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Clinical results of PRP application for Gonartrosis; Comparison of one or two week interval application achievements.

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ABSTRACT

Objective: Intra-articular platelet-rich plasma PRP (platelet-rich plasma) treatment can be applied at an early stage of Gonarthrosis in addition to medical treatment. There is no consensus in the literature regarding the dose interval of PRP. Our aim in this study is to compare the short-term clinical results of three doses of PRP administered at one and two-week intervals in the treatment of early-stage Gonarthrosis.

Material and Methods: Three doses of PRP were applied to one knee of the patients at intervals of one week and to the other knee at intervals of two weeks. All patients were clinically evaluated with McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Scale (VAS) before the PRP application and at the 1st, 3rd and 6th months after the application.

Results: The mean age of 61 (40 female, 21 male) patients included in this study was 56.75 years and the mean BMI (Body Mass Index) was determined as 25.45±3.15 kg/m2. In the clinical evaluation at the end of the 1st, 3rd, and 6th months after PRP, there was no significant difference between the one-week interval and two-week application. However, it was observed that PRP application provided statistically significant improvement in WOMAC and VAS scores in both applications ($p<0.05$).

Conclusion: According to the findings we obtained in our study, it has been determined that there was no difference between applying three doses of PRP at one- or two-weeks intervals.

Keywords: Platelet-Rich Plasma, PRP, Knee Osteoarthritis, Intra-articular Injection

INTRODUCTION

Knee osteoarthritis (Gonarthrosis) is a common due to the increased elderly population and prevalence of obesity. In various epidemiological studies that were conducted all around the world, it was determined that the symptomatic Gonarthrosis was present in 10-30% of individuals over the age of 65 years (1,2). Gonarthrosis is generally evaluated with Kellgren Lawrence (K-L) radiographic grading scale (3).

Although there are many current treatment methods for Gonarthrosis, the majority of treatments other than surgical treatment are palliative and the aim is to reduce pain and improve the quality of life (3,4). Palliative treatment includes lifestyle modifications such as losing weight and exercise. On the other hand, analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular injections are used as medical treatment. Hyaluronic acid (HA), corticosteroid, PRP and autologous mesenchymal stem cells are the most applied treatment modalities as intra-articular injections (5,6).

The use of PRP, which is obtained by centrifugation of whole blood and contains a higher concentration of platelets and growth factors than whole blood, has recently become widespread(1,7). Indications of PRP, ideal PRP preparation, dosage, number of doses and dose intervals are frequently discussed in the literature in order to obtain safe and effective applications of PRP in the treatment of early-stage Gonarthrosis (8,9). Although there is not a complete consensus in the literature about application intervals; several studies are present the literature reporting a dose interval of one- to four- weeks (10,11).

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Our aim in this study is to evaluate the clinical results of 3 doses of PRP, which we applied as a medical treatment option in our clinic in the treatment of early stage Gonarthrosis, at intervals of one and two weeks, according to WOMAC and VAS indexes, and to compare the short-term results of both applications.

MATERIAL and METHODS

Patients who applied to our clinic between 01.04.2021 and 15.06.2021 due to knee pain were evaluated. Patients with a BMI of 20-32kg/m2 and between the ages of 45-75 with bilateral knee stage 2-3 Gonarthrosis according to the American College of Rheumatology (12) clinically and the Kellgreen Lawrence classification(13) radiologically, were included in the study. A total number of 70 patients, who met the inclusion criteria, were included in this prospective randomized study. Nine patients, who did not attend their regular follow-ups and whose treatment was not completed were excluded from the study. The evaluation was performed on the remaining 61 patients and 122 knees. The study was started after the approval of the local ethics committee of our hospital. Three doses of PRP were applied to one knee at one-week intervals and to the other knee at two-week intervals of the patients who were included in this study with bilateral Gonarthrosis. In order to standardize the PRP application, three doses of PRP were applied to the right knee with one-week interval in the first 35 patients, and three doses of PRP were applied to the left knee with two-week intervals for the remaining 35 patients according to their order of admission to the hospital. All patients were clinically evaluated according to VOMAX and VAS scales before the PRP application and at the 1st, 3rd, and 6th months after the PRP application. Patients who had undergone knee surgery due to a history of Gonarthrosis or previous trauma, patients who had undergone intra-knee injection or arthroscopy in the last 6 months, those with immunosuppression and a history of malignancy, and those with arthrosis in one knee were excluded from the study.

Preparation of PRP

For the preparation of PRP, 10 ml of blood was collected using a vacuum system from the antecubital vein in a sterile way into the tubes, including sodium citrate. The blood sample was centrifuged at room temperature for 5 minutes at 3000 rpm and two layers were formed. The plasma in the upper layer was separated by pipetting method and then it was re-centrifuged at 3000 rpm for 10 minutes. The upper layer was discarded from the reconstituted two layers, and 4-6 ml of platelet-rich PRP was obtained from the lower layer.

Route of administration

PRP, prepared in the same way, was used in all patients to achieve standardization. Administration was performed by the same orthopedist from the same localization with the standard injection tip (21-gauge needle). After the patient is seated on the stretcher, the feet were hung down and the knee joint was flexed to approximately 90 degrees. Under sterile conditions, an appropriate dose of PRP was administered into the knee by entering the upper part of the tibial plateau (from the lateral portal) from the lateral side of the patella and patellar tendon junction. After covering the injection site with a sterile sponge, the knee was flexed and extended two or three times to distribute the PRP in the knee. No local anesthetic drug was used before PRP application. It was recommended not to use NSAIDs, not to exercise and long walk outside of daily routine activities, and not to use stairs if possible before the administration of the second dose.

Results of the measurement

All patients were interviewed by an experienced orthopedist using the Turkish version of the WOMAC and VAS questionnaires (21). VOMAC index consists of 24 questions, including five questions for pain, two questions for stiffness, and 17 questions for physical function. Each question was scored from zero (not at all) to four (extreme). The overall WOMAC score ranges from 0 to 96, with higher scores indicating worse results. For VAS index, using a ruler, the patient was asked to mark the place of pain on the ruler as zero (no pain) and ten (worst possible pain).Six months later, the VAS and VOMAC scores of both knees were compared.

Statistical Analysis

Statistical package program SPSS 23.0 was used for the analysis of data. The normal distribution of the data was determined by the Kolmogorov-Smirnov test. Paired sample t-test was used to evaluate the difference between repeated measurements of numerical data. Data were given as Mean±Standard deviation. $p<0.05$ was considered as a statistically significant difference.

RESULTS

The mean age of 61 (40 female, 21 male) patients included in the study was 56.75±7.58 and the mean BMI was 25.45±3.15 kg/m2. The VOMAC and VAS indices of all patients before PRP application and at the 1st, 3rd, and 6th months after PRP application are shown in **Table-1** and **Table-2**.The VOMAC scale of patients to whom PRP was applied at one-week and two-week intervals before and after the application is shown in **Figure-1** and **Figure-2**.

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There was no significant difference in terms of VOMAC and VAS indices between applications performed at one-week intervals and two-week intervals. In the clinical evaluation, it was observed that the total VOMAC and VAS scores of PRP applied at intervals of one and two weeks decreased from the first month, and this decrease was statistically significant($p<0.05$).

A statistically significant decrease in total VOMAC and VAS indices was detected at the end of six months in both application groups after treatment ($p<0.05$). This results show that PRP is effective on the clinical improvement. Superficial skin rash was developed in three of our patients, but it was not interpreted as an infection and completely healed within 2-3 days.

Table 1. PRP, which was applied with one-week intervals

VOMAC	Before PRP	1st month	3rd month	6th month
Pain (0-20)	10.3±1.52[a]	9.7±1.08[b]	5.45±1.19[c]	4.55±0.82[d]
Stiffness(0-8)	3,35±1.18[a]	3.0±1.07[b]	2.15±0.74[c]	2±0.72[c]
Function(0-68)	44.2±4.7[a]	43.1±4.29[b]	31.7±3.75[c]	29.1±3.75[d]
Total (0-96)	57.9±5.42[a]	55.8±5.06[b]	39.3±4.11[c]	35.6±3.36[d]
VAS(0-10)	5.55±1.09[a]	4.85±0.87[b]	2.45±0.61[c]	1.91±0.64[d]

Values with different letters in the same line are statistically significantly different $p<0.05$

Table 2. PRP, which was applied with two-week intervals

VOMAC	Before PRP	1st month	3rd month	6th month
Pain (0-20)	10.5±1.35[a]	9.5±0.88[b]	5.35±1.22[c]	4.7±0.81[d]
Stiffness (0-8)	3.4±1.18[a]	3.15±1.18[a]	2.0±0.85[b]	1.9±0.96[b]
Function (0-68)	44.0±4.42[a]	41.2±4.54[b]	31.5±3.95[c]	28.2±2.63[d]
Total (0-96)	57.8±4.91[a]	53.9±5.04[b]	38.9±4.14[c]	34.8±2.92[d]
VAS(0-10)	5.25±1.01[a]	4.85±1.04[b]	2.8±0.83[c]	2.05±0.61[d]

Values with different letters in the same line are statistically significantly different $p<0.05$

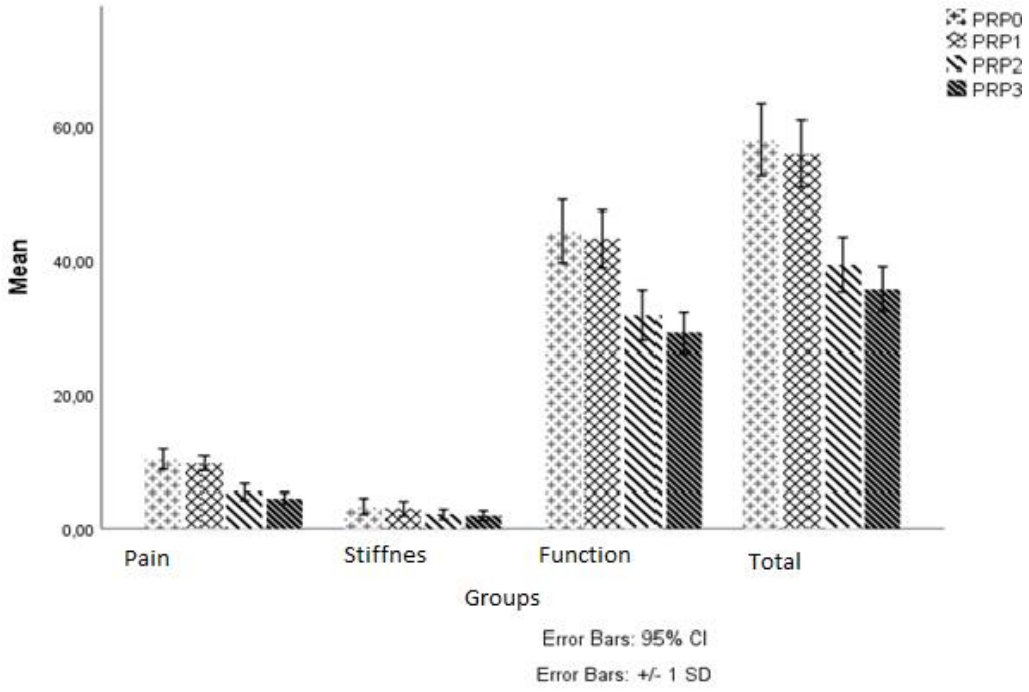

Figure 1: After PRP applied at one-week intervals; pain, stiffness, function, and total VOMAC scale distribution are shown. Error bar shows the SD. (PRP 0; before PRP administration, PRP 1; 1st month after administration, PRP 2; 3rd month after administration, PRP 3; 6th month after administration)

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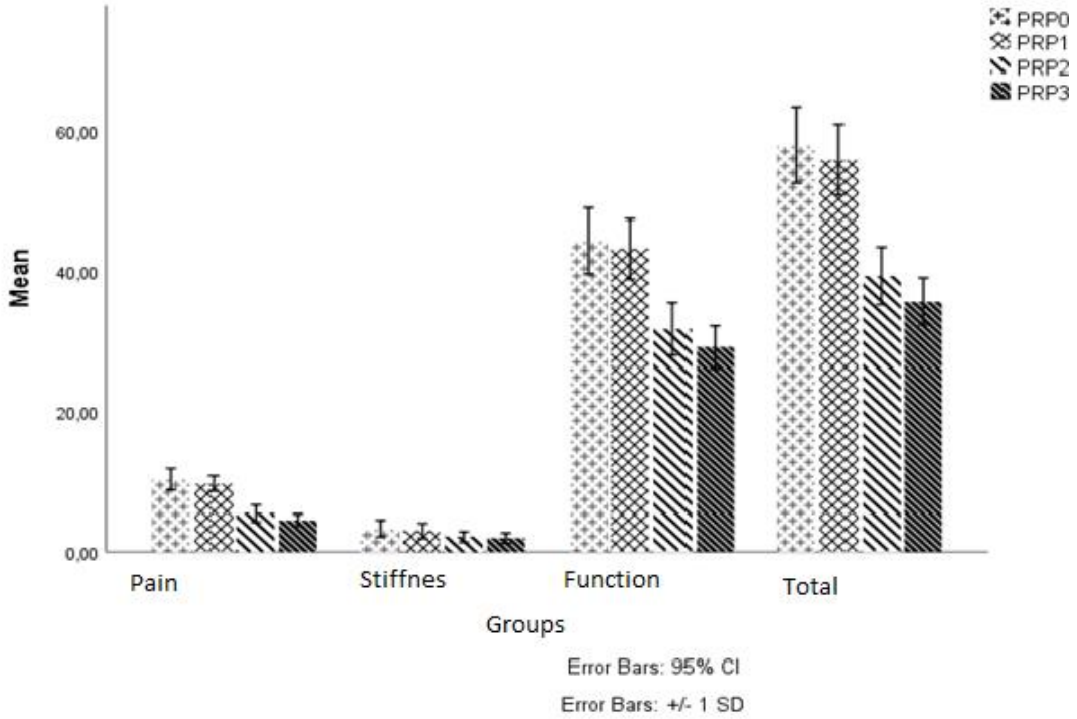

Figure 2: After PRP is applied at two-week intervals; pain, stiffness, function, and total VOMAC scale distribution are shown. Error bar shows the SD. (PRP 0; before PRP administration, PRP 1; 1st month after administration, PRP 2; 3rd month after administration, PRP 3; 6th month after administration)

DISCUSSION

When the demographic characteristics of the patients were evaluated, a similarity was found in the literature in terms of age, gender, and BMI (9,14). Gonarthrosis is seen in women in old age and especially in those with high BMI. In our study, the number of women was found to be higher, and their BMI was high.

Despite its common clinical applications, no consensus is present in the literature about the preparation, application method, number of doses and dose intervals of PRP. Nowadays, PRP is commonly applied in early stage Gonarthrosis that does not need surgery or in patients whose general condition is not suitable for surgical interventions. The results of these treatments are frequently discussed in the literature (15-19). When the dose intervals of PRP were compared in our study, there was no significant difference between the clinical results of three doses of PRP performed at one-week and two-week intervals. In both applications, clinically significant decreases were detected in VOMAC and VAS scores after six months of follow-up. As a result of our study, it was seen that PRP applied at intervals of one and two weeks as dose intervals were effective and successful in both applications. There are studies reporting that the ethnicity of the individual influences the platelet function during PRP administration (20). Considering this characteristic of PRP, this activity difference was tried to be eliminated by applying PRP to different knees of the same individual. Thus, specificity was achieved in our study with PRP applied in the same way on the same person.

PRP can be prepared as a result of one or two times of centrifugation (21, 22). It is known that the patient's age, comorbid diseases, the amount of blood taken at the beginning and the preparation technique are effective on the platelet concentration in the PRP (22). The PRP used in our study was obtained in the same standards by centrifuging twice with the help of our technician using the device in our center.

There are studies about the administration of a single dose or multiple doses of PRP in the literature (23-25). Clinical results were found to be more successful with multiple doses (21). In animal studies, the curative effect of PRP on synovial and cartilage tissue was found to be more effective with multiple doses (17). Based on such studies in literature and our clinical experiences, we applied three doses of PRP to all our patients.

Different recommendations are present in literature about the method of administration and the position of patient. Method of administration includes injection directly into the joint and administration via collagen membrane (22, 26).

Patient positions include administration to suprapatellar region at supine position of patient and full extension of knee or administration from the lateral portal of the knee in the sitting position with the knee flexed at 90 degrees (9,14).

Our routine practice in our study was administration of PRP in sitting position with the knee flexed, from the lateral portal directly into the joint, and no membrane was used.

Considering the mechanism of action of PRP, platelets, especially growth factors, cytokines and chemokines secreted from alpha granules, stimulate chondrocyte and chondrogenic structures and increase chondrocyte cartilaginous matrix secretion after intraarticular administration (27). Although this situation increases cartilage regeneration, the lack of vascular and nerve structure of the cartilage limits this regeneration (28). Although the duration of the PRP effect is not clear in literature, studies have shown that the duration of this effect may vary between 6 months and 2 years (21,26,29). In our study, the results of PRP in the first six months were evaluated based on the most effective time in the literature and various suggestions are present in the literature regarding the administration interval for PRP. However, there is still no consensus about this subject. Generally, this interval ranges from one week to four weeks (10,11). Some studies have reported that it is sufficient to repeat it once a year (21,30). We think that the evaluation of the clinical results of the same PRP at different time intervals with VOMAC and VAS scores for the same patient will provide more objective results. After this evaluation, no significant difference was found between clinical results in terms of dose intervals in our study.

There are also some limitations of our study. These limitations include; the low number of our patients, relatively short patient follow-up times, and lack of radiological evaluation.

CONCLUSION

In our study, no clinically significant difference was found between three doses of PRP which was administered at one- or two-week intervals in early-stage Gonarthrosis. However, it was determined that there was a significant clinical improvement in the knees for both administration intervals compared to pre-PRP values.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Local Ethical Committee.

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