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A clinical evaluation study of single spin vs double spin intra-articular PRP injection in patients with bilateral early OA knee: A novel technique

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Abstract

Purpose: To compare the clinical and functional outcomes of single spin versus double spin platelet rich plasma (PRP) intraarticular injection treatment for patients with bilateral early osteoarthritis knee (OA).

Methods: This study was a prospective, comparative, observational, time bound, hospital-based study conducted from November 2018 to August 2019, after obtaining institutional ethical committee (IEC) approval. The study involved 32 patients affected by bilateral OA knee. The patients were treated with single spin PRP injection in one knee and double spin PRP injection in the other knee in the same patient. The knee to which single spin or double spin PRP injection was to be given was picked using a simple randomization technique. The patients were evaluated at the time of presentation before intraarticular injection and at 1, 3 and 6 months follow-up with WOMAC, VAS and Oxford Knee scores.

Results: Patients were assessed before the first injection and after the intraarticular injection with a follow-up at 1 month, 3 months and 6 months. VAS score decreased after single spin PRP, by 3.94 points ($p < 0.001$), WOMAC-Score decreased by 22.09 points and Oxford knee score increased by 9.1 points. After double spin PRP, VAS decreased by 4.75 points ($p < 0.001$), WOMAC score decreased by 31 points and Oxford knee score increased by 11.06 points.

Conclusion: From our study, we can conclude that, PRP is a safe and effective for treatment of osteoarthritis and can be easily administered in normal clinical settings. Patients undergoing double spin PRP intra-articular injection have slightly better outcomes in terms of VAS and WOMAC scores as compared to single spin PRP intra-articular injection. The outcome difference is not much higher and hence both single and double spin PRPs can be used for treatment of knee OA and selection must be based on availability.

Keywords: Early osteoarthritis of knee, Platelet rich plasma, Single spin PRP, Double spin PRP, Functional outcome, VAS score, WOMAC score, Oxford knee score

Introduction

Osteoarthritis (OA) of the knee is a progressive disease involving the intra-articular (IA) tibiofemoral and patellofemoral cartilage^[1]. It is a multifaceted process in which the central role is played by mechanical factors and it has changes in structure and function of the whole joint. There is no cure and current therapeutic strategies are primarily aimed at reducing pain and improving joint function. The prevalence of OA varies according to the definition of OA, the specific joint under study, and the characteristics of the study population. The age-standardized prevalence of radiographic knee OA in adults age 45 years or older was 19.2% and 27.8% in two studies. It is a chronic progressive musculoskeletal disorder characterized by gradual loss of cartilage in joints, with a prevalence as high as 40% in India. OA has more preponderance in women than men, 44% of women over the age of 65 years have symptoms while 70% of those over 65 years show radiological evidence of OA, by 2050 people aged over 60 will account for OA more than 20% of the world's population.

Treatment of knee OA is difficult due to the avascular and aneural nature of adult knee cartilage, which results in a low regenerative capacity, and thus limited healing potential for the joints. The joint degeneration arising from OA occurs as a result of an imbalance in the equilibrium between the breakdown and repair of the joint tissue while both cellular changes and biomechanical stresses cause several secondary changes in the joint.

Conservative treatment modalities are the first choice in younger and middle-aged populations with cartilage damage and OA of the knee [2]. Treatment of knee OA includes non-pharmacological methods such as exercise and lifestyle modification, as well as pharmacological therapies, such as analgesics, non-steroidal and steroidal anti-inflammatory drugs, and corticosteroid injections. The pharmacological therapies often have side effects and sometimes do not provide adequate benefits [3,4].

Weight loss, physiotherapy and diet control remains one of the first treatments recommended for the treatment of OA. However, exercise has limitations as a treatment modality. One limitation being poor compliance, another limitation is that exercise can be painful for people with OA. According to AAOS evidence guidelines for knee osteoarthritis, oral NSAIDs were the only treatment modality that received a strong recommendation for treating osteoarthritis. But, it is known that continued NSAID can potentially lead to severe systemic side effects that limit their usefulness of as a long-term treatment method for OA, such as renal insufficiency, gastritis, peptic ulcer formation, and rare effects with the cardiovascular and cerebrovascular systems. Hyaluronic acid (HA), an integral part of synovial fluid, assists the joint in different ways, providing lubrication, stress reduction, and substance transport across the synovium. Since HA concentrations have been found to be reduced in knees with OA, visco supplementation with HA hopes to restore the elastic functions provided by HA back into the affected joint. But, it is important to note that unlike the autologous nature of PRP injections, HA injections are synthetically manufactured products. Several studies have shown that PRP injections gives better results when compared to HA injections.

Platelet-rich plasma (PRP) has been gaining popularity in treatment of knee OA due to its simplicity, safety and minimally invasive features [5]. PRP is an autologous blood product with an elevated platelet concentration that contains many different granules [6, 7]. Platelet granules include a variety of growth factors, including Platelet-derived growth factor, transforming growth factor beta, insulin-like growth factor-1 and epidermal growth factor. The concentrations of these growth factors may vary between patients and within the same patient at different times. These molecules are believed to be important in maintaining joint homeostasis, tissue healing and tissue regeneration [8, 10]. Platelet concentration is mentioned in the literature as an important factor in PRP treatment. Scientific evidence is currently limited with regard to optimal platelet concentration for the treatment of knee OA and requires further investigation. Although *in vitro* studies reveal that PRPs with higher platelet concentrations release more growth factors than PRPs with lower concentrations, it remains unclear whether more growth factors yield better clinical results [11].

Single-spinning centrifugation results in platelets up to three times that of baseline level whereas double-spinning centrifugation results in platelets up to eight times the baseline level with a high leucocyte content. However, there are very few studies which compare the use of the two techniques of preparation of PRP in early OA knee.

The aim of this study is to explore the treatment for early degenerative lesions of articular cartilage and OA by comparing two products, already used in clinical practice, which are based on different preparation approaches: single versus double spinning procedures, on a patient with bilateral OA knee and to assess the clinical and functional outcome after intraarticular injection of these two products.

Materials and Methods

It is a prospective, comparative, observational, time bound, hospital-based study conducted from November 2018 to August 2019, after obtaining institutional ethical committee approval. Thirty-two patients, who were in the age group of 40-70 years and diagnosed as Grade 1 and Grade 2 OA knee according to Kellgren and Lawrence grading were included in the study following the inclusion and exclusion criteria. Our exclusion criteria were, patients who underwent previous lower extremity surgery, poor diabetic control with HbA1c more than 7%, rheumatoid arthritis and gout and any history of infection or current infection at the affected joint. Using a simple randomization technique, the patient's knees were randomized into 2 groups, i.e. single spin PRP injection group and double spin PRP injection group. While one knee received single PRP injection, the other knee received double spin PRP injection in the same patient. Patients were selected on outpatient and in-patient basis. After clinical evaluation, radiographs of the knee joint in standing position (antero-posterior views and lateral views) were taken, blood sample of the patient was collected and PRP was prepared in the blood bank. Infiltration was done in operation theatre under strict aseptic conditions. Patients were assessed with VAS score (visual analogue scale) for pain, WOMAC (Western Ontario McMaster Universities Arthritis Index) scoring and Oxford knee scoring for functional outcome, before giving the PRP injection & after giving the injection at periods of 1 month, 3 months & 6 months. The decrease in WOMAC score & VAS score and increase in Oxford knee scores was suggestive of improvement in patient's condition.

Preparation of PRP

Single spin technique: 36-ml venous blood sample was collected in 4 tubes (9ml in each). Four tubes were centrifuged at 580g (gyrations) for 8 min, obtaining a concentration suspended in plasma that was extracted by pipetting carefully to avoid leukocyte aspiration. [Figure 1] [Figure 2] Double spin technique: 150ml of whole blood was collected in a double bag having 63 ml of Citrate phosphate dextrose adenine (CPDA) and was stored at room temperature of 20-24 degree Celsius till separation, which was done within one hour of collection. Two centrifugations (the first at 1,800 rpm for 15 min to separate erythrocytes and a second at 3,500 rpm for 10 min to concentrate platelets) were done. Next, blood bag was taken out and supernatant PRP was transferred into the transfer bag under laminar airflow. [Figure 3] This was followed by the sealing of the primary bag with a tube sealer. After one hour of resting, platelets will be re-suspended within the plasma. [Figure 4] A minimum of 15-20ml of PRP was collected and submitted for diagnostic evaluation with regard to the platelet count and relevant serological investigations before being injected into the joint.

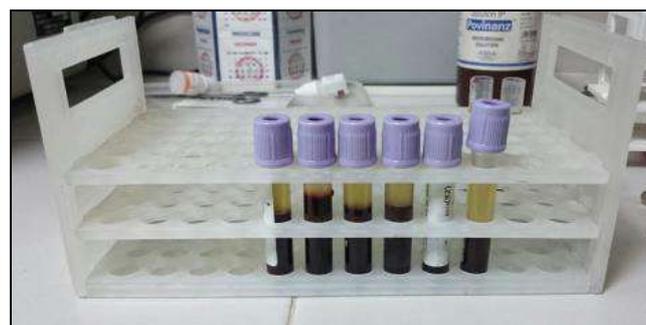


Fig 1: Vacutainers following 15 minutes of centrifuge with 1500 rpm used in single spin PRP.



Fig 2: Vacutainers containing PRP prepared using single spin technique.



Fig 3: 150ml blood bag with transfer bag used in double spin PRP technique.



Fig 4: Transfer bag containing PRP prepared using double spinning technique.

Procedure of PRP Injection

In operation theatre, the patient was put in supine position with the knee in flexion. Knee was thoroughly scrubbed & prepped. Under sterile aseptic conditions, about 10 ml platelet concentrate was injected into knee joint using 18-gauge needle without using any local anaesthetic. [Figure 5]

Post injection of PRP passive knee movements (flexion and extension) were performed. After the procedure, Jone's compression bandage was applied and the knees were immobilized for ten minutes. Patients were then observed for thirty minutes for possible side effects like sweating,

dizziness. During follow-up period, no analgesics were allowed.



Fig 5: Infiltration of PRP into the joint.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. Paired t test is the test of significance for paired data such as before and after quantitative data.

Results

The study group consisted of 32 patients (64 knees). The mean age was 50.34 ± 7.364 . [Graph 1] Using a simple randomization technique, the patient's knees were randomized into 2 groups, i.e. single spin PRP injection and double spin PRP injection. While one knee received single PRP injection, the other knee received double spin PRP injection. The mean VAS score in SS-PRP group was 7.94 ± 0.80 pre-injection and 8.00 ± 0.57 in DS-PRP group. The mean VAS score was 6.16 ± 0.63 in SS-PRP group after 1 month and 5.81 ± 0.64 in DS-PRP group. After 3 months, mean VAS score was 4.94 ± 0.67 in SS-PRP group and 4.53 ± 0.62 in DS-PRP group. After 6 months, mean VAS score was 4 ± 0.67 in SS-PRP group and 3.25 ± 0.67 in DS-PRP group. The difference in mean pre-injection VAS score between the study groups was not statistically significant. Whereas the difference between the two groups at 1 month, 3 months and 6 months was statistically significant.

The mean pre-injection WOMAC score was 77 ± 3.72 in SS-PRP, it was 74.84 ± 3.02 in DS-PRP. The mean WOMAC score at 1 month was 67.47 ± 4.27 in SS-PRP, it was 61.25 ± 2.75 in DS-PRP. The mean WOMAC score at 3 months was 60.41 ± 5.45 in SS-PRP, it was 52.72 ± 3.09 in DS-PRP. The mean WOMAC score at 6 months was 54.91 ± 5.91 in SS-PRP, it was 43.53 ± 2.99 in DS-PRP. The difference in mean pre-injection WOMAC score between the study groups and at 1 month, 3 months and 6 months was statistically significant.

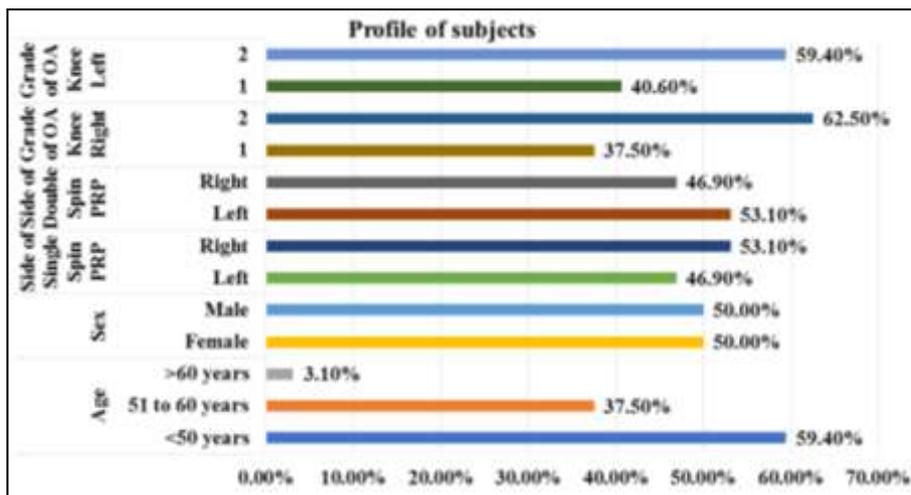
The mean pre-injection Oxford knee score was 18.84 ± 2.32 in SS-PRP, it was 19.28 ± 1.80 in DS-PRP. The mean Oxford knee score at 1 month was 22.63 ± 2.24 in SS-PRP, it was 24.22 ± 1.26 in DS-PRP. The mean Oxford knee score at 3 months was 25.75 ± 2.17 in SS-PRP, it was 27.5 ± 1.05 in DS-PRP. The mean Oxford knee score at 6 months was 27.94 ± 2.35 in SS-PRP, it was 30.34 ± 1.45 in DS-PRP. The difference in mean pre-injection and 1 month post injection of

Oxford knee score between the study groups was not statistically significant. Whereas the difference between the two groups at 3 months and 6 months was statistically significant. [Table 1] In the SS-PRP group, at the end of 6 months, mean reduction of VAS scores was 3.94, mean

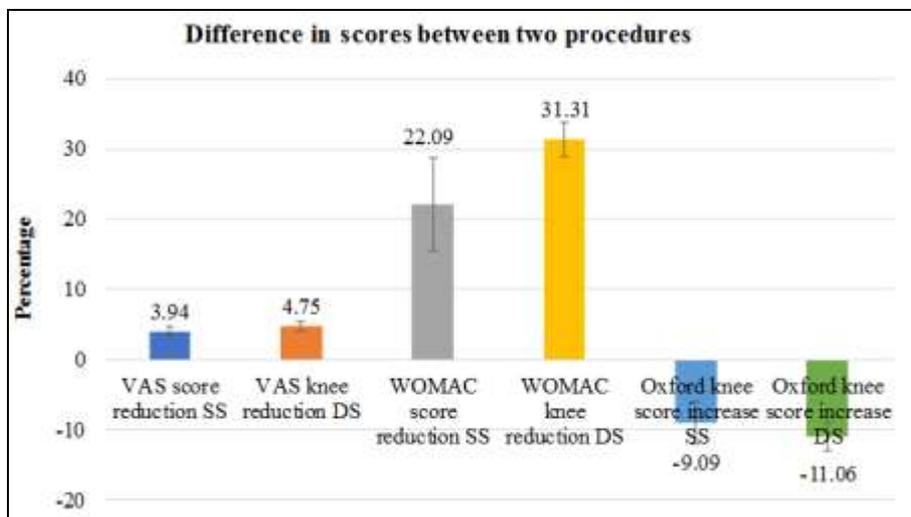
reduction of WOMAC score was 22.09 and mean increase in Oxford knee score was 9.09. In the DS-PRP group, at the end of 6 months, mean reduction of VAS scores was 4.75, mean reduction of WOMAC score was 31.31 and mean increase of Oxford knee score was 11.06. [Graph 2]

Table 1: VAS, WOMAC and OKS Scores among SS-PRP and DS-PRP at various intervals of follow up

	VAS Scores (SS-PRP)				VAS Scores (DS-PRP)				P value between SS and DS PRP groups
	Mean	SD	Median	P value with in SS PRP group	Mean	SD	Median	P value with in DS PRP group	
Pre-Injection	7.94	0.80	8		8.00	0.57	8		0.690
1 Month	6.16	0.63	6	<0.001*	5.81	0.64	6	<0.001*	0.009*
3 Month	4.94	0.67	5	<0.001*	4.53	0.62	5	<0.001*	0.005*
6 Month	4.00	0.67	4	<0.001*	3.25	0.67	3	<0.001*	<0.001*
	WOMAC Score (SS-PRP)				WOMAC Scores (DS-PRP)				P value between SS and DS PRP groups
	Mean	SD	Median	P value with in SS PRP group	Mean	SD	Median	P value with in DS PRP group	
Pre-Injection	77.00	3.72	76		74.84	3.02	76		0.015*
1 Month	67.47	4.27	68	<0.001*	61.25	2.75	61	<0.001*	<0.001*
3 Month	60.41	5.45	60	<0.001*	52.72	3.09	52	<0.001*	<0.001*
6 Month	54.91	5.91	54	<0.001*	43.53	2.99	43	<0.001*	<0.001*
	Oxford Knee Score (SS-PRP)				Oxford Knee Score (DS-PRP)				P value between SS and DS PRP groups
	Mean	SD	Median	P value with in SS PRP group	Mean	SD	Median	P value with in DS PRP group	
Pre-Injection	18.84	2.32	19		19.28	1.80	19		0.372
1 Month	22.63	2.24	23	<0.001*	24.22	1.26	24	<0.001*	0.001*
3 Month	25.75	2.17	26	<0.001*	27.50	1.05	28	<0.001*	<0.001*
6 Month	27.94	2.35	28	<0.001*	30.34	1.45	30	<0.001*	<0.001*



Graph 1: Bar diagram showing profile of subject



Graph 2: Bar diagram showing difference in scores (Pre-injection vs 6 months) between two procedures

Discussion

Osteoarthritis of the knee is a degenerative condition involving softening and focal disintegration of articular cartilage. The prevalence of osteoarthritis is more in developing countries like India. Studies have showed OA is more common in lower socioeconomic than higher socioeconomic population and also suggested that more active individuals have a lower risk of OA. The various modifiable risk factors are repetitive movement of joints, obesity, infection and injuries. The occupational physical activities include monotonous motions and great forces such as kneeling, squatting on joints, climbing and heavy weight lifting. Treatment of knee osteoarthritis is difficult because of avascular and aneural nature of adult knee cartilage [12].

Platelet rich plasma (PRP) injections are one of the four main injection therapies used for treatment of osteoarthritis [13]. The effect of PRP in osteoarthritis is mainly due to growth factors released from platelet activation. It has been observed that along with growth factors PRP also enhances type II collagen production, stimulates endogenous hyaluronic acid production and helps in mesenchymal cell survival and proliferation [14]. PRP is safe as it is an autologous blood product and hence will not cause any immunological reactions and disease transfer [15].

Though the rationale for use of PRP is strong there are still concerns regarding its clinical efficacy, mainly due to the heterogeneity of preparation methods and resulting products. Single-spinning centrifugation results in platelets up to three times that of baseline level whereas double-spinning centrifugation results in platelets up to eight times the baseline level with a high leucocyte content. However, there are very few studies which compare the use of the two techniques of preparation of PRP in early OA knee [16].

PRP can be prepared using single centrifugation, double centrifugation or blood selective filtration procedures. PRPs prepared by different methods differ in terms of proportion of platelets in PRP to platelets in whole blood which is called platelet enrichment factor, presence of absence of WBC and method of activation.

In our study from the observations made in VAS scores it can be deduced that PRP injections helps in reduction of pain in osteoarthritis over a period of 6 months which is evident by the reduction in VAS scores. This finding is supported by different studies which include study by Sanchez *et al.* in which effectiveness of intra-articular injections of autologous PRP for knee OA treatment in an observational retrospective cohort study on 30 patients was studied and results suggested the safety and usefulness of this treatment approach [17].

In a study by Sampson *et al.* single-spinning procedure was used for the treatment of a small group of patients affected by primary and secondary knee OA and reported a favourable outcome by reduction of VAS scores in the majority of the patients and maintained those positive results for at least 12 months [18].

Improvement in WOMAC scores in our study, after administration of PRP injections, was noted in a study by Sandeep Patel, *et al.* in which effect of single and two PRP injections on two different groups was studied and statistically significant improvement in all WOMAC parameters was noted in groups A and B within 2 to 3 weeks and lasting until the final follow-up at 6 months [19].

There was slightly higher reduction in WOMAC scores in DS-PRP group than in SS-PRP group which is different from the observation noted in similar study by Filardo, G., *et al.* in which same outcome was reported in both groups [20].

Improvements in Oxford knee scores were seen in both groups in our study and from our above observations it can be deduced that the improvement was same for both single spin and double spin PRP groups.

In the only study by Filardo G, *et al.* available in literature which compared the outcomes of single spin PRP and double spin PRP in knee osteoarthritis reported similar outcomes for both types of PRPs with only difference in that double spin PRP group (leucocyte rich) suffered from more swelling and pain reaction immediately after the injections.²⁰

Comparing the results of the present study with the above study and other studies on effect of single spin and double spin PRP on knee osteoarthritis it can be deduced that outcomes resulting from both PRPs are almost similar though small incremental reductions have been observed in VAS and WOMAC scores in double spin PRP group. These results cannot be used to conclude that double spin PRP will result in better outcomes because they are small and the sample size is also small and moreover not much difference was noted in knee scores between two groups. VAS and WOMAC scores are obtained by questionnaires and is dependent on patient's response and hence slight variations in outcomes between single spin and double spin PRP groups cannot be considered for concluding that double spin PRP will give better outcomes as these variations may be due to differences in individual perceptions.

It has been reported by many studies in literature that higher concentration of platelets within PRP may not result in enhanced tissue healing effect as it is observed that after certain threshold amount of concentration of platelets there will be inhibitory effect on tissue healing. In a study by Seyed Ahmad Raeissadat, *et al.* it was reported that PRP with 4 to 6 times concentration of platelets is only effective and concentration of more than 8 or less than 4 will not have any enhancing effect [21].

There were no systemic or long term complications except, mild to moderate pain immediately post intraarticular injection in both the groups. Sandeep Patel *et al.*, in 2013, in their study have documented some systemic adverse effects. Which were immediate and systemic rather than local and were of short duration not lasting more than 30 minutes. But they have not explained the characteristics of the adverse effects. They have attributed these adverse effects to the higher number of platelets in the infiltrating PRP sample and the possibility of CaCl₂, which was used as an activating agent. Sanchez *et al.* in 2007 have reported some injection pain, local inflammation of short duration and reaccumulation of effusion, but the exact numbers were not mentioned.

Conclusion

Our study concludes that PRP can be used for treatment of osteoarthritis as it results in reduction of pain and increase in range of movement. Regarding superiority of single spin or double spin PRP both can be considered to give similar outcomes in terms of pain reduction and range of movement and preference must hence be based availability of single or double spin PRP and physician's choice.

Double spin PRP preparation requires a haematology unit whereas single spin PRP can be easily prepared in normal clinical setting and hence the choice should be made accordingly depending on resource availability as there is not much difference in outcomes.

The salient findings of this study were that the PRP is a safe and effective for treatment of osteoarthritis and can be easily administered in a normal clinical setting. Double spin PRP

has slightly better outcomes in terms of VAS and WOMAC scores.

The outcome difference is not much higher and hence both single and double spin PRPs can be used for treatment of knee OA and selection must be based on patient selection criteria and availability of the suitable haematological equipment.

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Conflict of Interest

The author(s) declare(s) that there is no conflict of interest.

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