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Outcome of staged injection of autologous platelet rich plasma in treatment of mild to moderate knee osteoarthritis

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ABSTRACT

Background: Autologous platelet-rich plasma (PRP) offers an easy solution for delivering multiple growth factors needed for tissue repair. Intra-articular injections of PRP have been proposed as a simple low cost minimally invasive way to obtain the concentration of growth factors and biologically active molecules to promote cartilage healing in osteoarthritic (OA) knee joint. The objective of the present study was designed to evaluate the clinical efficacy of autologous platelet rich plasma injection in mild to moderate osteoarthritic knee and to assess the role of serial staged autologous platelet rich plasma injection.
Methods: 50 patients with mild to moderate osteoarthritis of knee were divided into two groups. Group A was given staged injection of freshly prepared autologous PRP in the affected knee. Group B was given single injection of PRP. The Results were evaluated on the basis of the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire and visual analog scale (VAS) before treatment and 3 weeks, 8 weeks, 16 weeks and 24 weeks after treatment.
Results: At 24-weeks follow up the following observations were made; the Mean VAS in Group A decreased to 3.30 whereas in Group B it increased to 4.54. The Mean WOMAC score in Group A was reduced to a mere 28.64 in Group A and in Group B it was 39.76.
Conclusions: It is concluded from our study that concomitant use of serial staged injection (two) of PRP over four months is more effective than single injection in patients with mild to moderate OA of knee.

Keywords: Platelet-rich plasma, Osteoarthritic knee, WOMAC

INTRODUCTION

Osteoarthritis (OA) is the most common form of arthritis.[1] Osteoarthritis commonly affects the hands, feet, spine, and large weight-bearing joints, such as the hips and knees. OA affects the knee more often than any other joint.[2] Synovium, bone, and cartilage are the main structures being destroyed during disease progression. Because of the complex pathophysiology of OA a wide variety of treatment options are available; pharmacologic and non-pharmacologic treatments are used for early and moderate cases of OA, but protection of articular cartilage has so far not been convincingly shown.[3,4] Surgical intervention is often indicated when the symptoms cannot be controlled and the disease progresses.

The use of intra-articular injections of platelet rich plasma has been proposed as a simple low cost minimally invasive way to obtain the concentration of many growth factors and biologically active molecules to promote cartilage healing. This is associated with reduced inflammation, pain relief, improved function, and possible cartilage regeneration and thus improving the lifestyle of the patient. Thus we intended to study the effect of autologous platelet rich plasma when injected

locally in knee with mild to moderate osteoarthritis and to assess the role of serial staged autologous platelet rich plasma injection.

METHODS

The study was carried out in Department of Orthopaedics, ESIC Model Hospital and PGIMSR, Basaidarapur, New Delhi for a period of 10 months i.e., from March 2018 to December 2018.

50 patients attending outpatient department (OPD) of ESIC Model Hospital and PGIMSR, Basaidarapur, New Delhi with mild to moderate primary osteoarthritis (Kellgren and Lawrence grade 2 and 3) between the age of 35-70 years of both male and female gender were included.[5] Patients who had severe OA knee, inflammatory arthropathies, rheumatoid arthritis (RA), coagulopathies, hyperuricemia were excluded from the study. After taking informed consent, the target population was randomization using lottery method in to two groups i.e., Group A and Group B of 25 people each with similar base line characteristics.

Group A

They were given two intra-articular injections of autologous platelet rich plasma after the interval of 16 weeks.

Group B

They were given single intra-articular injection of autologous platelet rich plasma at start and normal saline injection after interval of 16 weeks.

Method of collection of platelet-rich plasma

The platelet-rich plasma (PRP) required for injection was prepared using 40 cc of blood which was collected from ante cubital vein under aseptic conditions. In First spin it was centrifuged at 1800 rpm for 5 minutes. The serum and the buffy coat were drawn from the each syringe into another 10 cc syringe. After placing the syringes again in centrifuge machine, centrifuged at 4500 rpm for 10 minutes. After second spin the syringe contained platelet poor plasma on top and platelets and leucocytes at bottom. The supernatant was withdrawn and discarded leaving about 3.5 cc at the bottom as platelet rich fraction of plasma. Similarly, 3.5 cc of PRP was obtained from second syringe. In total 7 cc of PRP was available; of which 6 cc was available intra-articular injection and 1 cc was sent for culture and counts. The method of preparation of PRP in both the study groups remained the same.

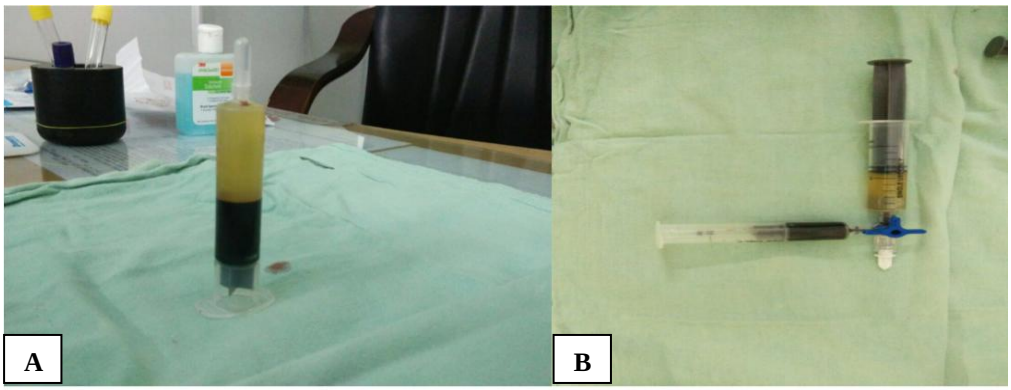

Figure 1: PRP preparation-after 1st spin, (A) 3 part separation after 1st spin and (B) plasma and buffy coat extracted.

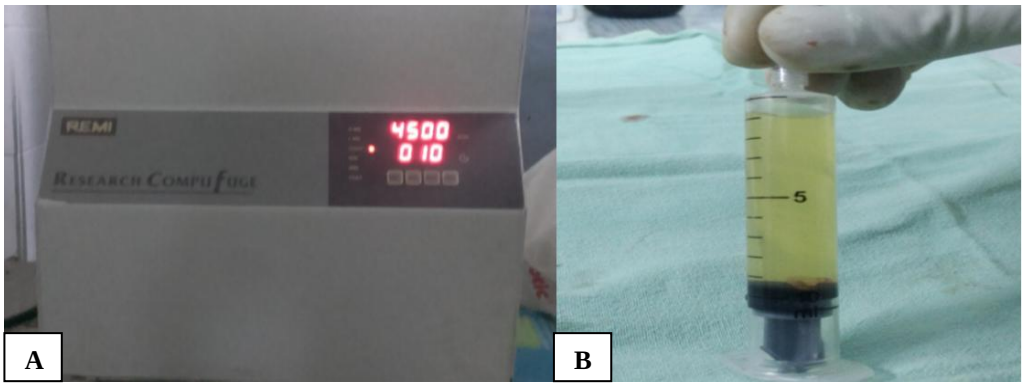

Figure 2: Final PRP after 2nd spin, (A) 2nd spin @4500 rpm for 10 mins and (B) final PRP.

Method of intervention in Group A

First injection

Under aseptic conditions, 6 ml of platelet concentrate and 1 ml of calcium chloride was injected into the knee joint through a supra-lateral approach.

Second injection (16th week)

The autologous platelet rich plasma injection was repeated again after 16 weeks and PRP was obtained by the method discussed above.

Method of intervention in Group B

First injection

Protocol followed was similar to Group A at time of first injection.

Second injection (16th week)

Same protocol steps were followed as discussed above but only difference is that instead of PRP normal saline was used. 0.1 cc of autologous blood was taken in injection to impart the colour similar to PRP injection.

Follow-up and assessment

The patients were then followed up at the interval of 3rd week, 8th week, 16th week, and final follow up at 24th week. No NSAIDs was prescribed during follow up period and paracetamol (dosage, 500 mg tds) was given in case of discomfort. All patients were asked to stop medications 48 hours before follow-up assessment.

Assessment was done by using two scores viz. visual analogue score and WOMAC score. Statistical analysis was done with the help of computer using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 22.0 for Windows). P value less than 0.05 was taken to denote significant difference.

RESULTS

The majority of the patients in Group A were between age group of 51 and 60 i.e., 60% (15) with the mean age of 56.2 years and in Group B were also between 51 and 60 i.e., 52% (13) with the mean age of 54.1 years. Majority of patients were females in both the groups i.e., in Group A are 17 (68%) and Group B is also 17 (68%).

Majority of the patients in both the groups i.e., in Group A is 12 (48%) and Group B is 14 (52%), had Grade II changes (Kellgren and Lawrence) in standard weight bearing radiographs. The mean concentration of platelets in PRP injected in patients of Group A was 708.6 × 10^3 per µl and in Group B was 692.96 × 10^3 per µl. The mean pre-injection VAS is Group A is 6.49±1.12 (mean±2SD) and in Group B is 6.32±1.06 (mean±2SD). The difference in VAS reduction in both the groups is statistically insignificant up to 16th week follow up. At 24th week the mean VAS in Group A is 3.3±1.02 (mean±2SD) whereas in Group B is 4.54±0.90 (mean±2SD); the reduction of VAS in Group A is statistically significant when compared to Group B ($p<0.0001$) at 24th week follow up. The mean pre-injection total the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score in Group A is 58.88±12.84 (mean±2SD) and in Group B is 57.92±10.70 (mean±2SD). The difference in the reduction of mean of both the groups is statistically insignificant up to 16th week of follow up. At 24thweek the mean total WOMAC score in Group A is 28.64±9.06 (mean±2SD) whereas in Group B is 39.76±8.08 (mean±2SD); Group A shows statistically significant reduction in total WOMAC score when compared to Group B ($p<0.0001$) at 24th week follow up. The patients receiving serial injections (two) had better WOMAC scores at final follow-up than the patients with single injection of PRP.

Table 1: Age distribution.

	Group A		Group B	
	No	**%**	**No**	**%**
Age group (years)				
Up to 50	5	20	9	36
51–60	15	60	13	52
Above 60	5	20	3	12
Total	25	100	25	100
Range (years)	45–68		42–66	
Mean (years)	56.2		54.1	
SD (years)	6.4		6.0	
P value	0.2426 not significant			

Table 2: Comparative efficacy of the two groups changes in visual analog score.

VAS at	Group A		Group B		P
	Mean	SD	Mean	SD	
Before injection	6.49	0.56	6.32	0.53	0.2807
3rd week	6.25	0.56	6.02	0.47	0.1115
8th week	5.3	0.57	5.1	0.43	0.1665
16th week	4.24	0.54	4.11	0.44	0.3815
24th week	3.3	0.51	4.54	0.45	<0.0001

*significant p value.

Table 3: Comparative efficacy of the two groups WOMAC Score-total.

WOMAC score-total at	Group A		Group B		P value
	Mean	SD	Mean	SD	
Before injection	58.88	6.42	57.92	5.35	0.5687
3rd week	53.84	5.67	53.36	4.34	0.7382
8th week	44.64	4.72	43.88	3.76	0.5315
16th week	36.84	4.06	35.76	2.31	0.2535
24th week	28.64	4.53	39.76	4.04	<0.0001*

*significant p value.

DISCUSSION

The results of this study showed positive effect of autologous PRP injection in patients affected with mild to moderate OA, with improved pain and symptom. In our study, PRP was prepared in lab using sterile disposable syringes and table top centrifuge (REMI-PR23). The PRP obtained was leucocyte rich PRP (type B) according to Dohan Ehrenfest classification as leucocyte filter was not used and type 2A according to Mishra's classification as platelet concentration in PRP was 2.84 times the baseline values in Group A and 2.70 times the baseline value in Group B and PRP was activated using calcium chloride.[6,7] No evidence of localised knee infection was reported and this can be attributed to antimicrobial effect of PRP observed *invitro* by Bieleckie T et al, 2007.[8]

In our study PRP prepared was fresh in both the groups A and B each time they were injected i.e., twice in Group A and once in Group B, this is because ours was open system and we were skeptical about platelet function being altered because of storage. This is similar to the PRP prepared by Sandeep Patel et al, who also injected freshly prepared platelet concentrate.[9]

Group A had 88% (22 out of 25) satisfied patients when compared to Group B that had 72% (18 out of 25) satisfaction level at end of 24th week. We have more number of satisfied patients in Group A than in Group B; though the percentage of satisfied patients in both the groups was significantly high. Kon et al reported 82% satisfaction level in PRP group whereas Patel et al had 67% and 64% satisfied patients in PRP group with single and double injection (given at interval of three weeks) respectively.[9,10]

Patel et al also noticed that pain scores were significantly decreased in those satisfied patients. In our study this is consistent finding with above study as we have more number of satisfied patients in Group A whose VAS scores are 3.30 when compared to patients in Group B, whose VAS score is 4.54 at 24th week (p<0.0001).[9]

Mean VAS score in Group A decreased from 6.49 at the start of study to 3.30 at 24th week follow up and in Group B from 6.32 to 4.54; however Group B showed slight deterioration in VAS scores at 24th week follow up when compared to 16th week.

Similarly, WOMAC score in Group A decreased from 58.88 at the beginning of study to 28.64 at 24th week follow up and in Group B from 57.92 to 39.76 at the end of study. This clearly shows significant improvement in patients of Group A as compared to Group B (p<0.0001). All WOMAC sub-scores were comparable in both the groups up to third follow up i.e. 16th week as both groups showed similar trend of decrease in WOMAC scores. However, in Group B slight deterioration was seen at 24th week when compared to 16th week.

Patel et al also reported slight deterioration of VAS and WOMAC scores at 6th month follow up when compared to 3rd month.[9] Similar findings were reported by Kon et al as they noticed slight worsening of International Knee Documentation Committee (IKDC) subjective and objective scores from second to sixth month follow up which was not significant thereafter significant deterioration was found at one year of follow up.[10]

Thus it is observed that the therapeutic benefit of PRP is temporary as there is no sustained long term effect and therapeutic effect begin to wane after a period of time, as

seen in Group B. However, if repeat injection PRP is given before the beneficial effect starts to decrease, significant improvement is seen; both VAS and WOMAC scores in group A were significantly lower. This is in line as suggested by Patel et al.[9]

CONCLUSION

The results of our study support the short-term effectiveness of intra-articular injection of platelet rich plasma (PRP) as effective measure in improving pain, stiffness and overall physical function in mild to moderate knee osteoarthritis (OA). Concomitant use of serial staged injection (two) of PRP over four months is more effective than single injection in patients with mild to moderate OA of knee.

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Ethical approval: The study was approved by the institutional ethics committee

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