

Efficacy of Intra-Articular Platelet-Rich Plasma Injections in Knee OsteoarthritisMallepogu Kiran Kumar¹, K. Udaya Kumar², M. Devender Reddy³, Sangem Srichandra Kumar⁴¹Senior Resident, Department of Orthopaedics, ESIC Medical College & Hospital, Sanathnagar, Hyderabad, Telangana²Senior Resident, Department of Orthopaedics, ESIC Medical College & Hospital, Sanathnagar, Hyderabad, Telangana³Senior Resident, Department of Orthopaedics, ESIC Medical College & Hospital, Sanathnagar, Hyderabad, Telangana^{4*}Senior Resident, Department of Orthopaedics, ESIC Medical College & Hospital, Sanathnagar, Hyderabad, Telangana

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Abstract:**Introduction:** Platelet-rich plasma (PRP) has been widely studied as a potential nonsurgical treatment for knee osteoarthritis. The current study was done to assess the effectiveness of PRP injections in terms of pain reduction and functional outcomes.**Materials and methods:** In this prospective randomized clinical study, 50 patients with early osteoarthritis knees who met the inclusion criteria received two intra-articular pure PRP injections. Follow-up assessments were performed at 6 weeks, 3 months, 6 months, and 1 year for pain reduction measured on the Visual Analog Scale (VAS) and functional improvement assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire. The pre and post injection WOMAC and VAS scores were compared. A p value < 0.05 was considered significant.**Results:** Two intra-articular injections of PRP were administered to 50 patients. Female patients were 27(54%) and male 23(46%). Majority (60%,n=30) of knees had grade II Osteoarthritis while 20(40%) knees had grade I Osteoarthritis. Each follow-up visit resulted in a significant improvement in pain reduction (VAS) and functional outcome (WOMAC), which maintained until the final follow-up appointment at one year. No complications were reported.**Conclusion:** Two intra-articular PRP injections in an early osteoarthritis knee resulted in a significant reduction in pain and improved functional results.**Keywords:** Intra-articular Injections; Knee Osteoarthritis; Platelet Rich Plasma.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Osteoarthritis (OA) of the knee joint is by far the most prevalent rheumatic disorder, and it is a primary cause of functional impairment in the elderly. [1,2] The characteristic abnormalities include articular cartilage degeneration and whole-joint failure. [3,4] As a result, cartilage begins to deteriorate and deep clefts are formed.

At the same time, the subchondral bone undergoes pathological changes, including the formation of subarticular cysts and osteophytes development. [5] These abnormalities cause joint dysfunction and pain, making standing, walking, and performing daily tasks difficult. They also have a significant negative impact on one's quality of life and psychological well-being. [6,7] Conservative

treatment of knee osteoarthritis include nonsteroidal anti-inflammatory drugs(NSAIDs),activity modification, physical therapy, intraarticular injections of steroid, Hyaluronic acid and Platelet-Rich Plasma (PRP).[8]Platelet Rich plasma (PRP) is produced after centrifugation of whole blood sample and is preferred over others because of its cost effectiveness, safety and long term efficacy.[9]

The α - granules of platelets contain Platelet Derived Growth factor (PDGF), Platelet Derived Epidermal Growth factor (PDEGF), Epidermal Growth factor (EGF), Transforming Growth factor- β (TGF- β), Insulin like Growth factor-1 (IGF-1), Fibroblastic Growth Factor (FGF), Vascular

Endothelial Growth Factor (VEGF), Hepatocyte Growth Factor (HGF), Cytokines and Chemokines.[10-12] PRP is an Orthobiologics autologous plasma with higher concentration (4 to 5 times) of platelets than plasma itself and release growth factors which are responsible for stimulation of cells and chondrocytes and enhances the repair and regeneration of damaged articular cartilage.[13]

Moreover PRP increases Hyaluronic acid and increases Aggrecan, an anti-inflammatory marker while pro-inflammatory markers like Cyclooxygenases, Interleukin-1, Metalloproteinases, Interferon gamma, Disintegrins, Selectins and Tumor Necrosis factor alpha are inhibited.[14] PRP injections have been shown to provide more pain relief and improved functional outcome at one year follow up than Hyaluronic acid, placebo or controls.[15-17] In addition statistically significant improvement has been detected on MRI in the volume of patellofemoral cartilage, lateral and medial meniscal disintegrity and synovitis in patients treated with PRP injections.[18]

The objective of our study was to determine the effectiveness of intra-articular injections of PRP in early Osteoarthritis knee in terms of pain reduction and improvements in functional outcome

Materials and Methods

This prospective randomised clinical study was conducted in the department of Orthopedics at ESIC Medical College & Hospital, Sanathnagar, Hyderabad, and Telangana. A total of 50 patients were recruited for the study after the fulfilment of inclusion and exclusion criteria.

The inclusion criteria were patients of either gender aged 40-70 years old, a history of knee pain for at least one month, a need for analgesics, and radiographic evidence of knee osteoarthritis (Kellgren-Lawrence grade 1-3) (19), with Grade 1 showing questionable narrowing of the joint space, Grade 2 showing definite osteophyte formation, and Grade 3 showing definite narrowing of the joint space with some sclerosis.

Diabetes or connective tissue problems, neoplasms, platelet abnormalities, coagulation disorders, and intra-articular steroid injections within the past six months were all considered exclusion criteria.

Method of PRP Preparation: 8.5 mL of the patient's venous blood was drawn via venipuncture and combined with 1.5 mL of anticoagulant citrate dextrose solution in a sterile vacutainer. A unit

(3ml) of PRP was obtained following two centrifugations (one at 1200 rpm for 15 minutes to separate erythrocytes and one at 1200 rpm for 10 minutes to concentrate platelets). All the procedures were performed at the same time. Within half an hour, one unit of PRP was delivered to the laboratory for platelet concentration assessment, while the other two units were used for injection. PRP contains up to ten times more platelets per milliliter than whole blood. The skin was sterilely prepped before being infiltrated with an 18-gauge needle using a standard lateral technique. Following the operation, the patient was urged to repeatedly flex and extend the leg to allow the PRP to disperse throughout the joint before transforming into a gel. Patients were told to contact their referring doctor if they had any side effects from the treatment. However, the injections were safe, and no adverse responses were observed afterward.

Outcome Measures: At the outset, we collected demographic information, clinical characteristics, and the Kellgren-Lawrence grading of knee OA. Additional measurements were performed at the start and four weeks after the third injection, including the subjective VAS, which is self-rated pain intensity at the moment of evaluation stated on a 10-cm horizontal scale, with 0 cm representing "no pain" and 10 cm indicating "worst pain." [20] The Western Ontario and McMaster Universities (WOMAC) OA index is a multidimensional self-assessment questionnaire that evaluates 17 functional activities, 5 pain-related activities, and two joint stiffness categories across three subscales. [21]

Statistics: The data was examined using SPSS version 21. Qualitative variables were computed using frequency and percentage, while quantitative variables were calculated using mean and standard deviation. The pre- and post-injection WOMAC and VAS values were compared, and the P value was calculated using the Student-T test. P value <0.05 was considered significant.

Results

We treated 50 patients with two PRP injections. Female patients were 27(54%) and male 23(46%). Majority (60%, n=30) of knees had grade II Osteoarthritis while 20(40%) knees had grade I Osteoarthritis. Right side effected were 28 (56%) and left side effected were 22 (44%).

Table 1: Characteristic features of the study subjects

	Number	%
Age (years) (mean±SD)	56.85±5.23	
Sex		
Male	23	46
Females	27	54
Side		
Left	22	44
right	28	56
Grade of osteoarthritis		
Grade-1	20	40
Grade-2	30	60

In each follow up visit a significant improvement ($P < 0.05$) in pain reduction (VAS) and functional outcome (WOMAC) was observed which persisted till last follow up visit at one year follow up.

Table 2: Outcome of PRP injections as measured with VAS and WOMAC questionnaire

Clinical parameter	Pre-Injection	Post injection				P value
		6 Weeks	3 Months	6 Months	1 Year	
VAS	7.65±1.5	6.74±2.7	4.8±2.3	3.6±1.1	1.24±2.43	0.001
WOMAC Pain	16.84±3.6	14.28±1.65	9.45±2.45	4.86±1.8	2.12±1.05	0.02
WOMAC Stiffness	6.12±2.45	5.45±1.2	4.2±2.1	2.54±2.86	2.02±3.1	0.002
WOMAC function	58.86±7.12	48.21±5.62	27.85±3.85	15.64±1.4	8.32±2.8	0.03

Discussion:

Previous studies have demonstrated that platelet-rich plasma (PRP) influences chondrogenesis and mesenchymal stem cell proliferation in a positive manner. Additionally, it may facilitate the healing process by enhancing the metabolic capabilities of impaired components. [22] Patel and Dhillon [23] showed that PRP-induced chondral remodelling can promote tissue healing and change inflammatory mechanisms by inhibiting the NFκB signalling system [24, 25], which leads to the development of OA.

In our study we administered 2 PRP injections (Leucocyte depleted) to 50 patients. Follow up visits at 6 weeks, 3 months, 6 months and one year showed statistically significant pain reduction (VAS) and functional improvement (WOMAC). The VAS score improved from pre injection value of 7.65±1.5 to post injection 1.24±2.43 at one year. The pre injection WOMAC pain score improved from 16.84±3.6 to 2.12±1.05. The WOMAC stiffness improved from pre injection 6.12±2.45 to post injection 2.02±3.1. The WOMAC function score improved from 58.86±7.12 to 8.32±2.8).

Rai and Singh et al. [26] treated 98 patients with knee osteoarthritis with two PRP injections spaced 3 weeks apart. The outcome with the WOMAC Questionnaire and VAS indicated statistically significant improvement at 6 weeks, 3 months, and 6 months, as well as a minor improvement at 1 year. Kavadar et al. [27] treated 120 osteoarthritis patients with one PRP injection (group 1), two PRP injections (group 2), and three PRP injections (group 3).

Post-injection follow-up assessments using the VAS and WOMAC questionnaires at 1 month, 3 months, and 6 months revealed significant improvements in all three groups, but particularly in group 2. Guillibert and Charpin et al. [28] treated 57 osteoarthritis knee patients with a single injection of pure PRP and found considerable pain relief and improvement in Knee Injury and Osteoarthritis Score at six months. Cole et al. [29] treated 49 osteoarthritis knee patients with leucocyte-depleted PRP and 50 with hyaluronic acid. There was no difference in the primary outcome WOMAC score between the groups.

Halpren et al. [30] treated 22 patients aged 30 to 70 with early osteoarthritis knee with PRP injection. At one year follow-up, pain score was reduced while WOMAC score was increased. Patel et al. [31] also documented significant improvement in WOMAC scores at 2 to 3 weeks, which lasted until the final follow-up at 6 months, but with minor worsening of some WOMAC scores.

Conclusion

From the study, it is concluded that two PRP injections in early osteoarthritis are a safe, efficient, minimally invasive, and cost-effective technique for clinical and functional outcomes.

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