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EFFECTIVENESS OF PLATELET RICH PLASMA FOR THE MANAGEMENT OF GRADE I, II, III AND IV KNEE OSTEOARTHRITIS

Original Research

Tariq Aziz[1]*
[1]Orthopedic Surgeon, Khyber Teaching Hospital Peshawar, Pakistan.
Corresponding Author: Tariq Aziz, Orthopedic Surgeon, Khyber Teaching Hospital Peshawar, Pakistan. nazargull.ta@gmail.com
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ABSTRACT

Background: Osteoarthritis is the most prevalent degenerative joint disease, characterized by cartilage degradation, pain, and functional impairment. Conventional treatments provide symptomatic relief but do not halt disease progression. Platelet-rich plasma (PRP) is emerging as a regenerative therapy due to its high concentration of growth factors, which promote tissue repair and inflammation modulation. The potential benefits of PRP in managing knee osteoarthritis warrant further clinical evaluation.

Objective: To determine the effectiveness of platelet-rich plasma in the management of knee osteoarthritis across different severity grades.

Methods: A prospective, double-blind, randomized, placebo-controlled trial was conducted at the Department of Orthopedics, Khyber Teaching Hospital, from December 2022 to July 2023, following ethical approval. A total of 104 individuals aged ≥35 years with radiographically confirmed knee osteoarthritis and persistent knee pain were enrolled. Participants were randomized into two groups: PRP (5 mL intra-articular PRP injections) and NS (5 mL intra-articular normal saline injections), administered weekly for three weeks. Pain severity was assessed at baseline, one, three, and six months post-treatment using the 100 mm Visual Analogue Scale (VAS). Statistical analysis was performed using SPSS 22.0, with a chi-square test for treatment efficacy ($p<0.05$ considered significant).

Results: At baseline, the mean VAS score was 52.2±16.9 in the PRP group and 50.9±14.8 in the NS group ($p=0.636$). In the PRP group, VAS scores significantly decreased to 42.6±16.2 at one month ($p=0.0203$), 29.54±11.8 at three months ($p<0.0001$), and 19.2±8.6 at six months ($p<0.0001$). The NS group showed minimal pain reduction with VAS scores of 47±22.7 at one month ($p=0.6714$), 44±16.6 at three months ($p=0.1123$), and 41±21.7 at six months ($p=0.0615$). PRP therapy demonstrated significantly greater effectiveness, with 47 individuals achieving >50% pain reduction compared to 16 in the NS group ($p<0.0001$).

Conclusion: Platelet-rich plasma is an effective treatment for knee osteoarthritis, significantly reducing pain and improving joint function. The findings support PRP as a promising alternative to conventional therapies, particularly in individuals with moderate disease severity.

Keywords: Knee osteoarthritis, Pain management, Platelet-rich plasma, PRP therapy, Regenerative medicine, Visual analogue scale, Intra-articular injection.

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INTRODUCTION

Osteoarthritis (OA) is a progressive degenerative joint disorder characterized by the erosion of articular cartilage, leading to pain, stiffness, inflammation, and reduced mobility. It primarily affects large synovial joints, with knee osteoarthritis being the most prevalent form, particularly among the elderly. As the disease advances, the loss of cartilage results in direct bone-on-bone contact, causing significant discomfort and functional impairment. While aging remains the primary risk factor, other contributing elements include obesity, genetic predisposition, joint trauma, and biomechanical stress. Additionally, factors such as repeated missed doses of steroids have been associated with joint laxity, muscle weakness, and osteoporosis, further exacerbating disease progression (1,2). Knee osteoarthritis is a significant public health concern, particularly in the United States, where approximately 10% of men and 13% of women over the age of 60 experience symptomatic knee OA. With an aging global population and rising obesity rates, the prevalence of OA is expected to increase substantially in the coming years. Despite its widespread occurrence, the exact burden of the disease in many regions remains unclear. Large-scale epidemiological studies are essential to accurately determine the incidence and identify at-risk populations. Currently, diagnosis is primarily based on clinical evaluation and radiographic findings, with X-ray imaging serving as the gold standard for confirming OA-related structural changes (3-5).

The symptomatic burden of knee OA extends beyond pain and stiffness, often leading to significant functional limitations, deformities, and a diminished quality of life. The Framingham study reported that 6.8% and 4.9% of individuals aged 26 and above experienced wrist and knee OA incidents, respectively. However, the Johnston County Osteoarthritis Project found a much higher prevalence, with 16.7% of participants aged 45 and older diagnosed with knee OA. Estimating the true prevalence is further complicated by the fact that OA predominantly affects older adults who frequently present with multiple comorbidities, making differential diagnosis challenging (6). Management of knee OA includes conservative treatments such as physical therapy, weight management, and pharmacological interventions, but these approaches often provide only temporary relief. For advanced cases, invasive procedures like total knee arthroplasty remain the definitive treatment. However, emerging regenerative therapies, particularly platelet-rich plasma (PRP), have shown promise in improving joint function and delaying surgical intervention. PRP, an autologous concentration of platelets derived from the patient's blood, is rich in growth factors that facilitate tissue repair, reduce inflammation, and promote cartilage regeneration. Clinical studies have demonstrated its effectiveness in alleviating pain and improving knee function. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) revealed that PRP treatment led to a 41.7% improvement in knee scores at six months, increasing to 55.9% at one year. Pain levels, as measured by the Visual Analogue Scale (VAS), decreased by 56.2% at six months and 58.9% at one year. Functional mobility also showed notable enhancement, with a 24.3% improvement in overall functional scores and a significant increase in daily living scores by 46.8% at six months and 55.7% at one year (7). Knee OA is highly prevalent in Pakistan, imposing a considerable burden on the healthcare system and affecting the quality of life of individuals. Given the limitations of conventional treatments and the need for cost-effective, minimally invasive therapeutic alternatives, this study aims to evaluate the effectiveness of PRP in managing Grade I, II, III, and IV knee OA. By assessing its impact on pain reduction, functional outcomes, and disease progression, this research seeks to provide evidence-based insights into the role of PRP as a potential therapeutic option for knee OA management (8).

METHODS

A prospective, double-blind, randomized, placebo-controlled trial was conducted at the Department of Orthopedics, Khyber Teaching Hospital, from December 2022 to July 2023, following approval from the institutional ethical committee. The study aimed to assess the effectiveness of platelet-rich plasma (PRP) in managing knee osteoarthritis (OA) across different severity grades. Written informed consent was obtained from all participants before enrollment, ensuring adherence to ethical guidelines (9). Individuals of both genders, aged 35 years and above, with a clinical history of knee pain persisting for six to twenty-four months, resistance to nonsteroidal anti-inflammatory drugs (NSAIDs), and radiographic confirmation of knee OA were included. Exclusion criteria comprised individuals who had received intra-articular knee injections of hyaluronic acid (HA) within the past 12 months, hemoglobin levels below 11 mg/dL, platelet counts below 150,000/μL, coagulopathies, ongoing anticoagulant therapy, or any hematological disorders. All participants were advised to continue physiotherapy and knee exercises as part of standard OA management. Additionally, supportive medication of no more than 1 g of paracetamol was permitted when necessary (10).

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Participants were randomized into two groups: the PRP group and the normal saline (NS) group, which served as the control. Each participant in the PRP group received 5 mL of autologous PRP, while those in the control group received 5 mL of normal saline. Randomization was performed to ensure baseline characteristics, including age, gender, height, weight, body mass index (BMI), and pre-injection visual analogue scale (VAS) scores, were comparable between the groups (11). For PRP preparation, 20 mL of venous blood was drawn from each participant using a syringe preloaded with 0.5 mL of heparin. The blood sample was divided equally into three sterile tubes and subjected to a two-step centrifugation process. The first centrifugation was performed at 1800 rpm for 15 minutes to separate erythrocytes, after which the supernatant, along with the buffy coat, was transferred into another sterile tube for further processing. A second centrifugation cycle was carried out at 3500 rpm for 10 minutes to concentrate platelets. The lower fraction, rich in platelets, was extracted into a sterile syringe for intra-articular injection, while the upper platelet-poor plasma (PPP) was discarded. PRP was activated with a few drops of 10% calcium chloride immediately before injection to enhance its therapeutic effect (12).

The intra-articular injection procedure was standardized for all participants. Each patient was positioned supine with the knee flexed at approximately 90 degrees. Using anatomical landmarks, a 20-gauge needle was inserted caudally and medially into the knee joint via the lateral patellar approach. Following the injection, participants were instructed to move their knee to facilitate the even distribution of the injected substance. Patients were advised to avoid strenuous activities for a few hours post-injection and were encouraged to engage in light physical activity thereafter. The use of NSAIDs was strictly prohibited for 48 hours following each injection to prevent interference with the treatment effects (13). Each participant received a total of three intra-articular injections at weekly intervals. Pain levels were assessed using the 100 mm visual analogue scale (VAS) at baseline, one month, three months, and six months after the completion of treatment. On the VAS scale, 0 indicated no pain, while 100 represented extreme pain. The treatment was considered "effective" if the pain reduction exceeded 50% from baseline at the six-month follow-up. Additionally, adverse effects related to the treatment were monitored throughout the study period. The evaluator, blinded to the treatment assignments, conducted all assessments to maintain objectivity (14). Data were analyzed using SPSS version 22.0. Descriptive statistics were used to summarize demographic and clinical characteristics. The chi-square test was applied to compare the effectiveness of PRP and normal saline groups. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 104 individuals were included in the study to evaluate the effect of platelet-rich plasma (PRP) treatment for the management of knee osteoarthritis. Among them, 65 (62.5%) were females, and 39 (37.5%) were males. The mean baseline pain score on the Visual Analogue Scale (VAS) was 52.2 ± 16.9 in the PRP group and 50.9 ± 14.8 in the normal saline (NS) group. There was no statistically significant difference in baseline VAS scores between the two groups ($p = 0.636$). The demographic and clinical characteristics of participants, including sex, age, disease duration, and body mass index (BMI), were analyzed. The classification of osteoarthritis stages, gender distribution, and disease duration did not show any statistically significant difference between the two groups ($p > 0.05$). VAS scores were measured at baseline and at one, three, and six months post-treatment. In the PRP group, the VAS score decreased from 52.2 ± 16.9 at baseline to 42.6 ± 16.2 at the one-month follow-up, a statistically significant reduction ($p = 0.0203$). This trend continued, with scores further decreasing to 29.54 ± 11.8 at three months and 19.2 ± 8.6 at six months ($p < 0.0001$ for both comparisons). Conversely, in the NS group, the VAS score showed only a slight decrease from 48.8 ± 19.5 at baseline to 47 ± 22.7 at one month ($p = 0.6714$), followed by reductions to 44 ± 16.6 at three months ($p = 0.1123$) and 41 ± 21.7 at six months ($p = 0.0615$), none of which were statistically significant. These findings indicate that PRP therapy resulted in a substantial improvement in pain reduction compared to the NS group.

Pain reduction of more than 50% from baseline at the six-month follow-up was considered an indicator of effective treatment. In the PRP group, 47 individuals (out of 52 participants) experienced significant pain relief, whereas only 16 individuals in the NS group showed comparable improvement. PRP therapy demonstrated superior effectiveness, and this difference was statistically significant ($p < 0.0001$), as confirmed by the chi-square test. Further analysis of potential effect modifiers showed that treatment effectiveness was significantly associated with age < 50 years ($p < 0.0001$), female gender ($p = 0.021$), osteoarthritis grade III ($p = 0.04$), and disease duration of less than five years ($p = 0.03$). However, there was no statistically significant association between BMI and treatment effectiveness ($p = 0.511$).

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Table 1: Demographic features of the study population

Features	Group of Platelet rich plasma	Group of normal saline	Value of P
Age in years	61.04±5.8	59.7±4.10	0.133
Weight in kilogram	83.13±8.7	80.6±7.8	0.082
Height (cm)	164.02±8.8	158.96±7.0	0.05
Body mass index	28.8±5.8	33.3±7.8	0.18
Disease duration	10.3±3.7	9.6±3.2	0.237
visual analogue scale score	52.2±16.9	50.9±14.8	0.66

Table 2: Study subjects' frequency

Features	Plasma group	Normal saline group	Total	Value of P
Age (years)				
<50	20	25	45	0.419
≥50	32	27	59	
Gender				
Male	18	21	39	0.681
Female	34	31	65	
Osteoarthritis grade				
II	14	10	24	0.27
III	19	27	46	
IV	19	15	34	
Duration of disease (years)				
<5	33	39	72	0.28
≥5	20	14	34	
Body mass index (kg/m2				
Overweight	7	5	12	0.81
Normal	11	26	37	
Obese	34	21	55	

Table 3: Relationship between the type of intervention and treatment efficacy

Type of intervention	Therapy effectiveness		Total
	Yes	No	
Platelet rich plasma group	47	5	52
Normal saline group	16	36	52
Total	63	41	104

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Table 4: Effect modifiers' correlation with therapy efficacy

Factor	Effectiveness of therapy		Total	Value of P
	Yes	No		
Age in years				
Below 50	38	7	45	Less than 0.0001
50 or above	25	34	59	
Sex				0.021
Female	32	32	64	
Male	30	10	40	
Grade of osteoarthritis				
II	17	7	24	0.04
III	31	15	46	
IV	15	19	34	
Disease duration in years				0.03
Below 5	49	23	72	
5 or above	14	18	32	
BMI(Kg per m2)				
Normal	7	5	12	0.511
Overweight	25	12	37	
Obesity	31	24	55	

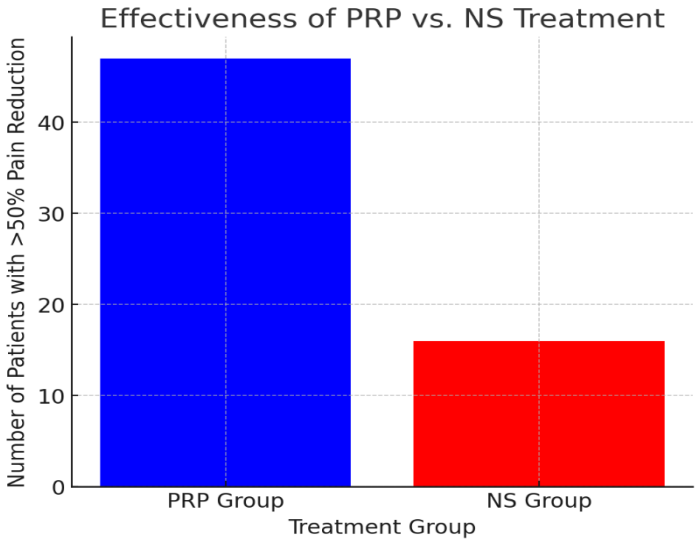

Figure 2 Effectiveness of PRP VS NS Treatment

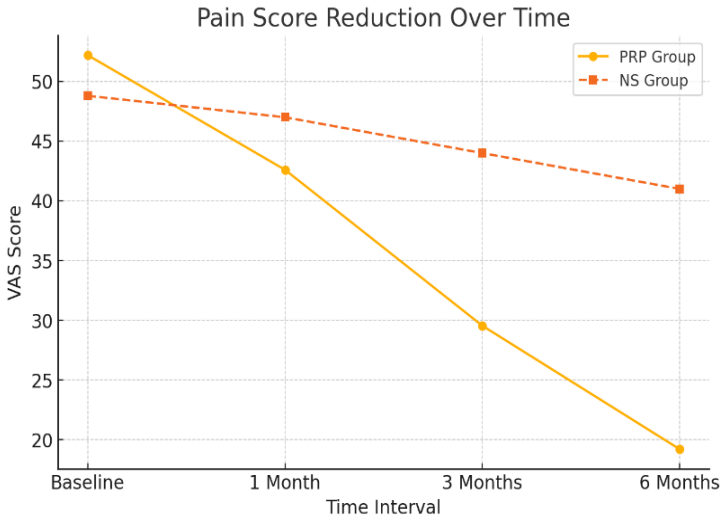

Figure 1 Pain Score Reduction Over Time

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DISCUSSION

Platelet-rich plasma (PRP) has emerged as a promising regenerative therapy in the management of musculoskeletal conditions, particularly in orthopedic and sports medicine. Its application in knee osteoarthritis has gained traction due to its potential to enhance tissue repair and modulate inflammation. PRP contains a high concentration of bioactive molecules, including transforming growth factor-beta (TGF-β1), vascular endothelial growth factor (VEGF), and platelet-derived growth factor (PDGF), which play a pivotal role in cellular proliferation, chondrocyte activation, and extracellular matrix synthesis. When administered intra-articularly, PRP is believed to facilitate cartilage healing and improve joint function by counteracting the degenerative processes of osteoarthritis (8). The findings of this study indicate that PRP is significantly more effective than normal saline in reducing knee pain and improving function among individuals with osteoarthritis. A substantial reduction in VAS scores was observed in the PRP group, with pain relief being sustained over six months. This aligns with existing literature, where PRP has been reported to provide prolonged symptom relief compared to placebo interventions. A previous randomized trial comparing PRP with hyaluronic acid (HA) demonstrated superior outcomes in terms of pain reduction and functional improvement, supporting the efficacy of PRP in osteoarthritis management (9). Another comparative study between PRP and corticosteroids showed that PRP-treated individuals exhibited greater long-term pain relief, reinforcing its regenerative potential over traditional anti-inflammatory therapies (10).

Despite these positive findings, some studies have reported mixed results regarding PRP efficacy, particularly in individuals with advanced osteoarthritis. A clinical trial evaluating PRP in individuals with high-grade osteoarthritis (Kellgren-Lawrence grades III–IV) found that pain reduction, though present, was less pronounced compared to individuals with early-stage disease. This observation aligns with the current study, where PRP demonstrated higher effectiveness in individuals with osteoarthritis grade III compared to grade IV. The diminished response in advanced cases could be attributed to extensive cartilage erosion and reduced chondrocyte viability, limiting PRP's regenerative potential (11,15). Age and disease duration were found to significantly influence treatment effectiveness in this study. Individuals younger than 50 years and those with a disease duration of less than five years exhibited better therapeutic responses. These findings are in agreement with prior research suggesting that younger individuals with early-stage osteoarthritis respond favorably to PRP due to the presence of a more viable chondrocyte population and a greater capacity for tissue regeneration (12). Conversely, studies have suggested that individuals with prolonged disease duration and severe cartilage degeneration may require adjunctive treatments such as mesenchymal stem cell therapy or surgical interventions to achieve meaningful clinical improvement (13,16).

One of the notable strengths of this study is its randomized, double-blind, placebo-controlled design, which minimizes bias and enhances the reliability of the results. The study also maintained strict inclusion and exclusion criteria, ensuring a homogenous participant population and reducing confounding variables. The assessment of treatment efficacy at multiple time points allowed for a comprehensive evaluation of PRP's effects over six months. However, certain limitations must be acknowledged. The sample size, while adequate for statistical analysis, may not fully capture variations in treatment response across different subgroups. Additionally, the study relied on VAS scores for pain assessment, which, although widely used, remains a subjective measure. Functional scores such as the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) or knee range of motion evaluations could provide a more detailed understanding of PRP's impact on joint function. Future studies incorporating these parameters would enhance the robustness of findings (14,17). Adverse effects associated with PRP were minimal in this study, with only mild post-injection pain and swelling reported, which resolved within 48 hours. This safety profile is consistent with previous reports, where PRP has been well-tolerated with no serious complications. The favorable risk-benefit ratio of PRP further strengthens its role as a viable therapeutic alternative for knee osteoarthritis, particularly in individuals seeking non-surgical interventions. Future research should explore optimizing PRP protocols, including the number of injections, concentration of platelets, and combination therapies, to maximize clinical benefits (15,18-20). The findings suggest that PRP is an effective and well-tolerated intervention for knee osteoarthritis, particularly in younger individuals and those with moderate disease severity. While PRP demonstrates significant pain relief and functional improvement, its efficacy in advanced osteoarthritis remains limited. Further investigations with larger sample sizes, longer follow-up durations, and objective functional assessments are warranted to refine PRP treatment strategies and establish standardized protocols for clinical practice.

CONCLUSION

This study highlights platelet-rich plasma as a viable therapeutic option for managing knee osteoarthritis, demonstrating its potential to significantly alleviate symptoms and improve joint function. The treatment showed the greatest effectiveness in individuals with moderate disease severity and shorter disease duration, reinforcing its role as a regenerative intervention that may delay the need for

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invasive procedures. The findings support the growing evidence that PRP can serve as a promising, minimally invasive approach for symptom relief in osteoarthritis, particularly for individuals seeking alternatives to conventional pharmacologic and surgical treatments.

AUTHOR CONTRIBUTIONS

Author	Contribution
Tariq Aziz*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published

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