

Effects of Intra-Articular Platelet Rich Plasma on Clinical Outcomes in Knee Osteoarthritis

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Abstract

Background and Aim: With increasing frequency, platelet-rich plasma (PRP) preparations have been used to treat cartilage lesions to regenerate tissue homeostasis and retard the progression of knee osteoarthritis (OA). The aim of our research was to study the effectiveness of intra-articular PRP injections in early-stage OA patients and to evaluate the clinical outcome and QOL at 6 months.

Material and Methods: Present study was conducted on 80 patients at tertiary care institute of Gujarat for the Period of 1 year. Intraarticular administration of PRP was done by injecting 5 mL of platelet concentrate in the supra-patellar pouch through supero-lateral approach with a 22-gauge needle. The patients were followed up for reduction in pain, reduction in stiffness and improvement in physical function in accordance with WOMAC scoring system on day 0 and at the end of 6th week, 3rd and 6th months and QOL in accordance with WHOQOL questionnaire before PRP therapy and at the end of 6th month.

Results: In our study of 80 patients 26 had very poor, 23 had poor and 1 had neither poor nor good QOL before PRP injection evaluated by WHOQOL. At 6 months post PRP therapy 5 had very good, 59 had good, 15 had neither good nor poor and 1 had poor QOL which showed highly significant improvement in QOL.

Conclusion: Intra-articular injection of autologous PRP is a safe, cheap, easy to prepare and use, and has a therapeutic role in early knee OA. Hence, PRP therapy can be used in management of early stage knee OA to provide relief from symptoms and to improve QOL with negligible complication, low cost and ultimately with good results.

Key Words: Osteoarthritis, Pain, Platelet-Rich plasma, Quality of Life

Introduction

Osteoarthritis (OA) is the fourth leading cause of years lived with disability at the global level. Increased longevity teamed with the epidemic of

obesity and the resultant motivation to exercise, often through sports, the burden and prevalence of OA are expected to grow further. Clinically, OA presents with recurring episodes of pain, particularly after prolonged activity and weight bearing that

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decreases with rest, stiffness felt after inactivity (gel phenomenon), progressive limitation of movement, and synovitis with effusion.^{1,2,3}

OA is one of the major causes of pain and disability in the elderly population (>70 years).⁴ OA alters the normal joint metabolism promoting increased catabolism and decreased anabolism. In OA knees, chondrocyte senescence and loss of cartilage integrity are prominent features. There is a surge in the water content of hyaline cartilage, accompanied by decrease in corresponding proteoglycan concentration, length and aggregation, causing cartilage stiffness and fibrillation of the cartilage surface. From this stage, cartilage proceeds to erode resulting in deep clefts. Concurrently, subchondral bone shows morphological changes. The synovial fluid infiltrates into subchondral bone causing the formation of subarticular cysts. Osteophytes are characteristic features of knee OA in non-pressure areas, caused due to the flattening of bone from pressure in high-wear areas.⁵

American College of Rheumatology (ACR) recommends various pharmacological and non-pharmacological treatment modalities for the management of knee OA.⁶ Weight reduction, joint offloading, exercises, Tai Chi, and therapeutic modalities are a few of the nonpharmacological therapies.^{7,8} Pharmacotherapy chiefly includes acetaminophen, non-steroidal antiinflammatory drugs (NSAIDS) oral as well as topical, intra-articular corticosteroids, opioids, and topical capsaicin. Surgical management includes arthroscopic debridement, osteotomy of the proximal tibia or distal femur, uni-compartmental knee replacement, total knee replacement, etc. are mostly reserved for more severely disabled patients who have failed conservative management.^{9,10} Conservative treatments increase the quality of life of patients, especially in the early phase. Current researchers are investigating new methods of stimulating repair or replacing damaged cartilage.¹¹ Platelet Rich Plasma (PRP) has the function of chondrogenesis, proliferation of fibroblasts in vitro, regulation of metalloproteinases, collagen synthesis, and stimulation of synovial fibroblast to produce hyaluronic acid that repairs the damaged articular cartilage.¹²

PRP is an autologous mixture of highly concentrated platelets and associated growth factors and other bioactive components produced by centrifugal separation of whole blood, which is used in orthopaedic and sports medicine practices to treat bone, tendon and ligament injuries.¹³ PRP may induce a regenerative response by improving the metabolic functions of damaged structures, and has been shown to have a positive effect on chondrogenesis and mesenchymal stem cell proliferation.¹⁴⁻¹⁶

The combined effects of PRP make it a potential option for management of knee OA, especially as a primary analgesic agent. This is due to an increase in proliferation of tenocytes, osteoblasts and mesenchymal stem cells resulting in decreased pain levels postoperatively.⁷ The aim of our research was to study the effectiveness of intra-articular PRP injections in early-stage OA patients and to evaluate the clinical outcome and QOL at 6 months.

Material and Methods

Present descriptive study was conducted on 80 patients at tertiary care institute of Gujarat for the Period of 1 year. The study included a total of 80 patients with clinically and radiologically diagnosed OA of knee joint/ joints with age of 50 years and above coming to the outpatient department of orthopaedics at tertiary care institute. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants.

Patients with active infective pathology around the knee joint, on anti-coagulant therapy or with bleeding disorders, platelet functional and morphological disorders, any primary or secondary malignancies, severely anaemic, uncontrolled diabetes mellitus, and OA other than knee joints were excluded from our study.

After proper informed consent and history taking, clinical assessment was done. Severities of symptoms were assessed by WOMAC score, the patients were explained about the procedure and the risks associated with it. For the preparation of PRP, 10 mL of peripheral blood was collected maintaining strict sterility protocol. The collected blood underwent a series of centrifugation process with 3000 rotations per minute for 10 to 12 minutes, thereby delivering the

desired PRP with four- to six-fold increase in platelet concentration. Intraarticular administration of PRP was done by injecting 5 mL of platelet concentrate in the supra-patellar pouch through supero-lateral approach with a 22-gauge needle. No form of local anaesthetic was used. Immediately after the injection, passive flexion and extension of the affected knee was performed.

The patients were observed for 30 minutes, following which they were given injection paracetamol for pain on "SOS basis" and prophylactic oral antibiotics for 3 days. They were instructed to limit the use of their affected knee for 24 hours. The patients were especially instructed not to use any/asked to stop medications 48 hours before the follow-up assessment. The patients were followed up for reduction in pain, reduction in stiffness and improvement in physical function in accordance with WOMAC scoring system on (pre-procedure) day 0 and (post-procedure) at the end of 6th week, 3rd and 6th months and QOL in accordance with WHOQOL questionnaire before PRP therapy and at the end of 6th month.

WOMAC consisted of a questionnaire which is aimed to assess three items in subscales of 0-4 containing total of 24 questionnaires.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results and Discussion

OA being a progressive degenerative and one of the oldest diseases in mankind still lacks a definite therapeutic or pharmacological agent to treat or stop the progression other than total knee replacement.¹⁷ Increased understanding of anatomy, pathophysiology and biochemical events occurring at the articular cartilage has led to invention of novel methods in treatment of OA knee lately. One among them is PRP therapy, which has gained popularity in the last decade worldwide mainly due to its promising results, easy availability, fewer complications and at

affordable cost. The PRP exerts multiple biological actions, including modulatory effects on inflammation and angiogenesis, which may translate clinically to pain relief.¹⁸ In isolated chondral lesions, healing has been seen as described in some studies.^{19,20} Hassan et al²¹ evaluated the osteoarthritic knees before and after the PRP injections and have found a significant decrease in the number of patients having increased Doppler activity after 6 PRP injections.

Our study included 80 patients with early-stage knee OA and given a single intraarticular injection of autologous platelet rich plasma and the outcomes of whom were assessed pertaining to improvement in their QOL and well-being

In our study we observed significant reduction in pain, reduction in joint stiffness and improvement in physical activities as shown by significant reduction in WOMAC score values at each successive follow-up with mean WOMAC scores of 60, 46 and 32 at 6 weeks, 3 months and 6 months respectively post PRP therapy. We observed significant mean differences in mean values with $p < 0.001$. In a study conducted by Mohammed et al in 55 patients with knee OA treated with PRP showed a significant improvement in pain and function in terms of WOMAC scores from baseline.²² In a comparative study conducted by Ramesh et al the patients showed improved range of movements with superior $p < 0.001$ for VAS, WOMAC and KOOS score which was statistically significant than corticosteroid injection.²³ In a study conducted by Naresh Kumar et al in 2017 concluded that PRP showed a significant improvement in pain and functional status of knee at 1, 3 and 6 months after single intra articular PRP injection.²⁴

In our study of 80 patients 26 had very poor, 23 had poor and 1 had neither poor nor good QOL before PRP injection evaluated by WHOQOL. At 6 months post PRP therapy 5 had very good, 59 had good, 15 had neither good nor poor and 1 had poor QOL which showed highly significant improvement in QOL with $p < 0.001$. (Table 1) In a study conducted by Wang-Saegusa et al evaluated the effects of plasma-rich growth factor (PRGF) on function and QOL of patients with knee OA and reported that the mean changes of WOMAC and related parameters and mean changes of physical parameters of SF-36 questionnaire for QOL were meaningful.²⁵ In a study

conducted by Raeissadat et al concluded that intra-articular knee injection of PRP can decrease joint pain and stiffness and improve patients' QOL in short term.²⁶

In our study of 80 patients 42 were females and 38 were males, with the mean age of 65 years with the most common age group being 61 to 70 years. (Table 2) In our study, we found age to be an important factor determining the clinical outcome. As OA is an age-related degenerative process, it may happen that PRP is more beneficial at incipient stages as compared with the later, when the disease has already progressed. According to studies by Felson et al showed there was a slightly higher prevalence of x-ray changes of OA in women than in men.²⁷ In a study conducted by Akinpelu et al indicated high prevalence of knee OA in women than in men.²⁸

Table 1: Quality of Life in patients before and after injection of PRP (evaluated by WHOQOL)

Quality of Life	Baseline	After 6 Month (Post PRP Thrapy)	P value
Very Good	2	5	0.01*
Good	28	59	
Neither Poor Nor Good	1	15	
Poor	23	1	
Very Poor	26	0	

* indicates statistically significance at $p \leq 0.05$

Table 2: Gender wise Distribution of study participants

Gender	Number	Percentage (%)
Male	38	47.5
Female	42	52.5
Total	80	100

This method appears to be quite safe in view of the fact that it is an autologous preparation, and hence chances of any immunological or allergic reactions are theoretically nil. Limitation of the study was the assessment of patients beyond 6 months and long-term follow-up were out of the scope of this study. Patients with multiple co-morbidities and internal derangements of the knee with previous history of

intra articular tibial plateau fractures or ligament injuries were not considered in our study.

Conclusion

OA knee was commonly observed in female patients with age more than 60 years with more sedentary lifestyle. There were no major complications or incidences of local infection in our study group. Intra-articular injection of autologous PRP is a safe, cheap, easy to prepare and use, and has a therapeutic role in early knee OA. Hence, PRP therapy can be used in management of early stage knee OA to provide relief from symptoms and to improve QOL with negligible complication, low cost and ultimately with good results. Outcome of treatment depends on age, sex and stage of the disease and the inherent potential of the articular cartilage to regenerate.

Ethical approval was taken from the institutional ethical committee and written

Informed Consent was taken from all the participants.

Conflict of Interest: None

Source of Support: Nil

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