ORIGINAL ARTICLE

Efficiency of Intra-Articular Platelet-Rich Plasma Injection in Grade I and Grade II Osteoarthritis in the Knee Joints: A Longitudinal Study

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ABSTRACT

Aim: To assess the efficiency of intra-articular platelet-rich plasma (PRP) injection in grade I and grade II osteoarthritis in the knee joints

Study design: A longitudinal study

Place and Duration: This study was conducted at Murshid Hospital and Health Care Center Karachi Pakistan from January 2021 to June 2021.

Methodology: The ages of the patients were between 35 years and 65 years. All the patients were diagnosed with osteoarthritis of grade I and grade II. A total of 3 injections of PRP were injected intraarticular in the knees at an interval of 4 weeks. Patients were asked to come for a follow-up in the outpatient department. They were assessed for physical mobility and pain related to arthritis using the WOMAC score. The assessment was done when the treatment was given and after 6 months. **Results:** A total of 250 patients were considered in the present study. The mean age of the patients was 55.63±5.65 years. The ratio of disease in females to males was 3:1. A total of 178 patients had grade I osteoarthritis and 72 patients had grade II osteoarthritis according to Kellgren–Lawrence classification. A total of 210 patients had reported experiencing symptoms for less than 2 years and the remaining 40 had been experiencing the symptoms for more than 2 years. The mean WOMAC score was 82.9 before the treatment was started and it was 39.15 after 6 months of the treatment. The improvement of WOMAC score was more in the patients having symptoms for less than 2 years. Minor hyperemia was seen in 4 patients and those patients were managed conservatively by ice application and activity limitation. None of the patients showed signs of infection.

Conclusion: The intraarticular injection of PRP proved to be beneficial and effective in the treatment of grade I and grade II early osteoarthritis.

Keywords: Osteoarthritis, Platelet-rich plasma, PRP, knee joint

INTRODUCTION

Osteoarthritis is a common disease of joints that occurs as a result of defects or damage in the articular cartilage. The quality of the life of the patients is greatly affected by this disease. It is one of the common causes of disability related to the musculoskeletal system of the body [1]. The disease has the potential to affect any joint of the body, however, it is commonly seen in the hip joint, knee joints, feet joints, and facet joint [2]. As time passes and the age of the patients advance, an increased prevalence of arthritis symptoms is observed. The annual incidence of the disease also increases with the increase in age. It is seen more in individuals between the age of 55 years and 65 years [3].

According to some theories, the wear and tear of the cartilage are called osteoarthritis. Nonetheless, it is not only the wear and tear of the cartilage. It is rather a complex disease that has been characterized by inflammatory secretions including cytokines. These mediators play an important role in the pathophysiology of osteoarthritis [4]. In a joint of normal anatomy and physiology, the chondrocytes are inactive with a smaller cartilage matrix turnover. The extracellular matrix receptors on the chondrocytes are converted into activated chondrocytes in osteoarthritis. They exhibit proliferation of the cell, formation of clusters, and the production of matrix leading to degradation of inflammatory cytokines and proteinases [5]. In addition to the destruction of the cartilage, this disease is also characterized by subchondral sclerosis, Synovial inflammation, osteophyte formation, and ligament laxity [6]. These changes in the pathophysiology of the joints have led researchers to consider it as a joint disease as an organ [5].

There are various treatments for osteoarthritis and almost all of them are supportive treatments including analgesics, corticosteroids, and viscosupplements. These are helpful in alleviating arthritis symptoms [7]. Another such treatment is intraarticular injections of hyaluronic acid. This treatment has been

used for a long time for this disease [8]. The PRP has been used for a few years as well, however, it is a more advanced treatment than hyaluronic acid. The blood of the patient is used for the derivation of PRP. It contains some growth factors which can activate the process of healing damaged cartilage. It also helps in the regeneration of the tissue [9]. The comparison of PRP and hyaluronic acid shows that PRP is more beneficial [10].

The present study aims at the observation of clinical outcomes and benefits of intraarticular injection of PRP in patients presenting with grade I and grade II osteoarthritis in the knees.

METHODOLOGY

The longitudinal study was conducted in the orthopedic department of our hospital. Permission was taken from the ethical review committee of the institute. A total of 250 participants were included in the study. The ages of the patients ranged from 35 years to 65 years. All the patients were diagnosed with osteoarthritic and classified as grade I and grade II according to the classification of Kellgren-Lawrence) [11]. According to the inclusion criteria, the participants must have a hemoglobin of more than 12 g/dL, symptoms persist for more than six months, platelets more than 150,000 μ/L , failure of physiotherapy, and failure of pharmacological intervention. As per the exclusion criteria of the study, the patients with an autoimmune disorder, platelet disorder, taking immunosuppressive or anticoagulant therapy, with a history of infection, diabetes, malignancy, or recent trauma were excluded from the study

Before the conduction of the study, all the included patients were demonstrated about the procedure, described the benefits of the treatment as well as the complications associated with the procedure. Written informed consent was taken from all the participants. A questionnaire was filled out by the participants or the researchers which included the demographic data such as the occupation of the patient, blood group, body mass index (BMI),

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grade of arthritis, and duration of the symptoms. A physical examination of all the patients was performed for the assessment of the physical activity and pain associated with osteoarthrosis. WOMAC scoring system was used in this regard [12].

There are two methods of preparation of PRP using differential centrifugation according to Dhurat and Sukesh [13]. One method is called the buffy-coat method and the other is called the PRP method. The PRP method was used in the present study. The preparation was done in the hematological department. The blood of the patient was taken from the cubital vein. About 4 to 6 mL of PRP was prepared from this blood. Blood was drawn and stored in a blood bag containing anticoagulants including adenine and citrate phosphate dextrose.

The blood was then poured into a tube. The tubes were centrifuged at a constant acceleration for the separation of red blood cells (RBCs) and the rest of the whole blood. The process of centrifugation separates the blood into three parts i.e. platelets and white blood cells (WBCs), buffy coat mostly containing WBCs, and layer of RBCs. The uppermost layer and buffy layer were centrifuged again for the formation of a soft pellet in the bottom of the tube. The upper two-thirds of the new volume was disposed of or discarded. PRP is formed from the remaining one-third by homogenization. A sterile syringe was used for dispensing the preparation of PRP. The PRP was then injected intraarticular in the knees in the suprapatellar pouch through a superolateral approach. Patients were asked to stay for another 20 minutes for observation. After 20 minutes, the patients were guided about the signs of infections such as redness, pain, inability to tolerate weight and warmth in the knee, and discharged from the hospital. Patients were instructed to take paracetamol in case of pain. Patients were instructed to come for regular follow-up visits in the outpatient department. During the course of treatment, 3 injections were given at the interval of 4 weeks.

A calculation of the WOMAC score was done for all the patients at the time of induction of the treatment and then six months intervals. This was helpful in the assessment of the effectiveness of the PRP injections. A comparison of the WOMAC score in the beginning and after six months of the treatment with PRP injection was done by using a t-test. The data was analyzed in the IBM SPSS version 26.

RESULTS

A total of 250 patients were included in the present study after strict inclusion criteria. A total of 12 patients were found to be noncompliant and they did not come for follow-up visits. The remaining 238 completed the study. The mean age of the patients included in the study was 55.63±5.65 years. Female patients were more than the male patients with a female to the male ratio of 3:1. The number of female patients was 165 (66%) and the number of male patients was 85 (34%). A total of 178 (17.2%) patients had grade I osteoarthritis and 72 (28.8%) patients had grade II osteoarthritis according to Kellgren-Lawrence classification. A total of 210 (84%) patients had reported experiencing symptoms for less than 2 years and the remaining 40 (16%) had been experiencing the symptoms for more than 2 years. The mean WOMAC score was 82.9±4.2 before the treatment was started and it was 39.15±5.6 after 6 months of the treatment. Table 1 shows a comparison in the WOMAC score at the induction of the treatment and six months after the treatment was given.

able 1: Comparison of WOMAC score		
	WOMAC (mean ±	P-value
	standard deviation)	
At the time of induction of the	82.9±4.2	0.000
treatment		
6 months after the treatment	39.15±5.6	

The WOMAC score was better in the patients who had been experiencing symptoms for lesser than 2 years. The difference was not significant in the individuals of both the genders as well as both the grades i.e. grade I and grade II. This comparison is given in Table 2. Minor hyperemia was developed in 4 of the patients. This was treated with ice application and activity limitation. Gross infection was not noted in any of the participants.

Table 2: Comparison of WOMAC score in different subgroups after 6 months of the treatment

	WOMAC (mean ± standard deviation)	P-value	
Gender			
Females	40.1 ± 5.3	0.765	
Males	37.6 ± 5.5		
Kellgren-Lawre	Kellgren–Lawrence grading		
Grade I	38.3 ± 5.1	0.167	
Grade II	39.7 ± 4.9		
Duration of the	Duration of the symptoms		
Less than 2	38.2 ± 5.8	0.005	
years			
More than 2	41.6 ± 4.2		
years			

DISCUSSION

In the present study, a remarkable improvement was seen in patients with osteoarthritis because of PRP injection therapy. The WOMAC score was significantly different at the time of induction of the treatment and after six months of the treatment. More improvement was seen in the patients who had reported the presence of symptoms for less than two years compared to those who had symptoms for more than two years.

Osteoarthritis greatly affects the quality of life and mobility of Non-surgical treatments of the disease corticosteroids, hyaluronic acid, and PRP. The treatment is prescribed by the physician according to the condition and feasibility of the patients. Recently, physicians have shown more interest in the regenerative and biological methods of therapy that also include PRP [14]. Nonetheless, it can be seen that all the invasive procedures have a placebo effect to some extent. It is better to make a comparative group while conducting a study regarding the treatment modality. A comparative group was not included in the present study due to certain reasons.

According to a meta-analysis and systematic review by Sadabad et al, the superiority of PRP in terms of efficacy has been given compared to the hyaluronic acid treatment for the alleviation of symptoms in two years. They also suggested a long-term study for the evaluation of PRP efficacy [10]. Another similar systemic review was given by Khoshbin et al. According to their study, a series of injections of PRP has much more efficacy compared to normal saline injections and hyaluronic acid injections over a follow-up duration of 6 months [15].

In the present study, a significant difference in the WOMAC score was seen in the PRP-treated patients in 6 months. PRP is a minimally invasive technique and a simpler alternative for tissue regeneration and the healing process of the cartilage in osteoarthritic patients. It is potent for improving the quality of life, enhancing the function of the knee joint, and relieve of pain [16].

The effect of PRP in chronic degenerative osteoarthritis of knee joints was studied by Kon et al in a similar study as that of the present study. They had included 115 patients in their study. The duration of the study was 12 months. The peculiarity seen by them in the study was that the results were favorable in the first six months, however, they were not as satisfactory in the next six months out of the total duration of the study. Moreover, the efficacy of PRP was better in the patients who reported symptoms recently [17]. In the present study, the results were favorable in 6 months of the treatment. The duration of the present study was shorter compared to the study of Kon et al.

Patel et al conducted a study to compare the effect of PRP on three groups. One of the groups had got one injection, the other group had got two injections and the other group received normal saline. The third group had shown deteriorating symptoms. Mild complications such as dizziness and nausea were observed. Similar to the results of their study, the present study also proved clinical improvement by the PRP injections. No major complications were observed in the present study except mild hyperemia in four patients. Cole et al conducted a study to compare the outcomes of hyaluronic acid and PRP in 111 patients. The results of PRP were better [18]

CONCLUSION

Treatment of osteoarthritis by sequential PRP injections was observed to be effective in the present study. The treatment was more effective in patients who had been experiencing symptoms for less than 2 years, grade I patients, and male patients.

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Permission: Permission was asked and taken from the ethical committee of the institute

REFERENCE

- Raeissadat SA, Rayegani SM, Babaee M, Ghorbani E. The effect of platelet-rich plasma on pain, function, and quality of life of patients with knee osteoarthritis. Pain research and treatment. 2013 Oct; 2013.
- Saqlain HAU, Hussain SS, Keerio NH, Qureshi MA, Valecha NK, Noor SS. Effect of Platelet Rich Plasma Injection Effect on Knee Osteoarthritis in Elderly: Single Dose versus Double Dose Randomized Clinical Trial. JPRI [Internet]. 2Mar.2021 [cited 13Jan.2022];33(6):84-9. Available from: https://www.journaljpri.com/index.php/JPRI/article/view/31191
- Deshpande BR, Katz JN, Solomon DH, Yelin EH, Hunter DJ, Messier SP, Suter LG, Losina E. Number of persons with symptomatic knee osteoarthritis in the US: impact of race and ethnicity, age, sex, and obesity. Arthritis care & research. 2016 Dec; 68(12):1743-50.
- Keerio NH, Aamir N, Kumar N, Qureshi MA, Amir us Saqlain H, Noor SS. Incidence of writing double NSAIDs in a single prescription for Osteoarthritis. Professional Med J 2021; 28(5):000-000. https://doi.org/10.29309/TPMJ/2021.28.05.4872.
- Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. Arthritis and rheumatism. 2012 Jun: 64(6):1697.
- Martel-Pelletier J, Boileau C, Pelletier JP, Roughley PJ. Cartilage in normal and osteoarthritis conditions. Best practice & research Clinical rheumatology. 2008 Apr 1; 22(2):351-84.
- Michael JW, Schlüter-Brust KU, Eysel P. The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. Deutsches Arzteblatt International. 2010 Mar; 107(9):152.

- Cheng OT, Souzdalnitski D, Vrooman B, Cheng J. Evidence-based knee injections for the management of arthritis. Pain medicine. 2012 Jun 1; 13(6):740-53.
- Smyth NA, Haleem AM, Ross KA, Hannon CP, Murawski CD, Do HT, Kennedy JG. Platelet-rich plasma may improve osteochondral donor site healing in a rabbit model. Cartilage. 2016 Jan; 7(1):104-11.
- Sadabad HN, Behzadifar M, Arasteh F, Behzadifar M, Dehghan HR. Efficacy of platelet-rich plasma versus hyaluronic acid for treatment of knee osteoarthritis: a systematic review and meta-analysis. Electronic Physician. 2016 Mar; 8(3):2115.
- Kellgren JH, Lawrence J. Radiological assessment of osteoarthrosis. Annals of rheumatic diseases. 1957 Dec; 16(4):494.
 McConnell S, Kolopack P, Davis AM. The Western Ontario and
- McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. Arthritis Care & Research: Official Journal of the American College of Rheumatology. 2001 Oct; 45(5):453-61.
- Ajmal Khan Silro, Muhammad Faraz Jokhio, Mohsin Aijaz Soomro, Raheel Akbar Baloch, Niaz Hussain Keerio, Najeeb Ur Rehman, & Syed Shahid Noor. (2021). Result of high Fibular Osteotomy (HFO) in Osteoarthritis knee. International Journal of Research in Pharmaceutical Sciences, 12(4), 2325-2329. https://doi.org/10.26452/ijrps.v12i4.4861
- Sheth U, Simunovic N, Klein G, Fu F, Einhorn TA, Schemitsch E, Ayeni OR, Bhandari M. Efficacy of autologous platelet-rich plasma use for orthopedic indications: a meta-analysis. JBJS. 2012 Feb 15; 94(4):298-307.
- Khoshbin, A., Leroux, T., Wasserstein, D., Marks, P., Theodoropoulos, J., Ogilvie-Harris, D., Gandhi, R., Takhar, K., Lum, G. and Chahal, J., 2013. The efficacy of platelet-rich plasma in the treatment of symptomatic knee osteoarthritis: a systematic review with quantitative synthesis. Arthroscopy: The Journal of Arthroscopic & Related Surgery, 29(12), pp.2037-2048.
- Filardo G, Kon E, Buda R, Timoncini A, Di Martino A, Cenacchi A, Fornasari PM, Giannini S, Marcacci M. Platelet-rich plasma intraarticular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. Knee Surgery, Sports Traumatology, Arthroscopy. 2011 Apr; 19(4):528-35.
- Filardo G, Kon E, Di Matteo B, Di Marino A, Sessa A, Merli ML, Marcacci M. Leukocyte-poor PRP application for the treatment of knee osteoarthritis. Joints. 2013 Jul; 1(03):112-20.
- Cole BJ, Karas V, Hussey K, Merkow DB, Pilz K, Fortier LA. Hyaluronic acid versus platelet-rich plasma: a prospective, doubleblind randomized controlled trial comparing clinical outcomes and effects on intra-articular biology for the treatment of knee osteoarthritis. The American journal of sports medicine. 2017 Feb; 45(2):339-46.