

A Prospective Observational Study of Platelet Rich Plasma as A Modality of Treatment for Primary Knee Osteoarthritis

K.N. Sandeep¹, Y. Panduranga Rao^{2*}

¹Assistant Professor, Department of Orthopaedics, Santhiram Medical College, Nandyal, Andhra Pradesh, India

²Assistant Professor, Department of Orthopedics, Santhiram Medical College, Nandyal, Andhra Pradesh, India

Received: 15-09-2021 / Revised: 30-11-2021/ Accepted: 16-12-2021

Abstract

Introduction: Osteoarthritis (OA) is the most common type of arthritis and degenerative disease affecting around 250 million globally. It affects patients socially, psychologically and economically and rates of the disease have been increasing due to obesity and old age. In the United States, the estimated prevalence of OA is 12% compared to 8.1% in China, accounting for around 110 million OA patients globally. **Materials and Methods:** This is a prospective observational study, conducted among 50 patients (selected at conveniences) with knee osteoarthritis who were studied in the outpatient Department of Orthopaedics, Santhiram Medical College, Nandyal. An informed written consent was taken from all the participants. Patients were diagnosed using The American College of Rheumatology (ACR) classification criteria of osteoarthritis. All patients were treated with 3 monthly intra-articular injections of autologous platelet-rich plasma into the knee joint, under local anesthesia on an outpatient basis. **Results:** After 6 months, all patients were re-evaluated according to Age, Sex, BMI (Body mass index), Side involved, Severity (Grade) of osteoarthritis, Pre and post-PRP injection comparison of crepitus, local temperature, Joint line tenderness, Effusion, Range of motion, Visual Analog Scale for pain, International Knee Documentation Committee (IKDC) score (Table 2). The maximum and minimum age in this study was found to be 41 years and 70 years. The average age of the patients was calculated as the total age of patients/ no. Of patients = 52.68 yrs. Out of 100 patients, 64 were females, and 56 were males. Out of 100 knee joints treated, 56 were the right side and 44 were the left side. 64 patients were found to be overweight, 24 were obese, and 12 were normal weight. The grading of osteoarthritis of the knee. **Conclusion:** PRP procedure showed a higher degree of efficacy as well as significant findings of more and longer pain reduction, improved function, and patient satisfaction. This was particularly noticeable in the treatment of younger patients with less severe articular cartilage degeneration. All of the comparative studies suggest that PRP injections are a useful approach and an alternative in the treatment of OA. This minimally invasive procedure appears to be safe and effective. It could be utilized as a reasonable treatment option when other therapies fail or are inappropriate for the particular patient.

Keywords: Osteoarthritis, American College of Rheumatology, Platelet rich plasma.

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Osteoarthritis (OA) is the most common type of arthritis and degenerative disease affecting around 250 million globally. It affects patients socially, psychologically and economically and rates of the disease have been increasing due to obesity and old age. In the United States, the estimated prevalence of OA is 12% compared to 8.1% in China, accounting for around 110 million OA patients globally[1]. Moreover, those under the age of 50 have a prevalence rate of 5.2% while individuals aged 60 are near 11%. In addition to aging and obesity, several risk factors for OA include gender, genetics, smoking and previous joint injury. Moreover, other illnesses such as rheumatoid arthritis and metabolic disorders can decrease bone density, increasing the susceptibility to develop OA[2]. OA patients' common complaints are usually pain, swelling, limitation of movement and stiffness. Such symptoms greatly affect the joint stiffness leading to a decreased range of motion leading to impairment of daily life activities. From the time of Hippocrates until 250 years ago, it was believed that the cause of joint pain was gout. In 1957, Kellgren and Lawrence reported one of the first radiographic classification and scoring systems of OA, grading it from 0 to 4 according to diminished joint space, loss of

cartilage, presence of cysts, sclerosis and osteophytes. However, a combined clinical approach with history, examination and radiological findings are still utilized collectively to be able to diagnose OA. The most common symptoms found with OA are joint pain, stiffness, swelling and decreased range of motion with the progression of OA being related to the progression of worsening symptoms[3]. In some studies, women have shown increased rates of cartilage loss and progression of knee cartilage defects than men. Analgesics, non-steroidal and steroidal anti-inflammatory drugs, glucosamine/ chondroitin supplementation, physical therapy, and hyaluronic acid injections are useful in the treatment of osteoarthritis. However, most of them not addressing the pathology or have shown only minor benefits and significant side effects[4]. New experimental studies have begun to target the biomechanical process of osteoarthritis with the focus on repairing cartilage or replacement. Autologous platelet-rich plasma therapy has got particular attention, in which high concentration of platelets achieved in a short volume of plasma after being placed in a centrifuge. Platelets play a vital part in tissue homeostasis[5]. Our chief aim was to study the effects of intra-articular injections of Platelet-rich plasma in the management of knee joint osteoarthritis and to compare the results with standard studies and draw conclusion.

*Correspondence

Dr. Y. Panduranga Rao

Assistant Professor, Department of Orthopedics, Santhiram Medical College, Nandyal, Andhra Pradesh, India.

E-mail: panduranga3@yahoo.com

Materials and Methods

This is a prospective observational study, conducted among 50 patients (selected at conveniences) with knee osteoarthritis who were

studied in the outpatient Department of Orthopaedics, Santhiram Medical College, Nandyal. An informed written consent was taken from all the participants. Patients were diagnosed using The American College of Rheumatology (ACR) classification criteria of osteoarthritis. All patients were treated with 3 monthly intra-articular injections of autologous platelet-rich plasma into the knee joint, under local anesthesia on an outpatient basis. All these cases were treated from January 2020 to December 2020. A detailed history was taken. A preliminary general and physical examination were done. Build and nourishment noted. Systemic examination of the cardiovascular, respiratory, gastrointestinal and genitourinary examination was followed as routine. A detailed local examination of the knee joint was done. Data was entered in MS Excel 2007 and analysed. Preparation of autologous platelet-rich plasma (PRP)-30 ml of venous blood was taken from every patient and collected in sterile sodium citrated tubes. The tubes with citrated blood were centrifuged at 1800 rpm for 15 min to separate erythrocytes, and at 3500 rpm for 10 min to concentrate platelets. By this method, 3-5 ml of platelet-rich plasma were obtained and injected immediately without storage. It has been stated that using freshly harvested PRP might preserve all the platelet functions better. PRP knee intra-articular injection technique- The injection was given in the supine position and with all aseptic precautions. The affected side was exposed up to the thigh and cleaned with betadine scrub (7.5%) and spirit. Then painted with 5% betadine solution and draped with linen towels. The knee joint was palpated, and good understanding of anatomical configuration was made. 2% Xylocaine injection was given in the skin and soft tissues of the lateral aspect of knee joint. The leg was held firm in neutral rotation, and intra-articular injection of autologous platelet-rich plasma was given by the lateral approach with knee in complete extension using a 23-gauge needle. After injection, patients were instructed not to use the injected leg for 24 h, use ice packs over the injected joint and not to use NSAIDs during this period.

Inclusion Criteria: Patients with history of chronic pain (of at least 4 months duration) or swelling of the knee, not responding to NSAIDs and/or physical therapy with radiographic findings of grade 1 (definite osteophyte, unimpaired joint space) and grade 2 (moderate

diminution of joint space osteoarthritis of the knee joint) according to Kellgren-Lawrence scale were included in the study.

Exclusion Criteria

Patients with diabetes, rheumatoid arthritis, major axial deviation (varus of more than 5 deg/valgus more than 5 deg), haematological diseases (coagulopathies), severe cardiovascular diseases, infections, immunosuppression, patients on therapy with anticoagulants-anti aggregants or nonsteroidal anti-inflammatory drugs within 5 days before blood donation, were excluded from the study. Follow up Assessment after 6 months, all patients were re-evaluated by physical examination, assessment of visual analog scale for pain, international knee documentation committee (IKDC) score.

Statistical Analysis

Chi-square test was used to assess differences between quantitative and qualitative data at baseline and after 3 PRP injections. Spearman's correlation coefficient analysis was performed to identify factors associated with better functional outcomes. The clinical features were evaluated using the chi-square test. The VAS scale and IKDC score were assessed using chi square test. A statistically significant cutoff value was set at $p < 0.05$.

Results

After 6 months, all patients were re-evaluated according to Age, Sex, BMI (Body mass index), Side involved, Severity (Grade) of osteoarthritis, Pre and post-PRP injection comparison of crepitus, local temperature, Joint line tenderness, Effusion, Range of motion, Visual Analog Scale for pain, International Knee Documentation Committee (IKDC) score (Table 2). The maximum and minimum age in this study was found to be 41 years and 70 years. The average age of the patients was calculated as the total age of patients/ no. Of patients = 52.68 yrs. Out of 100 patients, 64 were females, and 56 were males. Out of 100 knee joints treated, 56 were the right side and 44 were the left side. 64 patients were found to be overweight, 24 were obese, and 12 were normal weight. The grading of osteoarthritis of the knee.

Out of 100 study patients, 48 patients had grade 1 osteoarthritis, and 52 patients had grade 2 osteoarthritis. The clinical features were evaluated using the chi-square test. The VAS12 scale and IKDC13 score were assessed using the chi square test.

Table 1: Kellgren-Lawrence Grading of Patients with Primary Osteoarthritis

Kellgren-Lawrence Scale	No. of Patients	Percentage
Grade 1 (Doubtful)	48	48%
Grade 2 (Mild)	52	52%
Grade 3 (Moderate)	0	0%
Grade 4 (Severe)	0	0%

Table 2: Clinical Evaluation of Patients with Primary Osteoarthritis after PRP Injection

Clinical data	Baseline (No. Patients out of 100)	After 6 Months Follow Up (No. of Patients out of 100)	Chi Square Value	P Value
Local rise of temp	10	0	7.76	<0.005
Tender joint line	66	30	12.98	<0.001
Crepitus	66	40	6.78	<0.001
Effusion	10	10	0	1
Limited range of movements	36	10	9.54	<0.002

Discussion

Osteoarthritis is a major public health problem which causes pain and disability in one-third of all affected patients. The symptoms are often associated with notable functional impairment, as well as signs and symptoms of inflammation, including pain, stiffness, and loss of movement. Multiple factors are known to affect the progression of OA, including joint instability and/or malalignment, obesity, increasing age, associated intra-articular crystal deposition, muscle weakness, and peripheral neuropathy. Advances in molecular biology raise hopes that new therapeutic targets will be identified that will allow more than just symptomatic therapy. Joint replacement is still

the unsurpassed therapy for advanced and incapacitating OA[6]. However, with increasing appreciation of the contribution of all three joint compartments to disease progression, research in OA pathogenesis, biomarkers, and treatment has broadened immensely, and many new potential therapeutic targets have emerged over the past years. The growing interests in the use of PRP in OA treatment, which might provide cellular and humoral mediators to promote tissue healing and repair have gained momentum in the past few years and led to several studies[7]. Autologous plasma is a biological therapy approach with the goal of delivering concentrated platelets to accelerate and support the healing of injuries to hard and soft tissue

without exposing the patient to major risks. Growth factors, an essential part of PRP, induce differentiation of mesenchymal stem cells into chondrocytes and thereby increase cell proliferation. They also suppress inflammatory mediators such as interleukin-1, encourage matrix deposition, and slow down catabolism[8]. Hence, growth factors help stabilize cartilage homeostasis and possibly reverse articular degeneration. The use of autologous blood versus synthetic chemicals also eliminates the risk for allergic reaction or disease transfer in addition to limiting possible drug toxicity. The simple and efficient in-house preparation at the time of patient visit proves to be of advantage for the PRP procedure[9]. In our study 100 patients with Grade 1 or Grade 2 knee osteoarthritis treated with 3 monthly injections of platelet rich plasma and following conclusion made after six months of follow up. The average age documented was 52.68 years. Osteoarthritis of the knee was common in 5th and 6th decade of life, the commonest in between 51- and 55-years age group. In this study, 82 patients were found to be below the age of 60 years. Also, results were found to be better in the younger patients when compared to the older. In this study 64 patients (64%) were females, and 36 (36%) patients were male. The baseline visual analog score in female patients was 5.93 and 3.45 at 6 months, and that in males was 5.98 (Baseline) and 3.36 (at 6 Months) thus showing that there is no notable difference in response to treatment between males and females. The value of IKDC13 score in males was 38.75 (Baseline) and 76.08 (at 6 Months) and that in females was 38.42 (Baseline) and 76.14 (at 6 Months) therefore showing no significant difference in response to treatment in between males and females[10]. Side effects related to the injection of platelet-rich plasma are considered uncommon and, when present, usually manifest in a mild and self-limited form. In our study, 12 patients experienced slight pain at the site of injection which lasted for one week and only one patient experienced marked pain. One patient had skin discoloration in the form of bruising. No cases suffered from infection or allergic reaction. Local symptoms are the most usual adverse events, ranging from pain at the injection site to signs of arthritis[11,12]

Conclusion

PRP procedure showed a higher degree of efficacy as well as significant findings of more and longer pain reduction, improved function, and patient satisfaction. This was particularly noticeable in the treatment of younger patients with less severe articular cartilage degeneration. All of the comparative studies suggest that PRP injections are a useful approach and an alternative in the treatment of OA. This minimally invasive procedure appears to be safe and effective. It could be utilized as a reasonable treatment option when other therapies fail or are inappropriate for the particular patient.

References

Conflict of Interest: Nil

Source of support: Nil

1. Murray I, Mandelbaum B. Management of knee articular cartilage injuries in athletes: Chondroprotection, chondrofacilitation, and resurfacing. *Knee Surg Sports Traumatol Arthrosc.* 2015; 24:1617-1626.
2. Andia I, Maffulli N. Platelet-rich plasma and mesenchymal stem cells: Exciting, but are we there yet? *Sports Med Arthrosc Rev.* 2018; 26(2):59-63.
3. Boswell SG, Cole BJ, Sundman EA et al. Platelet-rich plasma: A milieu of bioactive factors. *Arthroscopy.* 2012; 28(3):429-439.
4. Akeda K, An HS et al. Platelet-rich plasma stimulates porcine articular chondrocyte proliferation and matrix biosynthesis. *Osteoarthr Cartil.* 2006; 14(12):1272-1280.
5. Pereira RC, Scaranari M, Benelli R et al. Dual effect of platelet lysate on human articular cartilage: A maintenance of chondrogenic potential and a transient proinflammatory activity followed by an inflammation resolution. *Tissue Eng Part A.* 2013; 19(11-12):1476-1488.
6. Altman R, Asch E, Bloch D et al. Development of criteria for the classification and reporting of osteoarthritis: Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum.* 1986; 29:1039-1049.
7. Sundman EA, Cole BJ, Karas V et al. The anti-inflammatory and matrix restorative mechanisms of platelet-rich plasma in osteoarthritis. *Am J Sports Med.* 2014; 42(1):35-41.
8. Anitua E, Sanchez M, Nurden AT et al. Platelet-released growth factors enhance the secretion of hyaluronic acid and induce hepatocyte growth factor production by synovial fibroblasts from arthritic patients. *Rheumatology (Oxford).* 2007; 46(12):1769-1772.
9. Stratz C, Nührenberg TG, Binder H et al. Micro-array profiling exhibits remarkable intra-individual stability of human platelet micro-RNA. *Thromb Haemost.* 2012; 107(4):634-641.
10. Ahlback S. Osteoarthrosis of the knee: A radiographic investigation. *Acta Radiol Diagn (Stockh) Suppl.* 1968; 277:7-72.
11. Gato-Calvo, Ruiz-Romero C, Blanco FJ, Burguera EF. Platelet-rich plasma in osteoarthritis treatment: Review of current evidence. *Ther Adv Chron Dis.* 2019; 10:2040622319 825567.
12. Yuan A, Farber EL, Rapoport AL et al. Transfer of microRNAs by embryonic stem cell microvesicles. *PLoS One.* 2009; 4(3):Article ID e4722.