



## THE ROLE OF INTRA-ARTICULAR INJECTION SODIUM HYALURONATE IN REHABILITATION OF OSTEOARTHRITIS KNEE

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### ABSTRACT

**OBJECTIVE:** To assess the effect of injection sodium hyaluronate in osteoarthritis knee as an add on treatment to routine Medication and Physiotherapy.

**PATIENTS AND METHODS:** 6 month observational study on total 60 patients suffering from primary osteoarthritis knee of grade II and III according to Kellgren-Lawrence Grading Scale was conducted. Patients were categorized in 2 groups: Group 1 patient opting for intra-articular injection sodium hyaluronate and Group 2 patients opting only routine line of treatment. Data was collected on demographic features of the individuals and changes in the VAS scores, KOOS scores and Lequesne index were measured.

**RESULTS:** Baseline characteristics were similar between the two groups. Group with visco-supplementation showed overall better outcome as compared to the control group at the end of 6 month. But at the end of 1 month no significant difference was felt in both the groups regarding the outcome. There was not much difference in side effect profile in both the groups.

**CONCLUSION:** a course of 3 sodium hyaluronate injections along with routine medication can improve the outcome of treatment for longer period.

**KEYWORDS :** Hyaluronic acid, Osteoarthritis, Intra-articular, Sodium Hyaluronate

### INTRODUCTION

Osteoarthritis is the most common form of arthritis, primarily a non inflammatory disorder of movable joints. It is a joint disease which primarily affects cartilage. This results in the wearing out of the joint surface characterized by pain, and increasing disability. The prevalence of documented knee OA in the general practice in those aged >45 years is found to be 12.5%.<sup>1</sup> The disease can have an impact on several aspects of a patient's life, including functional and social activities, relationships, socioeconomic status, body image, and emotional well-being. The treatment of osteoarthritis consists of pain reduction, modification of activities of daily living, maintenance of range of motion and improvement of joint functions.<sup>2</sup>

Decision on the choice of therapeutic approach need to consider comorbidities, co-medications, and relative cost and likely success of the intervention, as well as taking into account the age, wishes, lifestyle and previous experiences of the patients. Non-surgical therapies include physiotherapy, NSAIDs, cartilage protective drugs such as Diacerein, Glucosamine sulphate, oral and intra-articular steroids. Intra-articular corticosteroid injection provides relief of acute knee pain and inflammation, but the effects are relatively short lived (approximately 6 weeks).

Viscosupplementation is a novel, safe, and possibly effective form of local treatment for osteoarthritis. Viscosupplementation with hyaluronic acid [HA] helps to improve the physiological environment in an osteoarthritic joint by supplementing the shock absorption and lubrication properties of osteoarthritic synovial fluid. Addition of intra-articular injections of Hyaluronic acid along with physiotherapy, NSAIDs and Diacerein can show a significant effect on various symptoms of osteoarthritis knee and can improve the patient's quality of life. Thus effect of intra-articular viscosupplementation as adjuvant with other conservative therapy still needs further evaluation.

### MATERIALS AND METHODS

Outpatients fulfilling the American College of Rheumatology clinical or radiological criteria for the diagnosis of knee OA were recruited for the study<sup>3</sup>.

Patients included were age group of 50 to 70 yrs who had consented for the study with bilateral or unilateral primary osteoarthritis of knee grade 2 and 3 according to Kellgren-Lawrence Grading Scale<sup>4</sup>. Patients having pain as assessed with Visual Analog Scale > 30. Rescue drug in the form of Paracetamol 500 mg was advised. Evaluations were done after 2 days of wash off period during which patients were not allowed NSAIDs or other medication to reduce pain. Aspirin at an antiplatelet dose (<500 mg/day) was allowed.

Patients excluded during screening were those suffering from secondary osteoarthritis of knee (Due to injury/ inflammatory / metabolic/rheumatic disease, osteonecrosis etc...), knees with Grade 1 or 4 osteoarthritis changes according to Kellgren-Lawrence Grading Scale, patients with contraindications to intraarticular knee injections, patients with global pain < than 30 on Visual Analog Scale and patient with obesity i.e. BMI >28 kg/m<sup>2</sup>. Patients having neurological deficit or other co morbidity such as hip osteoarthritis, congenital deformities, varicosities, etc. were excluded.

### METHODOLOGY:

122 patients coming to the outpatient department of All India Institute of Physical Medicine & Rehabilitation were screened for the study from November -2017 to May -18 out of which 35 patient satisfying the inclusion criteria and opting for intra-articular injection of sodium hyaluronate were considered in Group 1 and 35 patient satisfying the inclusion criteria and opting for conservative treatment were considered in Group 2. Before the study was started, patients completed a two week washout period, in which treatment with oral steroids and non-steroidal anti-inflammatory drugs and other

analgesics was prohibited. 5 patient from Group 1 and 5 patients Group 2 were lost during follow up.

**Group 1:** Patients in this group were given intra-articular viscosupplementation i.e. 2.5 ml of 1% Sodium Hyaluronate [molecular weight 650,000-1,200,000 Daltons] every week for 3 weeks, along with oral medications, Diclofenac sodium 50 mg BD for 7 days and Diacerein 50 mg OD for 3 months and physical therapy [quadriceps strengthening exercises].

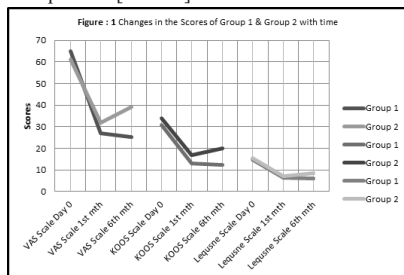
The injection used is available in form of prefilled syringes. Asepsis was maintained by cleaning the area with Betadine solution followed by surgical spirit. After draping the injection was given by 20 G 1 inch needle by superior-medial approach. Physical therapy where started after 2 days of injection.

**Group 2:** Patients in this group were given oral medication, Diclofenac sodium 50 mg BD orally for 7 days and Diacerein 50 mg OD for 3 months and physical therapy [quadriceps strengthening exercises].

**Table 1 - Baseline data of the two groups**

	Group 1(n=30)	Group 2(n=30)	P-value	T score	SE	Significance of difference
Age	61.5(5.69)	62.4(7.16)	0.59	0.5418	1.661	Not Significant
Weight	70.2(6.33)	72.33(6.71)	0.2107	0.2107	1.685	Not Significant
Height	165.9(5.56)	168.93(5.11)	0.0339	2.1733	1.38	Significant
BMI	25.53(1.69)	25.32(1.61)	0.6254	0.4908	0.428	Not Significant
Global VAS score at day 0	65.03(8.95)	61.26(10.44)	0.1391	1.4999	2.511	Not Significant
KOOS Total score at day 0	30.66(6.97)	33.95(6.92)	0.0717	1.8347	1.793	Not Significant
Lequesne index pain score at day 0	5.73(1.5)	5.5(1.33)	0.5277	0.6353	0.367	Not Significant
Lequesne index maximum distance score at day 0	3.6(1.13)	4.16(1.08)	0.0526	1.9785	0.286	Not Significant
Lequesne index ADL score at day 0	5.3(1.12)	5.88(1.15)	0.0854	1.7503	0.295	Not Significant
Lequesne index score at day 0	14.7(3.12)	15.36(3.22)	0.4196	0.8128	0.82	Not Significant

of Group 1 and Group 2 was not significant suggesting that the two groups are comparable. [Table 1].



At the end of 1 month the mean VAS scores of Group 1 and Group 2 were 27.1 and 31.83 respectively which were statistically similar with p =0.2109. But at the end of 6 month the mean VAS scores of the respective groups were 25.16 and 39 difference of which was statistically very much significant with p =0.0018, suggesting significant improvement in pain in Group 1 as compared to Group 2 end of 6 months. [Figure 1]

At the end of 1 month the mean KOOS Total score of Group 1 and Group 2 were 13.07 and 16.68 respectively which were statistically similar with p =0.0713. But at the end of 6 month the mean KOOS Total score of the respective groups were 12.16 and 19.18 difference of which was statistically very much significant with p =0.0011, suggesting significant improvement in overall symptoms of osteoarthritis knees in Group 1 as compared to Group 2 end of 6 months. [Figure 1]

At the end of 1 month the mean Lequesne index score of Group 1 and Group 2 were 6.4 and 6.93 respectively which were statistically similar with p =0.4904. But at the end of 6 month the mean Lequesne index scores of the respective groups were 6.11 and 8.51 difference of which was statistically significant with p =0.0071, suggesting significant improvement in overall symptoms of osteoarthritis knee in Group 1 as compared to Group 2 at the end of 6 months. [Figure 1]

**Adverse effects**

**Table 3 - Distribution of cases according to Adverse Effects**

Adverse effects	Group 1	Group 2
Knee pain during or after injection	7(23%)	0(0%)
Diarrhoea	9(30%)	11(37%)

In case of bilateral knee osteoarthritis though treatment was given bilaterally only the more painful knee was considered for study.

**Evaluations:** Evaluations were made at baseline, at the end of 1 month and at the end of 6 month according to the study performa. Patients were asked to fill the questionnaires at the time of visit. The patients were evaluated by three questionnaires, visual analog scale[VAS], KOOS scale and Lequesne index. KOOS scale which includes three sub scales i.e. for symptoms, stiffness, pain and function, daily living. Lequesne index also includes three subscales i.e. pain or discomfort, maximum distance walked and activities of daily living. Safety of the ongoing medications was assessed during follow-ups.

**RESULTS**

Statistical difference between the means of various parameters as age, weight, BMI, VAS score at day 0, KOOS total Score at day 0, Lequesne index pain score, Lequesne index maximum distance score and Lequesne index ADL score at day 0,

Gastritis	1(3%)	2(7%)
Symptoms of allergic reaction	0	0
Others	0	0

23% of patients complained of pain in the injected knee lasting not more than 3 days. 20 patients out of total patients of 60 gave history of diarrhea after starting Diacerein therapy.

**DISCUSSION**

The study was an observational controlled study done on 60 patients and was designed primarily to assess the efficacy of injection hyaluronic acid in management of osteoarthritis knees. It was found that inclusion of intra-articular *hyaluronic acid* is effective in reducing the symptoms for longer duration of time as compared to the patients managed with only NSAID's, Diacerein and physical therapy. The study also showed that the injections were well tolerated.

In our study we had observed 60 patients in two groups. Group 1 was the study group, it showed improvement in the form of change in mean global VAS scores from 65.03 to 25.16, KOOS score changed from 30.66 to 12.16 and Lequesne index from 14.7 to 6.11, similar changes could be seen in other studies. One of the study done in AIIMS showed change in Lequesne index of 10.58 at baseline to 5.7 at the end of 24 weeks.<sup>6</sup> Our study showed greater change in score which might be attributed to the combination of pharmacological management of NSAIDs and Diacerein and physical therapy with intra-articular injection of HA.

Another 3 armed study at Cochin hospital France showed change in VAS scale of 29.7 and change in Lequesne index of 4.8 at the end of one year in a sample of 131 patients, confirming the efficacy at the end of one year with a larger sample size.<sup>7</sup> Our studied showed more efficacy which might be attributed to smaller duration of follow up and combination of disease modifying drugs with intra-articular HA.

A study done in Whipps cross hospital in London was a randomized, blinded, placebo controlled trial with 6-month follow-up of 50 patients which showed statistically significant effect of intra-articular HA in improving walking pain and knee function.<sup>8</sup>

In our study 23% patients complained of knee pain lasting for more than 24 hrs after intra-articular injection during either of the weekly sessions of 3 intra-articular injections in Group 1. 30% patients from Group 1 and 37% patients from Group 2 complained of mild diarrhoea and 20% patients complained of gastritis in Group 1 and 17% patients in Group 2.

In study conducted in Cochin hospital France showed 17% patients had knee pain after intra-articular injection, which was similar to our study. 48% of the study sample complained of diarrhoea which was greater than our study which could be attributed to higher dose of Diacerein given to the patients. Also the incidence of gastritis was 4% was similar to our study.<sup>7</sup> In our study attempt was made to find the efficacy of the combination treatment that could be given, so as to optimize the effect of the overall therapy reducing the side effect of one particular drug. Thus in our study we could marginally reduce the diarrhoea associated with Diacerein.

One of the studies has suggested that intra-articular viscosupplementation is not significantly effective. This study had two major differences, first was the sample size was very large and secondly, this study had a huge placebo response hiding a real treatment effect. The placebo group in this study showed changes in global VAS scale of 31.1 and Lequesne index changed by 4.54 which were comparable with the patients given intra-articular viscosupplementation at the end of one year.<sup>7</sup> Thus the effect of placebo could not be ruled out in our study as the patients in control group were not given any sort of knee interventions.

In our study assessment was done for improvement in activities of daily living by KOOS subscale and Lequesne subscale both showed improvement in function. The mean scores reduced from 16 to 6.704 in KOOS subscale and 5.36 to 2.5 in the Lequesne's sub scale. Thus suggesting improvement in activities of daily living and thus improving the quality of life.

## CONCLUSION

In conclusion, in this observational controlled study, a course of 3 injections of sodium hyaluronate combined with pharmacotherapy and physiotherapy was well tolerated and effective in patients with osteoarthritis of the knee, with no systemic side effects attributed to the treatment. It effectively reduced the pain in the knee, and increased mobility, drastically reduce the morning stiffness. It also improved the quality of life by improving patients performance in activities of daily living and maximum distance walked in the of Kellgren's Grade II to III included in this study. And most of the improvements obtained from the baseline were maintained till the end of 6 months. The study also emphasised the role of pharmacotherapy with NASID's and Diacerein and physical therapy like quadriceps strengthening exercises which was obtained in control group without intra-articular hyaluronic acid therapy.

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