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Original Article

Efficacy of platelet-rich plasma administration in patients with severe knee osteoarthritis: can platelet-rich plasma administration delay arthroplasty in this patient population?

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Abstract: *Background/Objective:* The efficacy of PRP in knee osteoarthritis (OA) is still a matter of debate. There is evidence to support its use in early knee osteoarthritis but its effectiveness has not yet been established, especially in advanced knee osteoarthritis. The aim of this study was to determine the efficacy of PRP application on pain, function, and quality of life in patients diagnosed with severe knee osteoarthritis, with six months follow up, and to investigate whether injection of PRP delays arthroplasty. *Methods:* This study included 62 patients diagnosed as severe knee OA. Patients were randomized into PRP and control groups. Assessment and injections were performed by the same physician. The physician was not blinded and knew whether the patient was in the PRP or control group. One cc of PRP was obtained from 20 cc of venous blood after double centrifugations at 400 g for 10 minutes. Patients in the PRP group received 3 injections of PRP at 3-week intervals. Both groups were given home exercise programs. Clinical improvement was evaluated using Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaires, SF-36, and visual analogue scale (VAS) at 0, 3, and 6-month follow up visits. At the one year follow up, patients were called and asked for history of arthroplasty. *Results:* Statistically significant improvement in all WOMAC parameters (pain, stiffness, physical function) ($p<0.05$) and physical function, physical roles, pain, social function, emotional roles, mental health, general health, and vitality sub-scores of SF-36 ($p<0.05$) were noted in the group treated with PRP at 6-month follow up. One patient had arthroplasty in the PRP group in the first year of follow up, while none of the patients in the control group had arthroplasty. *Conclusion:* Significant clinical improvements in PRP-treated patients suggest that PRP injections may be a choice in symptomatic treatment of severe knee OA. Findings suggest that PRP-treated patients had better clinical status and quality of life than patients in the control group.

Keywords: Arthroplasty, gonarthrosis, growth factor, knee, knee osteoarthritis, osteoarthritis, platelet, platelet-rich plasma, regenerative, regenerative treatments

Introduction

Knee osteoarthritis is a significant cause of chronic pain and disability among the elderly [1]. Levels of cartilage degeneration and rates of disability increase with age. These patients generally present with a diagnosis of severe knee osteoarthritis. Although there are conservative treatment options, such as weight control, bracing, physical therapy, non-steroidal anti-inflammatory drugs (NSAID), analgesics, slow acting drugs, and intraarticular steroid and hyaluronic acid (HA) injections [2], treatment options are still limited as these patients are mostly older individuals with multiple comorbidities and comedications. They often face arthroplasty, eventually [3]. There is also a considerable patient population ineligible for surgical treatment due to their comorbidities or refusal of surgery. Therefore, questions such as which approach is preferred for severe knee osteoarthritis and how the course can be prevented have been discussed in recent years, with the concept of regenerative therapies gaining attention. Platelet-rich plasma administration is one of these regenerative methods.

Table 1. Patient Screening Criteria

Inclusion Criteria
• Age between 40-75 years
• Moderate - severe knee pain scored at least 4 over 10 points on a VAS or loss of joint range of motion
• Based on the diagnostic criteria of ACR as knee osteoarthritis
• Radiologically had grade - 4 knee osteoarthritis (including large osteophytes, marked joint, severe sclerosis and definite bony deformity) according to Kellgren-Lawrence classification
• Not responded to conservative therapy for at least 3 months
Exclusion Criteria
• Uncontrolled systemic disorder
• History of rheumatic disease
• Active malignancy
• Patients with another symptomatic joint or those with asymptomatic OA in >3 joints
• History of acute trauma, acute meniscopathy, anterior-posterior cruciate ligaments or collateral ligament injury or tear in the effected knee
• History of surgery, manipulation, mobilisation or arthroscopy in the effected knee
• History of steroid, local anesthetics or hyaluronic acid injection, kinesiotaping, prolotherapy or neural therapy over the last 3 months
• Reflex sympathetic dystrophy or neurodeficit of the effected extremity
• Anemia or thrombocytopenia (Hemoglobin <12 g/dl, platelet <150.000/uL), bleeding disorders, patients using anticoagulant or antiagregant medications
• History of medication use over a period of 10 days before and after treatment
• Infection or suspicious of infection
• Serious psychiatric disorder

Table 2. Demographic data of the patients

	Prp-Exercise n=30	Exercise n=30	*p* value
Age (mean ± SD) years	60.5 ± 7.8	56.3 ± 10.3	0.085
Min-Max	46-77	34-77	
Sex			
Female	24	29	0.103
Male	6	1	
BMI	33.6 ± 5.20	32.7 ± 12.06	0.616
Comorbidity	21	19	0.584
Flexion (mean ± SD)	78.83 ± 13.11	89.67 ± 11.89	0.808
Extentation (mean ± SD)	-9.63 ± 13.11	-1.33 ± 4.34	0.853
Exercise VAS (mean ± SD)	8.33 ± 1.83	7.47 ± 1.72	0.838
VAS at rest (mean ± SD)	6.97 ± 2.24	5.50 ± 2.01	0.590
Night pain	29	23	0.52

PRP is a fragment of plasma obtained from the patient's own blood by appropriate centrifugation methods, during which standard platelet levels are concentrated to reach very high levels per unit volume [4]. PRP has been considered to show activity through activation of processes such as cell proliferation, matrix generation, osteoid production, and collagen synthesis by growth factors released from the granules [5]. There are still multiple unanswered questions about the best PRP formulation. There is a lack of standardization in PRP preparation techniques for knee osteoarthritis [6]. PRP may be obtained with both the centrifuge method under laminar flow and standard cell separators. Single and double centrifuge methods may be used and leucocyte rich and leucocyte poor PRP may be obtained in these techniques, according to the literature [7-12]. The clinical efficacy of PRP in the treatment of knee OA remains unclear. There are variations in the treatment approach, including subject, knee, and outcome specific variables. These include PRP preparation techniques, platelet count, severity of OA, number of injections, interval/frequency of administration, and a lack of volume standardization [6].

Although there is no strong evidence for efficacy of PRP application in knee osteoarthritis, it is thought to be more effective than placebo [13] and more successful in early stage knee OA. However, the data regarding efficacy in patients with advanced stage knee OA has been limited [14-16]. The aim of this study was to determine the efficacy of PRP application on WOMAC and SF-36 scores in patients diagnosed with severe OA and to investigate whether injection of PRP delays arthroplasty.

Materials and methods

This was a prospective, randomized, and comparative clinical trial. All patients admitted to Outpatient Clinic of the Department of Physical Therapy and Rehabilitation at İzmir Katip Celebi University Ataturk Training and Research Hospital, between January 1, 2015 and December 31, 2015, with a diagnosis of knee OA were screened for participation.

Patient selection, sampling, and randomizaion

All patients were identified and recruited based on pre-established inclusion/exclusion criteria in a continuous fashion. A total of 90 patients were evaluated clinically and radiologically for inclusion and exclusion criteria. All radiographs were taken under weightbearing conditions. Of these 90, 62 patients were included in the study. **Table 1** shows inclusion and exclusion criteria. Power analysis was done with G power 3.0.8 software. Sample size was based on differences in final WOMAC scores (including subscores of pain, stiffness, and function) between the two groups with large effect size d type value of 0.8, power of 80%, and a false-positive rate of 5%. This study required 26 patients per treatment arm. Patients were randomized by the closed envelope method to either the PRP or control group. Each group consisted of 31 patients. Demographic data of patients are provided in **Table 2**. There were no differences in age, sex, BMI, comorbidity, VAS, and range of motion before the study between the two groups.

PRP preparation protocol

Protocol to obtain PRP was based on preliminary laboratory workup of a previous study investigating the efficacy of PRP in partial and total layer supraspinatus tears [17]. Fresh whole blood obtained from the blood bank was used for this purpose. After transferring the blood samples into 20-cc sterile tube under laminar flow, samples were processed by mono and double centrifugation at 200, 400, 600, and 800 g. This process was repeated four times for each sample. One cc PRP was obt-

Table 3. Mean platelet and leukocyte values at different g

		Blood PLT	PRP PLT ± SD	Platelet yield ± SD (fold)	Blood Leukocyte	PRP leukocyte ± SD	Leukocyte yield ± SD (fold)
200 gi	Mono centrifuge	167	405 ± 24.68	2.43 ± 0.06	5.49	14.365 ± 2.80	2.62 ± 0.51
	Double centrifuge	167	738 ± 27.78	4.42 ± 0.14	5.49	24.915 ± 4.97	4.54 ± 0.36
400 gi	Mono centrifuge	167	404 ± 49.01	2.42 ± 0.02	5.49	42.735 ± 3.36	7.78 ± 0.39
	Double centrifuge	167	1105 ± 147.08	6.62 ± 1.01	5.49	47.8 ± 0.51	8.71 ± 0.04
600 gi	Mono centrifuge	167	549 ± 128.53	3.29 ± 0.29	5.49	31.175 ± 4.29	5.68 ± 0.78
	Double centrifuge	167	713 ± 167.41	4.27 ± 0.58	5.49	29.15 ± 3.89	5.31 ± 0.10
800 gi	Mono centrifuge	167	539 ± 97.80	3.23 ± 0.89	5.49	25.705 ± 1.85	4.68 ± 0.16
	Double centrifuge	167	1062 ± 311.13	6.36 ± 1.86	5.49	45.27 ± 6.43	8.25 ± 0.28

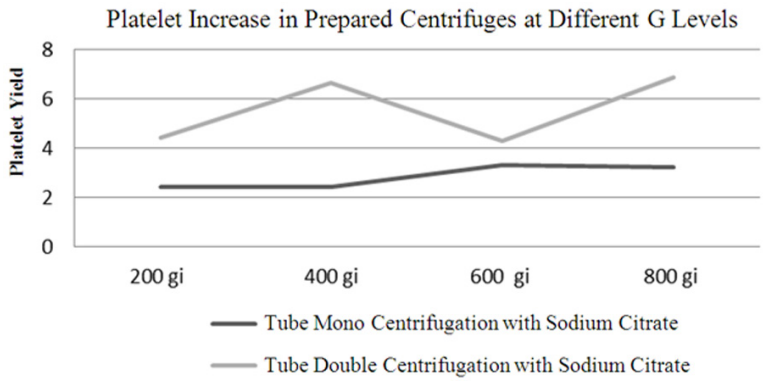

Figure 1. Platelet yields following mono and double centrifugation at different g levels.

ained from each and PLT was counted by a complete blood count analysis device. Samples were stored at -80 centigrade degrees. Obtained PRP samples were activated for 30 minutes with 10% calcium chloride ($CaCl_2$). Platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), transforming growth factor beta (TGF-β), and insulin like growth factor (IGF) were analysed by ELISA. A total of 32 samples were obtained and as all processes were repeated four times (for 200 gi mono-double centrifuge, 400 gi mono-double centrifuge, 600 gi mono-double centrifuge, 800 gi mono-double centrifuge). Mean values for platelet, leucocyte, and growth factors were calculated. Platelet and leucocyte levels are shown in **Table 3**. Obtained platelet enrichment rates are shown in **Figure 1**. Levels of growth factors are listed in **Table 4**. Results showed that the highest levels of platelet enrichment and growth factors were achieved by 10 minutes of centrifugation at 400 g and at 800 g. Since platelet fragmentation rates are known to increase at forces above 800 g [18, 19], the protocol to obtain PRP was 10 minutes of double centrifugation at 400 g.

Administration of PRP to patients and clinical follow up

Assessment of patients in the follow up visits and injections was performed by the same physician. The physician was not blinded and knew whether patients were in the PRP or control group. A total of 20 cc venous whole blood samples were collected from patients in PRP group and transferred to 10 cc sodium citrate tubes. Blood samples were transferred to sterile 10 cc tubes with sodium citrate. After first centrifuge for 10 minutes at 400 gi plasma, buffy coat above red blood cells was taken and transferred to a new sterile 10 cc tube with a sterile 21G syringe. After second centrifuge for 10 minutes at 400 gi, approximately one cc platelet rich plasma in the lowest 1/3 of the tube was taken with a sterile 21G syringe and leukocyte rich PRP was obtained. All fluid transfers were performed under laminar flow to obtain pathogen-free PRPs. Platelet concentrations and growth factors of PRP were analysed during a previous laboratory study. Although the platelets were activated in the previous study to measure growth factor levels, no activation was performed before applying to the knee joints because platelets were believed to have been activated after injection and in contact with collagen tissue. Patients in the PRP group were given three intraarticular injections of

Table 4. P selectin and growth factor levels at different g levels after mono and double centrifuge

		P selectin ± SD (ng/ml)	VEGF ± SD (pg/ml)	EGF ± SD (pg/ml)	IGF ± SD (ng/ml)	PDGF ± SD (pg/ml)	TGF-β ± SD (pg/ml)
200 gi	Mono centrifuge	2.87 ± 1.11	1336.06 ± 198.81	67.57 ± 12.52	18.70 ± 1.56	27528.45 ± 3662.79	15394.04 ± 1217.73
	Double centrifuge	2.26 ± 0.11	6664.57 ± 502.4	379.27 ± 14.46	19.74 ± 1.94	91446.50 ± 5808.79	16175.49 ± 7406.25
400 gi	Mono centrifuge	2.04 ± 0.46	2502.59 ± 377.72	110.60 ± 19.6	16.43 ± 2.38	38179.85 ± 11618.23	2988.78 ± 191.30
	Double centrifuge	2.57 ± 0.34	10381.33 ± 413.1	388.91 ± 9.68	19.96 ± 2.79	190927.96 ± 36619.33	8386.72 ± 1540.94
600 gi	Mono centrifuge	3.07 ± 0.86	5031.69 ± 485.79	212.70 ± 21.73	14.90 ± 1.66	134090.24 ± 89834.78	15357.10 ± 5817.64
	Double centrifuge	2.64 ± 0.44	4510.33 ± 960.01	198.76 ± 53.3	22.39 ± 1.46	354313.56 ± 117672.63	15199.06 ± 7761.36
800 gi	Mono centrifuge	3.46 ± 1.10	5727.53 ± 397.97	191.91 ± 38.62	16.12 ± 4.29	59618.94 ± 13366.02	11276.95 ± 4210.81
	Double centrifuge	2.18 ± 0.10	9245.67 ± 5195.24	276.19 ± 139.2	16.03 ± 0.61	211616.01 ± 7331.98	10437.75 ± 2472.14

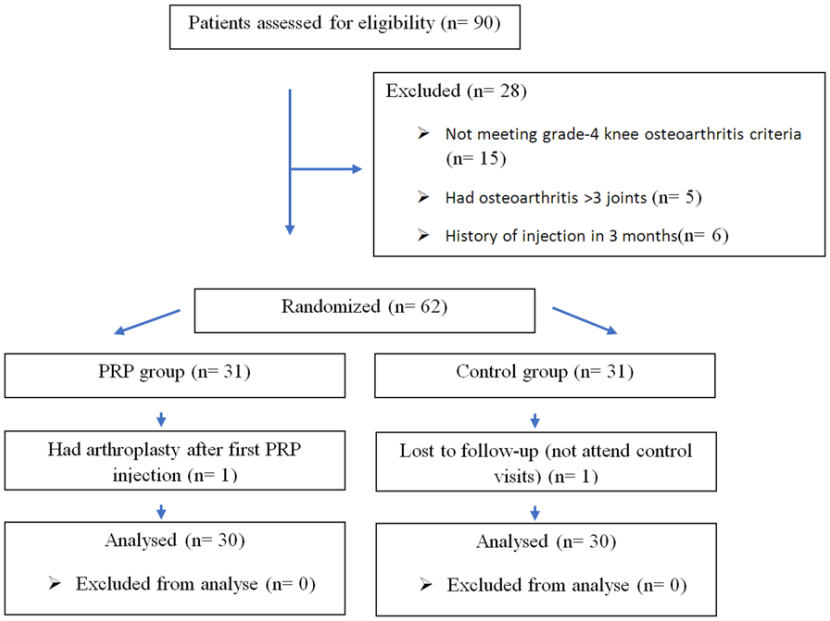

Figure 2. CONSORT (Consolidated Standards of Reporting Trials) flow diagram.

Table 5. Change in WOMAC scores after administration of platelet-rich plasma

		WOMAC SCORES		
		PAIN# Mean ± SD	STIFFNESS## Median (min-max)	FUNCTION## Median (min-max)
PRP+EXERCİSE	Baseline	6.167 ± 2.07	3.75 (0-7,50)	5.735 (1.18-10.58)
	At 3 mo	6.083 ± 2.45	3.75 (0-10)	5.735 (0.88-10.58)
	At 6 mo	6.417 ± 2.63	5 (0-10)	6.985 (1.76-10.58)
EXERCİSE	Baseline	6.667 ± 1.97	5.00 (0-10)	6.54 (3.68-13.50)
	At 3 mo	4.267 ± 2.40	3.25 (0-7.50)	4.55 (0.44-10.14)
	At 6 mo	3.717 ± 2.58	2.50 (0-7.50)	3.38 (0.29-10.14)
P value between groups		0.001#	0.001×	0.001×

The differences are statistically significant, p<0.05. #Bonferroni test. ##Freidman test. ×Wilcoxon signed ranks test.

PRP, every three weeks, by using a 21G needle with anterolateral approach under aseptic conditions. Patients both in PRP and control groups were given a home-exercise program consisting of knee ROM, isometric strengthening, and quadriceps strengthening exercises to be performed three days a week. Patients were advised to apply ice and use paracetamol as needed. They were advised not to use NSAIDs or any other medication that could potentially affect treatment outcome over the next 10 days. They were also advised to avoid strenuous activities for the next 48 hours. Clinical recovery of all patients was evaluated by Western Ontario and McMaster Universities Arthritis (WOMAC) questionnaires. Quality of life was assessed by Short form-36 (SF-36) scale. Pain levels were assessed by visual analogue scale (VAS) before injection and at 3-months and 6-months follow up visits. Patients were controlled 48 hours after injection and questioned regarding any side effects or complications. If any side effects or complications were detected, it was noted. Patients were called via telephone on the 1st year check-up time point. They were questioned on surgical intervention or arthroplasty history.

Statistical analysis

Statistical analysis was performed using SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). A patient from the PRP group had arthroplasty after first PRP injection and left the study. A patient from the control group did not come for control visits regularly and was excluded from the study. Analysis was performed for a total of 60 patients. Consolidated standards of reporting trials (CONSORT) flow diagram is shown in **Figure 2**. Analyses were performed by 80% power analysis at 95% confidence interval and 5% error rate. Shapiro Wilk test was used to chexck if data was normal distribtion. Changes over time in clinical parameters were tested by ANOVA and Bonferroni tests for parametric data. Freidman, Cochrane, and Wilcoxon signed tests were used for non-parametric data. Differences between the two groups were analysed by t-test, Mann Whitney test, and Chi-square test. *P* values <0.05 are considered statistically significant. Results were checked with intend to

Table 6. Short form-36 (SF-36) values after administration of platelet-rich plasma

	PRP+EXERCISE	EXERCISE	*P* value
Physical function##			
Median (min-max)	22 (11-33)	14.50 (11-33)	0.001*
Physical role××			
Median (min-max)	8 (4-8)	4 (4-8)	0.001*
Pain#			
Mean ± SD	7.283 ± 2.35	5.357 ± 1.95	0.001*
General health#			
Mean ± SD	16.980 ± 3.54	14.867 ± 3.22	0.033*
Vitality×			
Median (min-max)	18.00 (4-24)	13.50 (7-24)	0.001*
Social functionµ			
Mean ± SD	7.10 ± 2.04	5.37 ± 1.92	0.001*
Emotional role××			
Median (min-max)	6 (3-6)	3 (3-6)	0.001*
Mental health#			
Median (min-max)	22.00 (5-30)	17.00 (17-24)	0.001*

*The differences are statistically significant p<0.05. #Bonferroni test. ##Freidman test. ×Wilcoxon signed ranks test. ××Cochran test. µMc Nemar test.

treat (ITT) analysis after adding excluded patients.

Results

While WOMAC parameters of the control group did not show any significant changes on 3- and 6-months assessments, statistically significant improvements (p=0.001) were noted in all WOMAC parameters (pain, stiffness, physical function) of the PRP group. **Tables 5** and **6** show WOMAC and SF-36 results of patients regarding 3- and 6-months follow up visits. Changes in WOMAC sub-scores (pain, stiffness, physical function) over time are shown in **Figure 3**. Clinical recovery started on the third month and was significantly maintained on the 6th month. Statistically significant improvements were noted in physical function, physical roles, pain, overall health, vitality, social function, emotional roles, and mental health subscales of SF-36 in the PRP group (p=0.001). For physical roles, emotional roles, vitality, and mental health subscales, favorable effects were found to appear over the first 3 months, with a plateau between the 3rd and 6th months. Statistically significant improvements were still preserved on the 6th month control visit (p=0.001). In the control group, on the other hand, an improvement was noted only in physical function during the 6-months follow up visit (p=0.017), while no significant changes were observed in the other parameters. Patients in the PRP group were found to have statistically significantly increased clinical recovery and better quality of life. Results were checked after adding excluded patients with ITT analysis. According to ITT analysis, clinical recovery started in the third month in PRP group. All WOMAC scores (pain, function, stiffness) and SF-36 subscores (physical function, physical role, pain, overall health, vitality, social function, emotional role, mental health) were better in the PRP group at six months follow up (p=0.001). Telephone contacts performed at the end of the first year revealed that none of the patients in the control group underwent arthroplasty, while one patient in the PRP group underwent the procedure. Patients were asked for side effects 48 hours after injection. The most common side effect experienced was a temporary increase in pain. A total of 13 patients reported temporary increases in pain. In 6 of the patients, swelling in the knee joint was reported. Patients with side effects were treated with paracetamol and cold packs. Reported side effects disappeared within 3-7 days and the patients did not need further treatment. They did not develop any complications such as hypotension, vasovagal reaction, hematomas, and infections.

Discussion

Although none of the parameters, except for physical function, changed significantly in the control group, statistically significant improvements were noted in all WOMAC parameters (pain, stiffness, physical function) and SF-36 sub-scales (physical function, physical role, pain, overall health, vitality, social function, emotional role, mental health) in the PRP group. Previous studies have demonstrated that PRP is more effective in early stage osteoarthritis, whereas there are conflicting data concerning its efficacy in advanced stage knee osteoarthritis [14-16]. Findings of the present study support the efficacy of PRP application in severe knee osteoarthritis.

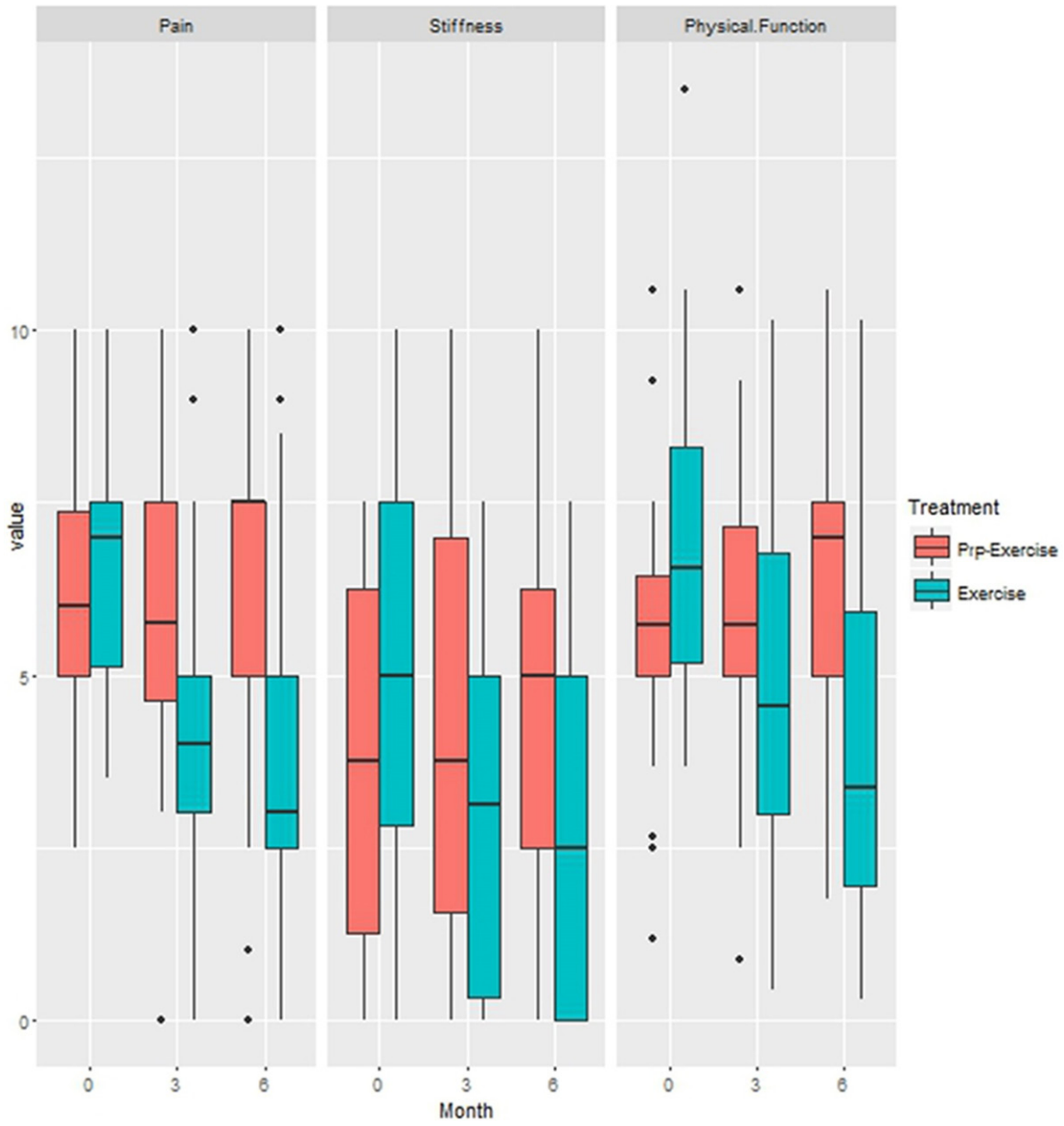

Figure 3. Change in WOMAC sub-scores (pain, stiffness, physical function) over time.

While there are several conventional treatment options for knee osteoarthritis, treatment response is generally limited in the presence of severe knee osteoarthritis, with eligible patients undergoing surgical intervention. However, there is a population consisting of patients that are ineligible for surgery due to comorbidities or refusal of surgical procedures. Thus, studies are ongoing to identify potential treatment options for this group of patients. Potential treatment options used in studies include prolotherapy injections, rESWT, fulranmumab (a nerve growth factor monoclonal antibody) therapy, low dose oral corticosteroid, combining hyaluronic acid (HA), and bracing [20-25]. There are a limited number of studies investigating potential treatments for severe knee osteoarthritis and available studies involve short follow up periods with low levels of evidence.

With regards to regenerative treatment modalities, there are options of stem cell, growth factor, and PRP application. Davatchi et al. [26] previously reported significant improvement in VAS and patient global assessment scores after 5 years of follow up with three patients given intraarticular injections of mesenchymal stem cells obtained from the bone marrow.

Raeissadat et al. reported both plasma rich in growth factor (PRGF) and HA were effective in knee OA and there was no significant difference between them [27]. In the future, regenerative treatments may become more popular as further research is conducted.

In terms of PRP applications, while some authors have argued that these therapies are not effective in advanced stage knee osteoarthritis since the cartilage structure of the joint is completely degenerated, others have reported that these might be effective in advanced disease [28-30]. It is believed that growth factors released from the granules within the platelets bind to the transmembrane receptors on the damaged sites they are applied to (graft, flap, wound), thereby activating endogenous signaling proteins of these receptors, effecting gene sequences, and activating processes such as cell proliferation, matrix generation, osteoid production, and collagen synthesis [31]. PRP is believed to show its main effects through the activities of these factors [32, 33]. There are many limitations and still a lot of questions concerning formulation, application method, efficacy, efficacy duration, delaying arthroplasty and combination of PRP with other treatments.

One of the major limitations of this study was the heterogeneity caused by autologous PRP applications. Although the mean number of platelets and level of growth factors achieved at each g had been previously analysed, no platelet and leucocyte counts were performed, as the same method of PRP preparation and application was used.

Concerning application method, Sanchez et al. [29, 30] suggested that PRP had limited activity in severe knee osteoarthritis and indicated that PRP injected into the subchondral bone might act on cartilage-bone intersection, as well as on subchondral bone, presenting a potential technique that might delay progression to arthroplasty. In their study, they administered PRP intraarticularly and intraosseously into tibial plateau and condyles. They reported an expert opinion supporting that intraarticular + intraosseous PRP application might reduce pain and enhance knee function, leading to a delay in arthroplasty. Combining methods of PRP application intraosseously and intraarticularly may be more thoroughly reported in the literature in the future.

Efficacy is another question because the cartilage structure of the joint is completely degenerated in severe knee OA. Jubert et al. found PRP application effective in patients with severe knee OA in their randomized, double blinded, and prospective study. However, they could not prove its superiority to corticosteroid application. The present results support the theory of efficacy of PRP application in severe knee OA, as improvement in VAS scores, WOMAC, and SF-36 scores were detected and persisted for six months [34]. Although PRP application seems to be effective, as assessment of patients and PRP injections were performed by the same physician and the physician was not blinded, there may be a bias in the evaluation of efficacy. Randomized controlled double-blind studies should be designed in the future. The option of injecting isotonic saline solution, as a placebo in the control group, should be considered.

There have been limited studies about efficacy duration in PRP application. In an open-ended study performed by Bottegoni et al. [29] on 60 elderly patients (65-86 years) with early-moderate stage knee osteoarthritis, patients were given three PRP applications at an interval of 14 days and followed-up for six months after therapy. While the patients displayed significant symptomatic recovery during the first two months, significant worsening was noted in clinical parameters over the following 2-6 months. The authors concluded that PRP application provides only short-term recovery in elderly patients. In the present study, patients given PRP experienced significant reduction in pain, improvement in functional levels, and a higher quality of life. All of these effects persisted after 6 months.

Regarding delayed arthroplasty, in the present study, while none of the patients in the control group required arthroplasty, one patient in the PRP group underwent arthroplasty. One year duration for follow ups was not long enough to draw conclusions regarding the delay of arthroplasty. Based on the present findings, it cannot be argued that PRP application can predict a delay in arthroplasty for knee osteoarthritis. Randomized controlled clinical trials with larger patient groups and longer follow ups are required in future studies.

Recently, combination of PRP application with other methods (HA application, prolotherapy)

have become popular. Chen et al. [35] gave PRP + hyaluronic acid combination to three patients with severe knee osteoarthritis. They reported a decrease in pain, an improvement in functional levels, in addition to findings of recovery on X-rays. The present findings support the efficacy of PRP application and its beneficial effects on symptomatic recovery in severe knee osteoarthritis. Further clinical trials are necessary to demonstrate the clinical impact of combination applications and their value in delaying arthroplasty.

Although the findings of this study cannot lead to a conclusion regarding delay of arthroplasty, PRP resulted in a decrease in pain levels, an improvement in functional levels, and improved quality of life, with favourable effects persisting after 6 months. Ferket et al. [3] reported that arthroplasty reduces costs but provides very limited change in quality of life. PRP can be preferred in severe knee osteoarthritis patients to achieve symptomatic recovery and elevate improve quality of life in cases that do not respond to conservative therapies or refuse arthroplasty. Delaying arthroplasty may be a more viable option in the future as results are obtained from studies investigating intraosseous or intraarticular + intraosseous PRP application, PRP + hyaluronic acid, prolotherapy, stem cell treatments, and their various combinations. As studies continue and data builds, PRP may become an option in severe knee osteoarthritis providing improvements in pain, functional levels, and quality of life. Decreases in costs due to disabilities associated with knee osteoarthritis and surgery rates can be reduced in this patient group.

Conclusion

In conclusion, PRP application in patients with severe knee osteoarthritis resulted in significant improvements in VAS, WOMAC, and SF-36 scores, compared to the control group, accompanied by clinical recovery and increased quality of life. PRP application provided symptomatic recovery in patients with advanced stage knee osteoarthritis, with these effects persisting for 6 months. Studies with a higher number of patients and longer follow up duration are required to draw conclusions concerning whether arthroplasty can be delayed in this patient group.

Disclosure of conflict of interest

None.

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