

Original Research Article

Clinical efficacy of single intra-articular platelet-rich plasma injections in mild to moderate knee osteoarthritis: a prospective study

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ABSTRACT

Background: Knee osteoarthritis (OA) is a degenerative joint disease that significantly impacts mobility and quality of life, particularly in older adults. Conventional treatments often provide limited relief, leading to interest in regenerative therapies like platelet-rich plasma (PRP) injections. This study aims to evaluate the clinical effects of a single intra-articular PRP injection in patients with mild to moderate knee OA.

Methods: A prospective, randomized study was conducted with 56 patients aged 40 to 70 years diagnosed with primary knee OA (Kellgren-Lawrence grades 1 and 2). Participants were treated with a single intra-articular PRP injection, prepared using the double-spin technique. Pain intensity was assessed using the Visual Analog Scale (VAS), and functional status was evaluated with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at baseline, and follow-up assessments were performed at 1 week, 4 weeks, 8 weeks, 12 weeks, and 6 months post-injection.

Results: Significant improvements in both pain and function were observed. The mean VAS score decreased from 7 at baseline to 4 at 12 weeks, and to 3 at 6 months. The mean WOMAC score improved from 53 at baseline to 30 at 12 weeks, and 24 at 6 months. These changes were statistically significant ($p < 0.05$). No major adverse events were reported during the study period.

Conclusion: A single intra-articular PRP injection significantly reduces pain and improves function in patients with mild to moderate knee OA. PRP therapy is a promising treatment option for managing knee OA, offering an alternative to more invasive procedures. Further studies are needed to explore the long-term effects and optimal treatment protocols.

Keywords: Platelet-rich plasma, Knee osteoarthritis, Intra-articular injection, Clinical efficacy, Pain relief, Functional improvement

INTRODUCTION

Knee osteoarthritis (OA), or degenerative joint disease, is a common chronic condition characterized by the progressive loss of articular cartilage due to wear and tear. It results in pain, fatigue, functional limitations, and increased healthcare utilization, imposing significant economic costs on society. The progression of OA varies among individuals and is expected to rise with increasing

obesity and an aging population. While OA is more prevalent in older adults, there is growing recognition that it also affects younger individuals. Primary knee OA typically begins after age 40 in 25-30% of the population, progressing to 60-90% by age 60. The knee, the largest synovial joint, consists of bones (distal femur, proximal tibia, and patella), cartilage (meniscus and hyaline cartilage), ligaments, and a synovial membrane that produces fluid for lubrication and nutrient supply to

avascular cartilage. Due to the knee's high usage and stress, it is particularly susceptible to OA.¹⁻⁴ Quadriceps weakness has been identified as a major contributor to knee OA, as it can significantly impair functional ability. Strengthening the lower extremities can help reduce pain and improve mobility. Dysfunction may result from quadriceps weakness or an imbalance between quadriceps and hamstring strength, which affects joint stability.⁵ OA is primarily caused by repetitive mechanical stress and aging, with etiological factors grouped into sex, anatomy, and body mass. The clinical manifestations of OA include joint pain, stiffness, reduced range of motion, and quadriceps weakness.¹ Muscle strength deficits are particularly problematic because they lead to a progressive loss of function. Individuals with OA often experience difficulty with activities like standing, walking, or climbing stairs, and may display a limp, misalignment of the limb, and instability. Crepitus is also commonly observed due to cartilage degeneration and irregular joint surfaces.⁶ Knee OA can be classified as primary or secondary. Primary knee OA results from age-related degeneration and wear and tear of cartilage. Secondary OA, on the other hand, is caused by factors like trauma, postsurgical changes, rheumatoid arthritis, or infective arthritis.⁷

Treatment goals for knee OA focus on pain relief and restoring joint mobility. Non-pharmacological treatments typically include weight loss, strengthening exercises for the knee muscles, and assistive devices like braces. Pharmacological treatments may involve non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and tramadol. Invasive procedures, such as intra-articular injections of corticosteroids, hyaluronic acid, or platelet-rich plasma (PRP), are used in some cases. Surgical options include arthroscopic lavage, cartilage repair, and knee replacement.⁸ PRP therapy has emerged as a promising treatment for knee OA. PRP is an autologous concentrate of platelets obtained from the patient's blood. The blood is centrifuged to separate the PRP from red blood cells and plasma, which is then injected into the affected joint. The first PRP studies, dating back to the 1950s, investigated its role in coagulation.^{1,9} When platelets degranulate after injection, they release growth factors like TGF-beta, PDGF, EGF, VEGF, FGF, and insulin-like growth factor. These factors are believed to have regenerative effects and may reduce inflammation in knee OA by inhibiting pathways involving NF-kB and IL-1.⁹

The primary objective of this study is to assess the clinical effects of intra-articular PRP injections in patients with mild to moderate knee OA. The study will evaluate the efficacy of PRP therapy by analyzing improvements in symptoms and functional outcomes using the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores over a defined follow-up period.

METHODS

This prospective, randomized study was conducted between August 2021 and October 2022 in the Department of Orthopaedics at a tertiary care hospital at SMIMER hospital, Surat. A total of 56 patients with clinically and radiologically confirmed primary osteoarthritis (OA) of the knee were included. Participants satisfied strict inclusion criteria, which required them to be 40 years or older with symptomatic knee OA (Kellgren-Lawrence Grades 1 and 2), and to have experienced minimal or no relief from conservative treatments, such as medication, physiotherapy, or knee braces, for at least two weeks.¹⁰ Exclusion criteria included previous knee surgeries, acute joint inflammation, uncontrolled diabetes, secondary OA, and significant peripheral vascular disease. Baseline demographic data, medical histories, and clinical examination findings were collected. Radiological staging of OA was performed using anteroposterior and lateral radiographs of both knees in a standing position, with staging based on the Kellgren-Lawrence grading system. WOMAC and VAS scores were recorded for each patient prior to intervention.

Measurement of pain and functionality

VAS was used to assess the intensity of pain. The scale ranges from 0 to 10, with 0 representing no pain and 10 indicating the worst imaginable pain. Patients marked their pain levels on a 10 cm line, allowing for a precise measurement of pain severity. The VAS provides a simple and sensitive method to monitor changes in pain perception over time.¹¹ WOMAC was used to evaluate pain, stiffness, and physical function. This index includes 24 items divided into three subscales: pain (5 items), stiffness (2 items), and physical function (17 items).¹² Each item is scored on a scale from 0 (none) to 4 (extreme), and the total score can range from 0 to 96. Lower scores indicate better outcomes, while higher scores signify greater pain, stiffness, or functional impairment. WOMAC is a well-validated tool for assessing the impact of osteoarthritis on daily living and has been extensively used in clinical trials.

Preparation and administration of PRP

PRP was prepared using the double-spin differential centrifugation technique.¹³ Blood samples were collected in acid citrate dextrose tubes and centrifuged at 1800 rpm for 12 minutes to separate erythrocytes. A second centrifugation at 4000 rpm for 5 minutes concentrated the platelets, yielding approximately 3 mL of PRP. Under strict aseptic conditions, PRP was injected intra-articularly into the affected knee using the superolateral approach. Following the injection, passive cycling movements were performed to ensure even distribution of PRP within the joint. Patients were monitored for immediate adverse effects for 30 minutes post-procedure and were discharged on the same day with weight-bearing ambulation advice.

Follow-up and outcome measures

Participants were followed up at 1 week, 4 weeks, 8 weeks, 12 weeks, and 6 months after the PRP injection. During each follow-up visit, patient-reported symptoms, clinical examination findings, and repeat radiographic assessments were recorded. VAS and WOMAC scores were re-evaluated at each visit and compared to baseline values to assess improvements in pain and functionality. A significant decrease in VAS and WOMAC scores over time was considered indicative of clinical efficacy.

Ethical clearance was obtained prior to the study (approval number IEC/Out No 104 dated 9th December 2022), and all participants provided informed written consent. Data analysis was conducted to evaluate the extent of symptom improvement and functional recovery, with a focus on determining the efficacy of PRP therapy in knee OA. A p-value of <0.05 was considered statistically significant.

RESULTS

The present study was conducted among 56 patients to assess the clinical effects of intra-articular PRP injections in patients with mild to moderate knee OA. Table 1 provides an overview of the baseline demographics and clinical characteristics of the study patients. The majority of patients were aged between 41-50 years (62.5%), followed by those in the 51-60 years range (28.5%), with a smaller group aged 61-70 years (9.0%). In terms of gender, 32 patients (57.0%) were female, while 24 patients (43.0%) were male. Regarding the distribution of knee osteoarthritis (OA), the left knee was more commonly affected, with 26 patients (46.0%) diagnosed with left OA, compared to 25 patients (45.0%) with right OA, and only 5 patients (9.0%) had bilateral OA.

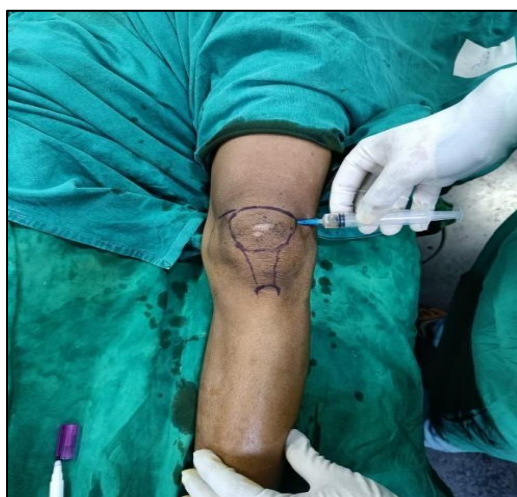


Figure 1: Marking of knee joint: the image depicts a medical procedure involving intra-articular injection into the knee joint, with marked anatomical landmarks guiding the needle placement. It suggests a therapeutic or diagnostic intervention, such as corticosteroid injection or joint aspiration.

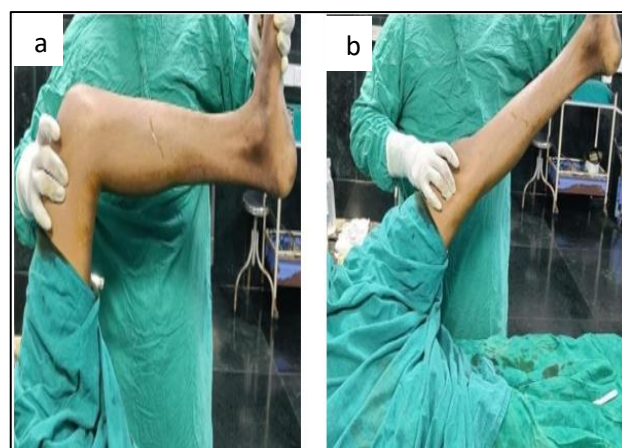


Figure 2: Post injection mobility (a, b) the images demonstrate clinical manipulation of a patient's knee and hip, likely assessing the range of motion or performing an orthopedic examination. Both images emphasize the angles achieved during flexion and extension of the lower limb.

Symptom duration varied, with the largest group reporting symptoms for 6-12 months (39.0%), followed by 13-24 months (29.0%), and 23.0% of patients had symptoms for less than 6 months. Only 9.0% of patients experienced symptoms for over 24 months. When classified according to the Kellgren-Lawrence (K-L) grading system, most patients were in grade 1 (61.0%), indicating mild OA, while 39.0% of patients were in grade 2, which represents moderate OA. This demographic breakdown helps provide context for the patient population in terms of age, gender, disease distribution, symptom duration, and OA severity.

Table 2 presents the distribution of patients based on gender and age in different Kellgren-Lawrence (KL) grades. The data shows that in the KL Grade 1 group, all patients (100%) are in the 41-50 age range, with 34 patients in this category.

In contrast, for KL Grade 2, the age distribution is more varied, with patients primarily in the 51-60 years age group (72.7%, 16 patients), followed by 22.7% of patients in the 61-70 years age range (5 patients). Regarding gender, KL Grade 1 consists of a higher proportion of females (64.7%, 22 patients), while KL Grade 2 has an equal distribution of males and females, with 54.5% males (12 patients) and 45.5% females (10 patients).

Table 3 compares the progression of pain and physical function over time, as measured by the WOMAC and VAS scores. The table shows a significant improvement in both scores from baseline to the 12-week and 6-month follow-up. The average WOMAC score decreases steadily from 53 at baseline to 30 at 12 weeks, and further to 24 at 6 months. Similarly, the VAS score drops from 7 at baseline to 4 at 12 weeks, and remains at 3 at 6 months. The p values for both the WOMAC and VAS scores at 12 weeks and 6 months are statistically significant ($p < 0.05$), indicating a

meaningful reduction in pain and improvement in function over time.

Table 1: Baseline demographics and clinical characteristics of patients.

Characteristic	No. of patients (%)
Age distribution (in years)	
41-50	35 (62.5)
51-60	16 (28.5)
61-70	5 (9.0)
Gender distribution	
Females	32 (57.0)
Males	24 (43.0)
Diagnosis distribution	
Bilateral OA	5 (9.0)
Left OA	26 (46.0)
Right OA	25 (45.0)
Symptom duration (in months)	
<6	13 (23.0)
6-12	22 (39.0)
13-24	16 (29.0)
>24	5 (9.0)
Kellgren-Lawrence (K-L) grade	
Grade 1	34 (61.0)
Grade 2	22 (39.0)

Table 2: Gender and age distribution in K-L grades.

Characteristic	No. of patients in KL grade 1 (%)	No. of patients in KL grade 2 (%)
Age distribution (in years)		
41-50	34 (100.0)	1 (4.5)
51-60	0 (0.0)	16 (72.7)
61-70	0 (0.0)	5 (22.7)
Gender distribution		
Females	22 (64.7)	10 (45.5)
Males	12 (35.3)	12 (54.5)

Table 3: Comparison of WOMAC and VAS scores over time.

Time period	Average WOMAC score	Average VAS score
Baseline	53	7
1 week	47	6
4 weeks	41	5
8 weeks	35	4
12 weeks	30	4
6 months	24	3
P value (baseline vs 12 weeks)	0.000	0.000
P value (baseline vs 6 months)	0.000	0.004

DISCUSSION

OA is a degenerative condition of the cartilage, also known as degenerative joint disease, degenerative arthritis, or hypertrophic arthritis, though some degree of synovitis is also present. Osteoarthritis, being the most common disease of the joints in the elderly, frequently affects the knee joint, causing a major source of disability due to pain and deformity, leading to significant loss of function. Current literature indicates that intra-articular (IA) knee injections are a promising modality in managing pain associated with OA knee. They are well tolerated and minimally invasive, especially in patients with comorbidities who either lack the fitness for surgery or are unable to tolerate oral analgesics for prolonged periods. Various IA injectables, including corticosteroids, infliximab, hyaluronic acid, botulinum neurotoxin, platelet-rich plasma (PRP), and even stem cells, are being used in the management of knee OA.

In recent years, there has been growing interest in exploring PRP as a treatment modality for OA knee. The platelet concentrates in PRP, when activated, results in the formation of platelet gel and the release of growth factors and bioactive molecules, which effectively participate in the healing process.¹⁹ Platelets contain significant amounts of cytokines and growth factors, which stimulate cellular growth, vascularization, proliferation, tissue regeneration, and collagen synthesis. This regenerative therapy is believed to promote healing by augmenting and accelerating the natural healing cascade. The injection of PRP to treat OA of the knee is considered a relatively new therapeutic approach.¹⁶

PRP can be prepared using single-spin or double-spin techniques. Studies suggest no clear advantage of the double-spin technique over the single-spin technique or vice versa. The two-stage centrifugation process involves a hard spin that separates low-platelet-concentrated plasma from red blood cells (RBCs) and PRP, followed by a soft spin to collect the PRP at the bottom of the test tube due to its high specific gravity.^{17,18}

This study aimed to assess the clinical implications of IA PRP injections in mild and moderate knee OA, specifically evaluating the clinical efficacy using the VAS and WOMAC scores. This prospective study aimed to evaluate the effect of a single IA PRP injection in Kellgren-Lawrence (KL) grade 1 and 2 OA knees in terms of the reduction in mean total WOMAC and VAS scores. There are few studies on the effectiveness of a single IA PRP injection, with most studies using 2-3 IA injections 1 to 6 weeks apart, reporting initial good results after the first injection. The study included 56 patients, with ages ranging from 40 to 70 years and a mean age of 49.39 years. In comparison, Sandeep Patel and colleagues included participants aged 33 to 80 years with a mean age of 53.11 years, and studies by Shu Fen et al, Farid et al, Ece et al showed comparable age ranges and means.¹⁹⁻²²

Regarding bilaterality and disease duration, 9% of patients had bilateral knee affection, with one knee being more symptomatic. The duration of symptoms in this study was 12.23 ± 7.27 months, a shorter duration compared to Hassan et al.²³

The KL grading system was used for clinical grading of OA severity. Only patients with grades I and II were included in the study, as studies have shown poor functional outcomes with PRP in grades III and IV. In total, 61% of the patients had KL grade 1, and 39% had grade 2, which is consistent with other studies.^{27,28} The results showed that OA knee is more prevalent in females than males, which is in agreement with other studies.¹⁹⁻²²

The clinical improvement in OA was evaluated by comparing WOMAC and VAS scores at 12-week and 6-month follow-ups with baseline values. At the 12-week follow-up, the improvement in functional outcomes was not significant, which aligns with studies by Guvendi et al and Akshay et al.²⁷ However, at the 6-month follow-up, the improvement in functional outcomes was significant in the present study, consistent with the findings of Guvendi et al and Akshay et al.^{26,27}

In comparison to other studies, the results of this study at 6 months were similar to those of Wang-Saegusa et al and Filardo et al who reported improvements in outcomes up to 6 months.^{28,29} Patel et al conducted a study with 78 patients, comparing single versus double injections of PRP and found that a single dose was as effective as multiple injections.¹⁹ The present study opted for a single dose and chose a longer follow-up period to evaluate the long-term effects. The decrease in mean total WOMAC score from baseline (52.75) was 29.75 (43.6%) at 12 weeks and 23.85 (54.8%) at 6 months, which is comparable to other studies.^{19,21,27}

Mohammed et al also conducted a study on patients with KL grade 1-3 OA knee who received two IA PRP injections and observed significant improvements in joint pain, stiffness, and knee function over 6 months.²¹ The baseline mean total WOMAC score in their study was 49.75, which decreased to 24.45 (56.3%) at 3 months and 27.18 (51%) at 6 months, while the present study showed a 43.6% reduction at 12 weeks and a 54.8% reduction at 6 months. This highlights the comparable efficacy of single IA PRP injections.

A study by Jubert et al compared single IA PRP injections with corticosteroids in late-stage knee OA and found that while both treatments improved patient outcomes, PRP showed greater improvement in quality of life (QOL) after 6 months.³⁰ The findings in the present study are similar, showing significant improvement in symptoms over 6 months.

In conclusion, IA PRP injections show promising results in managing knee OA, with significant improvements observed up to 6 months, particularly for patients with KL

grades 1 and 2 OA. The present study supports the growing evidence of PRP's effectiveness and highlights its potential as a viable treatment option for knee OA.

Limitations

This study used a single intraarticular injection, unlike most studies that use 2-3 injections, with no long-term follow-up for comparison. Platelet counts were not measured, and cases with severe knee OA (KL grade 3 & 4) or those over 70 years were excluded. Additionally, due to financial constraints, MRI scans to assess cartilage regeneration were not performed.

CONCLUSION

Primary knee osteoarthritis (OA) is a prevalent chronic condition that causes pain, fatigue, functional limitations, increased healthcare utilization, and significant economic burden on society. This study concludes that a single intra-articular injection of platelet-rich plasma (PRP) is a safe, simple, and cost-effective outpatient procedure, with minimal foreign body reaction. It significantly improves pain alleviation and overall functional outcomes in patients with knee OA of K-L grades 1 and 2. Furthermore, intra-articular PRP provides effective long-term pain relief and functional improvement, with sustained benefits up to 6 months, as evidenced by the significant improvements in WOMAC and VAS scores at 1, 4, 8, 12, and 6 months, with statistical significance determined using paired t-test analysis.

Future prospectives

Future research should focus on exploring the optimal number of PRP injections and their long-term efficacy in a broader patient population, including those with advanced knee OA (K-L grades 3 and 4) and older age groups. Additionally, studies investigating the exact platelet concentration and the mechanisms behind PRP's regenerative effects on cartilage would help refine treatment protocols. Further exploration of cost-effectiveness and comparison with other treatment modalities, such as stem cell therapy, would also be valuable to establish PRP as a widely accepted option for managing knee osteoarthritis.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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