

Platelet-Rich Plasma Treatment With Physical Therapy in Chronic Partial Supraspinatus Tears

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Received: September 15, 2014; Revised: December 1, 2014; Accepted: March 25, 2015

Background: Despite the insufficient evidence, due to potential contribution to the improvement, platelet-rich plasma (PRP) is emerging as a promising method.

Objectives: The aim of this study was to assess the effectiveness of PRP injection in partial supraspinatus tears by comparing with physical therapy (PT).

Patients and Methods: Seventy patients with chronic partial supraspinatus tears in magnetic resonance imaging were randomized into two groups; PRP (n = 35) and PT (n = 35). Before the treatment, at the end of the treatment and at the 12th month after the end of the treatment, range of motion (ROM), visual analog scale (VAS) for pain, Disabilities of Arm, Shoulder and Hand questionnaire (DASH), Neer's, Hawkins' and drop arm tests and Beck Depression Inventory were investigated.

Results: Statistical analysis was made for 62 subjects (PRP group, n = 30; PT group, n = 32). There were no differences between the groups according to demographic data. At the 12th month after the end of the treatment, significant improvement in ROM was detected in both groups, pain was reduced significantly in both groups and improvement of the DASH score was observed in both groups. At all the evaluation steps, increases in ROM degrees were significantly higher in the PT group than the PRP group. For VAS in activity and in rest, after the treatment, improvement was higher in the PT group than the PRP group. However, improvement of the DASH score of the PRP group was significantly better than the PT group.

Conclusions: When we compared with PT, PRP seemed to be a well-tolerated application which showed promising results in patients with chronic partial supraspinatus tears.

Keywords: Platelet-Rich Plasma; Shoulder; Tear

1. Background

Disability of shoulder caused by traumatic and degenerate rotator cuff tears, subacromial impingement, and osteoarthritis is a common morbidity. Nonoperative treatment methods include analgesics, local anesthetic and steroid injections, and physical therapy. Surgical interventions include debridement of the spurs of bone and osteophytes, debridement of the degenerate cuff and partial tears of the cuff with rotator cuff repairs. Repairs of torn and degenerate cuff are frequently failed due to many factors (1). In vitro and in vivo animal studies have shown the potential impact of platelet-rich plasma (PRP) on cellular anabolism and tissue regeneration (2-4). It is assumed that the importance of preventive interventions and the therapeutic options that regenerate tissue homeostasis has been increased (5) and these interventions might improve clinical outcomes (1). PRP is seemed to be a promising therapeutic application. Inflammation and cell proliferation are the important phases of bone and soft tissue injuries. Due to the possible contribution

to the healing process, it is important to investigate the PRP method. PRP is based on obtaining a high concentration of platelets from a patient's own blood plasma and applying to the damaged area. Platelet and plasma include growth factors and cellular signal factors supporting homeostasis and wound healing (6, 7).

In spite of the positive results, studies in humans are limited because of the study designs and the lack of number of subjects. Although evidence is insufficient, due to being an autologous application with low risk, low cost and potential contribution to improvement, PRP is emerging as a method to be investigated more.

2. Objectives

Although there are some studies in the literature which have investigated the effectiveness of intra-operative PRP in rotator cuff repairs (8-11), we could not find a comparative study of physical therapy (PT) and PRP

treatment in patients without surgical interventions. In this study, we aimed to assess the effectiveness of intra-articular PRP injection in partial supraspinatus tears by comparing with PT.

3. Patients and Methods

Subject number was calculated to be 52 to achieve an 80% power of study. Seventy patients were included in the study who were diagnosed with chronic partial supraspinatus tears. The diagnosis of the supraspinatus tear was made by magnetic resonance imaging. In accordance with the requirements of ethical standards (Helsinki declaration) and the approval of the institution, patients were randomized by computer and divided into two groups; PRP (n = 35) and PT (n = 35). Patients' written consents were obtained. Demographic data (age, gender, duration of complaints, and body mass index) were recorded. While three intra-articular injections with an interval of one week were applied to the PRP group, standard PT [hot pack for 15 minutes, ultrasound in continuous mode (1.5 watt/cm² for five minutes), trans-cutaneous electrical nerve stimulation in brief-intense mode for 15 minutes, range of motion (ROM), pandicular response, stretching and strengthening exercises with 10 repeats, and 500 mg acetaminophen as the rescue medication] was applied to the PT group for 15 sessions (five sessions per week for three weeks). After the physical therapy, the exercise program was continued as homework during the follow-up period.

For preparing the PRP, after extraction of 15 mL of peripheral blood, the sample was centrifuged for nine minutes at 3500 revolutions per minute. We obtained 6 mL of PRP and proceeded to the intra-articular infiltration under sterile aseptic conditions. Before every injection, calcium chloride was added to the PRP concentrate to activate the platelets for inducing rapid formation of fibrin clot. Patients were instructed to avoid the use of co-interventions within the follow-up period. Acetaminophen (500 mg) could be used as rescue medication. After the injection, patients were sent home with instructions to limit the use of shoulder for at least 24 hours and to use cold therapy for pain. After the third injection, ROM, pandicular, and stretching exercises were allowed and one month after the end of injections, patients were recommended to begin the strengthening program as tolerated. Exercise style and repeat number were similar to the PT group. Unlike the PT group, the strengthening program was started after the end of the injections in the PRP group and exercise program was given only as homework during the treatment as well as during the follow-up in the PRP group. The injections were applied by the same physician and the physician who collected the data was blind as well as the statistician.

Before the treatment, at the end of the treatment and at the 12th month after the end of the treatment, ROM,

visual analog scale (VAS) for pain during activity, rest and sleep, Disabilities of Arm, Shoulder and Hand questionnaire (DASH) (12) for interrogation of daily living activities, Neer's (13), Hawkins' (14) and drop arm tests (13) and Beck Depression Inventory (15) were investigated.

VAS (0 to 10) is used to assess the severity of pain and 10 indicates the worst pain. DASH is a questionnaire used to assess disability for disorders affecting the upper extremity by measuring the severity of symptoms and difficulty in completing specific tasks. The questionnaire includes a 30-item disability/symptom scale and two optional scales: work model (four items) and sports/performing arts model (four items). The score is transformed to a scale of 0 to 100, where a higher score indicates more severe disability (12). Beck Depression Inventory is a 21-item questionnaire used to assess the severity of depression, where a higher score indicates more severe depression (15).

Neer's test is the provocation of shoulder pain with the combination of internal rotation, abduction and flexion of shoulder while the elbow is extended (13). Hawkins's test is the provocation of shoulder pain with the combination of internal rotation, adduction and flexion of shoulder while the forearm is in flexion and internal rotation position (14). Drop arm test is defined as dropping the arm at 90 degrees abduction of shoulder, after asking the patient to put down his/her arm slowly from full abduction to 90 degrees abduction (13).

The exclusion criteria were age > 80 years, full thickness supraspinatus tears, other rotator cuff lesions with/without supraspinatus tears, systemic disorders such as diabetes, rheumatoid arthritis, hematological diseases (coagulopathy), severe cardiovascular diseases, infections, immunodeficiency, the use of anticoagulants or antiaggregants, the use of nonsteroidal anti-inflammatory drugs in five days before and during the treatment and hemoglobin value < 11 g/dL, and platelet value < 150,000 mm³.

3.1. Statistical Analysis

In this study, data analysis was made with SPSS 21 software package. For gender, the difference between patients treated with PRP and PT was tested by chi-squared test. Difference between the treatment groups according to variables was tested with independent two-sample t-test and nonparametric Mann-Whitney test due to not providing the assumption of normality. For difference between pretreatment, end of treatment and the 12th month after the treatment, one-way ANOVA was utilized. In case of not providing the assumption of normality, Kruskal Wallis H test was used. However, in case of providing the assumption of normality, to determine in which evaluation step the differences occurred, Tukey's multiple comparison test was used. P values less than 0.05 were considered statistically significant.

4. Results

In the PRP group, three patients with pain, one patient who used an analgesic except acetaminophen and one patient who did not complete the questionnaires were excluded from the study. In the PT group, one patient with pain, one patient who had personal reasons and one patient who did not complete the questionnaires were excluded from the study. Statistical analysis was performed for 62 subjects (PRP group, $n = 30$; PT group, $n = 32$).

There were no differences between the groups in terms of age (59.16 ± 10.76 years for the PRP group and 59.68 ± 9.88 years for the PT group, $P = 0.843$), gender (21 females and nine males in the PRP group and 24 females and 8 males in the PT group, $P = 0.665$), body mass index (28.91 ± 5.22 for the PRP group and 27.18 ± 3.48 for the PT group, $P = 0.135$) and the duration of complaints (7.33 ± 3.95 months for the PRP group and 7.15 ± 3.74 months for the PT group, $P = 0.857$). There was no significant difference between females and males for demographic variables except for the mean of age (Table 1). Sports/performing arts scale of DASH was not completed by any of the patients and so we did not include this optional scale in the statistical analysis.

The total number of platelets in the PRP per mL represented a mean increase of 2.1-2.5 times compared with whole blood values. In the plasma, the presence of leukocytes was also observed, with a concentration of 1.1-1.3 times with respect to the normal blood value.

When we compared the PRP and PT groups, while there was no significant difference between the PRP and PT groups for the flexion degree of shoulder before treatment, the increase of the flexion degree at the end of the treatment and at the 12th month after the treatment were significantly higher in the PT group than the PRP group ($P < 0.05$, Table 2). While before the treatment the extension degree of shoulder was significantly higher in the PRP group than the PT group, at the 12th month after the treatment the extension degree of shoulder was significantly higher in the PT group than the PRP group ($P < 0.05$, Table 2). The abduction degree of shoulder was significantly higher in the PT group than the PRP group at all the evaluation steps ($P < 0.05$, Table 2). At all the evaluation steps, there was no significant difference between the groups for the adduction degree of shoulder ($P < 0.05$, Table 2). While only the external rotation degree of shoulder at the 12th month after the treatment was significantly higher in the PT group than the PRP group, the in-

ternal rotation degrees of shoulder at all the evaluation steps were significantly higher in the PRP group than the PT group ($P < 0.05$, Table 2). While only the VAS in rest at the 12th month after the treatment was significantly higher in the PT group than the PRP group, VAS in activity at the end of treatment, VAS in sleep before the treatment and VAS in sleep at the end of the treatment were significantly higher in the PRP group than the PT group ($P < 0.05$, Table 2). The DASH score before the treatment and the work model score of DASH before the treatment and the work model score of DASH at the end of the treatment were significantly higher in the PRP group than the PT group ($P < 0.05$, Table 2). There was no significant difference between the groups for Beck Depression Inventory score at each evaluation step ($P > 0.05$, Table 2). No significant difference was found between the groups for Neer's, Hawkins' and drop arm tests ($P > 0.05$).

For flexion of shoulder in the PRP group, while there was no significant difference between the evaluations before and after the treatment, improvement at the 12th month after the treatment was significantly higher than the improvement after the treatment (Table 3). No significant difference was found between the evaluation steps for the extension of shoulder and Beck Depression Inventory score of the PRP group (Table 3). For Work model of DASH score, abduction and external rotation of shoulder in the PRP group, significant improvement was found only between the evaluation steps before the treatment and at the 12th month after the treatment (Table 3). Adduction and internal rotation of shoulder, for VAS in activity, in rest and in sleep and for DASH score improvement at the 12th month after the treatment, were significantly higher than the evaluation after treatment (Table 3).

In the PT group, for flexion, extension, abduction, adduction, internal rotation and external rotation of shoulder, for VAS in activity and rest, for DASH and DASH work model scores improvement at the 12th month after the treatment was significantly higher than the improvement after the treatment (Table 3). In the PT group, for VAS in sleep, improvement was found at the 12th month after the treatment, but there was no difference between the evaluation steps after the treatment and at the 12th month after the treatment (Table 3). When we compared the evaluation steps before and after the treatment in the PT group, we found no difference for Beck depression inventory score (Table 3).

Table 1. Comparison of Females and Males for Demographic Data

Variables	Female (n = 45)	Male (n = 17)	P Value
Age, y	57.62 ± 10.89	64.23 ± 6.29	0.005 ^a
Body mass index, kg/m ²	28.37 ± 4.80	27.08 ± 3.33	0.313
Duration of complaints, mo	6.86 ± 3.67	8.23 ± 4.10	0.210

^a Significance level: $P < 0.05$.

Table 2. Comparison of Platelet-Rich Plasma and Physical Treatment Groups for Range of Motion, Visual Analog Scale, Disabilities of Arm, and Shoulder and Hand and Beck Depression Inventory Scores ^{a,b}

Evaluation Steps (a, b, c)	PRP, n = 30	PT, n = 32	P Value
Flexion			
a	94.77 ± 40.83	111.09 ± 31.81	0.083
b	109.70 ± 36.86	132.03 ± 29.04	0.010 ^c
c	129.33 ± 30.47	157.65 ± 31.57	0.001 ^c
Extension			
a	25.53 ± 9.07	19.37 ± 9.73	0.013 ^c
b	27.86 ± 7.65	27.81 ± 9.49	0.980
c	28.70 ± 7.79	33.75 ± 9.91	0.030 ^c
Abduction			
a	84.66 ± 38.41	103.28 ± 27.28	0.031 ^c
b	94.33 ± 36.76	125.93 ± 29.60	0.000 ^c
c	109.83 ± 30.32	147.81 ± 33.93	0.000 ^c
Adduction			
a	24.16 ± 6.83	22.75 ± 7.13	0.429
b	28.50 ± 5.43	28.40 ± 7.72	0.956
c	34.00 ± 7.24	35.21 ± 7.64	0.522
External Rotation			
a	33.83 ± 16.95	31.40 ± 18.28	0.590
b	37.66 ± 15.68	44.06 ± 18.07	0.143
c	42.83 ± 16.85	60.15 ± 20.18	0.001 ^c
Internal Rotation			
a	65.66 ± 14.54	44.53 ± 19.27	0.000 ^c
b	76.50 ± 11.60	59.84 ± 18.55	0.000 ^c
c	84.16 ± 8.91	72.34 ± 19.00	0.003 ^c
VAS Activity			
a	7.80 ± 1.78	6.96 ± 1.95	0.087
b	5.43 ± 2.01	4.37 ± 1.93	0.039 ^c
c	2.70 ± 1.48	2.59 ± 1.73	0.798
VAS Rest			
a	2.86 ± 2.01	3.53 ± 2.07	0.206
b	1.56 ± 1.35	1.87 ± 1.47	0.396
c	0.30 ± 0.65	0.84 ± 1.32	0.045 ^c
VAS Sleep			
a	7.03 ± 2.07	4.12 ± 3.07	0.000 ^c
b	4.33 ± 2.39	2.00 ± 2.32	0.000 ^c
c	1.60 ± 1.92	1.00 ± 1.90	0.222
DASH			
a	66.26 ± 10.89	58.88 ± 14.07	0.025 ^c
b	51.35 ± 11.02	46.64 ± 14.03	0.150
c	35.62 ± 9.68	36.46 ± 14.58	0.790
DASH Work			
a	69.66 ± 19.02	56.25 ± 17.55	0.005 ^c
b	53.33 ± 14.22	41.56 ± 13.22	0.001 ^c
c	48.83 ± 77.40	30.78 ± 13.20	0.199
BECK			
a	22.64 ± 17.38	19.93 ± 15.58	0.520
b	20.78 ± 16.28	18.69 ± 14.41	0.593
c	17.87 ± 13.10	16.26 ± 12.67	0.625

^a Abbreviations: a, before the treatment; b, after the treatment; c, the 12th month after the treatment; BECK, Beck depression inventory score; DASH, disabilities of arm, shoulder and hand; DASH work, DASH work model score; PRP, platelet-rich plasma; PT, physical therapy; ROM, range of motion (flexion, extension, abduction, adduction, external rotation, and internal rotation in degrees); VAS, visual analog scale.

^b Data are presented as mean ± SD.

^c Significance level: P < 0.05.

Table 3. Comparison of the Differences of Means Between the Evaluation Steps for Platelet-Rich Plasma and Physical Treatment Groups ^a

Evaluation Steps (a, b, c)	PRP Group (n = 30), Difference of Means	PT Group (n = 32), Difference of Means
Flexion		
a-b	14.93	20.94 ^b
b-c	19.63 ^b	25.62 ^b
a-c	34.56 ^b	46.56 ^b
Extension		
a-b	2.33	8.43 ^b
b-c	0.83	5.93 ^b
a-c	3.16	14.37 ^b
Abduction		
a-b	9.66	22.66 ^b
b-c	15.50	21.87 ^b
a-c	25.16 ^b	44.53 ^b
Adduction		
a-b	4.33 ^b	5.66 ^b
b-c	5.50 ^b	6.81 ^b
a-c	9.83 ^b	12.47 ^b
External Rotation		
a-b	3.83	12.66 ^b
b-c	5.16	16.09 ^b
a-c	9.00 ^b	28.75 ^b
Internal Rotation		
a-b	10.33 ^b	15.31 ^b
b-c	7.66 ^b	12.50 ^b
a-c	18.50 ^b	27.81 ^b
VAS Activity		
a-b	2.36 ^b	2.59 ^b
b-c	2.73 ^b	1.78 ^b
a-c	5.10 ^b	4.37 ^b
VAS Rest		
a-b	1.30 ^b	1.66 ^b
b-c	1.27 ^b	1.03 ^b
a-c	2.57 ^b	2.69 ^b
VAS Sleep		
a-b	2.70 ^b	2.13 ^b
b-c	2.73 ^b	1.00
a-c	5.43 ^b	3.13 ^b
DASH		
a-b	14.91 ^b	12.24 ^b
b-c	15.73 ^b	10.17 ^b
a-c	30.64 ^b	22.41 ^b
DASH Work		
a-b	16.33	14.69 ^b
b-c	4.50	10.78 ^b
a-c	20.83 ^b	25.47 ^b
BECK		
a-b	1.85	1.24
b-c	2.91	2.43
a-c	4.76	3.67

^a Abbreviations: a, Before the treatment; b, After the treatment; c, the 12th month after the treatment; a-b, difference of means before the treatment and at the end of the treatment; b-c, difference of means at the end of the treatment and at the 12th month after the treatment; a-c, difference of means before the treatment and at the 12th month after the treatment; BECK, Beck depression inventory score; DASH, disabilities of arm, shoulder and hand; DASH work, DASH work model score; PRP, platelet-rich plasma; PT, physical therapy; VAS, visual analog scale.

^b Significance level: P < 0.05.

For Neer's, Hawkins' and drop arm tests of shoulder in the PRP group, improvement at the 12th month after the treatment was significantly higher than the evaluation after the treatment ($P < 0.05$). For Hawkins' and drop arm tests in the PT group, while there was no significant difference between the evaluation steps before and after the treatment, there was significant improvement at the 12th month after the treatment ($P < 0.05$). For Neer's test in the PT group, we found significant improvement after the treatment and at the 12th month after the treatment ($P < 0.05$); the improvement at the 12th month after the treatment was significantly higher than the evaluation after the treatment ($P < 0.05$).

Except for the patients excluded from the study due to pain, pain was controlled with acetaminophen. In both groups, we observed no complications of the treatment modalities, except pain.

5. Discussion

Platelets are rich of platelet growth factors, cytokines, chemokines, and other mediators, which are related to tissue regeneration (7, 16-19). Additionally to classical nonoperative treatment methods like analgesics, local anesthetic, steroid injections, and physical therapy (1), the importance of the therapeutic options like PRP that regenerate tissue homeostasis is increased (5) and these interventions might improve clinical outcomes (1).

Other than some studies in the literature investigating the effectiveness of intra-operative PRP in rotator cuff repairs (8-10), we could not find a comparative study of PT and PRP treatment in patients without surgical interventions. While some of these studies found intra-operative PRP ineffective for overall re-tear rates or the shoulder-specific outcomes after arthroscopic rotator cuff repair (8, 9), some of them found the PRP application ineffective for postoperative outcome measures but found lower re-tear rates (8). A study by Randelli et al. showed the effect of PRP on reducing postoperative pain and positive effect of PRP on rotator cuff, healing for grade 1 and 2 tears (10).

The subject number was calculated to be 52 and 70 patients were included in the study, whom were diagnosed with partial supraspinatus tears. Five patients from the PRP group and three from the PT group did not finish the study. All told, 62 patients were included in the statistical analysis and this number was acceptable for the trial.

Work model scale of DASH was calculated for all the patients, but none of them were concerned with sports or performing arts, so the sports/performing arts scale of DASH was not completed by any of the patients and we did not calculate this optional scale.

In an *in vitro* study, it was stated that PRP may result in a potential beneficial effect on target cells, but they could not support the "more is better" theory for higher platelet counts (20). Studies have shown that the clinical efficacy of PRP products is expected to increase to at least two to six folds of the platelets count from the base-

line value (5). In our study, the total number of platelets in the PRP per milliliter represented a mean increase of 2.1-2.5 times compared with whole blood values and this amount was appropriate for the treatment. In the plasma, the presence of leukocytes was also observed with a concentration of 1.1-1.3 times with respect to the normal blood value.

When we compared the PRP and PT groups for ROM, probably due to the tight exercise program of the PT patients during the PT sessions, the increases of flexion, extension, abduction, and external rotation degrees were significantly higher in the PT group than the PRP group, since for the PRP group the exercise program was only given as homework without the control of a therapist. For the adduction degree, there was an improvement in both groups, but we found no difference between the groups. Although there was an improvement in both groups for the internal rotation degree, in contrast with other motions, the internal rotation degree of shoulder was significantly higher in the PRP group than the PT group, similar to a study conducted for investigating the effectiveness of PRP application during arthroscopic rotator cuff repair (6). This result can also be due to already higher degrees of internal rotation, measured before the treatment in the PRP group.

In a study conducted on patients who had undergone surgical interventions and were the subject of PRP during surgery, reducing postoperative pain during first month and positive effect of PRP on rotator cuff healing were reported (10). In our study, VAS for pain (in activity, in rest and in sleep) was significantly improved in both groups. However, the higher improvement in the PT group at the end of treatment can show the early analgesic effect of transcutaneous electrical nerve stimulation in the PT group. In addition, during the intervention, additional pain due to PRP injection can lead to this finding.

Although before the treatment, the DASH score and the work model of DASH score were significantly higher in the PRP group than the PT group, both scores significantly improved in both groups till there was no difference between the treatment groups for these scores at the 12th month after the treatment. This result may show us the contribution of PRP treatment to functional improvement of patients with partial supraspinatus tear.

However, for Beck depression inventory score, no significant difference was found either between the treatment groups or in both groups at each evaluation step. The presence of depression that can exacerbate the severity of pain and restrict the functional capacity of the patient must be kept in mind; as well as other treatment modalities in depression, the effectiveness of additional cognitive therapy must be kept in mind, too (21). However, we could show neither the presence nor the improvement of depression in both groups.

Although for Neer's, Hawkins' and drop arm tests there were significant improvements at the 12th month after the treatment in both groups, the differences between

PRP and PT groups were not significant at none of the evaluation steps. This shows us the similar improvements of special shoulder tests in both groups.

Both treatment modalities seemed to be effective on chronic partial supraspinatus tears. However, we have to keep in mind that the effects of exercise program, rescue medication and cold therapy contribute to the effect of PRP treatment. We thought that the drop out number of study was acceptable as well as the rate of severe pain resulting the discontinuance of treatment.

PRP seems to be a well-tolerated therapeutic application which has shown encouraging clinical results in patients with chronic partial supraspinatus tears and may be as effective as PT. The standardization of PRP protocols, long-term follow-up and prospective blinded randomized studies should clarify the questions regarding the PRP effectiveness and the durability of clinical improvements.

Authors' Contributions

Study concept and design: Ilker Ilhanli, Necip Guder, and Murat Gul; analysis and interpretation of data: Ilker Ilhanli, Necip Guder, and Murat Gul; drafting of the manuscript: Ilker Ilhanli, Necip Guder, and Murat Gul; intra-articular injections and management of physical therapy: Necip Guder; acquisition of data: Ilker Ilhanli; randomization and statistical analysis: Murat Gul.

References

1. Mei-Dan O, Carmont MR. The role of platelet-rich plasma in rotator cuff repair. *Sports Med Arthrosc*. 2011;**19**(3):244-50.
2. Kon E, Filardo G, Di Martino A, Marcacci M. Platelet-rich plasma (PRP) to treat sports injuries: evidence to support its use. *Knee Surg Sports Traumatol Arthrosc*. 2011;**19**(4):516-27.
3. Torricelli P, Fini M, Filardo G, Tschon M, Pischedda M, Pacorini A, et al. Regenerative medicine for the treatment of musculoskeletal overuse injuries in competition horses. *Int Orthop*. 2011;**35**(10):1569-76.
4. Yoshioka T, Kanamori A, Washio T, Aoto K, Uemura K, Sakane M, et al. The effects of plasma rich in growth factors (PRGF-Endoret) on healing of medial collateral ligament of the knee. *Knee Surg Sports Traumatol Arthrosc*. 2013;**21**(8):1763-9.
5. Gobbi A, Karnatzikos G, Mahajan V, Malchira S. Platelet-rich plasma treatment in symptomatic patients with knee osteoarthritis: preliminary results in a group of active patients. *Sports Health*. 2012;**4**(2):162-72.
6. de Vos RJ, Weir A, van Schie HT, Bierma-Zeinstra SM, Verhaar JA, Weinans H, et al. Platelet-rich plasma injection for chronic Achilles tendinopathy: a randomized controlled trial. *JAMA*. 2010;**303**(2):144-9.
7. 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.
8. Barber FA, Hrnack SA, Snyder SJ, Hapa O. Rotator cuff repair healing influenced by platelet-rich plasma construct augmentation. *Arthroscopy*. 2011;**27**(8):1029-35.
9. Jo CH, Kim JE, Yoon KS, Lee JH, Kang SB, Lee JH, et al. Does platelet-rich plasma accelerate recovery after rotator cuff repair? A prospective cohort study. *Am J Sports Med*. 2011;**39**(10):2082-90.
10. Randelli P, Arrigoni P, Ragone V, Aliprandi A, Cabitza P. Platelet rich plasma in arthroscopic rotator cuff repair: a prospective RCT study, 2-year follow-up. *J Shoulder Elbow Surg*. 2011;**20**(4):518-28.
11. Chahal J, Van Thiel GS, Mall N, Heard W, Bach BR, Cole BJ, et al. The role of platelet-rich plasma in arthroscopic rotator cuff repair: a systematic review with quantitative synthesis. *Arthroscopy*. 2012;**28**(11):1718-27.
12. Hudak PL, Amadio PC, Bombardier C, Beaton D, Cole D, Davis A, et al. Development of an upper extremity outcome measure: The DASH (disabilities of the arm, shoulder, and hand). *Am J Ind Med*. 1996;**29**(6):602-8.
13. Neer C2. Anterior acromioplasty for the chronic impingement syndrome in the shoulder: a preliminary report. *J Bone Joint Surg Am*. 1972;**54**(1):41-50.
14. Hawkins RJ, Abrams JS. Impingement syndrome in the absence of rotator cuff tear (stages 1 and 2). *Orthop Clin North Am*. 1987;**18**(3):373-82.
15. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;**4**:561-71.
16. Anita E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. *Thromb Haemost*. 2004;**91**(1):4-15.
17. Mishra A, Woodall JJ, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. *Clin Sports Med*. 2009;**28**(1):113-25.
18. Sanchez AR, Sheridan PJ, Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. *Int J Oral Maxillofac Implants*. 2003;**18**(1):93-103.
19. Senet P, Bon FX, Benbunan M, Bussel A, Traineau R, Calvo F, et al. Randomized trial and local biological effect of autologous platelets used as adjuvant therapy for chronic venous leg ulcers. *J Vasc Surg*. 2003;**38**(6):1342-8.
20. Mazzocca AD, McCarthy MB, Chowanec DM, Dugdale EM, Hansen D, Cote MP, et al. The positive effects of different platelet-rich plasma methods on human muscle, bone, and tendon cells. *Am J Sports Med*. 2012;**40**(8):1742-9.
21. Hamidian S, Omid A, Mousavinasab SM, Naziri G. Comparison of the effect of mindfulness-based cognitive therapy accompanied by pharmacotherapy with pharmacotherapy alone in treating dysthymic patients. *Iran Red Crescent Med J*. 2013;**15**(3):239.