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Platelet-Rich Plasma Versus Hyaluronic Acid for Early Knee Osteoarthritis: A Comparative Study

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Abstract: Early knee osteoarthritis (KOA) is characterized by progressive cartilage degeneration, synovial inflammation, pain, stiffness, and functional impairment. Intra-articular hyaluronic acid (HA) and platelet-rich plasma (PRP) are commonly investigated injectable treatments intended to relieve symptoms and improve joint function. PRP contains concentrated platelets and associated growth factors that may influence inflammatory and reparative pathways, whereas HA primarily contributes to lubrication, viscoelasticity, and modulation of the intra-articular environment. Current comparative evidence suggests that both treatments can improve pain and function, although PRP may provide greater or more sustained clinical improvement in selected patients.The objective was to compare the clinical effectiveness of intra-articular PRP and HA in patients with early knee osteoarthritis, focusing on pain relief, functional improvement, duration of benefit, treatment-related adverse effects, and overall clinical utility.A comparative clinical research framework was used to evaluate PRP and HA for symptomatic early KOA. Relevant clinical studies, randomized controlled trials, systematic reviews, and meta-analyses were reviewed. Outcomes included pain severity, knee function, patient-reported improvement, duration of therapeutic benefit, and adverse events. The comparative evidence was synthesized qualitatively without generating unsupported patient-level numerical data. Both PRP and HA demonstrated beneficial effects on pain and knee function. PRP generally produced greater improvement in pain and patient-reported functional outcomes during intermediate and longer follow-up periods, particularly in patients with less advanced osteoarthritis. HA also provided clinically meaningful symptom relief, although its benefits were generally less pronounced or less durable in comparative studies. Both treatments showed favorable safety profiles, with mainly transient local reactions. Treatment response varied according to disease severity, PRP preparation, injection protocol, and patient characteristics. PRP and HA are both useful nonoperative injectable options for early knee osteoarthritis. PRP generally demonstrates a greater and more sustained improvement in pain and function, while HA remains a reasonable alternative because of its established clinical use and favorable tolerability. Patient selection,

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standardized PRP preparation, disease severity, and treatment expectations should guide the choice between the two therapies.

Keywords: Knee osteoarthritis, platelet-rich plasma, hyaluronic acid, intra-articular injection, pain, functional outcome, cartilage degeneration, regenerative medicine.

Introduction

Knee osteoarthritis (KOA) is a common degenerative joint disorder that causes progressive pain, stiffness, reduced mobility, and impaired physical function. The disease involves multiple joint tissues, including articular cartilage, synovium, subchondral bone, ligaments, and periarticular structures. Although structural degeneration is central to the disease process, inflammation and alterations in joint homeostasis also contribute to symptoms and functional decline [1,2].Early knee osteoarthritis is an important stage for conservative intervention because symptoms may be substantial even when structural changes remain relatively limited. Appropriate nonoperative treatment can improve pain and function and may delay the need for surgical procedures. Exercise, weight management, physical therapy, pharmacological treatment, and intra-articular therapies are commonly incorporated into individualized management strategies [1].Hyaluronic acid is a naturally occurring component of synovial fluid and extracellular matrices. Intra-articular HA injections are intended to improve the viscoelastic properties of synovial fluid and may also influence inflammatory and nociceptive pathways within the joint. The clinical response to HA varies among patients, and differences in molecular weight, formulation, injection frequency, and disease severity can influence outcomes [3].Platelet-rich plasma is an autologous blood-derived preparation containing a concentration of platelets and associated growth factors. Following intra-articular administration, PRP may influence the local inflammatory environment and promote biological processes involved in tissue repair and symptom modulation. Different preparation techniques produce PRP products with varying platelet and leukocyte concentrations, which contributes to heterogeneity among clinical studies [4].The comparative effectiveness of PRP and HA has been extensively investigated. A systematic review and meta-analysis of 18 randomized level-1 studies found that patients treated with PRP experienced greater improvement in WOMAC outcomes than patients treated with HA. PRP also produced better pain outcomes in several included studies, supporting its potential superiority for symptomatic treatment of knee osteoarthritis [5].

A larger meta-analysis of 26 randomized controlled trials involving more than two thousand patients similarly found that PRP produced better WOMAC total, physical-function, and pain outcomes than HA at several follow-up points. Improvements in stiffness, overall health status, and knee-specific functional outcomes also favored PRP at selected time points, while adverse events were not significantly different between the treatments [6].Evidence specifically relevant

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to early or mild osteoarthritis is also important. An earlier systematic review found that PRP improved pain, physical function, and stiffness and suggested that PRP could be particularly useful in patients with mild knee osteoarthritis [7]. This finding is clinically relevant because biological treatments may be more useful when the joint has not progressed to advanced structural destruction.Repeated PRP injections have also been studied. A systematic review and meta-analysis of randomized controlled trials found that multiple PRP injections were associated with lower pain scores than multiple HA injections at selected follow-up points, including later follow-up, suggesting that repeated PRP treatment may provide sustained symptomatic benefit in appropriately selected patients [8].More recent evidence continues to support the comparative effectiveness of PRP. A 2026 meta-analysis involving randomized and cohort evidence reported better WOMAC outcomes with PRP at six and twelve months, along with greater pain reduction at earlier follow-up points [9]. These findings further support the clinical interest in PRP for nonoperativenmanagement of symptomatic knee osteoarthritis.Nevertheless, PRP is not universally superior in every clinical setting. Differences in PRP preparation, platelet concentration, leukocyte content, injection number, dosing interval, disease severity, and outcome measurement can contribute to inconsistent findings. HA also remains an established intra-articular treatment with a substantial clinical evidence base [3,5].The decision between PRP and HA is therefore clinically relevant, particularly for patients with early knee osteoarthritis who seek nonoperative symptom control and functional improvement. This study compared PRP and HA with respect to pain, knee function, stiffness, patient-reported outcomes, durability of benefit, and treatment safety.

Materials and Methods

Study Design

A comparative clinical research framework was used to evaluate intra-articular PRP and HA for symptomatic early knee osteoarthritis. Published comparative studies, randomized controlled trials, systematic reviews, and meta-analyses were assessed to synthesize the available evidence.

Study Setting

The research was conducted through evaluation of evidence from orthopedic, sports medicine, rheumatology, and musculoskeletal medicine literature concerning intra-articular treatment of knee osteoarthritis at Lady Reading Teaching Hospital Peshawar.

Study Duration

The research was conducted for a time duration of 6 months from January 2026 till June 2026.

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Study Population

The reviewed population consisted of adults with symptomatic early or mild-to-moderate knee osteoarthritis who received intra-articular PRP or HA. Patients with advanced degenerative disease were considered separately because treatment response can differ according to radiographic severity.

Eligibility Criteria

Studies were considered relevant when they:

Evaluated adults with symptomatic knee osteoarthritis;

Compared intra-articular PRP with HA or provided clinically relevant comparative evidence;

Assessed pain, function, quality of life, or treatment-related outcomes;

Reported follow-up after injection therapy; and

Provided sufficient information for qualitative comparison.

Studies were excluded when they focused exclusively on advanced surgical disease, unrelated joint disorders, animal models, or interventions that did not allow meaningful comparison between PRP and HA.

PRP Intervention

PRP was prepared from autologous blood using centrifugation or other validated concentration techniques. Depending on the study protocol, PRP preparations differed in platelet concentration, leukocyte content, activation method, injection volume, and number of injections.

The biological rationale for PRP was based on the presence of concentrated platelets and associated growth factors. These components were considered capable of influencing local inflammatory and tissue-remodeling pathways.

Hyaluronic Acid Intervention

HA was administered intra-articularly according to the formulation and dosing schedule used in individual studies. Different molecular weights and injection schedules were included in the published evidence.

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HA was considered primarily a viscosupplementation therapy intended to improve joint lubrication and modify the intra-articular environment.

Outcome Assessment

The principal outcomes included:

pain severity;

knee-specific functional status;

patient-reported improvement;

duration of symptom relief;

quality of life;

treatment-related adverse effects; and

overall clinical response.

Pain and function were evaluated using validated patient-reported outcome instruments in the reviewed studies.

Follow-Up Assessment

Clinical outcomes were considered across early, intermediate, and longer follow-up periods. This approach was used because the relative effects of PRP and HA may change over time.

Short-term improvement was considered particularly relevant for initial symptom control, whereas intermediate and longer-term outcomes were considered important for evaluating durability of treatment response.

Safety Assessment

Treatment-related adverse events were evaluated, including injection-site pain, swelling, transient inflammatory reactions, stiffness, and other clinically reported complications.

Data Synthesis

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The comparative findings were synthesized qualitatively. Because no original patient-level dataset was supplied, numerical sample sizes, percentages, mean differences, or p-values were not generated.

Ethical Considerations

The study was based on previously published clinical evidence and did not involve direct recruitment or intervention involving human participants. Therefore, no new institutional ethical approval was required for the literature-based comparative analysis.

Results

The reviewed evidence showed that both PRP and HA improved symptoms in patients with early knee osteoarthritis. However, PRP generally demonstrated greater improvements in pain and function, particularly during intermediate and longer follow-up.

Table 1. Comparative Effect on Pain

Pain Outcome	PRP	Hyaluronic Acid	Overall Finding
Early pain relief	Improved	Improved	Both provided symptomatic benefit
Intermediate pain reduction	Greater improvement	Moderate improvement	PRP generally favored
Long-term pain relief	More sustained	Less consistent durability	PRP generally favored
Activity-related pain	Improved	Improved	Greater improvement generally reported with PRP

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Resting pain	Reduced	Reduced	Both demonstrated benefit
Patient-perceived pain improvement	More frequently reported	Frequently reported	PRP generally showed stronger improvement

Table 2. Comparative Functional Outcomes

Functional Domain	PRP	Hyaluronic Acid	Overall Finding
Knee function	Improved	Improved	Both beneficial
Walking ability	Improved	Improved	PRP generally showed greater improvement
Physical activity	Greater improvement	Moderate improvement	PRP generally favored
Stiffness	Reduced	Reduced	Both provided benefit
Daily activities	Improved	Improved	Greater sustained improvement generally occurred with PRP
Patient-reported quality of life	Improved	Improved	PRP generally demonstrated greater overall benefit

Table 3. Duration of Clinical Benefit

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Follow-Up Period	PRP	Hyaluronic Acid	Comparative Interpretation
Early follow-up	Clinical improvement	Clinical improvement	Both effective
Intermediate follow-up	Sustained improvement	Improvement maintained in many patients	PRP generally favored
Longer follow-up	More persistent benefit	Benefit may decline in some patients	PRP generally favored
Recurrent symptoms	Less frequent in comparative evidence	More commonly reported over time	PRP may provide greater durability
Need for additional treatment	Potentially delayed	May occur sooner in some patients	PRP showed potential advantage

Table 4. Safety and Clinical Utility

Parameter	PRP	Hyaluronic Acid	Overall Finding
Injection-site pain	Usually transient	Usually transient	Comparable overall
Local swelling	May occur	May occur temporarily	Generally mild

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	temporarily		
Serious adverse events	Uncommon	Uncommon	Both showed favorable safety
Systemic adverse effects	Minimal	Minimal	Favorable for both
Treatment standardization	More variable	More standardized	HA advantage
Biological activity	Multiple platelet-derived mediators	Primarily viscoelastic and biological effects of HA	Different mechanisms
Evidence of symptom improvement	Strong	Strong	Both useful
Longer-term effectiveness	Generally favorable	More variable	PRP generally favored
Practical clinical use	Increasing	Established	HA remains widely used

Discussion

The present comparative assessment showed that both PRP and HA improved symptoms of knee osteoarthritis, but PRP generally produced greater and more sustained improvements in pain and

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physical function. The advantage was particularly apparent at intermediate and longer follow-up, supporting PRP as a promising treatment option for early knee osteoarthritis.The findings were consistent with a systematic review of 18 randomized level-1 studies, which reported greater improvement in WOMAC outcomes among patients receiving PRP than among those receiving HA. Several included studies also reported superior pain outcomes with PRP [5]. These findings support the interpretation that PRP provides benefits extending beyond simple short-term symptom relief.The biological mechanisms of the two treatments differ. HA primarily functions through its effects on joint lubrication and the intra-articular environment, while PRP contains platelets and signaling molecules that can influence inflammatory responses and tissue-related biological processes. These differences may help explain why PRP demonstrates a more sustained clinical effect in some patient populations [3,4].The results also showed that the relative benefit of PRP became more apparent over time. A large meta-analysis of 26 randomized controlled trials demonstrated better WOMAC total, physical-function, and pain outcomes with PRP at three, six, and twelve months. Several other patient-reported outcomes also favored PRP at later follow-up [6].A separate meta-analysis similarly demonstrated greater pain reduction with PRP at six and twelve months compared with HA [10]. This longer-term advantage is clinically important for patients with early knee osteoarthritis because the goal of conservative treatment is not only immediate symptom relief but also sustained improvement in mobility and quality of life.The findings were particularly relevant to early disease. An earlier systematic review concluded that PRP could be an effective alternative treatment, especially in patients with mild knee osteoarthritis [7]. Early-stage disease may provide a more favorable environment for biological interventions because severe structural destruction and advanced joint-space loss can limit the potential for meaningful symptomatic improvement from intra-articular treatment.However, PRP should not be considered a uniform treatment. PRP preparations differ considerably in platelet concentration, leukocyte content, activation method, and injection number. Leukocyte-poor PRP has demonstrated favorable outcomes in some comparisons, although the optimal formulation remains incompletely established [5]. This heterogeneity can contribute to differences between clinical trials.HA also has several practical advantages. It does not require blood collection, its composition can be standardized, and dosing protocols are relatively well established. For patients who prefer a more standardized injectable treatment or who are not suitable candidates for blood-derived therapies, HA remains a reasonable conservative option.The safety findings were reassuring. The comparative evidence generally demonstrated similar adverse-event rates between PRP and HA. The 26-trial meta-analysis found no significant difference in adverse events between the two treatments [6]. Thus, the greater symptomatic benefit associated with PRP was not accompanied by a clearly established increase in overall adverse events.The nature of adverse effects also deserves consideration. Both treatments can produce temporary injection-site pain, swelling, or stiffness. These reactions are usually localized and self-limited. Appropriate injection technique, sterile precautions, and patient counseling remain important regardless of the selected

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treatment.Repeated injections may provide additional benefit in selected patients. Evidence comparing multiple PRP injections with multiple HA injections demonstrated lower pain scores with PRP at several follow-up points [8]. However, the optimal number of injections and interval between treatments remain uncertain because clinical protocols differ considerably across studies.Patient selection is therefore essential. PRP may be particularly appropriate for relatively younger or physically active patients with symptomatic early-to-moderate disease who seek longer-lasting symptom improvement without surgery. HA may remain appropriate for patients who value standardized treatment, have contraindications to blood collection, or prefer viscosupplementation.The severity of osteoarthritis also influences treatment response. Patients with advanced structural disease may experience less improvement from either injection compared with patients with early disease. The current study focused on early knee osteoarthritis because preservation of joint function and symptom control at this stage may provide greater opportunity for successful conservative management.Another important consideration is the heterogeneity of clinical outcomes. Some randomized trials have demonstrated little difference between PRP and HA, particularly at certain early follow-up points. This inconsistency means that PRP should not be represented as universally superior. Instead, the overall evidence suggests a favorable average treatment effect, particularly for pain and function over several months [5,6].The 2026 evidence further supports this interpretation. A recent meta-analysis reported significantly better WOMAC outcomes with PRP at six and twelve months and greater pain reduction at three and six months [9]. These findings strengthen the evidence for PRP while also demonstrating the importance of evaluating outcomes over an adequate follow-up period rather than relying only on immediate post-injection response.Treatment standardization remains an important research priority. Future clinical studies should use clearly defined PRP preparation methods, platelet concentrations, leukocyte classifications, injection numbers, and outcome thresholds. Standardized protocols would allow more reliable comparison between PRP and HA and help identify which patients are most likely to benefit.Cost and accessibility also influence clinical decision-making. PRP preparation may require specialized equipment and trained personnel, whereas HA is available as a standardized commercial preparation. Therefore, treatment effectiveness should be considered alongside availability, patient preference, local cost, and clinical expertise.Overall, the evidence supports PRP as a strong nonoperative treatment option for early knee osteoarthritis. HA remains clinically useful, but PRP generally provides greater improvements in pain and function, particularly over intermediate and longer follow-up. The choice should nevertheless be individualized according to disease severity, patient characteristics, treatment availability, and the specific PRP protocol used.

Conclusion

PRP and HA are both effective intra-articular treatment options for symptomatic early knee osteoarthritis. Both interventions provide meaningful improvement in pain, stiffness, and

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functional status and generally demonstrate favorable safety profiles.Comparative evidence indicates that PRP generally provides greater and more sustained improvement in pain and knee function, particularly during intermediate and longer follow-up. This potential advantage may be related to the broader biological activity of platelet-derived growth factors and signaling molecules.HA remains clinically relevant because it is an established treatment with predictable formulation, standardized administration, and generally good tolerability. It can provide meaningful symptomatic relief, particularly in patients who prefer conventional viscosupplementation or for whom PRP is not readily available.The choice between PRP and HA should therefore be individualized. Disease severity, patient age and activity level, treatment goals, PRP preparation characteristics, HA formulation, cost, availability, and clinician experience should all be considered.For appropriately selected patients with **early knee osteoarthritis**, PRP appears to offer a promising advantage in sustained pain reduction and functional improvement, while HA remains a reasonable and safe alternative within comprehensive conservative management.

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