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THE INFLUENCE OF PATIENT DEMOGRAPHICS, STAGE OF DISEASE, AND HISTORY OF CORTICOSTEROID INJECTIONS ON THE EFFECTIVENESS OF PLATELET-RICH PLASMA IN THE TREATMENT OF KNEE OSTEOARTHRITIS

DİZ OSTEOARTRİTİ TEDAVİSİNDE HASTA DEMOGRAFİK ÖZELLİKLERİNİN, HASTALIĞIN EVRESİNİN VE KORTİKOSTEROİD ENJEKSİYON GEÇMİŞİNİN TROMBOSİT AÇISINDAN ZENGİN PLAZMANIN ETKİNLİĞİ ÜZERİNDEKİ ETKİSİ

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ABSTRACT

Objective: Our study aimed to determine the impact of two PRP administrations, with an interval of four weeks, on pain, Cincinnati Knee Rating System and the Lysholm Knee Score evaluation in patients with knee osteoarthritis. In addition, we wanted to explore the relationship of PRP treatment and the stage of osteoarthritis, obesity, age, gender, and intraarticular steroid administration within the last 6 months.

Methods: Our study aimed to determine the impact of two PRP administrations, with an interval of four weeks, on pain, Cincinnati Knee Rating System and the Lysholm Knee Score evaluation in patients with knee osteoarthritis. In addition, we wanted to explore the relationship of PRP treatment and the stage of osteoarthritis, obesity, age, gender, and intraarticular steroid administration within the last 6 months.

Results: Pain intensity, the Cincinnati Knee Rating System and the Lysholm Knee Scores improved significantly when compared with baseline measurements. The stage of knee osteoarthritis, BMI, age, and intraarticular steroid injections within 6 months are important demographic data that require evaluation in patients for whom PRP treatment is planned. No relation between the effectiveness of PRP and age was found in this study.

Conclusions: Clinical improvement and a reduction in pain were experienced by all patients after the treatment; and the stage of knee osteoarthritis, BMI, age, and intra articular steroid injections within 6 months were directly related to the effectiveness of PRP treatment.

Anahtar Kelimeler: Osteoarthritis, PRP, Injection.

ÖZET

Amaç: Çalışmamızda 2 kez 4 hafta ara yapılan PRP uygulamasının diz osteoartirt hastalarında ağrı ve Cincinnati Knee Rating System and the Lysholm knee score üzerine olan etkisini belirlemek, bu etkinin osteoartrit evre- -obesite-yaş-cinsiyet-son 6 ay içinde yapılan intraartiküler streoid uygulaması ile olan ilişkisini araştırmak istedik.

Method: Bu çalışma tek merkezde, 295 hasta ve 371osteoartritli diz ile prospektive olarak yapıldı. Hastalarımız 40-65 yaş arasında idi. Dermografik belirteçleri yaş-cinsiyet- VKI- son 6 ay içinde yapılan intraartiküler streoid uygulaması sorgulandı. Hastaların bazal ağrı değerlendirmesi VAS ile diz osteoartrit evrelemes ikelgren skoru ile diz fonksiyonları Cincinnati Knee Rating System and the Lysholm knee scoreile yapıldı.4 hafta ara ile 2 kez intraartikuler PRP uygulamasını takiben VAS, Cincinnati Knee Rating System and the Lysholm knee score 1,3,6 aylarda tekrar değerlendirildi. Bu sonuçların dermografik veriler ile ilişkisi incelendi.

Bulgular: Pain intensity and Cincinnati Knee Rating System and the Lysholm knee scores improved significantly in compared with baseline. PRP uygulaması planlanan hastalarda uygulamanın etkinliği açısından diz evresi, VKI, yaş ve son 6 ay içinde yapılan intraartiküler streoid uygulaması değerlendirilmesi gereken önemli dermografik verilerdir. Çalışmada cinsiyetin PRP etkinliği ile ilişkisi ortaya konulmamıştır.

Sonuç: Bu çalışma ile PRP tedavisinin diz osteoartritinde uygulanabilir, güvenli ve etkili bir tedavi yöntem olduğu gösterilmiştir. Uygulamayı takiben bütün hastalarda ağrıda azalma ve klinik iyileşme saptanmakla birlikte özellikle osteoartritin evresi, VKI, yaş ve son 6 ay içinde yapılan intraartiküler streoid uygulamasının bu uygulamanın etkinliği ile direkt ilişkili olan belirteçlerdir. Cinsiyetin bu işlem üzerinde belirleyici bir rolü yoktur. PRP uygulaması için uygun hasta seçiminde bu parametreler gözönünde bulundurulmalı ve hasta bir bütün olarak ele alınmalıdır.

Keywords: Osteoartrit, PRP, Enjeksiyon.

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INTRODUCTION

Osteoarthritis is the most common type of non-inflammatory arthritis usually affecting the knee joint (Goldring MB 2007). Complaints about knee osteoarthritis increase as the population ages and sports participation rates increase (Goldring MB 2007). Healing can occur through regeneration of the avascular cartilage tissue. While pharmacological treatment, weight management, lifestyle changes, and physical therapy can improve symptoms in early osteoarthritis, surgical treatment can be recommended in late stages (S.B. Abramson S.B. 2009). Nonoperative treatments that accelerate regeneration are intended to promote healing in the periarticular tissue and prevent the progression of disease, and hence increase the patient's quality of life. The goal is to help preserve the patient's independence in activities of daily living for as long as possible using nonoperative treatment methods.

PRP is a nonoperative treatment method that promotes soft tissue and cartilage regeneration through injection of high concentrations of platelets into the knee joint. In contrast with conventional treatments, the main idea in this treatment is "triggering" inflammation instead of "suppressing" it, and PRP's effect is considered to stem from acceleration of cell proliferation, collagen synthesis, and vascularization (Monteforte P 2008, S.B. Abramson S.B. 2009, Khan KM1999). PRP consists of numerous growth factors, including but not limited to transforming growth factor-β (TGF-β), insulin-like growth factors 1 and 2 (IGF-1 and IGF-2), basic fibroblast growth factor (bFGF), hepatocyte growth factor (HGF), and vascular endothelial growth factor (VEGF) (Molloy T 2003). In the treatment of osteoarthritis, supraphysiological doses of growth factors, obtained through concentration of a patient's own platelets, stimulate the growth and differentiation of chondrocytes. Growth factors also increase proteoglycan synthesis while decreasing the breakdown, and they play an active role in cartilage regeneration and metabolism (Kon E 2011). With regard to PRP's effect on cartilage degeneration, PRP has been shown to inhibit the inflammatory process induced by interleukin-1 beta. Additionally, it diminishes the activation of nuclear factor kappa B, a pivotal factor in the pathogenesis of osteoarthritis (vanBuul GM 2011). Appropriate patient selection is crucial to the effectiveness and sustainability of this treatment. This study was designed to identify the patients for whom PRP treatment would predictably be successful through clinical evaluations in addition to a simple staging system. Therefore, the purpose was to contribute to the literature by providing a method of standardization for patient selection in PRP treatment. Identifying this standardization is important because it provides us with a method to avoid unnecessary treatments (cost and unnecessary procedure) and to offer an effective treatment (whether it is an operation or pharmacological treatment) in a timely fashion.

MATERIALS AND METHODS

This study was done on 371 knees of 295 patients who had osteoarthritis, who were 40 to 65 years of age, and who applied to Adnan Menderes University, Physical Medicine and Rehabilitation Clinic between March 2021 and February 2023. Informed consent forms were received from all patients.

Patients with a grade of more than 3 on Kellgren-Lawrence grading scale, an inflammatory arthritis, a severe deformity, a psychological disorder, and a history of drug addiction were excluded from this study. Furthermore, patients who had a cardiac disease, who were using antiplatelet medications, who had positive hepatitis markers, and who were either pregnant or nursing were also excluded.

To measure knee pain, the visual analog scale (VAS) was utilized. The VAS serves as a psychometric response scale applicable in surveys, where participants express their degree of agreement with a statement by marking a position on a continuous line between two endpoints. The VAS score is usually determined by measuring in millimeters between the left-hand end of the line and where the patient marks. Using the Cincinnati Knee Rating System and the Lysholm Knee Score, knee function was evaluated. The Cincinnati Knee Rating System encompasses a functional assessment that evaluates six key abilities deemed crucial for sports participation. This assessment proves valuable in gauging any alterations post-surgery or other interventions. The Lysholm Knee Scoring Scale has eight sections that are evaluated to generate an overall score of 0 to 100.

The categories of limp, support, and locking carry a potential score of 25 points each; pain and instability, 25 points each; swelling and stair-climbing, 10 points each; and squatting, 5 points.

Blood Sample Collection and PRP Production

From all patients who participated in the clinical trial, 27 mL of blood was obtained with a 20-6 needle from an antecubital vein to achieve a blood to anticoagulant ratio of 10:1. The blood sample was centrifuged at 3,000 RPM for 3 minutes. The buffy coat layer and the plasma in the upper portion were transferred to a concentration kit using a 10-mL syringe. The tubes were centrifuged again at 3,000 RPM for 3 minutes to acquire a concentrated PRP. Injection site was sterilized with an antiseptic solution, and 3 to 4 mL of PRP was injected into the knee joint. The patients were asked to bend and stretch their knees several times so that the PRP could spread evenly. After the second injection, stretching exercises were allowed. One month after the injections, patients were recommended to begin a strengthening program as tolerated.

Follow-up After PRP injections

PRP was injected twice, with an interval of 4 weeks, by the same physician. There were no complications after the injections. Baseline evaluation was done during the examination of the patient before the PRP injection. Second evaluation was done one month after the second PRP injection. Third evaluation was done 3 months after the second PRP injection. Fourth evaluation was done 6 months after the second PRP injection. The patients were evaluated for pain using VAS and for function using the Cincinnati Knee Rating System and the Lysholm Knee Score. The relation of these results with the stage of the knee, patient's age, gender, BMI, and additional diseases of the patient were analyzed.

While the descriptive statistics were shown as mean ± standard deviation for numerical data, number of cases and percentages were utilized for categorical variables. The Friedman test was employed to asses to the statistical significance of differences in VAS, Lysholm, and Cincinnati knee scores between measurement times. When the p value from Friedman test statistics were found as statistically significant, Wilcoxon Sign Rank test was employed to determine the measurement time that differed from the others.

The Mann Whitney U test was used to compare the differences between two independent groups, while to compare multiple independent groups, the Kruskal-Wallis test was employed. When the p value from Kruskal Wallis test statistics were found to be statistically significant, Conover's multiple comparison test was used to analyzes the group that differed from others. Spearman's Rank Correlation analyses were used to evaluate the degree of association between numerical data.

The analysis of data was conducted using IBM SPSS Statistics version 17.0 software (IBM Corporation, Armonk, NY, USA). Statistical significance was taken into account when the p value was less than 0.05. To prevent a Type, I error, the Bonferroni correction was performed for every possible multiple comparison.

RESULTS

Table 1 displays descriptive statistics about the demographic and clinical characteristics of the patients. The study comprised 295 participants, with an average age of 51.5 ± 6.4 years. Of those patients included in the study, 65.8% were women, and 34.2% were men. 49.8% of patients had an osteoarthritis of the right knee. There were no additional diseases in 95.3% of our patients, and 4.7% of the patients had a history of intraarticular injection within the last 6 months.

Table 1. Demographic and Clinical Data of Patients

	n=295
Age (years)	51.5±6.4
Range of age (years)	40-65
Gender	
Male	101 (34.2%)
Female	194 (65.8%)
Side	
Right	147 (49.8%)
Left	72 (24.4%)
Bilateral	76 (25.8%)
Stage	
I	40 (13.6%)
II	223 (75.6%)

III	32 (10.8%)
Body mass index	
Normal	182 (61.7%)
Borderline	60 (20.3%)
Obese	53 (18.0%)
Intraarticular steroid injection within the last 6 months	
No	281 (95.3%)
Yes	14 (4.7%)

Data regarding the VAS, Lysholm, and Cincinnati scores according to follow-up times is presented in Table 2. There was a statistically significant cumulative decrease in VAS scores between baseline and 6-month follow-up ($p<0.001$) (Figure 1). In the same period, both the Lysholm knee score and the Cincinnati knee score showed statistically significant cumulative increases ($p<0.001$) (Figure 1 and Figure 2, respectively). Statistically significant differences between follow-up times were noted in the table using symbols such as "a," "b," and "c.".

Table 2. VAS, Lysholm, and Cincinnati Scores According to Follow-Up Times

	VAS	LYSHOLM	CINCINNATI
Baseline	7.34±0.84[a,b,c]	49.77±4.99[a,b,c]	18.13±6.19[a,b,c]
1st month	4.41±1.65[a,d,e]	66.81±10.90[a,d,e]	22.45±1.70[a,d,e]
3rd month	3.56±1.82[b,d,f]	71.68±12.06[b,d,f]	23.88±1.32[b,d,f]
6th month	2.81±2.41[c,e,f]	76.89±13.96[c,e,f]	25.04±1.77[c,e,f]
p-value †	**<0.001**	**<0.001**	**<0.001**

The data were presented as mean ± SD. The Friedman test indicated significant differences: a) Baseline vs 1st month ($p<0.001$), b) Baseline vs 3rd month ($p<0.001$), c) Baseline vs 6th month ($p<0.001$), d) 1st month vs 3rd month ($p<0.001$), e) 1st month vs 6th month ($p<0.001$), f) 3rd month vs 6th month ($p<0.001$).

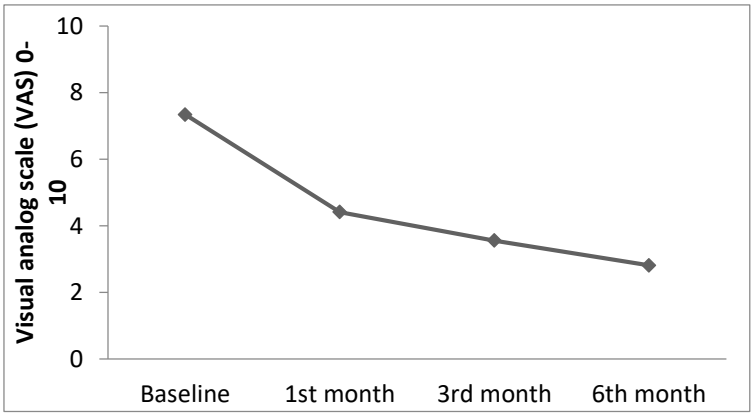

Figure 1. VAS Score

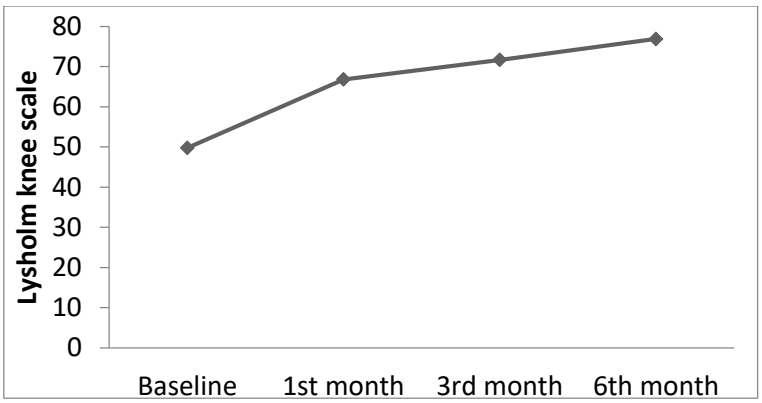

Figure 2. Lysholm Knee Score

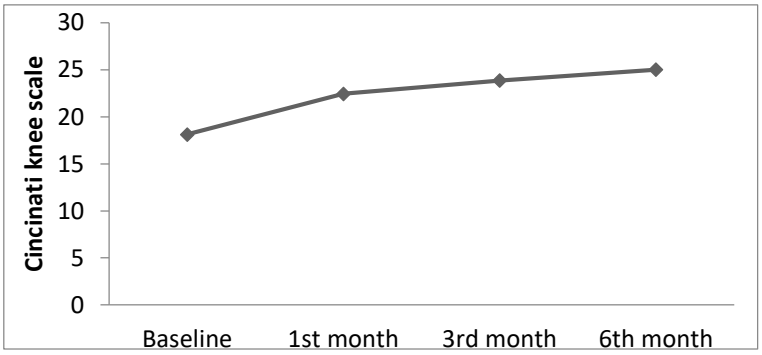

Figure 3. Cincinnati Knee Score

The VAS, Lysholm, and Cincinnati scores according to stages of patients are given for each follow-up time in Table 3. After the Bonferroni Correction, there were no statistically significant differences between stages, except for the baseline Lysholm and baseline Cincinnati scores, regarding the clinical scores ($p<0.0125$). The scores at various follow-up times and broken down according to stages are given in the following figures: VAS score in Figure 4, Lysholm score in Figure 5, and Cincinnati score in Figure 6. Statistically significant differences were noted using symbols such as "a," "b," and "c.".

Table 3. VAS, Lysholm, and Cincinnati scores according to stages

	Stage I	Stage II	Stage III	p-value †
VAS				
Baseline	7.13±0.82[a]	7.31±0.82[b]	7.78±0.83[a,b]	**0.004**
1st month	3.45±1.40[a,c]	4.39±1.49[b,c]	5.78±2.07[a,b]	**<0.001**
3rd month	2.50±1.13[a,c]	3.50±1.63[b,c]	5.28±2.47[a,b]	**<0.001**
6th month	1.23±1.58[a,c]	2.71±2.16[b,c]	5.50±2.78[a,b]	**<0.001**
LYSHOLM				
Baseline	51.15±5.10	49.78±5.02	48.00±4.18	0.026
1st month	74.30±8.18[a,c]	66.50±10.52[b,c]	59.63±11.17[a,b]	**<0.001**
3rd month	79.65±8.18[a,c]	71.56±11.62[b,c]	62.53±12.63[a,b]	**<0.001**
6th month	88.03±5.50[a,c]	76.45±13.61[b,c]	66.00±14.09[a,b]	**<0.001**
CINCINNATI				
Baseline	17.95±1.47	17.52±1.35	17.09±1.17	0.034
1st month	23.35±1.70[a,c]	22.42±1.67[b,c]	21.56±1.39[a,b]	**<0.001**
3rd month	25.05±1.04[a,c]	23.81±1.26[b,c]	22.94±1.01[a,b]	**<0.001**
6th month	26.80±1.09[a,c]	24.96±1.66[b,c]	23.41±1.21[a,b]	**<0.001**

The data were presented as mean ± SD. The Kruskal-Wallis test was applied, and, in accordance with the Bonferroni Correction, $p<0.0125$ was deemed statistically significant, a: Stage I vs Stage III ($p<0.01$), b: Stage II vs Stage III ($p<0.01$), c: Stage I vs Stage II ($p<0.01$).

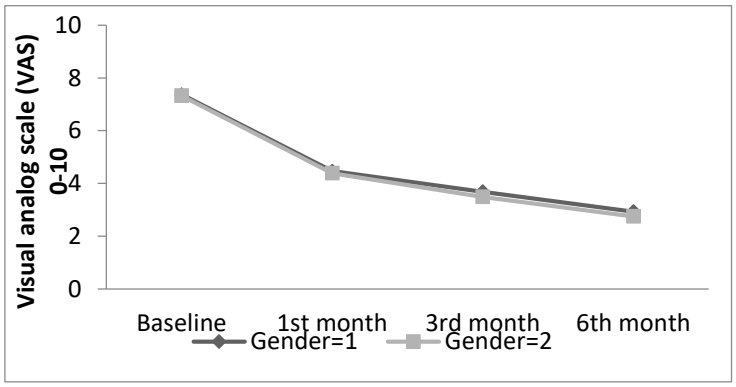

Figure 4. VAS Score

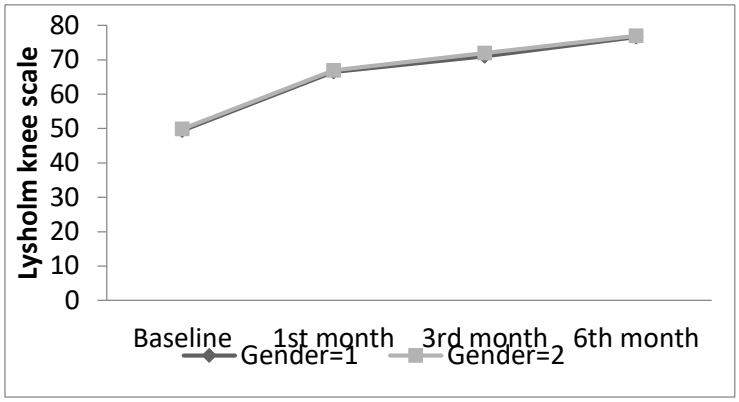

Figure 5. Lysholm Knee Score

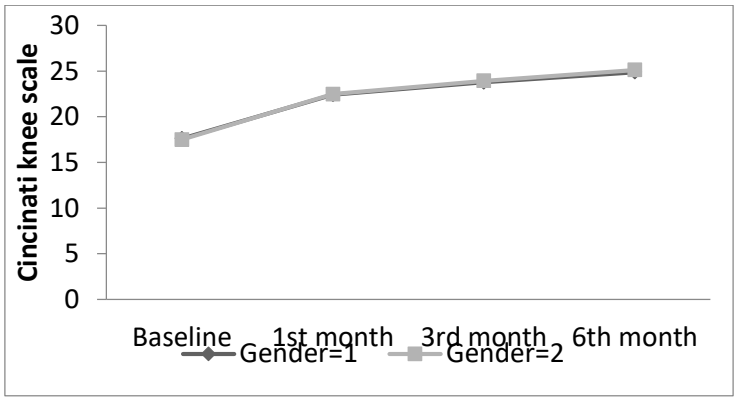

Figure 6. Cincinnati Knee Score

VAS, Lysholm, and Cincinnati scores broken down according to body mass index at each follow-up time are given in Table 4. The Bonferroni Correction revealed statistically significant differences between BMI groups, with the exception of the baseline VAS, baseline Lysholm, and baseline Cincinnati scores($p<0.0125$). VAS scores at each follow-up time within each category of BMI are shown in Figure 7. Similarly, Lysholm knee scores were given in Figure 8, and Cincinnati knee scores were shown in Figure 9. Statistically significant differences were noted using symbols such as "a," "b," and "c.".

Table 4. Comparison of changes in VAS, Lysholm, and Cincinnati scores according to BMI

	Normal	Borderline	Obesity	p-value †
VAS				
Baseline	7.27±0.81	7.47±0.85	7.42±0.91	0.395
1st month	3.91±1.45[a,b]	4.70±1.69[a,c]	5.81±1.37[b,c]	**<0.001**
3rd month	2.85±1.32[a,b]	4.00±1.89[a,c]	5.49±1.65[b,c]	**<0.001**
6th month	1.71±1.54[a,b]	3.55±2.50[a,c]	5.75±1.96[b,c]	**<0.001**
LYSHOLM				
Baseline	50.12±5.20	49.42±4.66	48.96±4.58	0.282
1st month	70.88±9.47[a,b]	64.27±9.86[a,c]	55.74±7.67[b,c]	**<0.001**
3rd month	76.76±9.31[a,b]	68.60±11.59[a,c]	57.72±8.23[b,c]	**<0.001**
6th month	82.99±9.85[a,b]	73.90±13.47[a,c]	59.30±10.09[b,c]	**<0.001**
CINCINNATI				
Baseline	17.56±1.38	17.45±1.41	17.55±1.28	0.823
1st month	23.01±1.61[a,b]	22.10±1.57[a,c]	20.96±1.07[b,c]	**<0.001**
3rd month	24.40±1.07[a,b]	23.52±1.20[a,c]	22.51±1.10[b,c]	**<0.001**
6th month	25.93±1.22[a,b]	24.38±1.51[a,c]	22.74±1.09[b,c]	**<0.001**

Data were shown as mean ± SD, † Kruskal Wallis test, according to the Bonferroni Correction $p<0.0125$ was considered as statistically significant, a: Normal vs Borderline ($p<0.001$), b: Normal vs Obesity ($p<0.001$), c: Borderline vs Obesity ($p<0.001$).

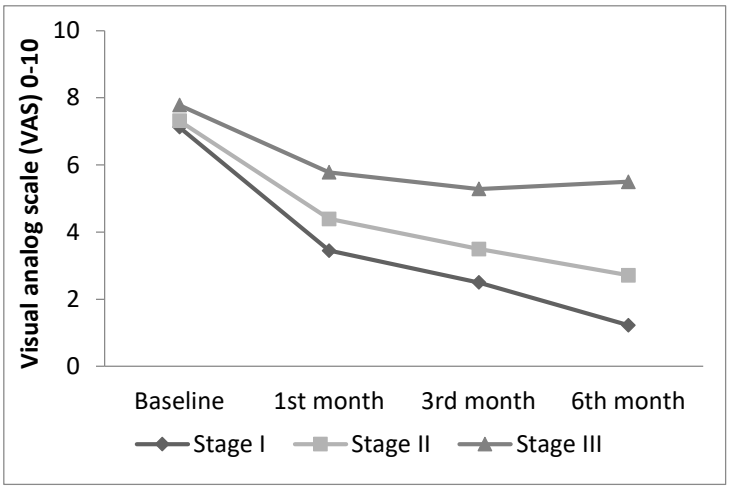

Figure 7. VAS Score

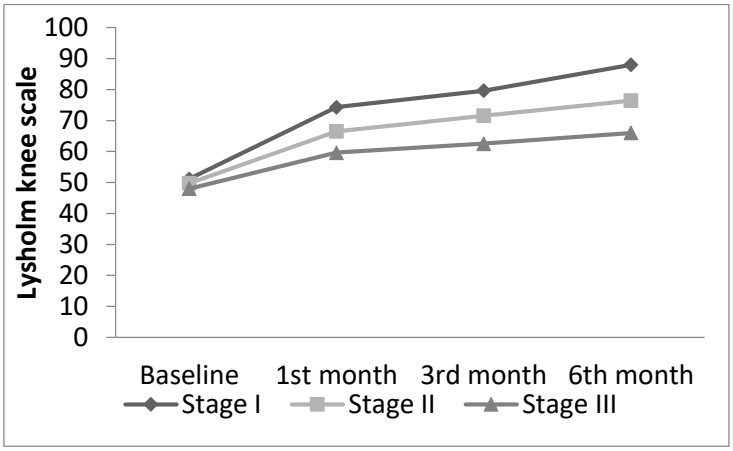

Figure 8. Lysholm Knee Score

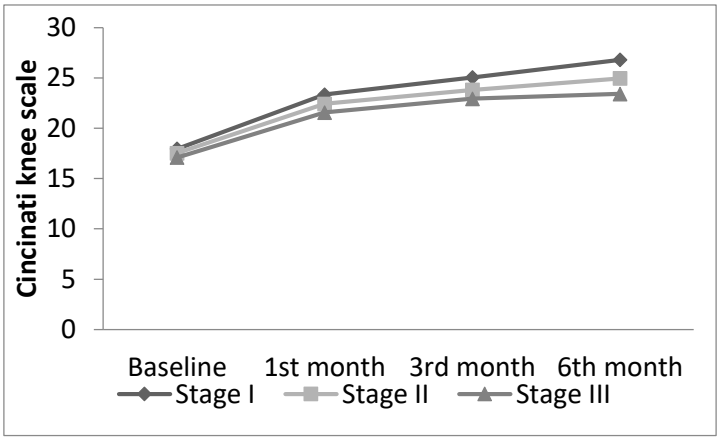

Figure 9. Cincinnati Knee Score

Data related to VAS, Lysholm, and Cincinnati scores at each follow-up time in patients who did and did not receive intraarticular steroid injections within the last 6 months are shown in Table 5. Except for baseline scores of VAS, Lysholm, and Cincinnati, all other Bonferroni corrected scores were observed to be statistically significant amongother follow-up times ($p<0.0125$). With respect to

intraarticular steroid injections within the last 6 months, data in each follow-up time are shown in Figure 10 for VAS score, Figure 11 for Lysholm score, and Figure 12 for Cincinnati knee score.

Table 5. Comparison of Changes in VAS, Lysholm, and Cincinnati Scores Regarding The History of Intraarticular Steroid Injection within The Last 6 Months

	Without injection (steroid)	With injection (steroid)	p-value †
VAS			
Baseline	7.35±0.85	7.21±0.58	0.420
1st month	4.35±1.65	5.64±1.22	**0.002**
3rd month	3.46±1.78	5.57±1.28	**<0.001**
6th month	2.65±2.33	6.00±1.66	**<0.001**
LYSHOLM			
Baseline	49.78±5.05	49.64±3.77	0.978
1st month	67.50±10.69	53.00±3.37	**<0.001**
3rd month	72.50±11.71	55.14±4.99	**<0.001**
6th month	77.88±13.43	57.00±8.56	**<0.001**
CINCINNATI			
Baseline	17.51±1.36	18.00±1.47	0.204
1st month	22.54±1.69	20.64±0.63	**<0.001**
3rd month	23.97±1.26	22.14±1.29	**<0.001**
6th month	25.15±1.70	22.79±1.63	**<0.001**

The data were presented as mean ± SD. The Mann Whitney U test was utilized, and in adherence to the Bonferroni Correction, p<0.0125 was deemed statistically significant.

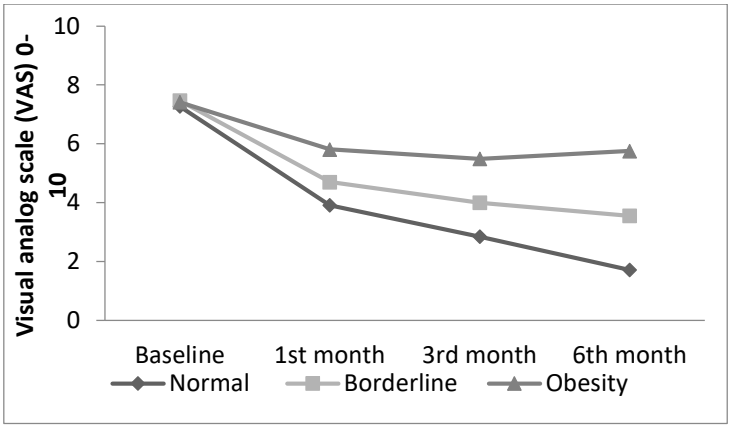

Figure 10. VAS Score

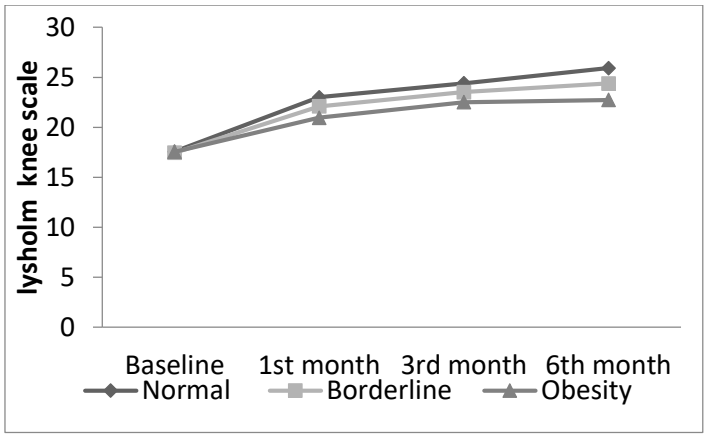

Figure 11. Lysholm Knee Score

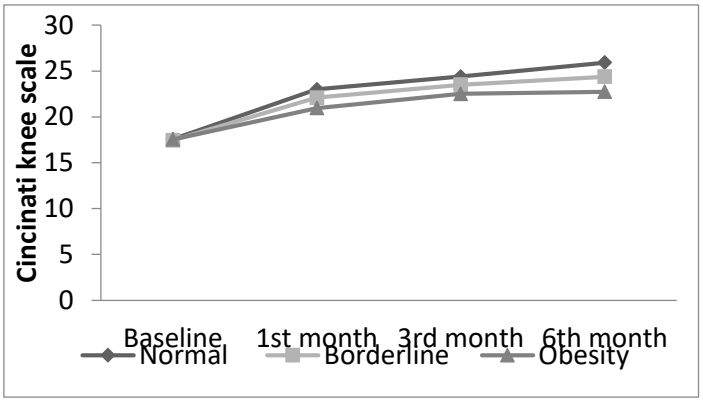

Figure 12. Lysholm Score

Table 6 shows the results of analysis of correlation between age and changes in VAS, Lysholm, and Cincinnati scores: first month to baseline, 3rd month to baseline, 6th month to baseline, 3rd month to 1st month, 6th month to 1st month, and 6th month to 3rd month.

Table 6. Correlation coefficients and levels of significance between age and VAS, Lysholm, and Cincinnati scores according to follow-up times

	Correlation coefficient	**p-value †**
VAS		
1st month - Baseline	-0.240	**<0.001**
3rd month - Baseline	-0.192	**<0.001**
6th month - Baseline	-0.081	0.168
3rd month - 1st month	0.187	**<0.001**
6th month - 1st month	0.287	**<0.001**
6th month - 3rd month	0.239	**<0.001**
LYSHOLM		
1st month - Baseline	0.288	**<0.001**
3rd month - Baseline	0.242	**<0.001**
6th month - Baseline	0.134	0.021
3rd month - 1st month	-0.099	0.089
6th month - 1st month	-0.195	**<0.001**
6th month - 3rd month	-0.182	**0.002**
CINCINNATI		
1st month - Baseline	0.305	**<0.001**
3rd month - Baseline	0.160	**0.006**
6th month - Baseline	-0.028	0.635
3rd month - 1st month	-0.309	**<0.001**
6th month - 1st month	-0.423	**<0.001**
6th month - 3rd month	-0.311	**<0.001**

† Spearman's rank correlation analysis, according to the Bonferroni Correction p<0.0083 was considered as statistically significant.

Table 7 shows the comparisons between gender and changes in VAS, Lysholm, and Cincinnati scores: first month to baseline, 3rd month to baseline, 6th month to baseline, 3rd month to 1st month, 6th month to 1st month, and 6th month to 3rd month. After Bonferroni Correction, clinical scores and there was no statistically significant difference between gender (p>0.0083).

Table 7. Comparison of VAS, Lysholm, and Cincinnati scores according to follow-up times with respect to gender

	Gender=1	Gender=2	p-value †
VAS			
1st month - Baseline	-2.90±1.81	-2.94±1.69	0.992
3rd month - Baseline	-3.68±1.99	-3.84±1.81	0.743
6th month - Baseline	-4.44±2.50	-4.57±2.35	0.941
3rd month - 1st month	-0.78±0.91	-0.90±1.06	0.302
6th month - 1st month	-1.53±1.66	-1.63±1.85	0.349
6th month - 3rd month	-0.75±1.29	-0.74±1.49	0.661
LYSHOLM			
1st month - Baseline	17.02±11.39	17.06±10.43	0.830
3rd month - Baseline	21.58±12.62	22.08±11.74	0.769
6th month - Baseline	27.18±14.37	27.09±13.89	0.775
3rd month - 1st month	4.56±3.47	5.02±4.21	0.533
6th month - 1st month	10.16±7.28	10.03±7.20	0.982
6th month - 3rd month	5.59±5.54	5.01±4.63	0.722
CINCINATI			
1st month - Baseline	4.78±2.11	4.99±2.25	0.412
3rd month - Baseline	6.15±1.92	6.45±2.00	0.158
6th month - Baseline	7.26±2.28	7.63±2.19	0.138
3rd month - 1st month	1.37±1.20	1.46±1.17	0.512
6th month - 1st month	2.48±1.66	2.64±1.55	0.245
6th month - 3rd month	1.11±1.19	1.19±1.07	0.256

Data were shown as mean ± SD, † Mann Whitney U test, according to the Bonferroni Correction p<0.0083 was considered as statistically significant.

The correlation coefficients and levels of significance, illustrating the relationship between the extent of change in Lysholm scores and the corresponding change in Cincinnati scores at each follow-up time, are presented in Table 8. The increase in Lysholm scores were associated with an increase in Cincinnati scores for baseline to 1st month, baseline to 3rd month, baseline to 6th month, 1st month to 3rd month, and 3rd month to 6th month (p<0.001).

Table 8. The correlation coefficients and levels of significance, illustrating the relationship between the extent of change in Lysholm scores and the corresponding change in Cincinnati scores at each follow-up time

	Correlation coefficient	p-value †
1st month - Baseline	0.776	**<0.001**
3rd month – Baseline	0.733	**<0.001**
6th month – Baseline	0.788	**<0.001**
3rd month - 1st month	0.060	0.302
6th month - 1st month	0.329	**<0.001**
6th month - 3rd month	0.382	**<0.001**

† Spearman's rank correlation analysis, according to the Bonferroni Correction p<0.0083 was considered as statistically significant.

DISCUSSION

According to the results in this study, PRP treatment is an effective method in relieving the symptoms of knee osteoarthritis. It also has a significant effect on clinical improvement. PRP treatment was tolerated well by all patients, and no allergic reactions were seen.

In the literature, PRP was found to be promising as a treatment method in early stage knee osteoarthritis (Filardo G, Kon E 2012, Soliman Hassan A 2015). Nevertheless, there are studies reporting its effectiveness in improving pain and functions in all ages and stages (Soliman Hassan A 2015, Campbell KA 2015, Lubowitz JH 2015). We found PRP to be effective in all ages and stages although its effect was more pronounced on clinical scores in the early stages. Jang et al. (2013) reported that the effectiveness of PRP decreased with advancing age and increasing degeneration (Jang SJ 2013).

Although we observed improvement in pain and functional scores across all age groups, the improvement was especially noticeable in young patients.

We showed that, in addition to age and degeneration, BMI and intraarticular steroid injection within the last 6 months were critical factors affecting the degree of improvement.

It is crucial to be aware of that the effect of PRP treatment is less in intensity and shorter in duration especially in overweight, obese, and morbidly obese patients so that the patients can be advised of the importance of weight loss, sports activities, and lifestyle changes in order to improve their participation in treatment. Studies are required using different approaches regarding the frequency and timing of PRP injections for these patients.

Our study suggests that the results of PRP treatment are negatively affected in individuals with a history of intraarticular steroid injections within the last 6 months for osteoarthritis treatment. Similar findings have been reported in the literature for patients with tendon injuries (Bradley Carofino 2012). Reviewing the frequency and the dose of intraarticular steroid treatment before the PRP treatment can be beneficial in order to obtain effective results. This can be explained with the mechanism of action of corticosteroids in that they affect the intracellular signals especially by negatively affecting the growth factors, that contribute to PRP's mechanism of action. In the case of tendons, for example, corticosteroids negatively affect tenocyte viability and proliferation; thus, they cause an increase in tendon injuries due to a decrease in matrix production (Bradley Carofino 2012, Wong MW 2005).

In randomized controlled studies comparing HA and PRP, both disease-modifying osteoarthritis drugs (DMOADs), PRP is reported to be more effective than HA. Sanchez et al. (2008), in their retrospective study comparing intraarticular hyaluronic acid with PRP, found a statistically significant improvement in the PRP group (Sanchez M 2008). Spaková et al. (2012) and Cerza et al. (2012) compared PRP to a control group of patients receiving hyaluronic acid injections, and they reported better pain scores and functional improvement in the PRP group in patients with osteoarthritis. On the other hand, Filardo G 2012 were unable to show any significant difference between the two methods of treatment.

Gobbi et al. 2012 compared patients receiving surgical treatment with patients receiving PRP injections, and they reported that return to daily activities was quicker in the PRP group.

İlhanlı et al.2015, in their study comparing physical therapy with PRP injections, found a more pronounced decrease in knee pain and increase in knee functions in the PRP group.

Halpern et al. 2013 reported an improvement in knee pain and knee functions in patients with knee osteoarthritis, and they showed a significant decline in the progression of disease.

Sampson et al.2010 reported a positive effect in 14 patients after receiving 3 PRP injections with intervals of 4 weeks. They showed an increase in cartilage thickness with ultrasound, but this study needed to be supported by studies with a larger cohort, because it was done on a small number of patients. Furthermore, there are studies stating that evaluations based on cartilage thickness would not be reliable, that knee complaints could be present in patients with adequate cartilage thickness, and that patients could be asymptomatic even though they have thin cartilages (Gandy SJ,2002). Therefore, we preferred to score pain and function instead of ultrasound measurements.

There are also studies reporting that PRP is effective for a short duration of time. In a study by Patel et al, the authors compared patients who received a single PRP injection, two PRP injections, and saline injection. They observed improvement in pain and function in patients who received PRP injections, but they reported that the improvement lasted for 6 months (Patel S 2013). Kon et al.2010 found that both pain and function improved in 100 patients who had three PRP injections with an interval of 3 weeks. Despite an improvement in parameters in the first year, results deteriorated in the second year, and the authors calculated a median value of 9 months for the asymptomatic period (Kon et al., 2010). We followed up our patients for a period of 6 months. During this follow-up period, we observed a significant improvement; however, studies with longer follow-up are needed.

CONCLUSION

Our study is meaningful in terms of identifying the relation of risk factors in osteoarthritis such as BMI, age, gender, and the severity of degeneration with the results of PRP treatment, along with indicating the negative effect of corticosteroid treatment administered within 6 months on the results of PRP treatment. With regard to its contribution to current literature, our study can be expected to contribute to future studies on standardization of PRP treatment.

Limitations of The Study

The limitations of our study are lack of a control group and reliance on patient evaluations in a self-preferred treatment.

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Conflict of interest

We declare that we have no conflicts of interest.

Author Contributions

Plan anddesing: YO; Data collection: YO; Analysis andcomments: YO; Reviewandcheck: YO; Writing: YO.

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