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Comparing the Effectiveness of Intra-articular Platelet-Rich Plasma and Corticosteroid Injection under Ultrasound Guidance on Pain Control of Knee Osteoarthritis

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Abstract

Background: Knee osteoarthritis is one of the most prevalent and disabling diseases worldwide, which decreases patients' quality of life (QoL). However, pharmacological and non-pharmacological treatments, apart from complications, could not desirably control the disease.

Objectives: The current study aimed at evaluating the effect of two methods of intra-articular injection of Platelet-Rich Plasma (PRP) and corticosteroid on pain control of knee osteoarthritis.

Methods: A randomized clinical trial was performed on 67- patients with grades II-III of knee osteoarthritis (OA) referring to pain clinic of a referral, university-affiliated hospital, Rasht, Iran, from April 2016 to June 2017. Patients were randomly divided into two groups: Triamcinolone (T) (n=34) and PRP (P) (n=33) by quadruple block. In the group T, 40 mg Triamcinolone and in the group P, PRP was injected intra-articularly, under ultrasound- guidance, once a month, for three consecutive months. Patients' pain intensity was evaluated based on the Visual Analog Scale (VAS), and their outcome was determined based on the Knee injury and Osteoarthritis Outcome Score (KOOS) monthly for three consecutive months, as well as six months after the treatment.

Results: There were no significant differences between the groups regarding demographic characteristics. VAS assessments indicated lower pain scores in the group P than group T; the difference between the groups was statistically significant two, three, and six months after the injections. In the group P, the mean initial VAS was 7.36 $\pm$ 0.92 compared with 7.12 $\pm$ 1.29 in the group T (P = 0.385). After six months, the scores dropped to 3.45 $\pm$ 0.86 and 4.81 $\pm$ 1.4, respectively (P = 0.0001). Examination of the KOOS parameters showed a significant association between treatment outcomes in the group P than the group T. Therefore, the test showed a significant difference between the groups regarding relief of pain, improvement of symptoms and activities of daily living (ADL) two, three, and six months after treatment. There was also a significant difference between the groups in terms of the quality of life (QoL) and doing sport activities three and six months after the treatment (P < 0.05). Based on the repeated measures analysis, a significant inter- and intra-group differences in the mean score of KOOS parameters was observed between the intervals (P = 0.0001).

Conclusions: The current study results showed that three intra-articular injections of Triamcinolone and PRP could reduce pain and improve articular function in patients with grades II-III knee osteoarthritis. However, pain relief and improvement in the outcomes were more effective and more prolonged secondary to PRP injections than corticosteroids.

Keywords: Corticosteroid, Injection, Intra-articular, Knee, Osteoarthritis, Pain, Platelet-Rich Plasma, Triamcinolone

1. Background

Osteoarthritis (OA) is the joint insufficiency. In OA, all of the joint structures have pathological changes (1). Knee OA is the most common type of OA in the lower extremity and constitutes 23% of all arthritis cases (2). It is probably a polygenic disease that may be affected by environmental factors. Higher age, female gender, overweight and obesity, knee injury, repetitive use of knee, bone density, muscle weakness, and joint laxity are associated with the progression of OA (3, 4). About 13% of females and 10% of males aged above 60 years have symptomatic knee OA (5). In a recent study on rural areas population in Iran, results

showed that about 20% of the studied population had OA in at least one of their joints. Also, the prevalence of OA in rural areas population of Iran was higher than those of Asian countries (4). Considering the increase in life expectancy and old population, it is one of the most challenging medical issues, worldwide (1, 6-8). Pain due to the knee or hip OA causes insufficient activity. Since OA is a common disease, inactivity is a public health problem that increases the risk of cardiovascular diseases.

The primary goal of the treatment is to relieve pain and minimize the loss of physical function, and then, inhibit the disease progression in order to maintain the patients' independence and improve their quality of life (QoL). Non-pharmacological (education and diet) and pharmacological (non-opioid oral analgesics) treatments are the initial recommended treatment for OA (9-13). Intra-articular injections can be used as an alternative treatment for oral medications in patients with poor response to such drugs (14).

Since synovial inflammation is probably one of the major causes of pain in patients with OA, topical anti-inflammatory therapies, administered intra-articularly, are effective to relieve the pain (15). Corticosteroids have anti-inflammatory and immunosuppressive effects, but their mechanism of action is complicated (16). These drugs reduce vascular permeability and inhibit the accumulation of inflammatory cells, phagocytosis, production of superoxide neutrophil, and prevent the synthesis and release of inflammatory mediators such as prostaglandin and leukotrienes (17). The anti-inflammatory effects of these drugs reduce erythema, swelling, warmth, and tenderness of the inflamed joints and increase viscosity by increasing the concentration of hyaluronic acid (18). Despite previous investigations, still, there is no consensus on the type of selected corticosteroid and the optimal dosage (19-21).

It is believed that the progression of OA results from an imbalance between pro-inflammatory cytokines such as interleukin (IL)-1a, IL-1β, tumor necrosis factor (TNF)-α, and anti-inflammatory cytokines including IL-4, IL-10, etc. It activates the proteolytic enzymes responsible for joint degeneration. Recently, treatments are used to eliminate this cytokine imbalance. One of these treatments is the use of platelet-rich plasma (PRP) (22). PRP is one of the new therapeutic approaches recently attracted interests and various researches were performed in this field. It is provided from the autologous blood centrifuge and is a volume of plasma containing a high concentration of platelets and white blood cells (WBCs). WBCs and platelets are the rich sources of cytokines used to regulate a number of healing and tissue regeneration processes. Platelets, in addition to cytokines, contain large amounts of growth factors and also release large amounts of bioactive proteins that increase the removal of necrotic tissues and accelerate the processes of tissue regeneration and healing (23-25). There is strong evidence of the efficacy of PRP in musculoskeletal diseases, wound healing, and OA in previous clinical trials (23, 26-29). However, according to the Filardo et al., there is a need for more organized studies with larger sample sizes to judge the effectiveness of these methods in the management of knee QA (30).

Since knee OA is one of the most prevalent and disabling diseases worldwide, it causes different levels of dysfunction. On the other hand, conventional and non-pharmacological treatments and surgical procedures, apart from complications, cannot optimally control the disease. Therefore, constant efforts to find new therapies with minimal complications and invasiveness and maximum efficacy are in progress (23, 26, 31). Intra-articular injections of PRP and corticosteroids are today popular therapeutic approaches. Although previous studies showed the effectiveness of each method in the treatment of knee OA (23, 26), based on the current review findings, only two studies examined the effectiveness of PRP injection versus intra-articular corticosteroids in the treatment of knee OA (32, 33). These studies administered only single dose of corticosteroid or PRP injection and the results were controversial; no study so far tried to compare the effect of multiple injections of these two compounds on knee OA treatment.

2. Objectives

The current study aimed at comparing the effect of three intra-articular corticosteroid and PRP injections, as two therapeutic methods, on pain relief and functional improvement of knee OA.

3. Methods

3.1. Setting

The current randomized, clinical trial was carried out after obtaining approval from the ethics committee of Guilan University of Medical Sciences (No: IR.GUMS.REC.1394.221), Rasht, Iran. The study was performed on patients with grades II - III of knee OA referring to pain clinic of Poursina educational and care hospital affiliated to Guilan University of Medical Sciences, Rasht, Iran, from April 2016 to June 2017. Poursina hospital is a state and referral center of orthopedic surgery in Guilan province. The study was registered in Iranian registry of clinical trials (Number: IRCT201601236186N12).

3.2. Study Participants

Before the enrollment, the method of the procedures as well as the advantages and disadvantages, the evaluation technique, and the necessary explanations regarding equal chance for attending in each group was given to the participants and informed consents were obtained.

3.3. Inclusion Criteria

Inclusion criteria were age 30 - 75 years, diagnosis of grades II - III knee OA according to the criteria of American College of Rheumatology (ACR) (34), or by tibio-femoral radiography based on Kellgren and Lawrence grading scale criteria (35), patients with debilitating knee pain for at least three months not responding to different treatments and causing dysfunction.

3.4. Exclusion Criteria

Exclusion criteria were knee joint deformities, cancer, rheumatoid lesions, body mass index (BMI) $>$ 35 kg/m^2, pregnancy, breastfeeding, acute infection, hemoglobin $<$ 11 g/dL, platelets $<$ 150,000 $\times$ 10^9/L, blood disorders, hemoglobinopathies, uncontrolled diabetes, acute knee pain, history of knee surgery, serious neurologic or psychological disorders, sciatica pain, history of treatment with anticoagulants, treatment of coagulation disorders, and corticosteroid consumption within last three months.

3.5. Sample Size

The sample size was calculated based on Forogh et al., protocol (32).

$\alpha = 0.05$

$\beta = 0.20$

z1-α/2 = 1.96

z1-β = 1.28

S1 = 15

S2 = 16.3

d = 12.5

$$n = \frac{\left(\left(z_1 - \frac{\alpha}{2}\right) + \left(Z_1 - \beta\right)\right)^2 \left(S_1^2 + S_2^2\right)}{\left(\mu_1 - \mu_2\right)^2} = 33$$

The sample size was set to 36 patients for each group, expecting 10% dropouts.

3.6. Randomizations

Using quadruple block, patients were assigned to one of the two groups of PRP intra-articular injection (group P) and intra-articular injection of Triamcinolone (group T).

3.7. Interventions

In the group P, to prepare PRP under sterile conditions, a 50-mL of blood was taken from an antecubital vein and placed in the centrifuge kit (standard kit) containing citrate phosphate dextrose (CPDA). Blood was centrifuged in standard kit at 1200 rpm for 15 minutes. Then, the sediment (red blood cells) was placed in the first bag and the supernatant (plasma) in the second bag. It was centrifuged again at 2700 rpm for six minutes. After extraction of free platelet plasma, 5 mL of platelet-rich plasma was injected into the knee joint. This procedure was performed once a month for three consecutive months. In the current study, the standard kit of Noavaran -Salamat - Arzhang Company, Iran, and a centrifuge device of Sahand -Azma- Tajhiz Company, Iran were used. Before the onset of study, the analysis of platelet counts on complete blood and PRP of five healthy subjects were conducted to confirm the quality of the PRP prepared based on the using method. Using this method, 4- to 6-fold increase in platelet count was obtained. For intra-articular injection of corticosteroids, in group T, 40 mg of Triamcinolone (EXIR Pharmaceutical Company, Iran) was injected into the patient's knee each month. To perform injections, the patient was placed in the supine position. Under sterile conditions and after putting the linear probe (6 - 12 MHz) at the top of the patella, a sono-visible needle gauge 21 (Pajunk Company, USA) was entered from the superio-lateral quadrant of the patella and directed with in-plane technique under ultrasound - guidance into the knee joint space. Then, the provided solution was injected into the knee. This monthly injection was performed for three times.

In both groups, after injection for through distribution in joint cavities, the anesthesiologist performed 10 passive knee flexion and extension movements. The patients then rested in the supine position for 10 minutes before discharge. In case of any complication, patients were monitored and discharged after full recovery.

Patients were advised to refrain from weight-bearing on the injected knee 24 - 48 hours after injection. To relieve the pain, patients were advised to use cold compresses (three to four times daily each 10 - 15 minutes), and take acetaminophen (500 mg every eight hours). If the pain was not controlled, acetaminophen could be used every six hours. Patients should avoid non-steroidal anti-inflammatory drugs (NSAIDs), steroids, and drugs affecting platelet count and function. Patients were advised to continue activities with mild to moderate intensity and gradually increase their activities based on personal tolerance.

3.8. Outcomes Measurement

The intensity of pain and knee function were evaluated based on Visual Analog Scale (VAS), and Knee injury and OA Outcome Score (KOOS) before the onset of treatment, once a month for three consecutive months, and six months after initiation of treatment. In VAS, zero represents pain relief and 10 scores indicate the highest intensity.

The KOOS is a 42-item, self-reporting questionnaire. It has five subscales including symptoms (seven items), pain (nine items), activities of daily living (ADL) (17 items), sport and recreation function (five items), and QoL (four items).

It is scored based on a five-option Likert scale from 0 to 4. Zero indicates the appropriate score and 4 the worst score. Total scores range from 0 to 100 in which 0 shows severe knee impairment and 100 indicates no problem. The higher total score shows lower disability. Reliability and validity of the Persian version of the questionnaire were confirmed by Salavati et al. (36).

The questionnaire was completed for all the patients by a physician who was blind to the type of treatment. Patients were asked to report any complications including pain, swelling, infection, and hematoma during a six-month follow-up.

3.9. Statistical Analysis

Normality of quantitative data was assessed by the Shapiro-Wilk test. Data were expressed by descriptive statistics (as the mean ± standard deviation); quantitative data were analyzed by independent test and repeated measures with SPSS software version 17.0 (SPSS Inc., Chicago, IL., USA). The p-value < 0.05 was considered the level of significance and 95% confidence interval (CI) was noted.

4. Results

The study subjects were selected from 123 patients with knee pain. Of these, 44 patients did not meet the inclusion criteria and seven patients were not interested to participate. The remaining patients were included in the study and allocated to each P and group T. Three patients from the group P and two patients from the group T were excluded from the study. In the group P, one patient was excluded due to distal femur fracture and orthopedic surgery caused by car crash three weeks after the first injection, another patient was also excluded due to migration two months after starting the treatment, and one patient did not respond to fill the questionnaire after the follow-up period. In the group T, two patients were excluded from the study since they did not cooperate for completing the questionnaires at three and six months follow-ups, and finally, 33 and 34 patients were assigned to P and Group Ts, respectively (Figure 1).

In the current study, there was no significant difference between the groups regarding demographic characteristics including age, gender, body mass index (BMI), and degree of OA (Table 1).

Table 1. Demographic Characteristics of the Patients[a]

Variables	Group T	Group P	P Value
Gender male/female	7/27	5/28	0.56
Age, y	58.55 ± 8.79	59.09 ± 7.79	0.794
BMI, kg/m^2	27.78 ± 3.29	28.4 ± 2.78	0.414
OA score, Grade II/III	11/23	9/24	0.65

Abbreviations: BMI, Body Mass Index; OA, Osteoarthritis.
[a]Group T received Triamcinolone and the group P received Platelet-Rich Plasma intra- knee injections.

Patients' pain was assessed based on VAS and test results showed a significant difference between the groups, except for baseline measures and one month after the treatment. Pain intensity in the group P was significantly lower than that of the group T. In the group P, the mean of baseline VAS was 7.36 ± 0.92 vs. 7.12 ± 1.29 in the group T. After six months, it was diminished to 3.45 ± 0.86 and 4.81 ± 1.4, respectively (P = 0.0001). Using repeated measures test, a significant difference in the mean intensity of pain was observed between the intervals in each group as well as two groups (P = 0.0001) (Table 2).

Table 2. The mean pain intensity based on VAS in the study groups (Mean ± SD)[a]

Time	Group T	Group P	P Value
T0	7.12 ± 1.29	7.36 ± 0.92	0.385
T1	5.42 ± 1.22	4.9 ± 1.04	0.071
T2	4.72 ± 1.09	4.06 ± 1.04	0.011
T3	4.24 ± 1	3.69 ± 0.88	0.022
T6	4.81 ± 1.4	3.45 ± 0.86	0.0001
P value intergroup[b]	0.0001	0.0001	
P value intragroup	0.0001		

Abbreviations: VAS, Visual Analog Scale.
[a]Group T received Triamcinolone and the group P received Platelet-Rich Plasma intra- knee injections.
[b]P < 0.05 was considered significant.

The parameters of KOOS including pain relief, symptoms relief, ADL, QOL, and sport were evaluated in two groups. Assessing the mean of KOOS parameters including pain relief, symptoms relief, and ADL, showed that except for baseline and one month after treatment, there was a significant difference between the groups. Hence, the level of pain reduction and symptoms relief, as well as increased ADL in the Group P was significantly higher than Group T (P < 0.05). Comparison of the mean QoL and sports pa-

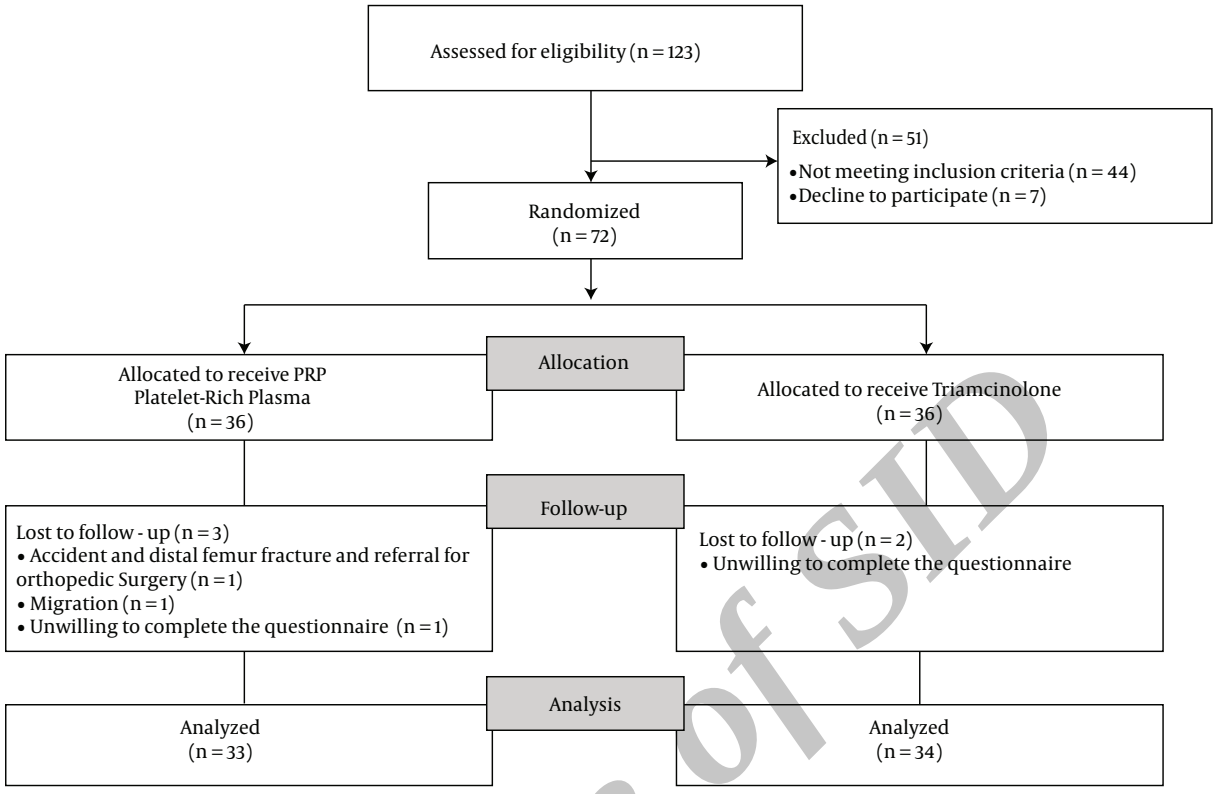

Figure 1. Consort form of the study

rameters in KOOS scale showed no significant differences between the groups except for three and six months post-treatment parameters (Table 3). Repeated measurement indicated a significant difference in the mean scores of KOOS parameters between the intervals in each group, as well as the two groups (P = 0.0001).

No major complications related to the injections were observed during the treatment and follow-up period. The most commonly observed complication was mild to moderate pain in the injection site, not considered as a serious complication.

5. Discussion

The current study mentioned the effectiveness of both intra-articular injections of PRP and corticosteroid, but patients receiving PRP had a greater and prolonged improvement in pain severity and physical function than those receiving corticosteroids.

The evaluation of patients in the current study was based on VAS and KOOS. VAS only measures the severity of pain, while the KOOS is a simple self-administered instrument that evaluates patient's short- and long-term term symptoms and functions.

The current study showed that both an intra-articular corticosteroid and PRP had beneficial effects on reducing the pain based on VAS. In both groups, the pain decreased until the third month. While the reduction of pain in the Group P prolonged for six months; in Group T, the pain increased in the sixth month compared with that of the third month. However, still, the pain level was significantly lower than the baseline, which suggested the effectiveness of both methods to control the symptoms in the patients. Hassan et al., (37) evaluated the efficacy of the PRP method to control symptoms in patients with OA; patients underwent six intra-articular PRP injections at the intervals of one month. Similar to the current study, the improvement of symptoms was observed at the end of the sixth month compared with the baseline values.

In a study by Kilincoglu et al., (38) patients received PRP and hyaluronic acid through injection once a week for three consecutive weeks. Patients' pain was assessed three and six months after injections. In their study, similar to the current study, patients' pain in both groups decreased up to six months. However, in their PRP group, the

Table 3. Comparison of the Groups Regarding Changes in KOOS Parameters (Mean ± SD)[a,b]

Time/ Group	Pain Relief		Symptom Relief		ADL		QoL		Sports	
T0										
Group P	35.26 ± 8.9	0.176	40.58 ± 15.17	0.683	40.5 ± 7.16	0.54	18.56 ± 15.02	0.437	14.24 ± 7.71	0.54
Group T	38.97 ± 12.89		42.12 ± 15.49		41.52 ± 6.3		21.5 ± 15.1		15.44 ± 8.19	
T1										
Group P	52.1 ± 9.16	0.481	54.43 ± 12.07	0.244	52.09 ± 6.22	0.324	26.13 ± 11.94	0.731	20.6 ± 6.34	0.582
Group T	50.16 ± 12.95		50.84 ± 12.95		50.56 ± 6.38		25 ± 14.83		19.7 ± 6.95	
T2										
Group P	61.61 ± 7.93	0.034	61.58 ± 9.65	0.021	59.13 ± 5.26	0.0001	31.62 ± 11.36	0.191	26.51 ± 6.05	0.115
Group T	56.45 ± 10.84		55.56 ± 11.09		53.54 ± 6.93		27.57 ± 13.59		24.11 ± 6.21	
T3										
Group P	67.84 ± 8.7	0.002	67.74 ± 7.54	0.0001	62.47 ± 6.74	0.0001	34.84 ± 10.36	0.023	31.36 ± 5.62	0.0001
Group T	60.62 ± 10.01		59.34 ± 10.62		54.45 ± 6.72		28.49 ± 11.93		24.55 ± 5.95	
T6										
Group P	71.63 ± 7.1	0.0001	70.34 ± 6.71	0.0001	65.99 ± 6.78	0.0001	36.36 ± 9.3	0.0001	33.03 ± 6.48	0.0001
Group T	54.65 ± 11.12		55.25 ± 8.58		47.44 ± 6.84		26.1 ± 11.66		19.41 ± 5.87	

Abbreviations: ADL, Activity of Daily Living; QoL, Quality of Life; T, Time after injection (month)
[a] Group T received Triamcinolone and the group P received Platelet- Rich Plasma intra- knee injections.
[b] $P < 0.05$ was considered significant.

pain, based on VAS, at the end of the sixth month was lower than that of the current study. The difference could be attributed to the difference in injection intervals (monthly versus weekly), the centrifugation method, and more importantly, the lower grades of OA in their study participants (grades I - II) compared to those of the patients in the current study (grades II-III).

In a study on the effect of intra-articular corticosteroid and hyaluronic acid on the treatment of knee OA, the effect of corticosteroid on pain reduction in a short period was greater than that of the hyaluronic acid, while the long-term effects of hyaluronic acid were greater than that of the corticosteroids (19). Forough et al., (32) compared intra-articular corticosteroid and PRP, similar to the current study, and observed a significant difference regarding the six-month reduction of pain between the two groups; therefore, pain reduction in the PR group P was significantly higher than that of the corticosteroid group. In the current study, the degree of pain reduction was significantly greater in the PRP than the corticosteroid group in the study by Forogh et al. This difference might be attributed to the more frequent corticosteroid injections in the current study (three times with one-month intervals (in contrast to one time in their study. Joshi Jubert et al., (33) compared corticosteroid and PRP; despite the reduction of pain in both groups, there was no significant difference between the groups. This difference might be noted regarding the higher degree of OA in their study (grades III-IV) compared with the current study.

To assess outcomes based on KOOS, the improvement of all parameters of this criterion was observed in the two groups at post-treatment time points, which indicated the effectiveness of both methods to treat knee OA. Although there was no significant difference between the groups in the first and second months regarding the improvement of parameters, improved parameters were noted more from the second and third months to the sixth month in the group P than the group T and indicated a more effective PRP treatment than corticosteroid.

In a systematic review performed to evaluate the effect of PRP injections on the knee OA, six studies were analyzed, and the results showed that PRP compared with placebo and hyaluronic acid in symptomatic OA patients could better improve symptoms for 12 months. From the six studied investigations, five studies compared PRP with hyaluronic acid, one study compared PRP with saline (placebo), and no study compared PRP with corticosteroids (38). Say et al., (39) compared one PRP injection with three injections of hyaluronic acid, and reported a clinical improvement in both groups, although the PRP Group showed better results. However, in a study by Filardo et al. (30), patients received three injections of PRP and intra-articular hyaluronic acid at three-week intervals. Patients were evaluated by the KOOS criteria at baseline as well as 2-, 6-, and

12-month follow-ups. Based on the results, there was no significant difference in the parameters of KOOS between the groups at all the times. The difference between the results of a study by Filardo and those of previous studies might be attributed to freezing PRP after centrifugation; since freezing the PRP solution causes a change in the morphology of cells, decreases platelets function, and reduces the effectiveness of injected PRP.

In a study by Raynauld et al. (40), patients received intra-articular Triamcinolone or saline every three months for two years. In a two-year follow-up, the symptoms of patients and the parameters of the WOMAC score included pain, stiffness, and physical function improved in the corticosteroid group compared with the placebo group without major complications. The results of their study supported the safety of long-term intra-articular steroids injection in patients with symptomatic knee OA. In a study by Forogh et al., (32), intra-articular injections of PRP resulted in prolonged pain relief, as well as improved LDAs and QoL compared with those of corticosteroids. In their study, there was a significant difference between the groups regarding the KOOS score parameters, except the sports parameter. The results were similar to those of the current study. However in the current study, in terms of sports parameter, at three and six months after treatment, PRP provided better statistical results, which might be attributed to more frequent injections of PRP in the present study.

Joshi Jubert et al., (33) showed that the effect of intra-articular PRP in elderly patients with advanced knee OA was equivalent to those of intra-articular corticosteroid injection. In addition to the number of injections that might cause a difference in the current study, the age, gender, weight, and grade of the disease also might affect the outcome of the study. Female gender, age increase, higher OA grade, and higher BMI score are the risk factors for symptomatic knee OA. According to Kon et al. (27), the highest PRP efficacy was observed in young male patients with lower BMI scores and lower OA grades. In a study by Jubert et al., patients with older ages (mean 67 years), higher BMI value (31 kg/m^2), and higher grades of OA (III or IV) were evaluated, which could justify the lower effectiveness of PRP in their study. But in the present study, the age of patients (less than 60 years), BMI < 30 kg/m^2, and OA grade of KL 2 - 3 could affect the outcome of the study and justify the better treatment outcomes for PRP.

Local complications were the most common side effects reported by the patients. Minor complications such as moderate pain, swelling, and mild sort effusion were occurred due to repeated intra-articular injections (41, 42).

The occurrence of allergic reaction is possible but rare. The most dangerous complication is an intra-articular infection, which could be prevented by considering the aseptic conditions. In different studies, the most common complication was arthralgia, which could be mild to moderate and resolved within a few days (43, 44). In the current study, the most common complaint was the pain in the injection site, which recovered in a few days. None of the current study patients reported major complications (hematoma, infection).

5.1. Strengths

Several studies are conducted on the efficacy and safety of these two methods in comparison with other therapies so far; but to the author's best knowledge, only two studies in the world compared the effectiveness of these two methods in the treatment of knee OA. In these two studies, a single injection of intra-articular drugs was used and contradictory results were noted. But, the current study used multiple injections of corticosteroids and intra-articular PRP (three injections versus single injection in the previous two studies), and the evaluation times of patients in the current study (T0, T1, T2, T3, T6) were more than those of the previous ones, which showed changes in symptoms and the patients' responses to treatment. These could be considered as the strength of the current study.

5.2. Weakness

One weakness of the present study was the duration of the assessment. In the current study, clinicians indicated six months as the duration of the investigation and could not evaluate the duration of response to treatment in patients. Also, the six-month-assessment was not enough to evaluate the chronic conditions such as knee OA. The lack of joint ultrasound or magnetic resonance imaging (MRI) to assess the thickness of articular cartilage before and after treatment was another weakness of the study. Although some previous studies suggested the safety of long-term use of intra-articular corticosteroid without adverse complications, some studies reported corticosteroid degenerative effects in joint and cartilage (45). Therefore, it seems that the use of an imaging method to evaluate joints is mandatory.

5.3. Study Limitation

One of the limitations of the study was the inability to perform a double-blind study since, in order to blind patients in the group T, researchers had to take blood, which was not ethical. Although patients were aware of their own therapeutic approach, the physician that evaluated the patients was not.

5.4. Conclusion

Results of the current study showed that three intra-articular injections of corticosteroids and PRP reduced joint pain and improved joint function. However, PRP injections were more effective and prolonged than corticosteroid therapy in terms of reducing pain and improving the outcomes. Up to three months, both treatments reduced pain and improved physical function. From the third month, the effects of PRP on pain relief and outcomes persisted, but in the corticosteroid group, these effects diminished. However, patients had better conditions in both groups at the end of the sixth month compared with the baseline status.

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