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Original Research Article

Short Term Outcome of Intra-Articular Viscosupplementation with HA In Early Primary Knee OA in North Bengal Population

Vipin Bijlwan[1], Shubham Pandit[2]

[1]Senior Resident, MS Orthopaedics, Department of Orthopaedics, North Bengal Medical College & Hospital, Sushrutnagar, Darjeeling, 734012

[2]Senior Resident, MS Orthopaedics, Department of Orthopaedics, NRS medical college , Sealdah, Raja Bazar, Kolkata, West Bengal 700014

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Corresponding author: Dr. Shubham Pandit

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Abstract

Introduction: OA is an age-related chronic degenerative joint disorder of multifactorial cause. It is mainly characterized by wear and tear of joint articular cartilage, joints marginal hypertrophy of bone, reduction in joint space and subchondral sclerosis.

Aims: To assess how effective HA injections are in reducing pain and improving joint function in patients with early-stage knee OA in the North Bengal population.

Materials and Method: The present study was a Prospective, Observational based study. This Study was conducted for 1 year. Total 50 patients were included in this study.

Result: In our study, 22 (44%) patients were Male and 28 (56%) patients were Female. In our study, 27 (54%) patients were 45-55 years of age, 12 (24%) patients were 55-65years of age, 11 (22%) patients were >65 years of age. In our study, 23 (46%) patients had Left side of knee, 25 (50%) patients had Right side of knee and 2 (4%) patients had bilateral side of knee. In our study, 18 (36%) patients had Grade 1 KL grade, 21 (42%) patients had Grade 2 KL grade, 11 (22%) patients had Grade 3 KL grade.

Conclusion: In conclusion, intra-articular viscosupplementation with hyaluronic acid (HA) in early primary knee osteoarthritis (OA) among the North Bengal population shows promising short-term outcomes. Patients experienced significant improvements in pain relief, joint function, and overall quality of life. These findings suggest that HA injections can be an effective early intervention for managing knee OA, potentially delaying the need for more invasive treatments. However, further studies with long-term follow-up are needed to confirm sustained benefits and broader applicability.

Keywords: Viscosupplementation, Hyaluronic Acid, Knee Osteoarthritis and Pain Management.

Introduction

Age-related chronic degenerative joint disease (OA) has multiple underlying causes. It is primarily distinguished by subchondral sclerosis, joint space decrease, articular cartilage deterioration, and marginal enlargement of bone in the joints. The pathophysiology of osteoarthritis (OA) involves multiple components, including mechanical, metabolic, and genetic factors.

The disease ultimately results in morphological alterations in the synovial membrane and joint capsule. In developing countries like India, where substantial physical activity is required for the livelihood, the increasing burden of the disease leads to increased morbidity and reduced quality of life. Since intra-articular drug administration shows promise for long-term effectiveness, it has been regarded as the ideal treatment technique. [1]

Currently, there are many non-invasive therapeutic modalities that focus on managing pain, enhancing function, and even altering the course of the disease and cartilage degradation. In OA, there is a gradual decrease in the concentration of hyaluronic acid in the joint space leading to degenerative changes in the joint with low-grade inflammation. The overall prevalence of Knee OA in India is 28.7%. It was found that OA knee had female, obese, and elderly age group preponderance. In an epidemiological study done recently, it was found that the prevalence of knee OA in females was 31.6% and was associated with obesity, old age, and sedentary lifestyle. [2]

Treatment options for knee OA are numerous. When the illness process is just getting started, conservative management techniques are taken into

account. Conservative treatments include mainly education, creating awareness, extra-articular functional devices, physiotherapy, weight reduction, exercises, lifestyle modifications, avoiding excessive weight bearing on the knee. In further stages of the disease, along with these non-pharmacological modalities, pharmacological treatment helps in effective control of symptoms. The pharmacological modalities include oral Non-steroidal anti-inflammatory drugs (NSAID's) and Opioid analgesics. Long term use of these drugs not only produces pain reduction but also causes multiple systemic side effects involving the cardiovascular system, gastrointestinal system, and renal system increasing morbidity. [3]

This led to the development of a new approach to the treatment of OA, which is comparatively safer and has fewer complications, i.e., intra-articular (IA) injections. Intra-articular injection of certain substances decreases the progression of the disease and hence delays the need for surgical treatment.[4] Most commonly used IA substances include corticosteroids, platelet-rich plasma (PRP), and hyaluronic acid, with PRP showing better outcomes among all these components.[5] In contrast, others have noted that among the intra-articular injection therapy for knee OA, the evidence was strongly favouring corticosteroids with promising results for HA and PRP.[6] The aim to assess how effective HA injections are in reducing pain and improving joint function in patients with early-stage knee OA in the North Bengal population.

Materials and Methods

Study Area: North Bengal Medical College

Study Design: Prospective observational study.

Study Period: 1 Year

Inclusion Criteria:

- Adults aged 40-65 years.
- Diagnosed with early-stage primary knee OA.
- No prior intra-articular injections within the last 6 months.

Exclusion Criteria:

- Patients with secondary OA (post-traumatic, rheumatoid, etc.).
- Severe OA (Kellgren-Lawrence grade III or IV).
- Significant deformities or prior knee surgeries.
- Systemic diseases affecting joints (e.g., rheumatoid arthritis).
- Recent corticosteroid or NSAID use that may interfere with outcome assessments.

Sample Size: A total of 50 samples have been included in this study.

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages.

Two-sample t-tests, which compare the means of independent or unpaired samples, were used to assess differences between groups. Paired t-tests, which account for the correlation between paired observations, offer greater power than unpaired tests. Chi-square tests (χ^2 tests) were employed to evaluate hypotheses where the sampling distribution of the test statistic follows a chi-squared distribution under the null hypothesis; Pearson's chi-squared test is often referred to simply as the chi-squared test. For comparisons of unpaired proportions, either the chi-square test or Fisher's exact test was used, depending on the context. To perform t-tests, the relevant formulae for test statistics, which either exactly follow or closely approximate a t-distribution under the null hypothesis, were applied, with specific degrees of freedom indicated for each test. P-values were determined from Student's t-distribution tables.

A p-value ≤ 0.05 was considered statistically significant, leading to the rejection of the null hypothesis in favour of the alternative hypothesis.

Result

Table 1: Demographic characteristics of the study patients and the disease

Parameters		Frequency (n = 50)	Percent (%)
Gender	**Male**	22	44
	Female	28	56
Age in years	**(45-55) Years**	27	54
	(55-65) Years	12	24
	>65 Years	11	22
Side Of Knee	**Left**	23	46
	Right	25	50
	Bilateral	2	4
KL Grade	**Grade 1**	18	36
	Grade 2	21	42
	Grade 3	11	22

Table 2: Mean and standard deviation values of SF36 scores for each subscale at baseline (0 weeks) and 8, 24, 52 weeks post-injection

SF-36	0 WEEK (mean ± SD)	8 WEEKS (mean±SD)	24 WEEKS (mean ± SD)	52 WEEKS (mean± SD)
Physical Functioning	27.2 ± 25.27	57.4± 25.27	66.9 ± 26.24	71.8 ± 28.26
Limitation due to physical health	8.5 ± 24.54	59 ± 47.04	74 ± 44.30	80 ± 40.40
Limitation due to an emotional problem	16.66 ± 35.15	66 ± 47.85	76 ± 43.14	80.66 ± 39.32
Energy/Fatigue	44.2 ± 28.43	60.4±21.38	69.8 ± 20.55	74.2 ± 21.83
Emotional well-being	46.64 ± 27.35	63.04±17.97	69.56 ± 18.11	73.68 ± 19.55
Social functioning	32.65 ± 26.27	53.5 ± 22.02	63 ± 23.54	67.75 ± 26.61
Pain	44.8 ± 23.12	66.05±22.13	75.65 ± 21.20	78.2 ± 21.94
General Health	47.6 ± 29.24	67.3 ± 20.40	74.6 ± 20.55	78.2 ± 23.83
Health change	28 ± 26.06	66 ± 20.05	75 ± 22.01	78.9 ± 25.95

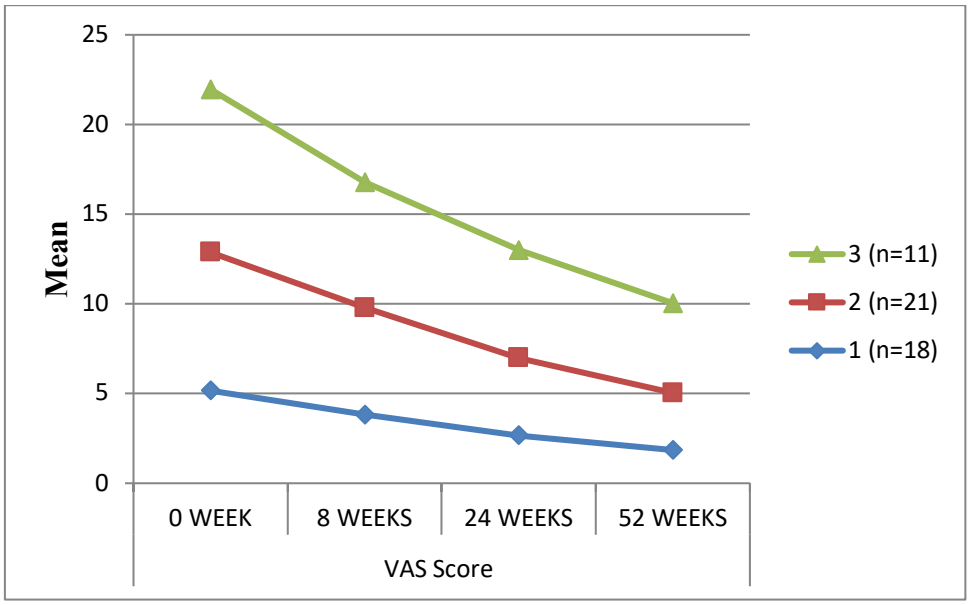

Figure 1: association between KL grade 1, 2, 3, and VAS scores

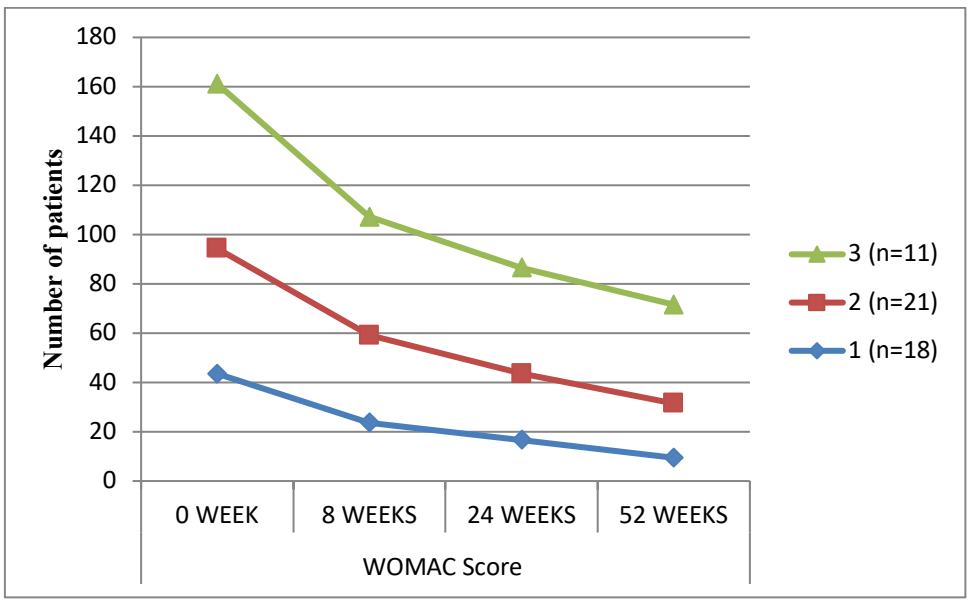

Figure 2: The association between KL grades 1, 2, 3, and total WOMAC scores

In our study, 22 (44%) patients were Male and 28 (56%) patients were Female. In our study, 27 (54%) patients were 45-55 years of age, 12 (24%) patients were 55-65years of age, 11 (22%) patients were >65 years of age. In our study, 23 (46%) patients had Left side of knee, 25 (50%) patients

had Right side of knee and 2 (4%) patients had bilateral side of knee.In our study, 18 (36%) patients had Grade 1 KL grade, 21 (42%) patients had Grade 2 KL grade, 11 (22%) patients had Grade 3 KL grade. In 0 week, the mean Physical Functioning (mean± s.d.) of patients was 27.2 ± 25.27. In 8 weeks, the mean Physical Functioning (mean± s.d.) of patients was 57.4± 25.27. In 24 weeks, the mean Physical Functioning (mean± s.d.) of patients was 66.9 ± 26.24. In 52 weeks, the mean Physical Functioning (mean± s.d.) of patients was 71.8 ± 28.26. In 0 week, the mean Limitation due to physical health (mean± s.d.) of patients was 8.5 ± 24.54. In 8 weeks, the mean Limitation due to physical health (mean± s.d.) of patients was 59 ± 47.04. In 24 weeks, the mean Limitation due to physical health (mean± s.d.) of patients was 74 ± 44.30. In 52 weeks, the mean Limitation due to physical health (mean± s.d.) of patients was 80 ± 40.40. In 0 week, the mean Limitation due to an emotional problem (mean± s.d.) of patients was 16.66 ± 35.15. In 8 weeks, the mean Limitation due to an emotional problem (mean± s.d.) of patients was 66 ± 47.85. In 24 weeks, the mean Limitation due to an emotional problem (mean± s.d.) of patients was 76 ± 43.14. In 52 weeks, the mean Limitation due to an emotional problem (mean± s.d.) of patients was 80.66 ± 39.32. In 0 week, the mean Energy/Fatigue (mean± s.d.) of patients was 44.2 ± 28.43. In 8 weeks, the mean Energy/Fatigue (mean± s.d.) of patients was 60.4±21.38. In 24 weeks, the mean Energy/Fatigue (mean± s.d.) of patients was 69.8 ± 20.55. In 52 weeks, the mean Energy/Fatigue (mean± s.d.) of patients was 74.2 ± 21.83. In 0 week, the mean Emotional well-being (mean± s.d.) of patients was 46.64 ± 27.35. In 8 weeks, the mean Emotional well-being (mean± s.d.) of patients was 63.04±17.97. In 24 weeks, the mean Emotional well-being (mean± s.d.) of patients was 69.56 ± 18.11. In 52 weeks, the mean Emotional well-being (mean± s.d.) of patients was 73.68 ± 19.55. In 0 week, the mean Social functioning (mean± s.d.) of patients was 32.65 ± 26.27. In 8 weeks, the mean Social functioning (mean± s.d.) of patients was 53.5 ± 22.02. In 24 weeks, the mean Social functioning (mean± s.d.) of patients was 63 ± 23.54. In 52 weeks, the mean Social functioning (mean± s.d.) of patients was 67.75 ± 26.61. In 0 week, the mean Social functioning (mean± s.d.) of patients was 44.8 ± 23.12. In 8 weeks, the mean Social functioning (mean± s.d.) of patients was 66.05±22.13. In 24 weeks, the mean Social functioning (mean± s.d.) of patients was 75.65 ± 21.20. In 52 weeks, the mean Social functioning (mean± s.d.) of patients was 78.2 ± 21.94. In 0 week, the mean General Health (mean± s.d.) of patients was 47.6 ± 29.24. In 8 weeks, the mean General Health (mean± s.d.) of patients was 67.3 ± 20.40. In 24 weeks, the mean General Health (mean± s.d.) of patients was 74.6 ± 20.55. In 52 weeks, the mean General Health (mean± s.d.) of patients was 78.2 ± 23.83. In 0 week, the mean Health change (mean± s.d.) of patients was 28 ± 26.06. In 8 weeks, the mean Health change (mean± s.d.) of patients was 66 ± 20.05. In 24 weeks, the mean Health change (mean± s.d.) of patients was 75 ± 22.01. In 52 WEEKS, the mean Health change (mean± s.d.) of patients was 78.9 ± 25.95. In 0 Week, the mean (n=18) KL Grade VAS Score (mean± s.d.) of patients was 5.16 ± 1.15. In 8 Weeks, the mean (n=18) KL Grade VAS Score (mean± s.d.) of patients was 3.83 ± 1.15. In 24 Weeks, the mean (n=18) KL Grade VAS Score (mean± s.d.) of patients was 2.66 ± 1.37. In 52 Weeks, the mean (n=18) KL Grade VAS Score (mean± s.d.) of patients was 1.85 ± 1.52.In 0 Week, the mean (n=21) KL Grade VAS Score (mean± s.d.) of patients was 7.71 ± 1.48. In 8 Weeks, the mean (n=21) KL Grade VAS Score (mean± s.d.) of patients was 5.95 ± 1.39.In 24 Weeks, the mean (n=21) KL Grade VAS Score (mean± s.d.) of patients was 4.33 ± 1.49. In 52 Weeks, the mean (n=21) KL Grade VAS Score (mean± s.d.) of patients was 3.19 ± 1.99.In 0 Week, the mean (n=11) KL Grade VAS Score (mean± s.d.) of patients was 9.09 ± 0.94. In 8 Weeks, the mean (n=11) KL Grade VAS Score (mean± s.d.) of patients was 7 ± 1.59. In 24 Weeks, the mean (n=11) KL Grade VAS Score (mean± s.d.) of patients was 6 ± 1.78. In 52 Weeks, the mean (n=11) KL Grade VAS Score (mean± s.d.) of patients was 5 ± 2.36. Distribution of mean KL grades 1, 2, 3 with VAS scores was statistically significant ($p< 0.01$). In 0 week, the mean (n=18) KL Grade WOMAC scores (mean± s.d.) of patients was 43.55 ± 17.88. In 8 weeks, the mean (n=18) KL Grade WOMAC scores (mean± s.d.) of patients was 23.72 ± 17.24. In 24 weeks, the mean (n=18) KL Grade WOMAC scores (mean± s.d.) of patients was 16.61 ± 16.34. In 52 weeks, the mean (n=18) KL Grade WOMAC scores (mean± s.d.) of patients was 9.44±13.31. In 0 week, the mean (n=21) KL Grade WOMAC scores (mean± s.d.) of patients was 50.81 ± 19.1. In 8 weeks, the mean (n=21) KL Grade WOMAC scores (mean± s.d.) of patients was 35.42 ± 18.15. In 24 weeks, the mean (n=21) KL Grade WOMAC scores (mean± s.d.) of patients was 26.95 ± 18.17. In 52 weeks, the mean (n=21) KL Grade WOMAC scores (mean± s.d.) of patients was 22.04±18.84.In 0 week, the mean (n=11) KL Grade WOMAC scores (mean± s.d.) of patients was 66.81 ± 19.48. In 8 weeks, the mean (n=11) KL Grade WOMAC scores (mean± s.d.) of patients was 48 ± 21.09. In 24 weeks, the mean (n=11) KL Grade WOMAC scores (mean± s.d.) of patients was 43 ± 25.77. In 52 weeks, the mean (n=11) KL Grade WOMAC scores (mean± s.d.) of patients was 40.09±28.81. Distribution of mean KL grades

1, 2, 3 with WOMAC scores was not statistically significant ($p< 0.05$).

Discussion

The primary goal of this study was to determine the effectiveness of a single intra-articular IAHA injection in treating patients with primary early OA knee (KL Grade<3) in terms of pain, physical functionality, and quality of life. We discovered that in individuals with early primary OA knee, a single IAHA injection was useful in lowering pain levels, enhancing functional abilities, and enhancing quality of life.

In our study there is a slightly higher representation of females (56%) compared to males (44%) in the sample. The majority of the population falls within the 45-55 years age group, representing 54% of the sample. The other two age groups, 55-65 years and those above 65 years, have lower representations at 24% and 22%, respectively.

In our study the distribution between left and right knees is nearly equal, with very few bilateral cases, suggesting that knee issues (in this context) typically affect only one knee at a time.

Synovial fluid in the joint space is required for the normal healthy functioning of the joint. The main component of synovial fluid is a polysaccharide chain known as hyaluronic acid, made up of repeating units of N-acetyl glucosamine and glucuronic acid with a molecular weight of 4–10 million Da. Normal joint space contains 2 ml of fluid with 2.5–4 mg/ml of HA concentration. The protective effect of HA is directly attributed to its concentration, molecular weight, and mechanical force exerted on the joint.[7]

There are multiple mechanisms of action of IAHA. Firstly, it allows lubrication and shock absorption, thus causing mechanical viscosupplementation to the joint. Secondly, it increases endogenous hyaluronic acid production and re-establishes joint homeostasis, the effect of which continues long even after the exogenous injection has left the joint space.[8] Further, it is also believed to inhibit the pain receptors, prevent enzymatic cartilage degradation and also act like a free radical scavenger.4 It has been shown to prevent the breakdown of joint matrix by inhibiting the proinflammatory factors (PGE2 and NFkB).[9]

Distribution of mean KL grades 1, 2, 3 with VAS scores was statistically significant ($p< 0.01$).

There are different products of HA used for intra-articular injections. The extent of benefit obtained from each product is different, because of the different molecular weights of HA. There are no proven studies for this, and hence it is controversial. In the index study, we had used single use agent (10 mL of Synvisc-One® containing 6 mL of Hylan G-F 20) for all cases. Hylan G-F 20 is an HA preparation consisting of hylan A, a 6000 kDa HA, and hylan B, a cross-linked derivative of natural HA.[10] This cross linking of the formulation is intended to improve the long-term efficacy of the preparation by resisting its degradation inside the knee joint.[9]

Distribution of mean KL grades 1, 2, 3 with WOMAC scores was not statistically significant ($p< 0.05$).

The effectiveness of this therapeutic approach for osteoarthritis (OA) knee in comparison to more widely used pharmaceutical treatments like NSAIDs has been the subject of numerous studies conducted worldwide.[11] Numerous meta-analytic studies have shown that intra-articular HA injections can effectively reduce pain and enhance quality of life.[12] On the other hand, limited research has demonstrated that using HA to treat osteoarthritis in the knee has a "small and clinically irrelevant benefit" and raises the possibility of major adverse events.[13] While earlier research on viscosupplementation in the treatment of osteoarthritis has yielded contradictory outcomes, more current data seems to support this therapy approach.

HA does not cause rapid effects, rather its clinical effect on pain and functional improvement shows a carryover effect which extends for a long time after initial administration. In Indian patients, a multicentric phase-4 study - OASIS (Osteoarthritis Synvisc-One® Indian Post-Marketing Study) was undertaken. The study concluded that at one-year, single dose of 6 ml Hylan GF 20 was safe and effective in treatment of symptomatic OA. The present study concurs with the findings of OASIS and noted statistically significant improvements SF-36, WOMAC and VAS scores.[14]

There are two types of Hylan G-F 20 formulations available in the market: a single-shot (wherein a higher volume (6 ml) is administered – Synvisc-One®) and the once weekly x 3 approach (wherein a lower volume (2 ml) is administered across multiple injections - Synvisc®3 × 2). A previous RCT reported that patients receiving more than one dose of Hylan GF-20 are likely to experience increased frequency of local adverse reactions.[15] A recent systematic review and meta-analysis was conducted to analyse the long-term (one year) efficacy and safety of single or 1–3 weekly injections of Hylan G-F 20. It was observed that there was no difference in level of efficacy based on injection schedule, nor between randomized and non-randomized studies. The meta-analysis revealed that there was statistically significant improvement in WOMAC (pain, physical function and stiffness), VAS, SF-36 scores (both mental and physical component summary). Furthermore, the

drug is well tolerated with low rates of adverse events. Since many clinical trials have demonstrated a differing response in the effectiveness of intra-articular HA in the treatment of OA, the level of recommendations afforded to HA by different international and national societies varies.[16] Despite the use of non-steroidal anti-inflammatory drugs (NSAIDs), in patients with OA knee who remain symptomatic, The European Society for Clinical and Economic Aspects of Osteoporosis and OA (ESCEO) treatment algorithm recommends intra-articular hyaluronic acid (HA) for pharmacological management. Similarly, The European League Against Rheumatism (EULAR) guidelines recommend Intra-articular HA based upon level 1B evidence for both joint functional improvement and pain reduction.[17]

Both the American College of Rheumatology (ACR) guidelines and ESCEO algorithm recommend IA HA, especially in patients whose symptoms persist even after prior treatments.

Conclusion

In conclusion, intra-articular viscosupplementation with hyaluronic acid (HA) in early primary knee osteoarthritis (OA) among the North Bengal population shows promising short-term outcomes. Patients experienced significant improvements in pain relief, joint function, and overall quality of life. These findings suggest that HA injections can be an effective early intervention for managing knee OA, potentially delaying the need for more invasive treatments. However, further studies with long-term follow-up are needed to confirm sustained benefits and broader applicability.

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