## **Research Article**

## Role of Intra Articular Injections of Autologous Platelet Rich Plasma in Osteoarthritis of Knee Joint

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Abstract: Osteoarthritis is the most common form of arthritis and a leading cause of chronic disability, to a great extent in knee and/or hip joints. Osteoarthritis, commonly known as wear and tear in which a protective cartilage on the end of the bones wears down over time. osteoarthritis of the knees is one of five leading causes for disability among noninstitutionalized adults. Osteoarthritis is the fourth leading cause of 'years lived with disability' (YLD), accounting for 3.0% of totals global YLD's. As per WHO by 2030. The most common symptoms of knee osteoarthritis are pain and physical limitations that have a significant effect on the individual's quality of life and her or his social and economic activities. Osteoarthritis diseases are a result of both mechanical and biological events that destabilize the normal biological coupling of degradation and synthesis of articular cartilage, chondrocytes, extracellular matrix, subchondral bone and subsequently synovial fluid. Current research efforts are focused on the identification of key biochemical pathways that can be targeted therapeutically through biological intervention for cartilage repair. 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. PRP therapy provides delivery of a highly concentrated of growth factors to accelerate healing. The present study has been undertaken in Gandhi Medical College, Hospital, Hyderabad, Telangana, India to study the role of PRP in the osteoarthritis of knee joint. In this study PRP from the patient's own blood i.e. autologous PRP has been immediately infiltrated into their knee joints with osteoarthritis and the results of injection of PRP have been observed and assess the functional outcome. It is a prospective longitudinal study on 100 patients with 161 primary osteoarthritic knee joints of Kellgren Lawrence radiological grade I-61 and II - 100. 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. In this study, the pain scores of the patients have decreased on the day of infiltration to one month and six months. Their mean scores have decreased from the day of infiltration to one month and six months. All the patients have started showing improvement at around two weeks and over all, the pain intensity has decreased in severity. It can be concluded that the efficacy of the PRP treatment from zero day to sixth month is statistically significant.

### Keywords: platelet rich plasma, osteoarthritis, knee joint

#### Introduction

Osteoarthritis is the most common form of arthritis and a leading cause of chronic disability, to a great extent in knee and/or hip joints. Commonly known as wear and tear arthritis, is a condition in which a protective cartilage on the end of the bones wears down over time<sup>1,</sup>. Osteoarthritis of the knees is one of five leading causes for disability among non-institutionalized adults, more common in females than in males<sup>2</sup>. Osteoarthritis is the fourth leading cause of 'years lived with disability' (YLD), accountings for 3% of total global YLD's. As per WHO by 2030, the demand for total knee arthroplasties will increase up to 67%<sup>3</sup>.Knee and hip joint replacement procedures account for 35% of the total arthritis procedures conducted during a hospitalization. The most common symptoms of knee osteoarthritis are pain and physical limitations that have a significant effect on the

individual's quality of life and her or his social and economic activities. Due to the increase in life expectancy, the number of elderly people, and the prevalence of obesity in society, it seems that the prevalence of knee osteoarthritis will increase<sup>3</sup>. It is of result of both mechanical and biological events that destabilize the normal biological coupling of degradation and synthesis of articular cartilage, chondrocytes, extracellular matrix, subchondral bone and subsequently synovial fluid. 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 antiinflammatory cytokines (including IL-4, IL-10, and IL-1ra). This cytokine imbalance is thought to activate proteolytic enzymes, leading to the destruction of cartilage<sup>5,6</sup>. The most common form of treatment for knee OA includes a

combination of non-pharmacological approaches and various pharmacologic therapies, including oral, topical, intra-articular medications, and intra-articular injections such as hvaluronic acid (HA)<sup>4,7</sup>. The final treatment option for knee OA is surgery. However, patients will often choose nonpharmacological and pharmacological treatments in order to delay the need for surgery. Current research efforts are focused on the identification of key biochemical pathways that can be targeted therapeutically through biological intervention for cartilage repair. 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. 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<sup>8,9</sup>.

PRP therapy provides delivery of a highly concentrated of growth factors to accelerate healing. However, at present, there are limited studies documenting the safety and efficacy of a nonsurgical PRP injectable for intraarticular use in knee Osteoarthritis.

Therefore, the present study has been undertaken in Gandhi Medical College, Hospital, Secunderabad to study the role of PRP in the osteoarthritis of knee joint. In this study PRP from the patient's own blood i.e. autologous PRP has been immediately infiltrated into their knee joints with osteoarthritis and the results of injection of PRP have been observed over a period of time.

### Aim of the Study:

• To study the effects of intra articular injections of autologous "Platelet Rich Plasma" in the osteoarthritis of knee joint.

#### **Objectives:**

- To assess the functional outcome after injecting platelet rich plasma in osteoarthritis knee joints.
- To compare the results with standard studies and draw conclusions.

### Pathogenesis of Knee Joint:

Osteoarthritis (OA) involves cartilage, bone, synovium, ligamentous capsular structures, and surrounding muscle. It is structurally by synovial inflammation, characterized degradation of articular cartilage, loss of joint function, active bone remodeling and angular deformity or malalignment<sup>10,11</sup>. Although a variety of synovial fluid markers provide insight into the biological response of joints to injury, no chemical or anatomic (imaging) biomarkers have been identified that monitor the development and progression of OA or the response to therapy<sup>12</sup>. OA is thought to be highly cytokinedriven, and is associated with mechanical stress resulting from of subchondral overloading bone from dysplasia, malalignment, and trauma. The small protein mediators (cytokines) provide chemical signaling or "cross-talk" among involved tissues. These signaling molecules incite inflammation in the synovium, remodeling subchondral bone, and enzyme activation and extracellular matrix degradation in articular cartilage. With the onset of OA, active remodeling including alteration in trabecular structure, sclerosis and osteophyte formation are seen<sup>13,14,16</sup>. Cytokines including IL-1, TNF- $\alpha$  and those of the fibrinolytic system including plasminogen, tissue and urokinase plasminogen activators (tPA, uPA), and plasmin play major signaling roles associated with cartilage degradation<sup>28</sup>.

#### Metabolic and Biochemical Changes In Osteoarthritis

Generalized increased hydration and swelling with loss of tensile strength is noticed in early OA, whereas increase in type I collagen synthesis and progressive fall occurs in proteoglycan concentration in later stage of OA. Specific collagens - Initial swelling of collagen fibrillary network with loss of type II collagen, specific cleavage of collagens and loss of tensile strength with increased content of collagen type IV. Type III and X collagen are also synthesized. Proteoglycans show increased extractability and decrease in monomer size because of specific cleavages by aggrecanases and metalloproteinases. Cytokines, proteinases and inhibitors increase pro-inflammatory There is in cytokines, aggrecanases, MMPs (matrix metalloproteinase), cathepsins and decrease in overall inhibitors<sup>29,27,21</sup>.

#### **Anabolic Growth Factors**

TGF (tissue growth factor beta- 1, 2 & 3) help in chondrocyte proliferation, matrix synthesis, modulate effects of IL-1 and increases proteinase inhibitors. Fibroblast and platelet derived growth factors also help in differentiation and proliferation of chondrocytes and MMP production. Insulin growth factor-1(IGF-1) increases glycosaminoglycan (GAG) and collagen synthesis. Bone morphogenetic proteins increase matrix synthesis<sup>25,16,13</sup>.

### **Catabolic Factors**

Interleukin-I (IL-1) and tumor necrosis factor (TNFa) increase MMPs, inhibit GAG synthesis and can further potentiate the degenerative cascade. Oncostatin-M combines with IL-1 and TNF topromote matrix breakdown. Others like IL-17 and IL-18 increase expression of IL-1 beta and IL-6 and increase MMP. NO (nitric oxide) can inhibit collagen and proteoglycan synthesis, NO is a major catabolic factor produced by chondrocytes can activate MMPs and cause an oxidative injury as well as produce apoptosis leading to degradation of articular cartilage. Prostaglandins effects on chondrocytes metabolism are complex and include enhanced type II collagen synthesis, activation of MMPs, and promotion of apoptosis. In cartilage explants, IL-1beta induces COX-2 expression and PGE2 production coordinate with proteoglycan degradation. Moreover, COX-2 inhibition prevents IL-1beta induced proteoglycan degradation<sup>12,20</sup>

IL-6 increases proteinase inhibitors production and proliferation of chondrocytes while IL-4, IL-13 and interferons oppose effects of proinflammatory cytokines.IL-1

receptor antagonist blocks effect of IL-1<sup>34,35</sup>.

#### **Physiology of Platelet Rich Plasma**

PRP has increased concentrations of PDGF, VEGF, TGFbeta1, and EGF compared with their concentrations in whole blood. PRP in OA knee joints delivers natural growth factors and their cytokines containing anabolic and catabolic factors in supraphysiologic concentrations directly into the site of injury to potentially optimize the healing environment. Maintaining a natural ratio of growth factors may provide a homeostatic environment and theoretically provide an abundance of healing factors without disrupting there in vivo relationships<sup>14,22,23</sup>.

#### **Material and Methods:**

It is a prospective longitudinal study on 100 patients with 161 primary osteoarthritic knee joints, selected from the outpatient Department of Orthopaedics in Gandhi Medical College, secunderabad, Telangana, India. Clinical examination and x rays of the knee joints were done and blood sample of the patients were collected and PRP prepared in the Blood Bank of the same Hospital. Infiltration was done in Operation Theatre under strict aseptic conditions. Patients were assessed with WOMAC (Western Ontario McMaster Universities Arthritis Index) scoring<sup>30</sup> 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**

- Age of the patient 30-70 years
- Kellegren –Lawrence scale grade 0-II With knee pain
- **1.** minimal (grade I –definite osteophyte, unimpaired joint space)
- 2. Moderate (grade II moderate diminution of joint space)

### **Exclusion Criteria**

- Patients of rheumatoid arthritis of knee joints.
- patients with haematological diseases(coagulopathies)
- Patients with active infections.
- Patients with immunosupression.
- Severe cardiovascular diseases.
- major axial deviation (varus more than 5degree ,valgus more than 5 degree)
- Patients on therapy with anti-coagulants-antiaggregants or use of NSAIDS within 5 days before blood donation.

All patients with primary osteoarthritis of knee joints were evaluated clinically using WOMAC scoring and radiographically. Based on kellgren and lawrence system<sup>4, 15</sup>.

# **Procedure for the Preparation of Platelet Rich Plasma** (**Prp**)

In the Blood Bank 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 with citrated blood were centrifuged at 1800 rpm for 15 min to separate erythrocytes, and at 3500 rpm for 10 min to concentrate platelets. Hereafter, the procedure was completely performed inside the biosafety cabinet. The PRP was then extracted through a pipette and transferred to a test tube. The final PRP was assessed for platelet count and was supplied for injection in a 10-mL syringe (approximately 5 mL per knee). Total leucocyte count and platelet 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.

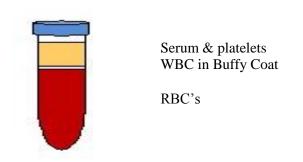
In the operation theatre with the patient in supine position, knee was scrubbed, painted and draped with sterile towels. With the patients knee in 45-90 degrees of flexion so that joint is opened for injection through lateral parapatellar approach. Under aseptic conditions, 8 mL platelet concentrate 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 Robert 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. During the follow-up period, nonsteroidal antiinflammatory drugs were not allowed and tramadol (dosage, 50 mg bid) was prescribed in case of discomfort; all patients were asked to stop medications 48 hours before follow-up assessment.



Fig 1: centrifuge 1<sup>st</sup> Spin 1800rpm x 15mins and 2<sup>nd</sup> spin: 3500rpm x 10mins



Fig2: Vacutaieners after 15 minutes of centrifuge with 1500 RPM

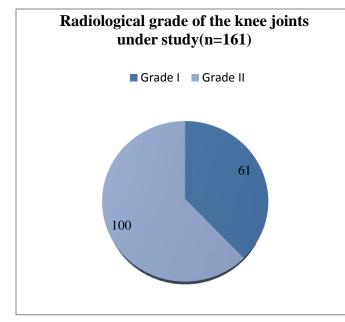


#### Fig 3: Residue of centrifuge

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 1<sup>st</sup> and 6<sup>th</sup> 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.

#### **Observations and Results:**

In this study on 161 osteoarthritic knee joints of Kellgren Lawrence radiological grade I-61 and II - 100 of total 100 patients. Patients were selected in the institutional Orthopaedic Inpatient Department. Out of which 61 patients were with bilateral early osteoarthritis and 39 patients were unilateral 23 patients selected were males and the remaining 77 patients were females.



#### Fig 3: number of patients in study and grading

In this study, the pain scores of the patients have decreased on the day of infiltration to one month and six months. 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 two cases pain has subsided completely.

### Table 1: Comparison of means of WOMAC Score -Pain on

	WOMAC Score - Pain mean(SD)		
0 day	1st month	6th month	After 6months
9.01(±1.98)	4.95(±1.14)	2.50(±1.05)	72.25
13.44(±1.50)	7.31(±1.32)	4.21(±1.54)	68.68
11.76(±2.74)	6.41(±1.70)	3.56(±1.60)	69.73
	9.01(±1.98) 13.44(±1.50) 11.76(±2.74)	0 day       1st month         9.01(±1.98)       4.95(±1.14)         13.44(±1.50)       7.31(±1.32)         11.76(±2.74)       6.41(±1.70)	0 day         1st month         6th month           9.01(±1.98)         4.95(±1.14)         2.50(±1.05)           13.44(±1.50)         7.31(±1.32)         4.21(±1.54)           11.76(±2.74)         6.41(±1.70)         3.56(±1.60)

o day, 1<sup>st</sup> month, 6<sup>th</sup> month based of ANOVA

In this study, the stiffness scores of the patients have decreased on the day of infiltration to one month and six months. In two cases there was no stiffness prior to the infiltration, and there was no stiffness in 43 knee joints at six months follow up, i.e. stiffness had completely subsided.

WOMAC Score - Stiffness mean(SD)				
	0 day	1st month	6th month	After
				6months
Grade I	3.26(±1.18)	1.52(±0.69)	0.47(±0.56)	85.59
Grade II	4.68(±1.03)	2.58(±0.71)	1.22(±0.57)	73.93
Total	4.14(±1.28)	2.18(±0.87)	0.93(±0.67)	77.54

# Table 2: Comparison of means of WOMAC Score-Stiffness

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.

		WOMAC Score - Functionality mean(SD)		
	0 day	1st month	6th month	After 6months
Grade I	39.80(±4.92)	21.31(±6.55)	11.04(±8.24)	72.26
Grade II	50.46(±4.07)	28.18(±7.80)	17.85(±9.23)	64.63
Total	46.42(±6.80)	25.57(±8.06)	15.27(±9.47)	67.11

 Table 3: Comparison of means WOMAC score

### Functionality

In the present study the total WOMAC scores of the patients have decreased from on the day of infiltration to one month and six months.

		WOMAC Score – total mean(SD)		
				After
	0 day	1st month	6th month	6months
Grade I	52.08(±6.49)	27.78(±7.46)	14.01(±9.20)	73.09
Grade II	$68.58(\pm 4.90)$	38.07(±8.62)	$23.26(\pm 10.53)$	66.09
Total	62.32(±9.78)	34.17(±9.59)	19.75(±10.98)	68.31
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 Table 4: Comparison of means of WOMAC score

• There was definite decrease in the mean WOMAC scores from "0" day (52.08) to 1<sup>st</sup> month (27.78), 1<sup>st</sup> month

(27.78) to  $6^{th}$  month (14.01) in grade I knee joints i.e. 73.09% of improvement.

- There was definite decrease in the mean pain scores from "0" day
- (68.58) to 1<sup>st</sup> month (38.07), 1<sup>st</sup> month (38.07) to 6<sup>th</sup> month (23.26) in grade II knee joints. i.e.66.09% of improvement.
- There was definite decrease in the mean pain scores from "0" day
- (62.32) to 1<sup>st</sup> month (34.17). 1<sup>st</sup> month (34.17) to 6<sup>th</sup> month (19.75) in both the grades of knee joints together i.e. 68.31% of improvement.

	Results
Excellent (85-100%)	19
Good (70-84%)	93
Fair (55-69%)	22
Poor (<55%)	27

# Table 5: Analysis of results of all knee joints according to the working classification (n=161)

• On doing the ANOVA (Analysis of variance), the calculated p-Value was less than 0.001. So the results were statistically significant.

	Grade I	Grade II
Excellent	14	5
Good	35	58
Fair	5	17
Poor	7	20

# Table 6: Comparison of results of grade I and grade II knee joints according to the working classification (n=161).

### **Discussion:**

Osteoarthritis is a major public health problem which causes pain and disability in one third of all affected patients. It is one of the crucial musculoskeletal disorders characterised by the imbalanced homoeostasis and destruction of the articular cartilage, in which pro-inflammatory cytokines are important catabolic regulators during osteoarthritis cascade<sup>24</sup>.

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<sup>12,13</sup>. Current pharmacologic interventions may only temporarily reduce chronic pain, but for the time being, no proven disease

modifying therapy is available  $^{9,10}$ .

In this prospective study, WOMAC scores were evaluated preinjection 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 spinning of the sample at 1800 rpm for 15 min to separate erythrocytes, and at 3500 rpm for 10 min to concentrate platelets and leucofilters were not used. Kon et al separated the blood sample twice at 1480rpm x 6 minutes and again at 3400rpm x 15 minutes with the baseline platelets more than 5 times activated with CaCl<sub>2</sub> and given more than three doses of injection with 2 weeks gap. In 2011, Filardo et al, used 5 ml PRP with 5 times the platelet count prepared from double spinning technique and activated with CaCl<sub>2</sub><sup>20,31</sup>

They have infiltrated three injections of PRP with one week gap. 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. Spakova et al used a stepwise approach of three centrifugations to concentrate the plasma (3200rpm x15min, 1500rpm x 10min, 3200rpm x10min) 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<sup>18</sup>.

Cerza et al in 2012 used 5ml of PRP not activated with CaCl<sub>2</sub>, platelet count less than the 5 times the baseline with single spinning and without leuco-filters. They have infiltrated four injections with each one week gap. The idea of using CaCl<sub>2</sub> was, it activates the platelets. Sanchez et al on the other hand, centrifuged the plasma only once at 640g x 8 minutes. Though not clearly stated, it appears that Sanchez et al utilized an enzyme linked immunosorbent assay kit to quantify the amount of platelets and growth factors. The preparation of PRP, number of platelets, amount of PRP infiltrated, and frequency of injections were not uniform<sup>19</sup>. Different researchers have used different methods of preparation, different amount of PRP and at different time periods. 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<sup>22</sup>.

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, 19 joints have shown excellent results, 93 joints have shown good results, 22 joints have shown fair results and 27 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. Twelve 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 showed better improvement in grade I osteoarthritis knee joints than grade II knee joints. Grade I patients shown 73.09 percentage of improvement, whereas grade II patients shown 66.09 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

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. 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 up to 6 months follow up. But the conditions 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 osteoarthritis. 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. Spakova et al. in 2012, in their study found statistically significant improvement in • WOMAC score, VAS and pain relief when compared to. viscoelastic supplementation <sup>14,18,32</sup>.

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, 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. 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<sup>17,20,31</sup>.

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.

Kon et al. in 2010 and Sanchez et al. in 2007 have reported some injection pain, local inflammation of short duration and reaccumulation of effusion, but the exact numbers were not mentioned. Sandeep Patel et al,in 2013, in their study have documented some systemic adverse effects <sup>19,32</sup>. Which were immediate and systemic rather than local and were of short duration not lasting more than 30 minutes. But they have not explained the characteristics of the adverse effects. They have attributed these adverse effects to the higher number of platelets in the infiltrating PRP sample and the possibility of CaCl<sub>2</sub>, which was used as an activating agent. Immediate post infiltration all patients have complained of severe pain but no systemic and long term complications noted during the course of this study.

All the patients have shown improvement at around two weeks. Therapeutic benefit might not be because of chondrogenesis, because it would have taken more time for the patients to perceive benefits. PRP may influence the overall joint homeostasis, reducing synovial membrane hyperplasia and modulating the cytokine level, thus leading to an improvement in the clinical outcome, even if only temporarily and without affecting the cartilage tissue structure and joint degeneration progression. 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. Filardo et al in 2012 have shown worsening of WOMAC score from nine months onwards, it implies that if the chondral remodelling was the cause for the improvement of symptoms, the benefit would have started later and lasted for a longer duration.

This study has its limitations,

No comparative group was included.

The Sex, Body Mass Index (BMI), was 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 is a common, debilitating disease and one of the main causes of musculoskeletal disability.
- Osteoarthritis 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 Kellgren Lawrence 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.

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