal over 100 million people worldwide suffer from OA, which is one of the most common causes of disability^[1, 2]. In addition, younger individuals may be susceptible to injury-induced OA. More than 50% of the population around the world (>65 years) show X-ray evidence of OA in one of the joints, thus demonstrating the high incidence of this disease. While OA is equally present in men and women, it appears to be more common among younger men (<45 years) and in the older women (>45 years)^[3, 4].

Between the ages of 30 and 65 years, the general incidence and prevalence of knee OA has been reported to increase by as much as 10 times that of younger age groups, affecting nearly 33.6% of people >65 years or an incidence of 1 in 10. Persons aged >65 years are more commonly affected by knee OA, due to the ongoing drop in birth rates and the overall increase in life expectancy; there is an alarming trend for future growth in the prevalence of knee OA in older population to be seen^[5]. Along with the increase in age, there is an exponential increase in the associated risk factor of obesity, due to progressive sedentary behavior, changes in lifestyle patterns, diet routine, and work environment conditions among the adult population⁶. About 80% of persons affected by OA already report having some movement limitation, and 20% report not being able to perform major activities of daily living; with an 11% of the total affected population reporting the need of personal care^[5].

Intra-articular (IA) injections provide an additional non-operative strategy for OA management when non-pharmacologic and medical therapies provide inadequate relief of symptoms. IA corticosteroids and hyaluronic acids (HA) are available for the treatment of OA, though the latter are approved by the US Food and Drug Administration solely for osteoarthritis of the knee^[7].

The efficacy of IA hyaluronates for the treatment of symptomatic knee OA has been previously reviewed [7, 8]. Similar to the findings for IA corticosteroids for knee OA, a Cochrane analysis of visco supplementation for the treatment of knee OA found HA derivatives as a class to be effective [8, 9]. There is increasing interest in the use of HAs for OA at sites other than the knee. Though preliminary reports suggest efficacy for shoulder and hip OA, these indications are currently considered off label [10].

The present study was conducted to evaluate the role of intraarticular hyaluronic acid in treatment of osteoarthritis of knee among the patients admitted in a north Indian hospital.

Material and Methods

This was a prospective study conducted in the Department of Orthopaedic Surgery, G.S.V.M Medical College, Kanpur & Era's Lucknow Medical College, Lucknow after the Ethical clearance from the Institutional Ethical Committee. The consent from each patient was taken before enrolling in the study. A total of 80 patients attending the out patient department of the hospital with a diagnosis of osteoarthritis of one or both knees were enrolled in this study. All the patients were symptomatic for osteoarthritis of knee and did not respond adequately to conservative treatment for osteoarthritis. Out of 80 patients, 60 were unilateral osteoarthritis & 20 were of bilateral osteoarthritis of knee, two patients of unilateral osteoarthritis & one patient of bilateral osteoarthritis were lost to follow-up, so excluded from the analysis. The results are finally presented on 96 knees of 77 patients who underwent series of 5 intraarticular injections of hyaluronic acid at weekly interval.

Included patients having systemic illness or major general medical conditions which can interfere with assessment of results, patients having associated osteoarthritis of hip, known or suspected joint infection, skin conditions overlying the joint which might make injection dangerous, patient suffering from Rheumatoid arthritis and other inflammatory disease and use of intra articular steroids within 3 months before the start of treatment.

All patients received five weekly intra articular injection of Hyaluronic acid (20 mcg/2ml, hyalgan). Intra articular injections were administrated by a single author using standard aseptic techniques after aspiration of any effusion present. Clinical assessments were made at baseline and during the treatment (at 6 month). During the treatment phase, the clinical assessments were made before each injection. Criteria used for assessment of treatment efficacy were pain at rest, pain at visual analogue score (VAS), Joint tenderness assessed by using Doyle's index as a 4 point scale (0- no

tenderness, 1- patient complained of pain, 2- patient complained of pain & winced, 3 patient complained of pain, winced and withdrew the joint), knee range of movements, patients global assessment of treatment and physician global assessment of treatment. The occurrences of adverse events were also assessed at 6 month.

Analysis

The results are presented in mean±SD and percentages. The unpaired and paired t-test are used to compare the scores. The p-value<0.05 is being considered as significant. All the analysis is being carried out by using SPSS 16.0 version.

Results

A total of 80 patients, 37 males & 43 females in the age group 45-80 years with a mean age of 59.13 ± 2.3 years were included in the study. Out of 80 patients, 60 were having unilateral involvement and 20 were having bilateral involvement (total of 100 knees). Two patients of unilateral involvement and one of bilateral involvement were lost during treatment and finally results were evaluated for 96 knees. Duration of symptom ranged from 6 months to 5 years with maximum between 25 – 60 months (Table not shown). Most of the knees (55.2%) had moderate grade of osteoarthritis according to Kellegren Lawrence criteria followed by severe (24%) and mild (20.8%) (Fig.1).

Table-1 describes the clinical assessment at baseline according to grade of osteoarthritis. The pain at rest and joint tenderness were significantly ($p=0.0001$) lower among mild grade of osteoarthritis as compared to moderate and severe. However, range of movement was significantly ($p=0.0001$) higher in mild grade of osteoarthritis than moderate and severe.

There was significant effect of intraarticular myaluronic acid in decreasing VAS and joint tenderness from baseline to 6 month. The decrease was higher among the patients of mild than moderate. There was no significant decrease in VAS and joint tenderness among the patients of severe. No change was observed in range of movement (Table-2).

Among 36 knees (37.5%) of patients, the assessment of outcome was good during the treatment, however, among 5 knees (5.2%), no improvement after complete course of Hyaluronic acid treatment was observed. Very good assessment among the patient's knees was found in 34 (35.4%) knees and excellent was in 7.3% knees. Almost similar observation was found among physician's global assessment (Table-3). As far as side effects are concerned, 6 knees (6.3%) showed local erythema which subsided with anti-inflammatory drugs (Table not shown).

Table 1: Clinical assessment at baseline

Clinical criteria	Mild (n=20)	Moderate (n=53)	Severe (n=23)	Total
Pain at rest (VAS)	4.40±0.51 ^{1,2}	6.58±0.71 ²	7.69±0.48 ¹	6.22±0.62
Joint tenderness	0.90±0.31 ^{1,2}	2.41±0.50 ²	2.76±0.43 ¹	2.02±0.39
Range of movement	117.50±6.34 ^{1,2}	103.54±6.50 ²	95.76±4.49 ¹	105.60±5.34

¹p=0.0001 (Significant, Unpaired t-test)

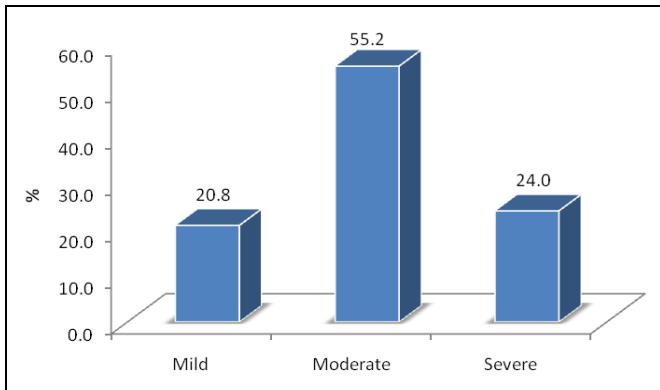
Table 2: Clinical assessment at 6 month

Clinical criteria	Mild (n=20)	Moderate (n=53)	Severe (n=23)	Total
Pain at rest (VAS)	2.21±0.41 ¹	4.32±0.21 ¹	6.79±0.58	4.19±0.72
Joint tenderness	0.51±0.11 ¹	1.11±0.13 ¹	2.45±0.13	1.78±0.29
Range of movement	116.32±5.14	101.14±5.60	94.16±3.59	103.62±3.36

¹p=0.001 (Significant decrease from baseline, Paired t-test)

Table 3: Patient's and Physician's global assessment during treatment

Assessment	Patient		Physician	
	No. of Knees	Percentage	No. of Knees	Percentage
Poor	5	5.2	4	4.2
Fair (1-25%)	14	14.6	9	9.4
Good (26-50%)	36	37.5	35	36.5
Very Good (51-75%)	34	35.4	39	40.6
Excellent (76-100%)	7	7.3	9	9.4

**Fig 1:** Grade of osteoarthritis according to Kellgren Lawrence criteria

Discussion

Corticosteroids and HAs are commonly used for the management of knee OA not responding to more conservative therapy. Few direct comparisons of IA corticosteroids to HA injections have been performed. Therefore, current guidelines make no recommendations as to which class should be initially employed once the decision is made to use injection therapy for knee OA. In one of the largest comparison studies reported, Leopold and colleagues^[11] randomized 100 patients with knee OA to receive a 3 injection series of Hylan G-F 20 or a corticosteroid injection. Both groups were followed for a total of 6 months and the corticosteroid group was allowed a second corticosteroid injection at any time during the study period. At study conclusion, there were no significant differences between the groups as assessed by 3 different pain scales commonly used to measure response in knee OA trials. In our study, we evaluated the efficacy of intra articular Hyaluronic acid for the treatment of osteoarthritis of knee based on few clinical criteria and physician and patient global assessment. Effect of intraarticular Hyaluronic acid was assessed by recording pain at rest, joint line tenderness and range of motion in all groups. In patients with mild osteoarthritis there was no significant improvement in pain at rest after two injections. After the third injection, there was clinical and statistically significant improvement in pain at 6 month pain.

The Osteoarthritis Research Society International (OARSI) has examined treatment effects of both corticosteroids and HAs for knee OA in a review of research published through January 2009^[12]. The effect size of corticosteroids on knee OA was estimated at 0.58, compared with 0.60 for HA derivatives (0.5 indicates a moderate effect). The number needed to treat (NNT) for each modality was also similar: 5 for corticosteroids and 7 for HA injections. This analysis suggests IA corticosteroids and HA can be expected to deliver similar results in clinical practice.

There was significant effect of intraarticular myaluronic acid in decreasing VAS and joint tenderness from baseline to 6 month in this study. The decrease was higher among the patients of mild than moderate. There was no significant

decrease in VAS and joint tenderness among the patients of severe. No change was observed in range of movement. Similar observations were made by other authors. Patients overall satisfaction favored hyaluronic acid compared with Placebo after 6 months ($p=0.006$). In a double blinded multi centre trial of 495 patients of osteoarthritis of knee, it was found that patients receiving Hyaluronic acid improved more with respect to pain on walking ($p<0.005$)^[13]. Albert *et al*^[14] reviewed 80 knees in the symptomatic osteoarthritis treated with Hyaluronic acid and reported more than 80% improvement in pain at rest. Improvements in the knee range of movement were not significant in all the groups in this study. In our study, most of the patients were satisfied after treatment with hyaluronic acid. On physician global assessment, was found to be good to very good.

Safety is an important consideration in choosing an initial agent for injection. In general, the rate of post-arthrocentesis septic arthritis is low and has been estimated at 1 in 14,000 to 1 in 50,000 following corticosteroid injections^[13]. Albert and colleagues^[14] described 2 cases of septic knee arthritis following intra-articular hyaluronate injection in elderly OA patients, but no estimates are currently available specifically for the rate of post-hyaluronate injection septic arthritis. Patients should be informed of the risk of infection when counseled about this procedure, because infection can occur following injection with either corticosteroid or HA.

In addition to septic arthritis, risks of HA injection include pseudoseptic injection reaction and flare of crystalline arthritis. Attacks of gout and calcium pyrophosphate dehydrate arthritis (ie, pseudogout) have been described following HA injection^[15, 16].

Conflict of interest

None

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