Section: Orthopaedics

Original Research Article

A PROSPECTIVE RANDOMIZED CONTROLLED STUDY FOR TREATMENT OF OSTEOARTHRITIS OF KNEE JOINT WITH INTRA-ARTICULAR INJECTION OF HYLAN GF 20 (SINGLE DOSE 6ML) VERSUS CONSERVATIVE MANAGEMENT

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ABSTRACT

Background: To determine the safety and efficacy of injection Synvisc (Hylan GF 20) on reducing pain and improving function among patients who are suffering from osteoarthritis knee by comparing patients who receive and who did not receive intraarticular injection Synvisc.

Material & Methods: Patients who came to OPD with grade 1 to grade 3 osteoarthritis were included in this study. The study group constituted total 248 adult patients (Range 30-70years)**.** The sample size was obtained on the basis of calculation by using statistical formula. The patients were randomized in to two groups by using computer generated randomization. Data collection was done preoperatively and at subsequent follow up at 1 week, 1 month, 3 months and 6 months for Pain, function, radiological and local parameter.

Results: The WOMAC pain score decreased to 4.18 after 6 months in injection group compared to 5.85 in conservative group. Similarly, WOMAC stiffness score decreased to 1.53 after 6 months as compared to 2.11 in conservative group. The WOMAC Physical function score decreased to 21.92 in injection group compared to 25.38 in conservative group. There was significant improvement in the WOMAC pain, stiffness and physical function scores and VAS pain scores.

Conclusions: Hylan GF 20 injection can improve the pain associated with osteoarthritis and is a useful modality in early stages of osteoarthritis or for the patients who are unable to undergo major surgery because of medical morbidity.

Keywords: Osteoarthritis knee, Injection Synvisc, Hylan GF 20, WOMAC pain score.

INTRODUCTION

Osteoarthritis is a chronic degenerative joint multifactorial disease and is a common public health problem encountered by Orthopedicians. The disease process of osteoarthritis is characterized by the progressive destruction of the articular cartilage, leading to joint space narrowing, subchondral sclerosis, subchondral cyst, synovial inflammation and marginal osteophyte formation.[1]

It is one of the most prevalent conditions resulting to disability particularly in elderly population. It is most common disease of the developed world and leading cause of chronic disability, mostly as a consequence of the knee OA and/or hip OA.[2] The economic burden of the of the disease is high including those related to the treatment, for those individuals and their families who must adapt lives and homes to the disease and those due to loss of work productivity.[3]

The treatment of OA includes non-pharmacological interventions such as patient education, physical therapy, weight loss and low impact exercises.[4,5] Pharmacological treatment options include acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), topical NSAIDs, glucosamine and/or chondroitin sulfate and intra articular corticosteroids. Opioid and non-narcotic analgesics may be prescribed in refractory pain patients. IA Hyaluronans (Has) have recently been used for the treatment of painful knee joints with OA.[6]

Administration of exogenous Hyaluronan (HA) preparations addresses this problem by replacing the low viscoelastic synovial fluid with solutions of higher viscosity.[7] There are also substantial data that exogenously provided HA may also improve pain and function by non-mechanical, biologically based mechanisms within the synovial and articular environment.[8]

Studies comparing the conservative management and efficacy and safety of intra articular injection of hylan GF – 20 (Exogeneous HA) are lacking in India and abroad. This study was mainly designed to compare the safety and efficacy of intra articular injection of hylan GF – 20 with the conservative methods of management of osteoarthritis of Knee joint.

MATERIALS AND METHODS

A prospective, randomized, controlled study was conducted among a total of 248 patients with osteoarthritis attending the Orthopaedics outpatient department of Northern Railway central Hospital, New Delhi between July 2016 to June 2017. Clearance from Institutional Ethical Committee was obtained before the study was started. All the subjects included in the study were approached for an informed and bilingual consent before they were included in the study. The sample size was calculated with the help of previous similar studies.9,10.

Inclusion Criteria

1. Primary osteoarthritis knee Grade-1,2 and 3 of osteoarthritis.
2. Age >40 years

Exclusion Criteria

1. Osteoarthritis knee grade-4 as per K-L classification.
2. Secondary osteoarthritis of knee.
3. Known case of hypersensitivity to hylan polymer.
4. Joint infection- acute subacute chronic.
5. Nonspecific inflamed knee joint.
6. Patient having cognitive dysfunction.
7. Patient not giving consent for injection.
8. Skin diseases or infection in the area of injection site.
9. Ligamentous laxity & meniscal instability.
10. Pregnant patients.
11. Valgus &Varus deformity of knee.

A total of 248 patients were enrolled from the outpatient department. The patients thus selected were divided into 2 groups depending on the computer-based randomization numbers.

Group A (conservative management group) received physiotherapy (quadriceps and hamstring strengthening exercises)

Group B (injection hylan GF20 group) received injection hylanGF20 under all aseptic precautions (Painting with savlon, betadine, spirit and draping with sterile sheets, towels.)

Patients from both groups received calcium (calcium carbonate 1000mg/day) and vit. D supplement (vit. D 600IU/day) during the study period. The patients were followed on 1stweek (skin color, local temperature, pain, swelling),1 month, 3 month, 6 month and evaluation were done on basis of WOMAC score (which includes knee pain, knee stiffness, knee functional limitations) VAS Score.

Injection Technique

Synvisc is supplied in 6-mL prefilled syringes. The recommended injection schedule is one injection single dose and Repeat courses of visco-supplementation can be performed after six months.

A knee joint can be injected several ways. One approach is to have the patient lie supine on the examination table with the knee flexed 90 degrees (figure 1). In this position, the anterior portions of the medial and lateral joint lines can easily be palpated as dimples just medial or lateral to the inferior pole of the patella. Often, the medial joint line is easier to palpate and define and can be chosen as the site of injection. Alternatively, the knee joint can be approached with the knee extended, again with the patient lying supine (figure 2). Most commonly the superolateral edge of the patella is the site of injection, but other quadrants of the knee near the patellar edges can also be chosen. With this approach (knee in extended position), the needle is generally aimed under the patella.

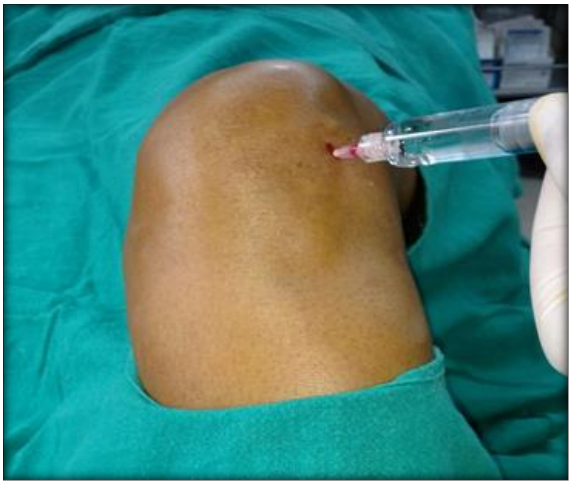

Figure 1: One method for injecting a knee joint. The patient is lying supine on the examination table with the left knee flexed to 90 degrees.

Figure 2

RESULTS

Alternative method for injecting a knee joint. The patient is lying supine on the examination table with the right knee extended. The injection site is marked along the superolateral corner of the patella. The needle is angled slightly toward the underside of the patella.

No excessive weight-bearing physical activity should take place for one to two days following injection. Otherwise, no specific post-injection instructions are necessary.

Table 1: Distribution of the study group according to Osteoarthritis of Knee grading

Osteoarthritis Knee grading	Group A n (%)	Group B n (%)
Grade 1	17 (13.7)	17 (13.7)
Grade 2	88 (71.0)	77 (62.1)
Grade 3	19 (15.3)	30 (24.2)
Total	124 (100)	124 (100)

χ^2 Value=3.203 df=2 p value=0.202, NS

Table 2: Distribution of the study group according to mean pre intervention WOMAC stiffness scores

Pre intervention WOMAC Stiffness	Group A	Group B	T value	P value, Sig
Mean ± SD	3.02 ± 1.38	2.96 ± 1.39	0.32	0.749, NS

Table 3: Distribution of the study group according to mean pre intervention WOMAC physical function

Pre intervention WOMAC Physical function	Group A	Group B	T value	P value, Sig
Mean ± SD	34.09 ± 3.78	33.9 ± 3.98	0.377	0.707, NS

Table 4: Distribution of the study group according to mean pre intervention VAS Pain

Pre intervention VAS Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	4.14 ± 1.4	3.82 ± 1.39	1.801	0.073, NS

Table 5: Distribution of the study group according to mean post intervention week 1 WOMAC Pain

Post intervention at week 1 WOMAC Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	6.99 ± 1.03	6.14 ± 1.44	5.376	0.000, Sig

Table 6: Distribution of the study group according to mean post intervention week 1 WOMAC Stiffness

Post intervention at week 1 WOMAC Stiffness	Group A	Group B	T value	P value, Sig
Mean ± SD	2.72 ± 1.08	2.04 ± 1.3	4.401	0.000, Sig

Table 7: Distribution of the study group according to mean post intervention week 1 WOMAC Physical function

Post intervention at week 1 WOMAC Physical function	Group A	Group B	T value	P value, Sig
Mean ± SD	31.8 ± 3.55	26.99 ± 4.12	9.832	0.000, Sig

Table 8: Distribution of the study group according to mean post intervention week 1 VAS pain

Post intervention at week 1 VAS Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	4.01 ± 1.11	3.48 ± 1.07	3.789	0.000, Sig

Table 9: Distribution of the study group according to mean post intervention at 1 month WOMAC pain

Post intervention at 1 month WOMAC Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	6.05 ± 0.92	4.16 ± 1.42	12.449	0.000, Sig

Table 10: Distribution of the study group according to mean post intervention at 1 month WOMAC stiffness

Post intervention at 1 month WOMAC Stiffness	Group A	Group B	T value	P value, Sig
Mean ± SD	2.42 ± 0.85	1.06 ± 0.85	12.553	0.000, Sig

Table 11: Distribution of the study group according to mean post intervention at 1 month WOMAC physical function

Post intervention at 1 month WOMAC Physical function	Group A	Group B	T value	P value, Sig
Mean ± SD	29.96 ± 3.32	21.96 ± 3.96	17.231	0.000, Sig

Table 12: Distribution of the study group according to mean post intervention at 1 month VAS pain

Post intervention at 1 month VAS Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	3.8 ± 0.93	3.24 ± 0.8	5.057	0.000, Sig

Table 13: Distribution of the study group according to mean post intervention at 3 months WOMAC pain

Post intervention at 3 months WOMAC Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	5.28 ± 0.83	3.18 ± 1.36	14.664	0.000, Sig

Table 14: Distribution of the study group according to mean post intervention at 3 months WOMAC stiffness

Post intervention at 3 months WOMAC Stiffness	Group A	Group B	T value	P value, Sig
Mean ± SD	2.27 ± 0.79	1.03 ± 0.78	12.356	0.000, Sig

Table 15: Distribution of the study group according to mean post intervention at 3 months WOMAC physical function

Post intervention at 3 months WOMAC Physical function	Group A	Group B	T value	P value, Sig
Mean ± SD	28.18 ± 3.19	19.5 ± 3.37	20.717	0.000, Sig

Table 16: Distribution of the study group according to mean post intervention at 3 months VAS Pain

Post intervention at 3 months VAS Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	3.08 ± 0.62	3.01 ± 0.66	0.896	0.371, NS

Table 17: Distribution of the study group according to mean post intervention at 6 months WOMAC pain

Post intervention at 6 months WOMAC Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	5.85 ± 0.83	4.18 ± 1.36	11.637	0.000, Sig

Table 18: Distribution of the study group according to mean post intervention at 6 months WOMAC stiffness

Post intervention at 6 months WOMAC Stiffness	Group A	Group B	T value	P value, Sig
Mean ± SD	2.11 ± 0.78	1.53 ± 1.15	4.655	0.000, Sig

Table 19: Distribution of the study group according to mean post intervention at 6 months WOMAC physical function

Post intervention at 6 months WOMAC Physical function	Group A	Group B	T value	P value, Sig
Mean ± SD	25.38 ± 2.95	21.92 ± 3.95	7.808	0.000, Sig

Table 20: Distribution of the study group according to mean post intervention at 6 months VAS pain

Post intervention at 6 months VAS Pain	Group A	Group B	T value	P value, Sig
Mean ± SD	3.06 ± 0.68	3.16 ± 0.75	1.064	0.289, NS

DISCUSSION

Osteoarthritis is a chronic degenerative multifactorial disease of joints and is more common in the society. The disease process of osteoarthritis is characterized by progressive destruction of the articular cartilage leading to joint space narrowing, subchondral sclerosis, subchondral cyst, synovial inflammation and marginal osteophyte formation.[1]

The treatment of OA remains a challenge to the orthopedic surgeon. Non pharmacological interventions include patient education, physical therapy, weight loss and low impact exercises.[4,5] Acetaminophen, Non-steroidal anti-inflammatory drugs (NSAIDs), topical NSAIDs, Glucosamine and/or chondroitin sulfate and intra articular corticosteroids forms the pharmacological treatment. Opioid and non-narcotic analgesics may be prescribed in refractory pain patients. Intra articular Hyaluronans (Has) have recently been used for the treatment of painful knee joints with OA.[6]

The administration of exogenous Hyaluronan (HA) preparations addresses the problem of osteoarthritis by replacing the low viscoelastic synovial fluid with solutions of higher viscosity.[7] The literature available had shown that the exogenously provided HA may also improve the pain and function by non mechanical, biologically based mechanisms within the synovial and articular environment.[11]

Hylan GF-20 is a high-molecular weight Hyaluronic acid derivative composed of two hylan polymers within a buffered physiological NaCl solution. The phenomenon of cross-linking (the first cross linking using formaldehyde and the second cross-linking forming sulfonylbis-ethyl cross-links between the hydroxyl groups of polymer chains) leads to the main characteristic of the product by the formation of a mixture of two different hylan polymers: hylan A (80%), which is a soluble high MW molecule (MW of 6.000.000 Da), hylan B (20%), which is an insoluble gel.[10]

The studies comparing the conservative management and efficacy and safety of intra articular injection of hylan GF – 20 are lacking. Hence, this study was taken up to compare the safety and efficacy of intra articular injection of hylan GF – 20 with the conservative methods of management of osteoarthritis of Knee joint.

The mean age of Group A patients was 54.09 (± 7.81) years and Group B patients was 54.48 (± 7.81) years. Majority of the patients belonged to 41 – 50 years of age group. Males outnumbered females in this study. The mean BMI of group A subjects was 22.5 and group B subjects was 22.4. About 13.7% of the subjects in Group A and Group B had grade 1 osteoarthritis, 71% of the group A and 62.1% of the group B had grade 2 osteoarthritis and 15.3% of the group A and 24.2% had grade 3 osteoarthritis in this study. The preoperative WOMAC pain among the group A patients was 8.02 and group B patients was 7.97. The pain scores decreased to 6.05 at 3 months and 5.85 at the end of 6 months in Group A. In group B, the pain scores decreased to 6.14 at 1 month, 4.16 at 3 months and 3.18 after 3 months of intervention and increased to 4.18 at the end of 6 months. There was a statistically significant difference between WOMAC pain scores of two different types of intervention at various intervals of time. The mean WOMAC stiffness score of the group A patients was 3.02 and group B patients was 2.96 at the baseline. The stiffness score was 2.72 at the end of one week, 2.42 at 1 month, 2.27 at the end of 3 months and 2.11 at the end of 6 months among the conservative management group. Among the patients who received hylanGF20 group, the scores were 2.04 at the end of 1 week, 1.03 at the end of 3 months and 1.53 at the end of 6 months. There was a statistically significant difference between WOMAC stiffness scores of two different types of intervention at various intervals of time. Before intervention, the mean WOMAC physical function score was 34.09 among the patients of conservative management and 33.9 among the patients of hylan GF20 group. The mean WOMAC physical function scores were 31.8 after 1 week, 29.96 at the end of 1 months, 28.18 at the end of 3 months and 25.38 at the end of 6 months. In hylan GF 20 group, the mean physical function was 26.99 at the end of 1 week, 21.96 after 1 month, 19.5 after 3 months and 21.92 after 6 months. There was a statistically significant difference between WOMAC physical function scores of two different types of intervention at various intervals of time. The mean pre intervention VAS pain among the patients of Group A was 4.[14] and group B was 3.82. The VAS scores decreased to 4.01 at the end of 1 week in conservative management group, 3.8 at the end of 1 month, 3.08 at the end of 3 months and 3.06 after 6 months. The VAS scores decreased to 3.48 at the end of 1 week, 3.24 at the end of 1 month, 3.01 at the end of 3 months and 3.16 at the end of 6 months. There was a statistically significant difference between VAS scores of two different types of intervention at various intervals of time.

CONCLUSION

This study was taken up with the aim of comparing the efficacy of Hylan GF 20 with the conservative management. This study had shown that, the mean age of osteoarthritis is above 50 years and males outnumbered females. The study had also demonstrated that there was significant

improvement in the WOMAC pain, stiffness and physical function scores and VAS pain scores. Hence, Hylan GF 20 injection can improve the pain associated with osteoarthritis. However this study is not without limitations as no blinding was done in this study and observational bias can occur in this study. But this study is able to bring out important facts about osteoarthritis and its treatment and importance of hylan GF 20, especially in patients who are unable to undergo major surgery because of medical morbidity like heart disease and in younger patients. Patients with severe pain awaiting surgery or in whom surgery has been deferred due to medical reasons can also benefit from this injection. Further researchers can do same study with blinding method to improve evidence of level of study.

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