A Study to Evaluate the Effect of Platelet Rich Plasma in Grade 1 and Grade 2 Osteoarthritis

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Abstract
Effectiveness of PRP injections for OA is still controversial. We investigated the effect of PRP injections in patients with knee osteoarthritis based on clinical parameters-decrease in pain, improving function and joint imaging parameters- global assessment and changes in specific components of the knee joint. The aim of this study was to evaluate the efficacy and safety of PRP injections in patients affected by knee osteoarthritis. Being an autologous blood product containing a high percentage of various growth factors [GF'S], cytokines and modulating factors, PRP has shown promising results in achieving this goal. This was the hospital based prospective, randomized clinical study. The study is conducted on patients who received 3 consecutive PRP injections and completed the follow ups. This study conducted from January 2022 to December 2023. Total 80 pts were allocated. The scores WOMAC, KSS and VAS were evaluated at 4 sittings, named T0, T1, T2, T3. T0 is the first sitting, before first PRP injection in the recruitment month. T1 is the second sitting, 1 month after T0. T2 is the third sitting, 3 months after T1. T3 is the fourth sitting-6 months after T2. All pts underwent X-ray evaluation at 6 months, at T3, after fourth sitting of PRP injection. PRP injections represent a valid conservative treatment to reduce pain, improve quality of pain, improve quality of life and functional score even at mid-term of 6 months follow up.

INTRODUCTION

Cartilage structure modifications are responsible for several degenerative joint diseases, such as chondroplasty and osteoarthritis[1-2]. OA is one of the most common progressive and degenerative knee disease, affecting the intra-articular, tibiofemoral and patellofemoral cartilage together with the adjacent joints and structures. Musculoskeletal pain and movement restriction are symptoms associated with OA, resulting in a reduction in daily performance among the conservative treatment, the use of NSAID'S, intra articular injections with steroid s or Hyaluronic acid and saline have been used to manage mild OA for several years. Various meta-analysis investigated the effectiveness of the PRP by comparing it with other procedures, the results highlighted a better pain relief and functional improvement observed at different time after injections. In particular, the PRP is an autologous blood products containing a high percentage of various growth factors, such as fibroblasts, growth factors, epidermal growth factors ,VEGF, TGF, PDGF[3-5].

A study suggested that these GF's and cytokines released by platelets after being damaged by an injury or pathology, might be involved in modulating the inflammatory process contributing to the tissue structures preservation or regeneration. Moreover, the effect of PRP injection on MRI changes remain unclear. The current study aims to assess the clinical effect of PRP in Pt affected by KOA of grades 1 and 2 at 1,3,6 months follow up, with VAS reduction as s definite primary end point.

MATERIALS AND METHODS

We used a 20-cc syringe with 2 cc of anticoagulant and 18 cc venous blood was drawn and mixed well. Blood was injected into the REMI centrifuge vial through the boundary by pulling the knob up and down. Plasma and the RBC layer were blocked completely. After the 2 Nd centrifugation in REMI PRP centrifuge, the upper silicon lid was opened and the PRP was then extracted done by pipette. A leucocyte filter was then used to filter was then used to filter off the leucocytes, PRP activation was done immediately before injection by adding 10% calcium chloride. PRP was injected out with the help of a 10 ml syringe. Finally, the platelet-rich plasma was divided into 2 units in disposable syringes. One unit was sent for analysis of platelet concentration and quality test and the second part was used for the first dose of intra-articular infiltration in patients within two hours of preparation.

The first injection was given on the Same day, under aseptic conditions. 10 ml of PRP was injected into the knee joint through the anterolateral approach with a 22-gauge needle. After the injection, the patient was encouraged to move the knee a few times to allow the platelet-rich plasma to spread in the joint after that knee was kept in extension for 20 min. All patients observed for 30 min for complications like sweating, dizziness and nausea and discharged. All pts were followed up at 1 month, 3 months 6 months and at 1 year. The quality of life was assessed using Western Ontario and McMaster Universities Arthritis Index [WOMAC] scoring and Visual Analog Scale [VAS] and Knee Society Score [KSS] for pain, before starting the treatment and then at 1 month, 3 months, 6 months and 1 year of treatment.

Inclusion Criteria:

- Age between 40-81
- BMI between 20-29.9
- Chronic history of knee joint pain (at least 4 months)
- Radiographically documented knee osteoarthritis of grade 1 and 2

Exclusion Criteria:

- Radiographic documented KOA of grade 3,4
- Previous femur and tibia fractures
- Previous knee surgery (arthroscopy)
- Hyaluronic acid infiltration with in previous 6 months
- Hemoglobin <10 g/dl
- BMI>30
- History of oncohematological diseases, infection, immune depression.
- Platelet count <150000/cu.mm

Statistical Analysis: Data analysis was done with the SPSS 26. The descriptive analysis was done for normally distributed parameters and their means were compared using the analysis of variance [ANOVA] tests. Within the groups, the data on pre and post levels were compared using the student t-test. Data of subsequent follow-ups were analyzed using repeated-measures ANOVA which was followed by post Hoc test -value of <0.05 was taken as significant in all the tests.

RESULTS AND DISCUSSIONS

Patients Screened for Clinical Trial: Eighty randomized patients were recruited and treated with PRP during. There were no significant difference in clinical characteristics between the group.

Patient Evaluation and Pain Score: Symptomatic outcome measure WOMAC composite score showed significant improvement from baseline in most of the patients in the group.

Womac Score: Statistically significant difference (p<0.05) occurred in the 4 time WOMAC for the functional limitations, pain and total WOMAC index.

the WOMAC functional limitation value, pain, stiffness demonstrated statistically significant reduction between T0 and T1 (3.4750+0.50574 SD vs 3.175+0.5006 SD, p≤0.001), between T1 and T2 (3.1750+0.5006 SD vs 2.425+0.5006 SD, p≤0.001), between T2 and T3 (2.4250+0.50064 SD vs 1.3250+0.47434 SD, p≤0.001).

Kss Score: Statistically significant difference (p≤0.05) occurred in the 4 -time KSS for the knee score and functional score.

The functional KSS score and knee score showed a statistically significant difference between T0 and T1 (57.07+1.52564 SD vs64.175+2.34124, p≤0.001), between T1 and T2 (64.175+2.34124 SD vs 72.750+2.3939, p≤0.001), between T2 and T3 (72.750+2.3939 SD vs 81.475+2.65047, p≤0.001), between T0 and T3 (57.07+1.52564 SD vs 81.475+2.65047, p≤0.001).

Vas Score: The VAS score improved statistically significant between T0 and T1 (5.900+0.95542 SD vs 5.22+0.76753 SD, p≤0.001), between T1 and T2 (5.22+0.76753 SD vs 3.875+0.75744 SD, P≤0.001), between T2 and T3 (3.875+0.75744 SD vs 2.700+0.60764 SD, p≤0.001), between T0 and T3 (5.900+0.95542 SD vs2.700+0.60764 SD, p≤0.001).

Recently PRP has been extensively explored as chondroprotective treatment for symptomatic knee osteoarthritis. PRP improves functional outcome and protects the articular cartilage from further wear and tear in patients with early stages of knee osteoarthritis[7-10].

Injections of PRP are a novel treatment for managing pain related to osteoarthritis of the knee. The platelet in our blood contains growth factors. It is believed that injecting PRP and growth factors from your own blood into an injured area will help tissue repair themselves by causing new cells to form. In this way, PRP could help reverse existing tissue damage. We noted the following at 3,6,12 months follow up.

- **Pain levels:** PRP injections significantly reduced pain scores at each follow up appointments.
- **Physical function:** PRP significantly improved physical function at these follow ups.

Most of the studies involving the use of PRP point towards some improvement in pain and function but lack proper documentation and analysis[11-16].

The results of WOMAC, KSS, VAS improved significantly in 1 st month itself with PRP injections, and despite slight worsening 3, 6 months follow ups, were still significsntly better.

As expected, the study demonstrated no structural efficiency of PRP unlike cellular therapy.

We observer, however, that PRP had a chondro protective structural benefit in terms of better maintenance of the JSW and cartilage thickness as an outcome measure.

Our results correlate well with earlier studies although, direct comparison is difficult because of difference in PRP processing, the dose [quantity and concentration of platelets] and no standard structural efficacy criteria. Patel *et al.* noted significant improvement in all WOMAC scores within 2-3 weeks which lasted up to 6 months[17].

In our study improvement was shown to continue till 1 yr. follow up on this may be attributed to the technique used by us. We used fresh PRP preactivated by calcium chloride before injection which has been found to be better than thawed PRP.
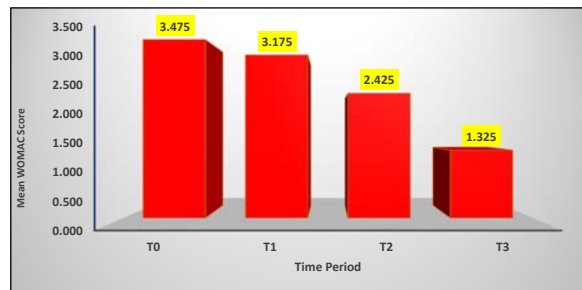

Fig. 1: The WOMAC pain score value showed statistically significant reduction between T0 and T1.
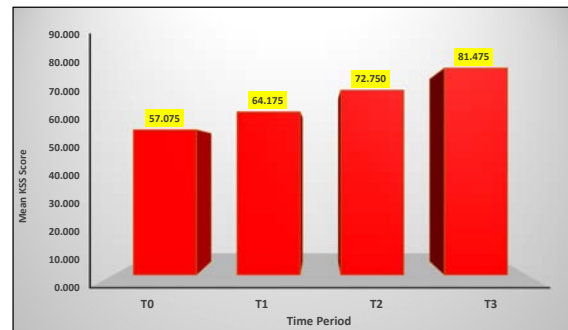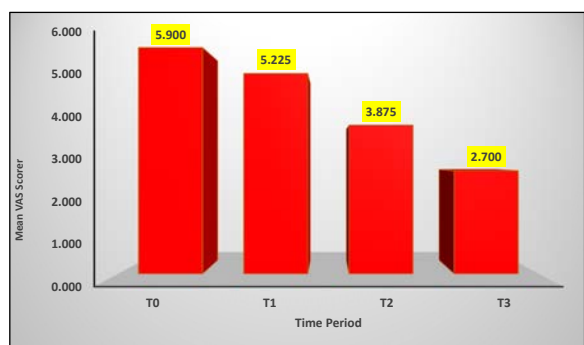

Fig. 2: Mean KSS Score

Fig. 3: Mean Vas Score distribution

Table 1 : Mean Distribution of WOMAC, VAS, and KSS among Study population

		N	Mean	SD	Minimum	Maximum	F-value	p-value
WOMAC	T0	40	3.47	0.505	3	4	149.483	<0.001
	T1	40	3.17	0.5	2	4		
	T2	40	2.42	0.5	2	3		
	T3	40	1.32	0.474	1	2		
KSS	T0	40	57.07	1.525	55	60	869.07	<0.001
	T1	40	64.17	2.341	60	69		
	T2	40	72.75	2.39	70	78		
	T3	40	81.47	2.65	75	85		
VAS	T0	40	5.9	0.955	4	8	132.931	<0.001
	T1	40	5.22	0.767	4	7		
	T2	40	3.87	0.757	3	5		
	T3	40	2.7	0.607	2	4		

Table 2 : Post hoc test for WOMAC, VAS, and KSS among Study population

Dependent Variable	(I) PERIOD	(J) PERIOD	Mean Difference (I-J)	P-value
WOMAC	T0	T1	.30000*	0.045
		T2	1.05000*	0
		T3	2.15000*	0
	T1	T0	-.30000*	0.045
		T2	.75000*	0
		T3	1.85000*	0
	T2	T0	-1.05000*	0
		T1	-.75000*	0
		T3	1.10000*	0
	T3	T0	-2.15000*	0
		T1	-1.85000*	0
		T2	-1.10000*	0
	T0	T1	-7.10000*	0
		T2	-15.67500*	0
		T3	-24.40000*	0
	T1	T0	7.10000*	0
		T2	-8.57500*	0
		T3	-17.30000*	0
	T2	T0	15.67500*	0
		T1	8.57500*	0
		T3	-8.72500*	0
	T3	T0	24.40000*	0
		T1	17.30000*	0
		T2	8.72500*	0
	T0	T1	.67500*	0.001
		T2	2.02500*	0
		T3	3.20000*	0
	T1	T0	-.67500*	0.001
		T2	1.35000*	0
		T3	2.52500*	0
	T2	T0	-2.02500*	0
		T1	-1.35000*	0
		T3	1.17500*	0
	T3	T0	-3.20000*	0
		T1	-2.52500*	0
		T2	-1.17500*	0

We believe that our slightly better results are due to standardized technique which has gradually evolved and should be preferred standard technique for further clinical use. In this study, we found a definite correlation of decrease in mean pain and other WOMAC SCORES and VAS score. This decrease in mean pain score is more in grade[1].

Intra articular infiltration of autologous PRP was well tolerated by all patients included in the study. our findings are also consistent with the results of Patel *et al.* Glynn *et al.* in their study observed that PRP has minimal associated adverse events and may have beneficial effects in terms of pain and patient satisfaction.

All the scores referring to stiffness and physical functions showed an improvement overtime, agreeing with a previous study, which pointed out a decrease in the WOMAC index and an increase in the KSS total score, suggesting a positive influence of the treatment. Bottegoni *et al.* in their study observed a statistically significant improvement of VAS at a follow up of 2 months[16].

Cavazos *et al.* suggest that while both single and multiple PRP injections improved pain and there was no difference between the two, triple PRP injections were more effective than single injection in enhancing joint functionality in individuals with early stage of knee osteoarthritis[1,18-20].

CONCLUSION

Our study shows that intra articular infiltration of PRP in the osteoarthritis knee is tolerable, very safe while being effective. The efficacy of the PRP injections on the Knee osteoarthritis, also suggesting that

decreasing pain was obtained already after month after injection with best results observed after 6 months.

REFERENCES

1. Vilchez, C.F., J.M.A. Millán, J.S. Blázquez, N.V. Álvarez and V.M.M. Peña,et al., 2019. Comparison of the clinical effectiveness of single versus multiple injections of platelet-rich plasma in the treatment of knee osteoarthritis: A systematic review and meta-analysis. Orthop. J. Spo Med., Vol. 7 .10.1177/2325967119887116.

2. Shen, L., T. Yuan, S. Chen, X. Xie and C. Zhang, 2017. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: Systematic review and meta-analysis of randomized controlled trials. J. Orthop. Surg. Res., Vol. 12 .10.1186/s13018-017-0521-3.

3. Huang, P.H., C.J. Wang, W.Y. Chou, J.W. Wang and J.Y. Ko, 2017. Short-term clinical results of intra-articular prp injections for early osteoarthritis of the knee. Int. J. Surg., 42: 117-122.

4. Samara O., Al, J. A., N.M. Al, M. Saleh and R.N. Al,et al., 2017. 1. Intra Articular Autologous Platelet Lysates produce positive MRI structural changes in early and intermediate knee osteoarthritis. Pak. J. Rad., 27: 14-18.

5. IPH. L., D.K. Nath, S.H. Sawleh, H. Kabir and N. Jahan, 2020. Regenerative Medicine for knee Osteoarthritis. The Efficacy and Safety of Intra-articular platelet -rich plasma Mesenchymal stem cells Injections: A Literature Review. cureus., Vol. 12.

6. Paterson, K.L., M. Nicholls, K.L. Bennell and D. Bates, 2016. Intra -articular injections of photo activated platelets -rich plasma in patients with knee osteoarthritis: A double -blind, randomized controlled pilot study. BMC musculoskeletal. Dis ord., Vol. 17, No. 67.

7. Ren, H., S. Zhang, X. Wang, Z. Li. and W. Guo, 2020. Role of platelet -rich plasma in the treatment of osteoarthritis: A meta – analysis. J. Int. Med. Res., 48: 1-10.

8. Dai, W. L., A.G. Zhou, H. Zhang and J. Zhang, 2017. Efficacy of platelets -rich plasma in the treatment of knee osteoarthritis: A meta- analysis of randomized controlled trials. Arthroscopy., Vol. 33.

9. Zhang, Y., X. Chen, Y. Ting, J. Luo and Q. Bi, 2020. 1. Development prospect of Intra -articular injection in the treatment of osteoarthritis: A review. j Pain Res., 13: 1941-1955.

10. Filardo, G., D. Previtali, F. Napoli, C.B. Candrian and S. Zaffagnini,et al., 2020. PRP injections for the treatment of knee osteoarthritis: A meta – analysis of randomized controlled trials. cartilage, Vol. 0.

11. Gato, C.L., J. Magalhaes, C. Ruiz-Romero, F.J. Blanco and E.F. Burguera, 2019. Platelet-rich plasma in osteoarthritis treatment: Review of current evidence. Ther. Adv. Chronic Dis., Vol. 10 .10.1177/2040622319825567.

12. Facr, M.D., 2021. 1. Medically reviewed by Nancy Carteron.

13. Himanshu, B., L. Jerry, L. Jeremy, D.A.W Pont, B. Anupama and A. Diwaker,et al., 2021. 1. Platelet-rich plasma in osteoarthritis knee: correct dose critical for long term clinical efficacy. Sci Rep., Vol. 11, No. 3971.

14. Glynn, L.G., A. Mustafa, M. Casey, J. Krawezyk and J. Blom,et al., 2018. platelet -rich plasma therapy for knee osteoarthritis: A feasibility study in primary care. Pil fea stu., Vol. 4, No. 1.

15. Bottengoni, C., G.L. Dei, S. Salvemini, E. Chiurazzi and R. Bencivenga,et al., 2016. 1. Homologous platelet rich plasma for the treatment of knee osteoarthritis in selected elderly patients: An open -label, uncontrolled, pilot study. Ther Adv mus Dis., 8: 35-41.

16. Patel, S., M.S. Dhillon, S. Aggarwal, N. Marwaha and A. Jain, 2013. 1. treatment with platelet rich plasma is worse more effective than placebo for knee osteoarthritis: A prospective, double -blind, randomized trial. AMJ sports med., 41: 356-364.

17. Ahlback, S., 1968. 1. Osteoarthritis of the knee: A radiographic investigation. Acta R adiol Diagn stoc suppl., 27: 7-72.

18. Altman, R., E. Asch, D. Bloch, G. Bole and D. Borenstein et al., 1986. Development of criteria for the classification and reporting of osteoarthritis: Classification of osteoarthritis of the knee. Arth amp Rhe., 29: 1039-1049.

19. Lai, L.P., T.P. Stitik, P.M. Foye, J.S. Georgy, V. Patibanda and B. Chen, 2015. Use of platelet-rich plasma in intra-articular knee injections for osteoarthritis: A systematic review. PM amp R, 7: 637-648.