Effect of Plasma Enriched with Platelets in Mild to Moderate Osteoarthritis of Knee Joint.

Faheem Sultan Ghori[1], Muhammad Annam Farooq[2], Kashif Mehmood Khan[3]

[1]Senior Registrar, Orthopaedic Surgery Ward 17, Jinnah Postgraduate Medical Centre, Karachi
[2]Senior Registrar, Orthopedic Department Ward 17, Jinnah Postgraduate Medical Centre, Karachi
[3]Associate Professor of Orthopedic Surgery Ward 17, Jinnah Postgraduate Medical Centre, Karachi

Authorship and contribution Declaration:
Each author of this article fulfilled ALL 04 Criteria of Authorship:
1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.
4. All authors agree to be responsible
for all aspects of their research work.

Corresponding author:
Dr. Faheem Sultan Ghori
E-mail: phaheemghori@gmail.com

ABSTRACT

Objective: To determine the effectivity of Plasma enriched with platelets in early knee articular-arthritis

Methodology: 125 patients who were added in the study, were of either gender with early knee osteoarthritis (kellgren and Lawrence type 1 and 2) .Patients with traumatic articular-arthritis, grade 3 and 4 articular arthritis, active infection, inflammation or tumour around knee, genu varum & who had an intra articular steroid injection in the last semester were excluded. Informed written consent was taken. Out Patients were chosen and dealt on day care basis. 5cc of Plasma enriched with platelets was introduced into the supra-patellar pouch using sterile measures. Patients were called to revisit at 6th week, 3rd month and 6th month. The clinical evaluation was determined by observation and interviews. End result was assessed by analyzing Western Ontario & Mc Master's University Osteoarthritis index and Visual Analogue Scale. Findings were put down on a pre-designed Performa and analyzed using SPSS v20. This is a longitudinal case study, conducted at department from July 2017 till June 2019.

Results: The average pain score was 17.07 ±3.08SD prior to PRP and decreased to 14.03 ±2.7SD after six months of PRP. The mean score for stiffness was 6.82 ±0.71SD and it decreased to 4.94 ±0.63SD after six months. The mean functional outcome score decreased from 58.57 ±2.29SD to 48.02 ±1.51SD. The comparison of the means before and after PRP showed significant results ($p<0.01$). Six months following injection, 49.6% (62 patients) were evaluated as having a satisfactory outcome (VAS 1-4),38 patients (30.4%) had a satisfactory outcome (VAS 5 to 7) whereas 25 individuals (20%) had a poor outcome (VAS 8-10).

Conclusion: Plasma enriched with platelets is an easy, inexpensive and less invasive procedure to cure early-stage progressive lesions of cartilage of knee-joint with minimal or no adverse-effects & has benefits in terms of relief from pain, patient contentment and improvement in knee range of motion & quality of life.

Keywords: Plasma enriched with platelets (PRP), Visual Analogue Scale (VAS), Nonsteroidal Anti-inflammatory drugs(NSAIDs), Western Ontario & Mc Master's University Osteoarthritis index (WOMAC), Osteoarthritis (OA).

This article may be cited as: Ghori F S, Farooq M A, Khan K M. Effect of Plasma Enriched with Platelets in Mild to Moderate Osteoarthritis of Knee Joint. J Pak Orthop. Assoc. (JPOA), Vol 35 (2) June, 2023

INTRODUCTION

Osteoarthritis a localized damage to the cartilaginous portion of a synovial joint in which the subchondral bone is sclerosed and accompanied by other alterations. It is closely correlated with advancing age[1,2]. It is the most prevalent kind of joint disease worldwide. According to the World Health Organization (WHO), osteoarthritis is the most prevalent cause of severe long-term pain and physical disability, affecting thousands of individuals worldwide[3,4]. More than 80% of people older than 55 have osteoarthritis in at least one joint, with hips, knees, spine, hands, and feet being the most affected[5]. It has a significant impact on daily living. It is categorized according to the Kellgren and Lawrence system[6,7].

Grade 0: OA is typically absent radiographically
Grade 1: decreased joint space is uncertain but presence of osteophytes is possible
Grade 2: possibility of decreased joint space on anteroposterior weight-bearing radiograph but definitive lipping with osteophytes is present
Grade 3: definitively decreased joint space, sclerosed margins, multiple osteophytes and possibly deformed bone
Grade 4: markedly decreased joint space, severely sclerosed margins, osteophytes are large & definitely deformed bone.

PRP is a supra-physiological concentration of human platelets[8]. Since 1987, PRP has been utilized in surgical operations to enhance cell regeneration, and it is a viable treatment for tendinosis, as demonstrated by a considerable body of evidence[9,10]. It is created by aspirating blood from a patient's peripheral vein and centrifuging it to obtain a tiny volume of plasma with a high concentration of platelets[11]. The PRP is then injected into the site of injury or surgery. Knee articular arthritis is predicted to impact approximately half of the population at some time in their lives. Hence, these people serve as samples for PRP research[12]. Plasma enriched with platelets (PRP) injections have been debated and studied to see whether they are an effective treatment for osteoarthritis[13,14]. Therefore, the primary objective of an orthopedist is to expeditiously return patients to their pre-injury level of activity while ensuring their complete and safe rehabilitation. In the realm of sports medicine, the use of autologous blood products, namely plasma enriched with platelets (PRP), is one of the most common approaches for biologically enhancing healing. Currently, plasma enriched with platelets is utilized to promote skin healing and soft tissue ulcers, hasten the healing of diabetic ulcers, and promote bone union in orthopedic trauma and sports surgery[15,16]. It can also be used in spinal and maxillofacial surgery[17], aesthetic and reconstructive surgery, heart surgery, and burns. This study was conducted to demonstrate that the injection of PRP into an osteoarthritic knee provides superior results in immediate and long-term treatment compared to injection of hyaluronic acid preparations and steroid, and that it is a beneficial technique for delaying the progression of OA.

METHODOLOGY

Sample Size: The calculated sample size is 125 by using WHO software "Sample Size Determination in Health Studies" considering 95% confidence interval with 5% margin of error and 0.201% SD difference between VAS score pre and post treatment.
Sampling Technique: Non-probability convenient sampling
Operational Definitions:
Visual analogue scale: VAS is one of the pain rating scales used in epidemiologic and clinical research to measure the intensity or frequency of various symptoms. The pain VAS is a unidimensional measure of pain intensity, used to record patients' pain progression, or compare pain severity between paints with similar conditions.
Womac score: The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is widely used in the evaluation of Hip and knee Osteoarthritis. It is a self- administered questionnaire consisting of 24 items divided into 3 subscales;

- Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing upright
- Stiffness (2 items): after first waking and later in the day
- Physical Function (17 items): using stairs, rising from sitting, standing, bending, walking, getting in / out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in / out of bath, sitting, getting on / off toilet, heavy domestic duties, light domestic duties.

Data Collection Procedure: Study was conducted from July 2017 till June 2019. Patients of either sex with early knee osteoarthritis (kellgren and Lawrence type 1 and 2) were included in the study. Patients with post traumatic osteoarthritis, grade 3 and 4 OA, patients with active infection, inflammation or tumour around knee, patients with deviation of mechanical axis (genu Varus) & patients receiving steroid injection into the knee joint during the last 6 months were excluded from this study. They were fully explained about the purpose, procedure, risks and the benefits of study and informed written consent was taken. Approval was taken from the ethical committee. OPD patients were selected and dealt on day care basis. All cases were done using strict sterile measure and were performed under supervision of Associate Professor.

To prepare 4-5cc PRP[35,36] with platelet concentration of 4-6 times above the normal value, venous blood sample of 30-40cc from ante-cubital vein was collected and stored in a sterilized tube containing anticoagulant dextrose solution A (ACDA) using a wide needle of 18G to avoid damage to platelets. The blood was centrifuged two times with anticoagulant, first at 3000 rpm, so that erythrocytes

are separated, then at 4000 rpm for 3 minutes & 15 minutes respectively to concentrate the platelets. 1 microgram of Prostaglandin E1 diluted in 0.005ml of saline was added before second cycle of centrifugation. 4-5cc of PRP- containing leucocytes [37] was the final product as a buffy layer. To activate the platelets, the final product was added with 0.05ml of 10% calcium chloride per ml of PRP. Under aseptic measures, PRP was injected into the knee with a 22G needle using a lateral approach, with patient in supine position and knee fully extended. With necessary instructions, patients were discharged home after 15 - 20 minutes. They were allowed immediate weight bearing and no antimicrobial cover was given. Patients were advised not to take NSAIDS during the trial period and were asked to follow-up at 6 weeks, 3 months and 6 months. On every visit, severity of pain was calculated using VAS. Outcome was assessed using WOMAC & VAS score. VAS Score of 0 indicated excellent outcome with completely painless walk. Score of 1-4 indicated satisfactory outcome with mild pain, 5-7 indicated fair outcome with moderate pain and limitation of activities while score of 8-10 indicated poor outcome with severe pain. Findings including VAS score, WOMAC score and improvement in range of motion were recorded on predesigned Performa. Inclusion and exclusion criteria was strictly followed to control biasness and cofounder.

Statistical Analysis: 20th version of Statistical Package of Social Sciences was used for analyzing data. Qualitative variables like gender and outcome were presented in frequencies and percentages. Quantitative variables like age, range of motion, VAS & WOMAC score were presented in the form of Mean ± SD. Effect modifiers like gender was controlled by stratification. To test significance for VAS scores, paired sample t-test between Pre PRP injection and post PRP injection was applied. To assess any significant difference among the groups one way ANOVA was performed. Less than or equal to 0.05 of P-value was considered significant.

RESULTS

This study comprised a total of 125 patients, of which 90 (72%) were females and 35 (28%) were males. 65(52%) had involvement of right knee, 42(33.6%) had left knee involvement and 18(14.4%) had bilateral involvement. 88 percent of 110 patients experienced discomfort sitting on the floor prior to PRP treatments. 118 patients (94.4%) experienced difficulty using the Indian restroom. The average patient was 56.144 years old and weighed 84.24 kilograms (Table 1).

The mean VAS score prior to PRP treatment was 7.312. The mean VAS score was 6.54 at six weeks, 5.8 after three months and declined to 5.1 after six months. The comparison of VAS scores before and after PRP was examined using the Paired Samples t-Test, which revealed statistically significant findings ($p<0.01$) (Table 2).

The researchers applied the WOMAC grading method to measure the pain, stiffness, and functional outcome. The average pain score was 17.07 prior to PRP and decreased to 14.03 after six months of PRP. While the mean score for stiffness was 6.82, it decreased to 4.94 after six months. The mean functional outcome score decreased from 58.57 to 48.02. The comparison of the means before and after PRP showed significant results (Table 3).

In terms of patient's assessment, six months after injection, 49.6% (62 individuals) had a satisfactory outcome (VAS 1-4). 38 patients (30.4%) had a fair outcome (VAS 5-7), while 25 patients (20%) had a poor outcome (VAS 8-10) (Table 4).

Table 1: Demographic Characteristics of the Patients

Demographics	Mean ±SD
Age (years)	56.14 ±5.2 SD
Male/Female Ratio	35/90
Weight (kilograms)	84.24 ±9.6 SD
Joint Involvement	
Right	65 (52%)
Left	42 (34%)
Bilateral	18 (14%)
Difficulty in floor sitting	110 (88%)
Difficulty using Indian Washrooms	118 (94.4%)

Table 2: Comparison of VAS score before and after PRP

VAS Score	Mean ±SD	p-Value
VAS Score before PRP	7.31 ±0.49	<0.01
VAS Score at 6th week	6.54 ±0.61	<0.01
VAS Score at 3 months	5.80 ±0.60	<0.01
VAS Score at 6 months	5.14 ±5.18	<0.01

Table 3: WOMAC Scoring System

WOMAC Score	Mean ±SD	p-Value
Pain		
Pain before PRP	17.07 ±3.08	
Pain at 6th weeks	15.67 ±2.70	<0.01
Pain at 3 months	14.81 ±2.70	
Pain at 6 months	14.03 ±2.71	
Stiffness		
Stiffness before PRP	6.82 ±0.71	
Stiffness at 6th weeks	6.03 ±0.67	<0.01
Stiffness at 3 months	5.02 ±0.64	
Stiffness at 6 months	4.94 ±0.63	
Physical Function		
Physical function before PRP	58.57 ±2.29	
Physical function at 6th weeks	55.42 ±2.17	<0.01
Physical function at 3 months	51.36 ±1.93	
Physical function at 6 months	48.02 ±1.51	

Table 4: Assessment of Patient's Satisfaction Post PRP

OA Grade	VAS Score	n (%)
Grade 1	Satisfactory (VAS 1-4)	62 (49.6)
Early Grade 2	Fair (VAS 5-7)	38 (30.4)
Advanced Grade 2	Poor (VAS 8-10)	25(20)

DISCUSSION

In the current study, PRP treatment showed significant reduction in joint pain, stiffness, and functional outcome. Prior to PRP, the average pain score was 17.07 which declined to 14.03. After six months. The mean score for stiffness lowered from 6.82 to 4.94 within six months. The mean score for functional outcome decreased to 48.02 from 58.57. Overall, 49.6% of the individuals received a satisfactory PRP score, while 30.4% reported a fair outcome.

According to the previous studies, knee osteoarthritis is one of the primary causes of knee joint discomfort in elderly persons around the world[18,19]. This ailment normally causes a great deal of discomfort for those suffering from it. OA is a matter of patience for anyone having conservative treatment for this ailment, as well as for the practitioner as the condition is permanent until surgically addressed[20]. Symptoms can range from moderate to severe, prompting patients to seek any treatment that will provide relief. Considering the duration, frequency, and severity of this condition's symptoms, numerous researchers have attempted to develop a treatment that is less invasive, cheaper, and effective with good results[21,22]. Various conservative and surgical therapies have been developed. There was a need for different treatment options because not every patient chooses surgery as it is invasive and expensive.

Different researchers injected various substances into the knee, including placebo, corticosteroids, hyaluronic acid, and platelet-rich plasma (PRP)[23,24]. As it is autologous, the use of PRP in the knee has yielded satisfactory outcomes with no adverse effects and no complications have been observed when PRP is injected under stringent aseptic conditions which is consistent with the results of current study[25,26].

Wang-Saegusa and his colleagues[27] examined 312 individuals with knee articular-arthritis and reported a significant improvement in pain function, knee stiffness, and the Lequesne Index. In another

study including 115 knees with osteoarthritis, all clinical scores improved significantly at 6 and 12 months[25]. The results of the previous studies were similar to the current study. Patel and his colleagues[28] discovered that patients treated with one or two PRP injections saw a reduction in pain intensity and knee joint stiffness, as well as a significant improvement in knee range of motion after 6 weeks and 3 months. Six months after PRP therapy, pain and functionality scores were no longer significantly better than they were before treatment. However, they remained significantly better than they were before treatment.

In a smaller trial, Halpern B. and colleagues[29] discovered that the majority of patients reported less pain one year after receiving a PRP injection than they had the year before (although pain had not disappeared necessarily). MRIs revealed that deterioration had not progressed in the majority of knees. In a study published in the journal Sports Health[30], 50 patients with knee articular-arthritis were tracked for a minimum of one year following therapy with two injections of autologous PRP into the knee joint. At 6 and 12 months, all patients (including those who had undergone an arthroscopic operation in the past) who had returned to their previous activities reported significant improvements in their complaints on all pain and function testing and measuring scores.

A study published in the physical therapy scientific journal[31] indicated that two or three injections were more beneficial than a single injection for improving physical function and reducing pain in grade 3 knee osteoarthritis. In Grade 3 arthritis, three PRP injections with a 15-day gap were found to be more beneficial than two injections for improving knee mobility and reducing discomfort. Immediately following a single injection of PRP, a considerable effect was observed; however, after an extremely brief duration, the effect subsided.

CONCLUSION

The injection of platelet-rich plasma (PRP) into a joint has become an effective treatment for knee osteoarthritis. Multiple randomized controlled studies (RCTs) have shown that PRP is a safe and effective treatment for knee arthritis. PRP is as effective as hyaluronic acid and is more useful than hyaluronic acid in younger, more active patients with low-grade arthritis. It can be a useful, less painful, and cost-effective method of reducing osteoarthritis symptoms and avoiding the need for more painful and costly treatments such as total knee arthroplasty. It can be used as an adjuvant to non-operative osteoarthritis therapy approaches. After 6 to 9 months, the benefits appear to diminish. Numerous PRP therapy variables that may be significant are accessible, however the best PRP technique is yet unknown. Future research, particularly well-designed randomized trials, is required to identify best practices, comprehend the mechanism of action, and assess outcomes and effect durability.

Conflict of Interest: None

Grants/Funding: None

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