

A CLINICAL STUDY ON ROLE OF INTRA ARTICULAR INJECTION OF PLATELET RICH PLASMA FOR OSTEOARTHRITIS OF KNEE AT GGH KADAPA

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Abstract:

Introduction: Osteoarthritis (OA) is chronic progressive, softening and disintegration of articular cartilage and new growth of cartilage and bone at joint margins. So many non surgical modalities of treatment are being developed to delay the surgery for osteoarthritis. Out of which PRP is being widely used. The purpose of this study was to evaluate functional outcome of intraarticular platelet-rich plasma in osteoarthritis knee joints. **Materials and Methods:** It is a prospective randomized study conducted from March 2021 to March 2022 on 100 osteoarthritis knee joints, selected from the Outpatient Department of Orthopedics, at Government Medical College, Kadapa. 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 Pathology of the same institute. Injection 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, 3 month and 6 months. A reduction in WOMAC score is suggestive of improvement in the patient's condition. **Results:** A Prospective study with 50 patients with bilateral primary osteoarthritis (100 knees) grade 1/2 to study clinical and functional outcome of intraarticular PRP. Out of 100 knees, 40 were males, 60 were females, 45 were grade 1, 55 were grade 2. According to Womac score, grade of result in group A – poor - 4, fair - 10, good - 32, excellent – 54. On assessing the results, there is a significant improvement in WOMAC score of all the patients and the results sustained for 6 months. Though clinically better results are seen in grade I knee joints than grade II knee joints, the difference is statistically not significant. **Conclusion:** We can safely conclude that Intraarticular Autologous PRP injection in Osteoarthritis (Grade I and Grade II) of Ahlback's radiological grading gives relief from pain, stiffness and improves physical functionality without major side effects and can be used as modality of treatment.

KEY WORDS: Platelet- rich plasma (PRP), Womac score, Ahlback's grading.

INTRODUCTION

Osteoarthritis (OA) is chronic progressive, softening and disintegration of articular cartilage and new growth of cartilage and bone at joint margins. Osteoarthritis is a common, debilitating and degenerative disease which is associated with a large economic burden¹. Osteoarthritis (OA) of the knee is one of the main causes of morbidity and disability². 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 demand for total knee arthroplasties will increase up to 670%.

This condition places a major burden on our current economy, with billions of dollars of annual expenditure associated with pharmaceutical treatment for pain relief, rehabilitation, and joint replacements³. Current opinion is that the disease progression results from an imbalance between pro inflammatory 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 system³. Autologous PRP is a volume of plasma having a platelet concentration above normative baseline values⁴.

Platelets are source of high concentrations of cytokines well documented to regulate a number of processes related to healing and tissue regeneration.^{5, 6, 7}. 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 underpowered⁸. However, at present, there are limited studies documenting the safety and efficacy of a nonsurgical PRP injectable for intraarticular use in knee Osteoarthritis^{9,10}.

Keeping in view these grey areas in our knowledge, this prospective study was designed to evaluate the role of PRP in the grade 1 and 2 of knee osteoarthritis. In this study PRP from the patient's own blood i.e. Autologous PRP has been immediately injected into their knee joints with osteoarthritis and the results of injection of PRP have been observed over a period of time.

MATERIALS AND METHODS

It is a prospective randomized study conducted from March 2021 to March 2022 on 100 primary osteoarthritis knee joints, selected from the Outpatient Department of Orthopedics, at Government Medical College, Kadapa. 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 Pathology, patients received single dose of PRP. Injection was done in Operation Theatre with strict aseptic precautions.

Patients were assessed with WOMAC (Western Ontario McMaster Universities Arthritis Index) scoring pre injection of PRP and post injection period of 1 month,3 month and 6 months. A reduction in WOMAC score is suggestive of improvement in the patient's condition. The collected data been computed in excel and analyzed through SPSS version 2.0,EPI.INFO and the p value and mean values been obtained.

Ahlback's Radiological Grading Of Osteoarthritis of Knee Joints

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)

Patient Selection

All patients with primary osteoarthritis of knee joints were evaluated clinically using WOMAC scoring and radio graphically based on Ahlback's radiological grading, patients with Grade I and II Osteoarthritis were selected irrespective of age, sex and socioeconomic status. Selected patient's blood samples were sent for complete blood picture, erythrocyte sedimentation rate, C-reactive proteins, and random blood sugar.

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- 160 range excluded from the study. Patients were enquired about oral medications like NSAIDS, steroids, if any was asked to stop one week before administration of PRP. 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.

Follow up: During the follow-up period, nonsteroidal anti-inflammatory drugs and steroids were not allowed, and tramadol (dosage, 50 mg bds) was prescribed in case of discomfort; all patients were asked to stop medications 72 hours before follow-up assessment.

RESULTS

A Prospective study with 50 patients with bilateral grade 1 and 2 osteoarthritis (100 knees) to study functional outcome of intraarticular PRP. Out of 100 knees, 40 were males, 60 were females, and 45 were grade 1, 55 were grade 2. According to Womac score, grade of result in group A – poor - 4, fair - 10, good - 32 , excellent – 54 .

On assessing the results, there is a significant improvement in WOMAC score of all the patients and the results sustained for 6 months. Though clinically better results are seen in grade I knee joints than grade II knee joints, the difference is statistically not significant. There is no significant difference between males and females.

Table 1 Grade of result in patients

Grade of result	50 patients
Poor	4
Fair	10
Good	32
Excellent	54
Total	100 knees

DISCUSSION

Hyaline cartilage has low healing potential, hence it's lesions and degeneration are difficult to treat. Present pharmacologic options available may only temporarily decrease chronic pain, but for the time being, no proven disease modifying agent is available¹². In this prospective randomized study, patients were given single dose of PRP.

WOMAC scores were evaluated pre-injection and post injection period on first month, three months 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 selected were having more than one lakh platelets, every patient got more than 5 lakh platelets per ml, which is prepared by double spinning of the sample for 5 minutes and 10 minutes with 3000 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 and given more than three doses of 2 injections with 2 weeks gap¹⁴.

Patel et al in 2013 used single spinning technique with leuco-filters. They have given two injections of PRP activated with CaCl each 8 ml, 2, with 3 weeks gap. Their platelet count is less than 5 times the base line^(2, 14). In 2011, Filardo et al used 5 ml PRP with 5 times the platelet count prepared from double spinning technique and activated with CaCl₂. They have infiltrated three injections of PRP with one week gap¹¹.

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 functionality¹⁷. Cerza et al in 2012 used 5ml of PRP not activated with CaCl, 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 was, it activates the platelets¹⁵.

Spakova et al in 2012 did a 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 leukocyte 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 joint¹³.

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. VAS- Visual analogue score, IKDC – International Knee Documentation Committee 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 not 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 stimulating the chondral anabolism or slowing the catabolic process. As we have given a working classification to assess the results, in patients, 54 joints have shown excellent results, 32 joints have shown good results, 10 joints have shown fair results and 4 joints have shown poor results. Though the mean pain scores have decreased in all the patients, the efficacy has been varied from patient to patient. Results were poor in obese, patients doing heavy work. The results have shown better improvement in grade I osteoarthritis knee joints than grade II knee joints. In every patient, there is decrease in WOMAC score, but in no one it has reached '0'.

It means that PRP delays the osteoarthritis progression in the joints, but it has not cured osteoarthritis. To evaluate its duration of action long term follow up studies are required. Spakova et al. in 2012, in their study found statistically significant improvement in WOMAC score, VAS and pain relief when compared to viscoelastic supplementation¹³.

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 oateoarthritis¹⁸. 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.

CONCLUSION

Osteoarthritis (OA) of the knee is one of the main causes of morbidity in elderly. It is a process of destruction and repair. Osteoarthritis is a common, debilitating disease with a large economic burden. The mechanism and duration of action of PRP is still not understood completely which requires further studies. We can safely conclude that Intraarticular Autologous PRP infiltration in early primary Osteoarthritis (Grade I and Grade II) of Ahlback's radiological grading gives relief from pain, stiffness and improves physical functionality without major side effects and can be used as modality of treatment. The efficacy goes off early in those who continue to do heavy work on comparison to those with sedentary lifestyle. The efficacy is more if patients undergo physiotherapy after injection. Immediate post injection, 10 patients have complained of severe pain. 5 patients had effusion on the day of injection, but no systemic and long term complications noted.

REFERENCES

1. Anna Litwic, Mark H Edwards, Elaine M Dennison, and Cyrus Cooper. Epidemiology and burden of Osteoarthritis, British medical bulletin 2015:1-15.
2. Sandeep Patel, Mandeep S. Dhillon, Sameer Aggarwal, Neelam Marwaha, and Ashish Jain. 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.
3. Steven Sampson, Marty Reed, Holly Silvers, Michael Meng, Bert Mandelbaum. Injection of Platelet-Rich Plasma in Patients with Primary and Secondary Knee Osteoarthritis- A Pilot Study, American Journal of Physical Medicine & Rehabilitation, 2010: 1961-69
4. Pietrzak WS, Eppley BL: Platelet rich plasma: Biology and new technology. J CraniofacSurg 2005; 16: 1043-54.
5. Eppley BL, Woodell JE, Higgins J: Platelet quanti • cation and growth factor analysis from platelet-rich plasma: Implications for wound healing. PlastReconstrSurg 2004; 114:1502-7.
6. Werner S, Grose R: Regulation of wound healing by growth factors and cytokines. Physiol Rev 2003;83: 835-70.
7. Anitua E, Sanchez M, Nurden AT, et al: New insights into and novel applications for platelet-rich • brin therapies. Trends Biotechnol 2006; 24:227-34.

8. Mishra A, Pavelko T: Treatment of chronic elbow tendinosis with buffered platelet rich plasma. *Am J Sports Med* 2006; 10:1-5 15.
9. Barrett S, Erredge S: Growth factors for chronic plantar fasciitis. *Podiatry Today* 2004; 17:37-42.
10. Sampson S, Gerhardt M, Mandelaum B: Platelet rich plasma injection grafts for musculoskeletal injuries: A review. *Curr Rev Musculoskelet Med* 2008; 1: 165-74.
11. Giuseppe Filardo, Elizaveta Kon, Roberto Buda, Antonio Timoncini, Alessandro Di Martino, Annarita Cenacchi, Pier Maria Fornasari, Sandro Giannini, Maurilio Marcacci. Platelet-rich plasma intra-articular knee injections for the treatment of degenerative cartilage lesions and osteoarthritis. *Knee Surg Sports Traumatol Arthrosc* (2011) 19:528-535.
12. Lucarelli E, Fini M, Beccheroni A. Stromal stem cells and platelet-rich plasma improve bone allograft integration. *ClinOrthop*2005; 435:62-8.
13. 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; 91:411-417.
14. Elizaveta Kon, Bert Mandelbaum, Robert Buda, et al Platelet-Rich Plasma Intra-Articular Injection versus Hyaluronic Acid Viscosupplementation as Treatments for Cartilage Pathology: From Early Degeneration to Osteoarthritis. *Arthroscopy* 2011; 11: 1490-1501.
15. Cerza, Carni S, Carcangiu A, Di Vavo I, et al. Comparison between hyaluronic acid and platelet-rich plasma, intra-articular in · ltration in the treatment of gonarthrosis. *Am J Sports Med.* 2012 Dec;40(12):2822-7.
16. Vaquerizo V, Placencia MA, Arribas I, et al. Comparison of intra-articular injections of plasma rich in growth factors versus Durolane hyaluronic acid in the treatment of patients with symptomatic osteoarthritis: a randomized controlled trail. *Arthroscopy* 2013; 29:1635-43.
17. Filardo G, Kon E, Di Martino 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 MusculoskeletDisord* 2012; 213:229.
18. Kon E, Buda R, Filardo G, et al. Platelet-rich Plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions. *Knee surg Sports traumatol Arthrosc* 2010; 18:472-479.