

Original Research Article

Comparison between single spin and double spin platelet rich plasma in pain and functional outcome of osteoarthritis knee: a randomized controlled trial

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ABSTRACT

Background: Osteoarthritis (OA) is condition characterised by progressive degeneration of joint cartilage, eventually leading to deformity of the joint. OA causes pain and disability and impacts on quality-of-life. Intra-articular platelet rich plasma gives favourable outcomes in OA knee; however, efficacy may be affected by method of preparation. Hence, this study comparing single spin and double spin platelet-rich plasma (PRP).

Methods: A randomised controlled trial done among patients of OA who visited Department of Physical Medicine and Rehabilitation, Regional Institute of Medical Sciences, Imphal during August 2019-July 2021. Patients with OA knee having radiological findings of Kellgren Lawrence (KL) grade 2 and 3 (n=62) randomized into single spin PRP, (n=31) and double spin PRP, (n=31) groups and intra-articular PRP injection was given.

Results: Baseline characteristics were not statistically significant. At the end of 1 week, improvement in mean difference of VAS was observe however not statistically significant (p=0.71). At end of 12 weeks and 24 weeks, there were statistically significant improvement in both mean difference of VAS (p=0.00) and WOMAC (p=0.002). Post intervention, out of the single spin PRP group, (64.51%, n=20) had complaints of adverse effects swelling, pain, redness whereas (6.45%, n=2) patients who received double spin PRP had adverse effects.

Conclusions: Platelet rich plasma obtained by double spin method has long term improvement in both pain and function in patients with KL grade 2 and 3 OA knee than PRP from single spin method. Patient who received single spin PRP has more frequent post injection flare ups.

Keywords: OA, PRP, Regenerative therapy, Single spin and double spin PRP, Intra-articular injection, Western Ontario and McMaster Universities OA Index (WOMAC)

INTRODUCTION

Osteoarthritis (OA) is condition characterised by progressive degeneration of joint cartilage, leading to sequelae of joint space reduction, osteophyte formation, subchondral sclerosis and cyst formation and eventually deformity of the joint. OA is a major cause of knee disability owing to an inadequate healing response in the inflammatory milieu. It is a major public health problem

worldwide and is projected to rapidly increase as the population ages and rates of obesity escalate.¹ According to World Health Organisation (WHO), OA is the second commonest musculoskeletal problem in the world and affects 30% of the population after back pain (50%). WHO, estimates that OA affects 9.6% of men and 18% of women older than 60 years of age. OA causes pain and disability and impacts on quality-of-life. The disability associated with OA results in a considerable economic

burden, both in direct costs related to treatment, particularly joint replacement surgery, and job-related indirect costs, including loss of productivity.

As such, there is no cure for OA and treatments are focused to alleviate pain and prevent functional decline. Pharmacological therapies (analgesics and anti-inflammatory agents) and non-pharmacological therapies are recommended. However, use of these drugs can have serious adverse consequences and compliance to exercise is often poor leading to lack of long-term benefit. Hyaluronic acid (HA) and corticosteroids are common intra-articular therapies for OA. HA has variable recommendations given across clinical guidelines. Intra-articular corticosteroids give short-term pain relief up to few weeks. With time, progressive structural deterioration occurs with worsening symptoms needing for joint replacement surgery.

There has been an increasing interest in the use of autologous growth factors, such as intra-articular injections of PRP for treatment of knee OA. The regenerative effect and anti-inflammatory potential of PRP is used for treatment of various musculoskeletal problems like tendinitis, ligament tears, including OA. A number of randomized controlled trials (RCTs) were reported with favourable outcomes of PRP injections for OA knee.²

PRP is an autologous blood product that contains 3-8 times elevated concentration of platelets above that of whole blood. Degranulation of the platelet's releases growth factors while the plasma contains cytokines, thrombin, and other growth factors with biological and adhesive properties. The concentration of platelets differs depending on the different systems and manufacturers, gravity forces and times of centrifugation, as well as patient's physiological status like the baseline platelet count. Basic centrifugation can follow single or double spin protocols, controversy exists about the effects of these two protocols on separation. This study aims to compare the effectiveness of single spin and double spin platelet rich plasma in pain and functional outcome of OA knee joint.

METHODS

A randomised controlled study was conducted for a period of 2 years, August 2019-July 2021 in patients of OA knee who visited Department of Physical Medicine and Rehabilitation, Regional Institute of Medical Sciences, Imphal, Manipur. Patients were diagnosed with OA knee based on the clinical presentation of knee pain, swelling and crepitations according to the American college of Rheumatology (ACR) 2016 revised criteria. Inclusion criteria were radiological findings of KL grade 2 and 3 in X-ray both knee in standing AP view, platelet count more than 1.8 lakh/microliter. Patients who received corticosteroid injection within last 12 weeks, history of platelet dysfunction syndromes, malignancy, systemic illnesses, haemoglobin level less than 10 mg%, were

excluded from the study. A sample size of 62 was calculated using formula

$$N=(Z\alpha + Z\beta)^2(S_1^2 + S_2^2)/(m_1 - m_2)^2$$

According to a study conducted by Socuoglu et al considering 95% power, and 5% level of significance and 10% for drop outs to counter attrition bias.³ Patients enrolled in study were assigned for single spin PRP and double spin PRP injection by block randomisation technique.

PRP was procured by using two methods, for which a 24 ml of blood was drawn under proper aseptic and antiseptic precautions, and put in 3 acid citrate dextrose anticoagulant containing tubes. The three tubes were centrifuged at 2400 revolutions per minute for 10 minutes. The clear supernatant fluid was taken out using a 20-gauge spinal needle. This was the single spin PRP that we used for injection in control group. For double spin PRP for the intervention group the single spin sample was put in plain vials and centrifuged again at 3600 rpm for 15 minutes. After centrifugation upper two-third of the resultant fluid, the platelet poor plasma is discarded. Remaining lower one-third was used for injection for double spin platelet rich plasma group.

For injection procedure, the patient was position in supine, with both legs hanging down from the edge of bed. Mid-thigh to mid-calf area was draped with sterile green sheets and using 5ml syringe the platelet rich plasma is injected into the knee joint from the lateral approach. And follow up was done at the end of 1 week, 12 weeks and 24 weeks. For subjective pain intensity numerical rating Visual analogue scale 1-10 was used. For functional improvement the Western Ontario and McMaster universities OA index (WOMAC) was used.

Ethics approval was sought from the Institutional Research Ethics Board.

Statistical analysis was done using statistical package for the social sciences (SPSS) version 25. Mean, frequency, percentage and standard deviation was used for descriptive data. For categorical data chi-square test was used and for continuous variable student's t test was used.

RESULTS

The baseline characteristics of the patients in control and intervention group was not statistically significant (Table 1). Therefore, we proceeded with the study. Females were more affected than males in both the groups (88.70%, n=55), coming with two-three years of symptoms (80.64 %, n=50) and most of them were housewife (64.51%, n=40). The participants in overweight category according to Asia Pacific body mass index (BMI) classification was maximum (62.90%, n=39). Outcome measures at baseline were not statistically significant (Table 2). Post intervention, out of the single spin PRP group, (64.51%,

n=20) had complaints of adverse effects swelling, pain, redness whereas (6.45%, n=2) patients who received double spin PRP had adverse effects (Table 5).

Table 1: Comparison of baseline characteristics between the group, (n=31).

Variables	Groups (%)		P value
	Single spin PRP	Double spin PPR	
Mean age ±SD	60.23±10.09	64.23±7.34	0.519
Gender			
Male	3 (0.9)	4 (14.28)	1.00
Female	28 (90.3)	27 (87.09)	
Duration (Months)			
<12	5 (16.1)	5 (16.1)	0.345
24	11 (35.485)	16 (51.61)	
36	13 (41.93)	10 (32.25)	
>4 years	2 (6.4)	0	
Occupation			
Housewife	22 (70.96)	18 (58.06)	0.202
Office worker	5 (16.1)	3 (0.9)	
Manual labourer	3 (0.9)	4 (12.90)	
Others	1 (3.22)	6 (19.35)	
Side of affection			
Right	18 (58.06)	15 (48.38)	0.611
Left	13 (41.93)	16 (51.62)	
KL grade			
2	7 (22.58)	7 (22.58)	1.00
3	24 (77.41)	24 (77.41)	
BMI (kg/m²)			
Normal (18.5-24.9)	11 (35.48)	4 (12.90)	0.11
Overweight (25-29.9)	17 (54.83)	22 (70.96)	
Obese (>30)	3 (9.67)	5 (16.12)	

Table 2: Comparison of baseline of outcome measures.

Outcome measures	Groups		P value
	Single spin PRP (mean ±SD)	Double spin PRP (mean ±SD)	
VAS	7.71±0.783	7.77±0.56	0.71
WOMAC	65.61±10.42	63.45±6.3	0.32

Table 3: Comparison of mean changes of VAS scores between the two groups from baseline to 1 week, 12 weeks and 24 weeks follow up, (n=62).

Mean difference VAS (Weeks)	Mean changes from base line		P value
	Single spin PRP	Double spin PRP	
1	-2.32±1.04	-2.74±0.89	0.95
12	-3.35±1.25	-4.45±0.85	0.00
24	-3.16±1.93	-5.41±1.17	0.00

Table 4: Comparison of mean changes of WOMAC scores between the two groups from baseline to 1 week, 12 weeks and 12 weeks follow up, (n=62).

Mean difference WOMAC (Weeks)	Mean changes from base line		P value
	Single spin PRP	Double spin PRP	
1	-16.12±7.20	-25.48±6.65	0.00
12	-30.38±9.30	-37.12±7.22	0.002
24	-30.38±9.30	-37.12±7.22	0.002

At the end of 1 week, there is statistically significant improvement in mean difference of WOMAC and improvement in mean difference of VAS was observe however not statistically significant. At end of 12 weeks and 24 weeks, there were statistically significant improvement in both mean difference of VAS and WOMAC (Table 3 and 4).

Table 5: Adverse effects following injection, (n=31).

Mean difference VAS	Mean changes from base line (%)		P value
	Single spin PRP	Double spin PRP	
No complications	11 (35.48)	29 (93.54)	0.000
Complications (pain, swelling, erythema, others)	20 (64.51)	2 (6.45)	0.000

DISCUSSION

OA knee is a chronic, progressive degeneration of joint which has a large impact on patients’ quality of life because of the pain and functional decline. No definitive treatment is available and therefore only short terms drug therapy to reduce pain and improve function by introducing exercises is the routine treatment that is employed. Local targeted approach into the joint became a fairly common practice, corticosteroids, ozone gas and HA preparations are injected intra-articularly, they may lead to short term benefits however in long term these are not promising. Randomized controlled trials showed favourable outcomes for intra-articular PRP. In a meta-analysis of randomized controlled trials done by Shen et al they have concluded that intra-articular PRP injections are more efficacious in the treatment of knee OA in terms of pain relief and self-reported function improvement at 3-, 6- and 12-months follow-up, compared with other injections, including saline placebo, HA, ozone, and corticosteroids.⁴ Since final product PRP may differ in concentration and potency according to methods of preparation, this study was conducted to compare the effectiveness of PRP obtained by single spin and double spin method. Treatment with PRP injections reduces pain, improves knee function, improves quality of life in short-term as concluded in a study by Filardo et al.⁵ Kon et al

also found that PRP is safe, reduces pain, and improves knee function and quality of life and has superior results in younger patients.⁶ A study by Patel et al concluded single dose of PRP is as effective as two injections therefore we proceeded with our study by comparing effects in pain and functional improvement after single dose intra-articular PRP.⁷ The study showed improvement in both VAS and WOMAC in the subsequent follow up.

Most of the patients who received single spin PRP had post injection flare ups, with pain, erythema and swelling at the injected knee which may be explained with the fact that single spin yield a leukocyte rich PRP, the presence of concentrated leukocytes increased the levels of catabolic and pro-inflammatory signalling molecules, including MMPs and IL-1 β , and that PRP formulations can be pro-inflammatory.⁸ A study confirmed the dual effect of platelet lysate on human chondrocytes-a transient pro-inflammatory activity followed by an inflammation resolution.⁹ Mean difference of VAS was not statistically significant in 1st week after injection. Follow up at the end of 12 and 24 weeks there was a statistically significant improvement in double spin method than in single spin method. It has also been concluded in a study by Hamza et al that PRP injections provided a meaningful improvement in chronic knee pain in patients with knee OA throughout a 12-week period. The pain reduction response to PRP was better in patients with early-stage knee OA.³

Limitation

The reproducibility of the study could have been more if done in a larger sample size. Quantification of platelet count as well as biochemical analysis of the platelet rich plasma prepared by different spin could not be done due to technical unavailability.

CONCLUSION

It was observed that platelet rich plasma obtained by double spin method has long term improvement in both pain and function in patients with KL grade 2 and 3 OA knee than PRP from single spin method. Patient who received single spin PRP has more frequent post injection flare ups. Further studies can be done in a greater number of patients with longer follow up.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Pereira D, Peleteiro B, Araujo J, Branco J, Santos RA, Ramos E. The effect of osteoarthritis definition on prevalence and incidence estimates: A systematic review. *Osteoarth Cart*. 2011;19:1270-85.
- Dai WL, Zhou AG, Zhang H, Zhang H. Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials. *J Arthroscop Related Surg*. 2016(9):1-12.
- Hamza S, Ustünsoy S. The short-term effect of PRP on chronic pain in knee osteoarthritis. *AGRI*. 2019;31(2):63-9.
- Shen L, Yuan T, Chen S, Xie X, Zhang C. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials. *J Orthopaed Surg Res*. 2017;12:6.
- Filardo G, Kon E, Buda R. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(1):528-35.
- Kon E, Buda R, Filardo G. Platelet-rich plasma: intra-articular knee injections produced favourable results on degenerative cartilage lesions. *Knee Surg Sports Traumatol Arthrosc*. 2010;18:472-9.
- Patel S, Dhillon MS, Aggarwal S. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *Am J Sports Med*. 2013;41:356-64.
- Sundman EA, Cole BJ, Fortier LA. Growth factor and catabolic cytokine concentrations are influenced by the cellular composition of platelet-rich plasma. *Am J Sports Med*. 2011;39:2135-40.
- Pereira RC, Scaranari M, Benelli R, Strada P, Reis RL, Cancedda R et al. Dual effect of platelet lysate on human articular cartilage: a maintenance of chondrogenic potential and a transient pro-inflammatory activity followed by an inflammation resolution. *Tissue Eng Part A*. 2013;19:1476-88.
- Hegaze AH, Hamdi AS, Alqrache A. Efficacy of Platelet-Rich Plasma on Pain and Function in the Treatment of Knee Osteoarthritis: A Prospective Cohort Study. *Cureus*. 2010;13(3):e13909.
- Bennell KL, Hunter DJ, Paterson KL. Platelet-rich plasma for the management of hip and knee osteoarthritis. *Curr rheumatol rep*. 2017;19(5):1-32.
- Xie X, Zhang C, Tuan RS. Biology of platelet-rich plasma and its clinical application in cartilage repair. *Arthritis Res Therapy*. 2014;16:204.
- Bhatia A, Ramya BS, Biligi DS, Panchakshari PBK. Comparison of different methods of centrifugation for preparation of platelet-rich plasma (PRP). *Indian J Pathol Oncol*. 2016;3(4):535-9.
- Abrams GD, Frank RM, Fortier LA, Cole BJ. Platelet-rich Plasma for Articular Cartilage Repair. *Sports Med Arthrosc Rev*. 2013;21(4):213-9.
- Kisiday JD, McIlwraith CW, Rodkey WG, Frisbie DD, Steadman JR. Effects of Platelet-Rich Plasma Composition on Anabolic and Catabolic Activities in Equine Cartilage and Meniscal Explants. *Cartilage*. 2012;3(3):245-54.
- Mascarenhas R, Saltzman BM, Fortier LA, Cole BJ. Role of Platelet-Rich Plasma in Articular Cartilage Injury and Disease. *J Knee Surg*. 2015;28:3-10.

17. Bendinelli P, Matteucci E, Dogliotti G, Corsi MM, Banfi G, Maroni P et al. Molecular Basis of Anti-Inflammatory Action of Platelet-Rich Plasma on Human Chondrocytes: Mechanisms of NF- κ B Inhibition Via HGF. *J Cell. Physiol.* 2010;225:757-66.

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