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## Pure platelet rich plasma injections in the management of knee osteoarthritis

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### Abstract

**Introduction:** Osteoarthritis is a degenerative joint disease. It is a slowly progressive disease that affects individuals from the fourth decade and continues to progress at a variable rate. Knee is the most common joint affected in this condition. Osteoarthritis of the knee is a common problem in India among the population above 40 years of age. Platelets have known roles in coagulation, inflammatory processes, and immunity modulation. Moreover, during degranulation, platelets release various cytokines and growth factors (vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor-B, insulin growth factor-I, and hepatocyte growth factor) which promote angiogenesis, tissue remodelling, and wound healing. In addition, platelets can reduce painful symptoms by an unknown mechanism which is apparently dependent on the release of proteases with analgesic properties. Pure Platelet rich plasma is a rapid and cost effective method which decreases the symptoms of osteoarthritis for a variable period and results in better functional outcome.

**Materials and Methods:** This is a prospective observational study conducted on 100 knees in 75 patients suffering from Osteoarthritis treated from Feb 2017 till Jan 2018, in the Department Of Orthopaedics, Dr D. Y. Patil Hospital, Pimpri, Pune. All the baseline characteristics of the patients, like demographics, symptoms, Kellegren and Lawrence criteria and functional outcome were recorded. The patients were treated at our hospital with Pure Platelet rich plasma and followed up for a minimum period of nine months. The follow-up information included range of motion, scoring, patient satisfaction and overall outcome of the procedure in terms of patient acceptance. The data was analyzed to determine the functional outcome at nine months.

**Results:** There was satisfaction in terms of symptoms of pain and range of movements of the knee. 37% patients showed excellent prognosis, good and fair prognosis was showed by 30% of the patients while only 3% people showed poor prognosis after a follow up of nine months duration.

**Conclusion:** Pure Platelet Rich Plasma was not only associated with excellent functional outcome and short term recovery in terms of patient satisfaction and range of movements of the knee with decrease in pain nine months post-procedure but also was found to be cost effective.

**Keywords:** knee, osteoarthritis, platelet rich plasma

### Introduction

Degenerative osteoarthritis of knee is frequent and difficult to treat. The risk factors include genetics, female sex, past trauma, advancing age, and obesity. A plain radiograph may help in the diagnosis of knee osteoarthritis. There are many proposed treatment options for osteoarthritis. The main function of knee joint is to bend and straighten for moving the body. The knee is more than just a simple hinge. It also twists and rotates. In order to perform all of these actions and to support the entire body while doing so, the knee relies on a number of structures, including bones, ligaments, tendons, and cartilage. "Osteo", meaning "of the bone", "arthro", meaning "joint", and "itis, meaning inflammation, although the "itis of osteoarthritis is somewhat of a misnomer – inflammation is not a conspicuous feature which is present in rheumatoid or autoimmune types of arthritis. Some clinicians refer to this condition as osteoarthrosis to signify the lack of inflammatory response [1]. Treatments in the form of injections with P-PRP are increasingly used in clinical practice. There are high expectations of these regenerative injections, and there is a clear need for effective conservative therapies. Many studies show that injections of autologous growth factors (whole blood and P-PRP) in patients with osteoarthritis of knee have a significant impact on improving pain and/or

Function over time. Platelets have known roles in coagulation, inflammatory processes, and immunity modulation. Moreover, during degranulation, platelets release various cytokines and growth factors (vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor- $\beta$ , insulin growth factor-I, and hepatocyte growth factor) which promote angiogenesis, tissue remodelling, and wound healing [2]. In addition, platelets can reduce painful symptoms by an unknown mechanism which is apparently dependent on the release of proteases with analgesic properties [3]. The use of autologous growth factors is thought to lead to tendon healing through collagen regeneration and the stimulation of a well-ordered angiogenesis [4, 5]. Thus, Pure-platelet-rich plasma (P-PRP) may represent a new therapeutic option for degenerative osteoarthritis of knee. P-PRP is easy to prepare, relatively low cost, and can be administered in a minimally invasive manner. A number of approaches to managing early osteoarthritis have failed to reliably alleviate pain, restore normal knee function and anatomy, or to slow the progression of osteoarthritis. Biological therapies for focal knee osteoarthritis, such as Pure-platelet-rich plasma, have been proposed to improve clinical and structural outcomes by delivering a high concentration of growth factors that mediate healing and remodelling [6, 7]. Some studies demonstrated that Platelet Rich Plasma (PRP) is able to start a reparative process. Platelet-rich plasma (PRP) is promoted as an ideal autologous response as biological blood-derived product that can be exogenously applied to various tissues, where it releases high concentrations of platelet-derived growth factors that enhance wound healing, bone healing, and tendon healing. In addition, PRP possesses antimicrobial properties that may contribute to the prevention of infections. When platelets become activated, growth factors are released which initiate the body's natural healing [10].

### Materials and Methods

The current study is a prospective observational study conducted at Dr D.Y. Patil Hospital, Pimpri, Pune for duration of 12 months from Feb 2017 to Jan 2018. A total of 75 patients were included in the study, the inclusion criteria being all adult patients (age > 40 years) presenting with osteoarthritis of Knee diagnosed on the basis of clinical symptoms like pain, knee effusion, medial joint line tenderness and morning stiffness while those patients not having any of these symptoms were excluded. Data was collected using a structured proforma. Patients were recruited on presentation to the orthopaedic consulting clinics according to the selection criteria. The purpose, procedure, risks and benefits of the study were explained to the patients and a formal written consent was taken. Patients were followed up for at least nine months after the procedure and on final follow-up patients underwent post procedure assessment of range of motion of the knee using a goniometer measuring all the ranges. Patient satisfaction with the procedure was assessed through direct questioning and a satisfactory or very satisfactory response was considered acceptable in the final follow-up. Results were presented according to improvement of knee pain as presented on the visual analogue scale at follow up of 1 month, 6 months, and nine months. All patients underwent therapy with Pure Platelet Rich Plasma Injections in the operation theatre after a formal written consent and by an orthopaedic surgeon.

### Procedure

The procedure is simple. With sterile technique, we obtained appropriate amount of venous blood and transferred it to the centrifuge machine. After the processing was completed, we extracted the P-PRP from the centrifuge. Cleansing of the patient's skin around the injection site was done; towels or drapes were used to create an aseptic field. Administration of a local anaesthesia was done. With sterile technique, we injected the P-PRP into the appropriate area; and dressing or bandage was applied to protect the needle entry site.

### Preparation of PRP

A closed system was used throughout the process to avoid contamination, at least 24 hours before injection. 20 millilitres whole blood was collected from the uninvolved arm into a 60-mL syringe that contained 5 mL sodium citrate. Autologous platelet concentrate contains concentrated white blood cells and platelets that are suspended in plasma. Since an acidic anticoagulant was introduced to the whole blood used to produce the platelet concentrate, the platelet concentrate was buffered to increase the pH to normal physiologic levels. This was accomplished with 8.4% sodium bicarbonate solution added at a ratio 0.05cc of sodium bicarbonate solution to 1 cc of platelet concentrate. From donated blood P-PRP separated by two-step centrifugation at ambient temperature [for 15 min at 320rpm (soft spin) then at 2000rpm for 15 min (hard spin)]. The resulting buffered platelet concentrate contained approximately a 6 to 8 times concentration of platelets compared to baseline whole blood. No activating agent was used. The total time from blood draw to injection in the patients was about 30 minutes. All patients were given an informed written consent, which was approved by local ethical committee.



**Fig 1:** Pure platelet rich plasma

### Pre-Injection Guidelines

1. No corticosteroids for 2 to 3 weeks before the procedure.
2. Non-steroidal anti-inflammatory drugs (NSAIDs) were discontinued
3. No anticoagulation use 5 days before the procedure.
4. Increased fluid intake in the 24 hours preceding the procedure.

### Injection technique

Initially, lignocaine was infiltrated into the skin and subcutaneous tissue of both groups as a local field block. Approximately 0.05cc was also injected directly into the area of maximum tenderness. Then 4 cc platelet concentrate was injected using a 22-g needle into the knee joint. This technique involved a single skin portal.



**Fig 2:** Injecting the P-PRP into the Knee

**Post-Procedure Protocol**

Immediately after the injection, the patient was kept in sitting position without moving the knee for 15 minutes. Patients were started with static quadriceps, static hamstrings, ankle toe movements, and knee ROM exercises.

**Evaluation of the Patients**

On admission, X-rays for AP view of both the knees in standing position were taken and osteoarthritis was graded as per Kellgren and Lawrence grading (1957). Before surgery

and at every follow up patient’s pain perception was evaluated as per his perception of pain as per Visual Analogue Scale (VAS) where the patient marked a dot on a line 100 mm long. Pain score was presumed to be at 100 mm mark at the start of treatment.

**Evaluation of results**

Depending upon improvement in pain score as per Visual Analogue Scale the results were graded as follows:

1. Excellent: 90-100% improvement
2. Good: 70-89% improvement
3. Fair: 40-69% improvement
4. Poor: <40% improvement

**Observations**

We enrolled patients of osteoarthritis of knee joint (Grades 1 to 3 per the Kellgren and Lawrence radiological grading) coming to the out-patient department of Orthopaedics of Dr D.Y. Patil Hospital, Pimpri, Pune for the purpose of the study. 100 knees in 75 patients were subject to Pure Platelet Rich Plasma Injections. All the patients turned up regularly for follow up at different intervals and observations were recorded as per Performa attached.

**Table 1:** Age and Sex Distribution

Age groups	No. of Patients				Total no. of patients
	One knee		Both knees		
	Female	Male	Female	Male	
40-49 years	5	6	4	-	15
50-59 years	10	9	12	3	34
60 years and above	16	4	4	2	26
Total	31	19	20	5	75

Total no. of female patients 51(68%)  
 Total no. of knees in female patients 71(71%).  
 Total no. of knees in male patients 29(29%)  
 Total no. of male patients: 24(32%)  
 Total no. of patients: 75  
 Average age of patient: 58 years

**Table 2:** Duration of Knee Pain

Duration of knee pain	Number of knees in patients	Percentage
<1 year	30	30%
1-2 year	25	25%
2-3 year	18	18%
3-4 year	15	15%
>4 year	12	12%

**Table 3:** Radiological Grading of Osteoarthritis Knee

Radiological grades	Number of knees	Percentage
Grade 0	None	-
Grade 1	5	5%
Grade 2	10	10%
Grade 3	55	55%
Grade 4	30	30%

**Results**

The results were graded according to improvement of knee

pain as recorded on the visual analogue scale at one, six and nine months.

**Table 4:** Results at 1 Month Follow up

Age groups	Number of knees	Kellgren and Lawrence grades → No. of knees
Excellent	37(37%)	Grade 1 → 4(10.8%)
		Grade 2 → 7(18.9%)
		Grade 3 → 26(70.2%)
		Grade 4 → 0
Good	37(37%)	Grade 1 → 1(2%)
		Grade 2 → 3(8%)
		Grade 3 → 20(54%)
		Grade 4 → 13(35%)
Fair	23(23%)	Grade 1 → 0
		Grade 2 → 0
		Grade 3 → 9(39.9%)
		Grade 4 → 14(59.1%)
Poor	3(3%)	Grade 1 → 0
		Grade 2 → 0
		Grade 3 → 0
		Grade 4 → 3(100%)
Total	100	100

**Table 5:** Results at 6 Month Follow UP

Age groups	Number of knees	Kellgren and Lawrence grades → No. of knees
Excellent	40(40%)	Grade 1 → 3(7%)
		Grade 2 → 7(17.5%)
		Grade 3 → 30(75%)
		Grade 4 → 0
Good	30(30%)	Grade 1 → 2(6%)
		Grade 2 → 3(10%)
		Grade 3 → 20(66%)
		Grade 4 → 5(16.6%)
Fair	27(27%)	Grade 1 → 0
		Grade 2 → 0
		Grade 3 → 5(18.6%)
		Grade 4 → 22(81.4%)
Poor	3(3%)	Grade 1 → 0
		Grade 2 → 0
		Grade 3 → 0
		Grade 4 → 3(100%)
Total	100	100

**Table 6:** Results at 9 Months Follow-Up

Age groups	Number of knees	Kellgren and Lawrence grades → No. of knees
Excellent	37(37%)	Grade 1 → 3(7%)
		Grade 2 → 6(16.2%)
		Grade 3 → 28(75.6%)
		Grade 4 → 0
Good	30(30%)	Grade 1 → 2(6%)
		Grade 2 → 4(13.3%)
		Grade 3 → 20(66.6%)
		Grade 4 → 4(13.3%)
Fair	30(30%)	Grade 1 → 0
		Grade 2 → 0
		Grade 3 → 7(23.3%)
		Grade 4 → 23(77.7%)
Poor	3(3%)	Grade 1 → 0
		Grade 2 → 0
		Grade 3 → 0
		Grade 4 → 3(100%)
Total	100	100

## Discussion

Osteoarthritis of knee is a degenerative joint disorder and its prevalence has increased in past three to four decades because of increase in life expectancy both in males and females. With increase in age, there is corresponding increase in geriatric problem like osteoarthritis of knee that too of moderate to severe grade especially in our country where knee joint is the most commonly affected joint because of social habits of squatting and sitting cross-legged<sup>[11]</sup>. In our OPD, patients of osteoarthritis of knee constitute more than 50% of total OPD attendance daily. Since total knee joint replacement is not socially acceptable because of immense cost of implant and squatting habits of Indian patients, Pure Platelet Rich Plasma Injection has a crucial role in management of osteoarthritis of knee in Indian patients<sup>[12]</sup>. Total knee replacement is also not advisable in middle aged patient because of need of revision surgery later in life. The pain relief after P-PRP lasts for a variable period of time, and is an economical, short duration procedure, can be repeated easily without blood loss or scarring of skin. The aim of this study was to achieve the objective of evaluating the results of Injection Pure Platelet Rich Plasma in osteoarthritis of knee joint with, reference to relief of pain. A total of 75 patients (100 knees) were included in the study. The age of patients varied from a minimum of 40 years to a maximum of seventy five years with an average of 58 years. In our series and most of the studies in literature the

average age lies between 40 and 70 years. It is also clear from the study that articular cartilage is strong enough to sustain the cyclic loading before the age of 40 years. The minimal cartilage changes that occur are not sufficient enough to cause any clinical problem<sup>[14, 15]</sup>. The patients showing no improvement have range from 50-75 years with an average of 59.2 yrs. The duration of knee pain in our study was >1 year in all patients and half of them had pain of >3 years. The average duration was 2.57 years. In our study the patients included had osteoarthritis of radiological grades one to four as per Kellgren and Lawrence grading (1957). The main outcome measure recorded in our study was knee pain and was recorded on the visual analogue scale. The results were evaluated at one, six and nine month follow up. At one month the results were excellent in 37% and good in 37% knees (Of the 37 knees showing excellent results 10.8% had radiological grade 1 osteoarthritis, 89% had grade 2 and 72% had grade 3 osteoarthritis and of the 37 knees showing good results. 8% had grade 2, 54% had grade 3 and 35% had grade 4 osteoarthritis. At six months results were excellent in 40% and good in 30% (of the 40 knees showing excellent results 7% had grade 1, 17.5% had grade 2 and 75% had grade 3 osteoarthritis. Of the 30 knees showing good results 6% had grade 1, 10% had grade 2, 66.5% had grade 3 and 16.6% had grade 4. At nine months the results were excellent in 37% and good in 30% knees (of the 37 knees showing excellent results 7% had grade 1, 16.2% had grade 2 and 75.6% had grade 3 osteoarthritis. Of the 30 knees showing good results 6% had grade 1, 13.3% had grade 2, 66.6% had grade 3, 13.3% had grade 4 osteoarthritis. Results were fair in 23% and poor in 3% knees at one month (Of the 23 knees showing fair results, 39% had grade 3, 60% had grade 4 osteoarthritis. Of the 3 knees showing poor results, all had grade 4 osteoarthritis. Results were fair in 27% and poor in 3% knees at 6 months (Of the 27 knees showing fair results. 18.6 had grade 3 osteoarthritis, 81.4% had grade 4 osteoarthritis. Of the 3 knees showing poor result all had grade 4 osteoarthritis). At 9 months follow up 30% knees had fair results and 3% had poor result (Of the 30 knees showing fair results. 23.3% had grade 3 osteoarthritis and 77.7% had grade 4 osteoarthritis, of the 3 knees showing poor result all had grade 4 osteoarthritis). From the above data it is observed that at 9 months out of 55 knees with grade 3 87.2% showed excellent or good results however, of the 15 knees with grade 1 and 2 osteoarthritis 100% showed excellent results. Moreover majority of the knees having fair or poor results had grade 3 osteoarthritis.

Hence it is inferred that the benefit of Injection P-PRP in osteoarthritis of knee is far better in patients with osteoarthritis of radiological grade 1 and 2 than grade 3 and 4 [16].

In a recent study of Peerbooms *et al.* [16] a positive effect of injection of PRP in the common extension origin for lateral epicondylitis was seen. This report describes the first comparison of an autologous platelet concentrate with corticosteroid injection as a treatment for lateral epicondylitis in patients who have failed non-operative treatment. It demonstrates that a single injection of concentrated autologous platelets improves pain and function more than corticosteroid injection. These improvements were sustained over time with no reported complications [17].

The individual cytokines present in the platelet  $\alpha$ -granules have been shown to enhance fibroblast migration and proliferation, up-regulate vascularization, and increases collagen deposition in a variety of in vitro and in vivo settings [18]. Additionally, many of these cytokines have been seen to work in a dose dependent manner [18].

Stacie Boswell, Brian Cole *et al.* performed a study of using Platelet-Rich Plasma in healing of musculoskeletal tissue. Components in this milieu have bioactive functions that affect musculoskeletal tissue regeneration and healing. Platelets are activated by collagen or other molecules and release growth factors from alpha granules. Additional substances are released from dense bodies and lysosomes. Soluble proteins also present in PRP function in haemostasis, whereas others serve as biomarkers of musculoskeletal injury. Electrolytes and soluble plasma hormones are required for cellular signaling and regulation. Leukocytes and erythrocytes are present in PRP and function in inflammation, immunity, and additional cellular signalling pathways [19].

Our results of 37% excellent, 30% good, 30% good, 30% fair and 3% poor at nine month follow up were compared thoroughly with the series in the literature and we are of the opinion that Injection P-PRP is more beneficial for patients with radiological grade 1 and 2. This treatment reduces the need for analgesic and hence reduces the likelihood of side effects that the patient may suffer as a result of NSAID intake. Hence this form of treatment can be used as an alternative or an adjunct to NSAIDs. It can also be tried in patients who are on high doses of NSAIDs, patients unwilling to undergo surgery, patients who require surgery but are medically unfit and patients with mild osteoarthritis who have peptic ulcer.

## Conclusions

Injection of Pure Platelet Rich Plasma of 100 knees in 75 patients of osteoarthritis knee ranging from grade 1 to grade 4 as per Kellgren and Lawrence radiological grading was done. The aim of the study was to see the effect P-PRP in relieving pain of osteoarthritis. It is a very safe and simple procedure and helps in relieving the pain in almost all the cases. This is a very simple procedure which can be used as outpatient treatment. The magnitude of pain relief is inversely proportional to the severity of the problem but some amount of pain relief is always there. Hence we strongly recommend the use of Injection Pure Platelet Rich Plasma in mild to moderate osteoarthritis of knee for short to medium term gains.

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