

## The efficacy of autologous platelet rich plasma vs homologous platelet lysate in patients with early knee osteoarthritis

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### Abstract

**Introduction:** Recently the idea of “Orthobiologics” leads to development of less invasive procedures and accelerated treatments which enhances functional recovery of musculoskeletal disorders. The desired therapeutic effect of autologous platelet rich plasma is facilitated by the ability of IL-1-Ra to limit the destructive inflammatory intra-articular (IA) actions of IL-1 $\beta$ .

**Objectives:** To evaluate the efficacy and functional outcome of autologous PRP injection and homologous platelet lysate to reduce pain, improve joint function and enhance quality of life in patients with early knee osteoarthritis and to investigate the advantages and disadvantages of PRP and homologous platelet lysate.

**Material and Methods:** A total of 121 cases of early osteoarthritis were equally divided into PRP and homologous platelet lysate group. Each patient in both groups has been given ultrasound guided PRP and homologous platelet lysate on day 0, at the end of 4 weeks and 8 weeks and all the patients were followed for up to one year. Treatment outcome measures were assessed at each visit using VAS and WOMAC scores.

**Results:** A statistically significant improvement is observed with VAS and WOMAC score in knee osteoarthritis patients over 12 months with greater advantages over homologous platelet lysate. The overall reduction of pain and enhanced joint function was observed within 1 week, 3 months and 12 months after the initial injection.

**Conclusion:** Homologous platelet lysate has the potential to offer chondroprotective and molecular approach in treating pain and functionality in patients with mild and moderate knee osteoarthritis with greater advantages over autologous platelet rich plasma.

**Keywords:** Platelet rich plasma; Homologous platelet lysate; Osteoarthritis; VAS score; WOMAC score.

### Introduction

Recent research in bioactive micromolecules leads to the discovery of minimally invasive techniques to combat patients with musculoskeletal disorders. The bioactive molecules bridged a gap between conservative and surgical management in treatment of osteoarthritis. Platelet rich plasma is a potent orthobiologic which helps in decreased morbidity and acts as a biological enhancer and improves the functional quality of life. The desired therapeutic effect of PRP is to induce IL-1Ra to limit the destructive process in the articular cartilage.<sup>(1,2)</sup> This article compares the efficacy and functional outcome of autologous platelet rich plasma and homologous platelet lysate in patients with early knee osteoarthritis.

### Material and Methods

Health care setup: Tertiary care hospital

Setting: JJM Medical College, Davangere, Karnataka.

Duration of the study: 2016 to 2018

Type of the study: Prospective cohort study

Sample size: 121

Selection of cases: 147 patients of knee osteoarthritis are clinically identified and radiologically confirmed grade 1 and 2 cases are included in the study. After excluding 26 cases according to our protocol, 121 cases were divided equally into two groups namely group A (n=57) who receive autologous platelet rich plasma injection and group B (n=64) who receive homologous platelet lysate injection as per our study protocol.

### Inclusion criteria

1. Patients with age between 30 – 70 years of both sex
2. Patients with radiological osteoarthritic knees (Kellgren Lawrence grade 1 & 2)
3. Patients with severe pain and under anti-inflammatory treatment without improvement > 3 months
4. Patients who have given consent for treatment as per our protocol
5. Regular visits in the out-patient department

### Exclusion criteria

1. Patients with h/o prior corticosteroid injection at treatment site within 3 month of duration
2. Patients with haemoglobin < 10 gm/dL and platelet count < 10<sup>5</sup>/ $\mu$ L
3. Patients with local infection at the site of the procedure, HIV, Hepatitis B or C, septicaemia and other systemic metabolic disorders
4. Patients with advanced osteoarthritis (Kellgren Lawrence grade 3 & 4 based on x ray findings)
5. Patients with rheumatoid arthritis or polyarticular arthritis
6. Patients refusal for PRP treatment as per our protocol

After getting IEC clearance from the institute and informed written consent from the patients enrolled in our study, they are subjected for thorough clinical examination to rule out the other causes of stiff and painful knee syndrome. The baseline investigations such as complete hemogram, ESR, CRP, renal function tests,

random blood glucose, serological testing for HIV 1 & 2 and HbsAg and radiographic analysis of affected knee joint are done.

**Preparation of autologous platelet rich plasma injection<sup>3</sup>**

The method by which autologous PRP prepared is called differential centrifugation. 20 ml of autologous venous blood are withdrawn into test tubes containing sodium citrate and are subjected first centrifugation of 3000 rpm for 15 minutes. Then the resultant plasma admixed with platelets are transferred into plain test tubes which are subjected for second centrifugation of 5000 rpm for 15 minutes. The resultant solution in the test tube contain upper 2/3<sup>rd</sup> portion of platelet poor plasma and lower 1/3<sup>rd</sup> portion of platelet rich plasma. 20 ml of autologous venous blood yield 3 – 4 ml of autologous platelet rich plasma solution. Before injecting autologous PRP injection, 10% of calcium chloride solution is added to autologous PRP in the ratio of 1:10.

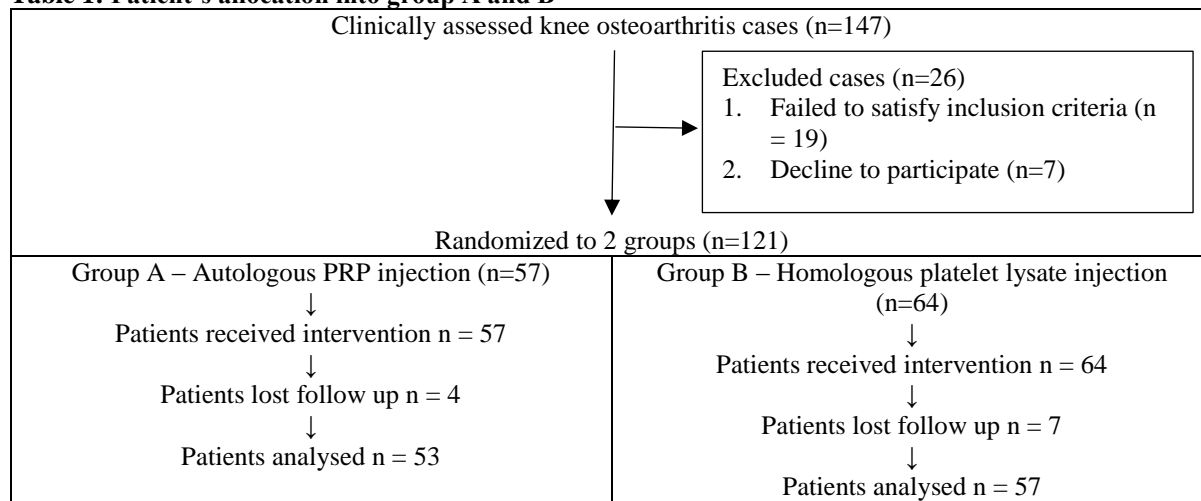
**Preparation of homologous platelet lysate injection<sup>1</sup>**

The human platelet units exclusively O positive are retrieved from blood bank and are subjected for removal of RBCs and WBCs and then subjected for freezing at -80 °C

& thawing at 30 °C for 3 cycles followed which the resultant solution are filtered by membrane filtration by 0.2 µ filter. Then finally lyophilisation of platelets are done at -30 °C to get homologous platelet lysate. The ELISA quantification of growth factors are done to quantitate the growth factors present in the homologous platelet lysate. Before injecting homologous platelet lysate, 3 ml of 0.9% NaCl is added and must be waited for 10 minutes for dissolution of platelet lysate equally in NaCl solution.

In both the groups, the knee joint is approached from anterior by tracing along the fanning of patellar tendon either in the medial or lateral joint line. The patients who got enrolled in group A (n = 57) are treated with 3 doses of 3 ml of autologous platelet rich plasma injection and group B (n = 64) with 3 doses of 3 ml of homologous platelet lysate injection on day 0, at end of 4 and 8 weeks under ultrasound guidance after securing all sterile precautions. After 10 minutes of post procedure in both the groups, a gentle knee mobilization was done. The patients were trained for home based knee strengthening programme.

**Table 1: Patient’s allocation into group A and B**



All the patients are advised to bear weight normally and the pain is combated with ice pack application. The patients are followed up for pain and range of movements in accordance with VAS and WOMAC scoring system on (pre-procedure) day 0 and (post-procedure) at the end of 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 12<sup>th</sup> months. All the recorded data were subjected for statistical analysis.

**Results**

The data obtained from participants of both the groups are subjected for statistical analysis with Mann–Whitney U test and p value.

**Table 2: Patient’s demography**

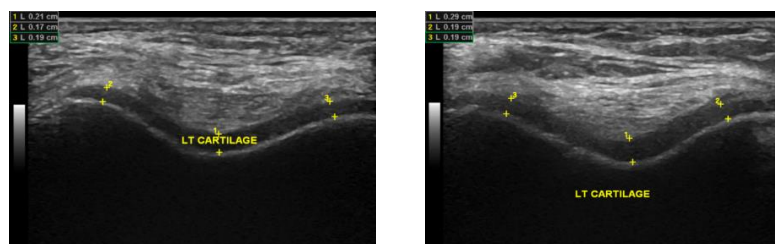
Variables		Group A (n=53)	Group B (n=57)	p value
Sex	Male	24	33	0.41
	Female	29	24	
Age	Mean±SD	51.85±10.14	57.49±10.00	0.01
	Range	(36 – 70)	(39 – 68)	

Group A – Autologous PRP group (n = 53)

Out of 53 cases, 24 (45.28%) were males and 29 (54.71%) were females. The age ranged from minimum of 36 years to maximum of 70 years. The mean age of patients in group A is  $51.85 \pm 10.14$ . The mean pre-procedural VAS and WOMAC scores were  $8.98 \pm 0.57$  and  $77.91 \pm 5.03$  respectively. At the end of 12<sup>th</sup> month, the mean VAS and WOMAC score improved to  $3.96 \pm 1.94$  and  $27.22 \pm 6.63$  respectively.



**Fig. 1: X ray of left knee in AP and lateral view showing medial joint line reduction**



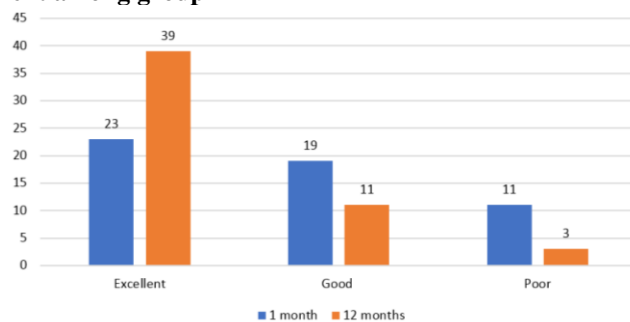
**Fig. 2: USG of left knee joint treated by autologous platelet rich plasma injections**



**Fig. 3: X ray of left knee in AP and lateral view showing post autologous PRP injection status after 15 months**

All patients are subjected to ultrasound of involved knee joint and joint space is measured and charted out both pre and post procedurally. In group A, the patients who received autologous PRP injection showed an average increase in joint space of 0.02 cm in ultrasound of knee at the end of 12 months. Out of 53 patients who underwent autologous PRP injection therapy, 23 (43.39%) patients reported excellent results, 19 (35.84%) patients reported good results and 11 (20.75%) patients reported poor results at the end of 1<sup>st</sup> month follow up. By the end of 12<sup>th</sup> month follow up, 39 (73.58%) patients reported excellent results, 11 (20.75%) patients reported good results and 3 (5.66%) patients reported poor results due to non compliance in the treatment protocol. The complications reported by group A participants are pain in 27 cases (50.94%) and swelling in 19 cases (35.84%).

**Graph 1: Quality of treatment among group A**

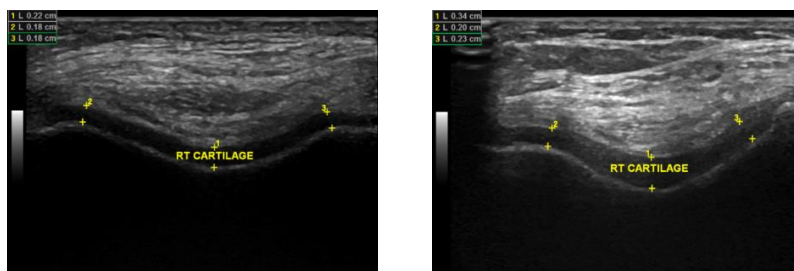


**Group B – Homologous platelet lysate group (n=57)**

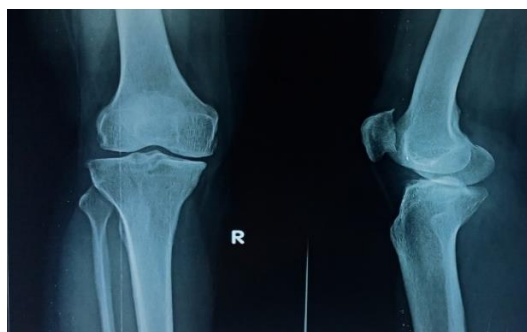
Out of 57 cases, 33 (57.89%) were males and 24 (42.10%) were females. The age ranged from minimum of 39 years to maximum of 68 years. The mean age of patients in group B is  $57.49 \pm 10.00$ . The mean pre-procedural VAS and WOMAC were  $9.10 \pm 0.38$  and  $78.08 \pm 5.03$  respectively. At the end of 12<sup>th</sup> month, the mean VAS and WOMAC score improved to  $3.76 \pm 1.41$  and  $25.63 \pm 4.49$  respectively.



**Fig. 4: X ray of right knee in AP and lateral view showing medial joint line reduction**



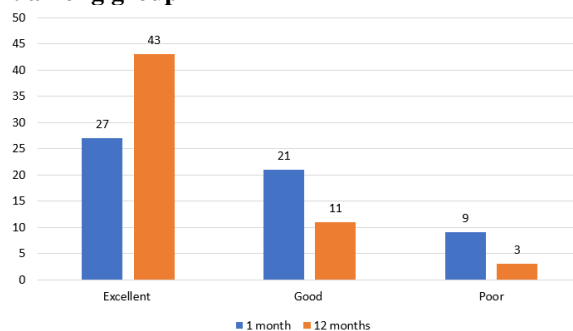
**Fig. 5: USG of right knee joint treated by autologous platelet rich plasma injections**



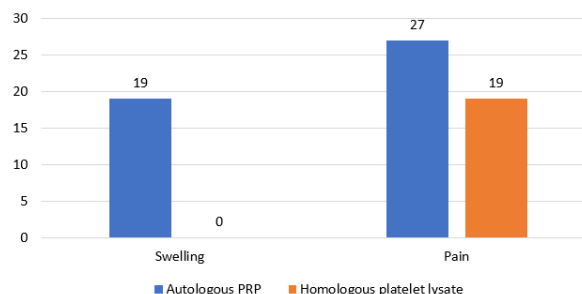
**Fig. 6: X ray of left knee in AP and lateral view showing post homologous platelet lysate injection status after 15 months**

All patients are subjected to ultrasound of involved knee joint and joint space is measured and charted out both pre and post procedurally. In group B, the patients who received homologous platelet lysate injection showed an average increase in joint space of 0.05 cm in ultrasound of knee at the end of 12 months. Out of 57 patients who underwent homologous platelet lysate therapy, 27 (47.36%) patients reported excellent results, 21 (36.84%) patients reported good results and 9 (15.78%) patient reported poor results by the end of 1<sup>st</sup> month follow up. By the end of 12<sup>th</sup> month follow up, 43 (75.43%) patients reported excellent results, 11 (19.29%) patients reported good results and 3 (5.26%) patients reported poor results. The complications reported by group B participants are pain in 19 cases (33.33%).

**Graph 2: Quality of treatment among group B**



**Graph 3: Complications**



**Table 3: VAS and WOMAC scoring**

Follow up	Group A	Group B	p value
VAS score			
Pre procedural	8.98±0.57	9.10±0.38	0.96
1 <sup>st</sup> month	7.56±7.45	8.56±3.25	0.71
2 <sup>nd</sup> month	6.91±0.93	6.23±1.93	0.09
3 <sup>rd</sup> month	4.65±3.21	5.01±2.47	0.04
12 <sup>th</sup> month	3.96±1.94	3.76±1.41	<0.001
WOMAC score			
Pre procedural	77.91±5.03	78.08±5.03	0.83
1 <sup>st</sup> month	71.45±3.92	69.34±7.12	0.67
2 <sup>nd</sup> month	55.74±1.53	54.69±4.29	0.24
3 <sup>rd</sup> month	49.02±7.32	45.06±3.10	0.02
12 <sup>th</sup> month	27.22±6.63	25.63±4.49	0.01

There is a statistically significant difference between two groups with p value for VAS score of <0.001 and WOMAC score of 0.01.

**Discussion**

Knee osteoarthritis (OA) is a chronic degenerative disease characterized by chronic pain, joint stiffness, reduced function, cartilage degradation, loss of

subchondral bone, and synovial inflammation. The histological hallmark of osteoarthritis is the destruction of articular cartilage by IL-1.<sup>4</sup>

The management options for osteoarthritis of knee are as follows., a) pharmacological management with analgesics, calcium and glycosaminoglycan supplementation, b) home based exercise programme in the form of hot fomentation and active range of knee movement exercises, c) physical therapy in the form of

active range of knee movements, wax bath and hot fomentation of the knee joint, d) intra-articular steroid injection in the form of 40 mg of triamcinolone into the affected knee joint, e) intra-articular sodium hyaluronate injection, which acts as a viscosupplement by increasing the viscosity of the synovial fluid, which helps lubricate, cushion and reduce pain in the joint, f) whole body cryotherapy with  $-110^{\circ}\text{C}$  to  $-140^{\circ}\text{C}$  provides anti-inflammatory and analgesic effect to the body, g) surgical management in the form of proximal femoral osteotomy in unicompartmental osteoarthritis, high tibial osteotomy in grade 1 and 2 osteoarthritis and total knee replacement in grade 3 and 4 osteoarthritis and varus knees and h) biological therapy with autologous platelet rich plasma injection, allogenic PRP injection, autologous conditioned serum, adipose derived mesenchymal stem cell injections.

The time duration of 4 weeks between successive injections are preferred for the formation of type 3 collagen. Three successive injections at 4 weeks interval are given to increase the concentration of growth factors at the local pathological site which act via tyrosine kinase receptor pathway which leads to transcription, translation, cell division, chemotaxis, proliferation, differentiation, neoangiogenesis, neovascularisation and production of extra cellular matrix. The process of freezing and thawing increases the production of extracellular matrix at the pathological site.<sup>4</sup>

Farid Mohammed et al studied the role of platelet rich plasma in patients of osteoarthritis knee with 55 patients which showed a significant improvement in pain and function in terms of WOMAC scores from baseline to 3 and 6 weeks, 3 and 6 months post injection. No severe adverse effects were observed during injections and follow up periods.<sup>5</sup>

Naresh kumar et al studied role of platelet rich plasma injection in osteoarthritis knee in 50 patients. The functional outcome were measured in terms of VAS and WOMAC scores which show a statistically significant outcome with p value of 0.001. They concluded PRP show a significant improvement in pain and functional status of knee at 1, 3 and 6 months after single intra articular PRP injection.<sup>6</sup>

Mishra et al described PRP enhanced mesenchymal stem cells proliferation and chondrogenic differentiation in vitro in osteoarthritis knee in view of cartilage repair.<sup>7</sup> Kon and Filardo et al evaluated the effectiveness of PRP in osteoarthritis and showed sustained efficacy. A statistically significant improvement of all clinical scores was obtained from the basal evaluation to 6-12 months follow-up ( $P < 0.0005$ ). The results remained stable from the end of the therapy to 6-12 months follow up from the basal level ( $P < 0.0005$ ).<sup>8</sup>

Forogh B et al used intra-articular platelet rich plasma in 41 patients in advanced osteoarthritis for subjective pain relief one month after intra-articular steroid injections. They concluded that one intra articular PRP injection decreases the joint pain more and longer

term, alleviates the symptoms and enhances the daily living activity and improved short term quality of life.<sup>9</sup> Sampson et al used three platelet rich plasma injections at one month interval in 14 patients with primary or secondary osteoarthritis, demonstrated improvement although statistically not significant in the cartilage thickness on sonography during first six months follow up.<sup>10</sup>

Gilbertie et al evaluated the effects of a pooled allogeneic platelet-rich plasma lysate (PRP-L) preparation on equine synoviocytes and chondrocytes challenged with inflammatory mediators in-vitro to mimic the OA joint environment. PRP-L treatment of inflamed synoviocytes would protect chondrocytes challenged with synoviocyte conditioned media by reducing synoviocyte pro-inflammatory cytokine production while increasing synoviocyte anti-inflammatory cytokine production. The challenge of chondrocytes with conditioned media from PRP-L treated synoviocytes resulted in increased collagen type II and aggrecan gene expression as well as decreased MMP-13 gene expression. They concluded that the use of pooled PRP-L for the treatment of osteoarthritis.<sup>11</sup>

Bottegoni et al observed the safety and the effect of platelet-rich plasma (PRP) intra-articular injections obtained from blood donors (homologous PRP) on elderly patients with early or moderate knee osteoarthritis (OA) who are not candidates for autologous PRP treatment with a total of 60 symptomatic patients. All patients were treated with 5 ml of homologous PRP intraarticular injections every 14 days for a total of three injections and functional assessment were documented by IKDC, KOOS and EQ-VAS scores. They observed a statistically significant improvement from baseline to the 2 month follow-up and 90% of patients were satisfied at the 6-month evaluation. They concluded that homologous PRP has an excellent safety profile but offers only a short-term clinical improvement in selected elderly patients with knee osteoarthritis.<sup>12</sup>

In our study, we have taken autologous platelet rich plasma and homologous platelet lysate into consideration in terms of safety, efficacy and functional outcome in the patients with grade 1 and 2 osteoarthritis of knee. Our study satisfied both primary goal which is concerned about safety and secondary goal which is efficacy and functional outcome of knee osteoarthritis. The overall safety profile with both autologous platelet rich plasma and homologous platelet lysate are favourable. The complications in autologous platelet rich plasma group were pain and swelling while in homologous platelet lysate was pain.

Following autologous PRP & homologous platelet lysate injection, on an average, the patients had pain relief within 10 days of injection and return to normal routine activities by end of 1<sup>st</sup> month in case of autologous PRP and 3<sup>rd</sup> week in case of homologous platelet lysate therapy. From our study, a subtle

differences are noted among both the groups which are tabulated below:

Variables	Autologous PRP	Homologous platelet lysate
Preparation method	Differential centrifugation	Lyophilisation
Amount of growth factors	Cannot be measured	Can be measured
Standardization	Non standardized	Standardized
Sterility	Unknown	100%
Need of platelet activator	Calcium chloride required	Not needed
Diluent	Absent	0.9% NaCl
Waiting phase	No waiting phase	10 mins after adding 0.9% NaCl to the platelet lysate
Safety	Highly safe	Highly safe
Efficacy	73% at the end of 12 <sup>th</sup> month	75% at the end of 12 <sup>th</sup> month
Complications	Pain 51%, Swelling 36%	Pain 33%

The short-term pain relief observed in both groups are robust in nature and are due to the anti-inflammatory effects of growth factors present in platelets. The long-term pain relief is attributed by improving joint homeostasis and quality of cartilage. But the study not only demonstrated robust improvements in mean outcome in VAS and WOMAC scores but also demonstrated good treatment effects in 73% cases in group A and 75% cases in group B at 12 months post-injection.

#### Limitation

1. Small sample size with small follow up time frame.
2. Unicentric study.
3. MRI of the knee joints have to be done to confirm the regenerative potential of chondrocytes under the influence of growth factors.

#### Conclusion

The minimally invasive technique offers the biological and natural healing cascade and cartilage augmentation in patients with grade 1 and 2 knee osteoarthritis. The homologous platelet lysate offer advantages over autologous platelet rich plasma in terms of swelling and pain. Further follow up of patients are needed to outline the analysis of long term outcome of the biological therapy.

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**Conflict of interest:** None declared.

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