



ISSN (P): 2521-3466
ISSN (E): 2521-3474
© Clinical Orthopaedics
www.orthoresearchjournal.com
2020; 4(3): 38-41
Received: 21-05-2020
Accepted: 23-06-2020

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Role of autologous platelet rich plasma in early stages of osteoarthritis of knee

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DOI: <https://doi.org/10.33545/orthor.2020.v4.i3a.234>

Abstract

Background: In the treatment of early stage osteoarthritis with intraarticular injection there are many available options as steroid, hyaluronic acid and platelet rich plasma. Platelet-rich plasma (PRP) is a concentrate of autologous blood growth factors which has been shown to provide some symptomatic relief in early osteoarthritis (OA) of the knee. The Aim of this study is to evaluate the effectiveness of Platelet Rich Plasma in reducing pain and improving physical function.

Materials and Method: A Prospective study of 30 Patient with Early stage (Stage 1 and 2) of Osteoarthritis who satisfies the inclusion criteria from August 2019 to June 2020 in Babuji Hospital and Chigateri Government Hospital attached to JJM Medical College, Davangere. All patients were injected with autologous platelet rich plasma and evaluated for VAS (Visual analog scale) and WOMAC (Western Ontario and McMaster Universities) scoring system on (pre-procedure) day 0 and (post-procedure) at the end of 4 weeks, 12 weeks, 24 weeks.

Result: In our study age distribution revealed mean age in is to be 46.6 years. The gender distribution of 66.66% of male and 33.33% of female. The mean BMI of the patient is 25.65. In this study 43.33% belong to Grade 1 and 56.66% patient belong to Grade 2 classification according to Kellgren Lawrence classification of OA knee. The Global WOMAC showed a mean of 61.3 at pre injection period which decreased to 48.46 at 4 weeks follow up and 37.90 at 12 weeks and declining to 27.33 at 24 week. The mean VAS score showed 6.33 at pre injection period which decreased to 4.4 at 4 weeks follow up and 2.5 at 12 weeks and declining to 1.76 at 24 week.

Conclusion: Platelet-rich plasma therapy is a simple, low-cost and minimally invasive intervention which is feasible to deliver to treat degenerative lesions of articular cartilage of the knee.

Keywords: Platelet rich plasma, osteoarthritis, WOMAC, VAS

Introduction

Osteoarthritis [OA] is a complex whole joint, chronic, degenerative disease caused by inflammatory mediators rather than purely a process of wear and tear. OA is a most common joint disease in India and major cause of pain and disability in adults [1]. Recent studies have shown that the incidence of OA of knee is increasing compared to other joints, especially in young adults.

Bilateral knee OA is more common than unilateral disease, affecting 5% versus 2%, respectively, of persons 45 to 74 years of age [2]. Having OA in one knee increases the likelihood of having OA in the contralateral knee [3]. It is believed that tibiofemoral OA is more common than patellofemoral OA.

OA is usually classified as primary (idiopathic) or secondary to metabolic conditions, anatomic abnormalities, trauma, or inflammatory arthritis.

The prevalence of radiographic knee OA rises in women from 1% to 4% in those 24 to 45 years of age to 53% to 55% in those of age 80 years and older. In men, the prevalence rises from 1% to 6% in those 45 years and younger to 22% to 33% in those 80 years and [4, 5, 6].

There are modifiable and non-modifiable risk factors. Modifiable risk factors include body weight and physical activity and non-modifiable risk factors include age, sex, race and genetic susceptibility [7].

Apart from cartilage degradation, it also involves synovitis, sub-condral bone re-modelling, degradation of ligaments and menisci and hypertrophy of the joint capsule takes part in its

pathogenesis. The hyaline cartilage provides friction free joint movement from underlying bone from excessive load and trauma. Cartilage has limited healing potential because it is avascular and few specialized cells with low mitotic activity. Once injured, cartilage degenerates leading to OA [8].

Currently treatment of OA mainly focuses on relieving of symptoms and improving day to day physical activities. Non pharmacological modalities are patient education, weight reduction, exercises, walking support, shoes and in sole modification. Pharmacological therapy include Non-steroidal anti-inflammatory drugs, opioids, and slow acting drugs like glucose amine and chondroitin sulfate. Intra articular injections like platelet rich plasma (PRP), corticosteroids, hyaluronic acid, autologous mesenchymal stem cells [7, 8]

The Aim of this study is to evaluate the effectiveness of Platelet Rich Plasma in reducing pain and improving physical function, as Platelet Rich Plasma provides a cocktail of growth factors directly into joint cavity. Platelet Rich Plasma is postulated to modify the disease process, unlike other methods of nonsurgical treatment which provide symptomatic relief.

Material and methodology

A Prospective study of 30 Patient with Early stage (Stage 1 and 2) of Osteoarthritis who satisfies the inclusion criteria who comes to Orthopaedics Outpatient Department in Bapuji Hospital and Chigateri Government Hospital attached to JJM Medical College, Davangere from August 2019 to June 2020. Patients will be taken for this study after obtaining the informed and written consent. Inclusion criteria includes Patient with age between 30-80yrs of both sex, patient with radiological osteoarthritis of knee (Kellgren Lawrence grade 1 and 2 based on x rays), patient with severe pain and under anti-inflammatory treatment without improvement for more than 3 months, consent from patient for treatment, regular OPD patient. Exclusion criteria includes Patient with age less than 20yrs and more than 80 yrs. Patient with Advanced OA (Kellgren Lawrence grade 3 and 4), patient with h/o prior intra articular injection at treatment within 3 months of duration, patient with Autoimmune disease, Polyarthrititis, Inflammatory arthritis, Rheumatoid arthritis, patient with local infection at the procedure site, patient with haemoglobin < 10mg/dl and platelet <10⁵ cells/microliter, patient with bleeding and coagulation disorder, patient with HIV, Hepatitis B or C, cellulitis, septicemia and other systemic metabolic disorder, patient not willing to participate.

Preparation of platelet rich plasma (PRP)

The preparation of the PRP begins by taking specific volume of autologous blood from the patient, through a syringe containing an anticoagulant. This sample is then centrifuged with double centrifugation technique. The patient is explained about procedure in there understandable language and 10ml of venous blood is withdrawn in 3.8% sodium citrate tube and subjected for 1st centrifugation at a spin rate of 3000 rpm for 10minutes. The centrifused sample has two layers, an inferior layer containing erythrocytes and a superior layer consisting plasma, in which the plasma layer will be isolated. This plasma is collected in a plain tube and subjected for 2nd centrifugation at rate of 5000 rpm for 10 minutes. The resultant solution contain upper 2/3 platelet poor plasma and lower 1/3rd platelet rich plasma. Every 10ml of blood yields 1-2 ml of platelet rich plasma solution.

Procedure

Having prepared the skin of the patient with iodine solution and

using a no touch technique, the autologous platelet rich plasma was injected into knee joint using anterior approach either through medial or lateral joint line after flexing the knee for about 50-60 degree. After the procedure, gentle knee immobilization for equal distribution of Platelet rich plasma, sterile dressing was done and crepe bandage was applied. The patient were trained for home based active quadriceps and knee strengthening exercise. The patients were advised for weight bearing immediately. The patient were followed up at 4 weeks, 12 weeks, 24 weeks.

Result

Out of 30 cases, 20 (66.66%) were males and 10 (33.33%) were females. The age ranged from minimum of 36 years to maximum of 58 years. The mean age of patients in is 46.6 years. In these patients 13 (43.33%) belong to Grade 1 and 17(56.66%) patients belong to Grade 2 according to Kellgren Lawrence classification. The mean BMI of patients is 25.65, of which 12 patients (40%) are in Normal (18.5-24.9) and 18 patients (60%) are in Overweight (25-29.9) group. The mean pre-procedural VAS and WOMAC score were 6.33 and 61.3 respectively. At the end of 24weeks, the mean VAS and WOMAC score improved to 1.76 and 27.33 respectively.

Table 1: Base line characteristics of patients

Base line characteristics	
Age (years)	36-58 (Mean-46.6)
Total participants	30
Male	20 (66.66%)
Female	10 (33.33%)
Male to Female ratio	2:1
BMI	25.65(mean)
Normal (18.5-24.9)	12 (40%)
Overweight (25-29.9)	18 (60%)
Obese (>30)	0
Kellgren-Lawrence Classification	
Grade 1	13 (43.33%)
Grade 2	17 (56.66%)

Table 2: Outcome Measure (Mean)

	VAS	WOMAC
Pre-procedure	6.33	61.3
4 weeks	4.4	48.46
12 weeks	2.5	37.90
24 weeks	1.76	27.33

Discussion

Osteoarthritis (OA) of knee is also called as osteoarthrosis, chondromalacic arthrosis, degenerative arthritis or arthritis deformans of knee. Osteoarthritis is a chronic, progressive and degenerative joint disease characterized by gradual loss of hyaline cartilage resulting in formation of bony spurs, subchondral sclerosis and cysts at the margins of the joints. Bilateral OA knee (5%) is more common than unilateral OA knee (2%). In the Framingham study, 2% of women per year developed radiographic knee OA, and 1% per year developed symptomatic knee OA, versus 1.4% and 0.7% of men, respectively.

It is hypothesized that osteoarthritis has the higher rate of cartilage degeneration than the rate of cartilage repair. OA destabilize the normal coupling of degradation and synthesis of articular cartilage chondrocytes and extracellular matrix, and subchondral bone. OA has a strong and significant evidence that

chondrocytes may transduce mechanical signals into biochemical responses through various intracellular and intercellular signaling pathways, including activation of second messenger pathways such as cyclic AMP (cAMP), inositol trisphosphate, or calcium ion [9]. OA is manifested by morphologic, biochemical, molecular, and biomechanical changes of both cells and matrix which lead to a softening, fibrillation, ulceration, loss of articular cartilage, sclerosis and eburnation of subchondral bone, osteophytes and subchondral cysts.

The platelet rich plasma act as a minimally invasive procedure which bridges the gap between pharmacological treatment and surgical treatment for osteoarthritis. It provides a strong and positive balance between pro-apoptotic and anti-apoptotic molecules, pro-inflammatory and anti-inflammatory cytokines & pro-angiogenic and anti-angiogenic factors for rejuvenation of degenerated cartilaginous tissues. Once PRP is activated, plasma fibrinogen polymerizes into a 3D fibrin scaffold, which contains heparan sulphate binding domains for growth factors, cytokines, chemokines, ECM components, cell adhesion molecules and acute phase proteins. This biodegradable 3D scaffold provides plastic-elastic stiffness and generates growth factors for cell proliferation, differentiation and migration. Once injected into the joint, 3D scaffold is converted into a viscous and malleable structure and further fibrinolysis begins and sustained release of growth factors occurs [10-11].

The growth factors rejuvenate the cartilage by producing IL-1Ra and other anti-apoptotic, anti-inflammatory and pro-angiogenic factors. The platelet rich plasma upregulates tissue inhibitor of metalloproteinases such as TIMPs -1, -3 and -4 by downregulating the signalling molecules of matrix metalloproteinases such as MMP-1, MMP-3, MMP-13 & MMP-28 and upregulation of ADAMTS-4 and 5 which lead to normal joint homeostasis [12].

In our study age distribution revealed mean age in is to be 46.6 years. The gender distribution of 66.66% of male and 33.33% of female. The mean BMI of the patient is 25.65. In this study 43.33% belong to grade 1 and 56.66% patient belong to grade 2 classification according to Kellgren Lawrence.

The Global WOMAC showed a mean of 61.3 at pre injection period which decreased to 48.46 at 4 weeks follow up and 37.90 at 12 weeks and declining to 27.33 at 24week.

The Visual analog score showed a mean 6.33 at pre injection period which decreased to 4.4 at 4 weeks follow up and 2.5 at 12 weeks and declining to 1.76 at 24week.

Soo Jin Jang *et al.* [13] studied the effectiveness of one dose of intra-articular PRP injections for early osteoarthritis in 65 patients who were evaluated at 1, 3, 6, 9 and 12 months after the procedure. They showed improvement of mean VAS score from 7.4 to 4.2 at 6 months follow up. The IKDC score showed a statistically significant outcome with p value < 0.05.

Pilot and prospective studies investigating the clinical efficacy of intra-articular injections of PRP in patients with knee OA have demonstrated clinical improvement in self-reported pain and functional capacity with no major adverse effects [14].

This study showed a significant decrease in global WOMAC score and VAS score, which was also consistent throughout the study period without any major side effect.

Conclusion

Osteoarthritis represents a failure of diarthrodial joint, characterized by degenerative changes in articular cartilage of joint. The management of Osteoarthritis has undergone change during the last century. Osteoarthritis has been managed by

conservative methods like lifestyle changes, physiotherapy and surgical methods like joint replacement arthroplasty, depending upon the stage of the disorder.

Platelet-rich plasma therapy is a simple, low-cost and minimally invasive intervention which is feasible to deliver to treat degenerative lesions of articular cartilage of the knee. Though it is not a permanent solution for knee OA but it relieves pain, improve function and quality of life in early stages of OA knee. This therapy appears to have minimal associated adverse event.

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