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To study the clinical and radiological outcome of treatment with leukocyte depleted platelet rich plasma and Hyaluronic Acid injections in early to moderate primary osteoarthritis

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Abstract
Introduction: *Osteoarthritis (OA) of the knee is a prevalent degenerative condition characterized by progressive cartilage deterioration and associated symptoms that significantly impact quality of life. Traditional treatments often provide only temporary relief with limited disease-modifying effects. Emerging biological treatments such as platelet-rich plasma (PRP) and hyaluronic acid (HA) injections have shown promise, but comparative evidence regarding their clinical and radiological efficacy remains limited, particularly for combined therapy approaches using leukocyte-depleted PRP formulations.*
Objectives: *To evaluate the clinical and radiological outcomes of treatment with combined leukocyte-depleted platelet-rich plasma (LP-PRP) and hyaluronic acid (HA) injections versus placebo in patients with early to moderate primary knee osteoarthritis over a 12-month follow-up period.*
Case: *In this prospective randomized controlled trial, 60 patients with early to moderate knee OA (Kellgren-Lawrence grades 1-3) were randomly allocated to either the treatment group receiving combined LP-PRP and HA injections (n=30) or the placebo group receiving saline injections (n=30). Patients were assessed at baseline, 3, 6, and 12 months using Visual Analog Scale (VAS) for pain, Knee Injury and Osteoarthritis Outcome Score (KOOS) for functional outcomes, International Knee Documentation Committee (IKDC) score, and MRI Osteoarthritis Knee Score (MOAKS) for cartilage assessment.*
Results: *Despite having higher baseline pain scores and more severe radiographic OA, the treatment group demonstrated significantly better outcomes across all clinical parameters at 12 months compared to the placebo group. The treatment group showed a 67.8% reduction in VAS pain scores (6.53 to 2.1) compared to a worsening in the placebo group (5.17 to 5.88). All KOOS subscales showed significantly greater improvement in the LP-PRP group, with improvements ranging from 60.5% to 72.5% from baseline. MOAKS Cartilage assessment revealed slight improvement in the treatment group (1.23 to 1.10) while the placebo group deteriorated (1.27 to 1.83, p=0.001).*
Conclusion: *Combined LP-PRP and HA injections provide superior clinical and radiological outcomes compared to placebo for patients with early to moderate knee OA over a 12-month follow-up period.*
Keywords: *Knee osteoarthritis; Platelet-rich plasma; Leukocyte-depleted PRP; Hyaluronic acid; Disease modification; MOAKS; KOOS; Visual analog scale; Cartilage regeneration*

INTRODUCTION

Millions of people worldwide suffer from osteoarthritis (OA), a serious global health concern that causes

severe physical impairment and financial hardship due to increasing joint degradation.[1] With an estimated global prevalence of 10-15% in persons over 45, osteoarthritis is the most common chronic joint disease, especially affecting weight-bearing joints like the knees and hips.[2] Biomechanical, inflammatory, and metabolic processes interact intricately in the multiple pathophysiological pathways of osteoarthritis, with the condition progressing due to a combination of subchondral bone remodeling, cartilage degradation, synovial inflammation, and altered joint biomechanics.[3]

Promising therapeutic options that target the underlying mechanisms of disease have been offered by recent developments in regenerative medicine. Injections of hyaluronic acid (HA) and leukocyte-depleted platelet-rich plasma (LD-PRP) are novel treatments that may be able to alter illness.[4] Rich in growth factors and bioactive proteins, platelet-rich plasma has the ability to promote cartilage healing, reduce inflammation, and stimulate tissue repair. A crucial component of synovial fluid, hyaluronic acid offers lubrication, stress absorption, and the potential to lessen inflammatory reactions in the joint environment.[5] The complementary modes of action of LD-PRP and HA provide justification for their combination, with PRP encouraging tissue regeneration and providing growth factors, while HA supports the joint structurally and biochemically, which may result in a synergistic therapeutic effect.[6]

A multimodal strategy to managing OA is advised by current clinical guidelines, with a focus on patient education, weight control, physical activity, and pharmaceutical therapies.[7] However, current therapies frequently fail to successfully stop the progression of the disease and offer only modest long-term relief. Hope for more thorough and possibly disease-modifying treatments is raised by the possibility of regenerative techniques like LD-PRP and HA injections. In patients with early to intermediate primary osteoarthritis, the goal of this study was to thoroughly assess the clinical and radiological results of combination LD-PRP and HA injections through systematic evaluation of functional enhancement, pain alleviation, and possible structural alterations.[8]

METHODOLOGY

This prospective randomized controlled trial was conducted in the Department of Orthopedics at Dr. D.Y. Patil Medical College, Pimpri, Pune, Maharashtra, from December 2023 to January 2025. The study was approved by the institutional ethics committee and informed consent was obtained from all participants. Sixty patients with early to moderate knee OA (Kellgren-Lawrence grades 1-3) were recruited and randomly allocated to either the treatment group (n=30) or placebo group (n=30).

Inclusion criteria comprised symptomatic knee osteoarthritis (Kellgren-Lawrence Grade 1, 2, and 3), patients aged 30-70 years, no ligament laxity, and no previous knee surgery within 2 years. Exclusion criteria included immunosuppressed patients, serious pre-existing medical conditions like diabetes mellitus or rheumatoid arthritis, secondary osteoarthritis, pregnancy, previous injections within 6 months, and positive infectious disease markers.

The intervention protocol involved preparation of autologous platelet-rich plasma from approximately 350ml of patient's venous blood by the Department of Transfusion Medicine. A specialized leukocyte depletion process was employed to create leucocyte-poor PRP concentrated to eight to ten times the baseline platelet value. The treatment group received 5ml of leucocyte-poor PRP combined with 6ml of high molecular weight hyaluronic acid (22mg/ml) injected into the supra patellar pouch under sterile conditions. The placebo group received 8ml of normal saline injection in the contralateral knee.

Patient assessments were conducted at baseline, 3, 6, and 12 months using comprehensive outcome measures including Visual Analog Scale (VAS) for pain assessment, Knee Injury and Osteoarthritis Outcome Score (KOOS) with five subscales (Pain, Symptoms, Activities of Daily Living, Sports, Quality of Life), International Knee Documentation Committee (IKDC) scores, and MRI Osteoarthritis Knee Score (MOAKS) for cartilage assessment at baseline, 6, and 12 months. Statistical analysis was performed using SPSS 20, with statistical significance set at $p < 0.05$.

RESULTS

Patient Demographics and Baseline Characteristics

Both groups demonstrated comparable demographic profiles with no significant differences in age distribution (p=0.951) or gender distribution (60% female in each group). However, the treatment group

had significantly more severe osteoarthritis cases, with 33.3% having Kellgren-Lawrence Grade 3 compared to only 3.3% in the placebo group (p=0.010). Duration of symptoms was comparable between groups (p=0.525), with the majority experiencing symptoms for 3-5 years.

Table 1: Pain Assessment (VAS Scores)

Time Point	Treatment Group	Placebo Group	P value
Baseline	6.53 ± 1.47	5.17 ± 1.05	<0.001
3 months	4.03 ± 2.17	6.63 ± 2.32	<0.001
6 months	2.7 ± 2.08	6.13 ± 2.3	<0.001
12 months	2.1 ± 2.01	5.88 ± 2.32	<0.001

Table 2: Functional Outcomes (KOOS Subscales at 12 months)

KOOS Domain	Treatment Group	Placebo Group	P value	% Improvement (Treatment)
Pain	85.22 ± 11.14	63.59 ± 9.9	<0.001	62.0%
Symptoms	81.75 ± 11.66	66.35 ± 9.72	<0.001	60.5%
ADL	86.96 ± 9.83	63.36 ± 9.84	<0.001	62.3%
Sports	82.27 ± 12.09	55.56 ± 10.58	<0.001	71.9%
QOL	76.78 ± 12.48	54.23 ± 9.89	<0.001	72.8%

Table 3: Radiological Outcomes (MOAKS Cartilage Scores)

Time Point	Treatment Group	Placebo Group	P value
Baseline	1.23 ± 0.858	1.27 ± 1.11	0.897
6 months	0.9 ± 0.88	1.83 ± 1.08	0.001
12 months	0.9 ± 0.88	1.83 ± 1.08	0.001

Table 4: IKDC Scores and Safety Profile

Parameter	Treatment Group	Placebo Group	P value
IKDC 12 months	66.8 ± 9.18	59.8 ± 6.5	0.001
Adverse Events:			0.194
None	27 (90%)	25 (83.3%)	
Mild Pain	3 (10%)	2 (6.7%)	
Swelling	0	3 (10%)	

Patients were evaluated using validated outcome measures at predetermined intervals. Pain was assessed using the Visual Analog Scale (0-10). Functional outcomes were measured using the comprehensive KOOS questionnaire covering five domains. Radiological assessment utilized MOAKS scoring for cartilage integrity on MRI. IKDC scores provided additional functional assessment. Statistical comparisons between groups were performed using appropriate tests with significance set at $p<0.05$.

DISCUSSION

The results of this randomized controlled trial demonstrate that combined LP-PRP and HA treatment provides superior clinical and radiological outcomes compared to placebo in patients with early to moderate knee osteoarthritis. Despite the treatment group having more severe baseline disease (higher proportion of KL Grade 3) and higher initial pain scores, they achieved remarkable improvements across

all outcome measures. The 67.8% reduction in VAS pain scores in the treatment group contrasts sharply with the worsening observed in the placebo group, suggesting genuine therapeutic benefits beyond placebo effects. This magnitude of improvement exceeds previous studies of either LP-PRP or HA alone, with Sánchez et al. reporting only 33.4% pain reduction with LP-PRP alone and Görmeli et al. demonstrating 44.2% improvement with PRP compared to 16.5% with controls.[9,10] The enhanced pain relief likely reflects synergistic mechanisms, with LP-PRP providing growth factors that modulate inflammation and promote tissue healing, while HA improves joint lubrication and exerts direct anti-inflammatory effects through CD44 receptor binding.[11]

The comprehensive functional improvements observed across all KOOS domains (60.5% to 72.8% improvement) indicate clinically meaningful benefits that extend beyond pain relief to impact daily activities, sports participation, and quality of life. These improvements exceed the minimal clinically important differences established for KOOS subscales and surpass results from previous combination therapy studies.[12] The progressive nature of improvement throughout the 12-month follow-up period suggests sustained therapeutic effects, contrasting with many injectable treatments that show peak efficacy at 3-6 months followed by gradual symptom return. This pattern aligns with mechanistic studies demonstrating that PRP can reduce synovial cell production of inflammatory mediators while stimulating HA synthesis, potentially creating positive feedback loops that enhance and prolong therapeutic effects.[13] The superior functional outcomes likely result from complementary actions addressing both biochemical and biomechanical aspects of OA pathophysiology.

Perhaps most significantly, the MOAKS cartilage assessment revealed potential disease-modifying effects, with the treatment group showing cartilage improvement while the placebo group demonstrated progressive deterioration. This finding is particularly noteworthy as cartilage damage has traditionally been considered irreversible in OA. Previous studies of either LP-PRP or HA alone typically reported stabilization but not improvement in cartilage status, suggesting that combined treatment may offer enhanced chondroprotective or chondroregenerative effects.[14,15] The mechanism likely involves LP-PRP providing growth factors that stimulate chondrocyte proliferation and matrix synthesis, while HA creates a favorable microenvironment for these regenerative processes and potentially serves as a scaffold for tissue repair. Both treatments demonstrated favorable safety profiles with no serious adverse events, confirming the safety of this combined approach and supporting its clinical utility across diverse patient populations.[16]

CONCLUSION

This prospective randomized controlled trial demonstrates that combined leukocyte-depleted platelet-rich plasma (LP-PRP) and hyaluronic acid (HA) injections provide significantly superior clinical and radiological outcomes compared to placebo in patients with early to moderate knee osteoarthritis over a 12-month follow-up period. The treatment group achieved a remarkable 67.8% reduction in pain scores and comprehensive functional improvements ranging from 60.5% to 72.8% across all KOOS domains, despite starting with more severe disease. Most importantly, radiological assessment revealed potential disease-modifying effects, with cartilage improvement in the treatment group contrasting with deterioration in the placebo group, suggesting this combination therapy may not only provide symptomatic relief but potentially alter disease progression. The favorable safety profile, with minimal adverse events and no serious complications, supports the clinical utility of this approach. These findings establish combined LP-PRP and HA as an effective and safe treatment option for knee osteoarthritis, offering hope for disease modification beyond conventional symptomatic treatments and warranting incorporation into treatment algorithms for patients seeking alternatives to traditional therapies.

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IMAGES

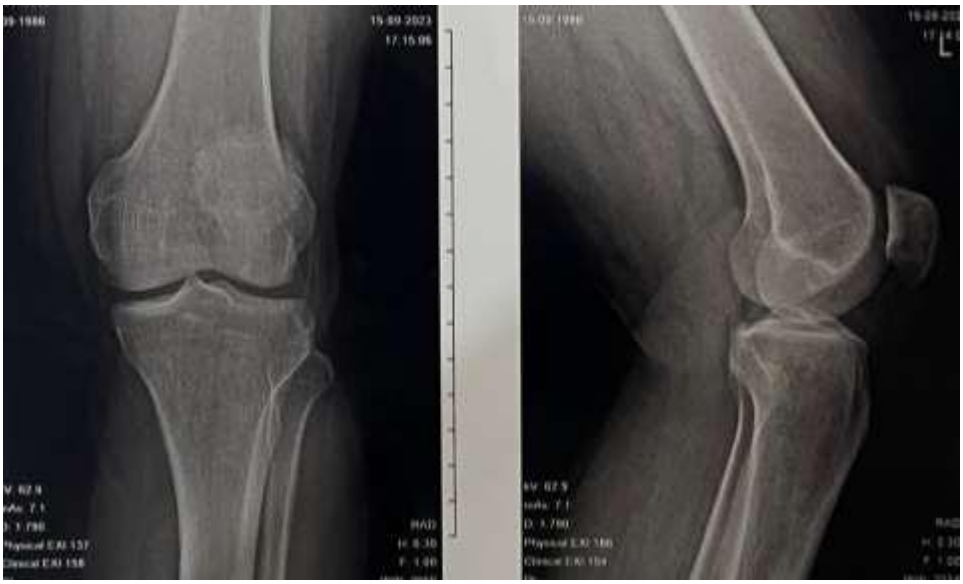

Figure 1: X-ray showing grade 2 OA

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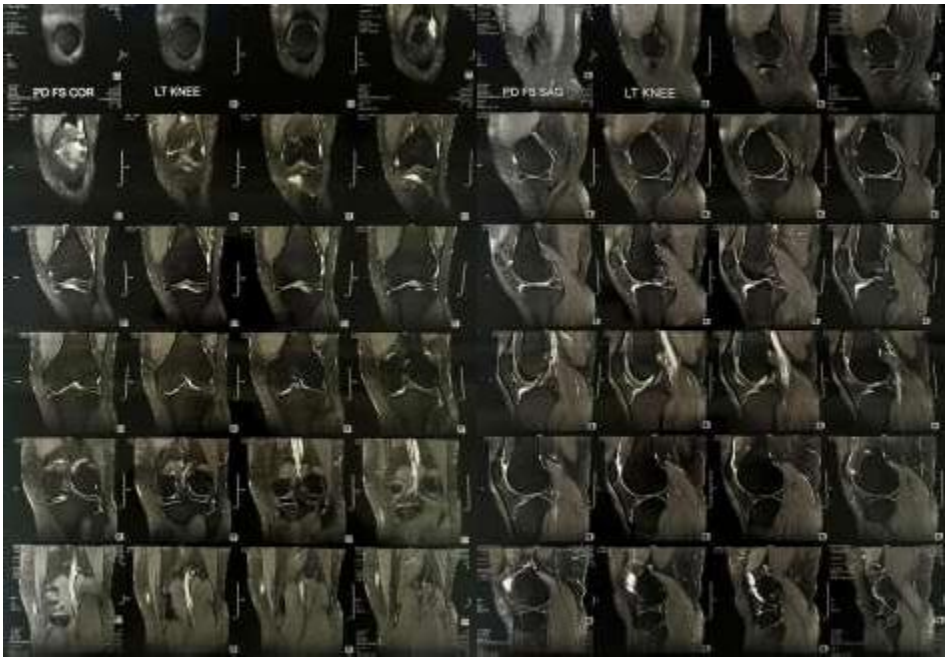

Figure 2: MRI showing damage to the articular cartilage of knee joint


Figure 3: Showing venesection procedure.

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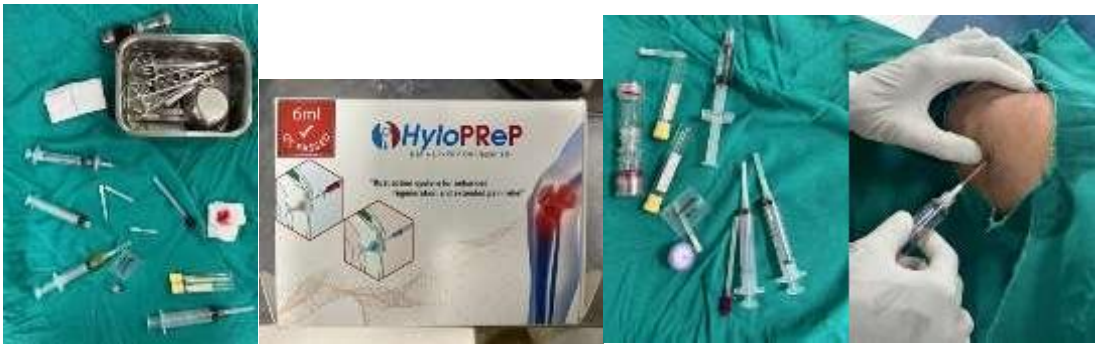
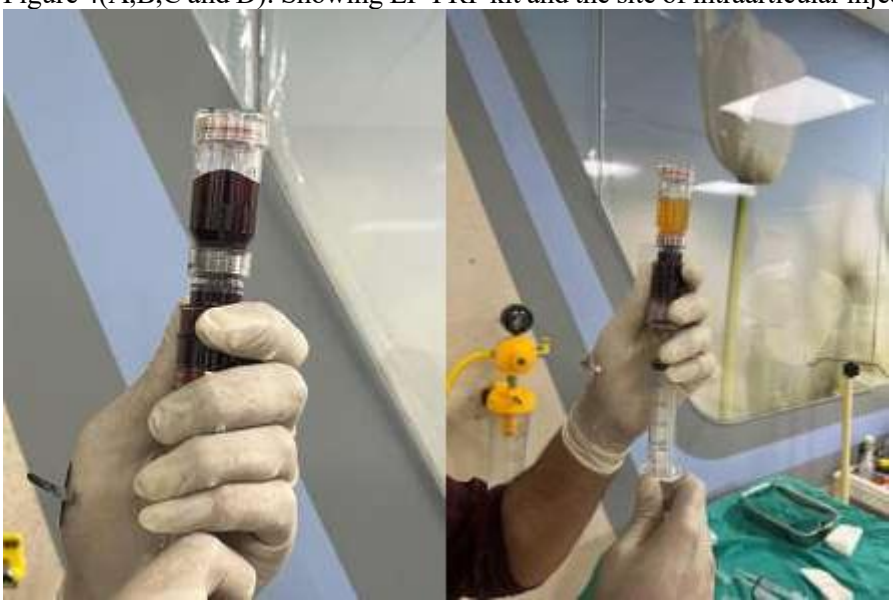


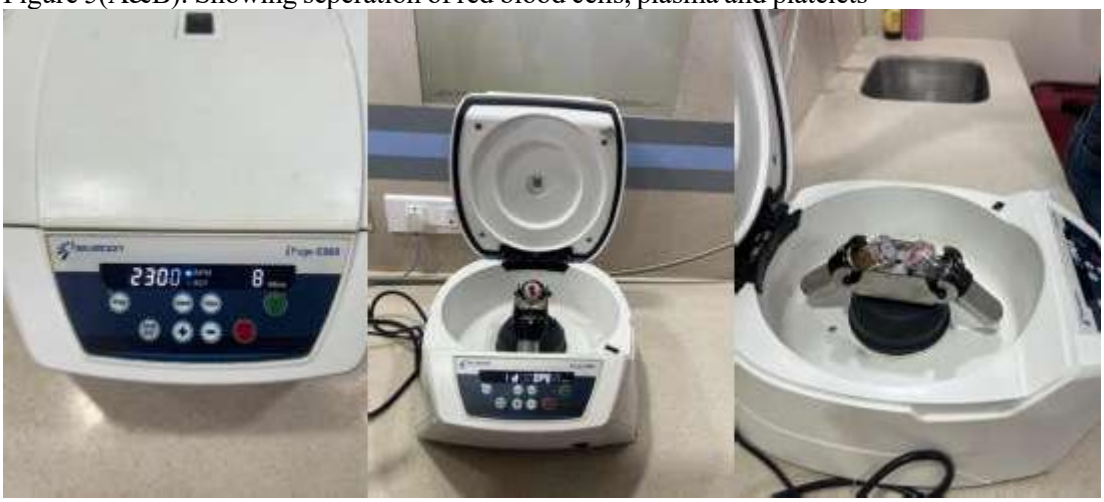
4A 4B 4C 4D

Figure 4(A,B,C and D): Showing LP-PRP kit and the site of intraarticular injection



5A 5B

Figure 5(A&B): Showing seperation of red blood cells, plasma and platelets



6A 6B 6C

Figure 6(A,B & C): Showing centrifugation of blood

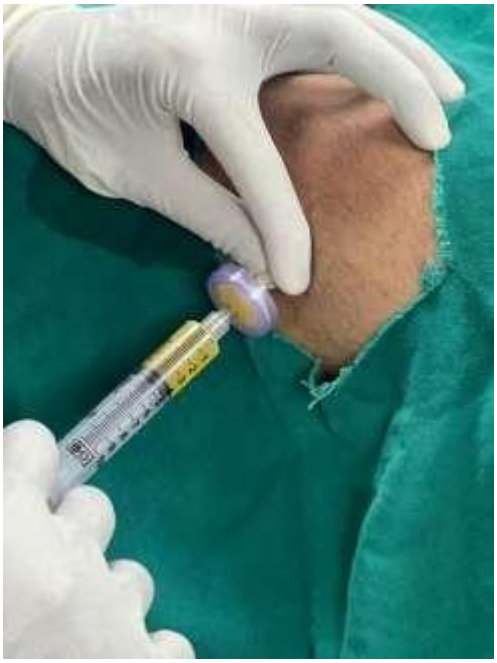


Figure 7: Showing injection of LP-PRP and HA and filter which separates platelets from PRP

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