International Journal of Orthopaedics Sciences

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2020; 6(1): 1003-1010

www.orthopaper.com
Received: 25-11-2019
Accepted: 28-12-2019

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A Study on the effects of injection of platelet rich plasma (Autologous) in the management of osteoarthritis of knee joints

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DOI: https://doi.org/10.22271/ortho.2020.v6.i1m.1949

Abstract
Background: PRP is a relatively new treatment for early osteoarthritic knee joints with increasing number of studies showing promising results.
Aim & Objective
Methodology: This is a prospective study done on 31 Ahlback's radiological grade I and grade II knee joints. Patients were selected in the outpatient department of orthopaedics, Kamineni Institute of Medical Sciences. 4 ml of autologous PRP prepared with single spinning technique at 1500 RPM for 15 minutes in the centrifuse in the Department of Transfusion Medicine, Kamineni Institute of Medical Sciences. Which was activated with 1 ml of $CcCl_2$.
Results: Total amount of sample infiltrated was 5 ml, in to each knee joint under aseptic conditions in Operation Theater. Each patient evaluated with WOMAC scoring on '0' day, 1 month and six months. Out of 31 knee joints infiltrated with PRP, 12 knee joints are grade I and 19 knee joints are of grade II. On assessing the results there is a significant improvement in WOMAC score of all the patients and the results sustained for more than 6 months. Though there is clinically better results are seen in grade I knee joints than grade II knee joints, these results are statistically not significant.
Conclusion: There were no long term local systemic complications noted through the course of the study except acute pain at the site of inject for immediate 10-15 minutes after the infiltration.

Keywords: osteoorthritis, platelate rich plasma, joints, womac score

Introduction
Osteoarthritis (OA) of the knee is one of the main causes of musculoskeletal disability [1]. Osteoarthritis is a common, debilitating disease which is associated with a large societal and economic burden, in addition to the physical and psychological sequelae it often manifests in the affected individual [2]. Osteoarthritis is the fourth leading cause of 'years lived with disability' (YLD), accountings for 3.0% of total global YLD's. As per WHO by 2030, the demand for total knee arthroplasties will increase up to 670%. This condition places a staggering burden on our current economy, with billions of dollars of annual expenditure associated with pharmaceutical treatment for pain relief, rehabilitation, and joint replacements [3].

Osteoarthritis is clinically heterogeneous, and the processes that cause deterioration are still poorly understood [1]. Current opinion is that the disease progression results from an imbalance between proinflammatory cytokines (including interleukin [IL]-1a, IL-1, and tumor necrosis factor-1 and anti-inflammatory cytokines (including IL-4, IL-10, and IL-1ra).This cytokine imbalance is thought to activate proteolytic enzymes, leading to the destruction of cartilage. The majority of recently proposed therapeutic modalities for osteoarthritis have a foundation in attempting to address this cytokine imbalance. In addition to cartilage loss, arthritis of the knee joint may adversely affect subchondral bone, synovium, ligaments, capsule, menisci, surrounding musculature, and perhaps the sensory nervous system [3].

At present, there are few options for patients with mild to moderate arthritis. Most of the approaches are palliative and address the symptoms rather than influencing the biochemical environment of the joint or the disease process [1]. Weight loss and exercise are excellent treatment options for OA, yet are often associated with poor compliance [3].

Current research efforts are focused on the identification of key biochemical pathways that can be targeted therapeutically through biological intervention and the testing of protein biotherapeutics for restoring the metabolic balance within the joint. In particular, the most recent knowledge regarding tissue biology highlights the potential use of specific growth factors as therapeutic proteins for cartilage repair, and this is now being widely investigated *in vitro* and in vivo. Some of the experimental orthobiological treatments include platelet-rich plasma (PRP) injection graft therapy, high concentrate PRP (HcPRP), autologous bone marrow aspirate concentration and adipose cells, IL-1 receptor antagonist, nerve growth factor inhibitor, and osteogenic protein-1among others [4]. Autologous platelet-rich plasma (PRP), which contains a pool of growth factors, appears to offer an easy solution for delivering multiple growth factors needed for tissue repair [1].

PRP therapy provides delivery of a highly concentrated cocktail of growth factors to accelerate healing. Currently, most studies on PRP therapy are anecdotal, nonrandomized, or involve insufficient sample sizes and are underpowered [5]. However, at present, there are limited studies documenting the safety and efficacy of a nonsurgical PRP injectable for intraarticular use in knee Osteoarthritis [6, 7]. PRP is being portrayed as a ‘‘wonder drug,’’ without sufficient evidence to support its application in almost all the areas in which it is used.

Keeping in view these grey areas in our knowledge, this prospective clinical trial was designed to evaluate the role of PRP in the early stages of knee OA.

Hence, In this study PRP from the patient’s own blood i.e. autologous PRP has been immediately infiltrated into their knee joints with early osteoarthritis and the results of injection of PRP have been observed over a period of time.

Materials and methods

It is a prospective longitudinal study on 31 primary osteoarthritic knee joints, selected from the Outpatient Department of Orthopaedics, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda District, Telangana State. Clinical examination and x rays of the knee joints were done and blood sample of the patients were collected and PRP prepared in the Department of Transfusion Medicine of the same institute. Infiltration was done in Operation Theatre under strict aseptic conditions. Patients were assessed with WOMAC (Western Ontario McMaster Universities Arthritis Index) scoring pre injection of PRP and post injection period of 1 month and 6 months. A reduction in WOMAC score is suggestive of improvement in the patient’s condition.

Inclusion criteria

- Patients with early osteoarthritic changes on clinical evaluation pain in knee joints, increasing with walking and exertion.
- Patients of primary osteoarthritis of knee joints with Ahlbacks's radiological grade I and II.

Exclusion criteria

- Patients of primary osteoarthritis of knee joints with Ahlbacks's radiological grade III, IV and V.
- Patients of secondary osteoarthritis of knee joints.
- patients with anemia
- patients with active infections
- platelet counts less than 1 lakh
- Abnormal random blood sugar levels

Ahlback Radiological Grading of Osteoarthritis of Knee Joints (Image – 1)

Grade I– Joint Space narrowing (< 3mm)
Grade II – Joint space obliteration
Grade III – Minor bone attrition (0-5mm)
Grade IV – Moderate bone attrition (5-10mm)
Grade V – Severe bone attrition (>10mm)

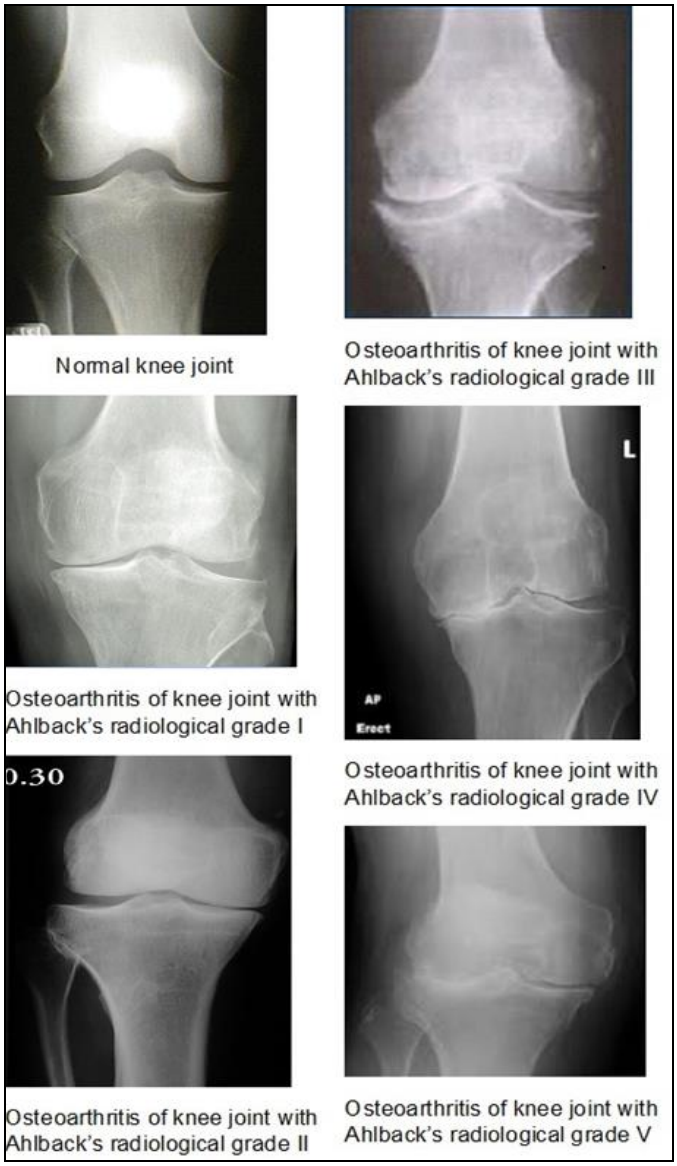

Fig 1: Ahlback Radiological Grading of Osteoarthritis of Knee Joints

Patient selection

All patients with primary osteoarthritis of knee joints were evaluated clinically using WOMAC scoring and radiographically. Based on Ahlback's radiological grading, patients with Grade I and II Osteoarthritis were selected irrespective of age, sex and socioeconomic status.

Parameters analysis

Selected patient’s blood samples were sent for complete blood picture, erythrocyte sedimentation rate, C-reactive proteins, random blood sugar and HIV and HbsAg status. Patients’ blood was evaluated to assess the white blood cell count and platelet count prior to the infiltration. Patients with elevated white blood cells, and platelet counts less than 100000/cubic mm, elevated erythrocyte sedimentation rate and positive C-reactive proteins, random blood sugar levels beyond 80-140

range, HIV and HBsAg reactive patients were also excluded from the study. Selected patients WOMAC score was recorded in a separate chart for each patient and follow up scorings were noted down in the same chart of the patient.

Standard operating procedure for the preparation of platelet rich plasma (PRP)

In the Department of Transfusion Medicine, from each patient 50 ml of venous blood was collected from the antecubital vein atraumatically in an effort to avoid irritation and trauma to the platelets with a syringe, blood was transferred to the vacutainers of 4.5 ml containing CPD-A1 (citrate phosphate dextrose and adenine) as an anticoagulant. The tubes were then centrifuged for 15 minutes at 1500 rpm on a table-top centrifuge, and the blood was separated into PRP and residual red blood cells. Hereafter, the procedure was completely performed inside the biosafety cabinet. The PRP was then extracted through a pipette and transferred to a test count were measured from the patient's peripheral blood as well as in the final PRP. Total leucocyte count was zero in our PRP, The mean platelet count achieved by our method was more than the five times the platelet count of blood of that patient.

In the operation theatre with the patient in supine position, knee was scrubbed, painted and draped with sterile towels. With the patients knee in 45-90 degrees of flexion so that joint is opened for injection through lateral parapatellar approach. Under aseptic conditions, 8 mL platelet concentrate was injected into the knee joint with an 18- gauge needle without local anesthetic. 1 mL of CaCl 2 (calcium chloride) was injected in a ratio of 1:4 for every 4 mL of PRP. After the procedure Jone's compression bandage applied and the knees were immobilized for 10 minutes. For any possible side effects like dizziness, sweating patients were observed for 30 minutes.

Followup

During the follow-up period, nonsteroidal anti-inflammatory drugs were not allowed, and tramadol (dosage, 50 mg bds) was prescribed in case of discomfort; all patients were asked to stop medications 48 hours before follow-up assessment.

Fig 2: Centrifuge for PRP separation with timer on the front side

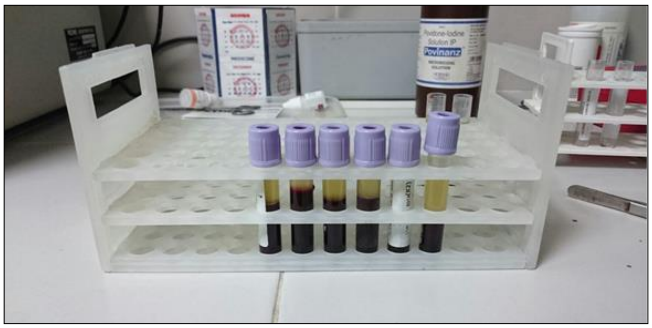

Fig 3: Vacutaieners after 15 minutes of centrifuge with 1500 RPM

Fig 4: PRP of 4ml activated with 1ml of $CaCl_2$, total 5ml of activated PRP in syringe

Fig 5: infiltration into the knee joint in Operation Theater

Outcome measures

Each patient was allotted a separate WOMAC chart till complete follow up. Each knee was scored separately as we were considering each as a separate unit, initial WOMAC score was recorded prior to the administration of PRP infiltration i.e. on day '0' and after the infiltration patients were asked to come for review on 1st and 6th months. A decrease in the WOMAC score is considered as improvement in the patient's condition. WOMAC score is measured in its individual variables and in total.

The WOMAC consists of 24 items divided into 3 subscales (components):

- Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing
- Stiffness (2 items): after first waking and later in the day
- Physical Function (17 items): stair use, rising from sitting, standing, bending, walking, getting in / out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in / out of bath, sitting, getting on / off toilet, heavy household duties, light household duties.

Each item of WOMAC score described in terms of - none, mild moderate, severe, and extreme. These correspond to an ordinal scale of 0-4. Each component of the WOMAC score ranges between 0-20 for pain, 0-8 for stiffness and 0-68 for functionality. A total WOMAC score is created by summing the items for all three subscales, ranges from 0-96 [8].

Outcome measured is quantified in percentage of improvement.

85-100% improvement – excellent
70-84% improvement – good
55-69% improvement – fair
< 55% improvement – poor

Statistical analysis
The means of the each parameter and total WOMAC score were calculated and ANOVA (Analysis of Variance) done for all the cases.

Observations and results
In this study on 31 osteoarthritic knee joints of Ahlback's radiological grade I – 12 and II - 19 of total 19 patients (table-1). Patients were selected in the institutional Orthopaedic Outpatient Department. Out of which 12 patients were with bilateral early osteoarthritis and 7 patients were unilateral (table- 2). 4 patients selected were males and the remaining 15 patients were females (table- 3).

Table 1: Radiological Grade of the knee joints under study (n=31)

Grade I	Grade II
12	19

Tables 2: Total no. of patients with knee joints injected with PRP (n=31)

Unilateral	Bilateral
7	12

Table 3: Sex distribution of patients with knee joints under study (n=31)

Male	Female
4	15

Effect of PRP on pain
In this study, the pain scores of the patients have decreased on the day of infiltration to one month and six months (table-4). Their mean scores have decreased from the day of infiltration to one month and six months. It means that there is definite decrease in the pain after infiltration, but on seeing the individual pain scores, for one case pain has subsided completely.
Over all, the pain intensity has decreased in severity. Since p-value is less than significance level ($p<0.05$), Null hypothesis cannot be accepted. Hence it can be concluded that the efficacy of the PRP treatment from zero day to sixth month is statistically significant. Similar results are seen from the results from one month to six months follow up. (Table-4 and table-10).

Table 4: Comparison of means of WOMAC Score -Pain on o day, 1st month, 6th month of grade I and grade II Osteoarthritis of knee joints (n=31) based of ANOVA

	WOMAC score – Pain mean(SD)			
	0 day	1st month	6th month	% of improvement after 6 months
Grade I	10.58 (±1.97)	5.33 (±1.43)	2.58 (±1.56)	76.62
Grade II	13.25 (±1.71)	7.47 (±1.54)	5.11 (±1.69)	73.86
Total	12.22 (±2.18)	6.61 (±1.76)	4.06 (±1.98)	66.78

There was definite decrease in the mean pain scores from '0' day-10.58 to 1st month (5.33), 1st month (5.33) to 6th month (2.88) in grade I knee joints i.e. 76.62% of improvement. There was definite decrease in the mean pain scores from '0' day (13.25) to 1st month (7.47), 1st month (7.47) to 6th month (5.11) in grade II knee joints. i.e.73.86% of improvement. There was definite decrease in the mean pain scores from '0' day (12.22) to 1st month (6.61). 1st month (6.61) to 6th month (4.06) in both the grades of knee joints together i.e. 66.78% of improvement. On doing the ANOVA (Analysis of variance), the calculated p-Value was less than 0.05. So the results were statistically significant.

Effect of PRP on stiffness
In this study, the stiffness scores of the patients have decreased on the day of infiltration to one month and six months (table-5, Fig-5). Their means have decreased from the day of infiltration to one month and six months. It means that there is definite decrease in the stiffness after infiltration, in one case there was no stiffness prior to the infiltration, and there was no stiffness in 10 knee joints at six months follow up, i.e. stiffness had completely subsided.
Over all, the stiffness intensity had decreased in severity. Since p-value is less than significance level ($p<0.05$), Null hypothesis cannot be accepted. Hence it can be concluded that the efficacy of the PRP treatment from zero day to sixth month is statistically significant and improved. Similar results are seen from one month to six months follow up (fig-5, table-5 and table-10).

Table 5: Comparison of means of WOMAC Score- Stiffness on o day, 1st month, 6th month of grade I and grade II Osteoarthritis of knee joints (n=31) based of ANOVA

	WOMAC score – Stiffness mean(SD)			
	0 day	1st month	6th month	% of improvement after 6 months
Grade I	3.25 (±1.54)	1.33 (±0.77)	0.25 (±0.45)	92.86
Grade II	4.76 (±1.25)	2.58 (±0.71)	1.17 (±0.63)	81.24
Total	4.19 (±1.51)	2.12 (±0.95)	0.80 (±0.69)	80.90

There was definite decrease in the mean stiffness scores from '0' day (3.25) to 1st month (1.33), 1st month (1.33) to 6th month (0.25) in grade I knee joints i.e. 92.86% of improvement. There was definite decrease in the mean stiffness scores from '0' day (4.76) to 1st month (2.58), 1st month (2.58) to 6th month (1.17) in grade II knee joints. i.e.81.24% of improvement. There was definite decrease in the mean stiffness scores from '0' day (4.19) to 1st month (2.12). 1st month (2.12) to 6th month (0.08) in both the grades of knee joints together i.e. 80.90% of improvement. On doing the ANOVA (Analysis of variance), the calculated p-Value was less than 0.05. So the results were statistically significant.

Effect of PRP on functionality
In the present study patients the functionality scores of the patients have decreased from on the day of infiltration to one month and six months (table-6). Their mean scores have decreased from the day of infiltration to one month and six

months. It means that there is definite improvement in the functionality after infiltration, but on seeing the mean functionality scores, in no joint the functionality scores have completely subsided. Over all the functionality restriction decreased in severity. Since p-value is less than significance level (p<0.05), Null hypothesis cannot be accepted. Hence it can be concluded that the efficacy of the PRP treatment from zero day to sixth month is statistically significant and improved. Similar results are seen from one month to six months. (Table 6).

Table 6: Comparison of means WOMAC score - Functionality on o day, 1st month, 6th month of grade I and grade II Osteoarthritis of knee joints (n=31) based of ANOVA

	WOMAC score – Functionality mean(SD)			
	0 day	**1st month**	**6th month**	**% of improvement after 6 months**
Grade I	41.91 (±5.83)	23.5 (±9.18)	12.33 (±11.6)	70.58
Grade II	51.70 (±3.82)	32.58 (±9.05)	2.702 (±10.83)	76.77
Total	48.03 (±6.70)	28.71 (±9.70)	18.13 (±11.76)	62.24

There was definite decrease in the mean functionality scores from '0' day (41.91) to 1st month (23.5), 1st month (23.50) to 6th month (12.33) in grade I knee joints i.e. 70.58% of improvement. There was definite decrease in the mean functionality scores from '0' day (51.70) to 1st month (32.58), 1st month (32.58) to 6th month (2.70) in grade II knee joints. i.e.76.77% of improvement. There was definite decrease in the mean functionality scores from '0' day (48.03) to 1st month (28.71). 1st month (28.71) to 6th month (18.13) in both the grades of knee joints together i.e. 62.24 of improvement. On doing the ANOVA (Analysis of variance), the calculated p-Value was less than 0.05. So the results were statistically significant.

have decreased from on the day of infiltration to one month and six months (table-7, fig-7). Their mean scores have decreased from the day of infiltration to one month and six months. It means that there is definite decrease in the total WOMAC score after infiltration, but on seeing the mean total WOMAC scores, in no joint the scores have reduced to zero. Over all there was decrease in severity. Since p-value is less than significance level (p<0.05), Null hypothesis cannot be accepted. Hence it can be concluded that the efficacy of the PRP treatment from zero day to sixth month is statistically significant and shows improvement. Similar results are from one month to six months follow up. (Fig-7, table-7 andtable-10).

Effect of PRP on total WOMAC score

In the present study the total WOMAC scores of the patients

Table 7: Comparison of means of WOMAC score - Total on o day, 1st month, 6th month of grade I and grade II Osteoarthritis of knee joints (n=31) based of ANOVA

	WOMAC score – Total mean(SD)			
	0 day	**1st month**	**6th month**	**% of improvement after 6 months**
Grade I	56.58 (±8.18)	30.16 (±10.71)	15.16 (±13.06)	73.01
Grade II	69.64 (±5.32)	43.17 (±9.90)	29.41 (±12.22)	56.82
Total	64.74 (±9.13)	37.74 (±11.58)	23.22 (±13.82)	64.13

There was definite decrease in the mean WOMAC scores from '0' day (56.58) to 1st month (30.16), 1st month (30.16) to 6th month (15.16) in grade I knee joints i.e. 73.01% of improvement. There was definite decrease in the mean pain scores from '0' day (69.64) to 1st month (43.17), 1st month (43.17) to 6th month (29.41) in grade II knee joints. i.e.56.82% of improvement. There was definite decrease in the mean pain scores from '0' day (64.74) to 1st month (37.74). 1st month (37.74) to 6th month (23.22) in both the grades of knee joints together i.e. 64.13% of improvement.

Table 8: Analysis of results of all knee joints according to the working classification (n=31)

	Results
Excellent (85-100%)	3
Good (70-84%)	16
Fair (55-69%)	3
Poor (<55%)	9

19 knee joints were showing good (16) and excellent (3), 12 knee joints were showing fair (3) and poor (9) results. When ANOVA done for the results, the calculated p-value was less than the 0.05, so the results were statistically significant.

Table 9: Comparison of results of grade I and grade II knee joints according to the working classification (n=31)

	Grade I	**Grade II**
Excellent	2	1
Good	8	8
Fair	0	3
Poor	2	7

Good (8) and excellent (2) results were more in grade I knee joints than in grade II knee joints, good (8) and excellent (1). Poor (7) and fair (3) results were more in grade II knee joints than in grade I knee joints, poor (2), fair (0). Though the results were clinically significant, when ANOVA was, the calculated p-value was more than 0.05, so the results were statistically not significant.

Discussion

Articular cartilage lesions and degeneration are difficult to treat and present a challenge for orthopaedic surgeons because of the distinctive structure and function of hyaline cartilage and its inherent low healing potential. For therapeutic intervention, laboratory investigations are focusing on the possibility of preserving normal homeostasis or blocking or at

least delay the need for more invasive surgical procedures. Current pharmacologic interventions may only temporarily reduce chronic pain, but for the time being, no proven disease modifying therapy is available [9].

In this prospective study, WOMAC scores were evaluated pre-injection and post-injection period on first month and sixth months. There is a correlation in Grade I and Grade II mean WOMAC scores. In Grade I, the mean WOMAC score of pain, stiffness and functionality is lower than the Grade II osteoarthritis knee joints. There was no control group in this study. The number of platelets used are more than 5 times the base line, as all the patients are selected were having more than one lakh platelets, so every patient got more than 5 lakh platelets per ml, which is prepared by single spinning of the sample for 15 minutes with 1500 RPM(Rotations per minute) and leucofilters were not used. Kon *et al.* in 2011, used double spinning with more than 5 times the base line platelets activated with $CaCl_2$ and given more than three doses of injection with 2 weeks gap [14]. Patel *et al.* in 2013, used single spinning technique with leuco-filters. They have given two injections of PRP activated with $CaCl_2$, each 8 ml, with 3 weeks gap. Their platelet count is less than 5 times the base line [1, 9]. In 2011, Filardo *et al.*, used 5 ml PRP with 5 times the platelet count prepared from double spinning technique and activated with $CaCl_2$. They have infiltrated three injections of PRP with one week gap [10]. In 2012 they compared the single versus double spinning and found no significant difference in the results. All the patients who have received the PRP have shown decrease in the pain, stiffness and functionality [11]. Cerza *et al.* in 2012 used 5ml of PRP not activated with $CaCl_2$, platelet count less than the 5 times the baseline with single spinning and without leuco-filters. They have infiltrated four injection with each one week gap. The idea of using $CaCl_2$ was, it activates the platelets [12]. Spakova *et al.* in 2012 did similar study, PRP prepared after spinning it for three times and without using leuco-filters and they have used three injections with one week gap. They have stated that the leucocyte content did not seem to induce negative effects or to impair the potentially beneficial effects of PRP, even when used in joints. However, they cannot conclusively claim that increased white blood cells in PRP have positive effect on knee joint [13, 14]. The preparation of PRP, number of platelets, amount of PRP infiltrated, and frequency of injections were not uniform. Different researchers have used different methods of preparation, different amount of PRP and at different time periods (table-9). Thus we can conclude that the method of preparation of PRP; the platelet count to be achieved before infiltration; the usage of leucofilters; the number of injections for each knee joints; the duration between injections; all are varying and nothing is standardized at present.

In this study all the patients have shown decrease in the WOMAC score. Their mean pain, stiffness and functionality scores have decreased. The decrease in WOMAC score continued upto six months. The improvement in our patients could be explained by the fact that injected platelets might have acted at different levels and were not stimulating the chondral anabolism or slowing the catabolic process.

As we have given a working classification to assess the results, 3 joints have shown excellent results, 16 joints have shown good results, 3 joints have shown fair results and 9 joints have shown poor results. Though the mean pain scores have deceased in all the patients, the efficacy had been varied from the patient to patient. Results were poor in obese, female patients with active labor work. Five patients who have used NSAIDS (Nonsteroidal anti-inflammatory drugs) against the medical advice have shown poor results. But it is not clear that how the obesity with active labor work and NSAIDS have their isolated effect on knee joints. The results shown better improvement in grade I osteoarthritis knee joints than grade II knee joints. Grade I patients shown 73.01 percentage of improvement, whereas grade II patients shown 56.82 percentage when evaluated with WOMAC score.

But the difference is not statistically significant. In every patient there is decrease in WOMAC score, but in no one it has reached '0'. It means that PRP delays the osteoarthritic progression in the joints, but it has not cured osteoarthritis. To evaluate its duration of action long term follow up studies are required. Filardo *et al.* in 2012, have also shown similar results, better results are seen in early osteoarthritis knee joints than advanced arthritic knee joints in their comparative study done between PRP and hyaluronic acid treatment of osteoarthritis of knee joints [11], though they have not found significant improvement in PRP group when compared with hyaluronic acid. in their previous study in 2011, the final evaluation confirmed that female patients showed the poor results, which probably due to gender-specific biological and biomechanical characteristics, which might influence the etiopathogenesis, the effects of the growth factors and ultimately, the clinical response to treatment. In this study no gender specificity was calculated.

Spakova *et al.* in 2012, in their study found statistically significant improvement in WOMAC score, VAS and pain relief when compared to viscoelastic supplementation [13]. Kon *et al.* in their study in 2011 had shown significant improvement in all parameters of the WOMAC score in the group of patients who were infiltrated with PRP upto 6 months follow up. But the condition of the patients were decreased from 6 months to 12 months follow up, i.e the effect of PRP decreasing from 6 months onwards. Some influencing factors were detected, in particular it was observed that young male patients were the best responding group, especially in case of simple chondropathy without signs of oateoarthritis [14].

In a later study evaluating the same patients at 24 months of follow up confirmed this trend with a further decrease in the clinical outcome, thus concluding that intra articular therapy with PRP is time dependent with an average duration of 9 months and better and longer results are achieved in younger patients with lower levels of joint degeneration. They have also stated that PRP has no beneficial effect in advanced Osteoarthritis. The biologic changes induced by PRP may only weakly influence older joints with higher degenration[10].

In this study the results have shown that the effect of PRP sustained for 6 months with continuous decrease in all parameters, i.e. pain, stiffness and functionality of the WOMAC score. As this study was done for only six months, this study cannot explain the duration of action of PRP in treating Osteoarthritis of knee joints. Filardo *et al.* in 2012 found that there was worsening of the condition of the patients from the end of 9 months, it means that the duration of action of PRP was 9 month, but still needs further studies to conclude the duration of action of PRP [11] (table-9).

Immediate post infiltration all patients have complained of severe pain but no systemic and long term complications noted during the course of study. Sandeep Patel *et al.*, in 2013, in their study have documented some systemic adverse effects. Which were immediate and systemic rather than local and were of short duration not lasting more than 30 minutes [1].

Filardo *et al.* in 2012 have shown worsening of WOMAC

score from nine months onwards [11], it implies that if the chondral remodeling was the cause for the improvement of symptoms, the benefit would have started later and lasted for a longer duration. Sandeep patel *et al.* in 2013, through their study stated that the improvement in patients of osteoarthritis of knee joints is not because of the stimulation of the chondral anabolism or slowing the catabolic process [1].

Table 9: Comparison of results of grade I and grade II knee joints according to the working classification (n=31)

Study	Type of study	Sample size		No. of Injections	Time of injection in weeks	Volume of PRP in ml	Platelet concentration	WOMAC score improvement
		PRP	Control					
Patel *et al.*[1] (2013)	PRP vs Placebo	54	50	2	0-3	8	<5×baseline	+
Filardo *et al.*[11](2011)	PRP vs PRGF	54	55	3	0-1-2	5	5×baseline	VAS
Cerza *et al.*[12] (2012)	PRP vs HA	60	60	4	0-1-2-3	5	>5×baseline	+
Spakova *et al.*[13] (2012)	PRP vs HA	60	60	3	0-1-2	3	<5×baseline	+
Filardo[11] *et al.* (2012)	Single vs Double spinning	72	72	3	0-3-6	5	<5×baseline	VAS
Kon etal[14](2011)	PRP vs HA	50	50	3	0-2-4	5	>5×baseline	VAS & IKDC
This study	PRP	31	NA	1	NA	5	>5×baseline	+

VAS- Visual analogue score, IKDC – International Knee Documentation Committee

This study has its limitations

- The sample size was low, and
- No comparative group was included.
- The age, sex, Body Mass Index (BMI), were not considered in selecting the patients.
- Cartilage mapping was not done because of its cost.
- No predefined classification system was there, though we have given a working classification to assess the results.
- Study follow up period was only six months, it would have given more understanding of its efficacy if it was followed for longer periods.

Further studies are required to better understand the mechanism of action of PRP, the dosage of PRP, duration of action, frequency of injections, its composition and role of $CaCl_2$ in its activation. It is necessary to understand the results of PRP, whether they are temporary or permanent. Different platelet concentrations and application modalities have to be studied further.

Conclusion

- Osteoarthritis (OA) of the knee is one of the main causes of musculoskeletal disability.
- Osteoarthritis is a common, debilitating disease which is associated with a large societal and economic burden, in addition to the physical and psychological sequelae it often manifests in the affected individual.
- The mechanism and duration of action of PRP is still not understood completely which requires further studies.
- We can safely conclude that Autologous PRP infiltration in early Osteoarthritis (Grade I and Grade II) of Ahlback's radiological grading does give relief from pain, stiffness and improves functionality without any major side effects and can be recommended as a viable modality of treatment.

Acknowledgement

The author thankful to Department of Orthopaedics, Kamineni Institute of Medical Sciences, Hyderabad, Telangana, India for providing all the facilities to carry out this work.

Conflict of interest

None

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