

Clinical and Radiological Benefits of Intra-Articular Platelet Rich Plasma (PRP) Injection in Patients with Knee Osteoarthritis

Original
Article

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ABSTRACT

Background: Although several studies had investigated the possibility of being effective in treating osteoarthritis, the use of PRP as a line of treatment in such cases is not yet approved.

Aim of the Work: To assess the potential clinical and radiological benefits of intra-articular PRP injection in patients with knee osteoarthritis.

Patients and Method: The study included 45 knee osteoarthritis patients following-up at the rheumatology clinic, Ain Shams University hospitals. Demographic, clinical data including the visual analogue scale (VAS), and Western Ontario and McMaster Universities (WOMAC) index, Magnetic Resonance Imaging (MRI) knee joint were analyzed. Intraarticular knee injection of PRP for 6 consecutive months was done. Patients were reassessed clinically and radiologically after 6 months from the last injection.

Results: There was 39 (86.7 %) females, 6 (13.3 %) males. There was a statistically significant reduction in VAS & WOMAC scores after PRP injection ($P < 0.001$). MRI showed statistically significant decrease in the subchondral bone marrow lesions ($P 0.004$) and statistically significant increase in the patellar cartilage volume ($P 0.02$), non-significant decrease in intercondylar synovitis ($P 0.51$). The patient's age and disease duration were significantly negatively correlated only with the VAS improvement percent ($P 0.04, 0.03$ respectively), BMI didn't show any significance with both scores. There was no major side effects of PRP injection like infection or bleeding. Minimal pain at site of injection reported by some patients.

Conclusions: The use of Intraarticular PRP injection improves the clinical and radiological outcomes of knee osteoarthritis without major adverse effects.

Key Words: Knee osteoarthritis, magnetic resonance imaging, platelet rich plasma.

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INTRODUCTION

Osteoarthritis (OA) is the commonest joint disease worldwide. It is a degenerative disease affecting the joint cartilage causing pain and disability. The chief features of osteoarthritis are subchondral bone anomalies, formation of osteophytes, bone remodeling, subchondral sclerosis^[1].

Treatment of cartilage disease is challenging as it is defective in blood vessels and nerve supply with poor ability to heal. Traditional treatment for osteoarthritis uncommonly improves patient's functional state^[2].

Platelet rich plasma (PRP) is rich in several growth factors & plasma proteins such as transforming growth factor beta 1 (TGF- β 1), platelet-derived growth factor (PDGF), insulin-like growth factor 1(IGF-1), vascular endothelial growth factor (VEGF), human growth hormone, and basic fibroblast growth factor (bFGF), thus it may have benefit in decreasing the cartilage loss in osteoarthritis^[3].

Various studies had suggested that PRP is hopeful in treatment of knee osteoarthritis as it may improve joint pain and function, increase range of movement, and decreasing the patient disability. More ever intraarticular PRP injection has been noticed to diminish the progression

of cartilage loss, therefore supporting its effectiveness in preventing the knee osteoarthritis degenerative effects and avoiding additional structural damage^[4].

Although several studies have investigated the possibility of being effective in treating osteoarthritis, the use of PRP as a line of treatment in such cases is not yet approved^[5].

AIM OF THE WORK

To assess the potential clinical and radiological benefits of intra-articular PRP injection in patients with knee osteoarthritis.

PATIENTS AND METHODS

This prospective study enrolled forty-five patients with knee osteoarthritis following-up at the rheumatology outpatient clinic, Ain Shams University hospitals. All patients were diagnosed according to the American college of rheumatology (ACR) criteria for knee osteoarthritis^[6]. Patients with Magnetic Resonance Imaging (MRI) or PRP injection contraindications were excluded (previous hyaluronic acid or corticosteroid injection, recent knee surgery or trauma, systemic or inflammatory joint disease, immunosuppression or acute infection, cancer, bleeding tendency).

An informed consent was obtained from all patients after approval from the Ethical Committee of Scientific Research, Faculty of Medicine, Ain Shams University. Detailed medical history was obtained from all patients including demographic data and disease duration. Assessment of joint pain was done using the visual analogue scale (VAS) as 0 = without pain; 10 = with maximum pain^[7]. Functional state of patients was assessed using the Western Ontario and McMaster Universities (WOMAC) index where the lower scores the better state (minimum is 0, maximum 96)^[8].

Full general examination and rheumatological examination of the knee joint were done. Laboratory investigations were done including erythrocyte sedimentation rate (ESR), C-reactive protein with titer (CRP), complete blood count (CBC), Prothrombin time (PT), Partial Thromboplastin Time (PTT) and international normalization ratio (INR).

Magnetic Resonance Imaging (MRI) knee joint was done and studied by radiologist, with especial comment on: (1) the subchondral bone marrow lesions were scored in 15 joint regions using the Whole-Organ Magnetic Resonance Imaging Score (WORMS score)^[9], each region scored from zero to three, with lower scores indicate better

state, (2) Inter-condylar synovitis was scored as zero or one (3) Patellofemoral cartilage volume was evaluated in millimeters (Normal: 4.5 ± 1.3 mm), (4) Medial and lateral meniscal integrity were scored from zero to three, zero referring to intact meniscus^[9].

All patients were subjected to intraarticular knee injection of autologous PRP monthly for 6 consecutive months. NSAIDs were stopped 2 days before injection. PRP was prepared by withdrawal of 30-mL patient's venous blood then centrifuged at room temperature with GPS II system for 10 minutes at a speed of 4000 rpm, then injected directly intraarticular under complete aseptic condition. Follow up and reassessment of patients after 6 months apart from the last injection were done including the VAS and WOMAC scores. MRI knee joint was also done on follow up.

The collected data was tabulated and statistically analyzed using statistical package of social sciences (SPSS) version 28. Data were presented as mean ± standard deviation (SD) or frequencies and percentages. Comparisons were done by Chi-square (χ^2) and Mann-Whitney tests. Correlation was done by Spearman's correlation coefficient (r) test. Significance was indicated by *P value* ≤ 0.05.

RESULTS

Thirty-nine (86.7 %) of the studied patients were females, 6 (13.3 %) were males, their mean age was 53±4.2 years, with a mean body mass index (BMI) 28.8±3.6 kg/m², and mean disease duration 4.1±2.9 years (Table 1).

Table 1: Demographic and laboratory data of the studied patients

Item	N (%) or Mean ± SD
Age (years)	53±4.2
Female	39 (86.7 %)
Male	6 (13.3 %)
Disease duration (years)	4.1±2.9
BMI (kg/m ²)	28.8±3.6
ESR (mm/hour)	13.4±5.6
CRP (mg/dl)	8.4±2.8
WBC (1000/microL)	7.3±1.7
Hb (gm/dl)	10.9± 0.8
PLT (1000/microL)	257±77
PT (seconds).	10.5± 0.6
PTT (seconds)	20±1.3
INR	1±0.5

BMI: Body mass index, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, WBC: White blood cell, PLT: Platelets, Hb: Hemoglobin, PT: Prothrombin time, PTT: Partial Thromboplastin, INR: International normalization ratio.

There was a statistically significant reduction in both VAS & WOMAC scores after the PRP injection as the VAS decreased from 6.9 ± 1.21 to 3.8 ± 1.7 , WOMAC decreased from 68.61 ± 15.22 to 37.7 ± 11.3 with *P* value <0.001 for both (Table 2).

Regarding the MRI changes after PRP injection, there was statistically significant decrease in the subchondral bone marrow lesions (*P* value 0.004) and statistically significant increase in the patellofemoral cartilage volume (*P* value 0.02) (Table 2, Figures 1,2).

Table 2: Comparison of clinical and radiological data at baseline and 6 months after last PRP injection in the studied patients

Item	Before PRP	After PRP	<i>P</i> value
WOMAC score	68.61 ± 15.22	37.7 ± 11.3	<0.001
VAS score	6.9 ± 1.21	3.8 ± 1.7	<0.001
MRI findings			
Subchondral Bone marrow lesions	5.1 ± 3.1	4.0 ± 2.7	0.004
Inter-condylar synovitis	6.7 %	3.3 %	0.51
Patellofemoral cartilage volume (mm)	2.51 ± 0.74	2.81 ± 0.61	0.02
Medial and lateral meniscal integrity	5.21 ± 2.92	4.91 ± 3.00	0.21

PRP: Platelet rich plasma, VAS: Visual analogue scale, WOMAC: Western Ontario and McMaster Universities, MRI: Magnetic Resonance Imaging. Bold values are significant at $p < 0.05$

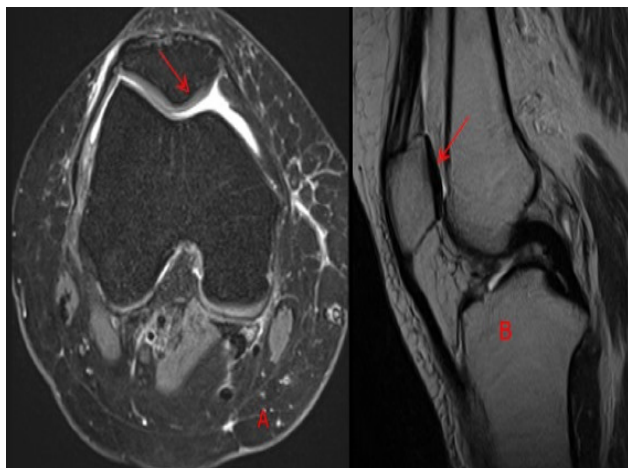


Fig. 1: MRI before PRP injection, (A) Axial T2WI revealed denuded articular cartilage and (B) sagittal STIR images revealed: denuded articular cartilage with subchondral bone edema.

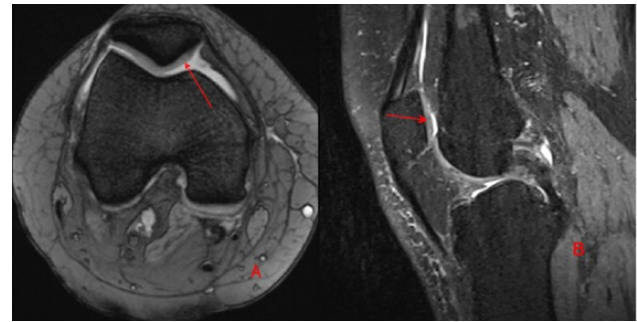


Fig. 2: MRI after PRP injection, (A) Axial T2WI revealed improvement as regards the articular cartilage volume and (B) Sagittal STIR images revealed improvement as regards the articular cartilage and subchondral bone edema.

Although the inter-condylar synovitis decreased from 6.7% to 3.3% after PRP injection, it didn't show statistical significance (*P* value 0.51), the same for medial and lateral meniscal integrity (*P* value 0.21) (Table 2, Figures 3,4).

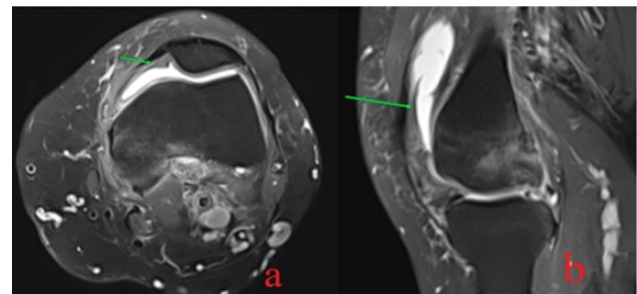


Fig. 3: MRI before PRP injection, (a) Axial T2WI and (b) Sagittal STIR revealed diffuse uniform synovial thickening suggestive of synovitis.

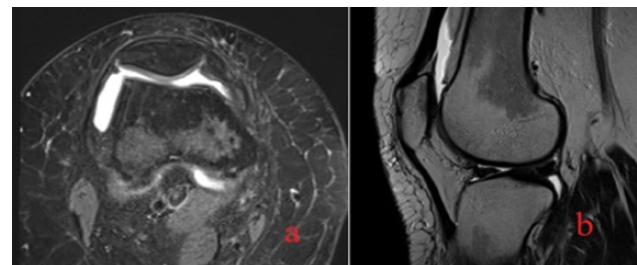


Fig. 4: MRI after PRP injection, (a) Axial T2WI and (b) Sagittal STIR revealed improvement of synovitis.

While correlating the different demographic data with the VAS & WOMAC improvement percent, patient's age and the osteoarthritis disease duration were significantly negatively correlated only with the VAS improvement percent (*P* value 0.04, 0.03 respectively), while the BMI didn't show any statistical significance with both scores (Table 3).

Table 3: Correlation between demographic data and the VAS & WOMAC improvement percent after 6 months from the last PRP injection

Item	Age (years)		BMI (kg/m ²)		DD (years)	
	r	p	r	p	r	p
VAS improvement %	-0.61	0.04	-0.04	0.80	-0.50	0.03
WOMAC improvement %	-0.14	0.47	0.26	0.17	-0.07	0.67

VAS: Visual analogue scale, WOMAC: Western Ontario and McMaster Universities, BMI: body mass index, DD: disease duration. Bold values are significant at $p < 0.05$

There were no major side effects of PRP injection like infection or bleeding, only minimal pain at site of injection for few hours after the procedure was experienced by some patients.

DISCUSSION

Osteoarthritis is a common degenerative joint disease that affects mainly knee and hip joints. It is usually manifested by pain and limited range of motion^[10]. Several studies had suggested the possible favorable effects of intraarticular injection of platelet-rich plasma in cases with knee osteoarthritis^[11].

While assessing the potential benefits of intra-articular PRP injection, 45 knee osteoarthritis patients were subjected to intra-articular knee injection of autologous PRP monthly for 6 consecutive months. While comparing the baseline findings with those after injection, there was a statistically significant reduction in both VAS & WOMAC scores after injection (p value < 0.001), that reflects clinical improvement of patients pain and functional ability, that was similar to results of *Halpern et al.*^[12], *Wang et al.*^[13], *Sdeek et al.*^[14], and *Dulic et al.*^[15] who found a clinical improvement indicated by decreased WOMAC and VAS scores after PRP injection in evaluated patients with knee osteoarthritis.

Similarly, studies by *Bansal et al.*^[16], *Rahimzadeh et al.*^[17], *Shahid et al.*^[18], *Gaballa et al.*^[19] and *Huang et al.*^[20] revealed similar findings concerning the WOMAC score. Additionally, *Hassan et al.*^[21] demonstrated a highly statistically significant reduction in the joint stiffness time, VAS score and international knee documentation committee osteoarthritis scale (IKDC score) ($p < 0.001$) after injection.

In 2016, Smith^[22] demonstrated 78% reduction in WOMAC scores in patients injected with PRP, while only 7% reduction in placebo injected patients. Furthermore, *Patel et al.*^[23], *Spaková et al.*^[24] and *Sampson et al.*^[25] concluded a linear improvement of pain scores and functional scores. Another study by *Cole et al.*^[26] found reduction in pain scores of 43.14% after PRP.

In 2019, Badr and colleagues^[27] concluded that combining PRP with therapeutic exercise resulted in significantly lower VAS and WOMAC scores than exercise alone in patients with knee osteoarthritis.

Although the VAS and WOMAC scores reflect the pain and functional ability of patients, but they are mainly patient self-administered tools, thus MRI knee joint was done to all the studied patients at baseline and 6 months after the last PRP injection trying to detect the possible significant radiological improvement. There was a significant decrease in the subchondral bone marrow lesions (P value 0.004) and significant increase in the patellar cartilage volume (P value 0.02), as well as a non-significant decrease in both inter-condylar synovitis and the meniscal integrity after injection. These results support the findings of *Özyalvaç et al.*^[28] who showed better functional scores and radiological improvement regarding the meniscal degeneration, and *Sampson et al.*^[29] who found increased cartilage thickness after PRP injection.

In accordance, *Ahmad et al.*^[30] observed clinical improvement after PRP injection as well as regression of the ultrasonographic findings of osteoarthritis in injected patients. And *Raeissadat et al.*^[31] concluded that adding to the benefits of PRP on VAS and WOMAC scores, PRP significantly improves the radiologic findings (patellofemoral cartilage volume and synovitis). Similarly, results of *Moretti et al.*^[32] showed a statistically significant VAS, WOMAC improvement, and non-significant increase in cartilage thickness. They concluded that PRP injection is valid in reducing pain and improving quality of life and functional scores.

Current results partially agree with those of *Küçükakkaş et al.*^[33] who found a statistically significant reduction in both pain and functional scores after PRP injection. However, their patients didn't show significant increase in cartilage thickness which differs from our findings.

In contrast with current results, *Bennell et al.*^[34] compared the effectiveness of placebo saline and PRP injections in knee osteoarthritis patients, and observed no statistically significant difference between both groups

regarding pain scores or cartilage volume in MRI, although the placebo group showed an extra minor loss of cartilage. In 2013, *Halpern et al.*^[12] concluded that MRI didn't show progression or regression of the cartilage loss after PRP injection.

These disagreements with our results could be attributed to the difference in patient's number, lower number of injections, different interval between injections and shorter follow up period in their studies.

While identifying the characteristics of patients with better response to PRP injection, we found that shorter disease duration and younger age showed better improvement of joint pain and or function, as the osteoarthritis disease duration and patient age were significantly negatively correlated with the VAS reduction percent. And they were negatively correlated with the WOMAC reduction percent although didn't show statistical significance.

These findings go hand in hand with those observed by *Meheux et al.*^[35] who found better response in patients with shorter disease duration.

In line, significant correlation of the disease duration and patient's age with VAS score after PRP injection was found by *Hassan et al.*^[21], but their results were different from ours regarding other parameters, as they found that BMI was significantly correlated with VAS and significantly negatively correlated with the international knee documentation committee osteoarthritis (IKDC) score after 6 PRP injections.

Intraarticular PRP injection seems to be safe causing no major adverse effects in the studied patients except for mild pain at injection site, the same was observed by *Hassan et al.*^[21] although *Patel et al.*^[23] recorded another side effects like nausea and dizziness in some of their studied patients, however it were mild and temporary.

CONCLUSION

From the current findings, we conclude that intraarticular injection of PRP has a promising effect in treating knee osteoarthritis via improving the pain, functional ability and increasing the cartilage volume. Consequently, the use of PRP seems to improve the clinical and radiological outcomes of knee osteoarthritis without major adverse effects.

Some limitations in this study should be considered such as small sample size, absence of control group of patients with osteoarthritis receiving different treatment to compare with the PRP results and lack of standard protocol for PRP injection with determined number of injections, interval between injections, and amount of PRP per injection.

CONFLICT OF INTERESTS

There are no conflicts of interest.

AUTHORS CONTRIBUTIONS

All authors have participated in the concept, design, collect, analysis and interpretation of data, writing, drafting and revising the manuscript.

FM: recruited patients, carried out clinical examination and assessment, and generated the result sheets.

MA: underwent data tabulation and statistical analysis, and interpreted the patient's data and wrote the final results.

MM: recruited patients, carried out clinical examination and assessment,

OB: revised data interpretation and manuscript.

AF: was the major contributor in writing and editing the manuscript, designed the protocol, carried out the Ethical approval, and data collection.

All authors have agreed to conditions noted on the Authorship Agreement Form and have read and approved the final version submitted. The content of the manuscript has not been published, or submitted for publication elsewhere. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests concerning this article.

ETHICAL APPROVAL

All procedures performed in the study were in accordance with the ethical standards of the faculty of

medicine, Ain Shams university research and ethical committee. We obtained approval from Research Ethics Committee (REC) No. FWA000017585. FMASU R 114/2023, On 1/5/2023. Written informed consent was obtained from participants for participation in this study.

The FMASU REC is organized and operated according to guidelines of the International Council on Harmonization (ICH) and the Islamic Organization of Medical Sciences (IOMS), the United States Office for Human research Protections and the United States Code of Feral Regulations and operates under Federal Wide Assurance No. FWA 000017585. FMASU 324/2018.

CONSENT FOR PUBLICATION

Not applicable due to patients' privacy concern.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and/or analyzed during this study are not publicly available due to patients' privacy, but are available from the corresponding author on reasonable request.

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الفوائد السريرية والإشعاعية لحقن البلازما الغنية بالصفائح الدموية داخل المفصل في مرضى خشونه الركبة

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الخلفية: على الرغم من أن العديد من الدراسات قد بحثت في إمكانية فعاليتها في علاج خشونه الركبة، إلا أن استخدام البلازما الغنية بالصفائح الدموية كخط علاج في مثل هذه الحالات لم تتم الموافقة عليه بعد.

الهدف من العمل: تقييم الفوائد السريرية والإشعاعية المحتملة لحقن البلازما الغنية بالصفائح الدموية داخل المفصل لدى المرضى الذين يعانون من خشونه الركبة.

المرضى والطريقة: شملت الدراسة 45 مريضاً مصاباً بخشونه الركبة الذين تتم متابعتهم بعيادة الروماتيزم بمستشفيات جامعة عين شمس. تم تحليل البيانات الديموغرافية والسريرية بما في ذلك المقياس التناظري البصري (VAS)، ومؤشر جامعات أونتااريو الغربية وماكاستر (WOMAC)، ومفصل الركبة بالتصوير بالرنين المغناطيسي (MRI). تم إجراء حقن البلازما الغنية بالصفائح الدموية (PRP) داخل المفصل لمدة 6 أشهر متتالية. تمت إعادة تقييم المرضى سريرياً وشعاعياً بعد 6 أشهر من الحقن الأخير.

النتائج: كان هناك 39 (86.7%) إناث، 6 (13.3%) ذكور. كان هناك انخفاض ذو دلالة إحصائية في درجات VAS و WOMAC بعد الحقن ($P < 0.001$). أظهر التصوير بالرنين المغناطيسي انخفاضاً ملحوظاً إحصائياً في آفات نخاع العظم تحت الغضروف ($P = 0.004$) وزيادة ذات دلالة إحصائية في حجم الغضروف الرضفي ($P = 0.02$)، وانخفاض غير ملحوظ في التهاب الغشاء المفصلي بين اللقمتين ($P = 0.51$). ارتبط عمر المريض ومدة المرض بشكل سلبي بشكل ملحوظ فقط مع نسبة تحسن الألم ($P = 0.04$ ، 0.03)، ولم يُظهر مؤشر كتلة الجسم أي دلالة إحصائية. لم تكن هناك آثار جانبية كبيرة لحقن PRP مثل العدوى أو النزيف، فقط القليل من الألم في موقع الحقن الذي أبلغ عنه بعض المرضى.

الاستنتاجات: يؤدي استخدام حقن البلازما الغنية بالصفائح الدموية داخل المفصل إلى تحسين النتائج السريرية والإشعاعية لالتهاب خشونه الركبة دون آثار ضارة كبيرة.