



EFFECT OF PLATELET-RICH PLASMA (PRP) IN OSTEOARTHRITIS OF THE KNEE

Orthodontics

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ABSTRACT

Introduction: Platelet-rich plasma (PRP) injections are challenging the current treatment options for knee osteoarthritis (KOA). Targeting the treatment to the optimal stage of the symptomatic KOA may be crucial in the success and failure of treatment. This study aimed to evaluate the effect of platelet-rich plasma (PRP) in knee osteoarthritis. **Methodology:** This prospective interventional study included 100 participants with Grade 1 to Grade 4 KOA. Baseline assessments had demographic details, medical history, and clinical and radiographic evaluations. Blood investigations and quality of life assessments using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale and the International Knee Documentation Committee (IKDC). Platelet-rich plasma (PRP) injections were administered with a structured schedule. Follow-ups at 1 week, 3 months, and 6 months assessed clinical outcomes and functional parameters. **Results:** The pre-treatment WOMAC and VAS scores showed a subsequent decline, and this change was statistically significant ($p < 0.001$). Similarly, during follow-up assessments, the pre-treatment IKDC score and flexion showed a consistent upward trend ($p < 0.001$). **Conclusion:** PRP injection represents a valid conservative treatment to reduce pain and improve quality of life and functional scores even at the midterm of 6 months follow-up.

KEYWORDS

Knee Osteoarthritis, Cartilage, Platelet-rich Plasma, Knee Injection.

INTRODUCTION

Osteoarthritis (OA) stands as a prominent cause of persistent, debilitating pain and disability, impacting approximately 10% of the global population. [1] Innovative regenerative solutions and tissue-engineering strategies offer promise for addressing moderate OA. [2] Manifesting as musculoskeletal pain and movement limitations, OA significantly hampers daily functioning. [3,4] A recent study has shown an anticipated increase in knee OA cases over the next decade, attributed to the rising rates of obesity and the advancing average age of the population. [5] Recent findings indicate diminished cartilage thickness and volume in 50-year-old individuals with a Body Mass Index (BMI) equal to or exceeding 25. [6] Diverse surgical and non-surgical interventions, especially recommended for early-stage OA in younger and middle-aged patients, aim to alleviate joint pain. [7,8] Conservative approaches encompass the use of non-steroidal anti-inflammatory drugs (NSAIDs) and intra-articular injections with corticosteroids (CS), hyaluronic acid (HA), and saline. [4] Numerous meta-analyses comparing Platelet-Rich Plasma (PRP) with alternative procedures have revealed superior pain relief and functional enhancement at various post-injection intervals. [4] PRP, an autologous blood product rich in growth factors (GFs) like fibroblast growth factor, epidermal growth factor, vascular endothelial growth factor, transforming growth factor- β , and platelet-derived growth factor, exhibits notable efficacy. [4] Recent studies propose that these GFs and cytokines, released by platelets in response to injury or pathology, play a crucial role in modulating inflammatory processes, contributing to the preservation or regeneration of tissue structures. [9] Autologous platelet concentrates (APCs), including plasma rich in growth factors (PRGF), advanced-platelet-rich fibrin (A-PRF), and injectable-platelet-rich fibrin (i-PRF), have demonstrated excellent outcomes in regenerative and reparative medicine, extending their application to fields such as maxillofacial surgery and orthopaedics. [10,11] Henceforth, we aimed to evaluate the effect of platelet-rich plasma (PRP) in knee osteoarthritis.

MATERIAL AND METHODS

This prospective interventional study took place at the Department of Orthopaedics, Hind Institute of Medical Sciences, Barabanki, spanning from June 2020 to May 2021, with a focus on patients suffering from Unilateral or Bilateral knee osteoarthritis characterized by chronic pain and radiological evidence (X-ray) of degenerative joint changes. A total of 100 participants from November 2016 to October 2017 exhibiting Grade 1 to Grade 4 osteoarthritis knees, according to the Kellgren and Lawrence staging, were enrolled following ethical approval and informed consent. Patients with a history of diabetes mellitus, inflammatory knee diseases, rheumatic conditions, haematological disorders (coagulopathies), severe cardiovascular issues, infections, or traumatic osteoarthritis were excluded from the study. Additionally, those currently receiving immunosuppressants or anticoagulants, as well as individuals with platelet counts below 150,000/cubic mm and haemoglobin levels below 9 gm%, were not included in the research. All participating patients underwent a comprehensive explanation of the study, and their informed consent was obtained before enrollment. Initial baseline assessments included the collection of demographic information and medical history. Clinical and radiographic evaluations were conducted to determine the clinical grade (KL grade) of each patient. Blood investigations, encompassing parameters such as Hemoglobin (Hb), Total Leucocyte Count, Differential Leucocyte Count, Erythrocyte Sedimentation Rate, C-reactive protein, RA Factor, Random Blood Sugar, Serum Uric Acid, and viral markers (HIV, HCV, HbsAg), as well as platelet counts in both the patient's blood and the Platelet-Rich Plasma (PRP) isolate, were performed to exclude alternative causes of knee pain. The assessment of patients' quality of life involved utilising the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale and the International Knee Documentation Committee (IKDC). Additionally, the level of pain experienced by patients was quantified using a ten-point visual analogue scale (VAS), where a score of 0 denoted no pain, and a score of 10 signified extreme

and intolerable pain. In the procedural phase, a 20 cc syringe with 2 cc anticoagulant was employed to draw 18 cc of venous blood for PRP preparation. Under strict aseptic conditions, the PRP was administered through the anterolateral aspect of the knee joint using a 22-gauge needle. The injection schedule commenced with the administration of the first injection on the same day, followed by two subsequent injections at two-week intervals, employing the same procedural approach. Post-injection, patients were actively encouraged to flex and extend their knees several times, facilitating the even distribution of Platelet-Rich Plasma within the knee joint. A systematic follow-up protocol was implemented, with patient assessments occurring at 1, 3, and 6 months. After the last injection, a comprehensive assessment of clinical outcomes and functional parameters was performed, including WOMAC score, IKDC score, and VAS score. This systematic approach allowed for thorough monitoring of the patient's progress and the overall effectiveness of the Platelet-Rich Plasma intervention over the designated follow-up periods.

Statistical Analysis:

The study data underwent statistical analysis using SPSS version 26.0 for further evaluation at a significance level of $p\text{-value}=0.05$. Continuous variables were presented as Mean $\pm$ standard deviation, while categorical variables were expressed in terms of frequency. Statistical analyses included Chi-square for categorical data, student's t-test for normally distributed continuous data, and the Wilcoxon Signed Rank Test for non-normally distributed continuous data. Additionally, paired t-tests were employed for comparisons within the same group over different time points.

RESULTS

The study included patients aged 34 to 79 years, with a mean age of 54.54 ± 11.24 years. The majority of participants were in the 41-60 age group (64.0%), female (68.0%), residing in rural areas (55.0%), and predominantly housewives (50.0%) or farmers (18.0%). The BMI of patients ranged from 21.0 to 30.0 kg/m², with a mean BMI of 26.52 ± 2.38 kg/m², and a significant proportion (78.0%) were either overweight or obese. (Table-1) The most common associated illness was diabetes mellitus (39.0%), followed by hypertension (14.0%). (Figure-1) Among the study population, 9.0% were taking medication for other illnesses, 12.0% had a past medical history, and none had associated tuberculosis or cardiovascular disease. Teetotallers constituted the majority (34.0%) of the patients, with 12.0% being smokers and 22.0% consumers of both alcohol and smoking. (Figure-2) Most patients presented with osteoarthritis in both knees (86.0%), predominantly at KL Grade 3 (62.0%). NSAIDs were used by 82.0% of patients, with 56.0% receiving only NSAIDs. (Table-1) Most (94.0%) received three injections, and 76.0% also underwent physiotherapy, with immediate active exercise advised post-injection. No treatment-related complications were reported by the majority (88.0%) of patients. (Table-2) 10.0% of cases were lost to follow-up, with 6 patients lost after 1 week and four more between 1 week and 3 months. Haematological investigations are detailed in Table 3. A significant improvement in effusion, swelling, and tenderness symptoms at follow-ups of 3 months and 6 months was also recorded. (Table-4) The pre-treatment WOMAC score was 43.11 ± 6.18 , demonstrating a subsequent decline in scores during follow-up assessments. Similarly, the pre-treatment IKDC score started at 35.10 $\pm$ 4.15 percentile, indicating a consistent upward trend at one week, three months, and six months. The mean pre-treatment VAS score for pain, initially recorded at 6.32 ± 0.81 , showcased a reduction during the follow-up periods. Pre-treatment flexion, measured at $101.20 \pm 17.14^\circ$, exhibited significant increases in subsequent assessments. All observed changes in scores were found to be statistically significant at each follow-up visit ($p < 0.001$). (Table-5)

DISCUSSION

The study was meticulously planned with two primary considerations in mind. Firstly, the investigation aimed to determine the feasibility of intra-articular platelet-rich plasma (PRP) use without encountering complications. Secondly, the study sought to evaluate whether the application of platelet-rich plasma could lead to clinical and functional improvements in patients diagnosed with knee osteoarthritis. To achieve these objectives, 100 patients with either unilateral or bilateral knee osteoarthritis underwent a PRP intervention. The age of patients ranged from 34 to 79 years, with a mean of 54.54 ± 11.30 years. Osteoarthritis is a condition which is strongly associated with age. The present study's findings also endorsed this viewpoint with a high prevalence of cases above 50 years of age. OA is often described as a

chronic degenerative disease and thought by many to be an inevitable consequence of growing old. In OA, degradation and loss of the articular cartilage is a central feature that is sometimes attributed to "wear and tear". Some studies have included patients as young as 18 years of age in their assessment [12]. In their series, Filardo et al. [13] also reported the mean age of patients as 56.5 years, which is close to the mean age of patients in present study. In the present study, most patients were females (68%), which is in accordance with the reported higher risk of all types of osteoarthritis among females than males [14]. The incidence of knee, hip, and hand OA is higher in women than men, and in women, it increases dramatically around the time of menopause [15]. However, in different clinical studies evaluating the role of platelet-rich plasma/ platelet-rich growth factors, the gender ratio has shown variability. In their study, wang-Saegusa et al. [16] had only 41.8% women. Kon et al. [17] also had only 37.4% women; however, Sanchez et al. [18], on the other hand, reported the proportion of females in two study groups as 60% and 66%, respectively. In another Indian study, Patel and Dhillon [19] reported 53/75 (70.7%) of their study population as women, thus showing a predominance of women as observed in the present study. In the present study, most patients were from rural areas (56%) and most were housewives (50%). The reason for the dominance of patients from rural areas could be that our facility is generally frequented by rural populations and that the dominance of housewives could be attributable to the majority of female patients. In the present study, the mean BMI of patients was 26.60 ± 2.37 kg/m². More than two-thirds (78.0%) of the patients were either overweight or obese (BMI > 25 kg/m²), and only 11 (22.0%) patients. The profile of the patients is in agreement with the observation that a sedentary lifestyle and associated obesity contribute to a higher risk of osteoarthritis [15]. Compared to the present study, Kon et al. [17] reported the mean BMI of patients in their series as 25 kg/m², Wang-Saegusa et al. [16], on the other hand, reported the mean BMI as 25.91 kg/m², Gobbi et al. [20] reported the mean BMI as 26.7 kg/m², Filardo et al. [13] reported it as 26 and 27 kg/m² in two groups of their study. In different study groups, Patel et al. [19] reported the mean BMI to be 25.81 to 26.28 kg/m². All these studies, in general, reflect that osteoarthritis knee is more common in overweight and obese patients, as observed in the present study. In the medical history assessment, we noted that 46% of patients had a history of diabetes mellitus, and 16% had a history of hypertension. A total of 10% were on medications for other illnesses, while 12% had relevant past medical history in our study. The study noted an association between osteoarthritis and cardiovascular diseases, consistent with existing literature [21,22]. Regarding lifestyle factors, 32% were smokers, and 20% used alcohol. Although clinical evidence linking osteoarthritis with smoking or alcohol is weak and inconsistent, these factors were considered [23,24]. Most (86%) cases presented with bilateral disease, and range of motion assessment was considered the worst of two legs for baseline and subsequent evaluations. In our study, the majority of patients (66%) had KL grade 3 followed by KL grade 2 (22%) and grade 4 (16%), respectively. Compared to Kon et al. [17], their study reported 57.9% patients in KL grade I-III and 42.1% in grade IV. Wang- Saegusa et al. [16], on the other hand, had 36.9% grade IV cases. However, some authors excluded patients of grade IV from their assessment [13,20,25]. In their study, Patel et al. [19] did not use KL grade as criteria but instead used Ahlback grade and included patients with grades 1-3 only while excluding the more severe grade 4-5 patients. However, in view of the promising evidence from some previous studies that included grade 4 cases, we also included these patients in the present study. In the present study, most % of patients (82%) had a treatment history. NSAIDs either alone (56%) or in combination with CPA (22%) and CPA+ high fibular osteotomy (8%) were the treatments being received by the patients. In the present study, the haematological profile of patients suggested mild anaemia and slightly prolonged erythrocyte sedimentation rest. The link between anaemia and osteoarthritis could be established based on two factors: first, the majority of our patients were females, and the prevalence of anaemia, especially in the post-menopausal age group, is quite high among females; secondly, a link between anaemia and osteoarthritis and rheumatoid arthritis has also been suggested. This link has been related to the continuous use of NSAIDs in these patients [26,27]. In this study, most of the patients (94%) required three injections, 38 (76%) cases underwent physiotherapy, and exercise was started immediately in 32 (64%) cases. Therapeutic exercise has been shown to positively impact the outcome [28]. Multiple PRP injections have also been reported in the literature [19,29]. Although we had planned 3-PRP injections in all the patients, owing to loss of follow-up, this protocol could not be completed in all the patients; hence, some

patients received fewer than 3 injections. In our study, we also found that there was an improvement in the range of motion of the knee joint due to the relief of pain, and also, the patients could carry out their activities of daily living with more ease. No post-operative pain or synovitis was reported in 44 (88%) cases. However, no serious complication was noted in any case.

CONCLUSION

Platelet-rich plasma (PRP) emerges as an effective and successful intervention for knee osteoarthritis, providing significant symptomatic improvement without severe side effects. This therapy exhibits promise as a treatment modality, particularly for grades 1 to 3 osteoarthritis. In grade 4 cases, its consideration is suggested, subject to the discretion of the treating doctor, especially for patients averse to surgery. However, the endorsement of PRP therapy is based on findings from a single-centric study with inherent limitations, notably a limited sample size.

While the current results are encouraging, further extensive evaluations are essential for a comprehensive understanding of the long-term benefits and limitations of PRP therapy in the management of knee osteoarthritis.

Conflict Of Interest:

All authors declare no conflict of interest.

Source Of Funding:

None

Consent:

As per international or university standards, the authors have collected and preserved written participant consent.

Ethical Approval:

As per international or university standards, the author(s) has collected and preserved written ethical permission.

Table-1: Clinico-Demographic parameters of enrolled patients (n=100).

Clinico-Demographics		No. of patients (N=100)	Percentage
Age Group (years)	≤40 yrs.	12	12.0
	41-50 yrs.	26	26.0
	51-60 yrs.	38	38.0
	61-70 yrs.	16	16.0
	>70 yrs.	8	8.0
Gender	Female	68	68.0
	Male	32	32.0
BMI	Normal (18.0-24.9 kg/m ²)	24	24.0
	Overweight (25-29.9 kg/m ²)	64	64.0
	Obese (≥30 kg/m ²)	12	12.0
Habitat	Rural	55	55.0
	Urban	45	45.0
Occupation	Housewife	50	50.0
	Retired	6	6.0
	Unemployed	2	2.0
	Farmer	18	18.0
	Labourers including Construction worker/Auto Rickshaw driver/Household worker	6	6.0
Laterality	Left	8	8.0
	Right	6	6.0
	Bilateral	86	86.0
KL Grade	Grade 2	22	22.0
	Grade 3	62	62.0
	Grade 4	16	16.0
Previous treatment	No treatment	34	34.0
	NSAIDs	42	42.0

NSAIDs + Chondroprotective agents (CPA) *	20	20.0
NSAIDs + Chondroprotective agents + High fibular Osteotomy	4	4.0

Table-2: Treatment and complications in the study population.

Treatment and Complications		No. of patients	Percentage
Number of Injections	One	2	2.0
	Two	4	4.0
	Three	94	94.0
Physiotherapy		76	76.0
Time of start of active exercise	Immediately after injection	64	64.0
	3-4 days after injection	14	12.0
	No Exercise	22	24.0
Complications	Post-PRP Pain	6	6.0
	Post-PRP Synovitis	6	6.0
	None	88	88.0
	Follow-up loss (3 patients were lost after 1 week and two more between 1 week and 3 months)	6	6.0

Table-3: Haematological parameters of the study population.

Haematological parameters	Mean Score (±SD)
Haemoglobin	10.963±1.1701
TLC	7995±1468.3
ESR	26.91±10.899
Platelet counts (lacs/mm ³)	2.9248±3.1839
Isolated Platelet counts (lacs/mm ³)	8.88±2.6244
RBS (mg/dl)	119.92±14.724

Table-4: Symptoms of the study population at follow-ups.

Symptoms		Pre-treatment (n=100)	1 week (n=97)	3 months (n=96)	6 months (n=94)	p-value
Effusion		27 (27.0%)	13 (13.4%)	6 (6.3%)	4 (4.3%)	Chi sq.= 27.71 p<0.001
Swelling		64 (64.0%)	57 (58.8%)	36 (37.5%)	28 (29.8%)	Chi sq.= 31.50 p<0.001
Tenderness	Level 1	9 (9.0%)	14 (14.4%)	35 (36.5%)	37 (39.4%)	Chi sq.= 37.80 p<0.001
	Level 2	66 (66.0%)	58 (59.8%)	45 (46.9%)	44 (46.8%)	
	Level 3	25 (25.0%)	25 (25.8%)	16 (16.7%)	13 (13.8%)	
Crepitus		96 (96.0%)	97 (100.0%)	96 (100.0%)	94 (100.0%)	NA
Deformities	Genu Recurvatum	3 (3.0%)	2 (2.1%)	2 (2.1%)	2 (2.1%)	Chi sq.= 0.46 p=0.998
	Valgus	8 (8.0%)	9 (9.3%)	9 (9.4%)	9 (9.6%)	
	Varus	41 (41.0%)	39 (40.2%)	39 (40.6%)	37 (39.4%)	
	Varus left	0 (0.0%)	4 (4.1%)	4 (4.2%)	4 (4.3%)	
	No deformity	48 (48.0%)	43 (44.3%)	42 (43.8%)	42 (44.7%)	

Table-5: Change in Score at follow-up visits.

Scores at Follow-ups		Mean Score (±SD)	Per cent Change	p' Value
WOMAC	1 week	39.28 ± 7.82	-8.88	t= -9.86 p<0.001
	3 months	36.15 ± 8.11	-16.14	t= -10.12 p<0.001
	6 months	33.67 ± 10.11	-21.90	t= -10.20 p<0.001
IKDC	1 week	36.82±3.64	4.90	t= 5.53 p<0.001
	3 months	38.16±3.22	8.72	t= 10.13 p<0.001
	6 months	40.12±3.69	14.30	t= 10.08 p<0.001
VAS	1 week	5.29±1.08	-19.24	Z= 5.801 p<0.001

	3 months	4.37±1.34	-33.28	Z= 5.663 p<0.001
	6 months	4.15±1.38	-36.64	Z= 5.788 p<0.001
Flexion	1 week	104.6±18.12°	3.360	t= 2.919 p<0.001
	3 months	105.70±17.52°	4.447	t= 4.382 p<0.001
	6 months	105.80±17.76°	4.545	t= 4.383 p<0.001

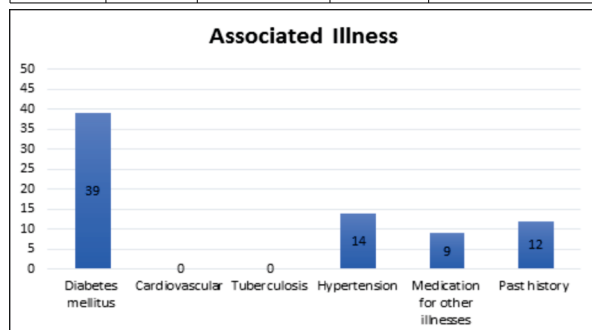


Figure-1: History of associated & past illness among study population.

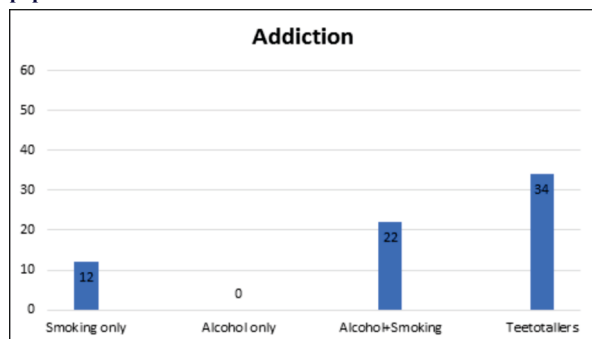


Figure 2: Addiction habits of study population.

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