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Original Research Article

Study of Treatment of Osteoarthritis of Knee by Intra-Articular Sodium Hyaluronate in South Karnataka Population (Retrospective Study)

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Abstract:

Background: Osteoarthritis is the slow and gradual development of joint pain, swelling, stiffness, and reduced joint movement. Hyaluronic acid is one of the visco supplements and alternative management options for OA.

Method: 30 patients with OA were selected for intra-articular Sodium Hyaluronate, and 30 patients with OA were treated with placebo. Routine blood exam; x-ray of the knee joint (MRI if necessary), Kellgran Lawrence radiographic scale were done to assess the severity of OA. Intraarticular 6 ml Hylan GF20 was injected by using a 23-gauge syringe in 30 OA patients and placebo in the other 30 OA patients.

Results: In the comparison of the VAS scale at week 25 between the Hyalgan and placebo groups, the primary outcome at week 25 was a highly significant p value ($p<0.001$). In comparison to the mean change from baseline to week 25 in the WOMAC Index score, all three parameters, including pain, stiffness, and function of the knee joint were highly significant ($p<0.001$).

Conclusion: Intra-articular therapy with sodium hyaluronate is a safe and easy method for treating OA of the knee joint.

Keywords: Osteoarthritis, Sodium Hyaluronate, Kellgren Lawrence Radiographic Scale, WOMAC Index Score.

Introduction

Osteoarthritis (OA) is a chronic, progressively degenerative disease with the slow and gradual development of fluctuating symptoms like joint pain, swelling, stiffness and reduced joint movements, which eventually lead to disabilities associated with functional and social activities, socio-economic status, emotional well-being, and image [1].

In India, OA is the second most common rheumatological disorder; with a prevalence of 28.7% and globally, it is the eighth leading cause of disability, with knee joints most commonly affected [2].

Physiotherapy, weight loss, ambulatory assistant devices and pharmacological therapies, including non-steroidal anti-inflammatory drugs (NSAID), opioids, muscle relaxants, antidepressants and intra-articular injections of steroids, platelet-rich plasma, and viscosupplements are being used, when these therapies fail and total knee replacement becomes inevitable. But total replacement treatment is costly, and poor and middle-class patients cannot afford such costly techniques [3]. Intra-articular visco-supplements are one of the most effective and safe alternatives for the management of OA. Hyaluronic acid is one such visco-supplement that results in pain relief, reduces the use of NSAIDs, and delays joint replacement surgeries.

Hyaluronic acid is a polysaccharide that forms the primary chemical component of synovial fluid [4]. Hylan GF-20 is FDA-approved and used for OA. Hence, an attempt is made to evaluate the efficacy of Hylan-G20 and compare it with placebo in OA patients.

Materials and Methods

30 patients aged between 40-65 years old, who regularly visited to the Akash Institute of Medical Sciences and Research Centre in Devanahalli, Bangalore-Pin: 562110 were studied.

Inclusion Criteria: Above 40 years and below 65 years of age, osteoarthritis was confirmed by x-rays or MRIs. The patients who gave written consent for treatment were selected for the study.

Exclusion Criteria: Osteoarthritis secondary to trauma, previous knee surgery, Non-cooperatives for treatment were excluded from the study.

Method: A detailed history of every patient was noted and a routine blood exam, including a CBC, RBS, and plain x-ray of AP and lateral view, MRI if necessary was done. The tibial plateau was identified by sliding the thumb upwards and into the joint space, as well as the edge of the patellar ligament. Lateral access point is about 1 finger strip lateral to patellar ligament.

A no-touch technique is used, once the area is cleaned; it was not touched with anything except sterile needles. The site was scrubbed, and 70% isopropyl alcohol was used for the scrub. Local anaesthesia was also used, with a 23-G needle with the knee flexed to 90 degrees to advance the HA syringe parallel to the floor in a postero-medial direction to a depth of about 2 cm. A give-way feel is there when the joint capsule is pierced; 6 ml of Hylan GF 20 was injected. Kellgren Lawrence radiographic grading scale 0–4 was used to assess the severity of osteoarthritis of knee, pain reduction based on VAS.

Technique for intraarticular injection:

1. patient in a sitting position with legs off the side of the table
2. Patient in supine position with knee flexed 20–30 degrees
3. Patient in supine position with knee extended as per the Murphy D, Scores JI **[5]**.

The side effects of the technique were skin rashes, itching, swelling of the face, lips, or tongue, coughing, wheezing or breathlessness, swimming or redness, arthalgia arthrosis, non-specific pain and headache. Patients were advised to take ice packs for such symptoms, which resolved in a week.

The duration of the study was from May 2021 to April 2022.

Statistical analysis: Comparison of Kellgren Lawrence grades and WOMAC Index score were analysed between sodium Hyaluronate and placebo patients. The VAS score was also analysed in those treated with placebo or sodium Hyaluronate. The statistical analysis was carried out in SPSS software. The ratio of males and females was 1:1.

Observation and Results

Table 1: Comparison of disease characteristics in Hyalgan with placebo, t test 0.24 and p>0.80(Insignificant)

Kellgren Lawrence grade –

- Grade-II – (mild) – 16 (± 2) in Hyalgan, 16 (± 2) in placebo group, t test was 0 and p>0.23
- Grade-III – 15 (± 2) in Hyalgan group, 15 (± 3) in placebo, t test was 0.01 and p>0.24
- Pain on 50 foot walking test - 45.35 (± 9.5) in Hyalgan, 43.38 (± 8.2) in placebo group, t test was 0.86 and p>0.804
- WOMAC-A pain – 44.38 (± 1.2) in Hyalgan group, 43.15 (± 12.03) in placebo group, t test was 0.41 and p>0.65
- WOMAC-C Function – 44.12 (± 9.2) in Hyalgan group, 44.28(± 12.1) in placebo group, t test was 0.09 and p>0.92

Table 2: Comparison of VAS pain scale in Hyalgan and placebo group of Osteoarthritis

- Baseline (W0) – 46.84 (± 8.35) in Hyalgan group, 44.12 (± 7.30) in placebo group, t test was 1.34 and p>0.18.
- W25 – 16 (± 13.3) in Hyalgan group, 20.52(± 14.6) in placebo group, t test was 1.82 and p<0.03 (p value is highly significant).
- Change from W0 to W5 – 23.70 (± 11.33) in Hyalgan group, 19.38 (± 13.3) in placebo group, t test was 1.34 and p>0.18.
- Change from W0 to W13 – 26.24 (± 13.8) in Hyalgan group, 23.02 (± 14.2) in placebo group, t test was 0.81 and p>0.812.
- Change from W0 to W25 (primary outcome) – 30.82 (± 13.15) in Hyalgan group, 23.60 (± 15.30) in placebo group, t test was 1.95 and p<0.005 (p value is highly significant.

Table 3: Comparison of Mean change from Base line to week 25 in WOMAC Index in both groups

- Pain (Change W0 to W25) – 28.27 (± 1.80) in Hyalgan group, 20.50 (± 1.82) in placebo group, t test was 16.6 and p<0.001
- Stiffness (Change from W0 to W25) – 23.80 (± 2.16) in Hyalgan group, 21.52 (± 2.18) in placebo group, t test was 4.06 and p<0.002
- Function (Change from W0 to W25) – 25.14 (± 1.60) in Hyalgan group, 18.22 (± 1.63) in placebo group, t test was 16.5 and p<0.001.

Table 1: Comparison of Hyalgan Osteoarthritis (OA) patients with placebo patients

Characteristics	Hyalgan patients (SD± mean)	Placebo	t test	p value
A) BMI	25.3 (± 3.3)	25.6 (±8.2)	0.24	p>0.80
B) Kellgran—Lawrence Grade-II (mild)	16 (± 2)	16 (± 2)	0	p>0.23
Grade-III Moderate	15 (± 2)	15 (± 3)	0.01	p>0.24
Pain on 50 foot walking test	45.35 (± 9.5)	43.38 (± 8.2)	0.86	p>0.804
WOMAC A-pain	44.38(±11.2)	43.15(± 12.03)	0.41	p>0.65
WOMAC –C Function	44.12 (± 9.2)	44.28 (±12.1)	0.09	p>0.92

P<0.001 = p value is significant

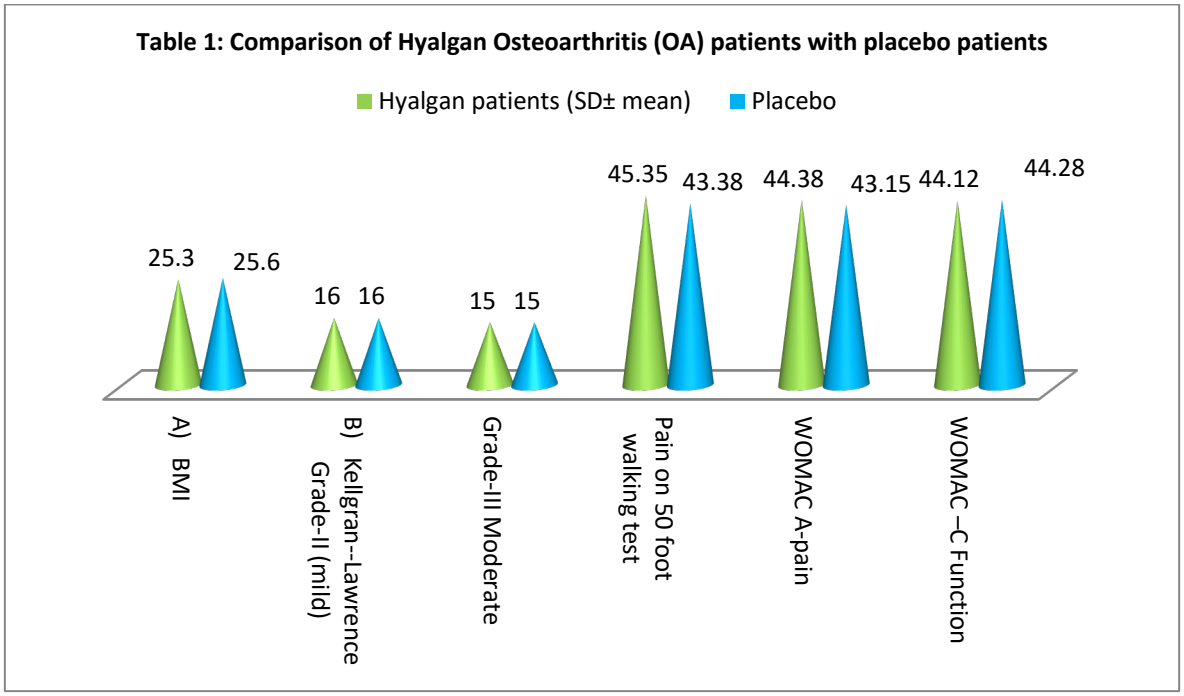

Figure 1: Comparison of Hyalgan Osteoarthritis (OA) patients with placebo patients

Table 2: Comparison of VAS pain scales in placebo and Hyalgan treatment groups on 50 foot walking test

Week (W)	Hyalgan (30)	Placebo (30)	t test	p value
Baseline (W0)	46.84 (± 8.35)	44.12 (± 7.30)	1.34	p>0.18
W 25	16 (± 13.3)	20.52 (± 14.6)	1.82	P<0.03 *
Change from w0 to w1	8.9 (± 10.30)	6.50 (± 8.46)	0.98	p>0.32
Change from W0 to W5	23.70 (± 11.83)	19.38 (± 13.3)	1.34	p>0.18
Change from W0 to W13	26.24 (± 13.8)	23.02 (± 14.2)	0.81	p>0.812
Change from W0 to W25 (primary outcome)	30.82 (± 13.5)	23.60 (± 15.30)	1.95	P<0.005 *

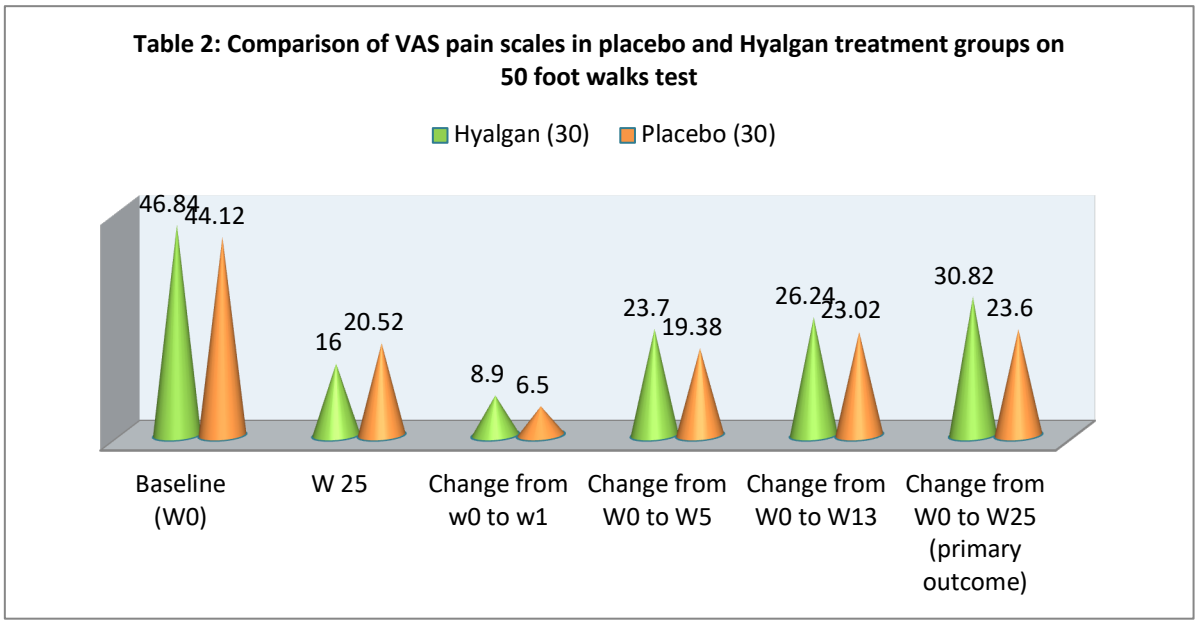

Figure 2: Comparison of VAS pain scales in placebo and Hyalgan treatment groups on 50 foot walks test

Table 3: Comparison of mean change from Base line to week 25 in WOMAC Index score in both groups

WOMAC Index score	Hyalgan Mean (± SD)	Placebo mean (± SD)	t test	p value
Pain change from W0 to W25	28.27 (± 1.80)	20.50 (± 1.82)	16.6	P<0.001`
Stiffness change from W0 to W25	23.80 (± 2.16)	21.52 (± 2.18)	4.06	P<0.002
Function change from W0 to W25	25.14 (± 1.60)	18.22 (± 1.63)	16.5	P<0.001

P<0.001 = p value is highly significant

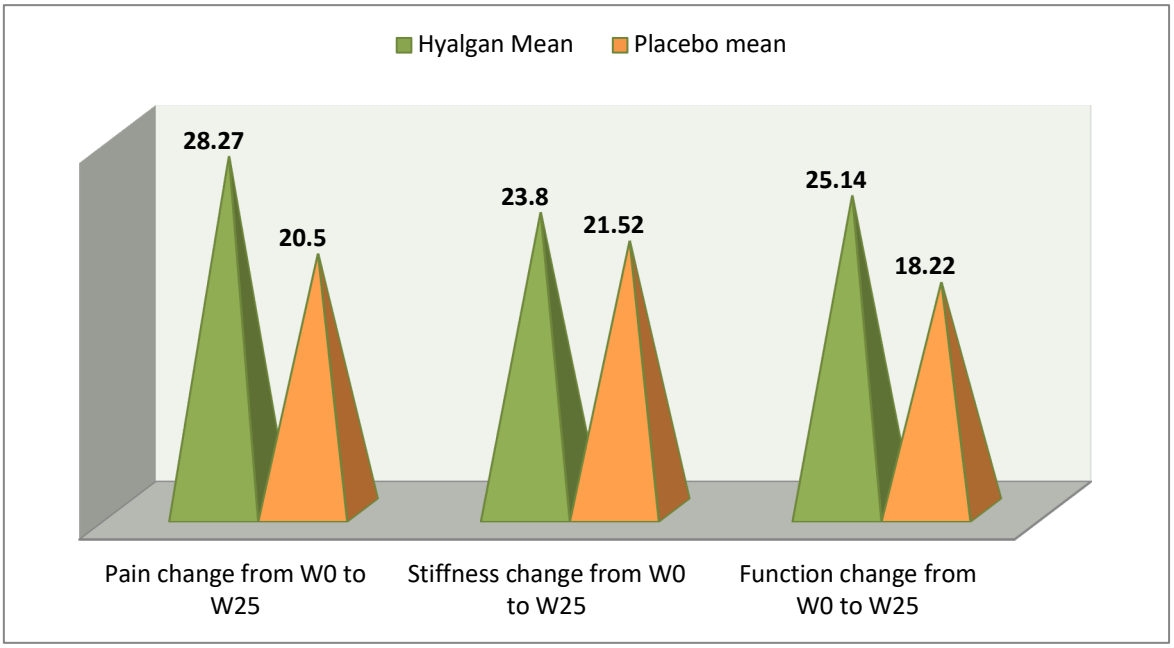

Figure 3:

Discussion

In the study of treatment of osteoarthritis of the knee joint by intra-articular sodium Hyaluronate in the south Karnataka population, in the comparison of characteristics in patients with Hyalgan with placebo, parameters like BMI, Kellgren Lawrence grading, pain on a 50-foot walking test, and WOMAC A pain and WOMAC C function were examined. Functions remain insignificant ($p > 0.80$) (Table 1).

In the comparative study of the VAS pain scale in the Hyalgan and placebo groups, W25 – 16 (± 13.3) in the Hyalgan group and 20.52 (± 14.6) in the placebo group. The t test was 1.82, and the p value was highly significant ($p<0.03$). Change from W0 to W25 (primary outcome): 30.82 (± 13.15) in the Hyalgan group, 23.60 (± 15.3) in the placebo group. The t test was 1.95 and $p<0.005$ (p value highly significant). (Table-2). In comparison of mean change from baseline to week 25 in the WOMAC Index score in both groups pain 28.27 (± 1.80) in the Hyalgan group and 20.50 (± 1.82) in the placebo group, the t test was 16.6 and $p<0.001$ (p value highly significant). Stiffness was 23.80 (±2.16) in the Hyalgan group and 21.52 (± 2.18) in the placebo group; the t test was 4.06 and $p<0.002$ (p value is highly significant). Function: 25.14 (± 1.60) in the Hyalgan group, 18.22 (± 1.63) in the placebo group; t test: 16.5; p value: highly significant ($p<0.001$) (Table 3). These findings are more or less in agreement with previous studies [6,7,8].

Overall treatment of Sodium Hyaluronate compared with placebo (2–3 injections followed by 25 weeks) demonstrated significant improvement in pain and stiffness. It was also reported by previous authors [9,10]. The results were also appreciated in knee pain efficacy for 1 injection; 2-4 injections, ≥ 5 injections of intra-articular have significant results in different patients depending on severity of pain [11].

The pathogenesis of OA is characterised by an imbalance between the synthesis and degradation of the cartilage matrix, resulting in the slow degradation of cartilage, subchondral bone, remodelling, osteophyte formation, and inflammation of the synovium [12]. These changes are influenced by several biochemical factors, including reduced hyaluronic acid content in the synovium, which results in acute as well as chronic pain. The viscoelasticity of hyaluronic acid is a critical regulator of OA pathology. It is reported that intraarticular hyaluronic products with a molecular weight ≥ 300 KDa and those derived from biological fermentation relate to superior efficacy and safety [13]. The low molecular weight (LMW) of hyaluronic acid does not meet the minimum clinical requirement.

Summary and Conclusion

Present study of treatment of OA of knee by intraarticular sodium hyaluronate, its high rate of pain relief and reduction of stiffness allow normalcy in the function of the knee joint. But this study demands that such clinical trials be conducted in a large number of patients with different molecular weights to get permanent relief from OA of the knee joint because the exact pathophysiology of OA is still unclear.

Limitation of study

Owing to the tertiary location of the research centre, the small number of patients, and the lack of

the latest technology, we have limited findings and results.

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