

Effect of Mean Platelet Volume on Platelet Rich Plasma Based Injection Therapy in Patients with Osteoarthritis of the Knee Joint- A Longitudinal Study

RAVI K KOTHARI¹, ROHIT V BHALARA², GYANENDRA SINGH³, RUSHANG M DAVE⁴, GAURAVI A DHARVA⁵



ABSTRACT

Introduction: There are different types of arthritis seen in elderly patients, of which Osteoarthritis (OA) is the most common. Platelet Rich Plasma (PRP), which is derived from blood, contains many growth factors. Platelet count and indices in PRP has association with pain score of OA, further study will prove its significance.

Aim: To find the correlation of platelet parameters like platelet count, Mean Platelet Volume (MPV) and Plateletcrit (PCT) with clinical OA improvement score in PRP-treated patients of OA.

Materials and Methods: The longitudinal study was done in the Department of Pathology, PDU Civil Hospital, Rajkot, Gujarat, India, from January 2021 to October 2021. Study was conducted on 40 patients, who were administered intra-articular injection of PRP prepared using double spin method. It was injected at the site of maximum pain in the knee joint. Platelet count, MPV and PCT were noted in the pre and post intervention. Patients were followed-up at two months and six months. The data was analysed using Friedman Analysis of Variance (ANOVA) and Pearson's correlation test.

Results: The mean age of patients was 58.57±4.95 years and there were 26 (65%) females and 14 (35%) males. Increase in platelet count, MPV, PCT in PRP prepared by double spin method and improvement in Visual Analog Scale (VAS) (Before-8.38±0.63; After-4.28±0.85), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Before-63.30±4.99; After- 43.67±5.22) and International Knee Documentation Committee (IKDC) (Before-45.04±6.06; After-66.14±5.78) score were found to be statistically significant. Correlation of platelet parameters WOMAC with Platelet count (p-value=0.052, R-value=-0.310), VAS with MPV (p-value=0.005, R-value=0.436) and IKDC with PCT (p-value=0.032, R-value=0.339) were also statistically significant at six months follow-up.

Conclusion: Single dose intra-articular injection PRP in OA knee with KL Grade 1 and 2 is valuable, efficient and cost-effective treatment to reduce or delay in knee replacement. The study showed the significant correlation of platelet parameters with OA improvement scores.

Keywords: International knee documentation committee, Plateletcrit, Visual analog scale, Western ontario and mcmaster universities osteoarthritis index

INTRODUCTION

Platelet Rich Plasma (PRP) is now very popular for treating hair loss, sports injuries, and various inflammatory diseases. Early research suggests that Osteoarthritis (OA) pain and stiffness may be treated with PRP injections by altering the joint environment and lowering inflammation, but more research is needed to find a correlation between platelet indices of PRP and relief of pain in OA [1,2]. The PRP is injected into the affected area, such as a tendon or knee, as needed. The treating doctor may occasionally utilise ultrasonography to direct the injection. To hasten the healing process, it is intended to raise the concentration of particular bioproteins or hormones, known as growth factors, in a particular location. The mechanism underlying PRP injections is not well understood. PRP contains a high concentration of growth factors. They stimulate and accelerate the healing process. Thus, reducing pain and even boosting hair growth [3]. The use of PRP to accelerate the healing of bones, cartilage, and soft tissues has revolutionised the field of musculoskeletal medicine [4].

Tissue recovery is a gradual and occasionally obstinate process. It's crucial to find a way to quicken tissue recovery, not just for athletes but also for everyone who deals with tendinopathy, OA, acute muscular injuries, etc. Musculoskeletal professionals started using PRP for the treatment of cartilage issues as early as 2003, despite the scant scientific proof [5,6]. PRP has been demonstrated to be at least as effective as intraarticular hyaluronic acid and steroid

injections for the management of symptoms in early OA of the knee [7]. The use of this therapy, a minimally invasive procedure, could help to promote tissue regeneration.

Alpha granules, which are present in PRP, release almost all of their stored growth factors in the first hour and around 70% of them in the first 10 minutes [8]. Some of the cells involved in tissue repair and bone and cartilage regeneration are activated by these growth factors [9]. PRP is an autologous blood product, thus there is no risk of immunological reactions or disease transmission, but there is always a chance of a local reaction with any injection technique.

Platelet count and indices in PRP has association with pain score of OA, further studies are required to prove the strength of the association. Intra-articular PRP injection is a safe treatment modality with limited financial cost. However, expertise is required for the same. A research on early OA knee patients found that PRP was more efficient than placebo in reducing pain and stiffness and enhancing knee functioning in the short term [1]. Thus, the present study aimed to find the correlation of platelet parameters like platelet count, Mean Platelet Volume (MPV) and Plateletcrit (PCT) with clinical OA improvement score in PRP-treated patients of OA.

MATERIALS AND METHOS

The present longitudinal study was conducted in the Department of Pathology, PDU Civil Hospital, Rajkot, Gujarat, India, from January 2021 to October 2021. Ethical approval (PDUMCR/IEC/155/2021)

was obtained from Institutional Ethical Committee of PDU Medical College, Rajkot, Gujarat, India.

Inclusion criteria: All patients aged 50 years and above of both sexes, patients with symptomatic osteoarthritic knee of Grade 1 and 2 of Kellgren-Lawrence Grade [10,11], patients with little pain relief or no pain relief after conservative treatment <2 weeks and patients having platelet count normal (range: 1.5-4.5 lakh/mm³) were included in the study.

Exclusion criteria: Patients with previous surgery of knee, significant joint swelling or clinical signs of acute inflammation, patients with septicaemia and local infection and patients with known platelet/bleeding disorder were excluded from the study.

Sample size calculation: According to hospital statistics there were 57 patients with knee OA in 2019 and 41 in 2020 (KL Grade 1 and 2) at the Orthopaedic Outpatient Department (OPD). During the study period, there were 40 consenting patients who wished to undergo PRP therapy and were included in the study.

Study Procedure

The 40 patients were administered intra-articular injection of PRP, over duration of six months from January 2021 to October 2021. A 15 mL of blood was collected from the patient in citrated centrifuge tube and subsequently centrifuged in two phases. PRP obtained after the 2nd spin was injected at the site of maximum pain in the knee joint. Platelet count and MPV were noted in the blood sample drawn prior to the centrifugation and repeated in the sample obtained after centrifugation. Then under the strict aseptic precautions PRP was injected intra-articularly into the affected knee, immediately (or within 30 minutes).

PRP preparation: Patients' vitals were measured to rule out any undiagnosed pathology or raised blood pressure secondary to anxiety.

Keeping the patient in the supine position, aseptic precautions were taken and 15 mL blood was collected from the antecubital vein in citrated centrifuge tube using 20 G needle. The collected blood sample was subjected to two spins. The 1st spin, called as the soft spin, was done for 1500 rpm for 15 minutes. The supernatant plasma containing platelets was transferred into another sterile tube (without anticoagulant). Centrifuge tube at a higher speed, i.e., 3000 rpm for 10 minutes (a hard spin) to obtain a platelet concentrate. The lower 1/3rd was PRP and upper 2/3rd was Platelet-poor Plasma (PPP). Platelet pellets are formed at the bottom of the tube. PPP was removed and suspended the platelet pellets in a minimum quantity of plasma (2-4 mL) by gently shaking the tube. The remnant was PRP which is usually around 2-3 mL. The procedure was done by orthopaedic doctor at the Department of Orthopaedic of the study institute. Sample collection and PRP injection was done by same orthopaedic doctor to avoid confounding bias. Collected sample processed at department of Pathology for preparation of PRP.

Blood sample prior to centrifugation and that of the sample obtained after centrifugation were put through 3 part NihonKohden Cell Counter and platelet count and platelet indices like MPV and PCT noted for evaluation. The improvement in patient condition was measured using WOMAC [12], VAS [13] and IKDC [14,15].

PRP injection [Table/Fig-1]: Two-three mL of PRP injections was injected on the patients at the study institute; every patient was given one injection. The patient's position was supine with the knees extended.

Following patella and soft spot palpation, a landmark was formed by the collision of two imaginary lines: one from the superior border of the patella and one from the lateral border of the patella. The needle was directly aimed towards the anterior femoral cortex [Table/Fig-1].

STATISTICAL ANALYSIS

The data was analysed using paired t-test, Friedman Analysis of Variance (ANOVA) and Pearson's correlation test.



[Table/Fig-1]: Freshly prepared PRP injection administered via superolateral approach.

RESULTS

The maximum number (57.5%) of patients was between the age group of 50-59 years and the mean age of patients was 58.57±4.95 years. Out of 40 patients, 26 (65%) were females and 14 (35%) were males [Table/Fig-2].

Age (years)	Gender		Laterality		KL Grade		Total (n)
	Males (n)	Females (n)	Unilateral (n)	Bilateral (n)	Grade 1 (n)	Grade 2 (n)	
50-59	7	16	16	7	10	13	23
60-69	5	10	13	2	2	13	15
70	2	0	2	0	0	2	2
Total (n)	14	26	31	9	12	28	40

[Table/Fig-2]: Age wise distribution of gender, laterality and Grade.

Mean value of blood platelet count was lower as compared to the platelet count found in PRP. Mean of PRP MPV was more than the normal MPV value. Average value of PRP PCT was also more as found in normal blood PCT [Table/Fig-3]. Mean±Standard Deviation (SD) of scores at the baseline and at all the follow-ups showed significant improvement (Friedman ANOVA test) [Table/Fig-4].

There was a significant correlation of platelet parameters WOMAC with Platelet count, VAS with MPV and IKDC with PCT [Table/Fig-5].

Variables	Mean±SD	p-value (paired t-test)
Blood platelet (cells/mm ³)	256775±51780.8	<0.001
PRP platelet (cells/mm ³)	456425±79492.6	
Blood MPV (fL)	5.16±0.76	<0.001
PRP MPV (fL)	5.56±0.93	
Blood PCT (%)	0.12±0.02	<0.001
PRP PCT (%)	0.21±0.05	

[Table/Fig-3]: Whole blood platelet, MPV, PCT and PRP platelet, MPV and PCT. The p-value in bold font indicates statistically significant values.

Score	Baseline Mean±SD	1 st follow-up Mean±SD	2 nd follow-up Mean±SD	p-value
VAS	8.38±0.63	6.43±0.78	4.28±0.85	<0.001
WOMAC	63.30±4.99	52.69±6.69	43.67±5.22	<0.001
IKDC	45.04±6.06	53.52±7.68	66.14±5.78	<0.001

[Table/Fig-4]: Mean score change of VAS, WOMAC and IKDC at baseline, 1st follow-up (two months) and 2nd follow-up (six months).

DISCUSSION

The OA, mostly seen in elderly patients, frequently affects the knee joint, with the advancement of diseases causing a major source of disability owing to pain and deformity [16]. PRP treatment is a well-tolerated and minimally invasive technique, particularly in patients who are unfit for surgery or unable to take oral analgesics for an extended period of time.

There has been an increase in the use of PRP as a treatment modality in recent years. When platelets are activated, they release various

Correlation between Haematological parameters and Osteoarthritis (OA) scoring	R-value	p-value
Platelets		
VAS	0.005	0.973
WOMAC	-0.310	0.052
IKDC	-0.064	0.695
MPV		
VAS	-0.436	0.005
WOMAC	0.173	0.286
IKDC	0.102	0.532
PCT		
VAS	0.093	0.567
WOMAC	-0.059	0.716
IKDC	0.339	0.032

[Table/Fig-5]: Pearson's correlation between haematological parameters (Platelets, MPV, PCT) and Osteoarthritis (OA) scoring (VAS, WOMAC, IKDC) prior to injections and at final follow-up at six months.

growth factors and bioactive molecules that enhance the healing process [17]. Platelets contain a high concentration of cytokines and growth factors, which stimulate cellular growth, vascularisation, proliferation, tissue regeneration, and collagen production.

Sánchez M et al., were the first to describe the importance of plasma-rich growth factors in treating articular cartilage avulsion in a soccer player [18]. Few other studies found PRP to be effective in treating mild to moderate OA [1,8,9,19,20].

KL Grade used to define severity of disease, which was first described in 1957. Several modifications of the Kellgren and Lawrence classification system have been utilised in studies [21].

Below is the original description [21,22,10]:

- Grade 0 (none): definite absence of X-ray changes of OA.
- Grade 1 (doubtful): doubtful joint space narrowing and possible osteophytic lipping.
- Grade 2 (minimal): definite osteophytes and possible joint space narrowing.
- Grade 3 (moderate): moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends.
- Grade 4 (severe): large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends.

This present study was directed to assess the clinical implication of intra-articular injection of PRP in mild and moderate knee OA (KL Grade 1 and 2 only) and to compare its clinical efficacy using VAS, IKDC and WOMAC scores.

Various studies on coagulation suggest its relationship with inflammation. So, coagulative parameters are utilised for diagnosis as well as prognosis purposes [23,24]. MPV suggests platelet size. In severe inflammation, the MPV value decreased, as per the study on rheumatoid arthritis and ankylosing spondylitis [25,26]. OA is a chronic inflammatory disease in which there is progressive destruction of cartilage and bone. The primary goal of the study was to correlate MPV and platelet value with OA stages. As diseases progress the value of MPV changes. Their value returns to normal after being treated with PRP. As a result, the diagnostic and prognostic role of MPV can be established in OA patients.

In the present study, the scores were noted at baseline (at the time of PRP injection) then at two and six month interval. The p-value from the baseline. At two months the improvement in functional outcome is not significant (p-value>0.05) in PRP, which is similar to studies done by UsluGüvendi E et al., and Patel A et al., [27,28]. However, at six months the improvement in functional outcome is significant (p-value<0.05) in the PRP group at six months which is also similar to studies done by UsluGüvendi E et al., and Patel A et al., [27,28].

Various studies have shown that coagulative parameters like a platelet count study with Complete Blood Count (CBC) should be done at least before three months of PRP therapy to assess the potential predictive role of circulating platelets as well as identify any absolute contraindications [29-31]. However, the correlation between platelet count and clinical response is uncertain [29,32]. So this study focused mainly on the platelet count and its indices like MPV and PCT cell transplantation to determine their significance in PRP.

The amount of platelets injected into PRP determines the outcome. The present study also found some significant role of MPV and PCT on improvement of clinical outcome scores, which can be helpful in further larger scale research. Anti-inflammatory cytokines, as well as Platelet-derived Growth Factor (PDGF), Transforming Growth Factor- β (TGF- β), Vascular Endothelial Growth Factor (VEGF), Insulin-like Growth Factor (IGF) and Fibroblast Growth Factor (FGF), are released after platelet activation [33]. PRP has an anabolic effect on cartilage tissue and chondrocyte metabolism [33-36].

Limitation(s)

The limitations of the present study were the small sample size and the follow-up period was brief. Unfortunately, the correlation between MPV and PCT and better OA scores was not quantified in the study. In order to minimise unnecessary procedures because of low MPV and PCT values, more research is needed to quantify the link.

CONCLUSION(S)

Platelet count was found to have a statistically significant association with WOMAC, VAS, and IKDC in this study. Additionally, a statistically significant association was found between MPV and VAS. It can be concluded that in patients with knee OA of Grade 1 and 2, a treatment that consists of a single dosage of PRP injected intra-articular is beneficial, efficient, and cost-effective. Patients experience a reduction in pain and an increase in their range of flexion as a result of this treatment. As a result, it postpones the time when a total knee replacement is necessary, and in certain situations, it may even prevent it.

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PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Pathology, PDU Medical College, Rajkot, Gujarat, India.
2. Associate Professor, Department of Pathology, PDU Medical College, Rajkot, Gujarat, India.
3. Assistant Professor, Department of Pathology, all India Institute of Medical Sciences, Rajkot, Gujarat, India.
4. Senior Resident, Department of Pathology, all India Institute of Medical Sciences, Rajkot, Gujarat, India.
5. Professor and Head, Department of Pathology, PDU Medical College, Rajkot, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rushang M Dave,
Aashutosh, 4 Tirupati Nagar, Near Hanuman Madhi,
Raiya Road, Rajkot-360007, Gujarat, India.
E-mail: ravidave94085@gmail.com

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Oct 04, 2022
- Manual Googling: Jan 11, 2023
- iThenticate Software: Feb 15, 2023 (17%)

ETYMOLOGY: Author Origin

Date of Submission: **Oct 03, 2022**
Date of Peer Review: **Nov 19, 2022**
Date of Acceptance: **Feb 16, 2023**
Date of Publishing: **May 01, 2023**