

Effect of Platelet Rich Plasma in Knee Osteoarthritis

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Abstract

Background and Aims: This study aims to evaluate the effectiveness of intra-articular injection of platelet rich plasma (PRP) in reducing pain and improving physical function, in osteoarthritis.

Method: Prospective longitudinal study comprising of 100 patients divided into 3 groups according to Kallgren & Lawrence grading of osteoarthritis of knee and followed up for period of 1 year (January 18 to October 19). All patients were treated with intra-articular PRP injection (C-arm guided) in affected knee at 4 weeks apart. VAS (Visual analog scale), KOOS (knee injury osteoarthritis outcome score) used for clinical evaluation. Data analyzed using SPSS software 22.0.

Result: Outcome were almost similar for grade 1&2 though intensity of pain showed significant improvement even in grade 3 ($p < 0.05$). On the basis of VAS SCORE Highly significant improvement in pain in Grade 1 and Grade 2 osteoarthritis having p value < 0.0001 and significant improvement in Grade 3 osteoarthritis having p value $= 0.003 (< 0.05)$. On the basis of KOOS SCORE all the parameters like pain symptom, functional daily activity, sport & recreational activity and quality of life highly significant improve in Grade 1&2 p value < 0.0001 and for Grade 3 significant improvement in all parameters having p value < 0.05 .

Conclusion: PRP injection is a cost effective, reliable, minimal invasive, no side effect, good efficacy & used in less equipped setting. And showed clinical as well as functional improvement in VAS score and KOOS score. It is highly significant for grade 1 and 2 and significant for grade 3 osteoarthritis.

Keyword: Platelet rich plasma (PRP); Knee injury & osteoarthritis outcome score (KOOS); Visual analogue scale.

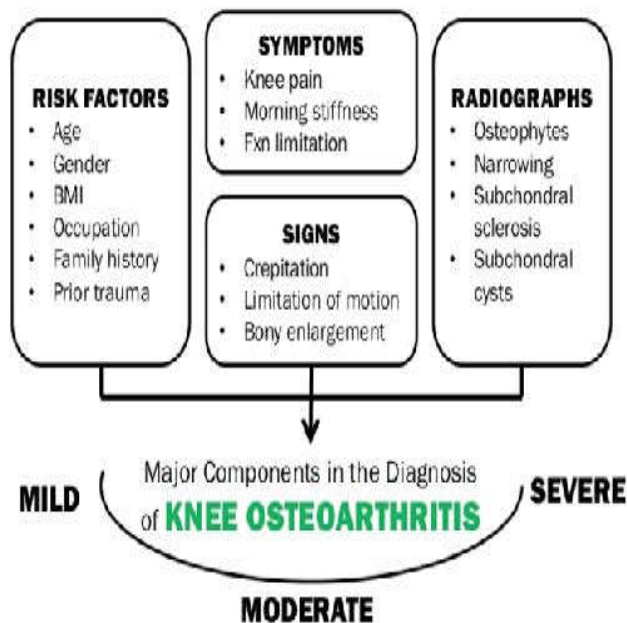
Introduction

Osteoarthritis is the leading cause of disability in human.¹ Knee osteoarthritis accounts for more than 80% disease burden comparative to other medical conditions.² India is likely to notice an endemic of osteoarthritis in 2013. Osteoarthritis in India affects over 15 million Indians each year with prevalence of

22 to 39% and this prevalence increased drastically with age after 50 years.³

The term osteoarthritis is defined as an idiopathic slowly progressive disease of diarthrodial (synovial) joints mainly occurring late in life and characterized pathologically by focal degeneration of articular cartilage, subchondral bone thickening

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Zhang W, Doherty M, Peol G, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis*. 2010;69(3):483-489.

(sclerosis), marginal osteochondral outgrowth (osteophytes), and joint deformity.⁴

There are various predisposing factor & sign-symptom are.⁵

Management Non Pharmacological

Education like life style modification , behavioural-intervention, weight loss, and physiotherapy like quadriceps strengthening.⁶

Pharmacological-Symptom Modifying Drugs:

Acetaminophen is recommended as first line therapy for osteoarthritis in addition to non-pharmacological therapy.⁷

Salicylate and NSAIDS for those who do not obtain adequate pain relief with paracetamol.⁷COX-2inhibitors like celecoxib, etoricoxib, valdecoxib for pain mangement and with better gastrointestinal tolerability, but having some cardiovascular general side effect.

Tramadol is good for pain, stiffness, physical function, in patient with chronic pain.⁸

Intraarticular corticosteroid injection most effective in patient with inflammation, effusion or both .⁹

Symptomatic slow acting drug for osteoarthritis/structure modifying oa drug-Hyaluronic acid (hyalgan and synvisc) are viscosupplementation use in OA knee & Diacerein and its active metabolite has capability to inhibit IL-1 β .



Operative Method- Includes 1- Joint debridement. 2- Realignment osteotomy 3- Joint replacement 4-Arthodesis.

Platelet Rich Plasma For Treatment of Knee Degeneration And Osteoarthritis

There are number of side effect after using the pharmacological drug in Osteoarthritis (gastric irritability, cardiovascular problems etc.) For operative management for osteoarthritis , it needs highly skilled and experienced surgeons and they are not cost effective.

Recently platelet rich plasma has been proposed as a useful modality in treatment of osteoarthritis knee joint which is cost effective and having less side effects comparative to existing treatment. Platelet rich plasma is autologous blood derived product Principally composed of a high concentration of Platelet. Platelet rich plasma therapy provides delivery of a highly concentrated cocktails of growth factors to accelerate healing.

Broadly platelet concentration are of 4 types:-¹⁰

Pure prp

Leukocyte rich prp .

Pure platelet rich fibrin (prf)..

Leukocyte rich prf

Platelets contain three types of granules -

Lysosomal granules,

Dense granules

Alpha granule

Alpha Granules-having GFs, like Platelet derived growth factor (PDGF), transforming growth factor(TGF-β), Platelet derived epidermal growth factor(PDEGF), Vascular endothelial growth factor(VEGF), Insulin-like growth factor(IGF-1) and epidermal growth factor(EGF); also contain cytokine and chemokines, which involved in stimulating chemotaxis, cell proliferation and maturation, modulating inflammatory molecules and maturation.

Dense Granules- Store ADP, ATP, calcium ions, histamine, serotonin and dopamine, which are also play a complex role in tissue modulation and regeneration.

Plasma itself help in healing mechanism of connective tissues and also contributing to the platelet stimulus in tissue regeneration.^{11,12}

Aims and Objective

The aim is to evaluate the effectiveness of platelet

rich plasma in reducing pain.

Objective is to assess the improving physical function in osteoarthritis knee.

Material and Methods

This study had been conducted in the Department of Anesthesiology critical care and pain medicine, GSVM Medical college & Associated Hospitals, Kanpur.

Study Group :

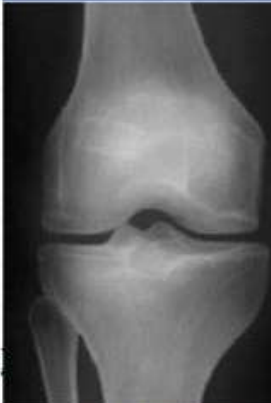

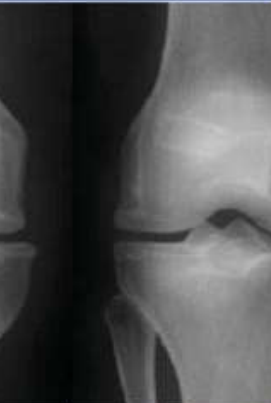
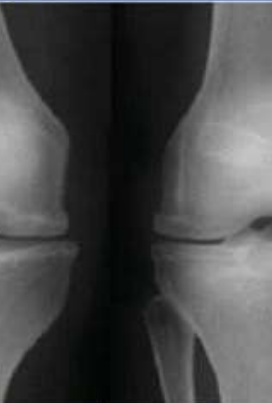


The study included patient of knee osteoarthritis admitted through Pain OPD of this Institution.

Study Design : Prospective Study, Single Arm, Open Label, to evaluate efficacy and safety of PRP technique in Knee Osteoarthritis

Study Duration : 1 year, January 2018 to October 2019.

Sample Size:- 100 Patient of OA Knee

Statistical Analysis : Analysis of data was done using the SPSS software 22.0 . The results were expressed as mean ± SD. Ap value of 0.05 or less

Kellgren-Lawrence Grading Scale					
					
Grade 1	Grade 2	Grade 3	Grade 4	Grade 4	Grade 4
Classification	Normal	Doubtful	Mild	Moderate	Severe
Description	No Features of OA	Minute Osteophyte: doubtful significance	Definite Osteophyte: normal joint space	Moderate Joint Space Reduction	Joint Space Greatly Reduced: subchondral sclerosis

is considered significant. A paired t test, Non parametric paired t test was used for comparison of the data. ANOVA (Analysis of variance) is used.

Inclusion criteria:

Unilateral / bilateral osteoarthritis knee patient of Grade 1 , 2 & 3 on basis of Kellgren -Lawrence classification.

Age more than 35 years
pain and swelling more than 4 months

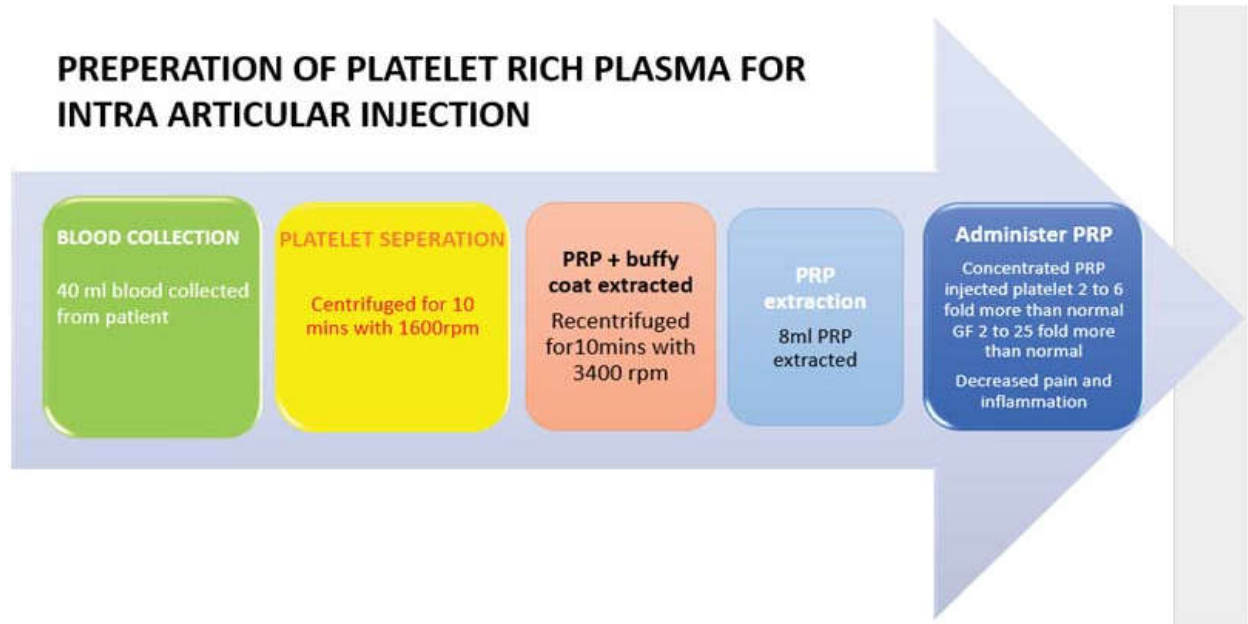
Exclusion Criteria:

Age more than 70 years
Grade 4 osteoarthritis knee.
3. disease like diabetes, rheumatoid arthritis,

hematological disease, severe cardiovascular diseases, infections, immunodepression, patients therapy with anticoagulants or anti-platelet aggregants

articular injection A 40ml venous blood sample drawn from patient itself under aseptic conditions in a 50ml syringe with 4ml CPD-A as anticoagulant for every knee treated. Then, 2 centrifuge twice the first at 1600 rpm for 10 minutes to separate

Preparation of platelet rich plasma and intra



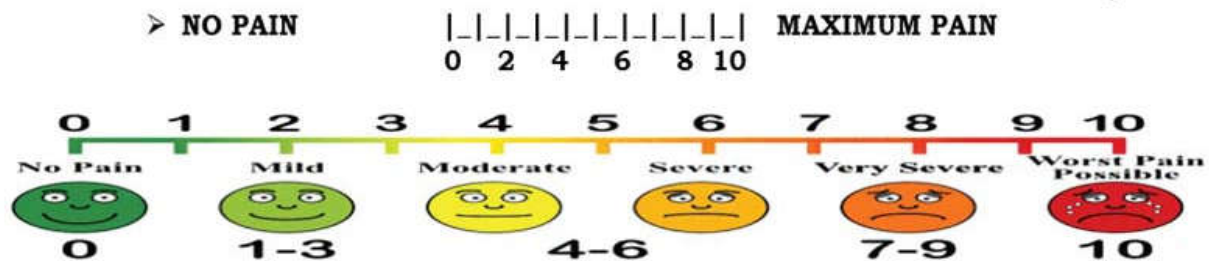
erythrocytes and a second at 3400 rpm for 10 minutes to separate concentrate platelets produced a unit (08ml) of PRP . The unit of PRP was divided into 2 small units of 2ml and 6ml.

After the injection, patients were sent home with instructions to restrict the use of leg for at-least 24 hours and to use cold therapy/ice on affected area to relieve pain. During this period of 72 hours, the use of non-steroidal medication was forbidden, however, if patient complain for pain we prescribe Paracetamol for pain management. patients were advised life style modifications, Physical therapies like Quadriceps strengthening exercises.

2ml was sent to the laboratory for analysis of platelet concentration and microbiological assessment. After getting the quality analysis of PRP. The remaining 6 ml PRP was injected in the knee^[18]. Followed by two similar injection cycle of PRP at a interval of 4 weeks.

We assess the effect of platelet rich plasma

> **VISUAL ANALOGUE SCALE**



on pain and functional activity of patient by using VAS Score and KOOS Score at 1,4,6 & 12 month from 1st day after intraarticular injection.

Visual Analogue Scale

Pain was further graded as –

0 – (VAS 0) comfortable

1 – (VAS 1-3) Mild Pain

2 – (VAS 4-6) Moderate pain

3 – (VAS 7 – 10) Severe pain

Knee Injury and Osteoarthritis Outcome Score (KOOS)¹⁷

The Knee Injury and Osteoarthritis Outcome Score (KOOS) is a questionnaire and it contain five item: pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life and. all items have five possible answer options scored from 0 (No problems) to 4 (Extreme problems).

Interpretation of scores

Scores are 0–100 scale, and zero represent extreme knee problems and 100 represent no knee problems. Scores between 0 and 100 represent the percentage of total possible score achieved.

Results

First we enrolled 150 patient 40 patient are exclude because 30 patient not meeting inclusion criteria 8 refused , 2 respond to conservative treatment. 10 patient lost to follow up. Hence, the wanalysis done on 100 patients.

Table 1: Distribution o f patients of osteoarthritis according to gender

Sex	No. of patients	%age
No. of males	55	55%
No. of females	45	45%

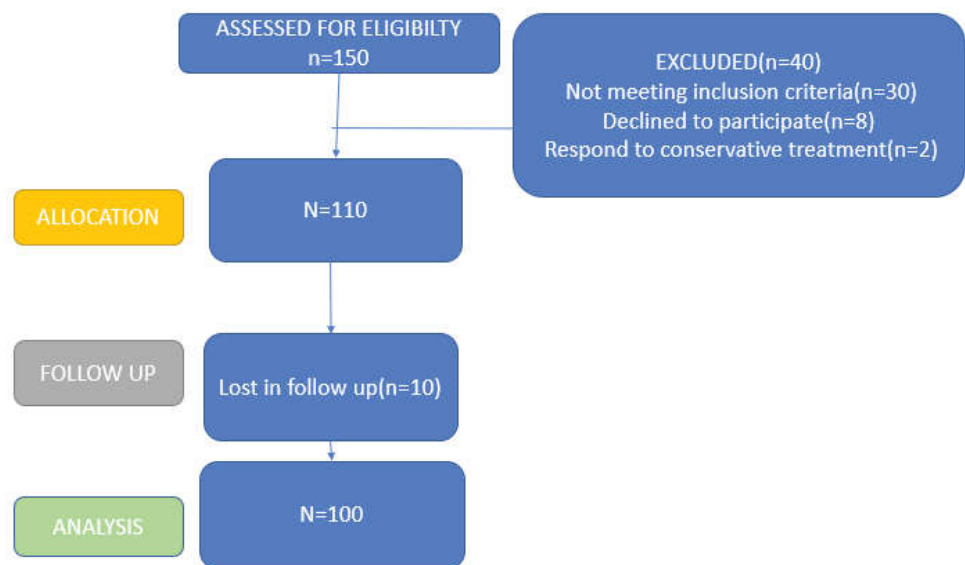
In our study there is 55% are male and 45% are female

Table 2: Age distribution of different grades of osteoarthritis in study subjects

Age distribution	No. of grade I Osteoarthritis		No. of grade II Osteoarthritis		No. of Grades III osteoarthritis	
	No.	%	No.	%	No.	%
35 – 44	9	9	1	1	0	0
45 – 54	16	16	9	9	0	0
55 – 64	5	5	33	33	2	2
65 – 75	0	0	11	11	14	14

Most of the patient are of 55 – 64 years of age having grade 2 osteoarthritis of total study subject. in 35 – 44 years of age maximum patients of grade

ENROLLMENT



1 osteoarthritis in 45 – 54 years of age maximum patients of grade 1 osteoarthritis while in 65 – 75 years of age 14 patients of grade 3 osteoarthritis and 11 patients are grade 2 osteoarthritis means severity increases with age.

Table 3: Comparison of VAS Score to study subjects before and after PRP administration

Determinant	PRE PRP		Post PRP	
	Mean	SD	Mean	SD
VAS Score	7.34	±.88	3.22	1.80±

P value < 0.0001

In our study mean pre injection VAS score is 7.34 ± 0.88 and it improved to score of 3.22 ± 1.80 at 12 months of follow up.

	Pre-PRP		Post-PRP		P value
	Mean	± S.D.	Mean	± S.D.	
Grade 1	6.8	±0.653	2.4	± 0.84	<0.0001
Grade 2	7.3	± 0.86	2.57	±0.80	<0.0001
Grade 3	7.8	± 0.85	6.8	± 1.01	=0.0029

In our study patient having grade 1, grade 2, grade 3 all are improved but grade 1 and grade 2 much better improved that grade 3.

In grade 1 and grade 2 osteoarthritis there has been very highly significant improvement in KOOS score while there has been highly significant improvement in a KOOS score in grade.³

Discussion

Platelet Rich Plasma has emerged as noble technique cost effective, reliable, good efficacy least side effect and can be used in less equipped setting in the treatment of osteoarthritis. Platelet rich plasma point to having a two to eight fold increase in platelet concentration and one to twenty five fold growth factor concentration of that of blood. PRP is an autologous blood derive product has been used as a treatment and has shown to have promising result in terms of clinical function. As per Laudy *et al*,¹⁴ the level of evidence regarding this association is not strong and needs further corroboration specially in different environmental and clinical situation as well as different other alternative treatment option.

There were two major consideration while planning the study First is whether intra-articular use of platelet rich plasma is feasible without complication Second whether platelet rich plasma provide a clinical/functional improvement in patient with osteoarthritis knee.

For this purpose, a total of 100 patients of with

unilateral or bilateral osteoarthritis underwent of PRP interventions and were subsequently followed up upto 12 month for symptomatic relief. Age of patient ranged from 35 to 70 years with a mean of 57.68 ± 8.77 years. Filardo *et al*¹⁵ too in their series reported the mean age of patient as 56.5year which is close to the mean age of present study. In present male female ratio is 55 and 45%. In different clinical study evaluating the role of platelet rich plasma the gender ratio has shown a variability. Wang-Saegusa *et al*.¹⁶ in their study had 41.8% women, as observed in present study. But in another Indian study Patel, Sandeep *et al*.¹⁸ reported 70.7% of their study population is women.

In our study we aimed to show the efficacy of PRP application in reducing pain & improving physical function in OA Knee and find that PRP application improved pain and clinical outcomes. PRP enhance synthesis of type 2 collagen and chondrocyte by stimulating the proliferation of chondrocytes and pluripotent mesenchymal.

In present study, majority of cases had bilateral disease (54%). and majority of patient is Grade 2 (54%) followed by Grade 1 (30%), and Grade 3 (16%) respectively. Compared to this. Filardo, KON *et al*¹⁵ in there study reported 57.9% patient in KL grade 1-3 and remaining 42.1% in KL grade 4. In Spakova T *et al*¹⁷ study total of 120 patient were included which include Grade 1, Grade 2, Grade 3 osteoarthritis patient.

Vas Score At Follow Up-

In our study over all VAS score after PRP decreased from 7.34±0.88 to 3.22±1.8 at 12 months of follow up. very highly significant improvement in VAS Score in Grade 1 and Grade 2 Osteoarthritis pvalue <0.0001 while there is significant improvement in Grade 3 osteoarthritis with pvalue of 0.0029. Sampson S *et al*¹⁹ conducted a study in which mean VAS score during moving decreased from 4.5 to 2.5 at 12 month of follow up. Sandeep *et al*¹⁸ conducted a study in which the VAS score decreased from 4.54 to 2.16 at 52 week followup. which is close to our study.

Koos Score Assesment

In our study KOOS Score there had been significant improvement in all 5 components p value in all cases had been less then 0.0001. there has been highly significant improvement in avg. KOOS Score in Grade 1 Grade 2 osteoarthritis and for grade 3 significant improvement, In Grade 3 osteoarthritis KOOS score for pain is .0041, for symptom 0.0065 and for functional daily activity

is 0.033 and for sports and recreational activity is 0.012 and for quality of life is 0.0004 which is significant but on other side for grade 1 and 2 is <.0001 which is very highly significant. with max improvement is in quality of life. Alberto Gobbi *et al*²⁰ conducted a study in which KOOS scoring showed significant improvement in all components at 12 months of follow up So on the basis of VAS SCORE AND KOOS SCORE we can say that PRP is effective for Grade 1,2 and 3 but most effective for grade 1 and 2

No serious complication was noted in any case.

Conclusion

The Platelet Rich Plasma showed clinical improvement in VAS score and KOOS score. It is highly significant for grade 1 and 2 and significant for grade 3 osteoarthritis. Thus The findings of study conclude that PRP is cost effective, reliable, good efficacy ,having no side effect & used in less equipped setting and useful in improving the symptoms and functions of patients knee joint.

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