Autologous Platelet Rich Plasma in the Treatment of Primary Osteoarthritis: A Review of 82 Knee Joints

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Abstract: *This prospective single centre study was conducted to investigate the efficacy of platelet rich plasma (PRP) on 82 knee joints (70 patients) of primary osteoarthritis of knee under treatment in department of orthopaedics. Patient received three injections of PRP and were followed up for 24 months using VAS, WOMAC score and radiologic Ahlback's grading. Significant improvement in VAS and WOMAC score was seen on first and second follow up visit. None of the patient reported worsening and no serious complications were reported by any of the patient following the procedure.*

Keywords: Osteoarthritis, platelet rich plasma (PRP) primary osteoarthritis, Ahlback's grading

1. Background and Introduction

Osteoarthritis is the most prevalent form of arthritis and a major cause of morbidity and disability in elderly and geriatric population. Majority of patients are in the age group of 50 years and more. It is the pathologic outcome of a multifactorial failure of synovial joints over a period of time. [1]

Though poorly understood, research questions on destruction of cartilage and possible etiologies has been carried out extensively in recent years. At first, articular cartilage may be the primary injury site but eventually all joint structures- bone, synovium, muscle, capsule, ligaments and meniscal cartilage become involved. [2]

Available options for management encompass symptomatic relief but do not in general, address the disease process itself. Moreover, adverse effects and complications with some of these interventions along with the age group where co-morbid conditions are coexistent is a source of major concern as it leads to restriction in their usage and patient compliance. Therefore there is a clear need of investigating treatment options that are widely applicable in this age group and directly targets the disease process and progression.

Reported therapies for osteoarthritis include the use of interleukin (IL-1) inhibitors that reverse cartilage destruction. [3]

Research efforts are being directed towards the testing of protein bio-therapeutics for restoring the metabolic balance within the capsular joint and potential role of specific growth factors as therapeutic proteins for cartilage repair. Bioactive growth factors and autologous platelet rich plasma(PRP) are recently being considered as therapeutic psssibilities to enhance healing of chondral injuries and modify early degenerative arthritis. [4,5]

There are over 1500 proteins within platelets and they are instrumental in normal tissue repair and regeneration. [5]

PRP derived from centrifugation of autologous whole blood contain a platelet concentration four to five times higher than that of normal blood. It concentrates a high number of platelets in a small volume of plasma. Five percent calcium chloride has been shown to be effective in activating PRP, resulting in formation of platelet gel and release of cascade of growth factors. The administration in the form of platelet gel provides an adhesive support that can confine secretion to a chosen site. [6]

However it should be realized that most questions on the role of PRP remains unanswered and treatment of cartilage injury is a longstanding task and it is unfair to treat it as a sort of wonder treatment. Relying on the lack of side effects and the fact that platelets take part in physiological healing processes in general, it is often used indiscriminately.

Considering all these facts, this study aimed at investigating the efficacy of PRP via a prospective study design in patients of primary osteoarthritis of the knee.

2. Materials and Methods

We did a prospective, randomized clinical trial and 82 knee joints (70 patients)of primary osteoarthritis. These patients were included in the study using the following criteria's, between August 2009 and December 2010 presenting to Department of Orthopedics. Approval was obtained from our institutional ethics committee, and informed consent was provided by all of the patients in the study. Osteoarthritis was diagnosed as per American College of Rheumatology Criteria. [7]

<u>Inclusion Criteria</u>
1) Grade 1 and 2 osteoarthritis as per Ahlback's radiological grading. [8]
2) Patients in age group of 35-70 years.
3) Patients who understood the treatment modality, our aims and gave a formal consent.

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<u>**Exclusion Criteria**</u>
1) Osteoarthritis secondary to joint inflammatory disease. (E.g. Rheumatoid arthritis, ankylosing spondylitis etc.)
2) Patients with other diseases, affecting the knee joint like crystal arthropathy, symptomatic chondrocalcinosis, acute synovitis, excessive joint effusion (>100 ml), cystic diseases around the knee joint (E.g. popliteal cyst)
3) Metabolic diseases of the bone.
4) Late stages of osteoarthritis.
5) Intra-articular injections within the previous three months.
6) Relative contraindications pertaining to platelet concentrate use – history of thrombocytopenia, use of anticoagulant therapy, active infection, tumour, metastatic disease.

All the patients were evaluated at first visit before giving injection using Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and thereafter at specific subsequent visits at 12 months, 24 months post injection while maintaining the regular follow up. After mean WOMAC score assessment, pairwise comparison of WOMAC parameters was done separately at each time frame. [9]

VAS score was self-completed by the respondents. 10 cm ruler was used and the patients were asked to draw a line perpendicular to the VAS line. Score was then assessed by measuring the distance in millimeters on 10 cm line with zero on the scale denoting no pain and 10 denoting worst imaginable pain, providing a range of scores from 0-100 mm. Level of pain was taken for the last 24 hours. [10]

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) consisted of 24 items divided in to 3 subscales. [11]
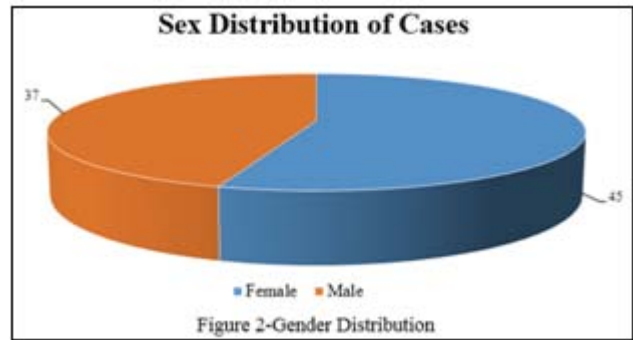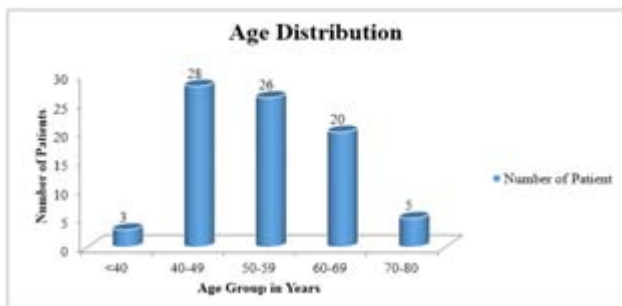
3. Aims and Objectives

To evaluate the efficacy, safety profile of intra-articular injections of platelet rich plasma (PRP) as a treatment option of primary osteoarthritis of the knee joint.

4. Results

Majority of the patients belonged to the age group of 40-49 years with a mean age group of 53.54. (Table 1, Figure 1)

Figure 1- Age Distribution

Figure 2-Gender Distribution

Number of females were 45 (54.8%) and males constituted 37 cases (45.2%). (Table 2, Figure 2)

Table 1: Age Distribution

Age Group	Number of Patient
<40	3 (3.66%)
40-49	28 (34.15%)
50-59	26 (31.71%)
60-69	20 (24.39%)
70-80	5 (6.10%)
Total	**82 (100%)**

Table 2: Gender Distribution

Sex	Number of Patient
Female	45 (54.88%)
Male	37 (45.12%)
Grand Total	**82 (100%)**

52(63.4%) of the patients presented with grade 2 Ahlback radiological grading while 30(36.6%) patients were grade 1. (Table 3, Figure 3) At 24 months repeat x-ray was done to look for radiological signs of improvement wherever possible as per Ahlback's grading and 36 (43.90%) were grade 1 and 46 (56.10%) were grade 2 at 24 months.
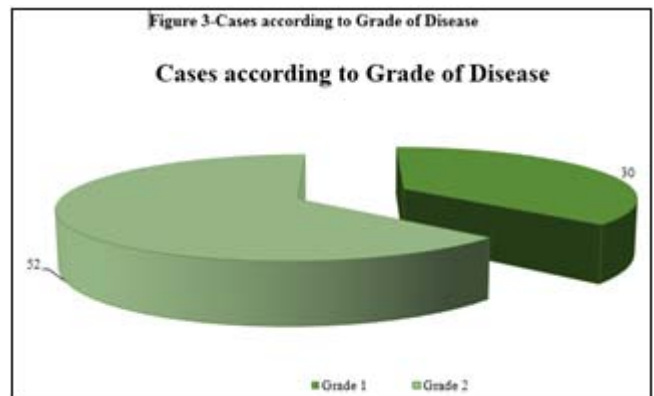

Figure 3-Cases according to Grade of Disease

Table 3: Cases according to Grade of Disease

Ahlback's Grading	Number of Knees
Grade 1	30 (36.59%)
Grade 2	52 (63.41%)
Grand Total	**82 (100%)**

Variables reviewed were WOMAC score and Visual Analogue Scale (VAS).Total WOMAC score, individual

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parameters of WOMAC score and VAS were analysed in all of the patients at pre-injection, and subsequent follow ups at 12 months, 24 months post injection. After mean WOMAC score assessment, pair wise comparison of WOMAC parameters was done separately at each time frame. Mean pain scores showed an overall trend of improvement as pre-injection mean pain score of 14.43±2.05 to 6.83±1.67 at last follow up. And change was statistically significant with p value of <0.05. (Table 4, 5 Figure 4)

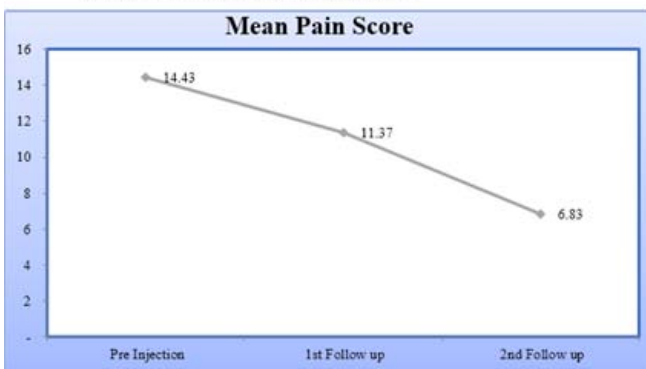**Table 4:** Pain Mean and Mean Comparison

Pain	Mean ± SD
Pre Injection	14.43 ± 2.05
1st Follow up	11.37 ± 2.12
2nd Follow up	6.83 ± 1.67

Table 4: Pain Mean and Mean Comparison at follow ups

Pain (I)	Pain (J)	Mean Difference (I-J)	P Value
Pre Injection	1st Follow up	3.06	0.000
	2nd Follow up	7.60	0.000
1st Follow up	Pre Injection	-3.06	0.000
	2nd Follow up	4.54	0.000
2nd Follow up	Pre Injection	-7.60	0.000
	1st Follow up	-4.54	0.000

Figure 4-Pain Mean and Mean Comparison

Mean stiffness score and stiffness value on pairwise comparison showed similar results at each time frame with a p value of 0.246 from pre-injection to first follow up and .000 at subsequent follow up and decreased from a mean of 4.79±1.53 at pre-injection to 2.99±1.94 at last follow up.(Table 6,7 and Figure 5)

Table 6: Stiffness Mean and Mean Comparison

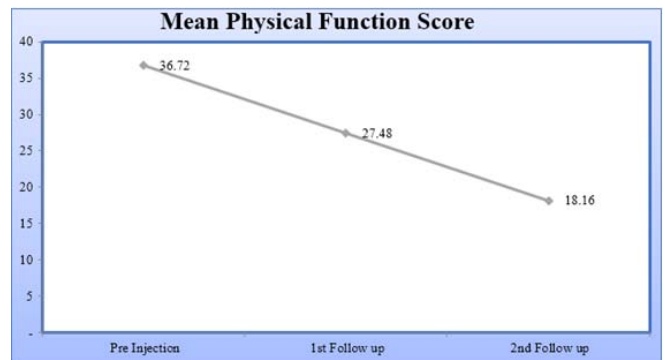| Stiffness	Mean ± SD
Pre Injection	4.79 ± 1.53
1st Follow up	4.54 ± 1.28
2nd Follow up	2.99 ± 1.94

Table 7: Stiffness Mean and Mean Comparison at follow ups

Stiffness (I)	Stiffness (J)	Mean Difference (I-J)	P Value
Pre Injection	1st Follow up	0.26	0.246
	2nd Follow up	1.80	0.000
1st Follow up	Pre Injection	-0.26	0.246
	2nd Follow up	1.55	0.000
2nd Follow up	Pre Injection	-1.80	0.000
	1st Follow up	-1.55	0.000

Figure 5: Stiffness Mean and Mean Comparison

Similarly mean physical function score and pairwise comparison of physical function values was done at each time frame. There was a decrease from a mean score of 36.72 ± 9.54 to 18.16 ± 5.51 at second follow up. The change had a p value of <0.01 to first follow up and the same to second follow up. (Table 8, 9 and Figure 6)

Figure 6: Physical Function and Mean Comparison

Table 8: Physical Function and Mean Comparison

Physical Function	Mean ± SD
Pre Injection	36.72 ± 9.54
1st Follow up	27.48 ± 7.98
2nd Follow up	18.16 ± 5.51

Table 9: Physical Function Mean and Comparison

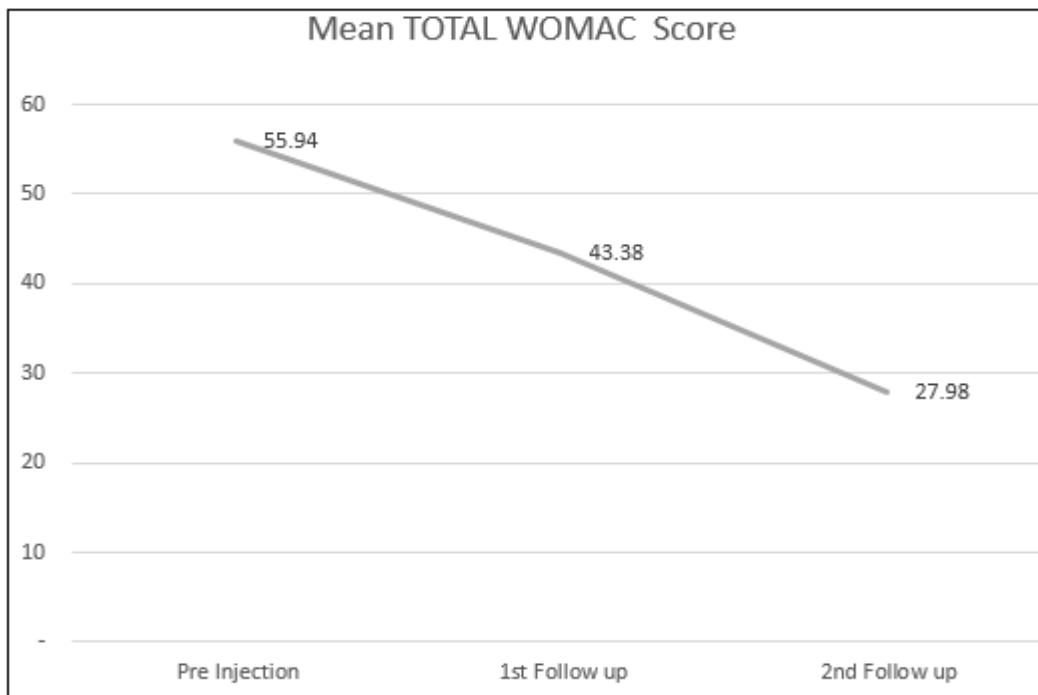| Physical Function (I)	Physical Function (J)	Mean Difference (I-J)	P Value
Pre Injection	1st Follow up	9.24	0.0000
	2nd Follow up	18.56	0.0000
1st Follow up	Pre Injection	-9.24	0.0000
	2nd Follow up	9.32	0.0000
2nd Follow up	Pre Injection	-18.56	0.0000
	1st Follow up	-9.32	0.0000

Analysis of mean Total WOMAC score and pairwise comparison was done. Total WOMAC mean score decreased from 55.94 ± 10.46 at pre-injection to 43.38 ± 8.54 at first follow up and subsequently to 27.98 ± 6.28 at second follow up with a statistically significant improvement (p value of <0.05) at both the follow up visits.(Table 10, 11 and Figure 7)

Table 10: TOTAL WOMAC Score Mean and Comparison

TOTAL WOMAC Score	Mean ± SD
Pre Injection	55.94 ± 10.46
1st Follow up	43.38 ± 8.54
2nd Follow up	27.98 ± 6.28

Table 10: TOTAL WOMAC Score Mean and Comparison at follow ups

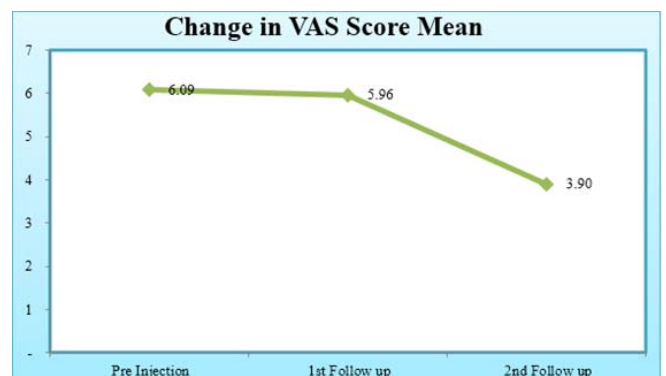| TOTAL WOMAC (I)	TOTAL WOMAC (J)	Mean Difference (I-J)	P Value
Pre Injection	1st Follow up	12.56	0.0000
	2nd Follow up	27.96	0.0000
1st Follow up	Pre Injection	-12.56	0.0000
	2nd Follow up	15.40	0.0000
2nd Follow up	Pre Injection	-27.96	0.0000
	1st Follow up	-15.40	0.0000

Figure 7: Total WOMAC Score Mean and Comparison

The improvement was observed in VAS score from pre-injection to second follow up with a p value 0.00. No improvement was observed at first follow up with a p value 0.5956.(Table 12, 13 and Figure 8)

Table 12: VAS Score Mean and Comparison

VAS Score	Mean ± SD
Pre Injection	6.09 ± 1.45
1st Follow up	5.96 ± 1.49
2nd Follow up	3.90 ± 1.38

Table 13: VAS Score Mean and Comparison at follow ups

VAS (I)	VAS (J)	Mean Difference (I-J)	P Value
Pre Injection	1st Follow up	0.12	0.5956
	2nd Follow up	2.18	0.0000
1st Follow up	Pre Injection	-0.12	0.5956
	2nd Follow up	2.06	0.0000
2nd Follow up	Pre Injection	-2.18	0.0000
	1st Follow up	-2.06	0.0000

Figure 8: VAS Score Mean and Comparison

The mean Total WOMAC score was calculated based on Ahlback's grading done at pre-injection and second follow up. It was observed that mean Total WOMAC score was less for grade 1 in comparison to grade 2. Table 14 shows mean Total WOMAC score versus Ahlback's grading.(Figure 9)

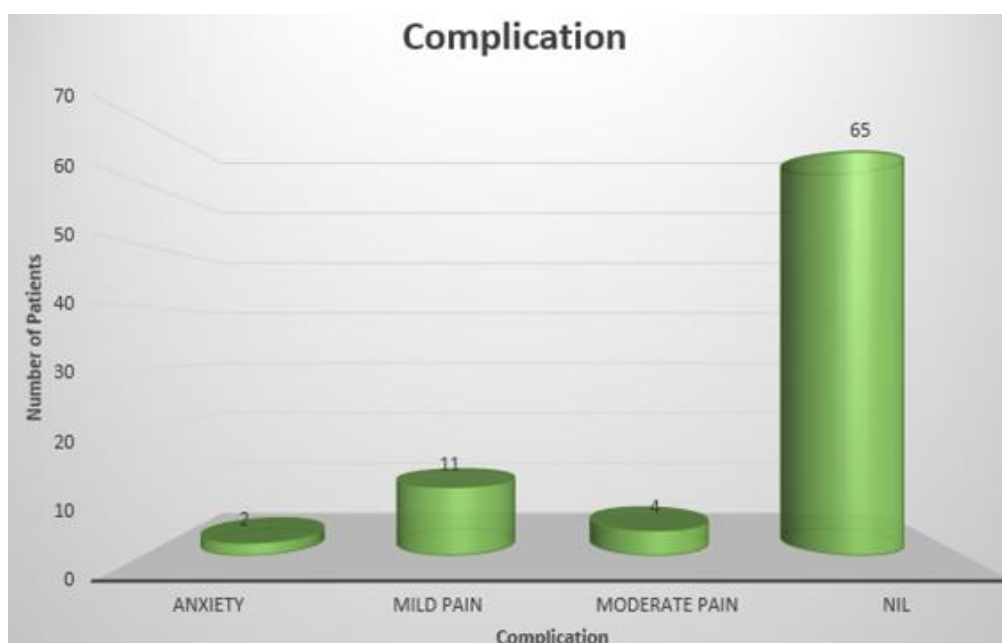**Figure 9:** Total WOMAC score for Ahlback's grading

Amount of PRP used in each case was 8 ml and none of the patients suffered any serious complication. 65 (79.27%) patients had no complications while 11 (13.41%) had moderate pain which subsided in 1-2 days without any intervention. Various side effects observed are shown in Table 15. (Figure 10).

Table 14: Total WOMAC Score for Ahlback's Grade

Ahlback's Grading		No. of Knees	Mean Total WOMAC Score	Standard Deviation
Pre Injection	Grade 1	30	54.23	11.83
	Grade 2	52	57.12	9.24
2nd Follow up	Grade 1	36	28.08	6.25
	Grade 2	46	27.89	6.37

Table 15: No. of cases according Complications

Complications	Number of Patient
Anxiety	2 (2.44%)
Mild Pain	11 (13.41%)
Moderate Pain	4 (4.88%)
Nil	65 (79.27%)
Total	**82 (100%)**

Figure 10: Number of cases according compliccations

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5. Conclusion

Patients were given three injections of PRP (8 ml) at four weeks interval and were followed up using VAS and WOMAC score. We conclude that platelet rich plasma has a role in the treatment of osteoarthritis as seen by improvement in VAS and WOMAC score at three weeks. Improvement in this duration suggests that anti-inflammatory mechanisms might be at work here as chondral remodeling takes much longer duration. At the same time we realize that efficacy should be measured in a larger cohort with a longer follow up as long term deterioration in symptoms is reported in literature.

Ethical Clearance

The informed consent for publishing for educational purposes was taken from patient.

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