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Original Research Article

Platelet rich plasma for the treatment of osteoarthrosis knee

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ABSTRACT

Background: New studies focused on modern therapeutic methods which stimulate cartilage healing and repair the damage, including the use of platelet-rich plasma (PRP) as a cocktail of growth factors. This study has the purpose to present the use of PRP in management of knee osteoarthrosis and its outcomes up to 6 month follow up.
Methods: 58 patients with 100 knees (32 male, 26 female) with Kellgren Lawrence grade 1, 2,3 and 4, aged between 50 to 65 years between February 2015 to December 2015 treated with 4 ml of intra-articular PRP injections at 4 week interval in each affected knee and evaluated using WOMAC and VAS scores before injection and on follow up at end of the 1st, 3rd, and 6th month.
Results: The mean age was 58.29 years. Improvement in WOMAC score for KL grade 1 (32.61%), grade 2 (31.12%), grade 3(26.54%) whereas only 13.68% in KL grade 4 at end of 6month follow up. Improvement in VAS score for KL grade 1 (41.30%), grade 2 (38.02%), grade 3 (47.68) whereas only 12.74% in grade 4 at the end of 6 month follow up. Results show statistically higher significant improvement seen in WOMAC and VAS for KL grade 1, 2, and 3 as compared to grade 4 at 6 months follow up.
Conclusions: The results of our study illustrated that the treatment with intra articular PRP injections is safe and effective in reducing pain and stiffness as well as improve knee function and quality of life in early stages of knee osteoarthrosis.

Keywords: Platelet-rich plasma, Kellgren Lawrence, Osteoarthrosis, WOMAC, VAS

INTRODUCTION

A relatively new strategy for the treatment of osteoarthrosis (OA) is application of cellular bio mediators for cartilage healing and repair by delivering a high concentration of growth factors. Its efficacy has been illustrated in vitro and in vivo studies; however its real efficacy in OA is not well established. Thus, this study has the purpose to present use of PRP in management of knee osteoarthrosis and its outcomes.

METHODS

Patients coming to the department of orthopedics at Jawaharlal Nehru Medical College and associated group of hospitals, Ajmer between February 2015 to December 2015 were included in the study.

Sample size

100 knees with osteoarthrosis.

Inclusion criteria

Patients with clinical symptoms of osteoarthrosis knee and the radiologic signs of knee with OA Grade 1, 2, and 3 and 4 according to Kellgren and Lawrence (KL) classification, all patients had previously been treated using analgesics without success and the patients between the age group of 50-65 years.

Exclusion criteria

Patients having systemic disorders such as diabetes, rheumatic diseases, hematological diseases (coagulopathies), severe cardiovascular diseases, infections, immunodeficit and patients with previous knee surgeries or significant trauma around knee, any malignancy, prosthesis in or near the knee, treatment with anticoagulant and antiplatelet medications 10 days before injection, use of NSAIDs 2 days before injection, history of knee intra articular injections of corticosteroids during the past 3 weeks or use of systemic corticosteroids 2 weeks before PRP injections, history of vasovagal shock, platelet count <1 lakh/uL, haemoglobin <10 g/dl.

Our research approved by ethical committee of JLN Medical College, Ajmer. All the mentioned information was given to the patients and signed the written consent form. All patients were treated with 2 intra-articular injections of autologous PRP (at 4 week interval) in each affected knee. Using 34 ml of autologous venous blood 3 to 4ml of PRP prepared using double spin centrifugation technique (using PRP centrifuge machine, Model–CM-8 plus, REMI Company ,WHO guidelines with ISO 9001/2008 certification). By above method we achieved average about 4 to 5-fold increase in platelet concentration over baseline platelet count. Patients were evaluated using Western Ontario and McMaster Universities Arthritis Index (WOMAC) and visual analog scale (VAS) before and at the end of the treatment 1st, 3rd and 6th month on follow up. Patient advised for dynamic and static quadriceps exercises for 1 hour daily.

Statistical analysis

Data were analyzed using Graph Pad Software (Inc.7825 Fay Avenue, Suite 230 La Jolla, CA 92037 USA). Data from Kellgren–Lawrence grade and WOMAC score/VAS score were evaluated by the paired t test. P value <0.05 was accepted as statistically significant for all tests.

RESULTS

Procedure was done in 58 patients under the present study. Participants were clinically evaluated. WOMAC score and VAS score for the affected knee was recorded. Cases were treated with local platelet rich plasma Injection. After the procedure patients were asked to report immediately if any increase in pain was there and were asked to follow up at end of 1st month, 3rd month and 6th month after the injection. Out of 58 patients in our study with 100 knees, 32 were female 26 were males as shown in Table 1. Maximum no. of knees were of grade 2 (47knees) and minimum were of grade 4 (13 knees) out of total 100 knees as given in Table 2. Patients with heavier weight (75.2 kg) and higher average age (59.38) have found to have higher grade of osteoarthritis knee (KL grade 4) as seen in Table 3. Out of total 58 patients, 42 patients have bilaterally affected knees whereas only 16 patients have only 1 affected knee as in Table 4. Higher age group (between 61 to 65 years) has higher mean WOMAC (total =50.38) score as compared to younger age group patients as presented in Table 5.

Table 1: Distribution of patients according sex.

Sex	No. of patients	No of knees
Female	32	57
Male	26	43

Table 2: Distribution of knees according to Kellgren Lawrence grading of osteoarthrosis.

KL Grade	No. of knees
1	14
2	47
3	26
4	13

Table 3: OA grade-specific average weight and average age.

KL grade	Average weight (in Kg)	Average age (in years)
1	68.625	54.5
2	69.66	58.14
3	72.9	59.38
4	75.2	60.69

Table 4: Distribution of patients according to involvement of knees.

Involved knee	No. of patients
Unilateral	16
Bilateral	42

Table 5: Age-specific prevalence of osteoarthritis and pre-treatment WOMAC scoring.

Age	No. of Patients	Mean WOMAC score at day 1st			
		Pain	Stiff-ness	Functional	Total
50-55	15	6.4	2.93	28.46	37.8
56-60	22	8.6	4.04	32.18	44.8
61-65	21	10.38	4.33	35.66	50.38

Table 6 presents the OA grade specific WOMAC (pain, stiffness and functional) scoring. It is evident from Table 7 that minimum total WOMAC score at the end of 6th month seen in KL grade-1 osteoarthritis knees and maximum in KL grade 4 osteoarthritis knees. Irrespective of grade minimum WOMAC score seen at the end of 3rd month.

Maximum decrement in total WOMAC score seen in Kellgren–Lawrence grade 1 osteoarthritis knees (32.61%) and minimum decrement in KL grade 4 (13.68%)

osteoarthritis knees at the end of 6th month. Irrespective of grade minimum total WOMAC score seen at the end of 3rd month of intra articular PRP injection therapy as given in Figure 1.

Minimum VAS score seen in KL grade 1 (2.43) and maximum VAS score seen in KL grade 4 of osteoarthritis knee (6.85) whereas % decrement in VAS is maximum in grade3 OA knee (47.68%) at the end of 6th month follow up. Irrespective of any grade of OA minimum VAS score is seen at the end of 3rd month follow up of PRP therapy as presented in Table 8.

Decrement in VAS score is more significant in KL grade 1, 2 and 3 OA knees (p <0.00 1) as compared to grade 4 OA knees (p= 0.036) at end of 6th month follow up.

Table 6: OA grade specific WOMAC (pain, stiffness and functional) scoring before treatment and on follow ups.

	Mean WOMAC score											
KL grade	At day 1st			At end of 1st month			At end of 3rd month			At end of 6th month		
	P	S	F	P	S	F	P	S	F	P	S	F
1	5	2.21	22.57	2.86	1.14	19.36	2.5	1	13.57	3.14	1.21	15.21
2	7.45	3.11	27.89	4.7	2	18.23	3.89	1.34	14.62	4.17	1.79	19.21
3	9.88	4.27	35.5	8.31	3.23	27.92	6.62	2.31	19.81	7.73	3.04	26.08
4	12.69	5.46	45.54	11.38	4.62	42.31	9.92	4.08	38.62	10.54	4.62	39.31

Table 7: OA grade specific total WOMAC scoring before treatment and on follow ups.

KL Grade	Mean of Total WOMAC score at day 1st	Mean of Total WOMAC score at end of 1st month	Mean of Total WOMAC score at end of 3rd month	Mean of Total WOMAC score at end of 6th month
1	29.78	23.36	17.07	19.57
2	38.45	24.94	19.85	25.13
3	49.65	39.46	28.73	36.85
4	63.69	58.31	52.62	54.46

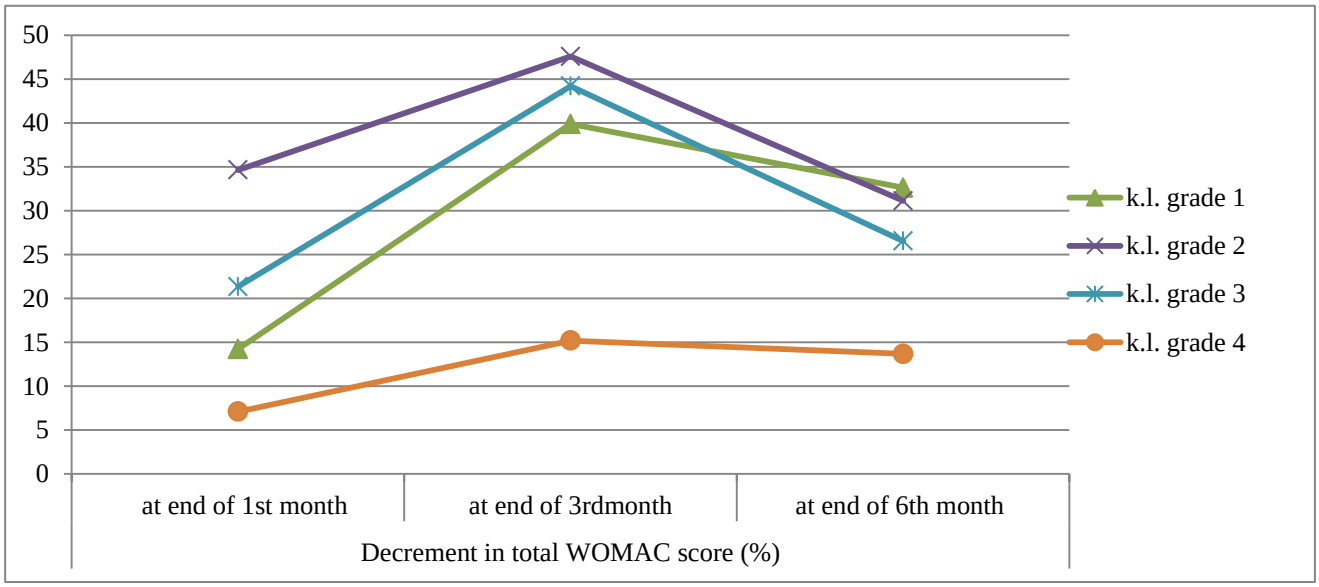

Figure 1: Line chart depicting OA grade specific decrement of WOMAC score in percentage on follow up.

Table 8: OA grade specific VAS scoring before treatment and on follow ups.

KL Grade	VAS at day1st	VAS at end of 1st month	VAS at end of 3rd month	VAS at end of 6th month
1	4.14	2.93	1.86	2.43
2	5.26	3.94	3.11	3.26
3	6.46	4.54	3.04	3.38
4	7.85	6.46	6.31	6.85

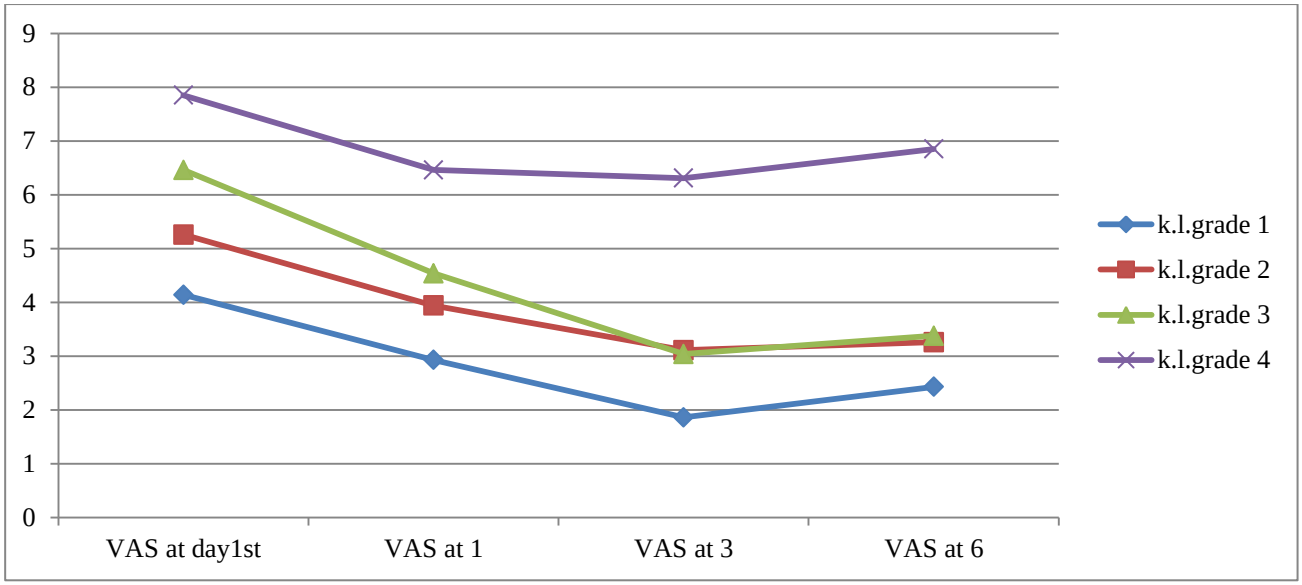

Figure 2: line chart depicting OA grade specific decrement of VAS score in percentage on follow up.

Mean platelet concentration in whole blood was about 263.48×10^3/µl and mean platelet concentration in PRP was about 1320.84×10^3/µl. So, there was about 5-fold increase in mean platelet concentration.

Table 9: Mean platelet concentration between whole blood and PRP.

Mean platelet concentration	In whole blood	In PRP
	263.48×10^3/µl	1320.84×10^3/µl

Complications

NO infection, marked muscle atrophy, deep vein thrombosis, fever, hematoma, tissue hypertrophy, adhesion formation, or other major adverse events occurred among study subjects. 7 patients with mild pain reaction and effusion after the injections, which persisted for not more than 2 days

DISCUSSION

The purpose of this study was to investigate the effectiveness of intra-articular PRP injections in active patients with symptomatic knee OA in terms of diminishing pain, improving quality of life, and returning to previous activities.

All patients showed significant improvement in all scores at 1, 3 and 6 months (P <0.01) except grade 4 OA knees where VAS score with p value=0.03, demonstrating that PRP injections can represent a valuable treatment in patients with early OA knee. . Irrespective of grade minimum total WOMAC score and VAS score seen at the end of 3rd month of intra articular PRP injection therapy.

We obtained significant improvement in all clinical scores up to 6 months follow up which is comparable to the study done by Kon et al. In their study illustrated statistically significant improvement of all clinical scores from the basal evaluation to the end of the therapy and at 6-12 months follow-up (P <0.0005). The results remained stable from the end of the therapy to 6 months follow up, whereas they became significantly worse at 12 months follow up (P =0.02).[1]

Anitua et al in their study on human synovial cells isolated from osteoarthritic patients showed that Intra-articular administration of PRGF might be beneficial in restoring HA concentration and switching angiogenesis to a more balanced status but does not halt the effects of IL-1beta on synovial cells. [2]

No major complications were noted in our study which is comparable with other study reports and signifies the safety profile of autologous PRP intra-articular injections.[1,3,4]

In our study we have found that low grade OA knee (KL grade 1, 2, 3) have better outcomes as compared to higher grade OA knee (KL grade 4) as well as younger age group (50-55 years) has lower WOMAC score as compared to higher age group (60-65 years) which is comparable to study done by Franca Vaccaro, Rita Guitaldi et al. which concluded that better results were achieved in younger patients with a lower degree of cartilage degeneration.[5]

Pre-treatment blood analysis of our patients showed an average platelet count of 263.48×10^3/µl. After centrifugation of 34 mL of peripheral blood, we obtain 4 mL of PRP with average 1320.84×10^3/µl of platelet concentration which is about 5-fold increase in mean

platelet concentration. The system we used includes a second centrifugation step to further concentrate platelets by removing poor platelets plasma. We did not activate PRP prior to injecting as activation could actually decrease their availability as compared to activation of platelets by collagen because thrombin activation result in an immediate release and collagen having a more sustained release pattern of growth factors as demonstrated by Harrison et al in their study.[6]

Platelet concentration in our PRP solution is similar to the PRP concentration obtained by the Amanda *et al* (about 5 fold increase). This level of platelet count may provide optimal benefit.[7]

In our study we have seen that heavier weight patients have found to have higher grade of OA which is comparable to study done by Lementowski and Zelic of which concluded association between osteoarthritis (OA) and obesity in their study and acknowledged as a risk factor for both the incidence and progression of OA.[8]

In our study statistically significant improvement in WOMAC score was seen till the final follow-up at six months, with slight worsening at the six month follow up as compared to third month which is comparable to study done by Patel et al. [9]

OA was more in women compared to men in our study (55.17% vs. 44.82% respectively). This difference can be possibly due to the lack of physical activity, mobility, social issues especially in our region and higher prevalence of obesity among women in general. A study done by Iqbal et al also observed that OA was more in women compared to men.[10] A similar observation was also made in a study done by Sharma et al.[11]

OA strikes women more often than men and it increases in prevalence after menopause. In our study premenopausal women (age <55 years) were 10 (31.1%) in number whereas 22 females (68.75%) were of postmenopausal age (age >55 years).The results of our study is comparable to study done by Das et al and Felson.[12,13]

The main limitation of our study was that we did not include a control group and no diagnostic evaluation like MRI and USG done to access effect on cartilage.

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

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