

## To Evaluate the Functional Outcome of Platelet Rich Plasma Therapy in Osteoarthritis of Knee

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### Abstract

**Background:** Osteoarthritis of knee is a chronic, degenerative condition associated with pain, deformity, disability, difficulty in movements and reduction in the quality of life. This study aims to assess the efficacy of intra-articular injection of autologous platelet rich plasma (PRP) therapy in the management of osteoarthritis of knee.

**Material and methods:** 50 patients with symptomatic knee osteoarthritis were treated by 5 ml autologous intra-articular PRP injection and were assessed for pain, quality of life and rate of satisfaction by WOMAC score.

**Results:** 50 cases (KL grade II 18 and grade III 22) were included in the study. In KL grade II, the mean WOMAC score, pretreatment was  $57.11 \pm 6.36$ , which improved to  $53.76 \pm 7.6$  ( $p=0.000$ ) at 2 weeks, to  $31.97 \pm 4.51$  ( $p=0.001$ ) at one month, to  $26.97 \pm 3.47$  ( $p=0.001$ ) at 3 months and to  $22.11 \pm 2.99$  ( $p=0.001$ ) at final follow-up of 6 months. In KL grade III, the mean WOMAC score pretreatment was  $59.21 \pm 5.63$ , which improved to  $55.76 \pm 7.6$  ( $p=0.000$ ) at 2 weeks, to  $48.79 \pm 5.42$  ( $p=0.001$ ) at one month, to  $36.46 \pm 4.36$  ( $p=0.001$ ) at 3 months, and to  $32.12 \pm 2.66$  ( $p=0.001$ ) at final follow-up of 6 months.

**Conclusion:** Use of single PRP intra-articular injection in the management of osteoarthritis knee provides excellent pain relief, improvement in quality of life and high rate of satisfaction, which is more effective in the early stages of osteoarthritis than the advanced stage. Relief starts immediately and it increases gradually with time. PRP is a safe, easy, minimally invasive and cheap alternative in the management of knee osteoarthritis.

**Keywords:** Platelet rich plasma, Osteoarthritis, WOMAC score.

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### Introduction

Osteoarthritis (OA) is a chronic degenerative disorder of synovial joints, which is characterized by progressive disintegration of articular cartilage, remodeling of adjacent bones by formation of new bone at joint margin (osteophytes), inflammation, sclerosis and cyst formation under the subchondral bone, synovitis and capsular fibrosis. This may be caused by any condition that can cause

articular damages, and all unfavorable biomechanical conditions, which result in the mechanical overload that exceeds the ability of a joint to maintain itself [1]. Coexisting symptoms are joint stiffness, swelling, deformity, muscular fatigue, loss of function, and disability in the activities of daily living [2].

The goals for the treatment of osteoarthritis are pain relief, enhance joint mobility,

prevention or correction of deformity, and slowing the disease progression process. NSAIDs and COX2 inhibitors provide symptomatic improvement in osteoarthritis but due to lack of proven disease-modifying potential, the relief is only temporary and the outcome deteriorates with time. Oral steroids decrease inflammation and have a role in reducing pain but due to side effects, they are not recommended for long-term use. Intra-articular injections of corticosteroids and visco-elastic supplementations have been tried but American Academy of Orthopedic Surgeons (AAOS) guidelines recently demonstrates inconclusive evidence and is against the use of hyaluronic acid visco-supplementation for patients with osteoarthritis knee [2-4].

Growth factors such as platelet derived growth factor (PDGF) and transforming growth factor beta (TGF- $\beta$ ) activate tissue healing and have the potential for bone and cartilage regeneration, changing the joint milieu and homeostasis. But genetically engineered growth factors are very expensive hence limits their clinical use. Autologous platelet rich plasma (PRP) contains a high concentration of these growth factors, which suppress inflammatory mediator concentrations and their gene expression and provokes healing and regeneration in synovium and cartilage tissue. This effect of PRP of improvement in pain score and early promising results has been demonstrated in some clinical series [5]. Hence we evaluated the efficacy & functional outcome of intra-articular injection of autologous platelet rich plasma therapy in the management of osteoarthritis of knee.

### Material and methods

This prospective study was conducted on 50 consecutive patients with symptomatic knee osteoarthritis which were treated by intra-articular autologous PRP injection at our institute from 2018 to 2020. The study was approved by the institutional ethical review committee and written informed consent was obtained from all the participants.

Patients presenting to OPD with clinical symptoms of knee pain, knee joint effusion,

and medial joint line tenderness were evaluated, and all these patients underwent knee joint AP and lateral weight bearing x-rays. Knee osteoarthritis was graded on these x rays as Kellgren and Lawrence classification (KL) of osteoarthritis knee [6]. Patients more than 40 years age with knee pain and joint tenderness having knee osteoarthritis of Kellgren-Lawrence classification grade II and III on weight bearing x-rays were included in the study. Patients with severe joint deformity (knee osteoarthritis KL grade IV), inflammatory or rheumatoid arthritis, hematological diseases (coagulopathies), infections or on immunosuppressive or anticoagulant therapy were excluded from the study.

Autologous PRP injection was prepared in the outpatient department itself by harvesting 30 ml of the patient's venous blood in acid citrate dextrose (ACD) vacutainers. The blood so collected was centrifugated in two steps, first at a lower rate of 2400 rpm for 10 mins, following this the obtained PRP containing platelets was poured into another sterile test tube (without anticoagulant). Then the second centrifugation was done for this test tube at 3600 rpm for 15 mins to get a platelet focus. From this centrifuged test tube the lower third platelet rich plasma (PRP) was isolated. Under all aseptic precautions, 5 ml of this PRP was injected using 18 G needle via a superolateral approach into the involved knee joint.

Post injection, all the patients were prescribed ice fomentation, locally and paracetamol orally along with range of motion exercises. All the patients were evaluated by WOMAC score (Western Ontario and Mac master universities osteoarthritis index) [5]. The results were described as the mean  $\pm$  standard deviation (SD). ANOVA test, paired t test, chi-square test, and the simple regression analysis were used to analyze correlations between the factors. P-value less than 0.05 was considered statistically significant.

### Results

50 cases of osteoarthritis knee treated with autologous PRP were included in the study. 37 (74%) patients were females and 13 (26%)

were males. The mean age in the study group was  $52.02 \pm 6.18$  years (range 42 to 64 years). There were 12 (24.0%) patients in the age group 40 to 50 years, 20 (40%) patients were in the age group 51 to 60 years and 18 (36%) were more than 60 years. 38 (76.0%) patients had BMI > 25 kg/m<sup>2</sup>. 32 (64.0%) patients had the K-L Grade III and 18 (36%) patients had K-L Grade II osteoarthritis.

In K-L grade II, the mean WOMAC score, pretreatment was  $57.11 \pm 6.36$ , which improved to  $53.76 \pm 7.6$  ( $p=0.000$ ) at 2 weeks, to  $31.97 \pm 4.51$  ( $p=0.001$ ) at one month, to  $26.97 \pm 3.47$  ( $p=0.001$ ) at 3 months and to  $22.11 \pm 2.99$  ( $p=0.001$ ) at final follow-up of 6 months. In K-L grade III, the mean WOMAC score pretreatment was  $59.21 \pm 5.63$ , which improved to  $55.76 \pm 7.6$  ( $p=0.000$ ) at 2 weeks, to  $48.79 \pm 5.42$  ( $p=0.001$ ) at one month, to  $36.46 \pm 4.36$  ( $p=0.001$ ) at 3 months, and to  $32.12 \pm 2.66$  ( $p=0.001$ ) at final follow-up of 6 months (table 1). All the patients were extremely satisfied with the treatment. We did not observe any adverse reactions or other possible serious complications after the PRP injection in any patient.

**Table 1:** Mean WOMAC score at different time intervals

Time interval	K-L Grade II (Mean $\pm$ SD)	K-L Grade III (Mean $\pm$ SD)	P value
Pre-treatment	$57.11 \pm 6.36$	$59.21 \pm 5.63$	-
At 15 days	$50.78 \pm 7.61$	$55.76 \pm 7.6$	0.000*
At 1 month	$31.97 \pm 4.51$	$48.79 \pm 5.42$	0.001*
At 3 months	$26.97 \pm 3.47$	$36.46 \pm 4.36$	0.001*
At 6 months	$22.11 \pm 2.99$	$32.12 \pm 2.66$	0.001*

## Discussion

The pathophysiology of osteoarthritis involves a combination of mechanical, cellular and biochemical processes, which lead to an imbalance in pro-inflammatory and anti-inflammatory cytokines. These cause changes in the composition and mechanical properties of the articular cartilage and finally leading to activation of proteolytic enzymes with

destruction of articular cartilage [7-9]. Among various modalities of treatment of knee osteoarthritis, including conservative and surgical methods, recent treatments focus on resolving these cytokine imbalances by using biologics [10-12].

Autologous platelet-rich plasma (PRP) contains a high quantity of growth factors including transforming growth factor-beta (TGF- $\beta$ ), platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF), fibroblast growth factor (FGF), and hepatocyte growth factor (HGF) which accelerate the healing process and cell proliferation. These growth factors regulate the expression of the chondrocyte phenotype that may play an important role in disease progression. PRP inhibits the catabolism of articular cartilage which has been confirmed in study by Goldring [13].

Transforming growth factor-beta (TGF- $\beta$ ) present in PRP, increases expression of the chondrocyte phenotype and stimulates the differentiation of mesenchymal stem cells and stromal deposits and suppresses the synthesis of the cartilage glycoprotein and inflammatory mediator IL-1 [14,15]. Platelet-derived growth factor (PDGF) plays an important role in cartilage cell proliferation and maintenance of the cartilage phenotype by increasing the synthesis of glycoprotein [16]. Vascular endothelial growth factor (VEGF) plays a role to induce cartilage and insulin-like growth factor (IGF) stimulates the synthesis of glycoprotein and degrades its catabolism [17]. Fibroblast growth factor (FGF) and hepatocyte growth factor (HGF) are additional growth factors that function independently or in cooperation for the regeneration of articular cartilage metabolism [18]. Thus growth factors present in the PRP lead to the regeneration of cartilage and prevent the degenerative process.

We evaluated the outcome of intra-articular injection of autologous PRP in KL grade II and grade III osteoarthritis knee in 50 patients with a mean age of 52 years. These patients were assessed for healing of cartilage and reduction in inflammation indirectly, by

improvement in pain, function and quality of life in osteoarthritis knee as assessed by WOMAC score. We found significant improvement in WOMAC scores from pre-treatment to final follow-up at 6 months in both grade II and grade III OA knee. Patient profile and demographics were almost comparable in our study to the reported studies of Filardo et al, Raeissadat et al, Patel et al and Srikanth et al [19-22]. Overall mean WOMAC score at final follow-up in our study was 28 (32 for grade III and 22 for grade II), whereas the mean score in the study by Rahimzadeh et al, Vamshi et al and Güvendi et al was 31, 23, and 24 respectively [23-25]. We also did not observe any adverse reactions or any other serious complications in our patients like in other series.

We included patients of only grade II and III OA knee for intra-articular autologous PRP injection therapy like all other series [20-25], except for series by Filardo et al and Meheux et al, who considered all grades of OA knee for

intra-articular PRP injection [19,26]. This is because the PRP injections work better in the early stages of osteoarthritis knee and do not provide the expected benefit in advanced osteoarthritis of knee. We also found better improvement in WOMAC score in grade II osteoarthritis compared to grade III, confirming that the PRP works better in the early stages of osteoarthritis rather than the advanced stage. Our study is limited by relatively shorter follow-up, small sample size, and absence of a control group.

### Conclusion

Early osteoarthritis and relatively younger age are the appropriate conditions for treatment with autologous intra-articular PRP injection. PRP is a safe, easy, minimally invasive and cheaper alternative in the management of OA knee which provides not only excellent pain relief but also improvement in quality of life and high rate of satisfaction. The relief starts immediately and it increases gradually with time.

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