

Original Research Article

A WINDOW OF OPPORTUNITY? PRP FOR SYMPTOMATIC EARLY KNEE OSTEOARTHRITIS

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ABSTRACT

Background: Symptomatic early knee osteoarthritis (OA) represents a potential therapeutic window preceding advanced structural degeneration. Although platelet-rich plasma (PRP) has demonstrated symptomatic benefit in knee OA, evidence specific to early-stage disease remains limited. This study evaluated clinical and functional outcomes following a single intra-articular PRP injection in patients with symptomatic early knee OA.

Materials and Methods: In this prospective observational study, 50 patients aged 50–75 years with persistent symptomatic knee OA (>6 months) and Kellgren–Lawrence (KL) grade 1–2 radiographic disease underwent a single intra-articular injection of autologous PRP. Patients with advanced OA, major previous knee pathology or surgery, coagulation disorders, systemic contraindications, or recent intra-articular corticosteroid use were excluded. PRP was prepared from 40 mL of peripheral blood using a two-step centrifugation protocol, with 5–7 mL administered intra-articularly. The primary outcome was change in WOMAC pain; secondary outcomes included physical function and quality of life, assessed at baseline and 1, 4, 12, and 24 weeks. Radiographic KL grade was reassessed at 24 weeks.

Results: Mean age was 62.4 ± 6.8 years; 64% were women. KL grade 1 and 2 disease accounted for 42% and 58%, respectively. WOMAC pain decreased from 62.5 ± 10.3 at baseline to 30.2 ± 7.9 at 24 weeks (51.7% reduction; $p < 0.001$). Physical function and quality-of-life scores improved by 49.8% and 53.1%, respectively (both $p < 0.001$). Pain reduction was numerically greater in KL grade 1 disease. Radiographic KL grade showed minimal short-term change.

Conclusions: A single PRP injection was associated with sustained improvements in pain, physical function, and quality of life over 24 weeks in symptomatic early knee OA. Given the uncontrolled design, these findings do not establish treatment efficacy or disease modification. Randomized controlled trials with standardized PRP characterization, clinically meaningful responder analyses, appropriate comparators, and longer-term structural endpoints are warranted.

Keywords: Intra-Articular Injection, Platelet-Rich Plasma, Kellgren–Lawrence. Knee osteoarthritis, Quality of Life, Treatment Outcome, WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index).

INTRODUCTION

Osteoarthritis (OA) is a progressive whole-joint disorder involving articular cartilage, subchondral bone, synovium, and periarticular tissues. Knee OA is a major cause of pain, functional limitation, and impaired health-related quality of life, with a substantial and increasing burden in India, particularly among women.^[1,2] Contemporary management of early knee OA emphasizes exercise, weight optimization, patient education, analgesia, and selected intra-articular interventions. Although these strategies provide symptomatic relief, the optimal timing and role of biological therapies capable of modifying the intra-articular environment during early disease remain uncertain.^[3]

Platelet-rich plasma (PRP) is an autologous blood-derived orthobiological therapy containing concentrated platelets and a heterogeneous array of bioactive mediators, including platelet-derived growth factor, transforming growth factor- β , and vascular endothelial growth factor. These mediators may influence synovial inflammation, nociceptive signalling, extracellular-matrix homeostasis, and cellular responses within the osteoarthritic joint. Clinical studies and meta-analyses have reported improvements in pain and function following intra-articular PRP, with potentially greater symptomatic responsiveness in patients with less advanced disease.^[4-6] However, substantial heterogeneity in PRP composition, leukocyte content, platelet concentration, preparation techniques, injection protocols, disease phenotype, and outcome assessment limits comparability across studies.^[7] Furthermore, symptomatic improvement should not be equated with structural disease modification, for which evidence remains limited.

Early symptomatic OA may therefore represent a potential therapeutic window in which intervention occurs before advanced structural degeneration. The present prospective observational study evaluated clinical and functional outcomes following a single intra-articular PRP injection in patients with symptomatic early knee OA. The primary outcome was change in WOMAC pain, with secondary assessment of physical function, quality of life, and radiographic Kellgren–Lawrence (KL) grade over 24 weeks.

MATERIALS AND METHODS

Study design and Ethical approval

This prospective observational study was conducted in the Department of Orthopaedics, Government General Hospital, Siddhartha Medical College, Vijayawada, Andhra Pradesh, India, between June 2024 and October 2025. Fifty consecutive patients with symptomatic early knee OA were enrolled, with one affected knee assessed per participant.

The study was approved by the Institutional Ethics Committee of Siddhartha Medical

College/Government General Hospital, Vijayawada (IEC reference: EC/SMC/GGH/2024/AP/088; approval dated 24 April 2024). The study adhered to the Declaration of Helsinki and applicable institutional requirements. Written informed consent was obtained from all participants.

Patient selection

Patients aged 50–75 years with symptomatic knee OA and persistent pain for >6 months despite conventional non-operative treatment were eligible. Early OA was defined by symptomatic disease with radiographic KL grade 1 or 2 changes on standard knee radiographs.

Exclusion criteria included KL grade 3 or 4 OA, active or previous knee infection, severe knee trauma, previous knee surgery, immunocompromising conditions, collagen vascular disease, malignancy, coagulation disorders, anticoagulant or antiplatelet therapy, and intra-articular corticosteroid administration within the preceding 6 months. These criteria were intended to minimize confounding related to advanced structural disease, previous major joint pathology, systemic disease, and recent intra-articular treatment.

PRP preparation and Administration

Approximately 40 mL of peripheral venous blood was collected into tubes containing an appropriate anticoagulant. PRP was prepared immediately before injection using a standardized two-step centrifugation protocol. A first, soft spin centrifugation at 1500 rpm for 15 minutes separated the plasma fraction from erythrocytes, followed by a second hard spin centrifugation at 3500 rpm for 7 minutes to concentrate platelets. The resulting PRP fraction was aspirated, and 5–7 mL was administered as a single intra-articular injection under strict aseptic conditions.

Platelet concentration, leukocyte content, erythrocyte contamination, and other cellular characteristics of the final PRP product were not quantitatively characterized. Accordingly, the intervention is defined by its preparation and administration protocol rather than by a quantified cellular composition.

Patients were advised to rest the treated limb for approximately 24 hours and avoid strenuous activity for 1 week. No additional PRP injection was administered during follow-up.

Clinical and Radiological outcomes

Patient-reported outcomes were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline and at 1, 4, 12, and 24 weeks. The primary outcome was change in WOMAC pain. Secondary outcomes included physical function and quality-of-life measures. The repeated assessments were intended to characterize both early response and persistence of symptomatic improvement over 6 months.

Standard knee radiographs were obtained at baseline and 24 weeks and graded using the KL classification. Radiographic assessment was primarily used to characterize structural disease

severity and explore interval change. Given the short follow-up and limited sensitivity of conventional radiography for early structural alterations, radiographic findings were interpreted independently from symptomatic outcomes.

Statistical Analysis

Continuous variables were summarized using descriptive statistics. Longitudinal changes in WOMAC outcomes were assessed using paired t-tests comparing baseline values with measurements at 4, 12, and 24 weeks. A two-sided $p < 0.05$ was considered statistically significant.

Because the study had no concurrent control group, observed changes were interpreted as temporal associations following PRP administration rather than definitive evidence of treatment efficacy or disease modification. Potential contributions from regression to the mean, natural symptom fluctuation, behavioural modification, concurrent conservative care, and contextual or placebo effects were therefore considered.

RESULTS

Baseline characteristics

Fifty patients were included. Mean age was 62.4 ± 6.8 years (range, 50–75 years), 32 (64%) were women, and mean BMI was 27.8 ± 3.2 kg/m². Eleven participants (22%) had normal BMI, 21 (42%) were overweight, and 18 (36%) had obesity. Mean symptom duration was 2.4 ± 0.8 years. Twenty-one patients (42%) had KL grade 1 disease and 29 (58%) had KL grade 2 disease.

Clinical Outcomes

WOMAC pain demonstrated progressive improvement during follow-up. Mean pain score decreased from 62.5 ± 10.3 at baseline to 48.7 ± 9.6 at 4 weeks, 37.8 ± 8.4 at 12 weeks, and 30.2 ± 7.9 at 24 weeks. The absolute reduction at 24 weeks was 32.3 points, corresponding to a 51.7% relative reduction from baseline ($p < 0.001$).

WOMAC physical-function scores decreased from 61.4 ± 9.5 at baseline to 49.2 ± 8.7 , 38.6 ± 7.9 , and 30.8 ± 7.2 at 4, 12, and 24 weeks, respectively. This represented an absolute reduction of 30.6 points and a 49.8% relative improvement at 24 weeks ($p < 0.001$).

Quality-of-life scores similarly decreased from 58.2 ± 9.1 at baseline to 45.6 ± 8.3 at 4 weeks, 34.7 ± 7.8 at 12 weeks, and 27.3 ± 6.9 at 24 weeks, representing a 53.1% relative improvement at 24 weeks ($p < 0.001$).

Subgroup observations

At 24 weeks, pain reduction was 52.2% among women and 50.9% among men. Patients with KL grade 1 disease demonstrated a numerically greater reduction in pain than those with KL grade 2 disease: 53.8% versus 49.5%, respectively. No formal between-group statistical testing was performed; therefore, these observations are exploratory and hypothesis-generating. Radiographic

KL grading demonstrated minimal short-term change at 24 weeks.

DISCUSSION

The principal finding of this prospective cohort study was progressive improvement in patient-reported pain, physical function, and quality of life over 24 weeks following a single intra-articular PRP injection in patients with symptomatic early knee OA. WOMAC pain, physical function, and quality-of-life measures improved by 51.7%, 49.8%, and 53.1%, respectively. These within-patient changes were statistically significant; however, their interpretation must account for the absence of a control group.

The observed trajectory is broadly consistent with previous clinical studies reporting symptomatic improvement following intra-articular PRP.^[8-12] Comparative trials have also reported benefits relative to saline or hyaluronic acid, although differences in PRP formulation, dosing schedules, patient selection, and outcome measures limit direct comparison.^[9,10] Recent meta-analyses generally support short- to intermediate-term improvements in pain and function following PRP, while also emphasizing substantial methodological heterogeneity.^[11-13] Conversely, placebo-controlled evidence suggests that the magnitude of benefit attributable specifically to PRP may be modest and may diminish over longer follow-up.^[13] These findings reinforce the need to distinguish observed symptomatic improvement from treatment-specific efficacy.

The focus on early OA is an important feature of this study. Restriction to KL grade 1–2 disease identifies a population with symptomatic disease but without advanced radiographic degeneration, potentially representing a clinically relevant therapeutic window. The numerically greater pain reduction observed in KL grade 1 compared with KL grade 2 disease is consistent with the hypothesis that disease stage may influence responsiveness. However, because no formal interaction analysis was performed, this finding cannot establish differential treatment efficacy and should be regarded as hypothesis-generating.

Biological plausibility for PRP in early disease arises from its complex repertoire of growth factors and signalling mediators, which may influence synovial inflammation, cellular signalling, extracellular-matrix turnover, and nociceptive pathways. Nevertheless, PRP is not a standardized biological product. Platelet concentration, leukocyte content, erythrocyte contamination, activation method, injection volume, and dosing frequency vary substantially between studies and may contribute to heterogeneous clinical outcomes.^[7,16] The present study used a reproducible two-step preparation and single-injection protocol, but did not quantitatively characterize the cellular composition

of the final product. This limits mechanistic interpretation and comparability with studies using fully characterized PRP preparations.

The single-injection approach also warrants consideration. Although improvement was observed progressively through 24 weeks, the study was not designed to establish whether repeated injections would provide superior or more durable benefit. Comparative studies of single versus multiple PRP injections have produced heterogeneous findings, emphasizing the need to determine the optimal dosing strategy.^[18]

Importantly, symptomatic improvement should not be interpreted as evidence of cartilage regeneration or disease modification. Conventional radiography showed minimal short-term change, but KL grading has limited sensitivity for detecting early structural alterations and a 24-week interval is insufficient to establish structural progression. Demonstration of disease modification would require longer-term controlled studies incorporating sensitive structural endpoints, such as quantitative MRI, alongside validated clinical outcomes.

This study has several strengths, including its prospective design, predefined early-OA population, standardized single-injection protocol, repeated longitudinal assessment, and inclusion of an Indian patient population that remains relatively underrepresented in the international PRP literature. However, several limitations require consideration. The sample size was modest and the single-centre design limits generalizability. Most importantly, the absence of a placebo or active comparator prevents causal attribution of the observed improvements to PRP. Regression to the mean, natural symptom variation, behavioural changes, concurrent conservative treatment, and contextual effects may have contributed. The 24-week follow-up cannot establish long-term durability or structural disease modification. Furthermore, PRP cellular composition was not quantified, and the study lacked MRI or biochemical biomarkers that could provide mechanistic or structural information. Subgroup analyses were descriptive and were not powered to establish effect modification.

Overall, the findings provide prospective evidence of substantial symptomatic and functional improvement following a single PRP injection in patients with early symptomatic knee OA. They support further investigation of the hypothesis that early-stage disease may represent an important therapeutic window, while recognizing that the present study cannot establish treatment efficacy or disease modification.

CONCLUSION

A single intra-articular PRP injection was associated with progressive improvements in pain, physical function, and quality of life over 24 weeks in patients with symptomatic KL grade 1–2 knee OA.

The findings suggest potential clinical utility of PRP in selected patients with early disease but should be interpreted cautiously given the uncontrolled observational design. Minimal short-term radiographic change further emphasizes the distinction between symptomatic improvement and structural disease modification. Adequately powered multicentre randomized controlled trials incorporating standardized PRP characterization, clinically meaningful responder thresholds, appropriate comparators, and longer-term clinical and structural endpoints are required to define the efficacy, durability, optimal dosing, and potential disease-modifying role of PRP in early knee OA.

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