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COMPARATIVE EFFECTIVENESS OF HYALURONIC ACID VS STEROID INJECTION AMONG OBESE PATIENTS WITH KNEE GRADE III OSTEOARTHRITIS

Original Research

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ABSTRACT

Background: Knee osteoarthritis (OA) is a progressive degenerative joint disorder and a major contributor to chronic pain, reduced mobility, and impaired quality of life, particularly among older adults and individuals with obesity. Non-surgical management strategies frequently include intra-articular injections to alleviate symptoms and improve functional capacity. Hyaluronic acid (HA) and corticosteroid injections are commonly used therapeutic options; however, their comparative effectiveness, especially when combined with structured exercise programs, remains an area of ongoing clinical investigation in patients with advanced disease.

Objective: To compare the effectiveness of intra-articular hyaluronic acid injections combined with exercise versus corticosteroid injections combined with exercise in reducing pain and improving functional outcomes among patients with Grade III knee osteoarthritis.

Methods: A randomized controlled trial was conducted involving 16 patients diagnosed with Grade III knee osteoarthritis and a body mass index of ≥30 kg/m². Participants were randomly allocated into two equal groups. Group A received intra-articular hyaluronic acid injections (20 mg/2 mL) along with an exercise program, while Group B received intra-articular corticosteroid injections consisting of triamcinolone acetonide (40 mg) combined with lidocaine, alongside the same exercise regimen. Pain intensity was assessed using the Numeric Rating Scale (NRS), and functional status was evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Assessments were performed at baseline, the second week, the sixth week, and the third month following intervention. Statistical analysis was conducted using repeated measures ANOVA and independent sample t-tests with a significance level set at $p < 0.05$.

Results: Participants in the hyaluronic acid group demonstrated a marked reduction in pain scores, with mean NRS values decreasing from 9.12±0.83 at baseline to 7.25±0.46 at two weeks, 5.00±1.19 at six weeks, and 2.37±0.51 at three months ($p<0.001$). In comparison, the corticosteroid group showed a decrease from 9.00±0.75 at baseline to 8.25±0.70, 7.12±0.83, and 6.00±0.75 across the same follow-up intervals ($p<0.001$). Functional outcomes also improved substantially in the hyaluronic acid group, with WOMAC scores declining from 83.62±6.54 at baseline to 72.37±5.39, 47.75±5.72, and 29.37±6.80 at subsequent evaluations ($p<0.001$). The corticosteroid group exhibited comparatively smaller improvements, with WOMAC scores decreasing from 83.75±4.62 to 80.12±5.54, 73.75±5.06, and 69.87±5.79 ($p<0.001$). Between-group analysis revealed significantly greater reductions in both NRS and WOMAC scores in the hyaluronic acid group at all follow-up time points after baseline ($p<0.01$).

Conclusion: Intra-articular hyaluronic acid injections combined with exercise demonstrated superior effectiveness in reducing pain and improving functional outcomes compared with corticosteroid injections combined with exercise among patients with Grade III knee osteoarthritis. These findings support the potential role of hyaluronic acid as a more beneficial conservative treatment option for sustained symptom management in this patient population.

Keywords: Exercise therapy; Hyaluronic acid; Injections, intra-articular; Osteoarthritis, knee; Pain measurement; Rehabilitation; Triamcinolone.

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INTRODUCTION

Knee osteoarthritis (KOA) is one of the most prevalent degenerative joint disorders and a leading contributor to chronic pain, disability, and reduced mobility worldwide. The global burden of KOA is expected to rise substantially, with projections suggesting an increase of nearly 74.9% in cases by 2050, highlighting the urgent need for effective and sustainable management strategies (1). Pathologically, KOA is characterized by progressive degeneration of articular cartilage, remodeling of subchondral bone, osteophyte formation, and varying degrees of synovial inflammation, all of which collectively contribute to pain, stiffness, and functional limitations (2). The condition is strongly associated with advancing age, obesity, genetic predisposition, and previous joint trauma, particularly injuries involving the anterior cruciate ligament and menisci (1,3,16). Beyond its clinical implications, KOA also imposes a substantial socioeconomic burden due to rising healthcare expenditures, productivity loss, and long-term disability (4). The pathogenesis of knee osteoarthritis is complex and multifactorial, involving the interplay of mechanical stress, inflammatory pathways, metabolic disturbances, and genetic susceptibility. Synovial inflammation triggered by damage-associated molecular patterns (DAMPs) contributes to cartilage degradation and joint degeneration (5,11). Metabolic alterations associated with obesity further exacerbate disease progression by promoting inflammatory mediators and disrupting normal chondrocyte function (6,12). Genetic factors, including polymorphisms such as those related to the angiotensin-converting enzyme (ACE), may also influence disease susceptibility and progression (7,13). In addition, emerging biomarkers, such as the monocyte-to-HDL ratio (MHR), have been explored as potential tools for early identification of osteoarthritis before radiographic changes become evident (8-11). Despite advances in understanding disease mechanisms, there remains a lack of disease-modifying treatments capable of halting or reversing osteoarthritic changes, emphasizing the importance of early detection and targeted therapeutic interventions (12-14,15-17).

Among the different stages of knee osteoarthritis, Grade III disease represents a clinically significant phase marked by substantial cartilage loss, joint space narrowing, osteophyte formation, and subchondral bone remodeling. Patients at this stage frequently experience persistent pain, joint stiffness, and notable limitations in mobility and daily functioning (18–24). These symptoms are often compounded by inflammatory processes within the synovium, further accelerating joint deterioration and negatively impacting quality of life. Obesity has been consistently identified as a major aggravating factor in the progression of KOA. Excess body weight increases mechanical loading on the knee joint while simultaneously promoting systemic inflammatory responses that accelerate cartilage degradation and synovitis (25). Patients with moderate to severe obesity, particularly those with a body mass index of ≥35 kg/m², often experience greater pain intensity, higher levels of functional impairment, and reduced physical activity compared with non-obese individuals (26). Consequently, obese patients with advanced osteoarthritis represent a challenging subgroup in which effective non-surgical treatment strategies are particularly important. Management of knee osteoarthritis typically involves a stepwise approach that includes non-pharmacological interventions such as patient education, lifestyle modification, exercise therapy, and weight management, followed by pharmacological treatments and surgical options in advanced cases (1,2). Total knee replacement remains the definitive treatment for end-stage disease; however, concerns regarding surgical costs, accessibility, and potential overutilization have prompted increasing interest in minimally invasive therapies that may delay or reduce the need for surgery (6). In this context, intra-articular injections have emerged as an important component of conservative management. Several biologic and pharmacologic injectables—including platelet-rich plasma (PRP), stromal vascular fraction (SVF), hyaluronic acid (HA), corticosteroids, and collagen preparations—have been investigated for their potential to alleviate symptoms and improve joint function (27–33). Among these therapies, PRP and SVF have demonstrated promising outcomes in terms of pain reduction and functional improvement; however, these modalities may not be readily accessible or cost-effective in many clinical settings (27–33).

Hyaluronic acid and corticosteroid injections remain among the most widely used intra-articular treatments in routine clinical practice. Hyaluronic acid acts as a viscosupplement, restoring synovial fluid viscoelasticity, improving lubrication within the joint, and potentially exerting anti-inflammatory and chondroprotective effects. Corticosteroid injections, in contrast, primarily reduce synovial inflammation and provide relatively rapid pain relief through potent anti-inflammatory mechanisms. While both treatment options are commonly employed for symptomatic management of osteoarthritis, their comparative effectiveness—particularly among obese patients with moderate to severe disease—remains an area of ongoing debate. Obesity-related inflammatory pathways and increased mechanical loading may influence treatment responsiveness, yet limited evidence specifically addresses how these two commonly used therapies perform in this high-risk population. Given the rising prevalence of obesity and its strong association with accelerated osteoarthritis progression, identifying effective non-surgical interventions for obese individuals with advanced knee osteoarthritis is of significant clinical importance. Comparative evaluation of commonly used intra-articular therapies may provide valuable insights into optimizing treatment strategies, improving pain control, and enhancing functional outcomes in this vulnerable patient group. Therefore, the present study aims to compare the effectiveness of intra-articular hyaluronic acid and corticosteroid injections in obese patients with Grade III knee osteoarthritis, focusing on their impact on pain relief and functional improvement in order to support evidence-based non-surgical management approaches.

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METHODS

This randomized controlled trial was conducted over a period of six months following ethical approval from the Ethical Review Board of Superior University, Lahore. The study was also registered in the U.S. Clinical Trials Registry prior to participant recruitment to ensure transparency and adherence to international clinical research standards. All procedures were performed in accordance with ethical principles for research involving human participants. Written informed consent was obtained from each participant after providing a detailed explanation of the study objectives, procedures, potential benefits, and risks. Participants were assured of confidentiality and their right to withdraw from the study at any stage without any impact on their clinical care. The sample size was determined using Epi Tool statistical software. The calculation was based on previously reported mean values ($mean_1 = 3.1$, $mean_2 = 4.8$) and variance of 1.33, with a confidence level of 95%, statistical power of 80%, and a two-tailed analysis. Based on these parameters, a total of sixteen participants were required, with eight individuals allocated to each group. Eligible participants were recruited through simple random sampling and were equally assigned to two intervention groups using random allocation procedures to minimize selection bias.

Participants included men and women aged between 40 and 70 years who had been clinically and radiographically diagnosed with Grade III knee osteoarthritis and had a body mass index (BMI) of ≥30 kg/m², indicating obesity. In addition, participants were required to have a history of chronic knee pain for at least six months prior to enrollment. Individuals were excluded if they had undergone previous knee surgery, had inflammatory arthritis, active local or systemic infections, neuromuscular disorders affecting lower limb function, or had received systemic corticosteroid therapy. Pregnant women were also excluded from the study to avoid any potential procedural risks. Following enrollment and baseline assessment, participants were allocated into two groups. One group received an intra-articular injection of hyaluronic acid (20 mg in 2 mL), while the other group received a corticosteroid injection consisting of 40 mg triamcinolone acetonide (1 mL) combined with 1 mL of 1% lidocaine to reduce injection-related discomfort. All injections were administered intra-articularly under strict aseptic conditions by a trained clinician using standard anatomical landmark techniques to ensure procedural consistency and patient safety.

Outcome measures were assessed using validated clinical instruments to evaluate pain and functional status. Pain intensity was measured using the Numeric Rating Scale (NRS), an 11-point self-reported scale ranging from 0 (no pain) to 10 (worst imaginable pain). Functional outcomes were evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), a widely validated questionnaire specifically developed for osteoarthritis assessment. The WOMAC index consists of 24 items divided into three subdomains: pain (5 items), stiffness (2 items), and physical function (17 items). Higher scores indicated greater symptom severity and functional limitation. Clinical assessments were performed at baseline prior to the intervention and subsequently at follow-up intervals of 2 weeks, 6 weeks, and 3 months after the injection. These time points were selected to evaluate both short-term and intermediate-term treatment effects on pain reduction and functional improvement. Data collected during these assessments were recorded systematically using standardized forms to ensure consistency across all participants.

Statistical analysis was conducted using IBM Statistical Package for the Social Sciences (SPSS) version 29. Descriptive statistics were calculated to summarize participant characteristics and outcome measures. Within-group comparisons were performed to evaluate changes in pain and functional scores across different time points, while between-group comparisons were conducted to determine differences in treatment effectiveness between hyaluronic acid and corticosteroid injections. Appropriate statistical tests were applied based on data distribution, and a p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of sixteen participants diagnosed with Grade III knee osteoarthritis and obesity completed the study and were equally distributed between the two intervention groups. The mean age of participants receiving hyaluronic acid injections combined with exercise was 56.25±5.17 years, whereas the mean age of those receiving corticosteroid injections combined with exercise was 60.25±9.72 years. Gender distribution showed that the hyaluronic acid group consisted of 2 males (25.0%) and 6 females (75.0%), while the corticosteroid group included 3 males (37.5%) and 5 females (62.5%). Body mass index distribution demonstrated that in the hyaluronic acid group, 2 participants (25.0%) had obesity class I (BMI 30–34.9 kg/m²), 5 participants (62.5%) had obesity class II (BMI 35–39.9 kg/m²), and 1 participant (12.5%) had obesity class III (BMI ≥40 kg/m²). In the corticosteroid group, 4 participants (50.0%) were classified as obesity class I and 4 participants (50.0%) as obesity class II, while no participant fell within the obesity class III category.

Within-group analysis of pain intensity measured through the Numeric Rating Scale (NRS) demonstrated a progressive reduction in pain scores across all follow-up intervals in both treatment groups. In the hyaluronic acid group, the baseline mean NRS score was 9.12±0.83, which declined to 7.25±0.46 at the second week, 5.00±1.19 at the sixth week, and further decreased to 2.37±0.51 at the third-month follow-up. Repeated-measures analysis revealed a statistically significant change in pain scores over time ($F=125.30$, partial $\eta^2=0.947$, $p<0.001$). Similarly, participants receiving corticosteroid injections demonstrated a reduction in pain scores over the follow-up period. The mean baseline NRS score was 9.00±0.75, which decreased to 8.25±0.70 at the second week, 7.12±0.83 at the sixth week,

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and 6.00±0.75 at the third-month assessment. Repeated-measures analysis also demonstrated a statistically significant change in pain scores across time points ($F=99.58$, partial $\eta^2=0.934$, $p<0.001$).

Functional status assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) showed a similar pattern of improvement within both groups over time. In the hyaluronic acid group, the baseline WOMAC score was 83.62±6.54, which decreased to 72.37±5.39 at the second week, 47.75±5.72 at the sixth week, and 29.37±6.80 at the third-month follow-up. Statistical analysis confirmed a significant reduction in WOMAC scores over time ($F=112.92$, partial $\eta^2=0.942$, $p<0.001$). In the corticosteroid group, the baseline WOMAC score was 83.75±4.62, which decreased slightly to 80.12±5.54 at the second week, followed by further reductions to 73.75±5.06 at the sixth week and 69.87±5.79 at the third-month evaluation. Repeated-measures analysis indicated a statistically significant change in WOMAC scores over time ($F=37.25$, partial $\eta^2=0.842$, $p<0.001$).

Between-group comparisons demonstrated comparable baseline pain levels between the two groups, with mean NRS scores of 9.12±0.83 in the hyaluronic acid group and 9.00±0.75 in the corticosteroid group (mean difference=0.12, $p=0.75$), indicating no statistically significant difference at baseline. At the second week, the mean NRS score was significantly lower in the hyaluronic acid group (7.25±0.46) compared with the corticosteroid group (8.25±0.70), with a mean difference of −1.00 ($t=-3.34$, $p=0.005$). This difference further increased at the sixth week, where mean scores were 5.00±1.19 and 7.12±0.83 respectively (mean difference=−2.12, $t=-4.12$, $p=0.001$). At the third-month follow-up, the hyaluronic acid group showed substantially lower pain scores (2.37±0.51) compared with the corticosteroid group (6.00±0.75), with a mean difference of −3.62 ($t=-11.19$, $p<0.001$). Baseline functional status assessed through WOMAC scores was also comparable between groups. The mean baseline WOMAC score was 83.62±6.54 in the hyaluronic acid group and 83.75±4.62 in the corticosteroid group (mean difference=−0.12, $p=0.965$). At the second week, the hyaluronic acid group demonstrated a significantly lower WOMAC score (72.37±5.39) compared with the corticosteroid group (80.12±5.54), with a mean difference of −7.75 ($t=-2.83$, $p=0.013$). This difference became more pronounced at the sixth week, where the mean WOMAC score was 47.75±5.72 in the hyaluronic acid group compared with 73.75±5.06 in the corticosteroid group (mean difference=−26.00, $t=-9.62$, $p<0.001$). At the third-month follow-up, the mean WOMAC score further decreased to 29.37±6.80 in the hyaluronic acid group, while it remained higher at 69.87±5.79 in the corticosteroid group (mean difference=−40.50, $t=-12.82$, $p<0.001$). Overall, numerical analysis demonstrated progressive reductions in pain intensity and functional limitations in both groups across the follow-up period, with greater reductions observed in participants receiving hyaluronic acid injections combined with exercise.

Table 4.1: Mean age of patients in group A and B

Variable	Groups	Mean	Std. Deviation
Age	Group A (Hyaluronic acid injections + Exercise)	56.25	5.17
	Group B (Steroid injections + Exercise)	60.25	9.72

Table 4.2: Gender distribution of patients in Groups A and B

Variable			**Groups**	
			Group A (Hyaluronic acid injections + Exercise)	**Group B (Steroid injections + Exercise)**
Gender	**Male**	**N**	2	3
		%	25.0%	37.5%
	Female	**N**	6	5
		%	75.0%	62.5%

Table 4.3: BMI of patients in Groups A and B

Variable			**Groups**	
			Group A (Hyaluronic acid injections + Exercise)	**Group B (Steroid injections + Exercise)**
BMI	**30-34.9 obesity class I**	**N**	2	4
		%	25.0%	50.0%
	35-39.9	**N**	5	4

	obesity class II	**%**	62.5%	50.0%
	Above 40	**N**	1	0
	obesity class III	**%**	12.5%	0.0%

Table 4.4: Comparison at 4-time points of observations of outcome variables within the group A

Variables	**Mean**	**Std. Deviation**	**F**	**Partial Eta Squared**	**p-value**
Baseline NRS score	9.12	.83	125.30	.947	.000
Second week NRS score	7.25	.46			
Sixth week NRS score	5.00	1.19			
Third month NRS score	2.37	.51			
Baseline WOMAC score	83.62	6.54	112.92	.942	.000
Second week WOMAC score	72.37	5.39			
Sixth week WOMAC score	47.75	5.72			
Third month WOMAC score	29.37	6.80			

Table 4.5: Comparison at 4-time points of observations of outcome variables within Group B

Variables	**Mean**	**Std. Deviation**	**F**	**Partial Eta Squared**	**p-value**
Baseline NRS score	9.00	.75	99.58	.934	.000
Second week NRS score	8.25	.70			
Sixth week NRS score	7.12	.83			
Third month NRS score	6.00	.75			
Baseline WOMAC score	83.75	4.62	37.25	.842	.000
Second week WOMAC score	80.12	5.54			
Sixth week WOMAC score	73.75	5.06			
Third month WOMAC score	69.87	5.79			

Table 4.6: Comparison of NRS at 4-timepoints of observations between the groups

Variable	**Groups**	**Mean**	**Std. Deviation**	**Mean difference**	**T value**	**p-value**
Baseline NRS score	Group A	9.12	.83	.12	.31	.75
	Group B	9.00	.75			
Second week NRS score	Group A	7.25	.46	-1.00	-3.34	.005
	Group B	8.25	.70			
Sixth week NRS score	Group A	5.00	1.19	-2.12	-4.12	.001
	Group B	7.12	.83			
Third month NRS score	Group A	2.37	.51	-3.62	-11.19	.000
	Group B	6.00	.75			

Table 4.7: Comparison of WOMAC at 4-timepoints of observations between the groups

Variable	Groups	Mean	Std. Deviation	Mean difference	T value	p-value
Baseline WOMAC score	**Group A**	83.62	6.54	-.12	-.04	.965
	Group B	83.75	4.62			
Second week WOMAC score	**Group A**	72.37	5.39	-7.75	-2.83	.013
	Group B	80.12	5.54			
Sixth week WOMAC score	**Group A**	47.75	5.72	-26.00	-9.62	.000
	Group B	73.75	5.06			
Third month WOMAC score	**Group A**	29.37	6.80	-40.50	-12.82	.000
	Group B	69.87	5.79			

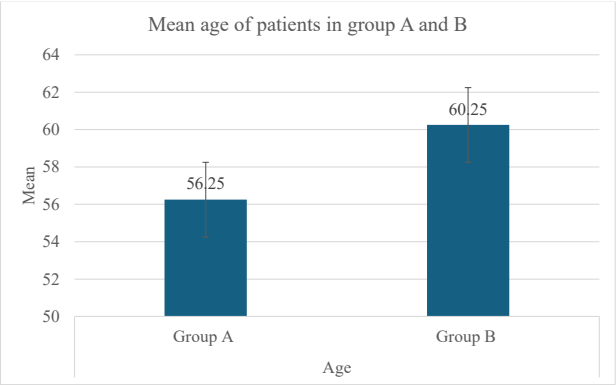

Figure: Mean age of patients in groups

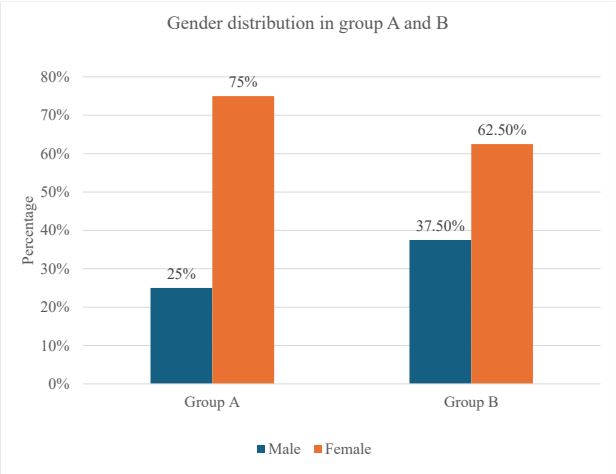

Figure: Gender distribution of patients in groups

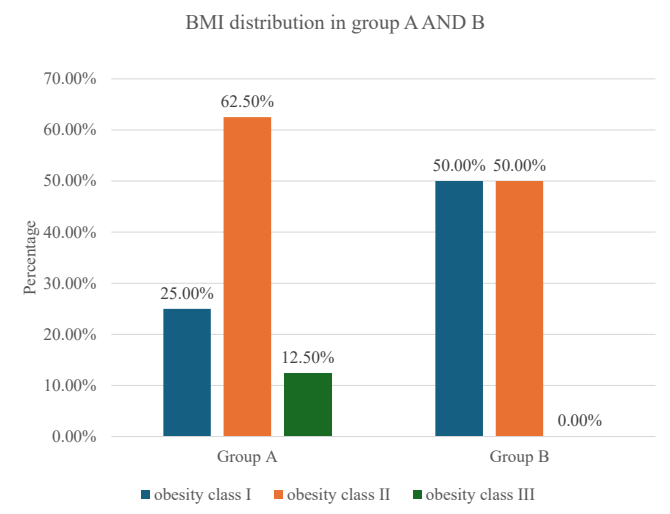

Figure: BMI distribution of patients in groups

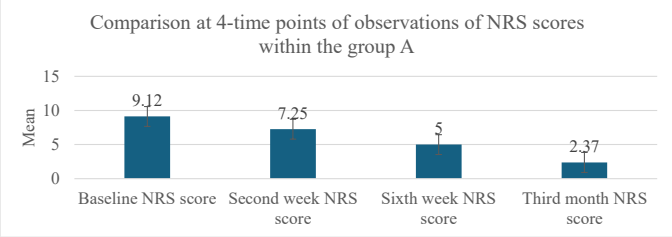

Figure: Comparison of NRS scores within the group A

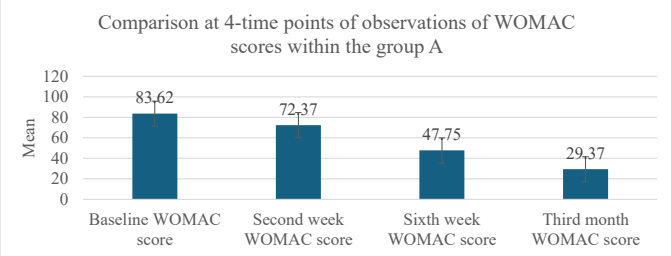

Figure: Comparison of WOMAC scores within the group A

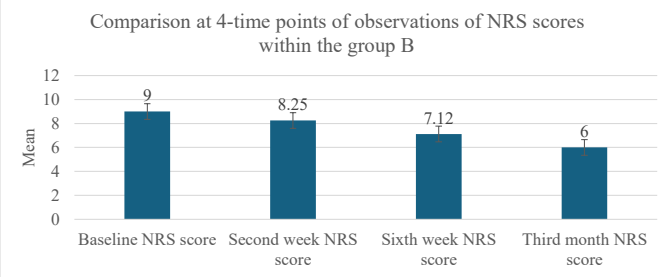

Figure: Comparison of NRS scores within the group B

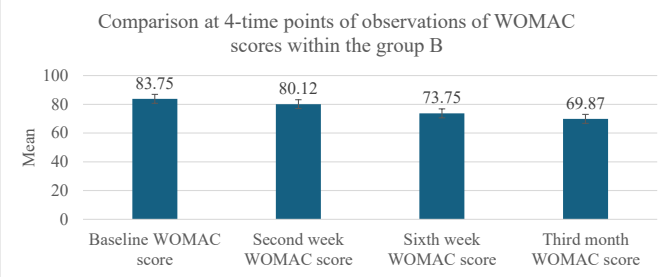

Figure: Comparison of WOMAC scores within the group B

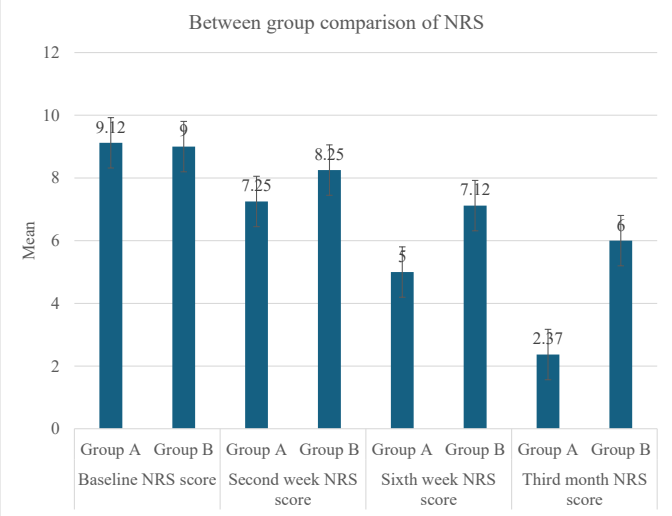

Figure: Comparison of NRS scores between group A and B

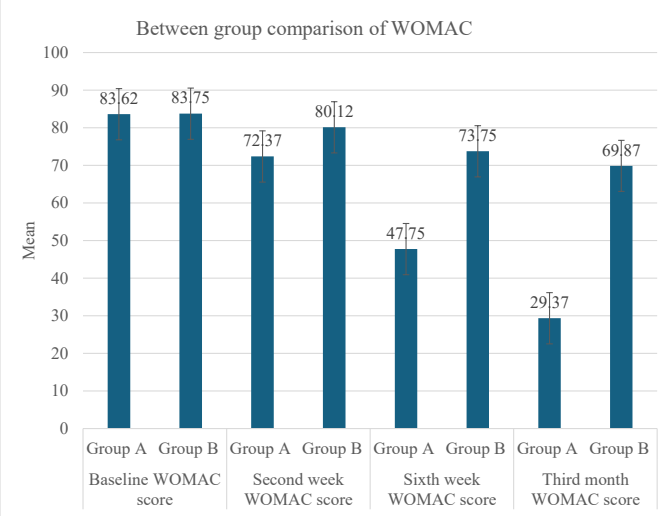

Figure: Comparison of WOMAC scores between group A and B

DISCUSSION

The present randomized controlled trial examined the comparative effectiveness of intra-articular hyaluronic acid and corticosteroid injections, both administered alongside exercise, in obese patients with Grade III knee osteoarthritis. The findings demonstrated that both treatment approaches were associated with statistically significant improvements in pain intensity and functional status over time; however, the magnitude and persistence of improvement were greater in the hyaluronic acid group. This pattern was evident in both within-group and between-group analyses and suggested that, in this specific patient population, hyaluronic acid combined with exercise provided a more substantial reduction in pain and functional limitation across the three-month follow-up period. The reduction in pain observed in the hyaluronic acid group was marked, with mean NRS scores declining from 9.12 at baseline to 2.37 at three months, while WOMAC scores decreased from 83.62 to 29.37 over the same period. In comparison, the corticosteroid group also improved, but the extent of change was comparatively modest, with NRS scores decreasing from 9.00 to 6.00 and WOMAC scores from 83.75 to 69.87. These findings suggested that although corticosteroid injections retained clinical value for symptom relief, hyaluronic acid produced a broader and more sustained therapeutic response in obese individuals with advanced disease. The absence of significant baseline differences between groups further strengthened the interpretation that the divergence in follow-up outcomes was more likely related to the intervention effect rather than pre-existing imbalance.

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These findings were broadly consistent with a substantial body of literature indicating that both hyaluronic acid and corticosteroid injections can provide symptomatic relief in knee osteoarthritis, although the duration, depth, and clinical profile of benefit differ between the two modalities (34). Several recent reviews and comparative trials have reported that corticosteroids may offer more rapid short-term analgesia, particularly in patients with inflammatory exacerbations, whereas hyaluronic acid tends to demonstrate a slower onset but more prolonged improvement in pain and function (34,35). The current findings aligned more closely with the latter perspective, as the superiority of hyaluronic acid became increasingly apparent from the second week onward and remained pronounced at six weeks and three months. This temporal pattern was clinically meaningful, particularly in the context of chronic degenerative disease where sustained symptom control is often more valuable than transient relief. At the same time, the wider literature has remained heterogeneous and at times contradictory. Some comparative studies have found corticosteroids to be superior at early follow-up intervals, including up to three months, particularly when outcomes were heavily weighted toward immediate pain suppression rather than broader functional restoration (35). Other syntheses have ranked corticosteroids among the more effective short-term intra-articular interventions, followed by hyaluronic acid, especially when pain reduction was considered in isolation (34,36-38). In contrast, other analyses have favored hyaluronic acid for longer-term functional recovery and durability of response, particularly beyond the acute post-injection phase. This inconsistency likely reflected differences in study populations, osteoarthritis severity, injection protocols, follow-up periods, outcome measures, and patient-level modifiers such as body mass index, inflammatory burden, and structural joint damage. In this regard, the present study contributed useful data by focusing specifically on obese patients with Grade III knee osteoarthritis, a subgroup that has often been underrepresented or insufficiently stratified in prior work.

The distinct response patterns observed in this study were biologically plausible. Corticosteroids exert their primary effect through rapid suppression of synovial inflammation and inflammatory mediators, which can translate into early pain relief, particularly in patients with an inflammatory component to their osteoarthritis. However, this effect is generally time-limited, and repeated exposure has raised concern regarding dose-related chondrotoxicity and potential acceleration of cartilage deterioration in susceptible joints (37,39). Hyaluronic acid, by contrast, appears to operate through a broader set of mechanisms that extend beyond simple viscosupplementation. In addition to improving joint lubrication and shock absorption, it has been associated with modulation of inflammatory cascades, support of extracellular matrix homeostasis, and possible chondroprotective effects, all of which may contribute to more durable clinical benefit (40). In obese patients, where mechanical overload and low-grade systemic inflammation coexist, a treatment capable of addressing both biomechanical and intra-articular biological disruption may reasonably offer greater medium-term benefit, which was reflected in the present results. The relevance of obesity in interpreting these findings was particularly important. Obesity is not merely a mechanical risk factor for knee osteoarthritis; it is increasingly recognized as a metabolic and inflammatory contributor to disease onset, progression, symptom severity, and treatment responsiveness (25,26). Excess adipose tissue promotes the release of pro-inflammatory cytokines and adipokines, while elevated body weight increases compressive stress across already compromised articular surfaces. In patients with Grade III disease, these overlapping mechanisms may amplify pain, accelerate structural degeneration, and limit recovery. Against this background, corticosteroid injections may still provide temporary suppression of inflammation, but their benefits may be less durable in a persistently adverse joint environment. Hyaluronic acid, by supporting synovial fluid properties and potentially preserving cartilage function without further compromising tissue integrity, may be better suited to the chronic pathophysiological demands of obese patients with advanced osteoarthritis. The present findings supported this clinical reasoning, though they should still be interpreted with due caution given the scale of the study.

The discussion surrounding combined or sequential use of hyaluronic acid and corticosteroids has also remained unsettled in recent literature. Some randomized trials have reported superior pain reduction when corticosteroids were co-administered with hyaluronic acid compared with hyaluronic acid alone, suggesting a possible additive or synergistic effect in carefully selected patients (36). Other controlled studies, however, have shown little or no meaningful incremental benefit, particularly when hyaluronic acid was already delivered in multi-injection regimens, and have emphasized that the theoretical gains must be weighed against the known biological concerns associated with corticosteroid exposure (37). This unresolved debate reinforced the value of direct comparative studies such as the present one. Rather than supporting broad generalizations, the current findings suggested that treatment choice may need to be individualized according to disease severity, body habitus, symptom chronicity, and therapeutic goals, with sustained functional improvement arguably carrying particular importance in obese patients with advanced osteoarthritis. A notable contribution of this study was its focus on a clinically challenging subgroup for whom high-quality evidence remains limited. Much of the contemporary literature has evaluated mixed osteoarthritis populations without adequate stratification by obesity status, or has included patients with milder disease severity and lower average body mass index, making it difficult to draw conclusions for obese individuals with Grade III knee osteoarthritis. By narrowing the study population to this specific group, the present trial addressed a meaningful evidence gap and offered findings with direct clinical relevance to non-surgical treatment decision-making in patients at heightened risk of progressive disability and eventual arthroplasty.

The study also had several strengths. The randomized controlled design reduced allocation-related bias and improved internal validity. The use of standardized and validated outcome measures, including the NRS and WOMAC, allowed assessment of both pain and function across multiple clinically relevant time points. The inclusion of exercise alongside injection therapy in both groups also reflected a more realistic therapeutic model, as intra-articular interventions are seldom used in complete isolation in routine musculoskeletal

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practice. Moreover, the repeated follow-up schedule allowed observation of the evolving treatment response rather than a single endpoint comparison, which strengthened appreciation of temporal trends. Despite these strengths, the findings should be interpreted within the context of important limitations. The most prominent limitation was the very small sample size, with only sixteen participants included in total. Although the sample size calculation was reported, such a limited cohort reduced statistical robustness, constrained generalizability, and increased the possibility that estimates of treatment effect were unstable. The short follow-up duration of three months also limited conclusions regarding long-term sustainability, recurrence of symptoms, structural progression, or delayed adverse effects. In addition, the methodology did not clearly describe blinding procedures, and the absence of participant, injector, or assessor blinding may have introduced performance or assessment bias, particularly for patient-reported outcomes such as pain and function. Baseline demographic characteristics were described, but formal statistical comparisons for age, sex, and obesity class were not reported, which would have strengthened the demonstration of group comparability. The study also did not report adverse events, rescue medication use, adherence to exercise, or changes in weight and activity level during follow-up, all of which may have influenced outcomes. Furthermore, reliance on clinical scales alone, without imaging reassessment or biomarker evaluation, limited insight into structural or biological response to treatment.

These limitations suggested several important directions for future research. Larger multicenter trials with adequately powered sample sizes are needed to validate these findings and improve external validity. Longer follow-up periods would be particularly valuable to determine whether the apparent advantage of hyaluronic acid persists beyond three months and whether either treatment meaningfully delays progression to surgical intervention. Future studies would also benefit from more rigorous reporting of allocation concealment, blinding procedures, adverse events, and adherence to co-interventions such as exercise and weight management. Stratified analyses according to obesity class, inflammatory phenotype, radiographic severity, and sex may help clarify which subgroups derive the greatest benefit from each therapy. Comparative trials involving repeated hyaluronic acid schedules, different corticosteroid preparations, combination regimens, and integration with structured rehabilitation or weight reduction programs would further strengthen the evidence base. Inclusion of imaging outcomes, inflammatory biomarkers, and patient-centered measures such as quality of life and treatment satisfaction would provide a more comprehensive understanding of treatment impact. Overall, the present study suggested that both intra-articular hyaluronic acid and corticosteroid injections, when combined with exercise, were associated with improvement in obese patients with Grade III knee osteoarthritis, but hyaluronic acid produced greater reductions in pain and functional limitation over the observed follow-up period. These findings supported the view that treatment selection in advanced osteoarthritis should extend beyond short-term symptom suppression and should consider durability of benefit, biological plausibility, and patient-specific risk profiles. While the results were encouraging, they should be interpreted as preliminary and hypothesis-supporting rather than definitive, given the limited sample and short duration of follow-up. Even so, the study added clinically relevant evidence to an area where targeted data remain scarce and underscored the importance of more focused research in obese patients with advanced knee osteoarthritis.

CONCLUSION

The findings of this study indicate that intra-articular hyaluronic acid injections combined with structured exercise provide greater improvement in pain relief and functional recovery compared with corticosteroid injections combined with exercise in obese patients with Grade III knee osteoarthritis. While both treatment approaches demonstrated clinical benefits, the hyaluronic acid regimen showed a more sustained and meaningful impact on symptom control and daily functional ability. These outcomes highlight the potential value of hyaluronic acid as a more suitable non-surgical management option for patients with advanced osteoarthritis, particularly in the context of obesity where long-term symptom control and preservation of joint function are essential. The study contributes to the growing body of evidence supporting the role of viscosupplementation as part of a comprehensive conservative treatment strategy for knee osteoarthritis.

AUTHOR CONTRIBUTION

Author	Contribution
Khadija Fareed	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Hafiz Muhammad Abu Bakar Rashid	Methodology, Investigation, Data Curation, Writing - Review & Editing
Ali Hayder	Investigation, Data Curation, Formal Analysis, Software
Ghazi Mustafa	Software, Validation, Writing - Original Draft
Rubab Naqvi	Formal Analysis, Writing - Review & Editing
Muhammad Abdullah Hamza	Writing - Review & Editing, Assistance with Data Curation

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