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Platelet-Rich Plasma Injection for Symptomatic Knee Osteoarthritis

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Background: Platelet-rich plasma (PRP) is plasma of enriched platelets with high concentration of platelet granules and growth factors. The platelet growth factors have a great potential of wound and connective tissue healing used to treat cartilage lesions and retarding the progression of knee osteoarthritis.
Objectives: This study was designed to evaluate PRP injection results in knee osteoarthritis.
Patients and Methods: This was a case-series study of 39 patients and all of them had three injections of PRP for the involved knee (every two weeks) and they were followed up at two weeks, two months and six months post-injection of PRP. All included patients filled the WOMAC (western Ontario and Mcmaster universities arthritis index) standardized and translated to our national language and culture. We analyzed the collected scores of before initiation of PRP injections, the second week, the second month and the sixth month after injections into the knees.
Results: Thirty-nine patients with a mean age of 55.24 ± 9.27 years (ranged 40 to 83) were evaluated in this study. Six patients (15.4%) were male and 33 patients (84.6%) female. There were significant differences in WOMAC score of patients in two months and six months after injection of PRP compared to before injection.
Conclusions: PRP had a great clinical improvement in short-term follow-up for early stages of knee osteoarthritis.

Keywords: Arthritis; Platelet- Rich Plasma; Knee; Osteoarthritis

1. Background

Osteoarthritis is the leading cause of disability among aged population and its incidence is increased (1). Relevant studies have shown that 10% of population older than 55 years have severe knee pain due to osteoarthritis (2).

Platelet-rich plasma (PRP) is one of the conservative options for osteoarthritic patients with promising preliminary clinical results (3, 4). PRP is a plasma of enriched platelets with high concentrations of platelet granules and growth factors. Platelet derived growth factors have a great potential of connective tissue, wound and vascular repair (5-7). There are so many proteins and over 1500 active proteins stored and identified in platelet alpha granules (8, 9).

Some of their important growth factors are fibroblastic growth factor (FGF), platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epithelial growth factor (EGF) and transforming growth factor beta (TGFβ). These factors help in matrix protein proliferation and cell development (10-12).

Recently, the use of PRP is increasingly gained attention in sport injuries as a therapeutic tool in orthopedic patients and few basic investigations systematically explored the content of PRP as well as its mechanism (s) of action (13). With increased usage of autologous PRP, various clinical studies reported ambiguous results and questionable efficacy (14, 15).

Whether PRP would improve body's natural healing response and facilitate faster rehabilitation, return to play and perhaps less bleeding and pain during recovery, resulted in extensive clinical use of PRP (16).

2. Objectives

The current study aimed to investigate the clinical results of PRP injection in osteoarthritic patients according to the western Ontario and Mcmaster universities arthritis index (WOMAC) knee scores after two and six months of intra-articular injection of PRP.

3. Patients and Methods

Our research project obtained the project number of 92-02-30-24008 from the research administration of Iran university of medical sciences. We selected 60 patients referred

to our clinic with symptomatic knee osteoarthritis, grades (I, II) of Kellgren-Lawrence classification (17), (Table 1).

The standard radiographic evaluations preoperatively included standing alignment view of both lower extremities, standing lateral X-ray, antero-posterior (AP), patellar view and MRI of involved knee.

3.1. Inclusion Criteria

1. Symptomatic osteoarthritis of knee (Kellgren-Lawrence grades 1 - 2).
2. Patients with stable knees, normal tibio-femoral alignment or patellofemoral tracking.
3. Patients with severe pain without improvement of symptoms after conservative treatments.

3.2. Exclusion Criteria

1. Inflammatory knee arthritis,
2. Advanced knee osteoarthritis (grades 3 - 4 Kellgren-Lawrence),
3. Mal-alignment (> 5 degree of varus or valgus deformity in coronal plane),
4. History of meniscectomy or meniscal injury proven by MRI.

Among 60 patients, only 39 patients completed the PRP injection courses and follow-up and 39 patients were regularly participated up to the end of our study. All the included patients before injection and at the second week, second month and six months after injection courses completed the WOMAC (western Ontario and McMaster universities arthritis index) score. We used the WOMAC score standardized and translated to our national language and culture (18). All patients participated in this study voluntarily and they filled the consent form.

3.3. PRP Preparation

As mentioned earlier, PRP is an autologous concentrate of human platelets in plasma, produced from own patient's centrifuged blood. Production of PRP consists of two steps. In the first step, 8 - 10 mL of autologous blood aspiration is centrifuged in a double-syringe system and the centrifuge is turned on for five minutes and adjusted to 5,000 rpm (rate per minute, Figure 1). After 5 minutes, RBC (red blood cell) fraction is completely separated from plasma and platelets and WBCs (white blood cells). At the second step, the separated serum is aspirated slowly via the inner syringe from the blood clot and buffy coat layer (Figure 2).

3.4. Sequences of PRP Injection

Each of included patients had three injections of PRP by interval of two weeks for the individual knee, in a sterile manner.

4. Results

In our study, we observed no major adverse events related to injection and at last 39 patients of 60 persons completed the follow-up. The mean age of patients was 55.24 ± 9.27 years (ranged 40 to 83). Six patients (15.4%) were male and 33 patients (84.6%) female. Injured knee was the right side in 17 patients (43.6%) and the left side in 22 patients (56.4%). All patients had significant improvement in their WOMAC score at 2 and 6 months after injections compared to before injection scores ($P < 0.05$).

Standardized WOMAC score according to Iranian culture and patients were filled before injection, at the second week, the second month and sixth months after the injections. We got the mentioned score from Mashhad university of medical sciences (18).

No major complications such as joint infection or hematoma were noted. There were significant differences in clinical satisfaction and knee scores at the completion of injections ($P = 0.027$). There was a significant difference between two months and six months after injections compared to before injections ($P = 0.03$, $P = 0.021$, respectively), Table 2.

Table 1. Kellgren-Lawrence Classification

Grade	Description
0	No radiographic features of osteoarthritis
1	Possible joint space narrowing and osteophyte formation
2	Definite osteophyte formation with possible joint space narrowing
3	Multiple osteophytes, definite joint space narrowing, sclerosis and possible bony deformity
4	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity

Table 2. WOMAC Score for Patient Evaluation in Four Times of Before Injection, Two Weeks, Two Months and Six Months After Injection

Variables	Minimum	Maximum	Mean ± SD
Age	40	83	55.24 ± 9.79
Before injection			50.77 ± 13.77
Two weeks after injection			53.65 ± 18.24
Two months after injection			57.74 [a] ± 19.51
Six months after injection			59.54 [a] ± 18.69

[a] A significant difference between two months and six months after injection and before injection times, ($P = 0.03$, $P = 0.021$, respectively).

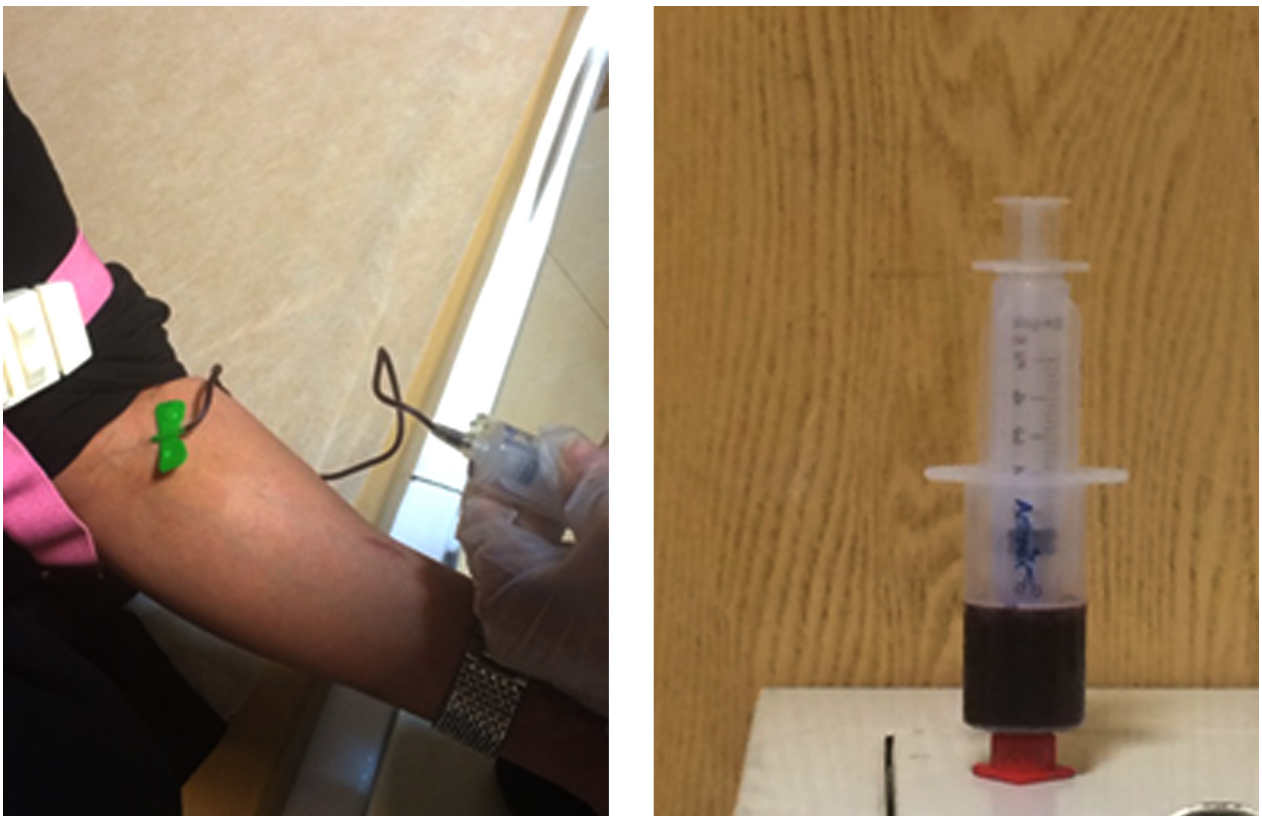

Figure 1. Aspiration of Autologous Blood (8 - 10 mL)

Figure 2. Centrifuger and Plasma Separation From RBCs and Ready for Intra-Articular Injection

Nearly 3 - 4 mL of PRP is aspirated from (8 - 10 mL) autologous blood. Total platelet count of PRP was 200,000 per mL.

5. Discussion

A number of biological approaches have been proposed to prevent progression of osteoarthritis. The purpose of this study was to investigate the effectiveness of intra-articular PRP injections in active and symptomatic knee osteoarthritis for diminishing pain, improvement in quality of life and activities.

Now PRP is used in many fields of orthopedic and in the management of tendinopathies, muscular lesions and cartilage damages (19, 20). The healing capacity of cartilage makes a challenging problem in knee osteoarthritis treatment (21).

In-vitro studies have shown the effectiveness of PRP in stimulation of chondrocytes in the treatment of osteoarthritis (22, 23). Other recent studies documented the effectiveness of platelet growth factors in prevention of joint degeneration by control of synthesis and decreasing extracellular matrix proteins (24, 25). Wu et al. in their animal study showed the effectiveness of PRP injections in new cartilage formation (26). Frisbie et al. reported clinical and histological improvement of osteoarthritis in horses (24). Saito et al. in another animal study reported good and promising results in osteoarthritis of rabbit models (25). They reported suppressed progression of osteoarthritis morphologically and histologically in their model. These preventive effects were attributed to stimulation of cartilage matrix metabolism caused by the growth factors contained in PRP.

Nakagawa et al. in their in-vitro study showed the efficacy of autologous PRP in cell proliferation and collagen synthesis of human chondrocytes and suggested a new method of osteoarthritis treatment and use of this method in the treatment of cartilage defects in human (27).

Kon et al. reported positive effect of PRP injection on symptoms and functions of chronic osteoarthritis of knee treated with three injections of PRP, one injection per week. They demonstrated positive effects in about 85% in scores for patients with a median age less than 60 years but improvement was only 30% (4).

In another study, authors showed that improvement in clinical results and knee scores deteriorated over 12 to 24 months of follow-up (28). Other authors used intra-articular injections of PRP in knee osteoarthritic patients and showed that PRP combined with proper nutrition, control of body mass index (BMI), exercise and lifestyle can act as a preventive agent in chronic and degenerative diseases (29-31).

All of our patients showed significant improvement at six months follow-up and it is in accordance with the preliminary results of other authors (29-31) with short-term follow-up of PRP injection for knee osteoarthritis.

Anitua et al. in their study on human synovial cells isolated from osteoarthritic patients showed that intra-articular injections of PRP could increase production of hyaluronic acid structure and promote angiogenesis and cell proliferation (32).

In our study, patients with advanced knee osteoarthritis were excluded and they had no associated pathologies such as knee instability, patellofemoral or tibiofemoral severe malalignment, which can affect clinical outcomes. Although in some studies, there have been worse results of PRP injection in female patients (28), but we found no significant differences between men and women results.

We found no adverse or major complications during PRP injection in our patients (such as acute pain or infection or hematoma) and other reports showed its safety without major complications (4, 30, 31). Intra-articular PRP injections could improve postoperative clinical outcome in these patients. The main limitation of our study was that we did not include a control group. A second limitation was that we followed our patients for six months; long-term follow-up and prospective randomized studies should be performed to clarify PRP effectiveness and durability of clinical improvements. PRP had a therapeutic application with positive and encouraging clinical results in active patients with knee osteoarthritis with mild to moderate grade of knee osteoarthritis.

Authors' Contributions

Study concept and design: Abolfazl Bagherifard, Mahmood Jabalameli, Ali Jahansouz. Analysis and Interpretation of data: Ali Jahansouz, Hooman Yahyazadeh, Tahmineh Mokhtari. Drafting of the manuscript: Abolfazl Bagherifard, Mahmood Jabalameli, Ali Jahansouz, Mahsa Khezri, Ramin Bozorgmehr, Hosein Karimi Heris, Parham Nikraftar. Critical revision of the manuscript for important intellectual content: Abolfazl Bagherifard, Ali Jahansouz. Study supervision: Abolfazl Bagherifard, Mahmood Jabalameli.

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