

# Comparative Study of Intra Articular Hyaluronic Acid and Intra Articular and Para Articular Dextrose Prolotherapy in Mild to Moderate Knee Osteoarthritis

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## ABSTRACT

**Introduction:** Osteoarthritis is the most common joint disease worldwide with a prevalence of 22 to 39% in India. Minimally invasive treatments are a success when conservative methods fail. The aim of the study was to compare the established treatment of intra-articular hyaluronic acid with the more novel approach of intra-articular and para-articular dextrose.

**Material and methods:** Thirty patients with Knee OA were divided into two groups of fifteen each and were either injected intra-articularly with high molecular weight hyaluronic acid (group H) or a mixture of 12.5% dextrose and 1% lidocaine (group D). Pre and post procedure Visual Analogue Scale and Western Ontario and McMaster University Arthritis Index assessment scale scores were compared before and two months after the procedure. Data were analysed using chi-squared test, unpaired and paired t-test.

**Results:** There was a significant reduction of both Visual Analogue Scale (VAS) and Western Ontario and McMaster University Arthritis Index assessment scale (WOMAC) scores at two months when compared to pre-procedure scores ( $p < 0.05$ ) for both groups. However, the reduction in both the scores were significantly lower in post procedure period for intra-articular dextrose when compared to hyaluronic acid ( $p = 0.011$  and  $p = 0.004$  respectively).

**Conclusion:** Intraarticular dextrose is certainly one of the better minimally invasive treatment for knee OA when compared to high molecular weight hyaluronic acid and at much lower cost.

**Keywords:** Osteoarthritis, Knee, Prolotherapy, Dextrose, Hyaluronic Acid, VAS, WOMAC

## INTRODUCTION

OA is the second most common rheumatologic disease and is the most frequent joint disease with prevalence of 22% to 39% in India.<sup>1</sup> Approximately 80-90% of individuals older than 65 years have evidence of radiographic primary osteoarthritis. the prevalence of osteoarthritis is higher among women than among men with a female-to-male incidence ratio of 1.7:1.<sup>2</sup> Osteoarthritis predominantly involves the weight-bearing joints, including the knees, hips, cervical and lumbosacral spine, and feet.

Traditionally, osteoarthritis was thought to affect primarily the articular cartilage of synovial joints; however, pathophysiologic changes are also known to occur in the synovial fluid, as well as in the underlying (subchondral) bone, the overlying joint capsule, and other joint tissues.<sup>3,4,5,6</sup> Risk factors for osteoarthritis include advancing age<sup>7</sup>, Obesity<sup>8</sup>, Trauma (including microtrauma) or surgery

(including surgical repair of traumatic injury)<sup>9</sup>, mal-alignment at the knee (esp. valgus)<sup>10</sup>, muscle dysfunction<sup>11</sup> and genetical predisposition<sup>12</sup>. Systemic diseases like crystal arthropathy, rheumatoid arthritis, Paget's disease, haemoglobinopathies etc can cause secondary osteoarthritis.

The treatment of OA mainly focuses on reducing pain and disability. The treatment modalities can be broadly divided into<sup>13</sup>:

1. Non pharmacological including physical methods and physiotherapy.
2. Pharmacological including analgesics and certain supplements like chondroitin sulphate and glucosamine. Intraarticular injections, of which low and high molecular hyaluronic acid preparations are very popular. Hyaluronic acids are long un-branched polysaccharides with repeated disaccharide units of glucuronic acid and glucosamine. It binds to aggrecan, retaining its concentration in the cartilage and thus increasing the resilience of the articular cartilage<sup>14</sup>.
3. Surgery including arthroscopy and arthroplasty.

Prolotherapy is an injection therapy for chronic musculoskeletal injury, including knee osteoarthritis. The most common prolotherapy agent used in clinical practice is dextrose, with concentrations ranging from 12.5% to 25%.<sup>15</sup> The mechanism of action behind prolotherapy is not completely understood. Current theory holds that the injected proliferant mimics the natural healing process of the body by initiating a local inflammatory cascade, which triggers the release of growth factors and collagen deposition, proliferation and strengthening of new connective tissue, joint stability, and a reduction in pain and dysfunction,<sup>16</sup>

The aim of the above study was to compare the effects of intra-articular high molecular hyaluronic acid and intra and para-articular dextrose prolotherapy on pain and function in patients with knee osteoarthritis by comparison of VAS scale and Western Ontario and McMaster University Arthritis

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Index (WOMAC) assessment scale respectively.

## MATERIAL AND METHODS

The study was done at ESI hospital, Sealdah, Kolkata. The patients were taken from the OPD pool of the pain unit run at the institute.

The period of the study was between Dec 2015 to April 2016. Comparative randomized single blind study.

After obtaining permission from the institutional ethics committee and informed written consent from the chosen patients, 30 patients were randomly selected and divided equally into two groups - Group D were treated with dextrose prolotherapy and Group H by high molecular weight hyaluronic acid.

Diagnosis of OA knee was done as per American College of Rheumatology Criteria<sup>16</sup>.

Pain in the knee and any THREE of the following:

- Over 50 years of age.
- Less than 30 mins. of morning stiffness.
- Crepitus on active movement.
- Bony tenderness.
- Bony enlargement.

No palpable warmth of synovium

Classification of the severity of OA was according to Kellgren - Lawrence grade (grade I, II, III, IV; IV being most severe).

The inclusion criteria were:

- Pain in the knee.
- Kellgren – Lawrence grade I, II, III on PA knee radiograph.
- Age 50 to 75 years.

The exclusion criteria were:

1. Systemic disease.
2. K - L Grade IV OA.
3. On anticoagulants.
4. Knee pain/ swelling due to inflammation, infection etc.
5. Previous intra articular injection.
6. Use of opioid analgesics.
7. Intra articular fluid accumulation.
8. Use of NSAIDS in past two weeks.

All patients were started on antibiotic (ciprofloxacin 500 mg

two times daily) one day before procedure and continued for three days.

In supine position after proper dressing and draping, the super lateral part of the knee joint is anaesthetised with 2% lignocaine. With an 18 gauge IV cannula, the joint space was approached.

In the Dextrose group (GROUP D) 25% dextrose and 2% preservative free Lignocaine (Xylocard 2%; Neon Laboratories) were mixed in a syringe to give a final concentration of dextrose 12.5% with 1% lignocaine. 4 ml of the mixture was injected into the joint. Also 0.5 ml of the mixture was also injected at peri articular tender points. Patients' knees were bandaged. They were also advised to use crepe bandage while walking or performing regular chores. Physiotherapy was advised in a graded fashion after the pain subsided. (GROUP D)

The group receiving high molecular weight hyaluronic acid (Synvisc One; Sanofi biosurgery, USA) (GROUP H) was injected with 4 ml of hyaluronic acid intra articularly after proper antisepsis. Periarticular tender points were injected with 0.5ml of normal saline. Post procedure they were advised the same as group D.

Each of the patients in dextrose group received a single session of intervention.

VAS score and WOMAC score were assessed before and two months after the procedure. Finally pre treatment and post treatment scores were compared.

All patients of group D had mild to moderate pain, swelling and mild stiffness of the injected knee for 7 to 20 days post procedure. All of them were managed with rest, paracetamol 1 gm 3 times daily for 3 to 5 days and hot and cold compress. Five patients of group H had mild to moderate pain swelling and stiffness for intra articular injection. They were also managed with paracetamol, rest and hot and cold compress.

## STATISTICAL ANALYSIS

Results were computed using Minitab 18. Paired t-test for pre and post procedure VAS and WOMAC score, and unpaired t-test between the groups for comparison of post procedure VAS and WOMAC score were calculated. A p-value of < 0.05 taken to be significant.

## RESULTS

Thirty patients with knee pain were selected according to the above criteria and divided randomly into two groups of 15 each. Table of random numbers was used to divide the subjects into two groups. Group D received dextrose prolotherapy and group H received high molecular weight hyaluronic acid.

There was no significant difference in the age of two groups.

Variables	Dextrose group (D) (Mean ± SE)	Hyaluronic acid group (H) (Mean ± SE)
No.	15	15
Age	58.27±1.6	58.20±1.3
Sex	F =10 M =5	F =10 M =5

Table-1: Demographic profile

Parameter Group	Pre-VAS	Post-VAS	P-Value	Pre-WOMAC	Post-WOMAC	P-Value
Group H	78.3±3.1	52.6±2.45	<0.05*	70.0±2.8	48.89±2.71	<0.05*
Group D	83.0±2.4	42.13±2.95	<0.05*	76.45±2.1	38.17±2.16	<0.05*
P value	0.237	0.011*		0.08	0.004*	

\*P value significant.

Table-2: Analysis of VAS and WOMAC score (Mean +/- SD). Group (rows). Parameter(columns).

The sex ratio is also comparable. The pre procedure VAS and WOMAC scores were comparable in both the groups. Over all the groups were similar in every respect. (Table 1)

However, pre and post procedure comparison of VAS and WOMAC score differed significantly for both group D and group H. Therefore both the treatments were effective in improving the condition of the patient. (Table 2)

From table 2 it is also evident, that on comparison of post procedure VAS and WOMAC scores in two groups, the dextrose group (group D) fared significantly better than the hyaluronic acid group (group H). The P value for post-VAS score and post-WOMAC score are 0.011 and 0.004 respectively.

## DISCUSSION

In the present study, 20 out of thirty participants are women (75%). Goorman et. al.<sup>18</sup> and Evanich et. al.<sup>19</sup> had 57% and 61% women in their study groups. Eslamian F et.al.<sup>20</sup> had a study group consisting of exclusively 24 women. It is a known fact that OA more in woman. Therefore, the study group reflects a more percentage of women.

The average age of both the study groups is 58 yrs. OA is more commonly manifested after 50 yrs and above 55 yrs women are more affected than men.<sup>2</sup>

There was no significant difference in proportion of male and female subjects in between the groups (P=1.0).

Patients were selected according to American College of Rheumatology criteria. Hence, weights of individual subjects were not taken into account.

Majority of the patients had a radiological diagnosis K-L grade II and III osteoarthritis.

Both groups had high VAS scores before the procedure (D=83±9.19; H=78±12.1), but were not significantly different (P=0.2).

Both groups had high composite WOMAC score before the procedure (D=76.4±8.31; H=70±11.0) but were not significantly different amongst themselves (P=0.8).

In the dextrose group, there was a significant difference (P<0.001) in the pre and post procedure VAS (83±9.19 vs. 42±11.43). Eslamian F et.al. found that after dextrose prolotherapy pain at rest and activity decreased from 8.82±1.37 and 9.37±1.31 to 4.87±1.39 respectively (P<0.001).<sup>20</sup>

The VAS score in the HA group decreased significantly (P < 0.005) from pre procedure value of 78.27±12.09 to post procedure value of 52.60±9.51. Miltner et.al. In his study showed a similar significant reduction in VAS score (P<0.001) post injection when compared to baseline<sup>21</sup>. Hashemi M et. al. also demonstrated a significant decrease in VAS score (p<0.001)<sup>22</sup>.

Comparing between groups, it shows that, there is significant decrease of post procedure VAS score in the dextrose group when compared to post injection value in hyaluronic acid group. (42.1±11.4 vs. 52.6±9.51, P = 0.011). Therefore, Dextrose prolotherapy relieves pain better than high molecular hyaluronic acid.

The WOMAC score in the dextrose group also decreased

significantly (P < 0.001) after the procedure (76.45±8.31 vs. 38.17±8.36; diff. 38.28± 15.48).Eslamian F et.al. showed a similar decrease in WOMAC score of 30.5±14.27 points (P <0.001) between pre and post procedure values.<sup>20</sup> Rabago et. al. also showed a decrease in WOMAC score of 15.3±3.5 (P <0.05)<sup>23</sup>. Hashemi M et. al. also registered a significant improvement in WOMAC score (p<0.001)<sup>22</sup>.

The hyaluronic acid group (H group) also showed a significant drop in the WOMAC score after the procedure (69.99±11.01 vs. 48.89±10.48; P <0.001). Altman et.al reported similar improvement in WOMAC score with hyaluronic injection.<sup>24</sup> Raynauld et.al also reported improved outcome after hyaluronic acid injections.<sup>25</sup>

However, comparing post procedure WOMAC score of the groups, the study reveals a significant decrease in the dextrose group (38.17±8.36 (D) vs. 48.9±10.5 (H); P = 0.004).

Conclusion is that dextrose prolotherapy works better than hyaluronic acid for knee osteoarthritis.

There are certain limitations in the study.

- i It is a single blind study. Therefore observer bias is likely to be present.
- ii The number of subjects in each group is small. Hence possibility of type 1 error is high.
- iii The subjects were followed for a very limited time (2 months). More extended periods of follow-up need to be done before drawing more plausible conclusions.
- iv Weights of the subjects have not been registered, considering that weight is an important factor in the pathogenesis of OA.
- v The protocol for dextrose prolotherapy is still empirical. Hence an empirical protocol was used for the above study.

## CONCLUSION

Osteoarthritis is the most common degenerative disease affecting the joints worldwide. It is also the most common cause of joint disability in India. Older age population are most affected and it is more common among the females.

Different types of treatment are available for osteoarthritis. Dextrose prolotherapy is a minimally invasive treatment for mild and moderate osteoarthritis. Our comparative study shows that dextrose is effective in reducing pain and improving disability in such patients. Furthermore it is shown to be more effective than the more popular and costly treatment of using high molecular weight hyaluronic acid. However more studies using larger number of samples are required to reinforce the findings.

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