Comparison of Single and Triple Platelet Rich Plasma Injections in the Treatment of Patellofemoral Pain Syndrome

Patellofemoral Ağrı Sendromu Tedavisinde Tek ve Üç Doz Trombositten Zengin Plazma Enjeksiyonlarının Karşılaştırılması

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ABSTRACT Objective: Patellofemoral pain syndrome (PFPS) is the most common problem in musculoskeletal system. Platelet-rich plasma (PRP) has been suggested to be beneficial in the treatment of sports injuries. The purpose of this study is to compare single and triple PRP injections in the treatment of PFPS and to show whether or not triple application of PRP injection may be more effective. **Material and Methods:** This is a randomized controlled clinical trial. A total of 30 patients with PFPS for more than 3 months, with age of 20 to 35 years, were included in this study. The patients were divided into three groups as single injection application group (n=20) or triple injection application group (n=10) and the unaffected opposite knees were used as controls (n=30). 2 mL of PRP injected into the knee joints. In triple injection group the injections were done a month apart. All patients received a six-week standard exercise program. The outcome measures proprioception, isokinetic test and Kujala patellofemoral score were assessed at baseline and 4 months after baseline. **Results:** Among the patients with PFPS treated with an exercise program, a triple PRP injection compared with a single PRP injection did not result in greater improvement in knee functions, balance and proprioception, isokinetic muscle strength and endurance during a 4-month follow-up ($p<0.05$). **Conclusion:** The triple PRP injection was found to be no more effective than single PRP injection.

Key Words: Patellofemoral pain syndrome; platelet-rich plasma

ÖZET Amaç: Patellofemoral ağrı sendromu (PFAS), en yaygın kas-iskelet sistemi problemidir. Trombositten zengin plazma (PRP) spor yaralanmaları tedavisinde önerilmektedir. Bu çalışmada, PFAS tedavisinde tek ve üçlü PRP uygulaması karşılaştırılarak, üç kez uygulanan PRP enjeksiyonunun daha etkin olup olmadığının gösterilmesi amaçlanmıştır. **Gereç ve Yöntemler:** Randomize kontrollü bu çalışmaya, üç aydan uzun süredir PFAS olan, yaşları 20-35 yıl arasındaki 30 hasta dâhil edildi. Hastalar tek enjeksiyon uygulama grubu (Grup 1, n=20) ve üçlü enjeksiyon uygulama grubu (Grup 2, n=10) olmak üzere ikiye ayrıldı, sağlam olan diğer dizler ise kontrol grubu (Grup 3, n=30) olarak değerlendirildi. Eklem içine 2 mL PRP enjeksiyonu yapıldı. Üçlü enjeksiyon uygulama grubuna bir ay arayla PRP enjekte edildi. Tüm olgulara altı haftalık standart egzersiz programı uygulandı. Katılımcılar başlangıçta ve başlangıçtan dört ay sonra izokinetik test, balans testi ve Kujala patellofemoral skorlama sistemi ile değerlendirildi. **Bulgular:** PFAS tedavisinde egzersiz ile birlikte tekli ve üçlü PRP enjeksiyonunun dört aylık takibi sonucunda diz fonksiyonu, denge ve koordinasyon, izokinetik kuvvet ve dayanıklılık açısından istatistiksel olaral anlamlı bir fark saptanmadı ($p<0,05$). **Sonuç:** Üçlü PRP enjeksiyon grubu, tekli PRP enjeksiyon grubundan daha etkin bulunmadı.

Anahtar Kelimeler: Patellofemoral ağrı sendromu; trombositten zengin plazma

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Patellofemoral pain syndrome (PFPS) is the most common problem in musculoskeletal system. PFPS frequency is 15-33% in young active people and 21-45% in puberty.[1] PFPS etiology is not very clear at the

moment, but many intrinsic and extrinsic factors may cause patellofemoral joint problems are thought to play a role.[2]

First choice of treatment in PFPS is conservative therapy. Rest, activity modifications, nonsteroid anti-inflammatory drugs, patellar braces, foot orthesis, patellar banding, exercise and "biofeedback" are the main conservative treatment methods.[2] The treatment should be planned personally, in accordance with the disorder causing factors and functional limitations.[3]

Platelet-rich-plasma (PRP) is the cellular component of the plasma with a higher percentage of platelets compared to total blood. It is made by centrifuging total blood samples.[4] Since it contains a number of growth factors, PRP injections in sports injury treatments became common today. In the literature, there are no studies about PRP usage in PFPS treatment; however there are some studies about the positive treatment results of intra-articular PRP injections in knee osteoarthritic patients.[5,6] The mechanism in knee osteoarthritis is platelets contain many types of growth factors such as PDGF, TGF-β, PDEGF, VEGF, IGF-1, FGF, and EGF. PDGF is a group of polypeptides that plays an important role on the growth and development of many tissues including cartilage tissue. In the light of this fact, clinical usage of PRP application in knee joint damage is frequently used.[5,7-9] There is a joint degeneration and cartilage tissue defect in PFPS and we think PRP can be effective in PFPS by the same mechanism in osteoarthritis. This study's main objective is to assess the efficiency of PRP injections in PFPS treatment by randomize controlled clinical study for the first time in the literature. In addition, the single and triple PRP injections are common and the efficiency is not clear between the applications in different articles. Therefore, our second purpose is to show the difference of the single and triple injections in PFPS.

MATERIAL AND METHODS

SUBJECTS

A total of 30 patients between the ages of 20 to 35 years who diagnosed with PFPS longer than 3 months, due to overuse or wrong training with physical examination, treated with exercise program, were included in the study. For this randomized controlled study, patients were evaluated in Gülhane Military Medical Academy Sports Medicine Clinic between January 2014 and July 2014.

Patients diagnosed with another condition other than PFPS on magnetic resonance imaging (MRI), presence of another pathology which may cause pain and loss of function in the knee (other joint pathologies, meniscopathy etc.) and patients with history or clinical features of patellar dislocation and subluxation were excluded from the study.

The study protocols were approved by the Ethics Committee of the Gülhane Military Medical Academy, Ankara, Turkey. Patients were informed about the purpose and scope of the study. All subjects voluntarily accepted to participate in the study and written informed consent was obtained at the beginning.

Patients' anamnesis information, demographic values, pain starting period, other diseases, platelet levels and systemic disease presence were evaluated. All subjects had unilateral PFPS. They had no contralateral lower extremity pathologies, neurological problems, or other conditions that could be aggravated by the testing protocol or could confound the test results. All patients were prescribed with a home exercise program. Standard range of motion exercises, stretching exercises and isotonic strengthening exercises program was taught to the patients and they were ordered to continue this exercise program for 3 weeks. All exercises were done with both extremities.

30 subjects included in the study were divided into single injection (Group 1, n=20), triple injection (Group 2, n=10) groups randomly and the unaffected opposite knees were used as controls (Group 3, n=30). For randomization all patients listed in order to arrival, than they were divided into three groups in the list, respectively.

Group 1 consisted of 13 (65%) males and 7 females (35%). Group 2 consisted of 6 (60%) males and 4 (40%) females. Group 3 consisted of 19 (63.3%) males and 11 (36.7%). Age mean values

were 27,2±5,7 in Group 1, 28,7±6,0 in Group 2 and 27,7±5,7 years in Group 3. There was no statistically significant difference between the groups in terms of researched properties (p>0.05) (Table 1).

PRP PREPARATION AND INJECTION

No kits were used in the preparation of PRP. 24 mL of blood, taken from patients' antecubital vein was drawn into 4.5 mL, 3.2% sodium citrate tube (Becton Dickinson Vacutainer System). No additional citrate was used since the remaining sodium citrate is enough to prevent clot formation. Blood samples were rested for 5 minutes before centrifuge. Six tubes of 27 mL of blood samples with anticoagulant agents were centrifuged for 15 minutes in 3500 rpm in the centrifuge (Model NF 800, Bench- Top Centrifuge, NÜVE Sanayi Malzemeleri İmalat ve Ticaret A.Ş. Ankara). Since the literature showed no advantage of double centrifuge over single centrifuge, the samples were centrifuged for one time only.[10,11] Following centrifugation, platelet poor plasma (PPP) was drawn using an injector and that part was not used. ~2 mL of PRP was removed from the remaining material in the tube. In order to check the platelet count, some of the PRP samples were sent to Gülhane Military Medical Academy Biochemistry Lab for thrombocyte counts, using Horiba ABX Pentra XL 80 hematology analysis machine. After counting platelet numbers in total blood samples drawn from the subjects, platelet numbers of PRP was reviewed. Platelet numbers of PRP cannot be calculated due to concentration on the first try, but after diluting the sample with 50% PPP, platelet numbers were seen to increase by approximately 5,7-17,6 times. At the end, patients were injected with 2 ml of PRP. No buffering or activating agents for PRP were used.

Injections were done by using a 22-gauge needle into the knee joint. Patients were in supine and knees were flexion position. Injections were done lateral site of the knee. Following injections, patients were asked to do knee flexion-extension movements for full solution coverage in the knee. Patients were rested in supine position for 15 minutes. In triple injection group the injections were done a month apart. All injections were prepared and performed by the same physician in Gülhane Military Medical Academy Sports Medicine Clinic.

Paracetamol and cold compresses were allowed whereas other NSAIDs were forbidden. Patients did not suffer from any of the side effects such as fever due to infection, infection, hematoma or rupture, except for localized increased pain that lasted for a few weeks due to local inflammatory response.

Following injection, all patients were put into a standard rehabilitation program. Patients were asked to avoid activities that might cause pain in the first two days of injection and told to rest their knees.

TABLE 1: Review of variable spread between the groups.

	1. group Mean±sd Max-Min	2. group Mean±sd Max-Min	3. group Mean±sd Max-Min	p value
Age, year	27.2±5.7	28.7±6.0	27.7±5.7	0.786
	20.0-35.0	21.0-35.0	20.0-35.0	
Height, cm	174.5±7.9	170.8±6.6	173.2±7.6	0.436
	160.0-188.0	160.0-179.0	160.0-188.0	
Weight, kg	73.4±12.8	71.1±12.5	72.6±12.5	0.984
	56.0-110.0	48.0-84.0	48.0-110.0	
Body mass	24.0±3.0	24.2±3.4	24.0±3.1	0.824
index, kg/m²	20.9-33.2	18.7-28.7	18.7-33.2	
Sex, n (%) Male	13 (65%)	6 (60%)	19 (%63.3)	0.965
Female	(35%)	4 (40%)	11 (%36.7)	

Sd: Standart deviation.

EXERCISE PROGRAM

After 2 days of injection, patients started a 3-week exercise program developed by the physiotherapist.

Exercise program started with range of motion exercises and stretching exercises that include iliotibial band, rectus femoris, gastrocnemius and soleus muscles. After 2 weeks, strengthening exercises for quadriceps femoris and hamstring muscles were added. Standard stretching exercises and isotonic strengthening exercises program was taught to the patients and they were ordered to continue this exercise program for 3 more weeks. An exercise protocol lasting for 6 weeks were prescribed. All exercises were done with both extremities.

MEASUREMENTS

In the study, muscle strength and endurance were tested by isokinetic test, balance and coordination was tested by using balance test. Knee function was reviewed by Kujala patellofemoral scoring system. The patients were reviewed in the beginning and 4 months later. In all rounds, patients were questioned about side effects. All those parameters of the patients were recorded in the same follow-up form.

KUJALA PATELLOFEMORAL SCORING SYSTEM

Kujala patellofemoral scoring system for PFPS was developed by Kujala et al. and widely used in the world. This questionnaire was used to evaluate subjective symptoms and functional limitations in patellofemoral disorders. There are a total of 13 questions. These questions assess knee pain when go up and down stairs, squatting, running, jumping, sitting for prolonged periods of flexion; limping, swelling or patella subluxation, the amount of quadriceps muscle atrophy, flexion deficits and to assess the need for walking. The scoring system is 0-100 points among the best to the worst.[12] Kuru et al. showed that Turkish translation of this questionnaire can be performed in Turkish patients in their study.[13]

BALANCE MEASUREMENT PARAMETERS

Measurements of balance and coordination were performed using the Biodex device (Balance System SD™, USA) with postural stability mode. The information about the test procedure was given to participants before the test. The balance positions of the foot were determined and measurements were performed both before the trial and during the test on the platform. Patient is trying to stay in balance on the mobile platform according to the patient's level of difficulty. For ensuring compliance with the test, participants on the right and left foot for a period of 60 sec at the 3 difficulty level.

ISOKINETIC MEASUREMENT

The knee to be tested was placed on the knee flexion extension plate of the Biodex Norm device [Biodex System 4 Pro (Biodex Medical Systems, New York, USA)] and secured with Velcro straps, according to the manufacturer's instructions for isolating knee flexion and knee extension. The length of the dynamometer was adapted to the length of the knee of each subject. To synchronise themselves with the testing device, subjects were instructed to perform three active repetitions of knee movement ranging from maximal flexion to maximal extension. Standard stabilisation strapping was placed across the distal thigh and chest, and placements were limited to grasping the waist stabilisation strap. Before the testing session started, the subject was allowed a 10 minute warm up at a light intensity (less than 50 W) on a cycle ergometer, followed by a 30 second stretch of the quadriceps and hamstring muscles. Selection of the extremity was random. The same investigator performed all the tests. Subjects were encouraged to give 100% effort and received positive feedback during testing. In order to adapt to the test conditions, patients were allowed three submaximal contractions of the quadriceps and hamstring muscle group at the beginning of the tests. They were given five maximal concentric contractions at 60°/sec and 10 maximal concentric contractions at 240°/sec for each test condition. The best peak torque and power contraction of the five and 10 test contractions for each test condition were collected for data analysis. Between each condition, the subjects were allowed to rest for one minute and gravitational corrections were performed.

STATISTICAL ANALYSES

Data analysis was done on SPSS (Statistical Package for Social Science) for Windows 15.0. Descriptive statistics were defined as mean±standard deviation or minimum-maximum for continuous variables and as case number (n) and percentage (%) for nominal variables. The comparison of continuous variables spread with the normal spread was done using Kruskal Wallis test. The comparison of discrete variables Chi- Square test was used. The significance of the continuous variable between 3 groups was done using Kruskal Wallis test, Mann-Whitney U test with Bonferroni correction was used as post hoc test. Comparisons of repeti-

tive measurements within groups were done by Wilcoxon Signed-Rank test. Examination of the linear relationship between platelet variables Spearman's rank order correlation test was used. Values of $p<0,05$ were defined as statistically significant.

RESULTS

30 patients diagnosed with PFPS were included in the study. Twenty patients received a single and 10 patients received a triple injection. Pre-injection balance and isokinetic tests cannot be performed in one patient in the single injection group for the affected side due to their pain levels in the beginning. The results of balance and isokinetic tests before and 4 month after the initial injection cannot be found in a patient in triple injection group.

Whole blood and PRP platelet values were present in the files of 6 cases. The mean platelet numbers in total blood specimens of those six cases was $256,8\times10^3$/mL. Platelet numbers in PRP samples of those patients was $3350,6\times10^3$/mL. That equals to an increase of ~5,7-17,6 times in platelet numbers compared to whole blood samples. There was no linear relationship between whole blood platelet count and PRP product platelet count ($p=0.111$).

No statistically significant difference was found in the pre-injection and post- injection balance coordination, muscle strength, endurance and pre- injection Kujala patellofemoral score between the groups ($p>0.05$). There was a statically difference in post- injection Kujala patellofemoral score between group 1 and 2 ($p=0.011$) (Table 2).

TABLE 2: Between the groups of the patients in terms of function, balance, coordination, muscle strength and endurance during pre- and post-treatment terms.

		1. group Mean±sd Max-Min	2. group Mean±sd Max-Min	3. group Mean±sd Max-Min	p value
KPFS	Pre-injection	27.8±15.1	32.5±15.7	29.3±15.2	0.789
		7.0-57.0	11.0-60.0	7.0-60.0	
	Post-injection	68.3±17.8	86.7±10.2	74.4±17.8	0.011
		24.0-100.0	74.0-100.0	24.0-100.0	
OSI	Pre-injection	2.7±1.1	3.5±1.5	2.4±1.1	0.100
		0.9-5.3	1.3-6.1	0.9-5.6	
	Post-injection	2.1±0.9	1.7±0.8	1.9±0.7	0.188
		0.9-5.2	1.0-3.9	0.9-4.7	
API	Pre-injection	1.9±1.0	2.6±1.1	1.7±0.8	0.078
		0.5-4.8	0.9-4.7	0.5-4.4	
	Post-injection	1.6±0.7	1.1±0.3	1.3±0.6	0.139
		0.5-4.2	0.5-1.8	0.5-3.8	
MLI	Pre-injection	1.7±0.6	2.1±1.0	1.6±0.8	0.263
		0.7-3.2	0.5-4.1	0.6-3.4	
	Post-injection	1.1±0.3	1.0±0.8	1.1±0.4	0.193
		0.7-2.1	0.5-3.3	0.4-2.3	
PT 60°/sec ex (N.m)	Pre-injection	112.6±56.4	118.2±46.7	127.1±54.1	0.687
		41.4-232.6	45.0-179.7	57.6-226.6	
	Post-injection	151.5±62.5	160.3±61.8	163.2±62.7	0.816
		49.0-261.2	57.9-251.3	65.4-284.9	
PT 60°/sec flex (N.m)	Pre-injection	62.6±30.8	60.3±27.5	71.8±28.6	0.340
		22-119.9	20.0-87.0	21.0-130.6	
	Post-injection	81.3±34.7	81.6±33.5	84.7±33.2	0.935
		35.3-138.1	21.7-124.3	29.9-152.3	

Continued→

TABLE 2: Between the groups of the patients in terms of function, balance, coordination, muscle strength and endurance during pre- and post-treatment terms *(Continued)*.

		1. group Mean±sd Max-Min	2. group Mean±sd Max-Min	3. group Mean±sd Max-Min	p value
PT 240°/sec ex (N.m)	Pre-injection	76.2±34.5	72.9±30.9	77.2±34.0	0.975
		28.0-147.5	25.0-135.0	24.0-139.3	
	Post-injection	96.9±34.6	95.8±37.3	97.4±38.6	0.999
		41.7-153.2	34.2-139.7	37.0-162.4	
PT 240°/sec flex (N.m)	Pre-injection	46.8±18.1	46.5±14.0	51.3±22.0	0.821
		19.7-80.2	20.3-69.4	21.5-95.3	
	Post-injection	57.2±24.8	54.9±19.1	58.9±24.1	0.959
		20.5-107.9	23.8-85.4	27.8-122.8	
PT/BW 60°/sec ex (%)	Pre-injection	167.7±72.7	166.9±53.1	182.7±55.7	0.899
		45.3-291.1	86.0-257.4	96.8-302.8	
	Post-injection	216.6±86.2	220.9±63.1	229.1±70.8	0.757
		84.3-364.4	119.2-299.2	106.9-347.0	
PT/BW 60°/sec flex (%)	Pre-injection	89.7±39.6	84.9±32.8	101.4±29.6	0.342
		23.7-164.4	33.0-122.7	45.5-151.8	
	Post-injection	122.0±45.3	112.7±37.3	122.5±39.6	0.741
		48.6-203.0	44.7-162.0	49.7-191.0	
PT/BW 240°/sec ex (%)	Pre-injection	111.1±42.5	105.7±34.6	110.7±34.9	0.846
		40.2-196.1	66.0-168.1	47.3-179.5	
	Post-injection	137.9±41.9	132.8±39.3	136.7±43.8	0.967
		63.0-214.6	70.4-171.5	57.8-207.1	
PT/BW 240°/sec flex (%)	Pre-injection	67.0±24.0	65.6±14.0	72.8±22.1	0.547
		36.7-129.6	42.0-82.6	29.0-118.3	
	Post-injection	84.7±32.4	75.6±19.0	87.9±33.0	0.609
		27.7-139.4	49.0-103.6	37.5-180.0	
TW 60°/sec ex (j)	Pre-injection	505.9±245.7	520.8±244.3	543.8±199.5	0.742
		150.6-972.0	196.0-967.0	263.2-958.4	
	Post-injection	798.0±508.1	697.2±298.0	789.0±390.4	0.854
		257.2-2199.4	267.0-1149.6	301.7-1932.7	
TW 60°/sec flex (j)	Pre-injection	306.9±170.6	296.5±153.0	355.0±136.7	0.409
		75.3-618.4	98.0-509.3	155.0-645.9	
	Post-injection	492.9±283.1	397.5±180.8	467.0±227.5	0.848
		189.7-1200.0	103.7-581.0	158.4-1199.3	
TW 240°/sec ex (j)	Pre-injection	770.5±332.4	869.0±548.1	808.3±372.6	0.983
		253.0-1463.7	360.7-2070.1	296.0-1795.0	
	Post-injection	1115.6±467.8	1141.4±595.4	1125.4±463.7	0.959
		326.1-1975.5	370.3-2175.9	368.0-1891.5	
TW 240°/sec flex (j)	Pre-injection	468.6±245.5	470.4±228.7	489.2±205.0	0.960
		58.9-877.7	180.1-915.6	157.2-857.0	
	Post-injection	672.0±316.2	555.4±237.3	612.3±272.5	0.663
		128.8-1302.2	180.1-915.6	160.7-1163.9	

KPFS: Kujala patellofemoral score; OSI: Overall stabilite index; API: Anteroposterior stabilite index; MLI: Mediolateral stabilite index; PT: Peak torque; Ex: Extantion; Flex: Flexion; BW: Body weight; TW: Total work.

There was a statistically significant difference was found in Kujala patellofemoral score, balance coordination, muscle strength and endurance in intragroups (p>0.05) (Table 3).

In comparison of percentage efficacy in treatment, there was a statistically significant difference in OSI and API between group 1 and 2 and group 2 and 3 (p=0.018, p=0.012, p=0.015, p=0.042 respectively) (Table 4). Other variables had no significant difference in post-injection term between groups (p>0.05). In comparison of percentage efficacy in balance and coordination was shown in Figure 1.

DISCUSSION

In this study groups were homogenous in terms of age, sex, height, weight and BMI. There was no

TABLE 3: Intergroup review of the patients in terms of function, balance, coordination, muscle strength and endurance during pre- and post-treatment terms.

	1. group		2. group		3. group	
Pre-post injection	**Mean±sd**	**p value**	**Mean±sd**	**p value**	**Mean±sd**	**p value**
KPFS	27.8±15.1	<0.001	32.5±15.7	0.005	29.3±15.2	<0.001
	68.3±17.8		86.7±10.2		74.4±17.8	
OSI	2.7±1.1	0.003	3.5±1.5	0.008	2.4±1.1	0.005
	2.7±1.1		1.7±0.8		1.9±0.7	
API	1.9±1.0	0.033	2.6±1.1	0.012	1.7±0.8	0.005
	1.6±0.7		1.1±0.3		1.3±0.6	
MLI	1.7±0.6	0.001	2.1±1.0	0.007	1.6±0.8	0.001
	1.1±0.3		1.0±0.8		1.1±0.4	
PT 60 ex	112.6±56.4	<0.001	118.2±46.7	0.005	127.1±54.1	<0.001
	151.5±62.5		160.3±61.8		163.2±62.7	
PT 60 flex	62.6±30.8	<0.001	60.3±27.5	0.005	71.8±28.6	<0.001
	81.3±34.7		81.6±33.5		84.7±33.2	
PT 240 ex	76.2±34.5	0.001	72.9±30.9	0.005	77.2±34.0	<0.001
	96.9±34.6		95.8±37.3		97.4±38.6	
PT 240 flex	46.8±18.1	0.001	46.5±14.0	0.005	51.3±22.0	0.001
	57.2±24.8		54.9±19.1		58.9±24.1	
PT/BW 60ex	167.7±72.7	0.001	166.9±53.1	0.005	182.7±55.7	<0.001
	216.6±86.2		220.9±63.1		229.1±70.8	
PT/BW 60flex	89.7±39.6	<0.001	84.9±32.8	0.005	101.4±29.6	<0.001
	122.0±45.3		112.7±37.3		122.5±39.6	
PT/BW 240ex	111.1±42.5	0.001	105.7±34.6	0.005	110.7±34.9	<0.001
	137.9±41.9		132.8±39.3		136.7±43.8	
PT/BW 240fle	67.0±24.0	0.001	65.6±14.0	0.005	72.8±22.1	<0.001
	84.7±32.4		75.6±19.0		87.9±33.0	
TW 60 ex	505.9±245.7	<0.001	520.8±244.3	0.005	543.8±199.5	<0.001
	798.0±508.1		697.2±298.0		789.0±390.4	
TW 60 flex	306.9±170.6	<0.001	296.5±153.0	0.005	355.0±136.7	<0.001
	492.9±283.1		397.5±180.8		467.0±227.5	
TW 240 ex	770.5±332.4	0.001	869.0±548.1	0.005	808.3±372.6	<0.001
	1115.6±467.8		1141.4±595.4		1125.4±463.7	
TW 240flex	468.6±245.5	<0.001	470.4±228.7	0.005	489.2±205.0	<0.001
	672.0±316.2		555.4±237.3		612.3±272.5	

KPFS: Kujala patellofemoral score; OSI: Overall stabilite index; API: Anteroposterior stabilite index; MLI: Mediolateral stabilite index; PT: Peak torque; Ex: Extantion; Flex: Flexion; 60: 60°/sec; 240: 240°/sec; BW: Body weight; TW: Total work.

TABLE 4: Comparison of percentage efficacy in treatment in terms of function, balance, coordination, muscle strength and endurance between groups.

	1.group Mean±sd	2.group Mean±sd	3.group Mean±sd	p value
KPFS	220.7±191.7	248.7±226.7	0.758	
OSI	18.5±24.8	46.6±22.0	12.3±34.8	0.008
API	9.8±29.7	48.3±28.9	14.8±39.5	$0.014^{\alpha,\infty}$
MLI	27.5±31.4	43.4±24.5	16.4±49.7	0.152
PT 60°/sec ex (N.m)	47.3±78.1	45.3±68.1	32.1±41.4	0.857
PT 60°/sec flex (N.m)	49.7±115.0	53.2±96.0	14.7±12.7	0.535
PT 240°/sec ex (N.m)	37.6±58.7	37.3±46.0	17.5±19.2	0.849
PT 240°/sec flex (N.m)	22.6±37.0	16.7±10.0	12.4±17.3	0.823
PT/BW 60°/sec ex (%)	41.4±82.2	42.3±64.9	16.8±16.3	0.847
PT/BW 60°/sec flex (%)	62.8±138.5	49.4±89.2	15.0±15.1	0.324
PT/BW 240°/sec ex (%)	30.3±46.4	31.9±49.8	15.9±16.9	0.724
PT/BW 240°/sec flex (%)	29.2±44.3	14.9±11.4	14.4±16.9	0.894
TW 60°/sec ex (j)	67.0±96.7	49.9±86.4	25.4±18.6	0.321
TW 60°/sec flex (j)	118.2±220.3	46.4±66.6	21.5±17.2	0.309
TW 240°/sec ex (j)	55.3±80.9	38.5±47.7	24.0±21.2	0.929
TW 240°/sec flex (j)	109.3±265.6	22.0±29.1	18.0±20.0	0.120

KPFS: Kujala patellofemoral score; OSI: Overall stabilite index; API: Anteroposterior stabilite index; MLI: Mediolateral stabilite index; PT: Peak torque; Ex: Extantion; Flex: Flexion; BW: Body weight; TW: Total work.

α: Comparison of group 1 and 2; ∞: Comparison of group 2 and 3.

statistically significant difference in the parameters measured during pre- and post-injection terms between the injection groups, except Kujala Patellofemoral Score. Triple PRP injection had an extra beneficial effect on balance parameters. In intragroup reviews of both groups, performance review measurement had similar improvements.

Both groups had a significant improvement with the treatment in balance, coordination, muscle strength and endurance. Kujala score is a functional parameter and increased in both groups but in triple injection group increased more than single injection group.

Our literature scan showed us that studies about using PRP in musculoskeletal diseases are on the rise lately and there is an increasing interest on this new treatment method. PRP application in musculoskeletal diseases is reported to be efficient in studies with a lower evidence level meanwhile studies with higher evidence levels have contradicting results.[14]

It is reported that platelet numbers over 1 x 10^6 per millimeter in PRP applications improve the healing process.[4,10] There are studies that used double centrifuge technique to get enough platelets[10,11] but there is no consensus in this subject. Some studies with a high evidence rate report enough platelet numbers using single centrifuge.[15,16] In our study, platelet numbers in our PRP product was

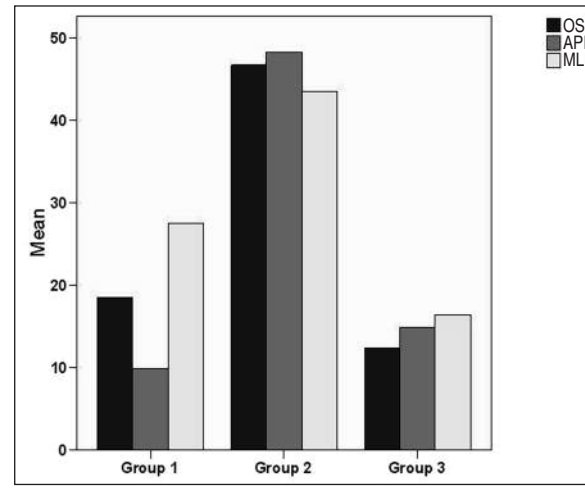

FIGURE 1: Comparison of percentage efficacy in treatment in terms of balance and coordination between groups.

OSI: Overall stabilite index; API: Anteroposterior stabilite index; MLI: Mediolateral stabilite index.

around 3356x10^3/mL. We used single centrifuge technique in our study.

There is no consensus on the amount of product used in PRP treatment, application frequency and interval and usage of platelet stimulating products during product formation.[17,18] In addition, the local anesthetic which is used frequently to ease the burning sensation of the injection is thought to have a negative effect on PRP efficiency by changing the pH of the area or diluting the area too much.[4,19,20] We didn't use local anesthetics in patients before PRP injections. Using buffering solutions such as bicarbonate in PRP in order to determine the proper pH or adding platelet activating agents such as calcium chloride or thrombin for optimal growth factor secretion to PRP are also controversial subjects.[4] We used pure PRP product without any additives for platelet activation in our study.

In the studies that report PRP's efficiency has no information about the healing effect period of PRP without surgical intervention. There are no studies about PRP application in treatment of PFPS but there are randomized controlled trials in knee osteoarthritis compared PRP with HA effect. Two of the present 3 studies on this subject reported the healing effect of PRP after 6 months.[19] When all those studies were reviewed, it is decided that PRP applications should be limited to young patients with a lesser degree of joint degeneration or patients that did not benefit from other conservative treatment methods.[5,7-9] Our study was also performed on young PFPS patients with low degree of joint damage.

Patel et al's double-blind, randomized and placebo controlled study reported a similar degree of improvement between two PRP injections two weeks apart and a single dosage of PRP injection in patients with early-term bilateral knee osteoarthritis and superiority over placebo group.[6] Our study also had similar improvement between single and triple injection groups.

In our study, both patient groups had a significant clinical improvement after 4 months of treatment. Those similar improvement rates can be connected to the positive effects of exercise programs administered after injections in both groups. Short and long-term healing effects of exercise treatment in PFPS are widely known.[21-23] In our study, exercise treatment may have increased PRP efficiency or could be the single contributing factor in healing.

Another point that might affect the study results is that invasive therapies increase patient expectations. This situation was reported in previous studies.[24] Another point is, in both groups, the needles used in injection that causes traumatization and focal bleeding might increase the biological inflammatory response and stimulate the healing mechanisms,[4] and the distension effect of product injected into joint space might increase this.[25] This situations could have been studied with a single exercise group and a placebo injection group but the applied amount was small and it can be ignored.

Another limitation of this study is small number of patients enrolled, but this is a pilot study.

PFPS mechanism is a complicated situation where intrinsic factors such as chronic degenerative period and extrinsic factors such as biomechanical problems play a part.[2] If the main reason for PFPS is a biomechanical problem or straining the knee joint over physiological limits during daily activities, significant improvement should not be expected before fixing those problems firsthand.

CONCLUSION

Our results did not support the usage of PRP injection for 3 times in PFPS treatment because of its invasive nature. More studies are necessary to define the musculoskeletal disorders that might benefit more from PRP, PRP product amount, application frequency and intervals, using platelet stimulating additives and standard rehabilitation protocol following PRP injection.

REFERENCES

1. Sanchis-Alfonsso V. Pathophysiology of anterior knee pain. In: Zaffagnini S, Dejour D, Arrendt EA, eds. Patellofemoral Pain, Instability, and Arthritis: Clinical Presentation, Imaging, and Treatment. 1st ed. Heidelberg; New York: Springer Science & Business Media; 2010. p.1-16.
2. Brukner P. Anterior knee pain. In: Crossley K, Cook J, Cowan S, McConnell J, eds. Brukner & Kahn's Clinical Sports Medicine. 4th ed. Australia: McGraw-Hill; 2012. p.689-700.
3. Houglum PA. Functional and activity-spesfic exercise. Therapeutic Exercise for Musculoskeletal Injuries. 3rd ed. USA, Pittsburg: Human Kinetics Publishers; 2010. p.295-319.
4. Nguyen RT, Borg-Stein J, McInnis K. Applications of platelet-rich plasma in musculoskeletal and sports medicine: an evidence-based approach. PM R 2011;3(3):226-50.
5. Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. BMC Musculoskelet Disord 2012;13:229.
6. Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. 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(2): 356-64.
7. Kon E, Filardo G, Di Matteo B, Marcacci M. PRP for the treatment of cartilage pathology. Open Orthop J 2013;7:120-8.
8. Sánchez M, Fiz N, Azofra J, Usabiaga J, Aduriz Recalde E, Garcia Gutierrez A, et al. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. Arthroscopy 2012;28(8):1070-8.
9. Spaková T, Rosocha J, Lacko M, Harvanová D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil 2012;91(5):411-7.
10. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent 2001;10(4):225-8.
11. Kon E, Filardo G, Delcogliano M, Presti ML, Russo A, Bondi A, et al. Platelet-rich plasma: new clinical application: a pilot study for treatment of jumper's knee. Injury 2009;40(6):598-603.
12. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. Arthroscopy 1993; 9(2):159-63.
13. Kuru T, Dereli EE, Yalıman A. [Validity of the Turkish version of the Kujala patellofemoral score in patellofemoral pain syndrome]. Acta Orthop Traumatol Turc 2010;44(2):152-6.
14. Paoloni J, De Vos RJ, Hamilton B, Murrell GA, Orchard J. Platelet-rich plasma treatment for ligament and tendon injuries. Clin J Sport Med 2011;21(1):37-45.
15. Mishra AK, Skrepnik NV, Edwards SG, Jones GL, Sampson S, Vermillion DA, et al. Efficacy of platelet-rich plasma for chronic tennis elbow: a double-blind, prospective, multicenter, randomized controlled trial of 230 patients. Am J Sports Med 2014;42(2):463-71.
16. Vetrano M, Castorina A, Vulpiani MC, Baldini R, Pavan A, Ferretti A. Platelet-rich plasma versus focused shock waves in the treatment of jumper's knee in athletes. Am J Sports Med 2013;41(4):795-803.
17. Anitua E, Sánchez M, Nurden AT, Nurden P, Orive G, Andía I. New insights into and novel applications for platelet-rich fibrin therapies. Trends Biotechnol 2006;24(5):227-34.
18. Fufa D, Shealy B, Jacobson M, Kevy S, Murray MM. Activation of platelet-rich plasma using soluble type I collagen. J Oral Maxillofac Surg 2008;66(4):684-90.
19. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. Am J Sports Med 2009;37(11):2259-72.
20. Liu Y, Kalén A, Risto O, Wahlström O. Fibroblast proliferation due to exposure to a platelet concentrate in vitro is pH dependent. Wound Repair Regen 2002;10(5):336-40.
21. Hazneci B, Yıldız Y, Sekir U, Aydin T, Kalyon TA. Efficacy of isokinetic exercise on joint position sense and muscle strength in patellofemoral pain syndrome. Am J Phys Med Rehabil 2005;84(7):521-7.
22. Dursun N, Dursun E, Kiliç Z. Electromyographic biofeedback-controlled exercise versus conservative care for patellofemoral pain syndrome. Arch Phys Med Rehabil 2001; 82(12):1692-5.
23. Yıldız Y, Aydın T, Sekir U, Cetin C, Ors F, Alp Kalyon T. Relation between isokinetic muscle strength and functional capacity in recreational athletes with chondromalacia patellae. Br J Sports Med 2003;37(6):475-9.
24. Zhang W, Robertson J, Jones AC, Dieppe PA, Doherty M. The placebo effect and its determinants in osteoarthritis: meta-analysis of randomised controlled trials. Ann Rheum Dis 2008;67(12):1716-23.
25. Virchenko O, Aspenberg P. How can one platelet injection after tendon injury lead to a stronger tendon after 4 weeks? Interplay between early regeneration and mechanical stimulation. Acta Orthop 2006;77(5):806-12.