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Comparative study of clinical and functional outcome of treatment of mild to moderate osteoarthritis of knee joint between intra articular platelet rich plasma and Hyaluronic acid injection

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Abstract

Aim: To compare the clinical and functional outcomes of treatment of mild to moderate osteoarthritis of knee joint by using intra-articular platelet-rich plasma injection versus hyaluronic acid injection.

Methods: Total of 60 patients with grade 0 to grade 2 osteoarthritis were included in the study, of which 30 were treated with intra-articular PRP and the other 30 with intra-articular HA. Patients was evaluated before and after the procedure using Visual Analogue Scale (VAS) and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) at 6, 12, 24 weeks respectively.

Results: Both groups had clinical improvement but excellent results were seen in the group of patients receiving platelet-rich plasma injections indicated by their VAS and WOMAC scores at 6, 12 week and 24 week follow-up. No severe adverse effects were observed in both the groups.

Conclusions: Our comparative study analyzed that application of autologous Platelet rich plasma is a safe and effective method in the treatment of mild to moderate stages of knee osteoarthritis. Significant better results was seen with 6 months of follow-up compared to hyaluronic acid. Moreover platelet rich plasma is cost effective than hyaluronic acid injection.

Keywords: Osteoarthritis of knee, Platelet rich plasma, Hyaluronic acid.

Introduction

Osteoarthritis (OA) is a chronic degenerative disorder characterised with pain, reduction and disability in the quality of life. It is associated by degeneration of articular cartilage and sub chondral bone changes [1]. The signs include joint line tenderness, crepitus, bony enlargement due to osteophytes, bony remodeling and deformity, restricted ability and stress pain [2]. The management of osteoarthritis is challenging due to its low healing ability and regenerative potential. Pharmacological therapies such as NSAIDs and DMOADs are non-curative and have their own limitations. As a result, the disease progresses and imposes a physical disability and financial burden to the individuals, family [3]. Total knee arthroplasty (TKR) is the treatment for severe OA knee to get rid of pain and to increase function. Due to the limited lifespan of joint replacement owing to implant wear conservative treatment modalities are becoming the central focus of management. There is a growing need for alternate cost effective and non-invasive treatment modalities. More recently PRP is used in treatment of osteoarthritis knee. Platelet-rich plasma (PRP) is an autologous blood containing a high concentration of platelets in and is obtained by centrifugation of blood. It contains growth factors, chemokines and cytokines which are shown to promote vascularization, tissue regeneration, cellular growth, proliferation and collagen synthesis and is a regenerative therapy that aids in promoting healing by augmenting and accelerating the natural healing cascade.

It thereby promotes chondrocyte proliferation, chondrocyte cartilaginous matrix secretion and decreases the catabolic effects by pro inflammatory cytokines. Platelet alpha granules contain growth factors such as insulin like growth factor(IGF-1), vascular endothelial growth factor(VEGF), and transforming growth factor β (TGF-B), fibroblast growth factor (FGF), platelet derived growth factor (PDGF), bone morphogenics protein (BMP) that are involved in each stage of the healing cascade.

Injection of autologous PRP into the joint space and surrounding painful soft tissues delivers a concentrated dose of these growth factors, which enhance the healing process and reduce pain. TGF- β induces chondrocyte proliferation and differentiation and decreases the catabolic effects of IL-1. IGF-1 promotes chondrocytes mitosis and extracellular matrix synthesis. BMP helps in migration of chondrocytes. FGF aids in cartilage repair. PDGF helps in cartilage regeneration by chondrocytes proliferation. VEGF increases the nutrient flow to the cartilage. Glycosaminogly can-proteoglycan matrix plays an important role in pathophysiology of osteoarthritis. Therefore, Hyaluronic Acid (HA), a large viscoelastic glycosaminoglycan has been used for the therapeutic management. It has traumatic energy dissipative, shock absorptive and lubricative properties. It provides a protective coating for the articular cartilage surface^[4]. Hyaluronic acid injections reduces the pain by antagonising the inflammatory mediators, decreases the cartilage degeneration and enhances the cartilage matrix synthesis. Therapeutic benefits were dependent on the variability of its molecular weight and duration of usage^[5-7].

Studies have shown clinical outcomes are better with PRP than comparison to HA. In this study, we are going to compare the clinical outcomes and therapeutic benefits of PRP and HA in patients with mild to moderate knee osteoarthritis.

Materials & Methods

Patients visiting the OPD of the orthopaedic department of Rajah Muthiah Medical College were selected and the study population consisted of 60 patients of both genders, between 40-60 years of age with grade 0 to grade 2 osteoarthritis of the knee joint diagnosed by using the Kellgren & Lawrence grading scale. Randomisation was done between the patients and the patients were divided into two groups. One group consisting of 30 patients received PRP injection and second group of 30 patients received HA injection.

Kellgren and Lawrence OA grading^[8]

- Grade 0 – No Radiographic features of OA are present
- Grade 1 – Doubtful joint space narrowing and possible osteophytic lipping
- Grade 2 – Definite osteophytes and positive joint space narrowing on antero posterior weight bearing radiograph
- Grade 3 – Multiple osteophytes, definite joint space narrowing, sclerosis, possible bony deformity
- Grade 4 – Large osteophytes, marked joint space narrowing, severe sclerosis, definite bony deformity

Exclusion criteria

Patients with

- Immunosuppressed patients
- Severe post traumatic arthritis
- Severe vascular disorder
- Secondary osteoarthritis
- Connective tissue disorders,
- Inflammatory disorders of joint,

- Who had received hyaluronic acid, steroid injections within past 8 months
- Haemoglobin less than 10 mg%
- Tumours

Data collection tools

The clinical and functional outcome were analysed before and post injection for the both groups using VAS and WOMAC scoring scale.

Interpretation of the score

VAS scoring scale^[9]

- No pain
- 1-3 – Low pain
- 4-6 – Moderate pain
- 7-10 – High pain

This score was measured for both HA and PRP groups prior to intervention. It was also measured on the 6th, 12th, and 24th week following intervention.

The western ontario and McMaster universities arthritis score (WOMAC)

This tool consists of evaluating pain, stiffness and physical function by rating over a scale of 5, where 0 is none and 5 is extremely difficult^[10]. The final score is computed by the formula: total score/ 96 (in %). This score was measured for both HA and PRP groups prior to intervention. It was also measured on the 6th, 12th, and 24th week following intervention.

Injection protocol

PRP group

Initially, 30 ml of venous blood was drawn from the participant's median cubital vein. This was centrifuged at 1800 rotations for the first 30 minutes followed by 3500 rotations for the next 30 minutes. After this, the Plasma Rich Platelets were separated in a special container. The participant was made to lie down supine on the examination couch, with the affected knee flexed at the joint. The knee was scrubbed with Povidone-iodine solution. After this, 5 ml of Platelet Rich Plasma was injected in either lateral or medial joint space. This was followed by performing of active range of movement exercise on that knee joint. Same procedure is repeated after 1 month in the same knee.

HA group

The participant was made to lie down supine on the examination couch, with the affected knee flexed at the joint. The knee was scrubbed with Povidone-iodine solution. After this, 2ml of Hyaluronic Acid was injected in either lateral or medial joint space. This was followed by performing active range of movement exercise on that knee joint. Same procedure is repeated after 1 month in the same knee.

Case 1



Fig 1: Platelet rich plasma injection



Fig 2: Pre injection range of movements



Fig 3: Post Injection range of movements

Case 2
Hylauronic acid injection



Fig 4: Pre Injection range of movements



Fig 5: Post injection range of movements

Statistical analysis

Data were entered in Microsoft Excel sheet. Statistical analysis were carried out using SPSS software ver.15. Background characteristics were carried out in percentages. Mean and SD were computed for VAS and WOMAC scores at different durations, prior to intervention and 6, 12, and 24 weeks after the intervention. Independent t test were used to

compare the outcome mean scores between both the groups. Paired t test were used to compare the functional outcomes for each group separately. Chi square test were used to compare the VAS scores between both the groups.

Results

Table 1: Background particulars of the study participants

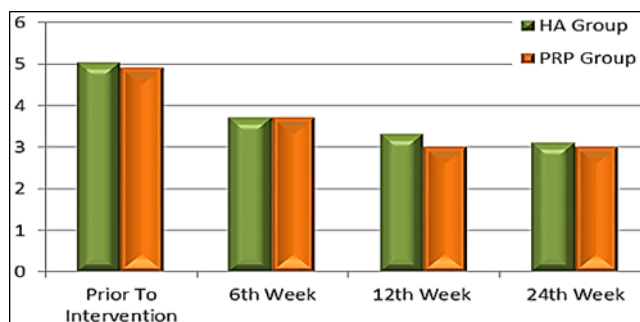
S. No	Particulars	HA group		PRP group	
		Frequency	Percentage	Frequency	Percentage
Age (in years)					
1.	40-45	4	13.3	3	10
	45-50	9	30	8	26.6
	50-55	9	30	14	46.6
	55-60	8	26.6	5	16.7
Sex					
2.	Male	14	46	12	40
	Female	16	54	18	60
Side of the limb					
3.	Left	15	50	13	44
	Right	15	50	17	56
Grading of Osteoarthritis (Kellgren and Lawrence)					
4.	Grade I	20	66.6	15	50
	Grade II	10	33.3	15	50

Table 2: Mean Scores of VAS and WOMAC for PRP Group

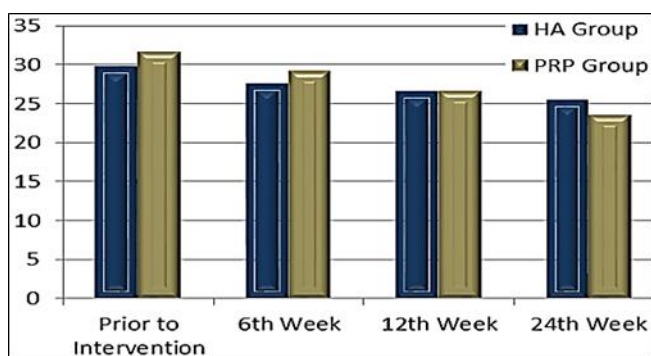
S. No	Duration	N	VAS		WOMAC	
			Mean	SD	Mean	SD
1.	Prior to intervention	30	4.86	0.850	31.67	2.963
2.	6 th Week	30	3.60	0.652	29.23	2.223
3.	12 th Week	30	3.00	0.831	26.77	1.960
4.	24 th Week	30	3.00	0.633	23.63	1.217

Table 3: Mean scores of VAS and WOMAC for HA group

S. No	Duration	N	VAS		WOMAC	
			Mean	SD	Mean	SD
1.	Prior to intervention	30	5.03	0.615	29.83	2.069
2.	6 th Week	30	3.70	1.119	27.67	2.090
3.	12 th Week	30	3.33	0.884	26.57	2.300
4.	24 th Week	30	3.20	0.923	25.57	2.528



Graph 1: Comparison of Mean VAS Scores Between HA & PRP Group



Graph 2: Comparison of Mean WOMAC Scores Between HA Group and PRP Group

The VAS Score for PRP group shows that nearly 67 percent of the study population belonged to high prior to intervention, while 83 percent of the study population have progressed to low score at 24 week, which shows the effect of treatment.

Table 4: Percentage of scores for VAS for PRP group

S. No	Duration of intervention	High		Moderate		Low	
		N	%	N	%	N	%
1.	Prior to intervention	20	66.6	8	26.6	2	6.8
2.	6 th week	0	0	23	76.6	7	23.4
3.	12 th week	0	0	8	26.6	22	73.33
4.	24 th week	0	0	5	17.6	25	83.3

The score for HA group is given in table 5 shows that nearly 63 percent of the study population belonged to high score, while 76 percent of the study population have progressed to low score at 24 week, which shows the effect of treatment.

Table 5: Percentage of scores for VAS for HA group

S. No.	Duration of intervention	High		Moderate		Low	
		N	%	N	%	N	%
1.	Prior to intervention	19	63	6	20	5	17
2.	6 th week	0	0	17	56.6	13	43.3
3.	12 th week	0	0	10	33.3	20	66.6
4.	24 th week	0	0	7	23.3	23	76.6

The mean WOMAC scores between pre and post intervention in PRP group were compared in table 6. There was a significant difference in the means as the duration increased. A statistically significant difference was seen between

priortothe intervention and at 6th week (t=10.656, p<0.0005), 12th week (t=13.266; p<0.0005) and 24th week (t=19.680; p<0.0005).

Table 6: Comparison of means for PRP group between pre and post intervention for WOMAC

S. No.	Factor	Mean Difference	Standard Error	t value	95% CI		p value
					lower	Upper	
1.	Prior to intervention Vs. 6 th week	2.433	0.228	10.656	1.966	2.900	0.001
2.	Prior to intervention Vs. 12 th week	4.900	0.369	13.266	4.145	5.655	0.001
3.	Prior to intervention Vs. 24 th week	8.033	0.408	19.680	7.198	8.868	0.001

The mean WOMAC scores between prior and post intervention in HA group were compared in table 7. There was a significant difference in the means as the duration increased. A statistically significant difference was seen between prior to the intervention and at 6th week (t=4.563, p<0.0005), 12th week (t=6; p<0.0005) and 24th week (t=6.579; p<0.0005).

Table 7: Comparison of means for HA group between pre and post intervention for WOMAC

S. No.	Factor	Mean Difference	Standard Error	t value	95% CI		p value
					lower	Upper	
1.	Prior to intervention Vs. 6 th week	2.167	0.475	4.563	1.195	3.138	0.0001
2.	Prior to intervention Vs. 12 th Week	3.267	0.544	6.000	2.153	4.380	0.0001
3.	Prior to intervention Vs. 24 th week	4.267	0.648	6.579	2.940	5.593	0.0001

The comparison between the WOMAC and VA scores between the PRP and HA group is shown in table 8. It was observed that the mean difference scores between PRP and HA group is statistically significant for WOMAC score (p<0.01).

Table 8: Comparison of difference in scores over the period of intervention for WOMAC score and VAS Score between PRP group and HA group

S. No	Factor	Mean difference	Standard error	t value	95% CI		P value
					Lower	Upper	
1.	WOMAC	1.81	0.55	3.3	0.6	3.01	0.006
2.	VAS	-0.73	0.42	-1.74	-1.6	0.2	0.113

Discussion

This study was carried out as a comparative study between HA and PRP. In our study, majority of the study population belonged to 40-60 years of age. In most of the other studies conducted, the mean age of the participants was over 50 years. Females were higher in HA group (53.3%) while males were higher in PRP group (60%). Prior to intervention the mean VAS scores were 5.03± 0.615 and WOMAC scores were 29.83± 0.06.

In a study done by Sandeep Patel [11] the mean VAS score was 4.6±0.62, which was comparable with our study, while the WOMAC score was 45.5±17.3. There was a significant reduction in WOMAC scores at the end of 24th week for HA group with a mean difference of 4.27 (p= 0.0001) and PRP

group's difference at the end of the 24th week being 8.03 ($p = 0.001$). There was a significant reduction in VAS scores at 6th week with mean difference 1.33 ($p=0.0001$), at 12th week with mean difference of 1.7 ($p=0.0001$), and at the end of 24th week for HA group with a mean difference of 1.933 ($p=0.0001$). For the PRP group, the mean difference was statistically significant ($p<0.001$).

In our study it was evident that as the duration increased the mean difference rose higher for PRP group in comparison to the HA group, which proves the long term efficacy of administration of PRP than HA group.

Our study showed a significant difference in WOMAC scores, when a comparison is made between both the groups, concluding that PRP is better than HA ($p = 0.006$)

Cole *et al.* [12] found that compared with HA, PRP significantly relieved pain in long term follow up (24 week). This conclusion has been confirmed in our meta-analysis. Cerza *et al.* [13] reported that PRP achieved superior clinical outcomes to HA.

Asfaha *et al.* [14] found that PRP has endogenous analgesic effects and alleviates inflammation related pain. In contrast HA can only increase the viscosity and elasticity of the joint fluid and reduce pain and lubrication with longer time after HA treatment, the lubrication effect decreases, and the pain usually reappears. In the study by raessadat *et al.*, the WOMAC score in PRP was superior to that HA group at 52 weeks of follow up.

In 2012, Sanchez *et al.* [15] conducted the first multicenter, double-blind randomized controlled trial comparing PRP to HA. The study of 176 patients with symptomatic knee OA found that 38% of patients treated with PRP had greater than 50% reduction of pain at 24 weeks compared to baseline. This was significantly higher than the pain reduction scores for patients treated with HA. Improvements in stiffness and physical activity were also higher in Platelet rich plasma group but were not significant. Age, severity of cartilage degeneration or knee osteoarthritis, duration of symptoms, prior therapeutic interventions, and patient activity level may all be relevant. Patient age impacts PRP outcomes, with younger individuals having greater benefits.

In a subgroup analysis of 150 patients with cartilage degeneration or OA, Kon *et al.* [16] found that patients younger than age 50 had greater benefit from PRP at 6 months follow-up than patients over age 50 and that younger patients had a better response to PRP than HA. In patients over age 50, HA and PRP had similar results. Hypotheses for age related efficacy include a less robust response of aging chondrocytes to growth factors and limited propensity for healing and regeneration in elderly patients. Patients with mild to moderate Osteoarthritis knee show better improvement after Platelet rich plasma treatment than patients with severe Osteoarthritis knee and joint deformity.

However in a study by gormeli *et al.* [17], no differences were observed between patients who receive single dose injection PRP and an HA injection, whereas the patient receiving multiple injection PRP experienced a greater improvement in function.

Yanhong *et al.* [18] done a meta-analysis to compare platelet rich plasma and hyaluronic acid in patients with OA knee and concluded that PRP injections is more effective than HA injections for knee osteoarthritis.

Raessadat *et al.* [19] had done a randomized clinical trial in 160 patients of OA knee from grade 1 to grade 3 out of which 87 patients received two intra articular PRP injections and 73 patients received three doses of HA injection. This study

suggests that PRP is more efficacious than HA injection in reducing symptoms and improving quality of life.

Considering the evidence intra articular PRP injection is more beneficial and cost effective when compared to Hyaluronic acid injection.

Conclusion

This study has highlighted the advantages of using PRP over HA in the treatment of OA knee through a randomized prospective trial. The benefits are witnessed with a remarkable improvement in VAS and WOMAC scores, and moreover, the effect of the intervention has been documented even at the 24th week. This study has also focused on the key benefits of PRP in reducing the physical, social and economic burden of OA knee.

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