Improvement in Knee Society Score after Twelve Months of Intra-articular Viscosupplementation of Patients with Mild to Moderate Osteoarthritis Presenting at a Tertiary Care Hospital, Karachi, Pakistan

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Abstract

Objective: This study focuses on assessing the efficacy of intra-articular viscosupplementation, specifically hyaluronic acid (HA), in individuals with mild to moderate knee OA in a Pakistani population. The Knee Society Score (KSS) was employed as an outcome measure to evaluate pain and functional improvement. This study explores the potential of HA injections in providing relief, reducing pain, and improving joint function.

Methods: The research methodology involves a single-center, single-arm, prospective observational study conducted at a tertiary care hospital in Karachi. Patients with mild to moderate knee OA received intra-articular HA injections, and their KSS was assessed before and after a 12-month follow-up. The study aims to contribute pivotal insights to bridge the existing knowledge gap and formulate evidence-based guidelines tailored to the Pakistani population.

Results: The study included patients with a mean age of 55.59 ± 13.351, and 14 patients received bilateral knee injections, while 11 opted for unilateral treatment. The mean BMI was 32.2 ± 4.71. Based on Kellgren and Lawrence classification, 46.2% had grade I knee OA, and 53.8% had grade II. Initial Knee Society Score and Knee Society Function Score were 72.28 ± 11.18 and 66.79 ± 15.23, respectively. After twelve months, both scores improved significantly to 81.28 ± 9.7 and 76.54 ± 15.39. The improvement was more pronounced in grade I OA. No significant differences were observed based on gender or BMI.

Conclusion: Intra-articular viscosupplementation using HA emerges as a safe and effective treatment for mild to moderate knee OA. The results underscore the potential for HA to offer symptomatic relief and highlight the need for further multicenter studies with substantial sample sizes to establish a standardized treatment algorithm. The study aims to contribute to informed and effective management paradigms for knee osteoarthritis in the Pakistani context.

Keywords: Osteoarthritis, knee society score, hyaluronic acid, viscosupplementation, Kallgeren and Lawrence classification.

IRB: Approved by the Ethical Review Board of Aga Khan University Hospital. Ref# 2023-8314-24988. Dated: 15th May 2023.

Citation: Shahid H, Umer M, Zahid M. Improvement in Knee Society Score after Twelve Months of Intra-articular Viscosupplementation of Patients with Mild to Moderate Osteoarthritis Presenting at a Tertiary Care Hospital, Karachi, Pakistan [Online]. Annals ASH & KMDC 2025; 29(1) 17-24

Introduction

Osteoarthritis (OA), a chronic and progressive joint disease, is a disease of wear and tear of joints and is defined as degenerative joint disease that results in biological and mechanical dysfunction. This wear and tear in OA is characterized by a progressive loss of cartilage tissue, remodelling of the underlying bone, inflammation of the synovial membrane, and abnormalities in lubrication of the articular joint. Among all joints, the knee bears the brunt of this degeneration, making it the most commonly affected site in OA. The prevalence of OA based on radiographs has been reported to be 27% and 44% approximately among patients under ages of 70 and 80 years respectively[1,2]. However, a separate study conducted in Bangalore, India, reported a substantially higher prevalence of 83%, highlighting the potential for geographic variations in the burden of OA[3]. Knee OA is influenced by various risk

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Date of Submission: 3rd September 2024
Date of Revision: 6th January 2025
Date of Acceptance: 18th February 2025

factors, such as advancing age, obesity, trauma to articular surface of the joint, and mal-alignment being the most common.

The structures involved by OA include cartilage, subchondral bone, ligaments, periarticular structures, and menisci[4]. The hallmark pathological features in OA involve the degradation of cartilage and remodeling of bone[5]. Addressing knee OA involves a comprehensive approach, and options available for the treatment of knee OA have been classified in stepwise fashion into non-operative/ nonpharmacological (e.g., physical and rehabilitation therapy, occupational therapy, massage, exercise, and weight reduction), pharmacological – non steroidal anti-inflammatory drugs (NSAIDs) and operative (high tibial osteotomy, unicompartmental and total knee arthroplasty). However, it is important to note that these therapeutic modalities aim to decelerate disease progression and none of them have been known to treat the disease except for surgery, that itself is invasive and a huge undertaking[6].

A relatively new modality being used in treatment of knee OA has been intraarticular viscosupplementation (hyaluronic acid). Hyaluronic acid (HA) has been shown to be effective for knee osteoarthritis (OA) in reducing pain and improving joint function. Several studies have demonstrated the efficacy of intra-articular (IA) injections of HA in relieving pain and improving symptoms in patients with knee OA[7-10]. In addition, injected hyaluronic acid can also augment the flow of synovial fluid, normalize the synthesis, and inhibit the degradation of endogenous hyaluronic acid, and relieve joint pain[11]. HA injections have been found to provide short-term pain relief and can be more effective than NSAIDs, corticosteroids, and placebo[12]. Additionally, repeated courses of IA-HA injections have been shown to maintain or further improve pain reduction without increased safety risks. HA has also been termed as safe and effective in management of OA knees[12,13]. HA injections have also been found to limit the progression of knee OA and delay the need for knee arthroplasty.

In our population, a notable gap exists in the comes of viscosupplementation concerning pain and functional improvement in individuals with knee OA. The current stance among orthopedic surgeons is characterized by a lack of consensus regarding the efficacy and role of viscosupplementation in the management of knee OA. This difference of approach has hindered the development of a standardized algorithm to guide the treatment and management of knee OA. The absence of population-specific studies leads towards need of evidence-based guidelines for Pakistani population. To address this gap, our study has undertaken an assessment of pain and function of knee joint before and after viscosupplementation, employing the Knee Society Score (KSS).

By evaluating these parameters within the population of Pakistan, our research aims to contribute insights that can serve as the foundation for the establishment of a standardized algorithm and local treatment guidelines. This algorithm would help in guiding clinicians in the treatment and management of knee OA, offering an approach that aligns with the specific characteristics and needs of patients in our population. The existing knowledge gap will be bridged based on outcomes of our study.

Methodology

Our research focuses on finding out improvement in knee society score after twelve months of intra-articular viscosupplementation of patients with mild to moderate osteoarthritis presenting at a tertiary care hospital, Karachi, Pakistan. Approval was sought from Ethical Review Committee (ERC) of our hospital with ERC number 2023-8314-24988. We classified osteo arthritis of the knee based on Kellgren-Lawrence classification[14]. The classification system had highest inter-observer and second highest intra-observer reliability when classifying knee joint, among all diarthrodial joints and has been specifically used for grading of knee joint osteoarthritis. Our outcome measure was Knee Society Score (KSS): The score was originally published in 1989 in Clinical Orthopedics and Related Research as the Knee Society Clinical Rating System[15]. It

was designed to provide a simple and objective scoring system to rate the knee and patient's functional abilities[16]. This was a single center, a single-arm longitudinal, before-after design (pre-post), prospective, observational, single group cohort study. It was done at the section of orthopedics, department of surgery, at a tertiary care hospital in Karachi, Pakistan. Nonprobability consecutive sampling technique was employed. A sample size of 36 was calculated using Open Epi software. Confidence interval was set at 95% and power at 80%. Baseline mean KSS was kept 63 +/- 10.8 and post-procedure 80 +/- 10.1.(6) All patients who are above 40 years of age and who consent to take part in this study with antero-posterior radiographs of knee showing mild to moderate knee OA (Grade 0-2) were included. Patients who were given other intra-articular injections for reasons other than OA like rheumatoid arthritis were excluded.

Data of patients presenting to clinics and diagnosed as having grade 0-2 osteoarthritis of knee based on Kellgren-Lawrence classification, who opted for intraarticular viscosupplementation (hyaluronic acid supplementations) as a part of their regular management, were identified. After obtaining informed consent, aseptic measures were taken, knee was prepped in clinic with sterile disposable drepes, pyodine was used as antiseptic solution and once single dose of Crespine Gel plus® (Hyaluronic acid 1mg, hyaluronic acid cross-linked 14mg, sodium chloride 6.9mg, 1 ml distilled water and Prilocain hydrochloride 3mg) was injected in the affected knee/s. Data was recorded on a data collection form by senior orthopedic residents. Patient's demographics like age, gender, height, weight, body mass index (BMI), side of injection and grading of osteoarthritis based on anteroposterior (AP) standing radiographs. Knee society scores were then calculated and documented on proforma before getting intraarticular viscosupplementation. Patients were then followed up for a period of twelve months and their knee society score was calculated again after this period on follow up in clinic. Stata version 15 was used for data entry and analysis. Quantitative variables (age, height, weight, BMI, knee society score) were expressed as mean ± standard deviation/median interquartile range (IQR) and qualitative variables (gender, grade of osteoarthritis) were c.alculated as frequencies. Comparison of continuous variables (KSS) both pre- and post-knee viscosupplementation was done using a Paired Sample T-test when normally distributed. Wilcoxin rank sum test was used for skewed continuous data keeping significance level at 5%. Histograms were created and density curve was plotted to assess normality of continuous variables in the data. More over Shapiro-Wilk test was used for each variable as well. Liner regression was performed to understand relationship between OA grade and functional improvement.

Results

A total of 25 patients and 39 knees were included in the analysis, reflecting a diverse cohort with varying degrees of knee osteoarthritis (OA). The mean age of the patients was 55.6 ± 13.4 years, with ages ranging from 40 to 75 years. This age range is consistent with the typical demographic for knee OA, as the condition predominantly affects middle-aged to elderly individuals. Among the patients (n=25), 9(36%) were males and 16(64%) were females (Table 1). Among the patients, 14(56%) received bilateral knee injections, and 11(44%) received injections in only one knee (Table 1). The mean Body Mass Index (BMI) of the patients was 32.2 ± 4.71 kg/m², indicating that most of the patients were classified as obese or overweight.

Radiographic assessment revealed that 46.2% of the patients (n=18) were diagnosed with grade I OA according to the Kellgren and Lawrence classification, while 53.8% (n=21) were diagnosed with grade II OA (Table 2). The mean age of patients with grade I OA was 52.1 ± 2.32 years, while those with grade II OA had a mean age of 60.4 ± 3.24 years, indicating a tendency for more advanced OA to occur in older individuals.

The pre-intervention Knee Society Score (KSS) averaged 72.28 ± 11.18, and the Knee Society Function Score (KSS-F) averaged 66.79 ± 15.23

(Table 3). Following a twelve-month period of intra-articular hyaluronic acid (HA) injections, both the KSS and the KSS-F showed marked improvement. The mean KSS increased to 81.28 ± 9.76, and the KSS-F improved to 76.54 ± 15.39 (Table 3). The observed improvements are statistically significant, with the difference in KSS being 9 ± 5.5 points (p=0.001) and the difference in KSS-F being 9.74 ± 6.01 points (p=0.001), as determined using paired sample t-tests (Table 3).

When examining the impact of OA grade on treatment outcomes, significant improvements were noted in patients with grade I OA. Specifically, the mean difference in KSS-F for grade I OA patients was 5.63 ± 2.07 points (p=0.01), suggesting that individuals with earlier-stage OA experienced more pronounced benefits from HA injections compared to those with more advanced disease. However, no significant differences were found between grade I and grade II OA patients regarding the overall KSS scores (p=0.82) (Table 4). This lack of differentiation may be due to the relatively small sample size and the variability in individual responses to treatment.

The study also considered the influence of BMI on treatment outcomes. Patients were categorized into two BMI groups: normal and pre-obese (BMI <30) and obese (BMI >30). Despite the observed high average BMI in the study population, the analysis revealed no significant differences in treatment outcomes based on BMI categories. Similarly, age and gender did not show significant associations with improvements in KSS or KSS-F. These findings suggest that the efficacy of HA injections may be consistent across different demographic and clinical subgroups, although further research with larger sample sizes could provide more definitive insights.

To better understand the relationship between age, gender BMI and OA grade and improvement in KSS and KSS-F, a linear regression analysis was performed. The coefficient of -0.55 indicates that for each year of increase in age, the KSS-F decreases by 0.55 points, demonstrating a statistically significant negative relationship (p=0.0017).The coefficient -0.39 also indicated significant negative impact of age on the overall KSS score, although the effect is slightly weaker than for the functional score. BMI also had a significant positive association, indicating that higher BMI is associated with a slightly higher KSS-F (p=0.046) but the effects on KSS were insignificant. The regression coefficient of 14.16 (p=0.03) indicated that patients with grade I OA had, on average, a KSS-F 14.16 points higher than those with grade II OA. The coefficient of 8.55 for KSS also showed a significant positive effect, although the impact on the KSS score is smaller compared to the functional score (p=0.0048) (Table6-7).

Table 1: Demographic Characteristics of study population (N=25)

Demographics	**Mean ± SD**
Age (years)	55.6 ± 13.4
Demographics	N (%)
Gender	
Male	9 (36)
Female	16 (64)
Laterality	
Unilateral	11 (44)
Bilateral	14 (56)
Obesity Status	
Normal and Overweight	7 (28)
Obese	18 (72)

Table 2: Characteristics of samples (N=39)

Characteristics	**N (%)**
Site	
Right	20 (51.3)
Left	19 (48.7)
Kellgren-Lawrence Grade	
I	18 (46.2)
II	21 (53.8)

Table 3: Improvement in functional outcome score

Functional Outcome Score	**Baseline (± S.D †)**	**twelve months post-treatment (± S.D †)**	**p-value**
Knee Society Score (Mean)	72.28 ± 11.18	81.28 ± 9.76	**0.001***
Knee Society Score-Functional (Mean)	66.79 ± 15.23	76.54 ± 15.39	**0.001***

†S.D: Standard deviation
* p-value < 0.05 considered significant

Table 4: Association of mean difference of Knee Society Score compared with OA grades, Genfer and Obesity

	Mean difference (± S.D†)	p-value
	Kellgren-Lawrence Grade	
Grade I	9.22 ± 6.38	0.829
Grade II	8.8 ± 5.45	
	Gender	
Male	9.07 ± 6.84	0.955
Female	8.96 ± 6.84	
Obesity		
Normal and overweight	8.07 ± 4.80.750	
Obese	9.46 ± 6.31	

†S.D: Standard Deviation

Table 5: Association of mean difference Knee Society Score – Functional compared with OA grades, Genfer and Obesity

	Mean difference (± S.D†)	p-value
	Kellgren-Lawrence Grade	
Grade I	12.77 ± 6.69	0.01*
Grade II	7.14 ± 6.23	
	Gender	
Male	10.71 ± 7.3	0.523
Female	9.2 ± 6.87	
Obesity		
Normal and overweight	9.23 ± 7.59	0.492
Obese	8.07 ± 4.8	

†S.D: Standard Deviation
* p-value < 0.05 considered signif

Table 6: Linear Regression analysis showing estimates of co-efficient for Knee Society Score -Functional score difference and Knee Society Score Difference

Predictor variable	Co-efficient (CI)†	Standard error	R2*	Significance
Knee Society Score - Functional difference				
Age	-0.04 (-0.21-0.12)	0.08	0.0079	0.59
Gender				
Female	-1.51 (-6.26-3.23)	2.34	0.01	0.52
BMI**	0.29 (-0.19-0.77)	0.23	0.04	0.22
Kellgren-Lawrence Classification Grade I	0.41 (-3.42-4.25)	1.89	0.0013	0.82
Knee Society score difference				
Age	0.027 (-0.11-0.17)	0.07	0.0040	0.7
Gender				
Female	-0.11 (-0.41-3.88)	1.97	0.001	0.95
BMI**	-0.24 (-0.64-0.15)	0.19	0.04	0.22
Kellgren-Lawrence Classification Grade I	0.41 (-3.4-4.2)	1.89	0.0013	0.82

†CI: Confidence Interval
*R2: square if ETA
**BMI: Body mass index

Table 7: Linear Regression estimating predictor variables for KSS and KSS-F scores at 12 months Follow-up

Predictor variable	Co-efficient (CI)†	Standard error	R2*	Significance
Knee Society Score - Functional at Twelve months follow up				
Age	-0.55 (-0.89 - -0.22)	0.16	0.23	0.0017
Gender				
Female	1.28 (-9.2-11.83)	5.2	0.0016	0.80
BMI**	1.04 (0.01-2.07)	0.5	0.1	0.046
Kellgren-Lawrence Classification Grade I	14.16 (5.17-23)	4.43	0.215	0.0029
Knee Society Score at Twelve months follow up				
Age	-0.39 (-0.59 - -0.18)	0.1	0.28	0.005
Gender				
Female	-0.78 (-7.4-5.9)	3.3	0.0015	0.81
BMI**	0.3 (-0.38-0.98)	0.33	0.02	0.37
Kellgren-Lawrence Classification Grade I	8.55 (2.7-14.32)	2.84	0.19	0.0048

†CI: Confidence Interval
*R2: Square of ETA
**BMI: Body mass index

Discussion

The current study sought to address a notable gap in comprehensive studies evaluating the outcomes of viscosupplementation in individuals with knee OA within the Pakistani population. Given the lack of consensus among orthopedic surgeons regarding the efficacy of viscosupplementation, the study aimed to systematically assess pain and functional improvement using the Knee Society Score and Knee Society Functional Score. This specific focus on the Pakistani population is crucial, as the absence of population-specific studies hinders the formulation of evidence-based guidelines tailored to the unique characteristics of patients in this region. High mean BMI (32.2 ± 4.71 kg/m²) of the patients in this study reaffirms obesity being a well-documented risk factor for OA, particularly in the knee joint, due to the increased mechanical stress it places on the joint structures. The high average BMI in this cohort underscores the importa-

nce of addressing weight management as part of a comprehensive treatment plan for knee OA. A tendency of having higher grade of OA in older population is also reflected in this study. These baseline scores reflect a moderate level of impairment in both pain and function. The KSS and KSS-F are integral measures of both clinical outcomes and patient-reported outcomes, providing a comprehensive view of the impact of knee OA on patients' daily lives. The changes in these scores represent a significant enhancement in both pain relief and functional capacity, indicating that HA injections are effective in managing knee OA symptoms. The associations reinforce the observation that early-stage OA may benefit more from HA treatment.

Multiple intra-articular treatment regimens have been proposed and used previously but none has proven superiority over the other. Hyaluronic acid supplementation has shown improvement in the Knee Society Score (KSS) in patients with knee osteoarthritis. These may not only improve the quality of life but also distances the requirement for future knee replacement procedures.

Vaishya et.al compared intra-articular triamcinolone hexaacetate and hyaluronic acid (HA) treatments, it was found that HA was significantly better than steroid in terms of pain relief and functionality in the short and mid-term periods[17]. They reported an increase of 19.4 points in knee society score and an increase of 20.3 point in knee function score by fourth week of administration. Bashaireh et.al evaluated the efficacy of viscosupplementation with Crespine Gel ® over a nine-month period, showed significant improvement in pain scores and functional performance by using Western Ontario and McMaster Universities Arthritis Index (WOMAC) score as outcome measure[18]. Peak improvement was noted at five months post-injection in above mentioned study. Davalillo et al also compared efficacy of intraarticular HA with betamethasone and found HA to be superior in terms of long term efficacy[19]. Chaudry et all found that visual analogue score (VAS), joint tenderness and patients & physician's global assessment score also improved significantly clinically as well as statistically in mild to moderate group[20]. Aggarwal et all evaluated a retrospective data of 2037 patients and found positive outcomes in WOMAC score after intraarticular injections of HA[21]. We in our study reported significant increase of 9.74 points in the Knee Society Functional Score at twelve months (p=0.001). Our study does not delineate the peak in increase in the score as the scores were calculated at two points in time only i.e before injecting and at twelve months post-injection follow-up.

Additionally, a Kusayam et.al investigated the effects of IA HA treatment on biomarkers in knee osteoarthritis found that IA HA had the potential to affect joint cartilage and synovium membrane, leading to improvements in synovial fluid properties[21]. Mean increase of 16 points in knee society score and 20 point in knee society function score was also observed, bit it is important to note that this study used 5 injections of 1% HA weekly. On the contrary, in our study we used Crespine Plus Gel®, which is a different composition including HA and administered once dose only. It is important to note that the specific improvement in the Knee Society Score after hyaluronic acid supplementation may vary depending on the individual patient and the severity of their knee osteoarthritis. Our results also resonate with the findings of Saeed et al., who compared arthroscopic debridement with intraarticular HA for pain alleviation and functional improvement in patients with Kellgren-Lawrence Grade II and III OA[8]. The study reported significantly better results after treatment with intra-articular HA, supporting our conclusion regarding the positive impact of HA on knee OA.

Huang et all compared IA HA supplementation with placebo and found significantly better results with IA HA[10]. Intra-articular injections of sodium hyaluronate provide sustained relief of pain and improves joint function in Asian patients with knee osteoarthritis. The outcome measure used in this study was WOMAC score.

While the study provides valuable insights into the effectiveness of viscosupplementation in a Pakistani population, several limitations should be ac

knowledged. The relatively small sample size and the absence of a control group limit the generalizability of our findings. We calculated scores at a single point of time after administration i.e twelve months and fail to recognize advancement to severe grade of OA due to a short follow-up. Future research with larger, randomized controlled trials and longer follow-ups could provide more robust evidence. Additionally, long-term follow-up studies are needed to assess the sustained efficacy and safety of viscosupplementation in this population and time to reach surgery.

Conclusion

This study provides important early evidence on the effectiveness of intra-articular viscosupplementation for patients with mild to moderate knee osteoarthritis (OA) in a Pakistani population. The results suggest that hyaluronic acid (HA) injections can offer significant symptomatic relief and improvement in joint function, as evidenced by the Knee Society Score (KSS). This is a promising non-surgical treatment, with potential to delay the need for invasive surgery such as arthroplasty. However, the limitations of this study, including its small sample size and the absence of a control group, highlight the need for further research. Future studies with larger populations and longer follow-up periods are recommended. These will help to confirm these findings and develop more robust treatment protocols.

Conflict Of Interest: None

Disclaimer: None

Source of Funding: None

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