International Journal of Research in Orthopaedics
Vamshi R et al. Int J Res Orthop. 2018 Jan;4(1):133-140
http://www.ijoro.org

Original Research Article

DOI: http://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20175661

A prospective study of intra-articular injections of platelet rich plasma in early osteoarthritis knee joint

Rentala Vamshi*, Vivekananda Bheemisetty, Raju Bollabathini, Vishwanath Mahadevuni

Department of Orthopedics, Osmania Medical College, Hyderabad, Telangana, India

Received: 20 October 2017
Revised: 01 December 2017
Accepted: 02 December 2017

***Correspondence:**
Dr. Rentala Vamshi,
E-mail: vamc.rentala@gmail.com

ABSTRACT

Background: Platelet-rich plasma (PRP) is a natural concentrate of autologous blood growth factors experimented in different fields of medicine in order to test its potential to enhance tissue regeneration. The aim of our study is to study the effects of intra articular injections of autologous "Platelet Rich Plasma" in the osteoarthritis of knee joint and to assess the functional outcome after injecting platelet rich plasma in osteoarthritic knee joints and compare the results with standard studies and draw conclusions.
Methods: This is a prospective study done on 161 Kellgren-Lawrence radiological grade I and grade II knee joints, between August 2013 and March 2016 which, were treated with PRP intra-articular injections. The procedure consisted of injection of 8 ml platelet concentrate into the knee joint with an 18- gauge needle without local anaesthetic. 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.
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.
Conclusions: 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.

Keywords: Platelet rich plasma, Kellgren Lawrence radiological grading, WOMAC score, Osteoarthritis knee

INTRODUCTION

Osteoarthritis, 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.[1] Osteoarthritis of the knees is one of five leading causes for disability among non-institutionalized adults.[2] Osteoarthritis is the fourth leading cause of 'years lived with disability' (YLD), accounting for 3.0% of total global YLD's. As per WHO by 2030, the demand for total knee arthroplasties will increase up to 67%.[3] Knee and hip joint replacement procedures account for 35% of the total arthritis procedures conducted during a hospitalization.[4] Knee osteoarthritis is more common in females than in males.[5] 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.[6,7] 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. 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. Osteoarthritis is clinically heterogeneous, and the processes that cause deterioration are still poorly understood.[8] Current opinion is that the disease progression results from an imbalance between proinflammatory cytokines (including interleukin [IL]-1a, IL-1, and tumour 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 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 hyaluronic acid (HA).[2] The final treatment option for knee OA is surgery. However, patients will often choose non-pharmacological and pharmacological treatments in order to delay the need for surgery. Because of limitations in the effectiveness of conventional management options, alternative options such as biological and regenerative methods are coming into vogue. 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.[9] 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.[8] PRP therapy provides delivery of a highly concentrated of growth factors to accelerate healing.[10] However, at present, there are limited studies documenting the safety and efficacy of a nonsurgical PRP injectable for intraarticular use in knee Osteoarthritis.[11,12] Therefore, the present study has been undertaken in Osmania Medical College, Hospital, and Hyderabad to study the role of PRP in the osteoarthritis of knee joint. In this study, PRP from the patients' 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.

METHODS

A prospective longitudinal study on 100 patients with 161 primary osteoarthritic knee joints, selected from the outpatient of Department of Orthopaedics in Osmania General Hospital, Hyderabad, under Osmania Medical College, Hyderabad, Hyderabad district, Telangana state. The study period was from November 2014 to October 2016. Clinical examination and radiographs 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 septic conditions. Patients were assessed with WOMAC (Western Ontario McMaster Universities Arthritis Index) (Table 1) 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. By using ANOVA (analysis of variance), the statistical significance was analysed and calculated.

Inclusion criteria

Age of the patient 30-70 years, Kellgren–Lawrence scale grade 0-II With knee pain.

Exclusion criteria

Patients of rheumatoid arthritis of knee joints, haematological diseases (coagulopathies) active infections, patients with immunosuppression, 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.

Standard operating 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 patients' 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 anaesthetic. 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 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.

Table 1: Western Ontario and McMaster universities osteoarthritis index.

Name_____Date_____ **Instructions : Please rate the activities in each category according to the following scale of difficulty : 0=None; 1=Slight; 2= Moderate; 3= Very; 4=Extremely** **Circle one number for each activity**		
Pain	1. Walking	0 1 2 3 4
	2. Stair climbing	
	3. Nocturnal	
	4. Rest	
	5. Weight bearing	
Stiffness	1. Morning stiffnes	
	2. Stiffness occuring later in the day	
Physical function	1. Descending stairs	
	2. Ascending stairs	
	3. Rising from sitting postion	
	4. Standing	
	5. Bending to floor	
	6. Walking on flat surface	
	7. Getting in/out of car/auto	
	8. Going shopping	
	9. Putting on socks/cleaning ankles	
	10. Lying in the bed	
	11. Taking off socks	
	12. Rising from bed	
	13. Getting in/out of bath	
	14. Sitting	
	15. Getting on/off toilet	
	16. Heavy domestic duties	
	17. Light domestic duties	
Total score : _____/96 = _____% **Comments/ Interpretation to be completed by therapist only**		

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 (Figure 1).

In order to suite the WOMAC score with Indian rural population, we had replaced the item getting in/out of a car with getting in/out of auto, and putting on/taking off socks with cleaning of ankles. 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. As in the literature we have not found the grading of results of WOMAC score, hence we have graded it to quantify the results. Outcome measured is quantified in percentage of improvement.

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

The means of the each parameter and total WOMAC score were calculated.

RESULTS

Grade II knee joints were more (100) than grade I knee joints (61) (Figure 1). Patients with bilateral knee joints (61) were more than unilateral knee joints (39) (Figure 2). Female patients (77) were more than male (23) in this study (Figure 3).

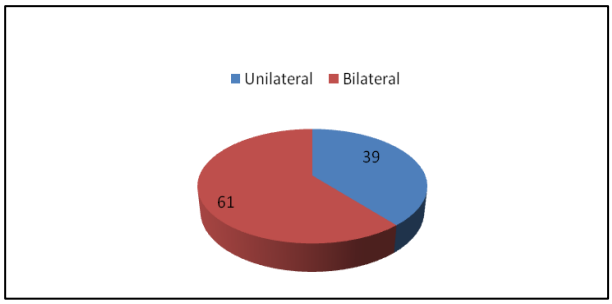

Figure 1: Total no. of patients with knee joints injected with PRP (N=161).

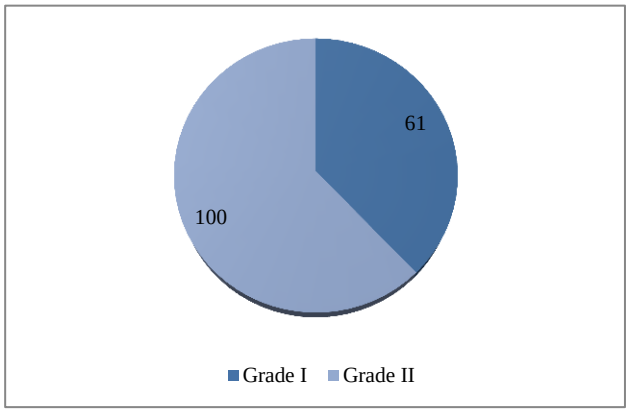

Figure 2: Radiological grade of the knee joints under study (n=161).

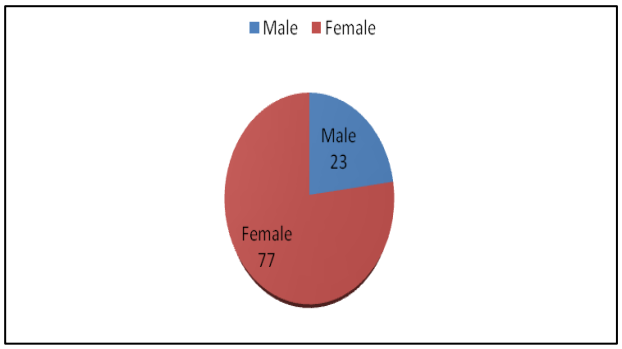

Figure 3: Sex distributions of patients with knee joints under study (n=100).

There was definite decrease in the mean pain scores from, 0 day-(9.01) to 1st month (4.95), 1st month (4.95) to 6th month (2.50) in grade I knee joints i.e. 72.25% of improvement (Figure 4). There was definite decrease in the mean pain scores from, 0 day (13.44) to 1st month (7.31), 1st month (7.31) to 6th month (4.21) in grade II knee joints. i.e.68.68% of improvement. There was definite decrease in the mean pain scores from, 0 day (11.76) to 1st month (6.41). 1st month (6.41) to 6th month (3.56) in both the grades of knee joints together i.e. 69.73% of improvement. On doing the ANOVA (Analysis of variance), the calculated p-Value was less than 0.001. So the results were statistically significant.

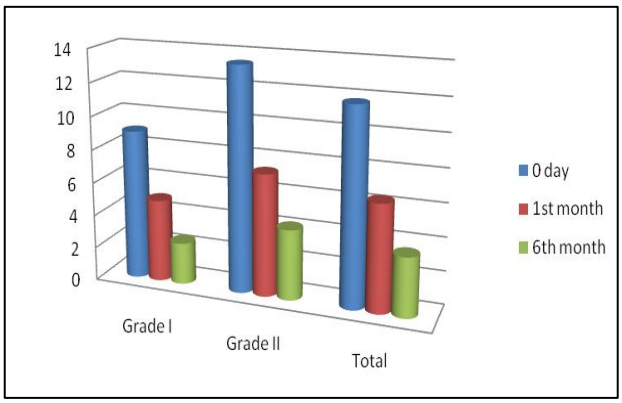

Figure 4: WOMAC score-pain mean (SD).

There was definite decrease in the mean stiffness scores from 0 day (3.26) to 1st month (1.52), 1st month (1.52) to 6th month (0.47) in grade I knee joints i.e. 85.59% of improvement (Figure 5). There was definite decrease in the mean stiffness scores from, 0 day (4.68) to 1st month (2.58), 1st month (2.58) to 6th month (1.22) in grade II knee joints i.e. 73.93% of improvement. There was definite decrease in the mean stiffness scores from, 0 day (4.14) to 1st month (2.18). 1st month (2.18) to 6th month (0.93) in both the grades of knee joints together i.e. 77.54% of improvement. On doing the ANOVA (Analysis of variance), the calculated p-Value was less than 0.001 so the results were statistically significant.

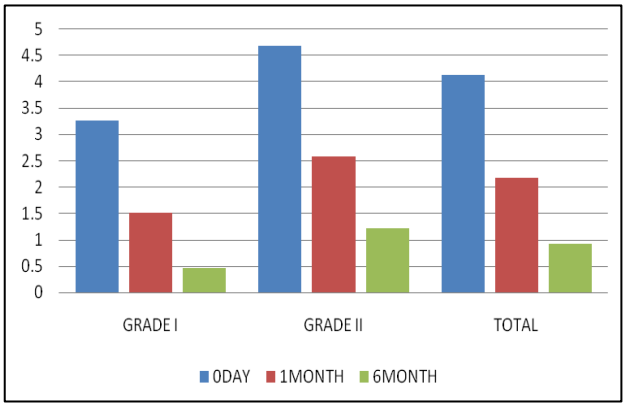

Figure 5: WOMAC score-stiffness mean (SD).

There was definite decrease in the mean functionality scores from, 0 day (39.80) to 1st month (21.31), 1st month (21.31) to 6th month (11.04) in grade I knee joints i.e. 72.26% of improvement (Figure 6). There was definite decrease in the mean functionality scores from, 0 day (50.46) to 1st month (28.18), 1st month (28.18) to 6th

month (17.85) in grade II knee joints i.e. 64.63% of improvement. There was definite decrease in the mean functionality scores from 0 day (46.42) to 1st month (25.57). 1st month (25.57) to 6th month (15.27) in both the grades of knee joints together i.e. 67.11% of improvement. On doing the ANOVA (Analysis of variance), the calculated p value was less than 0.001. So the results were statistically significant.

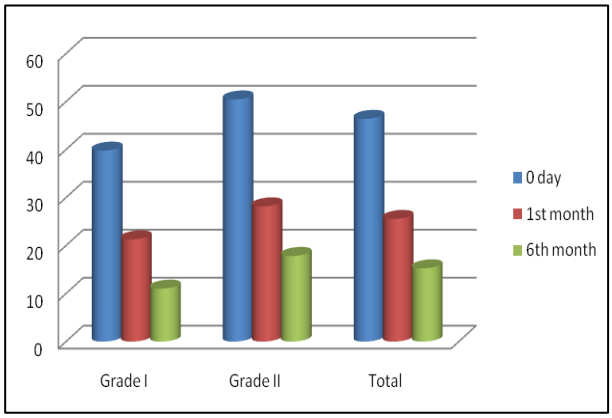

Figure 6: WOMAC score- functionality mean (SD).

There was definite decrease in the mean WOMAC scores from, 0 day (52.08) to 1st month (27.78), 1st month (27.78) to 6th month (14.01) in grade I knee joints i.e. 73.09% of improvement (Figure 7). There was definite decrease in the mean pain scores from, 0 day (68.58) to 1st month (38.07), 1st month (38.07) to 6th 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 1st month (34.17). 1st month (34.17) to 6th month (19.75) in both the grades of knee joints together i.e. 68.31% of improvement. On doing the ANOVA (analysis of variance), the calculated p-Value was less than 0.001. So the results were statistically significant.

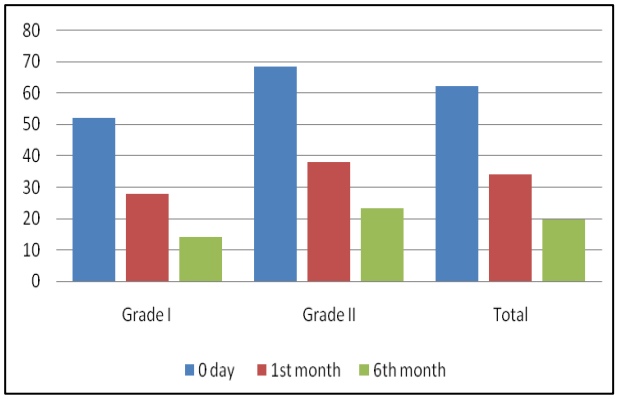

Figure 7: WOMAC score-total mean (SD).

161 knee joints were showing good (93) and excellent (19), fair (22) and poor (27) results. When ANOVA done for the results, the calculated p-value was less than the 0.05, so the results were statistically significant.

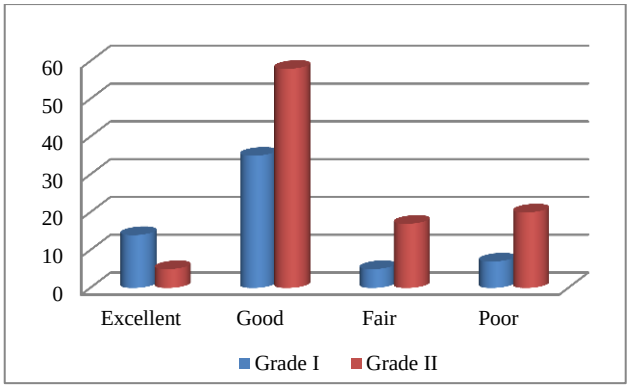

Figure 8: Comparison of results of grade I and grade II knee joints according to the working classification (n=161).

Excellent (14) results were more in grade I knee joints than in grade II knee joints, excellent (5) good (58) poor (20) and fair (17) results were more in grade II knee joints than in grade I knee joints, Good (35) poor (7), fair (5) (Figure 8). Though the results were clinically significant, when ANOVA was done, the calculated p-value was more than 0.05, so the results were statistically not significant.

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. 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.[13] 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 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 1480 rpm× 6 minutes and again at 3400 rpm×15 minutes with the baseline platelets more than 5 times activated with $CaCl_2$ and given more than three doses of injection with 2 weeks gap (Table 2).[13] In 2011, Filardo et al, used 5 ml PRP with 5 times the platelet count prepared from double spinning technique and activated with $CaCl_2$.

Table 2: Comparision of different studies of PRP in treating osteoarthritis of knee joints.

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					
Sandeep et al[8]	PRP vs. Placebo	54	50	2	0-3	8	<5×Baseline	+
Filardo et al[13]	PRP vs. PRGF	54	55	3	0-1-2	5	5×Baseline	VAS
Cerza et al[25]	PRP vs. HA	60	60	4	0-1-2-3	5	>5×Baseline	+
Spakova et al[25]	PRP vs. HA	60	60	3	0-1-2	3	<5×Baseline	+
Filardo et al[40]	Single vs. double spinning	72	72	3	0-3-6	5	<5×Baseline	VAS
Kon et al[41]	PRP vs. HA	50	50	3	0-2-4	5	>5×Baseline	VAS & IKDC
Our study	PRP	161	NA	1	NA	5	>5×Baseline	+

They have infiltrated three injections of PRP with one week gap.[14] 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.[15] Spakova et al[16] used a stepwise approach of three centrifugations to concentrate the plasma (3200 rpm×15 min, 1500 rpm×10 min, 3200 rpm×10 min) 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.[16,17] Cerza et al in 2012 used 5 ml 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.[18] Sanchez et al, on the other hand, centrifuged the plasma only once at 640 g×8 minutes.[19] 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. Different researchers have used different methods of preparation, different amount of PRP and at different time periods (Table 2). 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 up to 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 labour work. Twelve patients who have used NSAIDS (nonsteroidal anti-inflammatory drugs) against the medical advice have shown poor results. But it is not clear, how the obesity with active labour 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 73.09 percentage of improvement, whereas grade II patients shown 66.09 percentage when evaluated with WOMAC score. But the difference is not statistically significant. 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 condition of the patients was 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.[13] 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.[16] Filardo et al, 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.[17] 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 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.[15] 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.[17,20] Patel et al, 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 min. 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 $CaCl_2$, which was used as an activating agent.[8] 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. Patel et al, 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.[8] Filardo et al 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.[15]

This study has its limitations, no comparative group was included. The 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 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.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Osteoarthritis. Mayo Clinic Website. Available at: http://www.mayoclinic.org/diseases-conditions/osteoarthritis/basics/definition/con-20014749. Accessed October 2, 2014.
2. Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Pub Health. 1994;84(3):351-8.
3. Global Economic and Health Care Burden of Musculoskeletal Disease, 2001, World Health Organization. Available at: www.boneandjoint decade.org. Accessed on 3 August 2017.
4. Gabriel SE, Crowson CS, Campion ME, O'Fallon WM. Direct medical costs unique to people with arthritis. J Rheumatol. 1997;24(4):719–25.
5. Zhang Y, Xu L, Nevitt MC, Aliabadi P, Yu W, Qin M, et al. Comparison of the prevalence of knee osteoarthritis between the elderly Chinese population in Beijing and whites in the United States: The Beijing Osteoarthritis Study Arthritis Rheum. 2001;44:2065-71.

6. Michael JW, Schlüter-Brust KU, Eysel P. The epidemiology, etiology, diagnosis and treatment of osteoarthritis of the knee. Dtsch Arztebl Int 2010;107:152-62.
7. Zhang Y, Xu L, Nevitt MC, Aliabadi P, Yu W, Qin M, et al. Comparison of the prevalence of knee osteoarthritis between the elderly Chinese population in Beijing and whites in the United States: The Beijing Osteoarthritis Study Arthritis Rheum 2001;44:2065-71.
8. Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with Platelet-Rich Plasma Is More Effective Than Placebo for Knee Osteoarthritis - A Prospective, Double-Blind, Randomized Trial. The Am J Sports Med. 2013;41:356-64.
9. Pietrzak WS, Eppley BL. Platelet rich plasma: Biology and new technology. J Craniofac Surg. 2005;16:1043–54.
10. Werner S, Grose R: Regulation of wound healing by growth factors and cytokines. Physiol Rev. 2003;83:835–70.
11. Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet rich plasma. Am J Sports Med. 2006;10:1–515.
12. Barrett S, Erredge S: Growth factors for chronic plantar fasciitis. Podiatry Today. 2004;17:37–42.
13. Kon E, Mandelbaum B, Buda R. Platelet-Rich Plasma Intra-Articular Injection Versus Hyaluronic Acid Viscosupplementation as Treatments for Cartilage Pathology: From Early Degeneration to Osteoarthritis. Arthoscopy Related Surg. 2011;27(11):1490–501.
14. Filardo G, Kon E, Buda R, Timoncini A, Di Martino A, Cenacchi A, et al. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. Knee Surg Sports Traumatol Arthrosc. 2011;19:528–35.
15. Filardo G, Kon E, Di Martino A, Di Matteo B, Merli ML, Cenacchi A, et al. Platelet-rich plasma versus hyaluronic acid to treat knee degenerative pathology: study design and preliminary results of a randomized controlled trail. BMC Musculoskelet Disord. 2012;213:229.
16. Spakova T, Rosocha J, Lacko M, Harvanova D, Gharaibeh A. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil. 2012;91:411-7.
17. Kon E, Buda R, and Filardo G, et al. Platelet-rich Plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions. Knee Surg Sports Traumatol Arthrosc. 2010;18:472-9.
18. Cerza, Carni S, Carcangiu A, Di Vavo I, Schiavilla V, Pecora A, et al. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular infiltration in the treatment of gonarthrosis. Am J Sports Med. 2012;40(12):2822-7.
19. Sanchez M, Anitua E, Azofra J. Injection of an autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study, Clin Experim Rheumatol. 2008;26:910-3.
20. Sánchez M, Anitua E, Azofra J, Andia I, Padilla S, Mujika I. Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. Am J Sports Med. 2007;35:245-51.

Cite this article as: Vamshi R, Bheemisetty V, Bollabathini R, Mahadevuni V. A prospective study of intra-articular injections of platelet rich plasma in early osteoarthritis knee joint. Int J Res Orthop 2018;4:133-40.