

ISSN: 2395-1958
IJOS 2019; 5(3): 10-14
© 2019 IJOS
www.orthopaper.com
Received: 12-05-2019
Accepted: 14-06-2019

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A comparative study of 60 patients to compare the efficacy of P-PRP (Pure-platelet rich plasma) v/s hyaluronic acid injection in treatment of osteoarthritis of knee

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DOI: <https://doi.org/10.22271/ortho.2019.v5.i3a.1499>

Abstract

Objective: To compare efficacy of PRP v/s hyaluronuric acid administration in cases of osteoarthritis of knee.

Method: Analysis of two groups of 30 patients each who were administered PRP and Hyaluronuric acid respectively.

Results: Result was analysed in terms of VAS and WOMAC scores, with PRP showing better results all together.

Conclusion: Local administration of PRP gives better long term outcome.

Keywords: PRP (platelet rich plasma), osteoarthritis knee, hyaluronuric acid, WOMAC

Introduction

Osteoarthritis (OA) is a complex “whole joint” disease pursued by inflammatory mediators, rather than purely a process of “wear and tear”. Besides cartilage degradation, synovitis, subchondral bone remodeling, degeneration of ligaments and menisci, and hypertrophy of the joint capsule take parts in the pathogenesis. Osteoarthritis (OA) is a chronic degenerative disorder of multifactorial etiology characterized by the loss of articular cartilage, hypertrophy of bone at the margins, subchondral sclerosis, and range of biochemical and morphological alterations of the synovial membrane and joint capsule. [1] Pathological changes in the late stage of OA include softening, ulceration, and focal disintegration of the articular cartilage. Synovial inflammation also may occur. [2, 3] The incidence of knee OA increases by age and further increase with longer lifetime and higher average weight of the population. [6] It is painful and disabling disease that affects millions of patients. [7] of the knee is a major cause of mobility impairment, particularly among females. [2, 8] OA was estimated to be the 10th leading cause of nonfatal burden. [2, 9] X-ray findings do not always match symptoms, but prevalence based on radiography is probably a reasonable population estimate. 7 OA of the knee is more prevalent as per the literature available. [10] For the knee OA, various conservative treatment modalities are recommended by clinical guidelines. [11-13] If orally administered drugs are ineffective, intraarticular (IA) injection (corticosteroids, viscosupplements, blood-derived products) is the last nonoperative modality that can be preferred. [13-14] Platelets have known roles in coagulation, inflammatory processes, and immunity modulation. Moreover, during degranulation, platelets release various cytokines and growth factors (vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor-B, insulin growth factor-I, and hepatocyte growth factor) which promote angiogenesis, tissue remodeling, and wound healing. [15] In addition, platelets can reduce painful symptoms by an unknown mechanism which is apparently dependent on the release of proteases with analgesic properties. [16] The use of autologous growth factors is thought to lead to tendon healing through collagen regeneration and the stimulation of a well-ordered angiogenesis. [17, 18] Thus, Pure- platelet-rich plasma (P-PRP) may represent a new therapeutic option for degenerative

osteoarthritis of knee. P-PRP is easy to prepare, relatively low cost, and can be administered in a minimally invasive manner. A number of approaches to managing early osteoarthritis have failed to reliably alleviate pain, restore normal knee function and anatomy, or to slow the progression of osteoarthritis. Biological therapies for focal knee osteoarthritis, such as Pure-platelet-rich plasma, have been proposed to improve clinical and structural outcomes by delivering a high concentration of growth factors that mediate healing and remodeling. [19, 20] Recent studies in Asian patients with osteoarthritis of the knee suggests weekly intra-articular injections of sodium hyaluronate are well tolerated, can provide sustained relief of pain, and can improve function. [21]

Hence the present study was done at our tertiary care centre to assess the management of osteoarthritis by local injection of pure platelet rich plasma and injection hyaluronic acid and to study the radiological and functional outcome in the management of osteoarthritis with above stated modality.

Material and Methods

A hospital based prospective, comparative study was conducted with 60 patients in outpatient department of department of orthopaedics, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune between July 2016 to September 2018, to compare the efficacy of P-PRP (Pure-Platelet Rich Plasma) v/s Hyaluronic Acid injection in treatment of Osteoarthritis of Knee. The patients were selected randomly and were divided in the following two groups of 30 patients each:

Group A: Patients were treated with injection of Pure-Platelet rich plasma

Group B: Patients were treated with injection of Hyaluronic Acid

Eligibility criteria for age was kept between 18 to 70 years and was restricted to healthy individuals. The patients with previous history of being operated in the same knee were excluded. Other candidates who were excluded were with inflammatory disease, diabetes, ongoing infection and pregnancy.

Procedure

All patients informed written consent, which was approved by local ethical committee. Sterile extract was obtained with

appropriate amount of venous blood and transferred to the centrifuge. After processing is completed, extract the P-PRP from the centrifuge according to the manufacturer’s instructions. Cleanse the patient’s skin around the injection site; if desired, use towels or drapes to create an aseptic field. Administer a local anesthetic if necessary. With sterile technique, inject the P-PRP into the appropriate area; apply dressing or bandage to protect needle entry site.

A closed system was used throughout the process to avoid contamination, at least 24 hours before injection. 20 milliliters whole blood was collected from the uninvolved arm into a 60-mL syringe that contained 5 mL sodium citrate. Autologous platelet concentrate contains concentrated white blood cells and platelets that are suspended in plasma. Sodium bicarbonate solution was added at a ratio 0.05cc of sodium bicarbonate solution to 1 cc of platelet concentrate. The resulting buffered platelet concentrate contains approximately a 6 to 8 times concentration of platelets compared to baseline whole blood. 4 cc platelet concentrate or 6cc hyaluronic acid was injected using a 22-g needle into the knee joint using a peppering technique. Immediately after the injection, the patient was kept in sitting position without moving the knee for 15 minutes. After 48 hours, patients were given a standardized strengthening exercises protocol to follow for 2 weeks. At 4 weeks after the procedure, patients were allowed to proceed with normal activities as much as tolerated. In order to evaluate the systemic inflammation, the levels of CPR were measured in 30, 90, 180 and 360 days after the first application of PRP

Results

Comparison of VAS Score between Group A and Group B during Follow-up Period

The improvement in pain was significantly better in Group A when compared to Group B after 4 weeks, 12 weeks and 24 weeks as per ANOVA test (p<0.05).

Table 1: Comparison of VAS Score between Group A and Group B during Follow-up Period

VAS	Group A		Group B		p Value
	Mean	SD	Mean	SD	
Baseline	7.62	0.47	7.72	0.37	>0.05
4 weeks	4.69	0.97	3.45	0.58	<0.05
12 weeks	2.48	0.70	3.14	0.45	<0.05
24 weeks	1.49	0.55	2.67	0.32	<0.05

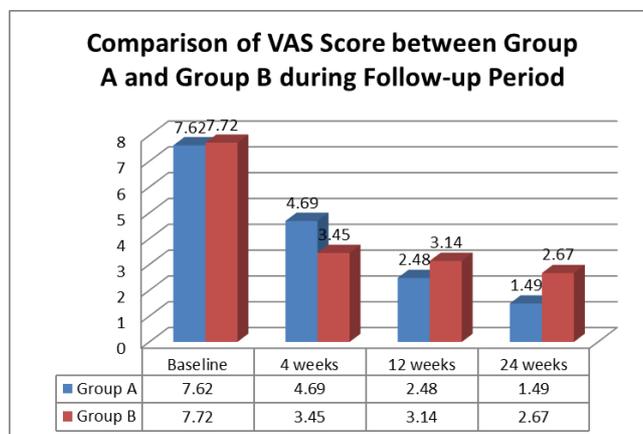


Fig 1: Comparison of VAS Score between Group A and Group B during Follow-up Period

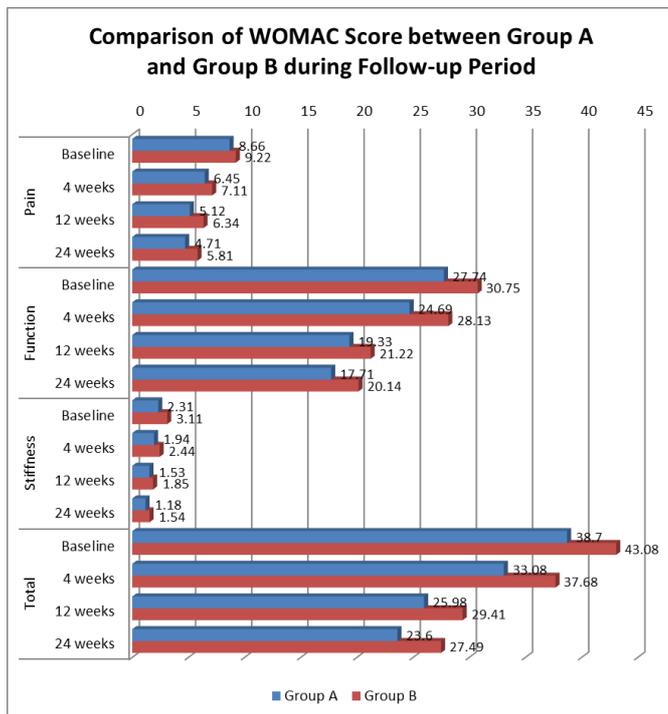
Comparison of WOMAC Score between Group A and Group B during Follow-up Period

The improvement in WOMAC Score was significantly better

in Group A when compared to Group B after 4 weeks, 12 weeks and 24 weeks as per ANOVA test (p<0.05).

Table 2: Comparison of WOMAC Score between Group A and Group B during Follow-up Period

WOMAC Scores		Group A		Group B		p Value
		Mean	SD	Mean	SD	
Pain	Baseline	8.66	1.14	9.22	0.40	<0.05
	4 weeks	6.45	0.35	7.11	0.79	<0.05
	12 weeks	5.12	1.37	6.34	0.33	<0.05
	24 weeks	4.71	1.02	5.81	1.26	<0.05
Function	Baseline	27.74	2.07	30.75	2.52	<0.05
	4 weeks	24.69	3.51	28.13	1.94	<0.05
	12 weeks	19.33	1.43	21.22	1.77	<0.05
	24 weeks	17.71	0.99	20.14	1.17	<0.05
Stiffness	Baseline	2.31	0.67	3.11	0.46	<0.05
	4 weeks	1.94	0.15	2.44	0.68	<0.05
	12 weeks	1.53	0.62	1.85	0.27	<0.05
	24 weeks	1.18	0.56	1.54	0.64	<0.05
Total	Baseline	38.70	2.51	43.08	2.67	<0.05
	4 weeks	33.08	3.53	37.68	2.51	<0.05
	12 weeks	25.98	1.57	29.41	1.79	<0.05
	24 weeks	23.60	1.41	27.49	1.65	<0.05

**Fig 2:** Comparison of WOMAC Score between Group A and Group B during Follow-up Period

Discussion

Platelet rich plasma and other regenerative injections represent a major paradigm shift and advancement in the treatment of knee osteoarthritis when compared to intra-articular corticosteroid injections. There is currently good in vitro evidence to suggest that tissue exposed to PRP has a propensity to undergo healing and self-repair.

Clinical trials are advancing to determine the role of PRP in clinical practice. Short-term follow-up studies show that PRP to be effective in reducing pain and increasing activity in patients with knee OA. Long-term follow-up studies and randomized clinical trials are now underway to better characterize how to incorporate PRP into patient care. Recently, there has been a lot of interest in new treatments aimed at stimulating repair or replacing damaged cartilage in joints. There are currently limited high-level studies in the literature to demonstrate the real efficacy of PRP injections.

Filardo G *et al.* [47], Spaková T *et al.* [34] and Lubowitz JH *et al.* [48] studies have suggested that the application of

hyaluronic acid and PRP may have potentially positive effects on cartilage repair and slow down the progression of OA.

Lana JFSD *et al.* [49] double-blind, randomized and controlled prospective study evaluating the effectiveness of HA and PRP as monotherapies for mild to moderate OA and comparing the results to the combination of PRP+HA found mean age of the patients was 60.9 years (45-70), 90 patients (84.8%) were female.

In our study, majority of the patients (36.7%) in Group A were overweight while 10 (33.3%) and 9 (30%) patients were in the normal range and obese respectively. The mean BMI of patients was 27.90 ± 4.63 kg/m². Majority of the patients (43.3%) in Group B were overweight while 11 (36.7%) and 6 (20%) patients were in the normal range and obese respectively. The mean BMI of patients was 27.19 ± 3.92 kg/m². There was no significant association between the groups as per Student t-test ($p > 0.05$). This is consistent with the study of Lana JFSD *et al.* [49] It was observed in the present study that as per Kellgren-Lawrence grade, 8 (26.7%) and 13 (43.3%) patients in Group A had Grade 1 and Grade 2 osteoarthritis in knee joint while 9 (30%) patients had Grade 3 osteoarthritis in knee joint. 8 (26.7%) and 12 (40%) patients in Group B had Grade 1 and Grade 2 osteoarthritis in knee joint while 10 (33.3%) patients had Grade 3 osteoarthritis in knee joint. There was no significant association between the groups as per Chi-Square test ($p > 0.05$). This is in concordance to the study of Lana JFSD *et al.* [49].

In our study, the mean baseline VAS score in Group A was 7.62 ± 0.47 which decreased to 4.69 ± 0.97 in 4 weeks with mean difference of 2.93. This difference was statistically significant as Student t-test ($p < 0.05$). Similarly the VAS score reduced significantly in 12 weeks and 24 weeks follow-up period as per ANOVA test ($p < 0.05$). The mean baseline VAS score in Group B was 7.72 ± 0.37 which decreased to 3.45 ± 0.58 in 4 weeks with mean difference of 4.27. This difference was statistically significant as Student t-test ($p < 0.05$). Similarly the VAS score reduced significantly in 12 weeks and 24 weeks follow-up period as per ANOVA test ($p < 0.05$). The improvement in pain was significantly better in Group A when compared to Group B after 4 weeks, 12 weeks and 24 weeks as per ANOVA test ($p < 0.05$). This is comparable to the studies of Lana JFSD *et al.* [49], Munde SL *et al.* [38], Sampson S *et al.* [32], Kon E *et al.* [20] and Raeissadat SA *et al.* [37]

In the advanced stages of OA, PRP might not have a direct effect on the chondrocyte anabolic process, but an anti-inflammatory effect through the regulation of joint

homeostasis and the cytokine level [20, 50]. Calis HT *et al.* [51] study showed that PRP administered three times at weekly intervals to patients with grade 3 and 4 knee OA reported improvements in their quality of life, and reduced levels of pain, and had increased cartilage thickness as measured by ultrasonography at the 6-month follow up.

In our study, the mean baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score in Group A was as follows WOMAC Pain - 8.66 ± 1.14 ; WOMAC Function - 27.74 ± 2.07 ; WOMAC Stiffness - 2.31 ± 0.67 ; WOMAC Total - 38.70 ± 2.51 . There was significant decrease in all WOMAC scores in 4 weeks, 12 weeks and 24 weeks follow-up period as per ANOVA test ($p < 0.05$). The mean baseline WOMAC score in Group B was as follows WOMAC Pain - 9.22 ± 0.40 ; WOMAC Function - 30.75 ± 2.52 ; WOMAC Stiffness - 3.11 ± 0.46 ; WOMAC Total - 43.08 ± 2.67 . There was significant decrease in all WOMAC scores in 4 weeks, 12 weeks and 24 weeks follow-up period as per ANOVA test ($p < 0.05$). The improvement in WOMAC Score was significantly better in Group A when compared to Group B after 4 weeks, 12 weeks and 24 weeks as per ANOVA test ($p < 0.05$). Similar observations were noted in the studies of Munde SL *et al.* [38], Lana JFSD *et al.* [49], Sanchez M *et al.* [52], Raeissadat SA *et al.* [37], Spakova T *et al.* [34], Kon E *et al.* [33] and Patel S *et al.* [53].

Thus according to VAS score initial results may appear superior for hyaluronic acid but on long term the results of prp are superior and in terms of WOMAC score prp is superior throughout.

Conclusion

In Ideal patients which have mild to moderate symptomatic osteoarthritis, this method ensures a lot of promise. we conclude that prp administration is superior in long term and also short term results of patients and thus we advocate the use of this procedure for better relief of patients suffering from osteoarthritis.

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