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Original Research Article

RATIONALE FOR USING PLATELET-RICH PLASMA IN OSTEOARTHRITIS KNEE

Aijaz Ahmed Ganai [1], Suhail Bashir[2], Syeed AalishanFatima[3]

[1]*Senior Resident, Department of Orthopedic, Government Medical College Anantnagl, J&K, India.*
[2]*Senior Resident, Department of Orthopedics, Government Medical College Anantnag, J&K, India.*
[3]*Senior Resident, Department of MD, DNB Radio diagnosis and Imaging, Government Medical College Srinagar, India.*

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Corresponding Author:
Dr. Suhail Bashir,
Senior Resident Department of Orthopedics, Government Medical College Anantnag, J&K, India.
Email:drsuhail624@gmail.com

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ABSTRACT

Background: Osteoarthritis (OA) of the knee is one of the most common causes of chronic pain and disability worldwide. Conventional treatments such as analgesics, NSAIDs, physiotherapy, corticosteroid injections, and viscosupplementation provide only temporary relief and do not address the underlying degenerative process. Platelet-rich plasma (PRP), an autologous concentration of platelets in plasma, is rich in growth factors and cytokines that may stimulate cartilage repair, reduce inflammation, and enhance joint homeostasis. This biological approach has emerged as a promising disease-modifying therapy in knee OA. **Aims:** This study aims to evaluate the rationale, clinical effectiveness, and therapeutic potential of platelet-rich plasma (PRP) in knee osteoarthritis by reviewing the disease pathophysiology and the need for biological therapies beyond conventional options. It analyzes the biological properties of PRP, particularly its growth factor profile and mechanisms in cartilage repair, inflammation modulation, and synovial fluid enhancement. Clinical outcomes of intra-articular PRP will be assessed in terms of pain reduction, functional improvement, and quality of life, with comparison to corticosteroids and hyaluronic acid for efficacy, safety, and durability of response.

Materials and Methods: This study was designed as a prospective, randomized, controlled, triple-blind clinical trial conducted on 70 patients diagnosed with primary knee osteoarthritis (Kellgren–Lawrence grade II–III). Participants were randomly allocated into two groups, with one group receiving intra-articular platelet-rich plasma (PRP) injections and the other receiving standard intra-articular therapy. Triple blinding was ensured at the level of the patient, treating physician, and outcome assessor. All patients were evaluated using standardized clinical outcome measures at baseline and at regular follow-up intervals.

Result: Both PRP and HA groups showed improvement in pain scores, but PRP consistently achieved greater reductions at all follow-up intervals. At 1 month, mean VAS reduction was −2.1 versus −1.2 ($p=0.003$), at 3 months −3.0 versus −1.9 ($p<0.001$), and at the 6-month primary endpoint −3.4 versus −2.1 ($p<0.001$), confirming the superior and sustained pain relief with PRP.

Conclusion: PRP showed superior efficacy over HA, providing greater pain relief, functional improvement, and higher responder rates, with the most notable benefits at 6 months.

Keywords: Platelet-rich plasma, Osteoarthritis knee, Biological therapy, Regenerative medicine, Intra-articular injection, Cartilage regeneration.

INTRODUCTION

Osteoarthritis (OA) of the knee is one of the most prevalent degenerative joint disorders, representing a major cause of pain, disability, and reduced quality of life worldwide. It is characterized by progressive loss of articular cartilage, subchondral bone remodeling, synovial inflammation, and osteophyte formation, ultimately leading to joint stiffness and functional impairment.[1] The increasing prevalence of knee OA, particularly in aging populations, poses a significant socioeconomic burden, as it is one of the leading causes of work disability and healthcare utilization.[2]Conventional treatment strategies, including non-steroidal anti-inflammatory drugs (NSAIDs), physiotherapy, intra-articular corticosteroid injections, and viscosupplementation with hyaluronic acid, primarily target symptomatic relief rather than modifying the disease process [3]. Although total knee arthroplasty remains the definitive treatment for end-stage disease, it is invasive, associated with complications, and not suitable for younger or less severely affected patients, thereby necessitating the exploration of novel biological therapies that may alter disease progression.[4]

In recent years, regenerative medicine has emerged as a promising field in the management of musculoskeletal disorders. Platelet-rich plasma (PRP), an autologous concentration of platelets derived from peripheral blood, has attracted considerable attention as a potential disease-modifying treatment in knee OA.[5]Platelets contain α-granules rich in growth factors, including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor (IGF), which play pivotal roles in tissue repair, angiogenesis, modulation of inflammation, and stimulation of extracellular matrix synthesis.[6]By harnessing these bioactive molecules, PRP offers the potential to promote cartilage regeneration, reduce catabolic processes, and modulate the inflammatory microenvironment within the osteoarthritic joint.[7]

The rationale for using PRP in knee OA is rooted in its multifaceted mechanism of action. First, PRP exerts chondroprotective effects by downregulating pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α), while simultaneously upregulating anti-inflammatory mediators.[8]This shift in the joint milieu helps mitigate synovial inflammation, which plays a critical role in OA pathogenesis. Second, PRP stimulates chondrocyte proliferation and extracellular matrix synthesis, thereby enhancing cartilage repair potential and delaying structural deterioration.[9]Third, PRP improves the viscoelastic properties of synovial fluid by increasing hyaluronic acid production, which translates into better lubrication, reduced friction, and improved joint biomechanics.[10]Collectively, these effects provide a biological basis for symptomatic relief and potential structural modification, distinguishing PRP from conventional intra-articular therapies that only provide transient symptomatic improvement.

Moreover, PRP is an autologous product, which minimizes the risk of immunogenic reactions and disease transmission, making it a relatively safe option compared to allogeneic or synthetic injectables. Clinical studies have reported improvements in pain, stiffness, and functional scores in patients treated with PRP, with some suggesting superiority over corticosteroids and hyaluronic acid, especially in early-to-moderate OA.[5,7,9]While variability in preparation methods, platelet concentration, leukocyte content, and injection protocols has led to heterogeneity in outcomes, accumulating evidence underscores the therapeutic potential of PRP as a minimally invasive, cost-effective, and biologically active alternative to conventional therapies.[6,8]

In this context, the rationale for using PRP in osteoarthritis of the knee lies in its ability to combine symptom relief with biological repair, addressing not only the clinical manifestations but also the underlying degenerative pathology. As research advances and standardized preparation protocols are established, PRP may serve as a valuable adjunct or bridge therapy, delaying the need for surgical interventions and improving the quality of life of patients with knee OA.

The present study aims to evaluate the rationale, clinical effectiveness, and therapeutic potential of platelet-rich plasma (PRP) in the management of osteoarthritis (OA) of the knee. The objectives are to review the underlying pathophysiological basis of knee OA and highlight the limitations of conventional therapies, thereby justifying the need for biological approaches; to analyze the biological properties of PRP, particularly its growth factor composition and mechanisms of action in promoting cartilage repair, modulating inflammation, and enhancing synovial fluid quality; to assess the clinical outcomes of intra-articular PRP injections with respect to pain reduction, functional improvement, and overall quality of life in affected patients; to compare the efficacy, safety, and durability of response of PRP with other commonly used intra-articular modalities such as corticosteroids and hyaluronic acid; and finally, to evaluate PRP as a minimally invasive, autologous, and cost-effective therapeutic strategy with the potential to delay the progression of disease and postpone the need for surgical intervention in osteoarthritis of the knee.

MATERIALS AND METHODS

Study design: A Triple-Blind Randomized Study

Study Design: Department of Orthopedics, Teerthanker Mahaveer Medical College and Research Centre (TMMC&RC).

Duration of study: Was conducted between January 2021- June 2022 after getting clearance from the college Research Centre and ethical committee.

Sample Size: 70 patients

Inclusion Criteria

- Patients with osteoarthritis (OA) knee, Grade II or III according to the Kellgren and Lawrence (K–L) radiographic grading system.
- Patients who fulfilled the American College of Rheumatology (ACR) clinical criteria for the diagnosis of knee osteoarthritis.

Exclusion Criteria

- Patients with previously operated knees.
- Patients with gouty arthritis or other inflammatory arthritides.
- Patients with an active knee infection.
- Patients with anemia, bleeding disorders, or rheumatoid arthritis.
- Patients with genu varum or genu valgum deformity > 5°.
- Patients with uncontrolled diabetes mellitus.
- Patients with ligamentous instability of the knee (confirmed by clinical examination).
- Patients with any malignancy.
- Patients with osteoarthritis involving any other joint

Statistical Analysis: Under the supervision of a statistician, we collected data compiled in an Excel spreadsheet. For statistical analysis, the means and standard deviations of the measurements for each group were used (SPSS 22.00 for windows; SPSS inc, Chicago, USA). The results were statistically examined at each evaluation point using one-way ANOVA. The significance threshold was chosen at p 0.05 for the chi-square test to measure the difference between the two groups.

RESULTS

Table 1: Baseline characteristics (n = 70)

Characteristic	PRP (n=35)	HA (n=35)	p-value
Age, years (mean ± SD)	59.0 ± 8.4	58.1 ± 9.1	0.62
Female, n (%)	19 (54.3)	20 (57.1)	0.82
BMI, kg/m² (mean ± SD)	28.4 ± 3.2	28.7 ± 3.5	0.71
Symptom duration, years (mean ± SD)	4.8 ± 2.3	5.0 ± 2.1	0.58
KL grade II, n (%)	19 (54.3)	18 (51.4)	0.81
KL grade III, n (%)	16 (45.7)	17 (48.6)	0.81
Baseline VAS pain (0–10)	7.1 ± 1.0	7.0 ± 1.1	0.64
Baseline WOMAC total (0–96)	58.2 ± 10.5	57.6 ± 11.1	0.79

Table 2: Primary outcome—change in VAS pain (0–10) from baseline

Time point	PRP Δ (mean ± SD)	HA Δ (mean ± SD)	Between-group Δ (mean, 95% CI)	p-value*
1 month	−2.1 ± 1.2	−1.2 ± 1.1	−0.9 (−1.4 to −0.4)	0.003
3 months	−3.0 ± 1.3	−1.9 ± 1.2	−1.1 (−1.6 to −0.6)	<0.001
6 months (primary)	−3.4 ± 1.4	−2.1 ± 1.3	−1.3 (−1.9 to −0.7)	<0.001

Table 3: Secondary outcomes at 6 months—WOMAC (0–96; higher = worse)

Outcome	PRP (mean ± SD)	HA (mean ± SD)	Mean difference (95% CI)	p-value*
Pain subscale improvement (0–20)	−12.8 ± 5.6	−8.5 ± 5.4	−4.3 (−6.8 to −1.9)	<0.001
Stiffness improvement (0–8)	−4.1 ± 2.2	−2.6 ± 2.1	−1.5 (−2.4 to −0.6)	0.001
Function improvement (0–68)	−26.4 ± 10.3	−17.8 ± 9.8	−8.6 (−13.1 to −4.1)	<0.001
Total WOMAC improvement (0–96)	−43.3 ± 15.2	−28.9 ± 14.6	−14.4 (−21.1 to −7.7)	<0.001

Table 4: Clinical responder and patient-reported outcomes at 6 months

Endpoint	PRP (n=35)	HA (n=35)	Risk difference (95% CI)	p-value
≥50% VAS pain reduction, n (%)	21 (60.0)	11 (31.4)	28.6% (7.6% to 49.6%)	0.010
OMERACT–OARSI responder, n (%)	26 (74.3)	16 (45.7)	28.6% (6.9% to 50.3%)	0.012
Patient satisfied/very satisfied, n (%)	27 (77.1)	20 (57.1)	20.0% (−1.6% to 41.6%)	0.071

Table 5: Safety, rescue medication, and retreatment through 6 months

Event	PRP (n=35)	HA (n=35)	p-value
Post-injection pain/flare, n (%)	8 (22.9)	4 (11.4)	0.21
Transient swelling/effusion, n (%)	5 (14.3)	3 (8.6)	0.71
Any infection, n (%)	0 (0)	0 (0)	—
Any NSAID rescue use, n (%)	9 (25.7)	15 (42.9)	0.12
Additional intra-articular injection requested, n (%)	4 (11.4)	10 (28.6)	0.08
Withdrawals due to AE, n (%)	0 (0)	1 (2.9)	1.00

A total of 70 patients were randomized into the PRP (n=35) and HA (n=35) groups. Baseline demographic and clinical characteristicswere comparable between groups, with no significant differences in age, sex distribution, BMI, symptom duration, Kellgren–Lawrence (KL) grade, baseline

VAS pain scores, or WOMAC totals (Table 1; all p > 0.5).

In terms of the primary outcome (VAS pain reduction), both groups showed improvement, but PRP consistently demonstrated greater pain relief at all follow-up points. At 1 month, mean VAS reduction was −2.1 ± 1.2 in PRP versus −1.2 ± 1.1 in HA (p=0.003). At 3 months, reductions were −3.0 ± 1.3 and −1.9 ± 1.2, respectively (p<0.001). At 6 months (primary endpoint), PRP maintained superior improvement (−3.4 ± 1.4 vs. −2.1 ± 1.3, p<0.001). [Table 2]

Regarding secondary outcomes, WOMAC scores at 6 months showed significantly greater improvement in the PRP group across all domains—pain (−12.8 vs. −8.5, p<0.001), stiffness (−4.1 vs. −2.6, p=0.001), function (−26.4 vs. −17.8, p<0.001), and total WOMAC (−43.3 vs. −28.9, p<0.001). [Table 3]

For clinical responder analysis, a higher proportion of PRP patients achieved ≥50% VAS pain reduction (60.0% vs. 31.4%, p=0.010) and fulfilled OMERACT–OARSI responder criteria (74.3% vs. 45.7%, p=0.012). Patient satisfaction also favored PRP (77.1% vs. 57.1%), though the difference did not reach statistical significance (p=0.071). [Table 4]

With respect to safety and tolerability, both treatments were generally well tolerated. Minor adverse events such as transient post-injection pain or effusion occurred more often with PRP but were self-limiting. No infections were reported. Use of NSAID rescue medication and requests for additional intra-articular injections were numerically higher in the HA group, though not statistically significant. No withdrawals occurred in the PRP arm, whereas one patient in the HA group discontinued due to adverse events. [Table 5]

Overall, PRP demonstrated superior efficacy in pain relief, functional improvement, and responder rates compared with HA, without significant safety concerns.

DISCUSSION

The present study demonstrated that intra-articular PRP provided superior clinical benefits compared with HA in patients with symptomatic knee OA, particularly with respect to pain reduction, functional improvement, and responder rates at 6 months. Our findings are in agreement with several previously published randomized controlled trials. Patel et al,[11] reported significantly greater improvements in VAS and WOMAC scores in the PRP group compared to HA at 6 months, consistent with our observation of a sustained analgesic and functional benefit. Similarly, Raeissadat et al,[12] found that PRP yielded superior WOMAC pain and function outcomes at both 6 and 12 months, supporting the durability of PRP effects beyond the medium term. A meta-analysis by Dai et al,[13] further confirmed that PRP offers greater clinical efficacy than HA, particularly in younger patients and those with lower KL grades, which aligns with our cohort where baseline characteristics were well balanced and still showed PRP superiority. Filardo et al,[14] reported that PRP provided better short-term improvement, but benefits plateaued after 12 months, highlighting the need for longer-term follow-up in our population. Another multicenter trial by Smith,[15] observed a higher proportion of OMERACT–OARSI responders in PRP-treated patients, consistent with our responder analysis (74.3% vs. 45.7%). Moreover, a network meta-analysis by Shen et al,[16] ranked PRP as the most effective injectable for knee OA in terms of pain relief and functional gain, surpassing HA and corticosteroids. Recent prospective studies by Lana et al,[17] and Kon et al,[18] also corroborated our findings, showing that PRP significantly outperformed HA in both pain and function, with safety profiles being comparable between groups. Interestingly, Di Martino et al,[19] reported that although PRP had more frequent transient post-injection reactions, overall tolerability was excellent and no major complications occurred, which mirrors our experience. Collectively, these findings reinforce the growing body of evidence that PRP represents a more effective biological approach to symptom modification in knee OA compared with HA, without significant safety trade-offs. However, as highlighted by Bennell et al,[20] further high-quality, long-term RCTs with standardized PRP preparation protocols are required to establish definitive recommendations for clinical practice.

CONCLUSION

In this randomized comparative study, intra-articular PRP demonstrated significantly superior efficacy over HA in terms of pain relief, functional outcomes, and responder rates at all follow-up intervals, with the most pronounced benefits observed at the 6-month endpoint. PRP was associated with greater reductions in VAS and WOMAC scores, as well as a higher proportion of clinical responders as per both ≥50% VAS reduction and OMERACT–OARSI criteria. While minor transient adverse effects were slightly more frequent with PRP, no serious safety concerns were noted, and overall tolerability remained favorable. Taken together, these findings suggest that PRP is a more effective and safe therapeutic option than HA for the management of knee osteoarthritis.

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