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CLINICAL OUTCOMES OF PURE PLATELET-RICH PLASMA VERSUS HYALURONIC ACID INJECTION FOR EARLY KNEE OSTEOARTHRITIS: A COMPARATIVE STUDY.

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Abstract

Background: Knee osteoarthritis (OA) is a common degenerative joint disorder associated with progressive cartilage loss, pain, stiffness, and functional limitation. Conventional intra-articular therapies such as hyaluronic acid (HA) provide symptomatic relief; however, their long-term efficacy remains variable. Platelet-rich plasma (PRP), particularly pure platelet-rich plasma (P-PRP), has emerged as a biological treatment option due to its potential regenerative and anti-inflammatory properties. This study was conducted to compare the clinical efficacy of intra-articular P-PRP and HA injections in patients with Kellgren–Lawrence Grade I–III knee osteoarthritis. ***Aim:*** To evaluate and compare the effectiveness of intra-articular pure platelet-rich plasma and hyaluronic acid injections in improving pain, functional outcome, and knee range of motion in patients with knee osteoarthritis over a 6-month follow-up period. ***Materials and Methods:*** A prospective comparative clinical study was conducted over a period of 6 months (September 2023 to February 2024). A total of 50 patients diagnosed with symptomatic knee osteoarthritis were included and divided into two groups of 25 patients each. Group A received a single intra-articular injection of pure platelet-rich plasma (P-PRP), while Group B received intra-articular hyaluronic acid injection. Patients with Kellgren–Lawrence Grade I, II, and III osteoarthritis were included. Clinical outcomes were assessed using the Visual Analog Scale (VAS) for pain, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and knee range of motion at baseline, 1 month, 3 months, and 6 months after injection. ***Results:*** Both groups demonstrated significant improvement in pain and functional outcomes following treatment. The mean VAS score decreased significantly in both groups; however, the reduction was greater in the P-PRP group at 3 months and 6 months follow-up ($p<0.05$). Similarly, improvement in WOMAC scores was significantly higher in the P-PRP group compared with the HA group at the final follow-up. Knee range of motion improved in both groups, with greater improvement observed among patients receiving P-PRP. At 6 months, a higher proportion of patients in the P-PRP group reported good to excellent clinical improvement compared with the HA group. No major complications were observed in either group. ***Conclusion:*** Intra-articular pure platelet-rich plasma and hyaluronic acid injections are effective in reducing pain and improving function in patients with Kellgren–Lawrence Grade I–III knee osteoarthritis. However, P-PRP demonstrated superior and more sustained improvement in pain relief, functional outcomes, and range of motion compared with hyaluronic acid at 6 months. P-PRP may be considered a safe and effective biological treatment option for patients with mild to moderate knee osteoarthritis, potentially delaying progression to advanced disease and surgical intervention.

Keywords: Knee osteoarthritis; Platelet-rich plasma; Pure PRP; Hyaluronic acid; WOMAC score; VAS score; Intra-articular injection; Biological therapy.

INTRODUCTION

Osteoarthritis (OA) of the knee is one of the most common degenerative disorders affecting the musculoskeletal system and represents a major cause of pain, disability, and reduced quality of life among the elderly population. It is characterized by progressive loss of articular cartilage, subchondral bone remodelling, osteophyte formation, synovial inflammation, and gradual deterioration of joint function. Knee osteoarthritis contributes significantly to global morbidity and imposes a considerable socioeconomic burden due to increased healthcare utilization and loss of productivity.[1]

The prevalence of knee osteoarthritis has increased with increasing life expectancy, obesity, sedentary lifestyle, and rising incidence of joint injuries. Early-stage knee osteoarthritis is a critical period where interventions aimed at reducing symptoms and modifying disease progression may delay or prevent the need for surgical procedures such as total knee arthroplasty.[2] Conventional conservative management includes activity modification, weight reduction, physiotherapy, non-steroidal anti-inflammatory drugs, and intra-articular therapies. However, these treatments mainly provide symptomatic relief and have limited potential for cartilage restoration.[3]

Intra-articular corticosteroid injections have traditionally been used for short-term pain relief but are associated with concerns regarding repeated administration and potential adverse effects on cartilage metabolism. Hyaluronic acid (HA) injections, also known as viscosupplementation, have gained popularity due to their ability to restore synovial fluid viscoelasticity, reduce inflammation, and improve joint lubrication. HA may provide longer-lasting symptom relief compared with corticosteroids, particularly in patients with mild to moderate knee osteoarthritis.[4] However, the clinical effectiveness of HA remains variable, and its role in disease modification is still debated.[5]

Platelet-rich plasma (PRP) therapy has emerged as a promising biological treatment option for early knee osteoarthritis. PRP is an autologous blood-derived preparation containing concentrated platelets and growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF). These bioactive molecules contribute to tissue repair by promoting chondrocyte proliferation, extracellular matrix synthesis, angiogenesis regulation, and modulation of inflammatory pathways.[6]

Pure platelet-rich plasma (P-PRP), classified according to the International Society for Cellular Therapy and platelet classification systems, contains a high concentration of platelets with minimal leukocyte contamination. Compared with leukocyte-rich PRP, P-PRP may reduce inflammatory responses and improve clinical outcomes by minimizing catabolic cytokine release within the joint environment.[7] Several studies have demonstrated that intra-articular PRP injections provide significant improvement in pain scores and functional outcomes in patients with early and moderate knee osteoarthritis.[8]

Comparative studies between PRP and hyaluronic acid have shown encouraging results, with several meta-analyses reporting superior and more sustained improvement in pain and functional scores with PRP compared with HA.[9] However, variations in PRP preparation methods, platelet concentration, number of injections, disease severity, and outcome measures have resulted in inconsistent conclusions. Therefore, further clinical studies evaluating standardized P-PRP preparations are required to determine its efficacy compared with established treatments such as HA.

The present study aims to compare the clinical efficacy of intra-articular pure platelet-rich plasma and hyaluronic acid injections in patients with early-stage knee osteoarthritis by evaluating pain relief, functional improvement, and patient-reported outcomes.

MATERIALS AND METHODS

Study Design: This was a prospective comparative clinical study conducted to evaluate and compare the efficacy of intra-articular pure platelet-rich plasma (P-PRP) and hyaluronic acid (HA) injections in patients with symptomatic knee osteoarthritis. The study was conducted in the Department of Orthopaedics after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants before inclusion in the study.

Study Duration and Study Population: The study was conducted over a period of 1 year, from 1st September 2023 to 28th February 2024. Patients presenting with symptomatic knee osteoarthritis to the Orthopaedics outpatient department were screened for eligibility. Patients fulfilling the predefined inclusion criteria were enrolled in the study.

Sample Size and Group Allocation

A total of 50 patients diagnosed with knee osteoarthritis were included in the study. Patients were divided into two groups of 25 patients each:

- Group A (P-PRP group): 25 patients received intra-articular pure platelet-rich plasma injection.
- Group B (HA group): 25 patients received intra-articular hyaluronic acid injection.

All patients were evaluated clinically and radiologically before intervention and followed up for a period of 6 months.

Inclusion Criteria

Patients fulfilling the following criteria were included in the study:

1. Patients aged > 18 years
2. Patients diagnosed with primary knee osteoarthritis
3. Radiological evidence of osteoarthritis classified as Kellgren–Lawrence Grade I, II, and III.

4. Patients with:
- Knee pain persisting for more than 3 months.
- Visual Analog Scale (VAS) pain score ≥4.
- Difficulty in performing activities of daily living due to knee symptoms.

5. Patients willing to participate in the study and provide written informed consent.

Exclusion Criteria

Patients were excluded from the study if they had:

1. Kellgren–Lawrence Grade IV osteoarthritis.
2. Previous knee replacement surgery or major knee surgery.
3. Acute knee trauma or ligamentous instability.
4. Inflammatory arthritis such as rheumatoid arthritis, gout, or septic arthritis.
5. Significant knee deformity (varus or valgus deformity >10°).
6. Intra-articular corticosteroid injection within the previous 3 months.
7. Bleeding disorders or patients receiving anticoagulant therapy.
8. Platelet disorders, significant anaemia, or active infection.
9. Uncontrolled diabetes mellitus.
10. Pregnancy or inability to comply with follow-up evaluation.

Clinical and Radiological Assessment

All patients underwent detailed clinical evaluation, including assessment of symptom duration, severity of pain, functional limitation, and physical examination of the knee joint. Radiological assessment was performed using standard weight-bearing knee radiographs, including: Standing anteroposterior view, lateral view and Skyline (patellofemoral) view. The severity of osteoarthritis was graded according to the Kellgren–Lawrence grading system. Patients with Grade I, II, and III osteoarthritis were included.

Outcome Assessment

Clinical outcomes were assessed using validated assessment tools at baseline and during follow-up visits at 1 month, 3 months, and 6 months after injection.

1. Visual Analog Scale (VAS)

Pain intensity was assessed using a 10-point Visual Analog Scale:
- 0: No pain
- 10: Worst imaginable pain

A reduction in VAS score was considered an improvement in pain symptoms.

2. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Functional outcomes were assessed using the WOMAC index, which evaluates:
- Pain
- Stiffness
- Physical function

Higher WOMAC scores indicated greater pain and functional disability.

3. Range of Motion (ROM)

Knee range of motion was assessed using a standard goniometer, measuring knee flexion and extension.

Injection Technique

Group A: Pure Platelet-Rich Plasma (P-PRP) Group

Approximately 40 mL of peripheral venous blood was collected under aseptic conditions into tubes containing acid citrate dextrose-A (ACD-A) anticoagulant. A double-spin centrifugation technique was used for preparation of P-PRP. First centrifugation (soft spin): Separation of plasma and platelet-containing layer. Second centrifugation (hard spin): Concentration of platelets to obtain pure platelet-rich plasma. Approximately 4–5 mL of P-PRP was prepared and injected intra-articularly into the affected knee. The injection was performed under strict aseptic precautions using the superolateral approach with the knee positioned in slight flexion, after infiltrating injection site with 2ml of 2% lignocaine (after test dose).

Following injection, patients were advised:
- Relative rest and avoidance of strenuous activities for 48 hours.
- Ice application if required.
- Avoidance of non-steroidal anti-inflammatory drugs (NSAIDs) for 1 week.

Group B: Hyaluronic Acid (HA) Group

Patients allocated to the HA group received an intra-articular injection of high molecular weight hyaluronic acid under sterile conditions after local anaesthesia infiltration at injection site. A single-dose HA preparation (6 mL formulation) was administered through the superolateral approach. Post-injection instructions and rehabilitation advice were similar to those provided to the PRP group.

Post-Injection Rehabilitation

All patients were advised regarding activity modification, quadriceps strengthening exercises, gradual return to normal activities, weight reduction measures wherever indicated.

Statistical Analysis

Statistical analysis was performed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Baseline demographic and clinical characteristics were compared between the two groups. Intragroup changes over time were analyzed using paired statistical tests, while intergroup comparisons were performed using independent statistical tests. Changes in outcome measures at different follow-up intervals were analyzed using repeated-measures analysis. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee. All participants were informed regarding the study procedure, expected benefits, possible complications, and alternative treatment options. Written informed consent was obtained from all participants prior to enrolment.

RESULTS

A total of 50 patients with symptomatic knee osteoarthritis were enrolled in the study and divided into two groups of 25 patients each. Group A received intra-articular pure platelet-rich plasma (P-PRP) injection, while Group B received intra-articular hyaluronic acid (HA) injection. All patients completed the 6-month follow-up period and were included in the final analysis.

Baseline Characteristics

The demographic and clinical characteristics of both groups were comparable at baseline. There was no statistically significant difference between the groups with respect to age, sex distribution, body mass index (BMI), duration of symptoms, or baseline clinical scores. The mean age of patients in the P-PRP group was 56.8 ± 7.2 years, while the mean age in the HA group was 57.4 ± 6.9 years. The majority of patients belonged to the 50–65 years age group. Both groups showed a similar distribution of Kellgren–Lawrence grades, with Grade II and Grade III osteoarthritis being the most common radiological grades.

Table 1: Baseline Demographic and Clinical Characteristics

Parameter	P-PRP Group (n=25)	HA Group (n=25)	p-value
Mean age (years)	56.8 ± 7.2	57.4 ± 6.9	0.76
Male/Female	14/11	13/12	0.77
Mean BMI (kg/m²)	26.8 ± 2.4	27.1 ± 2.6	0.68
Duration of symptoms (months)	18.6 ± 8.4	19.2 ± 7.9	0.81

No statistically significant difference was observed between the two groups at baseline.

Radiological Distribution

The distribution according to Kellgren–Lawrence grading was comparable between the groups.

Table 2: Kellgren–Lawrence Grade Distribution

KL Grade	P-PRP Group (n=25)	HA Group (n=25)
Grade I	5	4
Grade II	12	13
Grade III	8	8

Clinical Outcome Assessment

Visual Analog Scale (VAS) Pain Score

Both groups demonstrated significant reduction in pain scores after injection compared with baseline. However, the P-PRP group showed greater improvement in pain reduction at 3 and 6 months compared with the HA group.

Table 3: Comparison of VAS Score Between Groups

Follow-up	P-PRP Group	HA Group	p-value
Baseline	7.1 ± 0.9	7.0 ± 1.0	0.72
1 month	4.8 ± 1.1	5.2 ± 1.0	0.18
3 months	3.4 ± 1.0	4.5 ± 1.2	**0.001**
6 months	3.1 ± 1.1	4.3 ± 1.3	**0.002**

The reduction in VAS score within both groups was statistically significant ($p<0.001$). The improvement was significantly greater in the P-PRP group at 3 and 6 months.

WOMAC Score Analysis

Both treatment groups showed significant improvement in WOMAC scores during follow-up. Patients receiving P-PRP demonstrated greater functional improvement compared with HA at final follow-up.

Table 4: WOMAC Score Comparison

Follow-up	P-PRP Group	HA Group	p-value
Baseline	58.6 ± 7.8	59.2 ± 8.1	0.79
1 month	45.3 ± 7.2	47.8 ± 7.5	0.24
3 months	34.5 ± 6.8	40.6 ± 7.1	**0.003**
6 months	29.8 ± 6.5	37.9 ± 7.3	**<0.001**

The mean reduction in WOMAC score was significantly higher in the P-PRP group at 6 months.

Range of Motion

Both groups showed improvement in knee range of motion after treatment.

Table 5: Knee Flexion Improvement

Follow-up	P-PRP Group	HA Group	p-value
Baseline	112.4° ± 9.8°	111.8° ± 10.2°	0.83
6 months	124.6° ± 8.7°	119.2° ± 9.1°	**0.04**

The improvement in knee flexion was greater in the P-PRP group at 6 months.

Patient Satisfaction

At the final follow-up:

- **P-PRP group:** 21 out of 25 patients (84%) reported good to excellent improvement.
- **HA group:** 16 out of 25 patients (64%) reported good to excellent improvement.

The difference in patient satisfaction favoured the P-PRP group.

Adverse Events

No major complications were observed in either group.

- Three patients in the P-PRP group reported mild post-injection pain lasting less than 48 hours.
- Two patients in the HA group reported transient local discomfort after injection.

No infection, allergic reaction, or serious adverse events were noted.

Summary of Results

Both pure platelet-rich plasma and hyaluronic acid injections were effective in reducing pain and improving functional outcomes in patients with Kellgren–Lawrence Grade I–III knee osteoarthritis. However, patients treated with P-PRP demonstrated significantly greater improvement in VAS pain scores, WOMAC functional scores, and knee range of motion at 3 and 6 months compared with hyaluronic acid injection. The beneficial effect of P-PRP was more pronounced at longer follow-up, suggesting a sustained biological effect compared with HA viscosupplementation.

DISCUSSION

Osteoarthritis of the knee is a progressive degenerative joint disorder characterized by cartilage degradation, subchondral bone remodeling, synovial inflammation, and loss of normal joint biomechanics. Although several conservative treatment options are available, the management of early and moderate knee osteoarthritis remains challenging because most therapies provide symptomatic relief without significantly influencing the underlying degenerative process. Biological therapies such as platelet-rich plasma (PRP) have gained increasing attention due to their potential regenerative and disease-modifying properties. [1]

In the present study, we compared the clinical efficacy of pure platelet-rich plasma (P-PRP) with hyaluronic acid (HA) injection in patients with Kellgren–Lawrence Grade I–III knee osteoarthritis over a follow-up period of 6 months. Both treatment groups demonstrated significant improvement in pain and functional outcomes; however, the P-PRP group showed superior improvement in VAS pain scores, WOMAC scores, and knee range of motion at 3 and 6 months. The beneficial effects of PRP are attributed to the high concentration of platelets and the release of multiple growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), insulin-like growth factor-1 (IGF-1), and vascular endothelial growth factor (VEGF). These mediators promote chondrocyte proliferation, extracellular matrix synthesis, angiogenesis regulation, and reduction of inflammatory cytokine activity within the osteoarthritic joint environment. [6]

Pure PRP (P-PRP) contains a high platelet concentration with minimal leukocyte content. Compared with leukocyte-rich PRP, P-PRP may result in reduced inflammatory response due to lower levels of pro-inflammatory cytokines and matrix metalloproteinases. Dohan Ehrenfest et al. proposed a classification system for platelet concentrates and emphasized that the biological characteristics of PRP preparations significantly influence clinical outcomes. [7] In our study, both PRP and HA groups demonstrated significant reduction in pain scores at follow-up. However, the P-PRP group showed significantly greater improvement at 3 and 6 months. Similar findings were reported by Filardo et al., who demonstrated sustained improvement in pain and functional scores following PRP injection in patients with knee osteoarthritis, with benefits persisting beyond 6 months. [8] The prolonged effect of PRP may be explained by its biological activity and ability to modulate the inflammatory environment within the osteoarthritic joint.

Hyaluronic acid acts primarily through viscosupplementation by improving synovial fluid properties, enhancing lubrication, reducing mechanical stress, and modulating inflammatory mediators. HA also interacts with CD44 receptors on chondrocytes and synovial cells, contributing to reduced inflammatory activity. However, the clinical response to HA is variable and may diminish over time. [10] A meta-analysis by Shen et al. comparing PRP with placebo and other injectable therapies demonstrated significant improvement in pain and physical function following PRP treatment in knee osteoarthritis. The authors suggested that PRP may provide longer-lasting symptomatic improvement compared with conventional injection therapies. [9]

In a randomized controlled trial, Patel et al. evaluated the efficacy of PRP injections in knee osteoarthritis and reported significant improvement in WOMAC scores and pain reduction following PRP administration. They also observed that PRP was associated with better functional outcomes compared with baseline values. [11] Our findings are consistent with the study by Cole et al., who compared PRP and hyaluronic acid injections and found that both treatments improved clinical outcomes; however, PRP demonstrated greater improvement in pain and functional scores at longer follow-up intervals. [12] The authors suggested that PRP may have advantages due to its biological mechanism rather than merely providing mechanical lubrication.

The superiority of PRP over HA has also been demonstrated in several systematic reviews. Dai et al. reported that PRP provided better improvement in pain, function, and quality of life compared with HA, particularly at intermediate and long-term follow-up. [13] Similarly, Laudy et al. found that PRP was associated with clinically meaningful improvements in knee osteoarthritis symptoms compared with placebo and other injection therapies. [14] The present study included patients with Kellgren–Lawrence Grade I, II, and III osteoarthritis. While many earlier studies have focused on early-stage disease, inclusion of Grade III osteoarthritis provides clinically relevant information regarding the effectiveness of biological therapy in patients with moderate degenerative changes. Although advanced cartilage loss may limit regenerative potential, PRP may still provide symptomatic improvement through modulation of inflammation and enhancement of the joint environment.

The improvement in knee range of motion observed in the PRP group may be attributed to reduction in pain, decreased synovitis, and improved functional capacity. Similar observations were reported by Gobbi et al., who demonstrated improvement in clinical outcomes following PRP treatment in patients with different grades of knee osteoarthritis. [15] No major complications were observed in either group in our study. Mild post-injection pain was noted in a few PRP patients, which resolved spontaneously. The favorable safety profile of PRP is consistent with previous studies reporting PRP as a safe autologous treatment option with minimal adverse effects. [16]

The present study has certain limitations. The sample size was relatively small, and the follow-up period was limited to 6 months. Long-term follow-up with larger patient cohorts and imaging-based evaluation of cartilage changes would provide better understanding of the disease-modifying potential of PRP. Additionally, variations in PRP preparation protocols may influence outcomes and should be standardized in future studies. Despite these limitations, our findings suggest that pure platelet-rich plasma provides superior and more sustained clinical improvement compared with hyaluronic acid in patients

with Kellgren–Lawrence Grade I–III knee osteoarthritis. PRP may therefore be considered an effective minimally invasive biological treatment option for patients seeking symptom relief and functional improvement before progression to advanced disease.

CONCLUSION

Intra-articular injection therapy with both pure platelet-rich plasma (P-PRP) and hyaluronic acid (HA) demonstrated significant improvement in pain relief and functional outcomes in patients with Kellgren–Lawrence Grade I–III knee osteoarthritis over a 6-month follow-up period. However, patients treated with P-PRP showed superior and more sustained improvement in terms of Visual Analog Scale (VAS) pain scores, WOMAC functional scores, and knee range of motion compared with hyaluronic acid injection, particularly at 3 and 6 months after treatment. The biological properties of P-PRP, including the release of multiple growth factors and modulation of inflammatory pathways, may contribute to its prolonged clinical benefits compared with HA, which primarily provides viscosupplementation and symptomatic relief. P-PRP appears to be a safe, minimally invasive, and effective biological treatment option for patients with mild to moderate knee osteoarthritis, potentially delaying disease progression and the need for surgical intervention. Further studies with larger sample sizes, longer follow-up periods, and standardized PRP preparation protocols are required to establish its long-term disease-modifying effects and define its optimal role in the management of knee osteoarthritis.

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