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Original Research Article

Functional outcome and result of intra-articular injection hyaluronic acid in treatment of osteoarthritis of knee

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ABSTRACT

Background: Osteoarthritis (OA) is the most common disease of joints in adults around the world. Worldwide, it is estimated to be the fourth leading cause of disability. Objective of the study was to assess functional outcome and results of injection of hyaluronic acid in symptomatic osteoarthritis knee.
Methods: It was a prospective clinical study with 3 months of follow-up. Clinically proven sixty patients of osteoarthritis knee (OA) included in study according to inclusion and exclusion criteria on OPD basis after getting written and informed consent, treated by weekly intra articular injection of Hyaluronic acid (20 mcg/2ml) in affected knee joint for 5 weeks by single author . Functional outcome and clinical assessment was done by pain at visual analogue score (VAS) and by knee range of movements, patients global assessment of treatment and physician global assessment of treatment. The occurrences of adverse events were also assessed at 3 month.
Results: Sixty patients participated in study and reported statistically significant improvement in VAS score in mild and moderate osteoarthritis of knee from 4.46±0.52 and 6.57±0.72 points respectively pre-treatment level to 2.26±0.43 and 4.36±0.24 points respectively at three months post Hyaluronic acid injection follow up, improvement in joint tenderness and patients & physician's global assessment score also improved significantly clinically as well as statistically in mild to moderate group while in severe group no clinical and statistically significant improvement was observed in any parameters, change in range of motion at three months was not significant in any group.
Conclusions: Visco-supplementation with intra articular injection hyaluronic acid should be considered as safe and effective modality of treatment in selected group of mild to moderate osteoarthritis before mechanical changes takes place and patient complies with regular exercise, weight control and postural habits.

Keywords: Hyaluronic acid, OA knee, VAS, ROM

INTRODUCTION

Osteoarthritis (OA) is the most common disease of joints in adults around the world.[1] Worldwide; it is estimated to be the fourth leading cause of disability.[2] Nearly one-third of all adults have radiological signs of osteoarthritis.[3] Clinically too, significant osteoarthritis of the knee, hand, or hip is reported to affect around 8.94% of the adult population.[4] Its prevalence increases gradually in individuals older than 40 years. Studies suggests that prevalence of OA knee is >60% in subjects older than 70 years.[5,6] Community survey data in rural and urban areas of India shows the prevalence of osteoarthritis to be in the range of 17 to 60.6%.[7-9] The disease usually evolves with increasing levels of pain, mobility restriction, and physical disability.[5,10] 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.[11] 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 injections of hyaluronic acids (HA) are approved by the US Food and Drug Administration for osteoarthritis of the knee.[12]

Some studies have already been done regarding efficacy of IA hyaluronic acids in treatment of symptomatic Osteoarthritis knee, a Cochrane analysis of visco supplementation also found HA derivatives as a class to be effective in OA knee.[12-14] 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.[15]

The present study was conducted to evaluate the functional outcome and results of intra-articular hyaluronic acid in treatment of osteoarthritis of knee.

METHODS

After approval from institutional ethical committee (IEC), clinically diagnosed sixty adult patients of both sexes of symptomatic osteoarthritis knee (OA Knee) included in study and patients with any history of 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 steroid injection in past 3 months, Patient having significant cardiovascular disease, renal or hepatic disease, pregnancy, malignancy, diabetes, previous surgery around knee, joint instability and significant co morbidity of lower limb excluded from study.

All the patients were explained about the study and an informed consent was obtained. Only those providing consent to participate in the study were enrolled in. Participants were treated with five weekly intra articular injection of Hyaluronic acid (20mcg/2ml). Intra articular injections were administrated by a single author using standard aseptic techniques after aspiration of any effusion if present. Patients were followed up for 3 months post injection HA. No analgesic was prescribed during follow up except tab paracetamol (650 mg) SOS.

At baseline, the demographic information and medical history of the patients was obtained. Assessment of results done on the basis of VAS score, 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 and 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 3 month.

Statistical analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

RESULTS

Sixty patients participated in this study out of which 24 were males and 36 females of 38-78 years age group with a mean age of 52.78±10.31 years. Duration of symptom ranged from 6 months to 6 years with maximum ranging between 2-5 years (Table not shown). Most of the knees had moderate grade of osteoarthritis (58.3%) according to Kellegren Lawrence criteria followed by severe (23.3%) and mild (18.3%) (Figure 1).

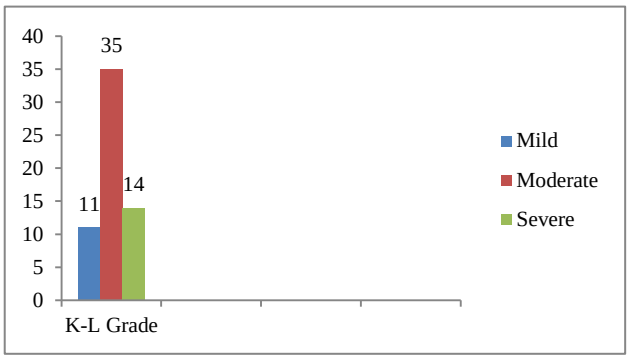

Figure 1: K-L grade OF OA knee.

Table 1: Clinical assessment pre-treatment.

Clinical criteria	Mild (n=11)	Moderate (n=35)	Severe (n=14)
Pain at rest (VAS)	4.46±0.52	6.57±0.72	7.67±0.46
Joint tenderness	0.92±0.32	2.43±0.51	2.71±0.43

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.

Table 2: Clinical assessment at 3 months.

Clinical criteria	Mild (n=11)	Moderate (n=35)	Severe (n=14)
Pain at Rest (VAS)	2.26±0.43	4.36±0.24	6.87±0.56
Joint tenderness	0.57±0.13	1.21±0.17	2.48±0.49

p=0.001 (Significant, Unpaired t-test)

Participants showed statistically significant improvement in VAS score in mild and moderate osteoarthritis of knee

from 4.46±0.52 and 6.57±0.72 points respectively pretreatment level to 2.26±0.43 and 4.36±0.24 points respectively at three months post Hyaluronic acid injection follow up, improvement in joint tenderness from 0.92±0.32 and 2.43±0.51 pretreatment level to 0.57±0.13 and1.21±0.17 respectively at three months was also significant.

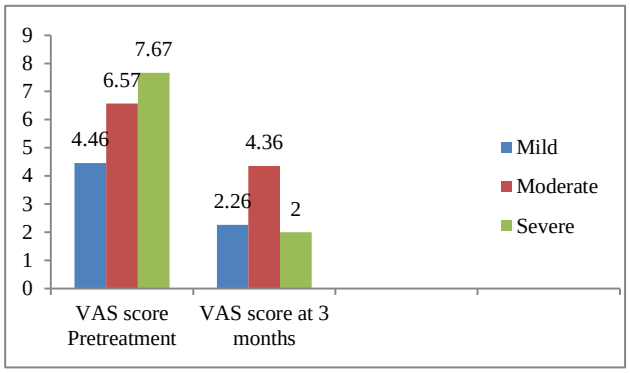

Figure 2: VAS Score pre-treatment and at 3 month.

Among 25knees (41.6%) of patients, the assessment of outcome was good during the treatment, very good assessment among the patient's knees was found in 20 (33.3%) knees and excellent was in 6.6% knees. However among 3 knees (5.0%), no improvement after complete course of Hyaluronic acid treatment was observed. Almost similar observation was found among physician's global assessment (Table 3).

Table 3: Patient's and physician's global assessment during treatment.

Assessment	Patient		Physician	
	No of knees	%	No of knees	%
Poor	3	5	2	3.3
Fair (1-25%)	8	13.3	5	8.3
Good (26-50%)	25	41.6	23	38.3
Very good (51-75%)	20	33.3	25	41.6
Excellent (76-100%)	4	6.6	5	8.3

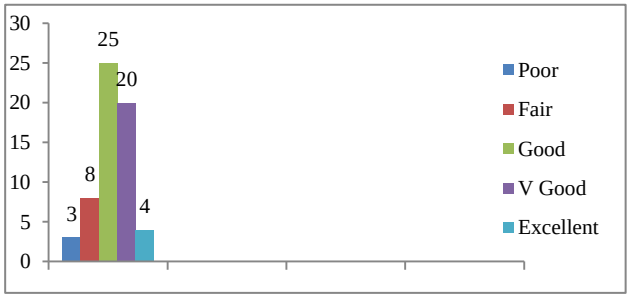

Figure 3: Patient's and physician's global assessment during treatment.

In severe group no clinical and statistically significant improvement was observed in any parameters, change in range of motion at three months was not significant in any group. Intra articular injections of hyaluronic acid resulted in clinically as well as statistically improvement in mild to moderate osteoarthritis group. As far as side effects are concerned, 4 knees (6.6%) showed local erythema which subsided with anti-inflammatory drugs (Table not shown).

Table 4: Range of motion.

ROM	Pretreatment	At 3 month
Flexion	128.78±3.41	128.69±3.56
Extention	0.57±0.98	0.62±1.02

p=0.463 (Not Significant, Unpaired t-test).

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 randomized 100 patients with knee OA to receive a 3 injection series of Hylan G-F 20 or a corticosteroid injection.[16] 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 present 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 intra-articular 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 3 months. 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.[17] 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 hyaluronic acid in decreasing VAS and joint tenderness from baseline to 3 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 favoured 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).[18]

Albert et al 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.[19] In present 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 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.[19] 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.[20,21]

CONCLUSION

Visco-supplementation with intra articular injection hyaluronic acid should be considered as safe and effective modality of treatment in selected group of mild to moderate osteoarthritis before mechanical changes takes place and patient complies with regular exercise, weight control and postural habits.

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