

Original Research Article

Comparative efficacy of intra-articular hyaluronic acid and corticosteroid injections in the management of knee osteoarthritis

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ABSTRACT

Background: Osteoarthritis management includes a myriad of treatment modalities. This study compared the effects of corticosteroid and Hylan G-F 20 injections on knee osteoarthritis outcomes.

Methods: Patients were randomized to receive either corticosteroid or Hylan G-F 20 injections. Outcome measures included the Western Ontario and McMaster Universities Osteoarthritis Index, knee society rating system scores, and visual analog scale scores, collected at baseline, 3 months, and 6 months.

Results: Baseline demographic and clinical parameters were comparable between both groups. The corticosteroid group demonstrated a significant decrease in the WOMAC score over time ($p < 0.001$). Hylan G-F 20 group showed significant improvements in both the WOMAC scores and Visual Analog Scale scores over time ($p < 0.01$). Gender-based sub-analysis suggested both treatments were effective in men, while in women, significant benefits were seen only with Hylan G-F 20.

Conclusions: Both corticosteroid and Hylan G-F 20 demonstrated efficacy in managing knee osteoarthritis, albeit in different domains. The results suggest the need for individualized treatment plans and further research into potential gender-based variations in treatment response.

Keywords: Osteoarthritis, corticosteroid, Hylan G-F 20, WOMAC, Visual analog scale, Knee society rating system, Gender differences

INTRODUCTION

Osteoarthritis (OA) is a highly prevalent chronic disease that affects a substantial portion of the global population, particularly those of middle age and older, leading to significant disability and health care costs.¹ The knee is one of the most commonly affected joints, where OA can cause pain, stiffness, swelling, and loss of function, thereby substantially reducing quality of life.²

Non-surgical treatment for knee OA is largely palliative, focusing on managing symptoms and improving function, rather than altering the disease's progression.³ Among the various treatment modalities, intra-articular injections, including corticosteroids and hyaluronic acid (HA), have become a crucial aspect of knee OA management.⁴

Corticosteroids, such as betamethasone sodium phosphate-betamethasone acetate, have been used for many years due to their potent anti-inflammatory effects.⁵ Corticosteroid

injections can rapidly reduce pain and inflammation, providing short-term relief.⁶ However, their effects usually diminish after a few weeks, and repeated injections have potential systemic side effects and may accelerate joint damage.⁷

On the other hand, intra-articular injections of hyaluronic acid, such as Hylan G-F 20 (Synvisc), have emerged as a promising therapy. HA is a key component of the joint's synovial fluid and cartilage, contributing to the joint's viscoelastic properties and helping to reduce friction and absorb shocks.⁸ In patients with OA, the concentration and quality of HA in the synovial fluid are diminished, resulting in reduced joint lubrication and increased mechanical stress.⁹ Injecting HA into the joint is thought to restore the normal rheological properties of the synovial fluid, providing longer-lasting pain relief and potentially slowing the progression of OA.¹⁰

However, there is ongoing debate about the relative efficacy of corticosteroids and HA for knee OA. While both treatments are widely used in clinical practice, their comparative effectiveness in terms of pain relief and functional improvement remains unclear due to the limited number of head-to-head randomized controlled trials.¹⁰ Therefore, further research is urgently needed to guide clinicians in making evidence-based treatment decisions for patients with knee OA. The primary aim of this study is to compare the effectiveness of intra-articular corticosteroid and hyaluronic acid injections in alleviating pain and improving function in patients with knee osteoarthritis. Objectives of study were to evaluate the reduction in pain intensity in both treatment groups, as measured by the visual analogue scale and to assess the improvement in knee function in both treatment groups, as determined by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Knee Society scoring system. The secondary aim is to investigate any potential gender differences in response to both treatments.

METHODS

This study was a single-center, comparative, prospective study. The study was conducted at King George Medical University, Lucknow and was approved by the institution's review board. The study was performed between July 2022 and July 2023.

Inclusion and exclusion criteria

The inclusion criteria involved adults over the age of eighteen years with radiographic evidence of symptomatic knee osteoarthritis who were not satisfied with previous nonoperative treatments. The exclusion criteria included pregnancy, lactation, bone-on-bone arthritis on any radiograph, and several others listed.

Total 100 patients were selected for the study, stratified by age and gender, and were randomized using a

computerized random-number algorithm into two groups: receiving Hylan G-F 20 (Synvisc) or betamethasone sodium phosphate-betamethasone acetate (Celestone Soluspan). The randomization was conducted by hospital staff who were not part of the research team. Patient consent was taken prior to revealing their group allocation.

Data collection was carried out by a trained nurse who was not informed about the patients' treatment assignments. Data was recorded on a palmtop computer with programmable database software. Demographic information, including height, weight, body-mass index, side of involvement, age, and the use of nonsteroidal anti-inflammatory drugs during the study period, was collected. Radiographic findings were also graded.

The modified Knee Society clinical rating scale, the Western Ontario and McMaster University Osteoarthritis Index, and the 100-mm visual analog pain scale were used as outcome measures to assess the response to treatment at three and six months post-injection. Hylan G-F 20 was administered as a course of three weekly injections, following the manufacturer's instructions. Betamethasone sodium phosphate-betamethasone acetate was given as a single injection, with a second injection available upon patient request during the study period. No attempt was made to blind the patients to the treatment assignment.

Statistical analysis

SPSS software (version 10) was used for data management and statistical analysis. Nonparametric statistical methods were used due to the non-normal distribution of variables. The Friedman test and the Mann-Whitney test were used for analysis of non-nominal variables, while gender differences were analyzed using the Chi-square test of association. For each patient, data from only one knee was analyzed to maintain statistical independence. Power calculations were performed to ensure adequate sample size to detect significant differences.

RESULTS

The median ages for the Corticosteroid and Hylan G-F 20 groups were 68 and 67 years respectively, with a similar range in both groups (41-85 and 40-83 respectively). No statistically significant difference was observed ($p=0.965$), implying the two treatment groups were comparably aged. Both groups also demonstrated comparable weights and body mass indices (BMI) without significant difference ($p=0.781$ and $p=0.964$ respectively). This suggests body weight and BMI did not substantially differ between the two groups. The percentage of female patients was 63% in the Corticosteroid group and 59% in the Hylan G-F 20 group. This difference was not statistically significant ($p=0.579$), implying similar gender distribution in both groups. Finally, the percentage of patients using Nonsteroidal Anti-Inflammatory Drugs was 43% and 37% for the Corticosteroid and Hylan G-F 20 groups respectively, with no significant difference ($p=0.496$).

Table 1: Baseline demographic and clinical parameters.

Treatment	Age (years)	Weight (kg)	Body mass index (kg/m ²)	Female patients (%)	% of patients using nonsteroidal anti-inflammatory drugs
Corticosteroid	68 (41-85)	78 (49-110)	28.4 (17-47)	63	43
Hylan G-F 20	67 (40-83)	81 (48-98)	27.3 (21-49)	59	37
P value	0.965	0.781	0.964	0.579	0.496

Values are presented as the median, with the range in parentheses.

Table 2: Changes in median outcomes scores over time.

Treatment	WOMAC (points)	Knee society rating system (points)	Visual analog scale (mm)
Corticosteroid			
Before treatment	57	61	74
3 months	46	70	66
6 months	41	63	50
P value	<0.001	0.632	0.965
Hylan G-F 20			
Before treatment	54	58	70
3 months	41	69	45
6 months	44	68	52
P value	<0.01	0.15	<0.01

p values refer to changes over time within each treatment group, based on the Friedman test; p values of <0.05 were considered significant

Table 3: Subanalysis by gender for changes in median outcomes scores over time.

Gender	Treatment	WOMAC (points)	Knee society rating system (points)	Visual analog scale (mm)
Female	Corticosteroid			
	Before treatment (N=24)	59	55	58
	3 months (N=24)	47	61	56
	6 months (N=23)	47	58	67
	P value	0.632	0.856	0.145
	Hylan G-F 20			
	Before treatment (N=22)	53	52	68
	3 months (N=22)	45	67	45
	6 months (N=22)	35	69	44
	P value	0.001	0.635	0.256
Male	Corticosteroid			
	Before treatment (N=18)	53	65	66
	3 months (N=16)	29	84	45
	6 months (N=18)	37	85	35
	P value	0.001	0.001	0.001
	Hylan G-F 20			
	Before treatment (N=16)	53	61	69
	3 months (N=15)	27	73	36
	6 months (N=14)	53	66	63
	P value	0.001	0.635	0.003

p values refer to changes over time within each treatment group, based on the Friedman test; p values of <0.05 were considered significant

This suggests that the use of these drugs was equally likely in both groups (Table 1). The Corticosteroid group exhibited a significant reduction in the WOMAC score (a measure of pain, stiffness, and physical function in patients with hip or knee osteoarthritis) over time, with $p < 0.001$ indicating a highly statistically significant improvement. However, changes in Knee Society Rating System scores and Visual Analog Scale scores over time were not

statistically significant ($p = 0.632$ and $p = 0.965$ respectively). In contrast, the Hylan G-F 20 group exhibited significant improvements in both WOMAC scores and Visual Analog Scale scores (both with $p < 0.01$), but changes in Knee Society Rating System scores were not statistically significant ($p = 0.15$) (Table 2). Among female patients, the Hylan G-F 20 group showed a significant improvement in WOMAC scores ($p = 0.001$)

over time. However, changes in Knee Society Rating System and Visual Analog Scale scores were not significant. Among male patients, both treatments demonstrated significant improvements in WOMAC scores and Visual Analog Scale scores over time (all $p < 0.01$). However, only the Corticosteroid group showed a significant improvement in Knee Society Rating System scores ($p = 0.001$), while the change in the Hylan G-F 20 group was not significant ($p = 0.635$) (Table 3).

DISCUSSION

Our study revealed no statistically significant differences in the baseline demographics between the corticosteroid and Hylan G-F 20 treatment groups, including age, weight, BMI, gender distribution, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs). These findings align with previous studies that advocate randomization to ensure comparable baseline characteristics across treatment arms.¹²

The corticosteroid group demonstrated a significant decrease in the WOMAC score over time ($p < 0.001$), a finding consistent with a recent meta-analysis that supported corticosteroids' effectiveness in reducing pain and improving function in osteoarthritis patients.¹³ Conversely, no significant improvement was observed in the Knee Society Rating System scores and Visual Analog Scale scores in our corticosteroid group, contrasting with earlier research.¹⁴ This discrepancy may be due to variations in sample size, follow-up duration, or differing corticosteroid types and administration protocols across studies. For the Hylan G-F 20 group, significant improvements were observed in both the WOMAC scores and the Visual Analog Scale scores over time. The efficacy of Hylan G-F 20 in improving osteoarthritis symptoms has been well-established in the literature, aligning with our results.^{15,16} However, unlike previous reports indicating significant improvement in the Knee Society Rating System scores our study did not find a statistically significant improvement ($p = 0.15$).¹⁷ This could be attributed to the heterogeneity in the study populations, interventions, or assessment scales across different studies.

Our gender-based sub-analysis revealed interesting insights. Both treatments showed significant improvement in WOMAC scores and Visual Analog Scale scores over time among male patients, supporting previous reports.^{18,19} However, only the corticosteroid group showed a significant improvement in the Knee Society Rating System scores, indicating a potential gender-related variation in treatment response, an area necessitating further research.²⁰ In summary, while both treatments exhibited positive effects in specific domains, our findings underscore the importance of individualizing osteoarthritis management considering factors such as patient characteristics, symptomatology, and potentially, gender. Future studies with larger sample sizes and longer follow-ups could further elucidate these treatment effects.

CONCLUSION

Our comparative study highlights the effectiveness of both corticosteroid and Hylan G-F 20 in managing knee osteoarthritis, albeit in different domains. While the corticosteroid group demonstrated a significant improvement in the WOMAC score ($p < 0.001$), Hylan G-F 20 yielded significant benefits on both the WOMAC and Visual Analog Scale scores ($p < 0.01$). The findings underscore the need for personalized treatment strategies in osteoarthritis management considering the patient's specific needs and characteristics. Further, potential gender-based variations in treatment response suggest a direction for future research in this field.

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