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Original Research

Short-term clinical results of intra-articular PRP injections for early osteoarthritis of the knee

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HIGHLIGHTS

- PRP injection appears to be effective in early symptomatic OA knees.
- There were significant reduction in pain and improvement in knee function at 12 months after treatment.
- Three injections at monthly intervals appear to show better results in short-term clinical follow-up.

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ABSTRACT

Purpose: To assess the short-term results of repeated intra-articular platelet rich plasma (PRP) injections into the knee in patients with early osteoarthritis (OA) and to determine a better treatment protocol.
Methods: This is a retrospective study in 191 knees (127 patients) with minimum of 12 months follow-up. We compared the clinical results of three types of injection method, once a month, twice monthly, and three injections at monthly interval. The outcomes were assessed using Visual Rating Scale (VRS), functional score, knee score, range of motion (ROM), WOMAC Stiffness/Pain/Function score, IKDC score, before the first injection and at 12 months post treatment.
Results: There were significant improvements in all scores after treatment as compared to the pre-treatment values ($p < 0.05$), except Knee score after 1st and 2nd injection and ROM in three groups. The parameters of Visual Rating Scale (VRS), functional score, and WOMAC Stiffness/Pain/Function score showed significant differences among the three groups in favour of the three injections group ($p < 0.05$). At 12 months, the effects began to decline in one injection and two injections groups, and the data in one injection group showed significant difference compared to two injection group ($p < 0.001$). Three injections group had higher scores and more improvement at 12 months after treatment when compared to the other two groups.
Conclusion: PRP injection appears to be effective in early symptomatic OA knees. The results after treatment are encouraging with significant reduction in pain and improvement in knee function at 12 months after treatment when compared to the pre-treatment status. Three injections per month yielded significantly better results in short-term follow-up.

1. Introduction

Degenerative osteoarthritis of the knee (OA) affects approximately 250 million people (nearly 27 million Americans). It is a major source of knee pain that affects 35% of population older than 65 years [1,2]. Non-invasive treatment is indicated in the early knee of OA by means of rest, oral anti-inflammatory drugs, analgesics, physical therapy, and intra-articular injections of different drugs including hyaluronic acid (HA), corticosteroids (CS), and platelet-rich plasma (PRP). Since 1950, PRP has been used to manage dermatologic and oromaxillofacial conditions [3,4]. More recently, interest has grown exponentially in the use of PRP in orthopaedic

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applications such as bone formation, soft-tissue injury and osteochondral pathology and osteoarthritis. Platelet-rich plasma is an autologous blood product that contains concentration of platelets. Platelets have a high concentration of growth factors and cytokines with their α-granules and dense granules. The growth factors, including hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), insulin-like growth factor-1 (IGF-1), epidermal growth factor (EGF), and transforming growth factor−β (TGF-β) [5], stimulate the soft tissue healing, and bone or cartilage regeneration. Numerous basic science and clinical studies had demonstrated the positive effects of PRP on cartilage degeneration or injury. Moreover, recent reports indicate that intra-articular PRP injection could have a better performance than HA in younger patients with early degeneration [6]. Although PRP has been shown to be a safe and effective treatment option for knee osteoarthritis, there are numerous PRP treatment variables. Previous study [7], the clinical benefits of PRP injection for respect to pain and function seemed to decline starting at 6–9 months after treatment, and further loss of benefit at 24 months [8–10]. At present, the optimal number of PRP injection frequency remains unclear.

The purpose of this study was to assess the short-term results of repeated intra-articular platelet rich plasma (PRP) injections into the knee in patients with early osteoarthritis (OA).

2. Materials and methods

This is a retrospective study from May 2014 to February 2015 including 191 knees (127 patients) with the diagnosis of early knee osteoarthritis by American College of Rheumatology criteria [11]. All patients received the radiographic evaluation including standing anteroposterior, lateral, and Merchant views of the knee. The stage of knee osteoarthritis was calculated according to the Ahlback radiological classification [12]. Patients with symptomatic early stage OA of the knees (Ahlback classification stage 1–3), failure to previous conservative or surgical treatment, and had received intra-articular autologous platelet-rich plasma (PRP) injections (Regen ACR-C, Regen Lab, Switzerland), were included in this study. All patients were systematically followed up for a minimum of 12 months after the last PRP injection. Patients were excluded for systemic disease, active tumor or hematologically malignant disease, infection, history of anticoagulant use, Hb value < 11 g/dl, thrombocyte count <150,000/mm^3, radiologically osteoarthritis at Ahlback Stage 4, or loss to follow up. Patients were divided into three groups according to three types of intra-articular PRP injection method, once a month, twice monthly, and three injections per month.

2.1. PRP preparation and application

The PRP processing was performed using the Regen Kit. The Regen Kit is a fully enclosed system that maintains sterility throughout the entire process and uses a dual spin system. In order to prepare PRP with concentrations of four to six times the average of normal values, 10 mL of blood was first collected from the patient's upper limb cubital vein using an 18G needle, subsequently 5 mL of acid citrate dextrose solution-A was added to the sample as an anticoagulant. Local anesthetic agent was not injected. This was due to the fact that resources stated that anesthetic agents not only could have toxic effects on chondrocytes but could also influence the activation of platelet by changing the pH of the environment [13]. Patient was placed in a sitting position with the knee in 90° of flexion. The skin of the injection site was prepped and draped, and the liquid PRP was injected in sterile condition using a 23G needle through the classic approach for intra-articular injection (anterolateral portal). After 15–20 min of rest, patients were asked to actively flex and extend their knees so that the PRP could spread evenly across the knee joint space. Limited movement was allowed for 24 h. Resting or ice packing for 3 days was recommended in case of pain or swelling. The patient did not receive non-steroidal inflammatory drugs (NSAIDs) for two weeks after PRP injection to avoid PRP concentration [14]. In addition, an exercise program was given to the patients, and performance of normal daily activities was recommended after 3 days of injection when tolerable.

2.2. Outcome measures

The outcome was assessed by using Visual Rating Scale (VRS) [15], with a score from 0 (no pain) to 10 (extremely severe) to evaluate the pain, functional score, knee score, range of motion (ROM), Western Ontario and McMaster Universities Arthritis Index (WOMAC) Stiffness/Pain/Function score [16,17], and International Knee Documentation Committee (IKDC) score [18] were also used to measure the functional result before the first injection and 12 months post last treatment. The stage of knee osteoarthritis was reevaluated by the radiographic examination at last follow up.

An institutional review board approved the study (Chang Gung Medical Foundation Institutional Review Board at TAIPEI, TAIWAN, with protocol number 201600470B0) and date of approval May 11, 2016.

2.3. Statistical analysis

All continuous data were expressed in terms of the mean ± standard deviation of the mean. One Way MANOVA was performed to assess differences among groups when the Levene test for homogeneity of variances was not significant ($p < 0.05$); otherwise, the Mann Whitney test (2 groups) or the Kruskal Wallis test (more than 2 groups) were used. The Least Significant Difference test was performed as a post-hoc pair-wise analysis of the Kruskal Wallis test. The generalized linear model for repeated measures with Sidak correction for multiple comparisons was performed to test differences of the scores at different follow-up times. The non-parametric Pearson's Chi square test evaluated by exact methods was performed to investigate the relationships between grouping variables. For all tests, $p < 0.05$ was considered significant. Statistical Analysis was carried out by using the Statistical Package for the Social Sciences (SPSS) software version 15.0 (SPSS Inc., Chicago, USA).

3. Results

64 patients (98 knees) received single injection of PRP, 18 patients (27 knees) received twice PRP injection at monthly interval, and 45 patients (66 knees) received three injections at monthly interval. Demographic information of 3 groups is summarized in Table 1. The baseline characteristics of the 3 groups in age, gender, BMI, side of lesion, duration of symptoms, and length of follow up were analyzed.

The one injection group consisted of 27 men and 37 women, with a mean age of 60.9 years (range, 21–83 years; standard deviation [SD], 13.0 years). The mean BMI was 27.2 (range, 16.4–49.8; SD, 5.5). The one injection group consisted of 47 right knees, 51 left knees, and 34 bilateral knees with the mean duration of symptoms for 22.6 months (range, 1–120 months; SD, 18.6 months). The mean length of follow-up was 12.8 months (range, 10–13 months; SD, 3.2). The osteoarthritis was graded according to the Ahlback radiographic classification: that included 63 knees stage 1, 30 knees stage 2 and 5 knees stage 3.

The two injections group consisted of 8 men and 10 women with