Original Article

Comparison of Efficacy of Single Injection of Platelet-Rich Plasma versus Corticosteroid in Patients with Knee Osteoarthritis: A Randomized Controlled Trial

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ABSTRACT

Introduction: As the most prevalent musculoskeletal condition, osteoarthritis (OA) is a multifactorial, chronic illness that begins with the breakdown of articular cartilage, resulting in the loss of joint space and the development of regional osteophytes. Growth factor-containing platelets can stimulate anabolism in any type of cell, including chondrocytes, and can also repair damaged cells. From this angle, platelet rich plasma (PRP) has been proposed as a therapy for lesions with limited regenerative capacity, such as articular cartilage lesions.

Aims/ objective: To compare efficacy of single injection of platelet-rich plasma versus corticosteroid in patients with knee osteoarthritis.

Materials and Method: 60 patients with knee osteoarthritis were divided into two groups with 30 patients in each group receiving PRP or corticosteroid intra-articular injection. The following measures were taken prior to the injection: flexion contracture, both active and passive range of motions (ROM) of knee, 20MW test, VAS-based pain severity, and one and six months later. The portions of the KOOS questionnaire were evaluated prior to the procedure, as well as one, and six months later.

Results: Most the patients had grade 3 osteoarthritis from radiological examination. Patients in PRP group had comparatively better score with respect to KOOS parameters than corticosteroid group at 1 and 6 months of follow-up and the difference was statistically significant ($p<0.05$). Patients in PRP group had comparatively better outcome with respect to VAS, 20 MW test, and range of motion parameters than corticosteroid group at 1 and 6 months of follow-up and the difference was statistically significant ($p<0.05$).

Conclusion: The result of our study demonstrated than platelet rich plasma is safe and effective in reducing pain and enhancing physical functions in patients with osteoarthritis.

Keywords: Osteoarthritis, Knee, Platel Rich Plasma, Corticosteroid, Pain, Range of Motion.

INTRODUCTION

As the most prevalent musculoskeletal condition, osteoarthritis (OA) is a multifactorial, chronic illness that begins with the breakdown of articular cartilage, resulting in the loss of joint space and the development of regional osteophytes. [1, 2] There is no permanent treatment that can stop the underlying cause of degeneration of articular cartilage in the short term due to the poor propensity for articular cartilage repair. Presently available techniques are all symptomatic and do not help patients regain their previous range of motion or quality of life. Autologous blood, and particularly its mediators such as growth factors (GFs), have been proposed as a potential substitute for current OA treatments.

A plasma volume that has a higher concentration of platelets than the plasma itself is known as platelet-rich plasma (PRP).[3] Growth factor-containing platelets can stimulate anabolism in any type of cell, including chondrocytes, and can also repair damaged cells.[4-6] From this angle, PRP has been proposed as a therapy for lesions with limited regenerative capacity, such as articular cartilage lesions. PRP has been safely used and reported in various domains, such as musculoskeletal illnesses, wound healing, cardio-thoracic, and oro-mandibular surgery, for the past 20 years. [7]

The use of PRP in the management of chronic rotator cuff tendinopathy, Jumper's knee, partial rupturing of the Achilles tendon, Hamstring rupture, osteo-chondritis dissecant lesions, MCL repairs, regeneration of nerves, ACL repairs, plantar fasciitis, bone healing, and chondral defects regrowth is currently the subject of numerous studies for this condition. [6, 8, 10-16] The impact of PRP on chondrocyte differentiation, HA, proteoglycan, and collagen type-2 formation have been the subject of numerous research.[17-23] Additionally, a number of research on the clinical use of PRP in treating articular cartilage defects among humans and animals have been conducted. [19, 20, 24-33]

These trials show that PRP is a safe procedure with no significant side effects noted at follow-up.[3, 4, 19, 25–33] Nonetheless, the majority of current research consists of pilot or prospective research with no control groups. [3, 4, 25–27, 29–30, 32] Furthermore, there are differences in the quantity and timing of injections amongst these investigations. Without any particular rationale or scientific basis, nearly all of them need three shots.[33] It appears that the conventional protocol of three hyaluronic

acid (HA) injections is being adhered to in these investigations.[3, 4, 6, 18, 19, 26, 27, 30]

Injections of corticosteroid (CS) intra-articular are commonly used to treat both acute and chronic inflammatory diseases. [38] By suppressing inflammatory cytokines and obstructing the mechanisms that allow them to function, CS mostly has anti-inflammatory effects. [39] None of the current studies have compared PRP and corticosteroid injection, regardless of the fact that corticosteroid intra-articular injection has been widely utilized for managing osteoarthritis for over half a century and is advised as the treatment for OA in up to 11 guidelines, including the American College of Rheumatology (ACR).[36, 38] So, this study was planned to compare efficacy of single injection of platelet-rich plasma versus corticosteroid in patients with knee osteoarthritis.

MATERIALS AND METHODS

This was an open label randomised controlled trial with parallel 1:1 allocation done on patients with osteoarthritis of knee in Department of Orthopaedics of tertiary care hospital of eastern India from July 2022 to June 2023. The study was started after taking approval from institutional ethics committee and then patients' recruitment was done after taking their written informed consent as per the guidelines of Good Clinical Practice and Declaration of Helsinki.

Inclusion Criteria:

- Patients with clinical and radiological diagnosis of osteoarthritis of Knee Joint.
- Patients pain intensity of 6 or more in the Visual Analogue Scale (VAS) at time of recruitment
- Patients having knee pain for greater than three months
- Patients whose symptoms are not under control despite at least two OA treatments (including life style changes, oral drugs, physiotherapy, or orthotic devise).

Exclusion Criteria:

- Patient on anticoagulant or antiplatelet drugs
- Patients with history of collagen vascular disease or hematopoietic disease, or any systemic illness
- Use of Immunosuppressive drugs
- Patients with active infection of the knee
- Patients who had undergone arthroscopy or surgery within 6 months of recruitment
- Patients with any other neurological disorders

60 patients were divided into two groups with 30 patients in each group.

Group PRP: Using a 10-cc syringe, 20 ml of blood was drawn from the ante-cubital vein and, in accordance with aseptic protocols, transferred into sterilized disposable test tubes smeared with anticoagulant. The test tube was first placed directly into the centrifuge, and the entire blood was spun. The first spin, which lasts for three minutes at 3,000 revolutions per minute, is referred to as "soft spin". This results in the separation of blood into red blood cells, platelets, buffy coat, and the upper layer of platelet poor plasma. The top layer of plasma, which contains platelet-rich plasma and buffy coat, was put into a separate test tube using a long-bore, sterilized micropipette. This is subjected to a second centrifugation procedure called a "hard spin," which operates at 4500 rpm for 15 minutes. Platelet rich and platelet poor plasma got separated as a consequence of this. The layer of platelet-poor plasma was removed using a long-bore, sterile micropipette, and around 4-5 ml of platelet-rich plasma was recovered. A calcium gluconate solution (1 g/10 ml) was added to 0.5 ml of PRP solution to activate it. The PRP solution was then injected into knee via intra-articular route.

Group CS: 40 mg of methylprednisolone acetate (1 ml) was injected in the affected knee via intra-articular route.

The following measures were taken prior to the injection: flexion contracture, both active and passive range of motions (ROM) of knee, 20MW test, VAS-based pain severity, and one and six months later. The portions of the KOOS questionnaire were evaluated prior to the procedure, as well as one, and six months later.

In this study, 42 questions from the five areas of Pain Relief, Symptom Relief, Activities of Daily Living (ADL), Quality of Life (QOL), and Sporting Abilities of the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire were employed. A prior study validated the validity and reliability of KOOS questionnaire. [37]

Every subject underwent two 20-meter jogging performances, known as the 20-meter-walk test (20MW test), after each follow-up visit. An occupational therapist recorded the mean score of the test, which was measured using a chronometer. The patients' active and passive ROMs were assessed with a goniometer in prone position and knee flexion contracture while they were supine.

Statistical Analysis:

The data obtained from patients of OA receiving PRP or corticosteroid injection were transferred into Microsoft Excel 365 and analysed using Graph Pad version 8.4.3. Categorical variables such as gender and grade were presented as frequency and compared using Fisher's exact test. Continuous data such as KOOS scores, range of motions, VAS, and 20 MW test were presented as mean ± SD and compared using unpaired t test with p-value of 0.05 as cut-off for significance.

OBSERVATIONS AND RESULTS

Table 1: Comparison of Baseline Demographic and Clinical Characteristics between PRP group and CS group

Parameters	PRP Group	CS Group	P-Value
Age in years (mean ± SD)	60.32 ± 6.14	61.13 ± 5.69	0.60*
BMI in kg/m^2	27.86 ± 3.02	28.26 ± 3.55	0.29*
Sex			
Male	11	12	>0.99**
Female	19	18	
Osteoarthritis Grade			
Grade 2	10	9	>0.99**
Grade 3	20	21	

*Unpaired t-test **Fisher's Exact Test

Most of patients were female and of age greater than 50 years in both group PRP and CS. Most the patients had grade 3 osteoarthritis from radiological examination. There was not any statistically significant difference between two groups with respect to age, sex, and osteoarthritis grade.

Table 2: Comparison of KOOS Parameters after 1 Month between PRP group and CS group

Parameters	PRP Group	CS Group	P-Value Unpaired t-test
Pain Relief	74.6 ± 11.4	61.2 ± 9.7	<0.0001
Symptoms Relief	75.3 ± 8.7	60.5 ± 7.8	<0.0001
Activities of Daily Life	76.5 ± 9.2	56.2 ± 8.4	<0.0001
Quality of Life	26.5 ± 5.3	18.7 ± 4.7	<0.0001
Sport	14.4 ± 4.0	11.7 ± 2.8	0.009

Table 3: Comparison of KOOS Parameters after 6 Months between PRP group and CS group

Parameters	PRP Group	CS Group	P-Value Unpaired t-test
Pain Relief	79.1 ± 8.6	55.5 ± 6.5	<0.0001
Symptoms Relief	79.2 ± 7.9	59.4 ± 7.3	<0.0001
Activities of Daily Life	76.0 ± 9.1	64.0 ± 8.2	<0.0001
Quality of Life	31.6 ± 5.4	18.5 ± 3.1	<0.0001
Sport	12.4 ± 1.9	12.7 ± 1.5	0.50

Patients in PRP group had comparatively better score with respect to KOOS parameters than corticosteroid group at 1 and 6 months of follow-up and the difference was statistically significant ($p<0.05$).

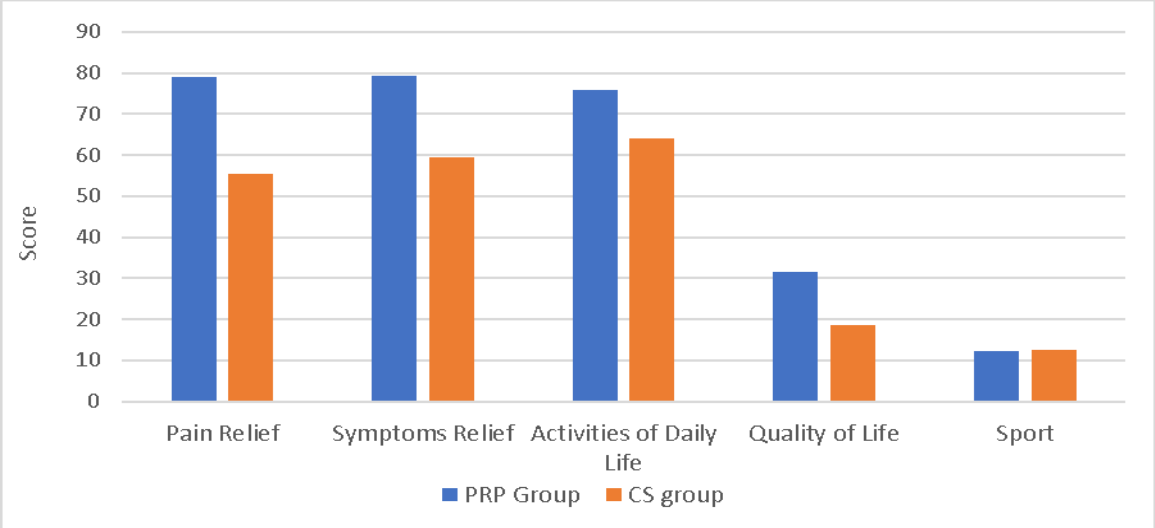

Figure 1: Comparison of KOOS Parameters

Table 4: Comparison of Mean VAS, time duration for 20 MW test and knee ROMs after 1 Month between PRP group and CS group

Parameters	PRP Group	CS Group	P-Value Unpaired t-test
Pain Intensity (VAS)	4.5 ± 2.3	6.5 ± 1.9	0.0005
20 MW test in seconds	14.3 ± 3.2	18.1 ± 4.7	0.0005
Active Flexion ROM in degree	104.3 ± 13.1	100.5 ± 10.4	0.22
Passive Flexion ROM in degree	114.9 ± 12.9	120.1 ± 18.3	0.21
Flexion Contracture in degree	0.9 ± 0.2	0	<0.0001

Table 5: Comparison of Mean VAS, time duration for 20 MW test and knee ROMs after 6 Months between PRP group and CS group

Parameters	PRP Group	CS Group	P-Value Unpaired t-test
Pain Intensity (VAS)	45.7 ± 9.7	71.6 ± 11.3	<0.0001
20 MW test in seconds	14.9 ± 2.9	18.4 ± 3.6	0.0001
Active Flexion ROM in degree	104.9 ± 11.4	98.7 ± 9.8	0.03
Passive Flexion ROM in degree	115.7 ± 10.2	118.7 ± 19.7	0.46
Flexion Contracture in degree	0.9 ± 0.2	0	<0.0001

Patients in PRP group had comparatively better outcome with respect to VAS, 20 MW test, and range of motion parameters than corticosteroid group at 1 and 6 months of follow-up and the difference was statistically significant (p<0.05).

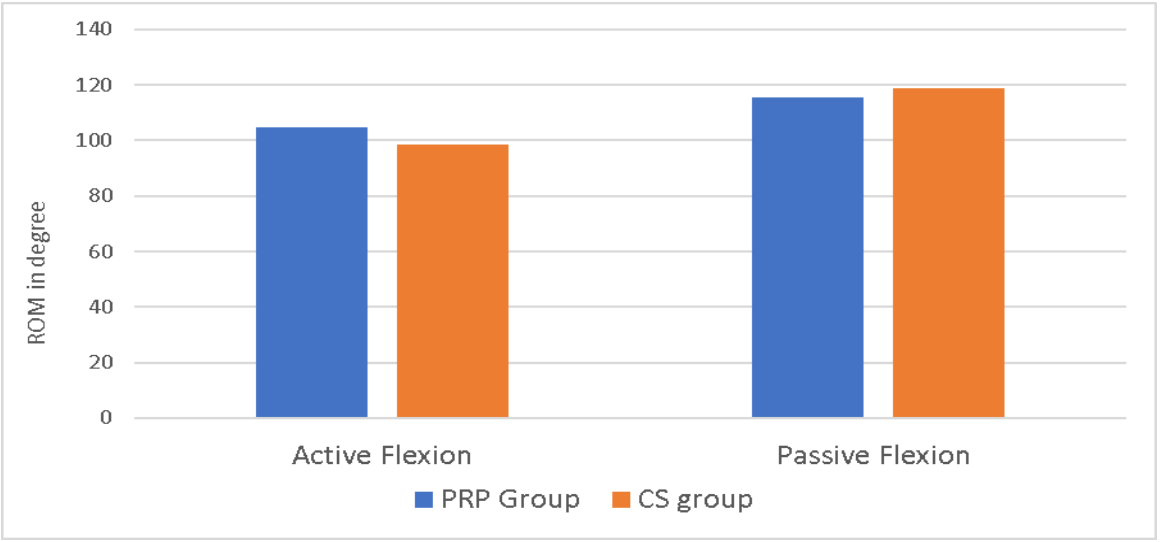

Figure 2: Comparison of knee ROMs after 6 Months between PRP group and CS group

DISCUSSION

In this study, we examined the effects of a single PRP injection and methylprednisolone acetate for the first time. This study showed that, when compared to corticosteroids, PRP treatment was more advantageous for patients' pain and symptom reduction, quality of life, and routine tasks of daily living. Furthermore, it was observed that PRP therapy outperformed corticosteroid therapy in improving the 20-meter walk test. Furthermore, there was no statistically significant difference between the two groups' knee flexion contractures and active and passive ranges of motion based on the therapy strategy or time.

A comparison between PRP and CS injection and the outcomes of intra-articular CS and PRP for the treatment of osteoarthritis (OA) has been evaluated in few studies. A meta-analysis of 7 randomized controlled studies including individuals with knee OA, wherein IA CS and IA HA were directly compared, provided support for this. Corticosteroids were more successful in reducing pain in the first two weeks, but by week four, both were equally successful. From week eight onward, HA was more successful until the final assessment at week twenty-six. Analyses of the data for additional endpoints, like decreased stiffness and enhanced function after IA HA, showed comparable findings. [39]

PRP and high- and low-molecular-weight HAs were compared by Kon et al. [3] in the treatment of osteoarthritis in the knee. The outcomes demonstrated that PRP was

superior to HAs in terms of longer-lasting benefits, greater pain reduction, and symptom improvement. [3] On the other hand, Filardo *et al.*'s study contrasting these two approaches revealed that while patients' symptoms improved following PRP injection for a year, the improvement was not statistically greater than HA. [28] According to Cerza et al., PRP produced better clinical outcomes up to a 6-month follow-up than HA. [31]

In a study conducted by Raiessadat et al. at Shahid Beheshti University of Medical Sciences, Iran, 65 individuals received two PRP injections spaced four weeks apart. WOMAC and SF36 questionnaires were used to measure the patients' outcomes at a six-month follow-up. The outcomes showed that PRP is useful for improving quality of life and relieving pain and other symptoms. Platelet concentration ranged from 3 to 7.8 times on average. There was no correlation seen between the concentrations of platelets in PRP and the results of therapy. [29]

One-course and two-course injections containing PRP were compared in a 2013 study by Patel et al., with saline injections used as the control group. The findings showed that there was no discernible difference between the outcomes of the first and second PRP injection courses. Overall, patients' osteoarthritis pain and symptoms were greatly reduced by PRP injection. [33]

Platelets containing growth factors (GFs) such as TGF-B, ILGF-1, Platelet-Derived Growth Factor, and Fibroblast Growth Factor (FGF) in their alpha granules are included in platelet-derived plasma (PRP), which is made from blood centrifugation. Studies both in vivo and in vitro have shown how important these elements are for cartilage regeneration and homeostasis. [3, 4, 6, 17–19, 25–27, 30, 33]

One month following the injection, VAS and 20 MW test evaluations in our study showed significant enhancements . Similarly, Patel et al. noted that after an average of 17 days following injection, the patients claimed improvement (during that time chondrogenesis was not started).[33] Therefore, it appears that other mechanisms are involved in PRP operation and that chondrogenesis isn't the sole active process. The platelets influence joint homeostasis overall, reduce synovial cartilage hyperplasia, control cytokine levels in joint fluid, promote anabolism, and slow down the breakdown of joint cartilage. [3, 33]

After the initial injection course, several researchers extracted 150 milliliters of blood and stored the platelets at -30 °C for subsequent injection courses. [3, 17] Platelet-rich plasma could lose part of its advantageous qualities and cause platelets to degranulate at temperatures below -30 °C. [33] Therefore, care should be used while evaluating the beneficial effects in the publications using comparable methodologies. Certain research has indicated an inverse connection between aging and treatment response. The results for younger individuals were superior to those for patients who were older than 50. [3, 27, 29]

The absence of biologic evaluations pertaining to the intra-articular surface of growth factors and imaging assessments such as MRI for assessing the amount of thickness of articular cartilage prior to and following therapy were limitations of this study.

CONCLUSION

The result of our study demonstrated than platelet rich plasma is safe and effective in reducing pain and enhancing physical functions in patients with osteoarthritis. In contrast to corticosteroids, our study showed that a single PRP injection reduced joint pain significantly for a longer period of time, relieved symptoms, and improved quality of life and activities of daily living in the short term. Nevertheless, there is no evidence that either of the intra-articular injections will result in cartilage regeneration or a regression of osteophyte growth in these patients.

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