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## Research Article

### EFFICACY OF INTRA-ARTICULAR HYALURONIC ACID INJECTION COMPARED TO LIFE STYLE MODIFICATION IN TREATING OSTEOARTHRITIS OF KNEE JOINT

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#### ABSTRACT

**Aim & Background**-The aim of this study was to determine whether hyaluronic acid (HA) injections or life style modifications (LSM) can improve functional parameters in patients with knee osteoarthritis (OA).

**Material and methods**-In this prospective clinical trial, a total of 100 Cases with primary knee osteoarthritis as defined by American College of Rheumatology with radiographic Kellgren-Lawrence grade 2 and grade 3 knee OA were randomized and received treatment either in the form of three intra-articular injections of hyaluronic acid at one-week intervals or life style modifications for 6 weeks. Patients were evaluated by use of WOMAC Score and followed-up for 6 months.

**Result**-In HA group, mean WOMAC score before treatment was  $67.32 \pm 7.90$ , a decline of  $28.29 \pm 6.28$  in WOMAC score after treatment ( $38.73 \pm 5.95$ ) was observed while in LSM group, mean WOMAC score before treatment was  $68.36 \pm 8.55$ , a decline of  $27.80 \pm 7.04$  in WOMAC score after treatment ( $40.47 \pm 6.62$ ) was observed. This change in WOMAC score was statistically significant ( $p < 0.001$ ) in both the group

**Conclusion**-The study suggests that at 6 month follow up, WOMAC score showed significant improvement in both the groups, however slight better results were determined in the HA treated group as compared to LSM treated group. Early outcomes (at 1 month) were better in HA group as compared to LSM group.

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#### INTRODUCTION

Osteoarthritis (OA), a complex disease entity is primarily non-inflammatory, degenerative joint disease characterized by progressive loss of articular cartilage, subchondral bone sclerosis, osteophyte formation, changes in the synovial membrane, and an increased volume of synovial fluid with reduced viscosity and hence changed lubrication properties<sup>1</sup>.

With the rapidly aging population, the worldwide prevalence of osteoarthritis is approximately 10%. More authentic and well documented data on osteoarthritis (OA) is available from the United States<sup>2</sup> where nearly 13% of women and 10% of men aged 60 years and older have symptomatic knee OA. Today more than 100 million people are above 60 years or more in India<sup>3</sup>. Nearly half of them have evidence of Osteoarthritis in at least one joint<sup>4</sup>. Epidemiological studies have shown that its prevalence increases from 19.2% among those aged <50 years to 30.7% among those aged 50-59 years and then shoots up to 54.1% among those aged more than 70 years<sup>5</sup>.

This progressive and disabling disease can be resulted from a combination of risk factors, including advancing age, genetics, trauma, knee mal-alignment, increased biomechanical loading of joints through obesity, augmented bone density and an imbalance in physiological processes<sup>6</sup>. A higher risk in women has been reported with increasing age<sup>7</sup>.

Primarily OA occurs due to imbalance in tissue wear and repair and involves the articular cartilages and connective tissues. The effects of the OA can be seen as sclerosis of the subchondral bone, formation of osteophyte, laxity in ligaments and weakening of the periarticular muscles<sup>8</sup>. The disease is also responsible to bring down the quality of life and to have direct and indirect costs which include expensive care, joint replacements and other surgeries under direct expenses and early retirement and loss of labour as indirect costs of the disease<sup>9,10,11</sup>. The patients affected by the disease also face decreased joint function and increased rates of comorbidity. Osteoarthritis can also be associated with induction of depression due to limited mobility<sup>12,13</sup>.

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Hyaluronic acid (HA) is the most well associated marker for efficacy in diagnosis of osteoarthritis. Exogenous HA visco-supplementation improve viscoelasticity within the joint and also work through other mechanisms in OA such as inhibition of leukocyte chemotaxis, inhibition of lymphocyte proliferation, inhibition of phagocytosis, inhibition of apoptosis, enzymatic cartilage degradation, prostaglandin E2, and other arachidonic activities.

An association between obesity and osteoarthritis had been established<sup>14</sup>, opening a door for lifestyle behavioural weight management programs more relevant for individuals with OA. Increased weight had been indicated as a contributor to the development and progression of OA and negatively impacts adjustment to OA pain and disability<sup>15</sup>. It has been established that exercise along with diet intervention can produce the greatest benefit in knee pain and physical function<sup>16</sup>.

A variety of physical modalities can be used to relieve pain, reduce stiffness, and limit muscle spasm while strengthening periarticular structures to provide improved joint support. Physical measures in OA management include- Exercise (Muscle Strengthening and resistance exercises-isometric, isotonic, iso-kinetic (e.g. Quadriceps Strengthening exercises), Dietary modifications, Alterations in activities of daily living and Thermal modalities<sup>17</sup>. The aim of the study was to assess the efficacy of Intraarticular Hyaluronic Acid Injections compared to Life Style Modification in treating knee osteoarthritis

## MATERIAL AND METHODS

This prospective study is carried out at Era's Lucknow Medical College, between January 2015 to June 2016. This study involves 100 Cases with primary knee osteoarthritis as defined by American College of Rheumatology. The Cases recruited after history taking and physical examination, taking into consideration all inclusion criteria, whereas all the exclusion criteria were meticulously sought and ruled out had grade 2 and grade 3 knee OA. All the cases were asked to fill WOMAC questionnaire and were advised to get a bilateral knee radiograph done, in order to confirm the severity of disease with the help of Kellgren Lawrence Scale.

**Inclusion Criteria** includes patients with age - 40-80 years, patients who have failed to get relief by other treatment options such as - oral NSAID>3weeks, Patient with K-L grade 2-3 OA on X-ray and patient with WOMAC scores >40.

**Exclusion Criteria** includes patient with secondary Osteoarthritis, Patient with Systemic diseases, patient allergic to NSAIDs, Pregnant and Lactating mothers, patient with joint replacement of the knee within the previous 12 months, patient with K-L grade 4 knee OA, patient who have undergone arthroscopy of either knee within 3 months.

The case group was divided into two groups. The first group received intra-articular hyaluronic acid injections and the second group received life style modifications as treatment. Before treatment, knee function of all patients was evaluated by WOMAC score. The Knee Score criteria consists of 24 questions (5 pain, 2 stiffness and 17 physical function). This produces a reported WOMAC Score of between 0(worst) to 100(best).

Patient receiving NSAIDS were asked to discontinue them for the duration of study, beginning from 15 days before the study. During the course of the study patient complaining of pain received Paracetamol (10 mg/kg) as a rescue drug.

**Intra-articular HA injections**-High Molecular Weight Hyaluronic acid injections were injected once a week for 3 weeks. In bilateral cases, both the knees were injected. The cases were regularly followed at 1month, 3 months and 6 months after the last injections.

**Procedure** - The patient was placed in the supine position and under proper aseptic precautions a prefilled 2-ml syringe, containing 8 mg HA was injected Supero-laterally into the Supra-patellar pouch of affected knee. The patients was advised to refrain from strenuous activity for a day following the intra-articular injections. The patient was given two more HA inj. at weekly interval.

Life Style Modifications included series of alteration in daily activities (such as avoid squatting, cross legged sitting, climbing staircases), diet modification, weight reduction, muscle strengthening and resistance exercises with range of motion exercises. The Exercise program was taught to the participant by physical therapist on the day of enrollment in the study (day 0) and then performed in home based regime with the patient coming to the hospital at 1 and 2weeks after the initiation of the study and then followed up at 1, 3 and 6 months.

### Analyzed parameters

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software.

## RESULTS

The study included 100 cases (186 knees) of knee osteoarthritis. Demographic data and baseline clinical characteristics of these patients were recorded at the start of the clinical trial.(Table1). There were no statistically significant differences between demographic data or clinical data used in the study.

**Table 1** Demographic data and Baseline characteristic of the 100 cases of knee OA

| Baseline Characteristics   | HA GROUP (n=92) | L.S.M GROUP (n=94) |
|----------------------------|-----------------|--------------------|
| Age (years)                | 52.60±9.95      | 50.98±8.16         |
| Sex ( male : female ratio) | 1:2.33          | 1:1.94             |
| Unilateral Oa Cases        | 8 (16%)         | 6(12%)             |
| Bilateral Oa Cases         | 42 (84%)        | 44(88%)            |
| Grade 2 Knee Oa            | 38              | 38                 |
| Grade 3 Knee Oa            | 54              | 56                 |
| Loss of follow up          | 2               | 5                  |
| Mean Womac Score           | 67.32±7.90      | 68.36±8.55         |

The Age distribution of the cases ranged from 40-78 years and mean age was 51.79±9.09 years. Majority of the patients were females (68.00%) and rest were males (32.00%). Male: Female ratio was 1:2.13 in overall population while ratio was 1:2.33 in Group I and 1:1.94 in Group II. Out of 186 osteoarthritis affected knees, 76 (40.86%) were of Grade 2 osteoarthritis and rest 110 (59.14%) were of Grade 3 osteoarthritis. In present study, mean WOMAC scores at baseline were 67.32±7.90 and

68.36±8.55 respectively in HA and LSM groups. Both the groups were matched statistically for age, gender, grade, side, bilaterality, weight category and functional scores, thus showing that confounding effect of these factors, if any, was equivalent in both the groups. A total of 2 patients in Group I and 5 in Group II were lost to follow up and the causes of discontinuation of treatment in HA treated group was one patient took NSAIDS and the other patient took corticosteroid injection while in L.S.M treated group, two patients continued exercises with NSAIDS, one patient opted for corticosteroid injection and one patient was lost to follow up.

**Table 2** Intragroup Change in Nutritional Status of Study Population after Treatment

| Group           | Nutritional Status (BMI kg/m <sup>2</sup> ) | Before treatment |       | After treatment |       | Statistical significance |       |
|-----------------|---|------------------|-------|-----------------|-------|--------------------------|-------|
|                 |   | No.              | %     | No.             | %     | χ <sup>2</sup>           | P     |
| Group I (n=48)  | Normal wt.                                  | 6                | 12.50 | 6               | 12.50 | 0.031                    | 0.985 |
|                 | Overweight                                  | 26               | 54.17 | 24              | 50.00 |                          |       |
|                 | Obese                                       | 16               | 33.33 | 18              | 37.50 |                          |       |
| Group II (n=45) | Normal wt.                                  | 1                | 2.22  | 9               | 20.00 | 9.309                    | 0.009 |
|                 | Overweight                                  | 29               | 64.44 | 29              | 64.44 |                          |       |
|                 | Obese                                       | 15               | 33.33 | 7               | 15.56 |                          |       |

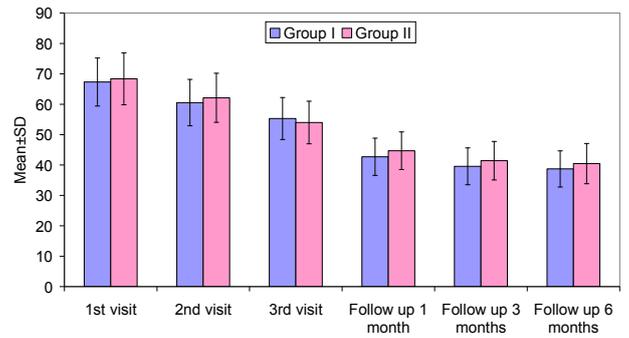
Treatment outcomes measured in terms of % improvement in mean WOMAC score, as the change from the baseline, are given in Table 4. In Group I, mean WOMAC score before treatment was 67.32±7.90, a decline of 28.29±6.28 in WOMAC score after treatment (38.73±5.95) was observed while in Group II, mean WOMAC score before treatment was 68.36±8.55, a decline of 27.80±7.04 in WOMAC score after treatment (40.47±6.62) was observed. The change in mean WOMAC score for both the group was found to be statistically significant (p<0.001).(Fig:2)

**Table 3** Treatment outcome measured in terms of % improvement in Mean WOMAC Score between Group I & Group II at Intervention Visits and follow up visits

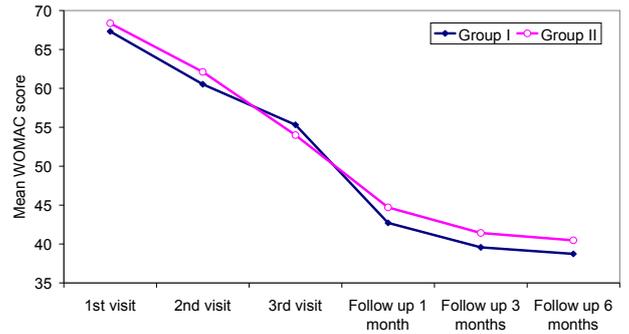
|                       | Group I |       |      | Group II |       |      | Statistical significance |       |
|-----------------------|---------|-------|------|----------|-------|------|--------------------------|-------|
|                       | No.     | Mean  | SD   | No.      | Mean  | SD   | 't'                      | 'p'   |
| 1 <sup>st</sup> visit | 92      | 67.32 | 7.90 | 94       | 68.36 | 8.55 | -0.857                   | 0.392 |
| 2 <sup>nd</sup> visit | 88      | 60.53 | 7.63 | 92       | 62.12 | 8.07 | -1.360                   | 0.176 |
| 3 <sup>rd</sup> visit | 88      | 55.31 | 6.91 | 84       | 53.99 | 7.00 | 1.245                    | 0.215 |
| Follow up 1 month     | 88      | 42.71 | 6.13 | 84       | 44.71 | 6.17 | -2.137                   | 0.034 |
| Follow up 3 months    | 88      | 39.57 | 6.07 | 84       | 41.42 | 6.33 | -1.957                   | 0.052 |
| Follow up 6 months    | 88      | 38.73 | 5.95 | 84       | 40.47 | 6.62 | -1.812                   | 0.072 |

**Table 4** Intragroup Change of Mean WOMAC Score from first intervention visit (Baseline)

| Group                              | Time interval                      | Mean ch. | S.D.   | % Change from baseline | 't'     | 'p'    |
|------------------------------------|------------------------------------|----------|--------|------------------------|---------|--------|
|                                    |                                    |          |        |                        |         |        |
| 3 <sup>rd</sup> intervention visit | -11.71                             | 3.88     | -17.47 | -28.304                | <0.001  |        |
| Follow up at 1 month               | -24.31                             | 6.40     | -36.27 | -35.612                | <0.001  |        |
| Follow up at 3 months              | -27.45                             | 6.20     | -40.96 | -41.532                | <0.001  |        |
| Follow up at 6 months              | -28.29                             | 6.28     | -42.21 | -42.255                | <0.001  |        |
| Group II                           | 2 <sup>nd</sup> intervention visit | -5.99    | 2.34   | -8.79                  | -24.493 | <0.001 |
|                                    | 3 <sup>rd</sup> intervention visit | -14.28   | 5.08   | -20.92                 | -25.765 | <0.001 |
|                                    | Follow up at 1 month               | -23.55   | 6.99   | -34.50                 | -30.891 | <0.001 |
|                                    | Follow up at 3 months              | -26.85   | 7.01   | -39.33                 | -35.090 | <0.001 |
|                                    | Follow up at 6 months              | -27.80   | 7.04   | -40.72                 | -36.208 | <0.001 |



**Fig 1** WOMAC Score at every follow up visits.



**Fig 2** Mean WOMAC Score of the two group before and after completion of treatment.

A significant functional improvement was observed in both the groups from first follow up (1 week post-intervention) itself. By one month, a reduction in WOMAC scores to the extent of 36.27% was observed in HA group as compared to 34.50% in LSM group. By the end of six months the mean % reduction in HA group was 42.21% as compared to 40.72% in Lifestyle modification group.

At all the follow up intervals, except at 1 month follow up interval, mean WOMAC scores did not show a significant difference between two groups. At 1 month post-intervention follow-up, functional improvement was significantly better in HA group as compared to LSM group.

Throughout the study no complications arising from HA injection, for example pain, joint effusion, synovitis, haemarthrosis, or septic arthritis, were recorded.

**DISCUSSION**

For symptomatic treatment of knee OA, different therapeutic options other than NSAID may benefit patients by reducing the morbidity associated with the disease. Intraarticular hyaluronic acid injection, one of the most common pharmacological treatment option that potentiates the synovial fluid around the bony joint in order to keep the joint lubricated and reduce the stresses on joints during their functioning<sup>18</sup> whereas amongst various non-pharmacological treatment options, exercise and lifestyle modification is one of the most commonly recommended treatment modalities however, its efficacy has often been questioned<sup>19,20</sup>. In present study, 92% patients were overweight and obese. Overweight and obesity is a recognized risk factor for knee OA<sup>2,3</sup>. That is why weight reduction is a recommended strategy for treatment of OA especially when lifestyle modification is planned.

Weight reduction is the mainstay of lifestyle modification treatment strategies<sup>21</sup>. Similar to present study, Huang *et al.*

(2000)<sup>22</sup> also observed weight reduction of 12-15% in patients undergoing lifestyle modification therapy in their study. Usefulness of combined dietary and exercise intervention in weight loss has also been indicated by Messier *et al.* (2000)<sup>23</sup> who reported an 8.5 kg reduction following lifestyle modification. The reason for this difference could be difference in focus of intervention between two studies. In present study, the focus of intervention was change in functional status whereas the cited study was focused towards attaining a weight reduction for functional improvement.

In present study, effect of treatment on functional outcome was visible within one week itself, however, the pace of improvement was faster in hyaluronic acid group throughout the study period with first week, first month, third month and 6 month follow up interval % decline in WOMAC scores was being 9.69%, 36.27%, 40.96% and 42.21% respectively as compared to 8.79%, 34.50%, 34.50%, 39.33% and 40.72% respectively in LSM group. Notwithstanding these percentage differences, the route of reduction in WOMAC scores was similar in both the groups and did not show a statistically significant difference between two groups except at one month when HA group had significantly lower mean WOMAC scores as compared to that in LSM group.

In a similar study, Karatosun *et al.* (2006)<sup>24</sup> who compared intraarticular hyaluronic acid therapy to exercise therapy over a period of one year has shown improvement in functional scores to be 41.9% in HA group as compared to 35.02% in exercise group. Compared to this in present study which spanned over six months period, the improvement in functional scores was 42.21% in HA group which can be considered to be close to that reported in the cited study, however, the improvement in functional scores in LSM group was slightly higher than their study. The reason for this could be that in present study, the LSM regimen included both physical exercises as well as dietary and lifestyle management.

## CONCLUSION

On the basis of above findings this study suggests that at 6 month follow up, WOMAC score showed significant improvement in both the groups, however slight better results were determined in the HA treated group as compared to LSM treated group. This study also concluded that lifestyle modifications provided a viable treatment option for increasing functional quality of life of knee OA patients which was comparable to intraarticular hyaluronic acid visco-supplementation therapy. Both the groups brought about optimum response within one month and thereafter a sustenance of results was seen till the end of study. The primary mechanism of LSM success was weight reduction and conditioning of muscles and cartilage and thus making them more flexible. Early outcomes (1 month) were better in HA group as compared to LSM group. Whether the change in functional ability of patients as a result of both the treatments was sustainable in long-term remains to be studied, for which further studies on larger sample size and longer follow-up duration are recommended.

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