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Original Article

A Comparison of Intra-Articular Platelet-Rich Plasma, Steroids and Normal Saline Injection in Treatment of Grade 2 and 3 Knee Osteoarthritis

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ABSTRACT

Background: Knee osteoarthritis (OA) is a widespread condition among the Indian population, with several intra-articular treatment options available for managing the disease in its early to mid-stages. This study aims to evaluate and compare the effectiveness of intra-articular steroid injections and platelet-rich plasma (PRP) against normal saline used as a placebo.
Methods: Between January 2018 and January 2020, 150 patients diagnosed with grade 2 and 3 knee OA received intra-articular injections. The participants were divided into three groups of 50 each: Group I received platelet-rich plasma, Group II received steroids, and Group III received normal saline in a sequential manner. Over a nine-month follow-up period, the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and Visual Analog Scale (VAS) scores were assessed and analyzed at baseline, and then at one, three, six, and nine months post-treatment.
Results: All three groups exhibited a significant reduction in VAS and WOMAC scores ($p < 0.05$) after one month. Groups I (PRP) and II (steroids) showed similar levels of improvement, while Group III (normal saline) demonstrated lesser improvements. In Group III, VAS and WOMAC scores continued to decline at three and six months, eventually exceeding baseline levels by the nine-month mark. In contrast, both Group I and Group II maintained lower VAS and WOMAC scores at three, six, and nine months, although the extent of reduction was less significant in Group II. While both Group I and Group II experienced some increase in scores after the first month, the deterioration was less severe in Group I.
Conclusion: Intra-articular injections of PRP and steroids are effective conservative treatments for reducing pain, enhancing quality of life, and improving functional scores in patients with Grade 2 and 3 osteoarthritis. PRP injections, in particular, offer more favorable long-term outcomes compared to steroid injections.

***Keywords**: Osteoarthritis (OA), Platelet rich plasma (PRP), intra-articular injection, steroid, Visual analogue score (VAS), Western Ontario and McMaster University Osteoarthritis index (WOMAC).*

INTRODUCTION:

Knee osteoarthritis is a degenerative disease that involves the progressive loss of articular cartilage, making it one of the leading causes of lower limb disability among older adults (1). As life expectancy rises and obesity rates increase, the occurrence of osteoarthritis has significantly grown worldwide, including in India, where approximately 80% of knee osteoarthritis cases are found in people aged 55 and older (2). The disease is rooted in an imbalance between cartilage maintenance and repair processes, leading to cartilage breakdown, abnormal bone growth, and the development of bony outgrowths known as osteophytes. Consequently, therapies aimed at stimulating cartilage repair are seen as promising strategies for managing the condition. In India, estimates suggest that the prevalence of knee osteoarthritis, considering both symptomatic cases and radiographic findings, ranges from 22% to 39% (3-5). Given the chronic nature and substantial impact of osteoarthritis, there is an increasing demand for new treatments to improve patient care. While traditional approaches, both medical and surgical, remain key to management, ongoing research is focused on discovering innovative therapies (6).

One of the emerging treatments in this field is platelet-rich plasma (PRP), which has gained considerable attention since it was first introduced roughly a decade ago. PRP has become well-established in the fields of physical rehabilitation and orthopedic treatment (7). This treatment is created from the patient's own blood, reducing the risk of side effects due to its autologous origin. When injected into the affected area, PRP enhances various local biological processes, such as promoting type I collagen synthesis, encouraging the proliferation of tenocytes, and raising levels of platelet-derived growth factor (PDGF). These actions collectively aid in the formation of ligament matrix, a critical aspect in addressing osteoarthritis (8).

Previously, corticosteroid injections were frequently used for osteoarthritis management. However, it is now recognized that these injections come with a range of complications, including skin discoloration, nerve damage, calcification within the joint, elevated blood sugar, and disruptions to the hypothalamic-pituitary axis. Repeated corticosteroid use has also been linked to more severe risks, such as tendon rupture (9). Despite PRP showing potential as an alternative therapy, research is still hindered by variations in study designs, preparation methods, and outcome evaluations. Therefore, further studies are necessary to establish a clearer understanding of PRP's efficacy.

METHODS:
The research took place at a tertiary care hospital, specifically within the Orthopaedics Department, and included both outpatient and inpatient populations. Approval was granted by the Institutional Ethics Committee and Review Board, and all participants provided written informed consent before the study began.

A comparative hospital-based study was conducted on 150 patients to assess the effects of intraarticular injections of platelet-rich plasma (PRP), corticosteroids, and normal saline on pain levels in individuals diagnosed with grade 2 and 3 knee osteoarthritis. The participants were split into three equal groups of 50: Group I received PRP injections, Group II was treated with corticosteroid injections, and Group III was administered normal saline. The research was conducted over an 18-month period, from August 2020 to January 2022. The sample size was determined using the formula $n = [z^2p(1-p)]/d^2$, where z represents the standard value for the alpha error from the Standard Normal Distribution table (0.95). This calculation determined that 50 patients per group were sufficient to detect a significant difference, leading to a total of 150 patients.

Inclusion criteria consisted of individuals over the age of 40, experiencing chronic knee pain for more than 3 months, and having a clinical diagnosis of grade 2 or 3 knee osteoarthritis. Patients with trauma-related knee pain, inflammatory arthritis, conditions like ankylosing spondylitis, rheumatoid arthritis, psoriatic arthritis, pregnancy, severe infections, malignancy, blood disorders, nerve issues (e.g., radiculopathy), previous knee injections, immunodeficiency, anticoagulant use, or a platelet count below 150,000/mm^3 were excluded.

Each patient went through a comprehensive history-taking and physical examination, including assessments for knee tenderness, range of motion, and stability. Baseline scores for pain and function were recorded using the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Visual Analog Scale (VAS). Diagnosis was based on patient history, clinical signs, and findings from standing knee radiographs, with osteoarthritis severity classified using the Kellgren-Lawrence (K-L) scale.

Intra-articular injections were administered under sterile conditions in an operating room. Patients were positioned supine, with knees flexed at 90 degrees, and the injection site was sterilized. The injections were delivered using a 21-gauge needle inserted into the anterolateral soft spot of the knee, followed by sterile bandaging.

- Group I (PRP) received manually prepared PRP through a single-spin centrifugation technique. Thirty milliliters of peripheral blood were drawn into tubes with 3.2% sodium citrate and centrifuged at 1800 rpm for 8 minutes, resulting in 3.5 ml of PRP. Platelet count analysis showed that the PRP concentration was four times higher than peripheral blood levels. PRP was activated with calcium chloride (50 µl per 1 ml of PRP) before being injected.
- Group II (Corticosteroid) received 1 ml of 40 mg/ml methylprednisolone acetate mixed with 5 ml of 1% lidocaine.
- Group III (Normal saline) received 2 ml of normal saline.

Post-injection, patients were monitored in a lying position for 30 minutes and discharged the next day. They were advised on lifestyle adjustments, such as avoiding squatting, maintaining weight, and adhering to physiotherapy and exercise routines.

Patients were followed up at intervals of 1 month, 3 months, 6 months, and 9 months post-treatment. The primary outcome was pain relief during knee movement, assessed using the VAS, which employed a 10 cm line ranging from "no pain" to "worst pain imaginable." The VAS scores were compared across the three groups. Additionally, changes in WOMAC scores, which assess pain, stiffness, and physical function with a total score of 96, were tracked at each follow-up and compared to baseline data.

Statistical Analysis:

Quantitative data were summarized as means and standard deviations, and comparisons between the groups were made using unpaired t-tests based on the results of normality tests. Qualitative data were presented in frequency and percentage tables. Group associations were analyzed using Fisher's exact test, the Student's t-test, and the Chi-Square test. A p-value of less than 0.05 was deemed statistically significant, and results were visually represented where applicable.

RESULTS:

Demographic details such as age, gender, BMI, affected side, osteoarthritis grading, and symptom duration are summarized in Table 1. Statistical evaluations using the Student's t-test and Chi-square test showed no significant differences between the groups.

Participant Characteristics	Variables	Group I (PRP) N=50	Group II (Steroid) N=50	Group III (Normal saline) N=50
Age	Mean	61.92 ± 11.03 (SD)	61.12 ± 10.47 (SD)	60.44 ± 10.78 (SD)
	Range	42 – 78 years	46 – 76 years	44- 75 years
Gender	Male	27 (54%)	26 (52%)	24 (48%)
	Female	23 (46%)	24 (48%)	26 (52%)
BMI (kg/m^2)	Mean	27.21 ± 5.26 (SD)	27.49 ± 4.10 (SD)	26.63 ± 3.65 (SD)
	Range	20.3 – 35.4 kg/m^2	22.6 – 34.8 kg/m^2	21.3 – 33.9 kg/m^2
Side	Right	24 (48%)	27 (54%)	26 (52%)
	Left	26 (52%)	23 (46%)	24 (48%)
Kellgren-Lawrence Grade	Grade 2	23 (46%)	20 (40%)	27 (54%)
	Grade 3	27 (54%)	30 (60%)	23 (46%)
Duration of symptoms	Mean (Months)	5.85 ± 1.63 (SD)	5.74 ± 1.23 (SD)	5.52 ± 0.96 (SD)

The study revealed significant improvements in the Visual Analog Scale (VAS) scores at the 1-month mark across all groups: Group I (3.2 ± 2.11 SD), Group II (3.4 ± 1.85 SD), and Group III (4.5 ± 2.65 SD), with a p-value of ≤ 0.05 indicating statistical significance. Continued improvement was observed between baseline and 3 months for both Group I and Group II (Group I: 3.4 ± 1.51 SD, Group II: 3.9 ± 2.03 SD, p ≤ 0.05), and from baseline to 6 months (Group I: 3.9 ± 2.45 SD, Group II: 4.6 ± 2.96 SD, p ≤ 0.05). By the 9-month follow-up, Group I still showed significant improvement (4.6 ± 2.63 SD, p ≤ 0.05), but no significant change was found in Group II (5.5 ± 2.39 SD, p > 0.05) or in Group III at the 3-month (5.7 ± 2.62 SD, p > 0.05) and 6-month (6.1 ± 2.92 SD, p > 0.05) points. Notably, Group III had an increase in VAS scores at 9 months (6.7 ± 3.14 SD). Figure 1 provides a comparative overview of these findings.

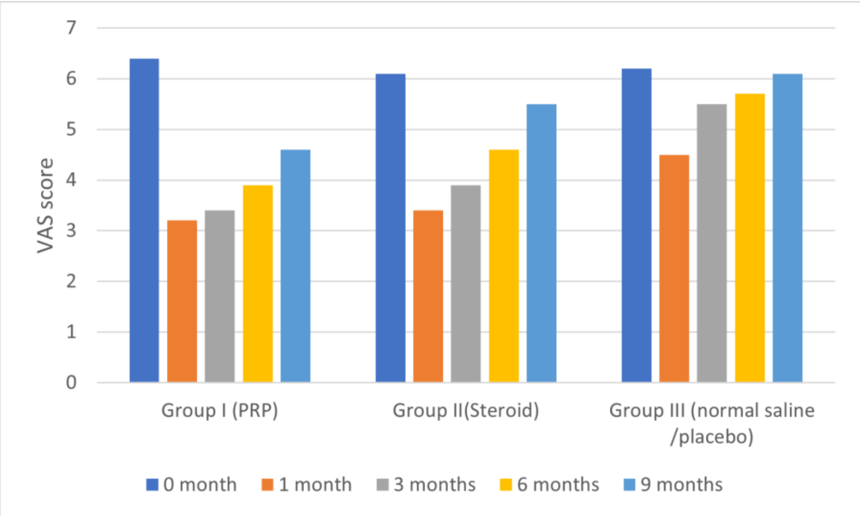

Figure 1

Similarly, the WOMAC composite scores demonstrated significant improvements from baseline to 1 month across all groups: Group I (30.1 ± 8.11 SD), Group II (30.3 ± 8.56 SD), and Group III (37.4 ± 10.72 SD), with p-values of ≤ 0.05. Between baseline and 3 months, both Group I and Group II showed continued improvement (Group I: 30.9 ± 12.63 SD, Group II: 34.8 ± 11.43 SD, p ≤ 0.05), and this trend persisted through 6 months (Group I: 35.6 ± 11.59 SD, Group II: 41.4 ± 13.85 SD, p ≤ 0.05). By 9 months, Group I still had significantly improved scores (43.8 ± 12.65 SD, p ≤ 0.05), whereas

Group II did not show a significant change (55.2 ± 14.32 SD, $p > 0.05$). Group III did not show significant differences at 3 months (56.2 ± 12.43 SD, $p > 0.05$) or 6 months (59.2 ± 13.23 SD, $p > 0.05$), but an increase above baseline was observed at 9 months (61.9 ± 13.32 SD). These results are illustrated in Figure 2.

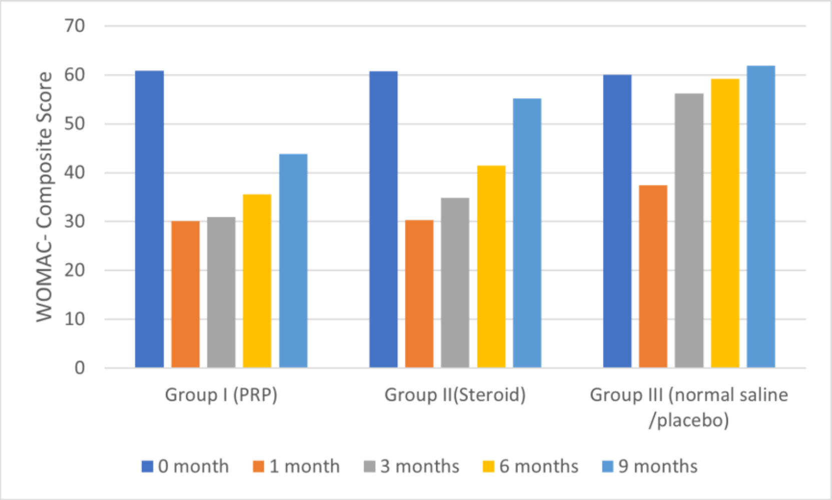

Figure 2

For WOMAC pain scores, a significant reduction was observed from baseline to 1 month in all groups: Group I (6.8 ± 1.43 SD), Group II (7.1 ± 1.85 SD), and Group III (9.2 ± 2.63 SD), with a p-value of ≤ 0.05. Continued improvement was observed between baseline and 3 months in Group I and Group II (Group I: 7.2 ± 1.97 SD, Group II: 9.5 ± 2.65 SD, $p \leq 0.05$), and from baseline to 6 months (Group I: 7.7 ± 3.16 SD, Group II: 10.1 ± 3.73 SD, $p \leq 0.05$). At 9 months, significant improvements remained in Group I (9.7 ± 3.42 SD, $p \leq 0.05$), while no significant change was observed in Group II (11.5 ± 5.65 SD, $p > 0.05$). Group III did not show significant differences at 3 months (11.8 ± 4.96 SD, $p > 0.05$) or 6 months (12.2 ± 4.69 SD, $p > 0.05$), but an increase above baseline was noted at 9 months (13.1 ± 5.12 SD). These results are depicted in Figure 3.

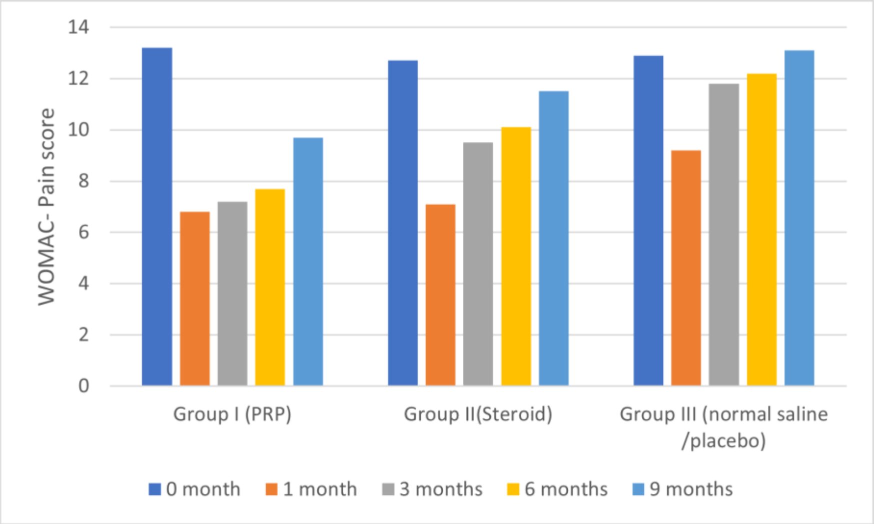

Figure 3

WOMAC stiffness scores showed significant improvement from baseline to 1 month across all groups: Group I (2.9 ± 1.02 SD), Group II (2.7 ± 0.98 SD), and Group III (3.3 ± 1.32 SD), with a p-value of ≤ 0.05. Improvements persisted between baseline and 3 months across all groups (Group I: 2.8 ± 1.51 SD, Group II: 3.1 ± 1.72 SD, Group III: 4.7 ± 2.31 SD, $p \leq 0.05$). At 6 months, Groups I and II showed further improvement (Group I: 3.1 ± 1.61 SD, Group II: 4.2 ± 1.56 SD, $p \leq 0.05$), and this trend continued to 9 months (Group I: 3.9 ± 1.95 SD, Group II: 4.4 ± 1.92 SD, $p \leq 0.05$). Group III did not show significant differences at 6 months (5.3 ± 2.43 SD, $p > 0.05$), but an increase above baseline was observed at 9 months (5.5 ± 2.12 SD). These findings are illustrated in Figure 4.

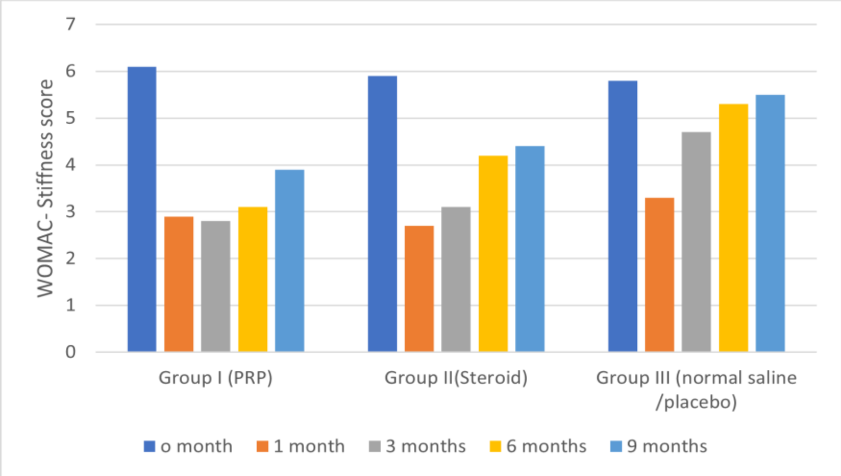

Figure 4

Finally, WOMAC physical function scores also improved significantly from baseline to 1 month in all groups: Group I (20.4 ± 5.32 SD), Group II (20.5 ± 5.41 SD), and Group III (24.9 ± 5.65 SD), with a p-value of ≤ 0.05. Continued improvement was observed between baseline and 3 months in Group I and Group II (Group I: 20.9 ± 6.23 SD, Group II: 22.2 ± 8.12 SD, $p \leq 0.05$), and from baseline to 6 months (Group I: 24.8 ± 7.23 SD, Group II: 27.1 ± 6.15 SD, $p \leq 0.05$). By 9 months, Group I still showed significant improvement (30.2 ± 6.82 SD, $p \leq 0.05$), while no significant change was found in Group II (39.3 ± 11.43 SD, $p > 0.05$). In Group III, no significant differences were observed at 3 months (39.7 ± 10.54 SD, $p > 0.05$); however, an increase above baseline was noted at 6 months (41.7 ± 10.34 SD) and 9 months (43.3 ± 10.68 SD). The comparative results are shown in Figure 5.

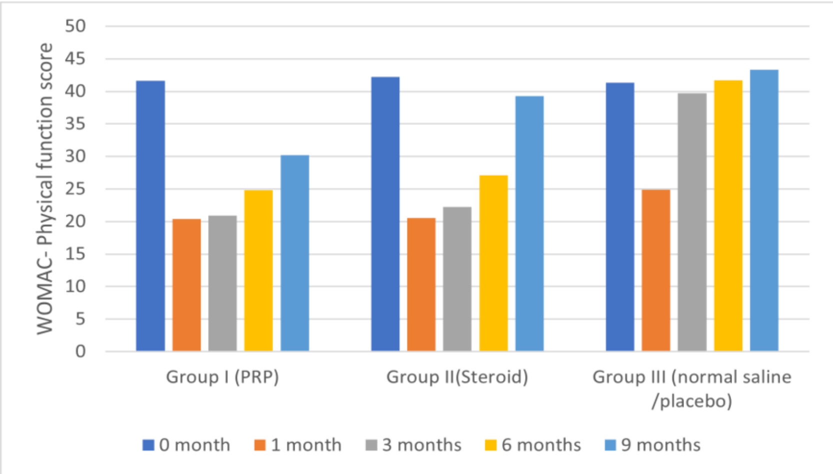

Figure 5

X-ray evaluations at 9 months indicated that there was no improvement in joint space width across all groups, with deterioration observed instead.

DISCUSSION:

The study revealed notable improvements in both WOMAC and VAS scores across all groups—PRP, steroid, and normal saline—within the first month. These enhancements persisted up to 3 months for the PRP and steroid groups, although there was a slight decline at the 6- and 9-month follow-ups. The PRP group, in particular, maintained significantly better scores compared to the steroid group over time. Conversely, the normal saline group showed initial improvements at 1 month, but these benefits did not last through the 3-, 6-, and 9-month follow-ups.

These results are especially interesting given that preclinical studies suggest PRP primarily enhances the articular environment through homeostasis rather than providing a lasting regenerative effect. This homeostatic impact may influence the balance between pro- and anti-inflammatory cytokines, potentially disrupting the inflammatory pathways that contribute to the progression of osteoarthritis. Since inflammation plays a crucial role in both the symptoms and progression of osteoarthritis, strategies aimed at reducing inflammation may help mitigate these processes. Additionally, PRP may affect the entire joint environment, impacting synoviocytes, meniscal cells, and mesenchymal stem cells, and its chemoattractant properties could help recruit other cells that contribute to the overall therapeutic effect. This combination of actions could lead to anabolic effects, a reduction in overall joint inflammation, and potentially decreased chondrocyte apoptosis, which might explain the sustained clinical benefits observed beyond the initial follow-ups.

Several researchers have highlighted the benefits of PRP injections for joint conditions, noting improvements in pain relief and physical function as measured by WOMAC, KSS, and VAS indices. Although there was no statistical comparison of KSS scores between the 1- and 3-month follow-ups, significant improvements were recorded in both subjective and objective measures. Previous studies have consistently reported the analgesic effects of PRP injections, with many researchers documenting the pain-relief properties of platelets. A recent meta-analysis found that PRP reduces pain by modulating levels of mediators such as prostaglandin E2, substance P, dopamine, and 5-hydroxy-tryptamine. Furthermore, the growth factors in PRP concentrate support cartilage matrix production, promote chondrocyte growth, and help suppress local inflammation.

Two studies comparing PRP with steroids reported WOMAC scores at the 6-month follow-up, showing a significant advantage for PRP. Y. Huang et al. noted that while intra-articular PRP has comparable efficacy to hyaluronic acid and corticosteroids at 3 months, PRP demonstrates superior long-term efficacy. A meta-analysis concluded that a single PRP injection is as effective as multiple injections for pain improvement, though multiple injections may be more beneficial for enhancing joint function at 6 months. In our study, a single injection was chosen to minimize complexity and reduce the risk of complications associated with multiple injections.

It is important to note that most similar studies have employed a comparable methodology—being prospective, longitudinal, and non-randomized. A prospective approach is essential for interventions, particularly given that PRP is a relatively new treatment option. The longitudinal design allows for repeated assessments over time using consistent methods, enabling effective comparisons. In our study, VAS and WOMAC scores were repeatedly assessed and compared, whereas other studies have utilized additional assessment tools such as the International Knee Diagnostic Committee (IKDC) score, Lequesne Algofunctional Index, and Japanese Knee Osteoarthritis Measure (JKOM).

Study Limitations:
This study did not include Hyaluronic Acid (HA), despite its known chondroprotective effects and evidence suggesting that PRP may be more effective than HA at a 36-month follow-up [26]. Other limitations include the absence of long-term follow-up data, lack of a standardized protocol for PRP preparation and injection dosage, non-randomization, and the absence of stratified analysis based on gender, BMI, and OA grading, which would require a larger sample size.

CONCLUSION:
The study demonstrated that PRP provided the most favorable outcomes compared to corticosteroids and placebo in patients with grade 2 and 3 knee osteoarthritis over a 9-month period. Both PRP and corticosteroids were effective, particularly at the 1- and 3-month marks, but PRP maintained its benefits longer, with noticeable effects persisting up to 9 months. In contrast, the efficacy of corticosteroids began to diminish more significantly after 3 months. Further investigation into PRP is necessary to establish standardized protocols for its preparation, optimal dosing schedules, platelet concentration, and to evaluate the role of leukocyte-rich PRP in order to enhance its therapeutic effectiveness.

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