Intra Articular PRP Injection for Stage 1&2 Osteoarthritis of Knee

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Abstract: _Background: Platelet rich plasma (PRP) is defined as a volume of the plasma fraction of Autologous blood having a platelet concentration above baseline. Platelets contain bioactive proteins responsible for attracting macrophages, mesenchymal stem cells, and osteoblasts which not only promote removal of necrotic tissue, but also enhance tissue regeneration. Osteoarthritis of knee is a chronic and progressive joint disease that leads to articular cartilage damage, bone deformation, osteophyte formation and synovial inflammation. Treatment options for knee OA vary from simple analgesia in mild cases to knee replacement for advanced disease. Knee pain and early degeneration due to early stages of OA can be targeted with regenerative techniques such as use of intra articular platelet rich plasma was proposed. In this review, we present a comprehensive overview of the efficacy of Intra articular PRP for stage 1&2 OA of knee. Materials and Methods: A Prospective study was carried out in orthopaedics department from the month of January 2020 to December 2020, patients with Osteoarthritis of knee stage 1&2 have been included in this study and been followed up till December 2021 and have been evaluated based on WOMAC and VAS score system. Results: Among 31 patients who were willing and consented for study with Osteoarthritis of knee stage 1 (11 Males and 20 Females) the mean WOMAC score and VAS score were improved statistically following intra articular PRP injection. Conclusions: PRP plays an important role in tissue repair, regeneration, and the differentiation of mesenchymal stem cells to treat degenerative lesions of articular cartilage of the knee. This therapy appears to have minimal associated adverse events and have beneficial effects in terms of pain, stiffness, patient satisfaction and better functional outcomes._

Keywords: Intra Articular PRP, Platelet Rich Plasma OA Knee, Osteoarthritis Knee, PRP IN OA Knee, Stage 1 & 2 OA Knee

1. Introduction

Osteoarthritis of knee is a chronic and progressive joint disease that leads to articular cartilage damage, bone deformation, osteophyte formation and synovial inflammation[1]. Osteoarthritis of the knee is one of the most common disorders in the elderly, with a prevalence of 22-39% in India and is more common in women than men [2, 3]. Nearly 45% of people of over age of 65 years have symptoms while radiological evidence is found in 70% of those over 65 years[4, 5]. Without adequate treatment, the condition progresses continuously due to cartilage damage and inflammatory change. This gradual progression is due to the limited regeneration potential of articular cartilage[2]. Thus, repetitive trauma, injuries, and aging lead to thinning of the joint space and eventually, limited and painful joint movement. Given the high incidence of this disease and costs of medical treatments, OA can be considered an economic burden on society. Available treatments for OA can be classified into three groups: drug, nondrug/ nonsurgical (eg, physical and rehabilitation therapy, occupational therapy, massage, exercise)-which are the primary line of treatment-and surgical therapies[6, 7]. However, nonsurgical treatment has recently garnered greater attention. The sequence of treatment application begins with drug therapies and ends with surgical therapies. There are several different options which have been extensively studied that have been shown to be effective at symptom relief: these include non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular hyaluronidase injections, corticosteroids, and more recently, PRP [6, 7].

Platelet-rich plasma (PRP), a blood derivative that has a higher platelet concentrate than whole blood, after activating releases a group of biologically active proteins that bind to the transmembrane receptors of their target cells, promoting cellular recruitment, growth, morphogenesis and modulating inflammation as well.[8]

Platelet rich plasma was activated by addition of 0.5ml of a 5% solution of $CaCl_2$ in PRP tube. The gelation was determined by the visualization of the clot and the gel remaining attached to the tubes after turning it upside down.[9]

Growth factors released from platelet includes platelet-derived growth factor (PDGF), epidermal growth factor (EGF), insulin-like growth factor (IGF-I), transforming growth factorβ-I (TGFβ-I), vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), stromal cell derived factor (SDF 1alpha), Platelet factor 4 (PF 4), and basic fibroblast growth factor (bFGF), which provide stimulus for the healing of tissues through interaction with specific cells.[10, 13]

The active secretion of growth factors by platelets begins within 10 min after activation with 10% calcium chloride with more than 95% of the pre-synthesized growth factors secreted within 1 hour.[11]

OA Knee is associated with a degenerative process that occurs in the articular cartilage with other changes. Therefore, PRP due to its high content of various growth factors may be more effective as a healing agent. Injectable medications that can cause regenerative changes in tissue

structure manage and alleviate OA symptoms, and help cope with the underlying tissue pathology are very important. This importance is due to the fact that these medicines are not only palliative but also reconstructive and preventive against replacement surgeries. Platelet-rich plasma (PRP) exists in this category. Platelets-besides contributing to the process of haemostasis-play different critical roles in the body. For example, following a tissue injury, platelets attract white blood cells to the site of injury and prevent damaged cells from being infected. Moreover, platelets contain a growth factor (i. e. Platelet derived growth factor [PDGF]) that increases the production of stem cells. This characteristic has made platelets attractive in OA treatment[7].

2. Objectives

To evaluate pain, stiffness and functional limitation of knee joint following Autologous platelet rich plasma (PRP) injection among adults with Stage 1 &2 Osteoarthritis of knee in a tertiary care centre.

3. Material and Methods

A Hospital based prospective study was conducted among 31 adults (35-70 years) who presented with knee pain due early OA knee to the out-patient department of Orthopaedics at GSL Medical College, Rajahmundry, for a period of 1 year (January 2020 to December 2020)

3.1 Inclusion Criteria:

1) Patients above age 35 yrs with complaints of Knee pain due to stage 1&2 OA knee based on the Kellgren-Lawrence [KL] radiological classification with failed conservative management of at least 4 weeks duration.
2) Patients of either sex
3) Age between 30 years to 70 years

3.2 Exclusion Criteria:

1) Patients with known case of Diabetes Mellitus,
2) Patients who had received steroid injection within 3 months
3) Refusal of consent
4) previous history of knee surgery
5) use of anticoagulant or non steroidal anti-inflammatory drugs (NSAIDs) in the previous 7 days
6) Knee pain due to inflammatory arthritis like rheumatoid Arthritis, crystal arthropathies like gout and haemophilia
7) Infection or ulcer at the injection site

Ethical clearance from Institutional Ethical Committee of GSL Medical College, was obtained before initiating the study. Prior to the commencement of the study, informed consent was taken from the study participants after explaining the purpose of the study in vernacular language in an understandable manner.

1. Data Collection

All the patients who presented to the orthopaedic OPD and satisfied the inclusion criteria were considered for the study. A total of 37 cases of stage 1 OA knee came to Orthopaedic OPD during the study period, among which 6 of them did not give consent for treatment with injection PRP. Hence, data for study was collected from 31 patients.

2. Procedure:

5.1 Initial Assessment

The primary information, including age, gender, body mass index (BMI), was recorded for all patients. Patients were assessed clinically, a thorough history and clinical examination was carried out. The subjective symptoms and objective signs were recorded in a pre defined proforma. This was followed by routine investigations as well as an X-ray of the knee followed by its staging using Kellgren-Lawrence [KL] radiological classification and other causes that cause knee pain were ruled out. Once the diagnosis of early OA Knee was established, PRP injection was given to the patient. Then the patients were followed up for a period of 12 months. Assessment of functional outcome was done using Visual Analogue Scale (VAS) scores and WOMAC scores recorded before treatment and follow up at 1st month, 6th month and 12th month based on following criteria.

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The WOMAC measures five items for pain (score range 0-20), two for stiffness (score range 0-8), and 17 for functional limitations (score range 0-68). Thus, the possible WOMAC score is between 0 and 96 [12].

5.2 Injection of PRP:

A 20-mL blood sample was drawn under sterile conditions and placed in specialized centrifuge kits for the preparation of PRP. Then, the blood was centrifuged for 20 minutes at a rotation speed of 3, 200 rpm. The plasma was separated and recentrifuged for 5 minutes at a rotation speed of 1, 500 rpm. Then, 4 mL of the separated plasma was prepared for intra-articular injection for patients. After administration of local anesthesia, under aseptic precautions, a 50 mm long 22-gauge needle was inserted into the knee joint at the upper outer quadrant of the patella and injection given into the joint space. Using the WOMAC index and VAS score, levels of pain and knee function were evaluated and recorded for each patient at specified time points-immediately prior to the first injection, 1 month later, 6 months later, and 12 months later.

3. Statistical Analysis

Data extraction and analysis was done using Microsoft Excel 2007 and SPPS version 2.0. Results were expressed as percentages for categorical variables.

Continuous variables were expressed as mean and standard deviation. Paired 't' test was applied to compare the mean

scores at every follow-up. A 'P' value of <0.05 is considered as statistically significant.
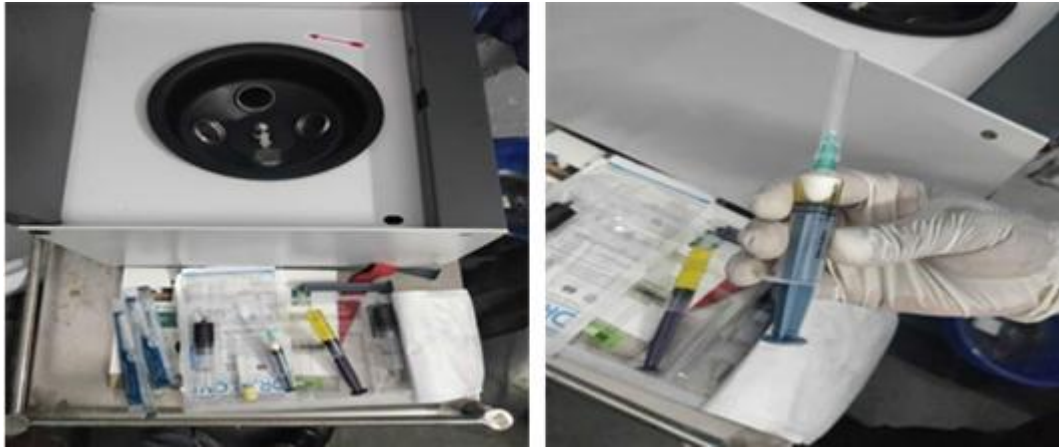

4. Results and Discussion

A total of 31 patients of stage 1&2 OA knee were evaluated. About 4 (12.9%) belonged to 30-40 years age group, 9 (29%) belonged to 41-50 years age group, 13 (41.9%) belonged to 51-60 years age group and 5 (16.2%) belonged to 61-70 years age group. Females constituted majority, 20 (64.5%) while Males were 11 (35.5%). Mean age of the study subjects in this study was 50.61 years ±9.01. Mean age of the patients in PRP group in a study by Poupak Rahimzadeh et al is 65.5 years, and participants' age ranged between 41 to 70 years[13]. In the present study, majority 22 (70.9%) of the subjects were aged 41-60 years and 4 (12.9%) were below 40years and 5 (16.2%) were above 60 years. Right side was predominantly involved with 17 (54.8%) of subjects and 14 (45.2%) on left side.
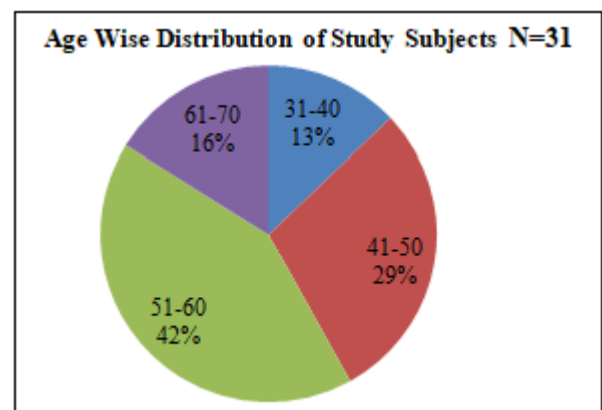
Graph 1: Age Wise Distribution of Study Subjects N=31
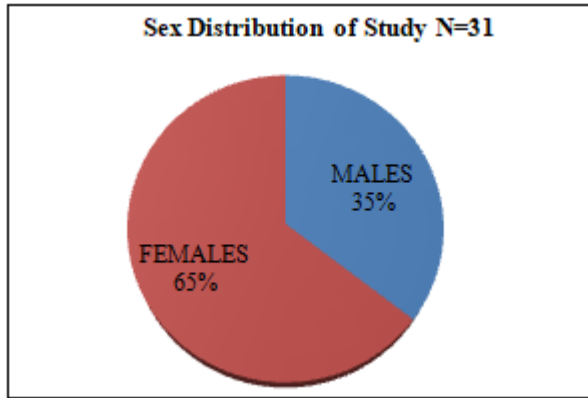
Graph 2: Sex Distribution of Study N=31
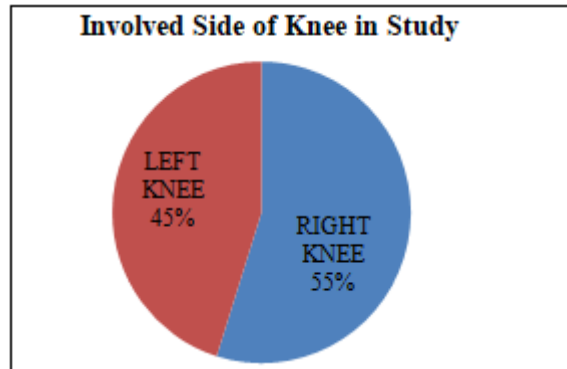
Graph 3: Involved Side of Knee in Study N=31

Table 1: Mean VAS score at pre and post injection at different follow up visits

Variables	Mean	Standard Deviation	P Value
At the time of injection	7.709	1.51	
1ST Month After Injection	3.806	1.42	<0.000001
6 Months After Injection	2.290	1.24	<0.000001
12 Months After Injection	4.225	1.47	<0.00001

Table 2: Mean WOMAC score at pre injection of PRP

Variables	Mean	Standard Deviation
Pain Level	13.064	3.66
Stiffness	5.258	2.01
Functional Limitation	46.612	10.80
WOMAC Score	64.934	12.51

Table 3: Mean Pain Level at pre and post injection at different follow up visits

Variables	Mean	Standard Deviation	P Value
At the time of injection	13.064	3.66	
1ST Month After Injection	7.709	2.73	<0.00001
6 Months After Injection	5.225	2.20	<0.00001
12 Months After Injection	8.258	2.74	<0.00001

Table 4: Mean Stiffness at pre and post injection at different follow up visits

Variables	Mean	Standard Deviation	P Value
At the time of injection	5.258	2.01	
1ST Month After Injection	3.266	1.99	<0.00001
6 Months After Injection	2.677	1.11	<0.00001
12 Months After Injection	3.354	1.30	<0.00001

Table 5: Mean Functional Limitation at pre and post injection at different follow up visits

Variables	Mean	Standard Deviation	P Value
At the time of injection	46.612	10.80	
1ST Month After Injection	31.806	12.07	<0.00001
6 Months After Injection	23.419	7.736	<0.00001
12 Months After Injection	25.741	4.774	<0.00001

Table 6: Mean WOMAC SCORE at pre and post injection at different follow up visits

Variables	Mean	Standard Deviation	P Value
At the time of injection	64.934	12.51	
1ST Month After Injection	42.781	10.35	<0.00001
6 Months After Injection	31.321	12.01	<0.00001
12 Months After Injection	37.353	10.28	<0.00001

The mean pain scores at baseline have been mentioned in Table 3. As we can see the pain score dropped from 13.064 before treatment to 5.225 in the sixth month and then rose to 8.258 in the 12th month. In detail, all pair wise comparisons of pain in different time periods for pre and post PRP were statistically significant by t test with t value of 10.28 and p value obtained was <0.00001

The mean stiffness score from the baseline values have been mentioned in Table 4. As we can see the stiffness score dropped from 5.258 before treatment to 2.677 in the sixth month and then rose to 3.354 in the 12th month. In detail, all pair wise comparisons of physical activity in different time periods for pre and post PRP injections were statistically significant by t test T value of with P value <0.00001.

The severity of knee OA was assessed using the patients' WOMAC scores (ie, the sum of functional limitations, stiffness, and pain-level scores). Mean physical activity (or functional limitation) scores recorded at baseline values are mentioned in Table 5. As we can see the physical activity score dropped from 46.612 before treatment to 23.419 in the sixth month and then rose to 25.741 in the sixth month. In detail, all pair wise comparisons of physical activity in different time periods for pre and post PRP injections were statistically significant by t test T value of 5.08 with P value <0.00001.

The mean WOMAC scores at baseline are reported in Table 6., the WOMAC score dropped from 64.934 before treatment to 31.321 in the sixth month, and then rose to 37.353 in the 12th month. In detail, all pair wise comparisons of physical activity in different time periods for pre and post PRP injections were statistically significant by t test T value of with P value <0.00001.

Results of the present trial indicated that PRP therapy is effective and was shown that PRP therapy can significantly decrease pain, functional limitations, and stiffness in patients with knee OA for up to 12 months.

5. Conclusions

The findings of this study show that platelet rich plasma injection is an effective mode of treatment for patients with stage 1 Osteoarthritis of knee. Though many modalities of

treatments are available, Autologous PRP injection is also a safe and useful modality for treatment of early Osteoarthritis of knee. The response of patients with early OA knee to PRP injection was found to be good with highly significant results. No significant side effects were observed

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