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Effect of Single Injection of Platelet-rich Plasma in Comparison with Corticosteroid on Knee Osteoarthritis: A Double-blind Randomized Clinical Trial

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Abstract

Aim: Evidence on the effect of Platelet-Rich Plasma (PRP) in treating osteoarthritis (OA) is insufficient. Therefore, the present study compares the effects of a one-time injection of PRP and corticosteroid (CS) as two types of treatment for the patients suffering from osteoarthritis.

Methods: In the present randomized double blind clinical trial, the participants who suffered from knee osteoarthritis (Grades II/III), were randomly divided into two groups: intra articular injection of PRP and CS. Knee injury and osteoarthritis outcome score (KOOS), the 20-meter-walk test, active and passive ranges of motions (ROM), flexion contracture, and pain intensity based on Visual Analog Scale (VAS) were assessed before, 2-months, and 6-months after interventions.

Results: 41 participants (48 knees) were involved in the research (66.7% women; average age of 61.1±7.0 years old). Compared to the group treated with corticosteroid, pain relief (df:6 ,35 ;F=11.0 ;p=0.007), symptom free (df:6 ,35 ;F=23.0 ;p<0.001), activities of daily living (ADL) (df:6 ,35 ;F=10.7 ;p=0.005) and quality of life (df:6 ,35 ;F=5.2 ;p=0.02) in the RPR group were significantly higher, but sporting ability was not different between the 2 groups (df:6 ,35 ;F=0.6 ;p=0.55). PRP prescription was significantly more helpful for relieving patients' pain (VAS) compared to corticosteroids (df:6 ,35 ;F=32.0 ;p,0.001). It's also notable that using PRP was more helpful in improving the 20-meter-walk test than corticosteroid treatment (df:6 ,35 ;F=7.4 ;p=0.04) but none of the treatments had any impact on active flexion ROM .passive flexion ROM and flexion contracture (p>0.05).

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Conclusion: Our study demonstrated that one shot of PRP injection, decreased joint pain more and longer-term, alleviated the symptoms, and enhanced the activity of daily living and quality of life in short-term duration in comparison with CS.

Keywords: Platelet-rich plasma; osteoarthritis; glucocorticoids; treatment outcome

Introduction

Osteoarthritis (OA), as the most common musculoskeletal disease (1), is a multifactorial chronic condition, which starts with the destruction of articular cartilages and leads to joint space loss and formation of peripheral osteophytes (2). Considering the low possibility for articular cartilage repair, at present there is no decisive cure to halt the pathophysiology of articular cartilage degeneration. All the current methods are symptomatic treatments that fail to return the patients to their original movements and quality of life. Recently, autologous blood and mainly its mediators, like growth factors (GFs), have been suggested as an alternative for treatment of OA.

Platelet-rich Plasma (PRP) is referred to as a plasma volume in which concentration of platelets is higher than that of the plasma itself (3). Platelets, containing growth factors, have the potential of cellular repair and anabolic stimulation of any type of cells, including the chondrocytes (4-6). From this perspective, use of PRP has been introduced as a treatment modality for lesions, like that of articular cartilage, which have a low potential for regeneration. For the past 20 years, PRP has been safely used and documented in several fields, including musculoskeletal diseases, wound healing and cosmetic, cardiothoracic and oromandibular surgery(7). Currently, a multitude of studies areunderway on the treatment of chronic rotator cuff tendinopathy (6,8,10), jumper's knee (8,11), partial rupture of the Achilles tendon (6), hamstring tear (8),

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osteochondritis dissecans lesions (8), MCL repair (8), nerve regeneration (12), ACL repair (6,8), plantar fasciitis (13), bone healing (14-16) and chondral defect regeneration (3,4,17-20) using PRP. A large number of studies have addressed the effects of PRP on chondrocyte differentiation, hyaluronic acid (HA), andproteoglycan and type 2 collagen synthesis (8,21-23). Moreover, several studies have been carried out on the clinical use of PRP in the treatment of articular cartilage lesions in animals (20,24) and humans (3,4,19,25-33). According to these studies, PRP is a safe method with no serious complications reported during the follow-up periods (3,4,19,25-33). However, most of the existing studies are either pilot or prospective studies with no control groups (3,4,25-27,29,30,32). In addition, the number and the frequency of injections in these studies are different. Almost all of them require three injections without any scientific reasons or specific justification (33). As it seems, in these studies the traditional practice of three injections of HA is followed (3,4,6,18,19,26,27,30).

Intra-articular corticosteroid (CS) injections are frequently used to treat acute and chronic inflammatory conditions (38). The effects of CS are mainly anti-inflammatory, brought about by inhibiting inflammatory cytokines and blocking the pathways leading to their actions (39). Despite the fact that intra-articular injection of CS has been used to treat osteoarthritis for more than 50 years and it is recommended in up to 11 guidelines, such as The American College of Rheumatology (ACR),as a treatment modality for OA (36,38), in none of the existing studies, has there been a comparison between PRP and CS injection. Therefore, the present study compared the effects of a one-time injection of PRP and CS as two types of treatment for patients suffering from osteoarthritis.

Materials and Methods

Study Setting and Design

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This double-blind randomized clinical trial (RCT) was carried out on patients aged 50-75, who were referred to the Physical Medicine and Rehabilitation Clinic, Firouzgar Hospital, Tehran, Iran, from March to August 2012. The study was approved by the local Ethics Committee. The research was carried out according to Helsinki Declaration. The study was registered at the Iranian Clinical Trial Center under the code IRCT2013041413012N1. All the treatment objectives, procedures, possible benefits and risks of intra-articular injection of PRP or CS were explained to the subjects. It was made clear that it was equally possible for them to be included in the PRP- or CS (Depo-Medrol)-receiving group. Only the participants who signed the written consent form issued and certified by the Department of Medical Ethics, Tehran University of Medical Sciences, were included in the study.

Participants

Based on the ACR criteria (36), the participants who suffered from knee osteoarthritis were assessed for eligibility. The inclusion criteria consisted of a pain intensity of 60 in the Visual Analogue Scale (100-mm VAS) at the admission time, knee pain with a duration of more than three months, residing in Tehran and its suburbs, and a history of undergoing, but not benefiting from, at least two OA treatments (including lifestyle changes, weight loss, oral medications, physiotherapy, acupuncture, laser, using insole, cane or orthotic devise). Radiography was conducted for all the patients under weight-bearing conditions to determine their arthritis grade based on Kellgren-Lawrence (KL) Grading Scale criteria (35). Only those with Grades II or III of arthritis (based on radiologist's report) were included in the study. If a patient used anticoagulants or anti-platelet medications or systemic CSs, the injections were delayed for at least 10 days. Patients with a history of collagen vascular or severe cardiovascular and hematopoietic diseases, diabetes mellitus, history or presence of cancer, malignant disorders or immunosuppression, hepatitis B or C, HIV infection, any active infection or wound of the knee,

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history of any knee articular injections, infection, arthroscopy or surgery during the previous 6 months, active lumbosacral radiculopathy and/or drug abuse were not included. Moreover, those who had experienced physiotherapy treatment modalities, laser or acupuncture on their knees during the 6 months following the injection were not included in the study. Participants' characteristics, age, sex, height, weight, BMI (Body Mass Index), education level and history of smoking were recorded in their profiles. The subjects were consecutively enrolled in the study and divided into PRP-receiving and CSs-receiving groups through permutated blocks of four (stratified to VAS and arthritis KL grades) in block randomization method. During the period of the study (six months), the participants were advised not to use any other modalities like physiotherapy, laser or acupuncture on their knees. Otherwise, they would be excluded from the study (Consort Chart).

Procedures

PRP was prepared by harvesting 20 mL of autologous blood, and 2 mL of ACD-A (Anticoagulant Citrate Dextrose Solution, Solution A,) were added to it. Two centrifugation procedures, the first at1600 relative centrifugal force (RCF) for 6 minutes to separate the erythrocytes and the second at 2000 RCF for 6 minutes to concentrate platelets, produced 5 mL of PRP. The PRP solution was activated by adding 0.5 mL of a calcium gluconate solution (1 g/10 mL). Within minutes, before its gelation, the solution was injected into each patient's knee. TUBEX 25-mL kit (MOOHAN Co., South Korea), which is certified by CE and Iranian Health and Medical Education Ministry, and Selex Centrifuge Device (South Korea) were used in this study. Platelet count analysis was carried out on whole blood and PRP from 6healthy persons before the study to confirm the quality of PRP preparation process. The average whole blood platelet count was 283×10^3 platelets/μL while the average PRP platelet count was 1501×10^3

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platelets/μL. Thus the concentration of the platelets in the PRP was more than 4 times that of the whole blood. Platelets exhibited normal morphology in PRP smears.

In the control group, however, only 5 mL of blood was taken to make the participants blind to the study. One mL of Depo-Medrol (containing 40mg of methylprednisolone acetate) was injected in an intra-articular technique.

It should be noted that all the syringes were prepared outside the room and covered to prevent patients from seeing the injectant. Injections were carried out by the same person (the second author) following the standard method from the supra-lateral patellar area. In both groups, after the injection, the participants carried out ten passive knee flexion and extension movements to distribute the solution throughout their joint cavities before its gelation. Then, they rested in a supine position for 10 minutes. They were recommended to put cold compresses on the joints at home 3 times, each time for 15 minutes with 10-minute intervals. They were also asked to avoid weight pressure on the injected knee for the next 24 hours and to use only acetaminophen or cold compresses every six hours if they felt any pain. The patients in both groups were also asked to carry out a number of range motions 24 hours after the procedure, and isometric exercises were taught to them. They were also recommended to walk in water and on a flat surface with moderate intensity three weeks after the injection up to 40 minutes daily. However, during the six months of the study period, they were allowed to use oral analgesics in case they felt any pain on the condition that they informed the researchers of the dose of the analgesics they used. Each time, only one knee in each patient was treated. If the other knee had clinical indications for intra-articular injection, it was carried out at least 3 weeks after the first one.

Outcome Measurements

An experienced occupational therapist who was blind to the participants' group evaluated the patients' VAS-based pain intensity, 20-meter-walk (20MW) test, active and passive knee ROMs

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and flexion contracture before the injection, as well as 3 weeks, 2 months and 6 months after that. The KOOS questionnaire's sections were assessed before the injection, as well as 2 months and 6 months after that.

Knee injury and osteoarthritis outcome score (KOOS) questionnaire, which contains 42 questions on the five sections of pain relief, symptom relief, activities of daily living (ADL), quality of life (QOL) and sporting abilities, was used in this study. Reliability and validity of the Persian version of this questionnaire was certified by a previous study (37). The questions were in the multiple-choice format. The participants' answers were scaled from zero to four in the Microsoft Excel software. The scores in each section were calculated from 0 to 100. The higher grades indicated better conditions, whereas the lower ones showed worsening of the symptoms. The 20MW test (20 meters of jogging) was carried out twice for all the subjects in each follow-up session. The test was measured via a chronometer and the mean score was recorded by the occupational therapist. Using a goniometer, the patients' knees' active and passive ranges of motions (ROMs) in prone position, as well as their knee flexion contracture, were measured in supine position. To calculate pain intensity based on 100-mm VAS, a 100-mm line was drawn in each patient's profile. They were also investigated in relation to the severity of their pain during the previous week in order to determine the relevant point on the line.

Statistical Analysis

Data were analyzed with SPSS 21. Descriptive analysis was used for reporting frequencies, percentages, means and standard deviations (SD). Paired-sample t-test and Cramér'sV were used for comparison of data before injection between the two groups. Repeated-measures ANOVA was used to determine the effect of time(several follow-up sessions during 6 months in each group) and injections (PRP or CS) on the outcomes. Statistical significance was set at $P<0.05$.

Results

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Overall, 48 knees in 41 patients were studied, with 24 knees in each group. In the PRP group, one patient did not refer for 2- and 6-month follow-ups due to deep dissatisfaction due to increased knee and lumbar pain after PRP. In the CS group, one patient missed the 6-month follow-up due to travelling abroad. In this group we excluded four persons. One for incidence of acute L3-L4 radiculopathy 12 days after the injection and finally lumbar disc surgery 5 months later and three participants (6 knees) for prescription of physiotherapy and acupuncture by a physician who was not aware of our research instructions. Finally a total of 39 knees were included in the statistical analysis, 66.7% of which were women with an average age of 61.1±7.0. There were no significant differences in age (P=0.32) and sex (P=0.54) distributions between the two groups. In addition, average weight (P=0.98), height (P=0.84) and body mass index (P=0.71) were similar in patients of both groups. The affected knee (P=0.23) and OA severity (P=0.76) were not different between the two groups, either (Table 1). Assessing KOOS parameters, significant pain relief was detected in both groups (P<0.001). Pain relief in the group treated with PRP was significantly higher compared to the group treated with corticosteroids (df:6,35;F=11.0; P=0.007). Moreover, relief of symptoms was seen in both groups (P<0.001). Also in this regard, the group treated with PRP exhibited more pain relief (df:6,35;F=23.0;P<0.001). Similar results were found regarding activities of daily living (ADL) (df:6,35;F=10.7; P=0.005) and quality of life (df:6,35;F=5.2; P=0.02). Therefore, we can conclude that PRP treatment was more effective than corticosteroid treatment in improving both ADL and quality of life. However, sporting ability was not different between the two groups (df:6,35;F=0.6; P=0.55)(Table 2). Mean pain severity in the group treated with corticosteroid was 79.1±13.4before intervention, which decreased to 63.2±19.7 after two months and 72.5±16.2 after six months. Therefore corticosteroid treatment was only effective in relieving the patients'

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pain at2-month follow-up (df:3,15;F=10.8; P=0.005). Pain severity in the group treated with PRP was 80.4±14.4 before intervention, which decreased to 45.1±23.4 and 44.6±15.6 at 2- and6-month follow-ups, respectively. PRP treatment significantly relieved the patients' pain at 2- and 6-month follow-ups (df:2,21;F=42.8; P<0.001). Two-way ANOVA measurements showed that PRP prescription was significantly more effective in relieving the patients' pain compared to corticosteroid (df:6,35;F=32.0; P<0.001). Assessing the 20MW test showed that corticosteroid treatment was only effective in improving the test results at the2-month follow-up (df:3,15;F=11.5; P=0.02), not at the 6-month follow-up (df:3,15;F=2.5; P=0.13).However, PRP treatment was effective in both 2- and 6-month follow-ups (df:2,21;F=26.1; P<0.001) and was more effective than corticosteroid in improving the 20MW test results (df:6,35;F=7.4; P=0.04). However, none of the treatments had any impact on active flexion ROM, passive flexion ROM and flexion contracture (P<0.05) (Table 3).

The numbers of analgesic tablets taken by the patients during the 6-month period after injection were 14.13±6.62 and 17.69±10.48 in the PRP and CS groups, respectively, with no significant differences.

Considering the small sample size (13 knees with grade II and 29 knees with grade III), no analysis was performed to compare responses to treatment based on the osteoarthritis grading.

Discussion

In the current study, we compared a single shot of PRP with that of methylprednisolone acetate for the first time.

This study demonstrated that PRP treatment was more beneficial for the patients' pain relief, symptom relief, quality of life and activities of daily living in comparison to corticosteroids. Moreover, it was noted that PRP treatment improved the 20MW test more than corticosteroid

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treatment did. In addition, the changes in knees' active and passive flexion ROMs and flexion contracture in the two groups were not statistically significant in terms of the therapeutic approach and time.

Several studies have compared the effects of intra-articular (IA) CS with HA, and PRP with HA for OA treatment but there is no comparative study between PRP and CS injection. In the Cochrane reviews of trials comparing IA corticosteroids with IAHA injections, there were no significant differences 4 weeks after the injection but IAHA injections were shown to be more effective 5-13 weeks after injection. This was further supported by a meta-analysis of seven randomized controlled trials in patients with knee OA, in which IAHA injection was compared directly with IACS injection. In the first two weeks, corticosteroids were more effective in relieving pain, but at week 4, both were equally effective, and from week 8 on, HA was more effective until the last assessment at 26th week. Analysis of the results for other outcomes, such as reduction in stiffness and improvements in function following IAHA injection, were similar (39). Kon et al. (3) compared PRP with low- and high-molecular-weight HAs for treating knee osteoarthritis and reported that PRP was effective in improving patients' symptoms in addition to more pain reduction and longer effects compared with HAs (3).In contrast, Filardo et al. compared these two methods and showed that although improvements in patients' symptoms after PRP injection lasted for one year, this improvement was not significantly more than that with HA (28). Cerza et al. showed that the clinical outcomes of PRP were better compared to the results of HA up to 6 months of follow-up (31).In a study performed by Raiessadat et al. in Shahid Beheshti University of Medical Sciences, Iran, 65 patients were treated by two PRP injections with 4-week intervals and the results were assessed after 6months using WOMAC and SF36 questionnaires. The results demonstrated that PRP was effective in pain and symptom

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relief and quality of life improvement. The mean platelet concentration was 3-7.8 times the initial values. No relationship was observed between platelet concentrations in PRP and therapeutic outcomes (29).

In a study in 2013 by Patel et al., one-course and two-course PRP injections were compared while saline injection was used for the control group. The results indicated no significant differences between outcomes of one and two courses of PRP injection. Overall, PRP injection significantly decreased the pain and symptoms of osteoarthritis (33).

PRP is produced from blood centrifugation and includes platelets containing GFs, such as tissue growth factor (TGF-β), insulin-like growth factor (ILGF-1), platelet-derived growth factor (PDGF-αβ) and fibroblast growth factor (FGF) in their alpha granules. In vitro and in vivo studies have demonstrated the role of these factors in homeostasis and regeneration of cartilage (3,4,6,17-19,25-27,30,33). In the present study, VAS and 20MW test assessments showed a considerable improvement three weeks after the injection (data not shown). Likewise, Patel et al. (33) reported that the patients mentioned improvements after an average of 17 days from injection (during this period chondrogenesis had not occurred). Thus, it is probable that chondrogenesis is not the only active process regarding PRP function and it seems that other mechanisms are involved; the platelets affect the overall joint homeostasis, decrease the hyperplasia of synovial cartilage and regulate the levels of cytokines in joint liquid, in addition to stimulating anabolism and slowing the catabolic process of joint cartilage (3,33).

In the current study, 22 mL of blood was drawn and fresh PRP was injected. Some researchers have drawn 150 mL of blood and after the first course of injection, have kept PRP at -30°C for later courses (3,17). At -30°C, PRP may lose some of its beneficial properties and the platelets may become degranulated (33). Thus, in the assessment of therapeutic outcomes in the articles

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with similar methods, caution should be exercised. An inverse relationship between age and response to treatment has been reported in some studies. In younger patients the outcome was better than those for patients over 50 (3,27,29). In the current study only patients over 50 years of age were included (based on ACR criteria) for adjusting the potential confounding effect of age.

Limitations and Advantages of the Study

The present study was a double-blinded trial. The patients and the assessor were unaware of the treatment groups. To decrease bias, all the injections were performed by the same person. For blinding the patients, blood was also drawn from those in CS group (of course, with lower content of 5 mL instead of 22 mL). All the syringes were prepared outside the room and covered to prevent patients from seeing the injectant. For more accurate assessments and to decrease the probability of subjects' bias, in addition to subjective criteria such as KOOS questionnaire and pain intensity based on VAS, objective criteria, including 20MW test and measurement of active and passive knee ROMs, were also used. As for its limitations, this study had a rather small sample size (48 knees).The sample size was not sufficient for evaluating the association of the PRP effect level with osteoarthritis grade and age. Another limitation of this study was lack of imaging assessments like MRI for evaluating the thickness of articular cartilages before and after treatment, as well as lack of biologic assessments regarding the intra-articular surface of growth factors due to high costs. The physician who carried out injections was not blind and this might have caused some biases. Follow-up period in this study was 6 months. Thus, the present findings cannot be generalized to long-term effects of PRP. One of the reasons for selecting a rather short follow-up period was comparison of PRP with CS. Since the patients in the CS group were likely to have to seek another treatment modality after some months, this study was designed for only 6 months.

Conclusion

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Our experience indicates that IA injection of CS and PRP are safe and have positive effects on knee OA. Our study demonstrated that one shot of PRP decreased the joint pain more and for a longer term, alleviated the symptoms, and enhanced the activity of daily living and quality of life in short-term duration in comparison with CS. However, there is no data that any of the IA injections will cause osteophyte formation regression or cartilage regeneration in these patients.

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References:

1- Pereira D, Peleteiro B, Araújo J, Branco J, Santos RA, Ramos E.The effect of osteoarthritis definition on prevalence and incidence estimates:a systematic review. Osteoarthritis Cartilage. 2011 Nov;19(11):1270-85.

2- MiglioreA, Giovannangeli F, Granata M,Laganà B. Hylan G-F 20: Review of its Safety and Efficacy in the Management of Joint Pain in Osteoarthritis.Clin Med Insights Arthritis Musculoskelet Disord. 2010 Sep;20(3):55-68.

3- KonE, Mandelbaum B, Buda R, Filardo G, Delcogliano M, Timoncini A,and et al. Platelet-Rich Plasma Intra-Articular Injection Versus Hyaluronic Acid Viscosupplementation as Treatments for Cartilage Pathology: From Early Degeneration to Osteoarthritis. Arthroscopy. 2011 Nov;27(11):1490-501.

4- Kon E, Buda R, Filardo G, Martino AD,Timoncini A, Cenacchi A, and et al. Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions.Knee Surg Sports Traumatol Arthrosc. 2010 Apr;18(4):472-9.

5- Creaney L, Hamilton B. Growth Factor Delivery Methods in the Management of Sports Injuries: The State of Play.Br J Sports Med. 2008 May;42(5):314-20.

6- Kon E, Filardo G, Martino A.D, Marcacci M. Platelet-rich plasma (PRP) to treat sports injuries:evidence to support its use. Knee Surg Sports Traumatol Arthrosc. 2011 Apr;19(4):516-27.

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7- Sampson S, Gerhardt M, and Mandelbaum B.Platelet rich plasma injection grafts for musculoskeletal injuries: a review. Curr Rev Musculoskelet Med. 2008 Dec;1(3-4):165–174.

8- Lopez-Vidriero E, Goulding KA, Simon DA, Sanchez M, Johnson DH.The use of platelet-rich plasma in arthroscopy and sports medicine: optimizing the healing environment. Arthroscopy. 2010 Feb;26(2):269-78.

9- Mishra A, Gosens T. Clinical indications and techniques for the use of platelet-rich plasma in the elbow. Oper Tech Sports Med. 2011;19:170–176.

10- Garbis N, Romeo AA, Thiel GV, Ghodadra N, Provencher MT, Cole BJ, and et al. Clinical Indications and Techniques for the Use of Platelet-Rich Plasma in the Shoulder. Oper Tech Sports Med. 2011 Sep;19:165-169.

11- Kon E, Filardo G, Delcogliano M, Presti ML, Russo A,Bondi A, and et al. Platelet-rich plasma: New clinical application .A pilot study for treatment of jumper's knee. Injury. 2009 Jun;40(6):598-603.

12- Elgazzar RF, Mutabagani MA, Abdelaal SE, Sadakah AA. Platelet rich plasma may enhance peripheral nerve regeneration after cyanoacrylate reanastomosis: a controlled blind study on rats. Int J Oral Maxillofac Surg. 2008 Aug;37(8):748-55.

13- Jia X, Peters PG, Schon L. The Use of Platelet-Rich Plasma in the Management of Foot and Ankle Conditions.Oper Tech Sports Med. 2011 Sep; 19(3):177-184.

14- Ogino Y, Ayukawa Y, Kukita T, Atsuta I, Koyano K. Platelet-rich plasma suppresses osteoclastogenesis by promoting the secretion of osteoprotegerin. J Periodontal Res. 2009 Apr;44(2):217-24.

15- Mooren A,Merkx A, Bronkhorst A,Jansen A,Stoelinga A.The effect of platelet-rich plasma on early and late bone healing: an experimental study in goats. Int J Oral Maxillofac Surg. 2007; 36(7): 626–631.

16- Nagata M, Messora M, Okamoto R, Campos N, Pola N, Esper L,and et al. Influence of the proportion of particulate autogenous bone graft/platelet-rich plasma on bone healing in critical-size defects: An immunohistochemical analysis in rat calvaria. Bone. 2009 Aug;45(2):339-45.

17- Napolitano M, Matera S, Bossio M, Crescibene A, Costabile E, Almolla J, and et al. Autologous platelet gel for tissue regeneration in degenerative disorders of the knee. Blood Transfus. 2012 Jan;10(1):72-7.

18-Filardo G, Kon E, Buda R, Timoncini A, Di Martino A, Cenacchi A, and et al. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis.Knee Surg Sports Traumatol Arthrosc. 2011 Apr;19(4):528-35.

19-Jang SJ, Kim JD, Cha SS.Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol. 2013 Jul;23(5):573-80.

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20- Milano G, Sanna Passino E, Deriu L, Careddu G, Manunta L, Manunta A , and et al. Fabbriciani C. The effect of platelet rich plasma combined with microfractures on the treatment of chondral defects: an experimental study in a sheep model. Osteoarthritis Cartilage. 2010 Jul;18(7):971-80.

21- Fortier LA, Hackett CH, Cole BJ. The effects of platelet rich plasma on cartilage: Basic Science and Clinical Application. Oper Tech Sports Med. 2011;19 (3):154-159.

22- Akeda K, An HS, Okuma M. Platelet rich plasma stimulates porcine articular condrocyte proliferation and matrix biosynthesis. Osteoarthritis Cartilage. 2006;14(12):1272-1280.

23- Mejia HA, Bradley JP.The Effects of Platelet-Rich Plasma on Muscle: Basic Science and Clinical Application .Oper Tech Sports Med. 2011 Sep;19(3):149-153

24- Brehm W, Aklin B, Yamashita T, Rieser F, Trüb T, Jakob RP, and et al. Repair of superficial osteochondral defects with an autologous.scaffold-free cartilage construct in a caprine model: implantation method and short-term results. Osteoarthritis Cartilage. 2006 Dec;14(12):1214-26.

25- Sampson S, Reed M, Silvers H, Meng M, Mandelbaum B. Injection of platelet-rich plasma in patients with primary and secondary knee osteoarthritis: a pilot study. Am J Phys Med Rehabil. 2010 Dec;89(12):961-9.

26- Sánchez M, Anitua E, Azofra J, Aguirre JJ, Andia I. Intra-articular injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study. Clin Exp Rheumatol. 2008 Sep-Oct;26(5):910-3.

27- Giannini S, Vannini F, Timoncini A,Ghemandi R, Ruffilli A.The treatment of severe chondropathies of the knee with autologous platelet rich plasma injections:preliminary results. Osteoarthritis and Cartilage 2008 Sep;16:126-S127.

28- Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, and et al. Platelet-rich plasma vs hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trial. BMC Musculoskelet Disord. 2012 Nov; 23(13):229.

29-Raeissadat SA, Sedighipour L, Rayegani SM, Bahrami MH, Bayat M, Rahimi R. Effect of Platelet-Rich Plasma (PRP) versus Autologous Whole Blood on Pain and Function Improvement in Tennis Elbow: A Randomized Clinical Trial. Pain Res Treat. 2014;2014:165967.

30-Spaková T1, Rosocha J, Lacko M, Harvanová D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil. 2012 May;91(5):411-7.

31-Cerza F, Carnì S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, and et al. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. Am J Sports Med. 2012 Dec;40(12):2822-7.

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32-Jang SJ, Kim JD, Cha SS. Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol. 2013 Jul;23(5):573-80.

33- Patel S, Dhillon M.S, Aggarwal S,Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial.Am J Sports Med. 2013 Feb;41(2):356-64.

34- Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, and et al. OARSI recommendations for the management of hip and kneeosteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage. 2008 Feb;16(2):137-62.

35- Kijowski R, Blankenbaker D, Stanton P, Fine J, De Smet A. Arthroscopic validation of radiographic grading scales of osteoarthritis of the tibiofemoral joint. AJR Am J Roentgenol. 2006 Sep;187(3):794-9.

36- Hochberg MC. Proposed 2011 American College of Rheumatology recommendations for the use of non-pharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip and knee. Semin Arthritis Rheum. 2012;41(1):92–93.

37- Salavati M, Mazaheri M, Negahban H, Sohani SM, Ebrahimian MR, Ebrahimi I, and et al. Validation of a Persian-version of Knee injury and Osteoarthritis Outcome Score (KOOS) in Iranians with knee injuries. osteoarthritis and cartilage 2008;16:1178-1182.

38- Shimizu M, Higuchi H, Takagishi K, Shinozaki T, and Kobayashi T. Clinical and biochemical characteristics after intra-articular injection for the treatment of osteoarthritis of the knee: prospective randomizedstudy of sodium hyaluronate and corticosteroid. J Orthop Sci. 2010;15:51–56.

39- Ayhan E, Kesmezacar H, and Akgun I. Intraarticular injections (corticosteroid, hyaluronic acid, platelet rich plasma) for the knee osteoarthritis. World J Orthop. Jul 18, 2014; 5(3): 351–361.

Title of tables

Table 1: Demographic and clinical characteristics of patients in two study groups

Table 2: Mean scores of 5 parts of KOOS questionnaire in several follow-ups

Table 3: Mean VAS, time duration for 20 MW test and knee ROMs in several follow-ups

Title of figures

Figure: Consort Flowchart

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Table 1: Demographic and clinical characteristics of patients in two study groups

Variables	PRP group (n=24)	Corticosteroid group (n=24)	p
Age (mean±SD)	59.13±7.03	61.13±6.7	0.33
sex(female:male)	17:7	15:9	0.54
Height (cm)	161.9±9.4	161.4±8.5	0.85
Weight (Kg)	75.8±11.0	75.8±8.6	0.98
BMI (Kg/m^2)	28.9±2.8	29.2±3.4	0.71
Smoking (%)	0 (0.0)	3 (12.5)	0.23
Right knee:Left knee	12:12	11:13	0.99
Education (%)			
Illitrate or elementary	8 (33.3)	10 (41.7)	0.94
Middle school	2 (8.4)	2 (8.4)	
High school	9 (37.5)	8 (33.3)	
University	5 (20.8)	4 (16.6)	
Osteoarthritis grade (%)			
II	7 (29.2)	8 (33.3)	0.76
III	17 (70.8)	16 (66.7)	

PRP: Platelet-Rich Plasma

BMI: Body Mass Index

VAS: Visual Analog Scale

ADL: Activities of Daily Living

ROM: Range Of Motion

20 MW test: 20 Meters Walk Test

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Table 2: Mean scores of 5 parts of KOOS questionnaire in several follow-ups

Parameters of KOOS	PRP group (n=23)			Corticosteroid group (n=16)			P*
	before	2-month	6-month	before	2-month	6-month	
Pain relief	45.8±13.5	73.5±15.0	78.0±10.5 $P_{for\ trend} < 0.001$	52.3±11.8	60.0±16.3	54.4±20.4 $P_{for\ trend} < 0.001$	0.007
Symptoms relief	55.2±14.0	74.1±18.6	78.1±8.0 $P_{for\ trend} < 0.001$	54.6±16.8	59.4±14.7	58.3±16.4 $P_{for\ trend} < 0.001$	<0.001
ADL	51.9±14.2	75.4±13.1	74.9±15.0 $P_{for\ trend} < 0.001$	46.1±21.5	55.1±20.3	62.9±19.1 $P_{for\ trend} < 0.001$	0.005
Quality of life	7.4±8.4	25.4±19.2	30.5±15.3 $P_{for\ trend} < 0.001$	5.1±7.4	17.6±12.6	17.4±11.0 $P_{for\ trend} < 0.001$	0.02
Sport	5.9±6.8	13.3±9.9	11.3±8.0 $P_{for\ trend} < 0.001$	5.0±7.1	10.6±6.8	11.6±10.4 $P_{for\ trend} < 0.001$	0.55

* Significant level for between groups comparison

KOOS: Knee Osteoarthritis Outcome Score

PRP: Platelet-Rich Plasma

Table 3: Mean VAS, time duration for 20 MW test and knee ROMs in several follow-ups

Variables	PRP group (n=23)			Corticosteroid group (n=16)			P*
	before	2-month	6-month	before	2-month	6-month	
Pain intensity (VAS)	81.3±13.4	45.1±23.4	44.6±15.6 $P_{for\ trend} < 0.001$	77.8±13.8	65.3±19.3	72.5±16.2 $P_{for\ trend} = 0.02$	0.01
20 MW test (second)	16.33±4.4	14.4±3.3	15.6±3.4 $P_{for\ trend} < 0.001$	19.3±5.3	17.7±4.9	18.2±5.5 $P_{for\ trend} = 0.04$	0.03
Active flexion ROM (degree)	98.6±13.9	103.2±12.2	103.8±12.5 $P_{for\ trend} = 0.07$	95.6±11.1	99.4±11.3	97.6±10.9 $P_{for\ trend} = 0.09$	0.27
Passive flexion ROM (degree)	114.9±13.3	115.8±13.1	114.6±11.3 $P_{for\ trend} = 0.52$	108.5±9.8	119.8±47.3	106.1±9.8 $P_{for\ trend} = 0.37$	0.34
Flexion contracture (degree)	0.9±2.4	0.9±2.4	0.9±2.4 $P_{for\ trend} = 0.99$	0.3±1.2	0	0 $P_{for\ trend} = 0.23$	0.21

* Significant level for between groups comparison

PRP: Platelet-Rich Plasma

VAS: Visual Analog Scale

20 MW test: 20 Meters Walk Test

ROM: Range Of Motion

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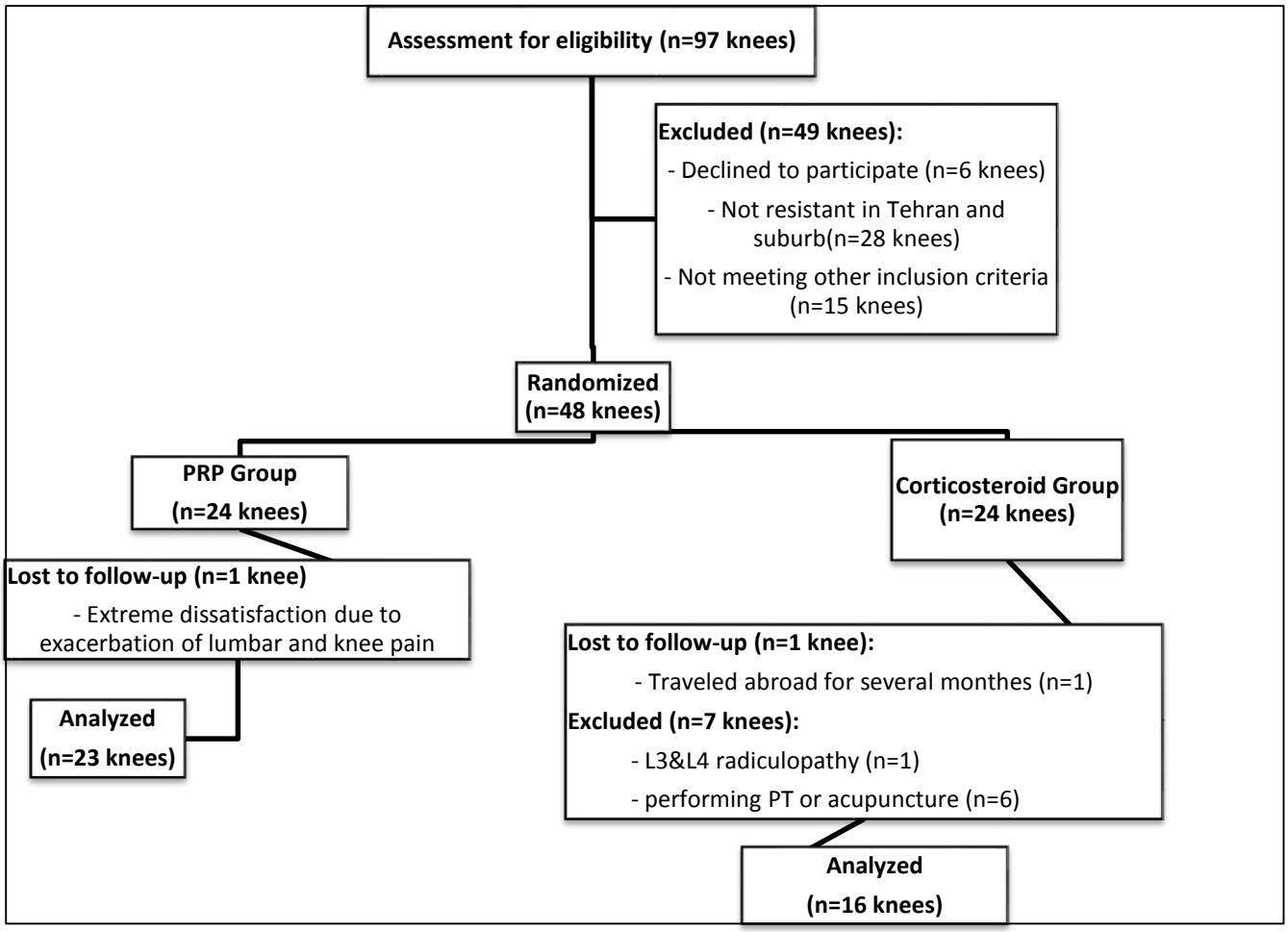

Figure Consort Flowchart

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