Factors Associated with The Efficiency of Platelet-Rich Plasma Injection Among Patients with Knee Osteoarthritis: A Retrospective Data Analysis

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Research article

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Abstract

Objectives: Intra-articular application of platelet-rich plasma (PRP) are found to effectively improve knee function in patients with Knee osteoarthritis (KOA). This study is to identify the factors that influence the effect of PRP in the treatment of KOA.

Methods: PRP was performed with a rich-leukocyte autologous conditioned plasma (ACP) system in 82 patients who were diagnosed with KOA. A Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to score the level of KOA by 3 features as the evaluation indicator of therapeutic effect. Visual Analogue Scale (VAS), X-ray and subsequent Kellgren-Lawrence (K-L) scale level evaluation were performed before the treatment. Basic information of participants and disease duration were also collected. Simple correlation analysis, single-factor ANOVA and multivariant regression analysis were used for identifying factors associated with the efficiency of PRP injection.

Results: WOMAC decreased after PRP therapy by 10.12 ± 0.98 points (P < 0.001). Simple correlation analysis and ANOVA suggest BMI, pre-treatment VAS scores, and pre-treatment K-L scale level positively correlated with the therapeutic effect of PRP treatment ($P < 0.05$), while the other factors were not significantly correlated with the effect ($P > 0.05$). Further multivariate model indicates that the responsible variable Y (Post-treatment changes of WOMAC scores) was affected by exploratory variables BMI (X_1), VAS (X_2), K-L scale level (X_3) and Gender (X_4) (F = 7.857, $P < 0.001$). The exploratory variable X_3 had the biggest effect on Y.

Conclusion: This study found that the therapeutic effect of PRP is better in male patients with higher BMI, higher VAS and lower K-L scale level.

This study was qualified and registered in the Chinese Clinical Trial Registry as ChiCTR2000039856.

Introduction

Knee osteoarthritis (KOA) is common and often lead to significant physical disability. While classic conservative therapeutic approaches aim for symptoms like pain and inflammation, procedures like the intra-articular application of platelet-rich plasma (PRP) are found to promote tissue regeneration and improve cartilage tissue. PRP has made great success for patients with KOA, which restores the knee function and improves patients' satisfaction. An increasing number of researches have proven that intra-articular application of PRP, with less adverse reactions and more effective results, is a better choice for KOA patients than the injection of hyaluronic acids (HA).

However, factors that might influence the therapeutic effect of PRP in KOA patients remained to be identified. Some relevant research and our preliminary experiment suggest that patients' situation and their pre-injection knee function might play parts in the treating efficiency of PRP injection. This study aims to investigate factors affecting the therapeutic effect of PRP in KOA patients using a retrospective analysis.

Materials And Methods

The Medical ethics committee of Sun Yat-sen Memorial Hospital approved this study (Approved number of the ethic committee: SYSEC-KY-KS-2020-170). Written informed consent was obtained from all study participants before participation. This study was qualified and registered in the Chinese Clinical Trial Registry as ChiCTR2000039856.

82 patients with diagnosed KOA and indication for PRP treatment were enrolled in the study in 2020 after informed consent was obtained. Inclusion criteria: (1) Adults aged 38 and 85 years; (2) Confirmed clinical diagnosis of unilateral or bilateral KOA in accordance with the 2010 Clinical Diagnostic Criteria for the Diagnosis and Treatment of Osteoarthritis by the Chinese Medical Association Rheumatology Branch. Specifically, the diagnosis is confirmed by meeting items 1 + 2 + 3 + 4, items 1 + 2 + 5 or items 1 + 4 + 5 (item 1: knee pain most of the time in the past month; item 2: crepitus; item 3: morning stiffness lasting ≤ 30 min; item 4: age ≥ 38 years; and item 5: palpable bony enlargement); (3) Report average knee pain over the past week ≥ 20 on a 100 mm visual analogue scale; (4) No history of musculoskeletal pathology or trauma in the past 6 months. Exclusion criteria: (1) Acute, infectious diseases or other systemic diseases; (2) Knee function affected by another disease of the nervous or musculoskeletal system, such as stroke, fractures and rheumatoid arthritis; (3) hemoglobin concentration is lower than 12 g/dL or platelet counts is lower than 150,000 /uL; (4) anticoagulant or antiplatelet drugs were taken within 10 days before injection; (5) hormone was taken within 2 weeks before injection; (6) not suitable for X-rays test.

A total of 36 ml of blood sample was drawn from the antecubital vein into 10-ml syringes containing 1 ml 3.8% (w/v) sodium citrate. The blood samples were centrifuged for 10 min at 1600 rpm at room temperature (RT, 23°C) to separate the red blood cells from the buffy coat (containing platelets and white blood cells) and plasma. The supernatant buffy coat and the upper plasma layer were then harvested and transferred into new centrifuge tubes without disturbing the red blood cell layer. Then, the samples were centrifuged again for 10 min at 3200 rpm at RT. The lower fraction of the plasma was collected, which contained approximately 10 ml of concentrated PRP. A sample of 1 ml PRP was sent to the laboratory for quantitative analysis of platelet and leukocyte counts. All procedures were performed under sterile conditions.

To evaluate the treatment effect of PRP in KOA patients, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were surveyed before the first injection and after a mean follow-up of 6 weeks. Post-treatment changes of WOMAC scores were specified as evaluation indicator of the treatment effect for KOA.

Variables analyzed in the study included the following: (1) demographic characteristics: age, gender, mass, height, and body mass index (BMI); (2) pre-injection test data: Kellgren-Lawrence (K-L) scale level, Visual Analogue Scale (VAS) score, and KOA duration.

Statistical analysis

All statistical analyses were carried out by SPSS software (version 22.0). The data is represented by mean ± standard deviation. The single factor adopted the chi-square test, and the multi-factor adopted the linear regression analysis. $P < 0.05$ is considered statistically significant.

Results

Eighty-two patients (72% female) with a mean age of 67.09 ± 1.04 years and a BMI of 24.77 ± 0.28 underwent PRP therapy for KOA. To analyze clinical outcome and patient satisfaction with PRP therapy, WOMAC scores were surveyed before the first injection and after a follow-up of 6 weeks. WOMAC decreased after PRP therapy by 10.12 ± 0.98 points ($P < 0.001$, Fig. 1).

Post-treatment changes of WOMAC scores were considered as the evaluation indicator of PRP. To preliminary explore whether a positive response to PRP therapy was associated with the patients' pre-treatment situation, simple correlation analysis and single-factor ANOVA were performed. Shown as Table 1 and Table 2, the results suggest that BMI, pre-treatment VAS scores, and pre-treatment K-L scale level positively correlated with the therapeutic effect of PRP treatment ($P < 0.05$), while the other factors were not significantly correlated with the effect ($P > 0.05$).

Table 1
Simple correlation analysis between the post-treatment changes of WOMAC and factors

Factor	Mean ± SD	*r* value	*P* value
Age (year)	67.09 ± 9.40	-0.078	0.489
BMI (kg/m^2)	24.77 ± 2.52	-0.281	0.010
VAS	5.77 ± 1.79	-0.223	0.044
Duration (weeks)	5.90 ± 2.93	-0.113	0.311

Table 2
Single-factor ANOVA of the potential factor classifications

Factor	Classification	Number	Percent	Mean ± SD	F value	*P* value
Gender	Female	59	72.0	-9.08 ± 8.78	1.72	0.890
	Male	23	28.0	-12.78 ± 8.62		
K-L scale level	I	20	24.4	-12.75 ± 9.19	4.499	0.006
	II	29	35.4	-11.45 ± 7.59		
	III	23	28.0	-9.91 ± 9.37		
	IV	10	12.2	-1.5 ± 5.23		

Table 3
Multivariant linear regression analysis

Factor	β	Std. Error	Standardized Coefficients	t value	P value
Intercept (Constant)	31.50	8.98		3.51	0.001
BMI (X_1)	-0.98	0.33	-0.28	-2.94	0.004
VAS (X_2)	-1.66	0.49	-0.03	-3.38	0.001
K-L scale level (X_3)					
IV	(reference variable)				
III	-8.47	2.74	-0.43	-3.09	0.003
II	-12.03	2.73	-0.66	-4.41	< 0.001
I	-15.66	2.94	-0.77	-5.33	< 0.001
Gender (X_4)					
Male	(reference variable)				
Female	3.69	1.83	0.19	2.02	0.047

To further analyze the contribution of these factors to the efficiency of PRP therapy, a multivariate model with ordinary least squares regressions was performed by stepwise method. The results indicated that the responsible variable Y (Post-treatment changes of WOMAC scores) was affected by exploratory variables BMI (X_1), VAS (X_2), K-L scale level (X_3) and Gender (X_4) ($F = 7.857$, $P < 0.001$). The exploratory variable X_3 had the biggest effect on Y according to the values of standardized coefficients. R^2 suggested that these independent variables could explain 39% variation of Y, indicating that the model fitted the data well. Moreover, “higher BMI”, “higher VAS”, “lower K-L scale level” and “male” were the favorable factors for PRP injection to effectively improve knee function.

Discussion

To analyze what factors are associated with the positive effects of PRP injections, the improvement of knee function was reflected by the post-treatment changes of WOMAC scores. Regression analysis provided a prediction model, indicating that therapeutic effect of PRP injection was affected by many variables, such as BMI, pre-treatment VAS scores, pre-treatment K-L scale level and Gender. Similar to this result, an advantage of PRP therapy compared to HA application was frequently reported for the treatment of mild-moderate knee osteoarthritis in younger patients and in male patients[1–3]. Nevertheless, all of these studies either used a different PRP preparation protocol or did not provide

details to reproduce the treatment algorithm[4]. In this study, we have unified injection standards for recruited participants and collected data, which suggested that “higher BMI”, “higher VAS”, “lower K-L scale level” and “male” were the favorable factors for PRP injection to effectively improve knee function.

Although fewer study identified the factors that influence the effect of PRP in the treatment of KOA, some researches have found that the intra-articular injection of PRP might improve KOA symptoms independent from the level of cartilage damages quantified by a whole-organ MRI scoring method (WORMS)[5]. However, our results suggest K-L scale level, another scoring method for cartilage damage, is correlated with the efficiency of PRP treatment. Here, we found that KOA patients would receive better rehabilitation when they only have mild cartilage damage. This divergence may be due to the differences in evaluation scoring systems and radiological technologies.

An increasing number of studies have clarified the underlying molecular mechanisms of PRP treatment. Especially, PRP treatment can significantly decrease the expression of inflammatory factors (IL-18, IL-1β, and TNF-α) and suppress relevant inflammation pathway[6]. Such pathways are proven to be over-active in knee pain model[7], which might explain why PRP treatment have a greater performance in KOA patients with more pain. Besides, PRP treatment is famous for its excellent pain relief function.

It was reported that there are some differences in the composition of PRP between men and women, with sex being a greater factor than age[8], suggesting gender might be the factor affecting the PRP effect, while age might not. However, fewer studies have noticed the relationship between BMI and the therapeutic effect of PRP injection. Some latest researches focus on the combined use of PRP and adipose tissue-derived mesenchymal stem cells (MSCs), which shows a synergistic effect in spinal cord injury [9]and severe KOA[10]. It is possible that PRP have better performance in fatter KOA patients because of their activation of MSCs. Even though this study has clarified important factors that may affect the therapeutic effect of PRP treatment, there are still some potential variants that needs further investigation. For example, the patients’ post-discharge activity intensity might be different, which is hard to assess and might be another influence factor.

Conclusion

This study found that the therapeutic effect of PRP is better in male patients with higher BMI, higher VAS and lower K-L scale level.

Declarations

Consent for publication

All authors have approved this manuscript and concurred in its publication.

Availability of data and materials

Please contact the author for data requests.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Shaoling Wu and Chao Ma conceived the design of the study and collected the data. Yaochao Zheng and Shuo Luan carried out the statistical analysis and prepared the manuscript. Caina Lin assisted with the statistical analysis and revision of the manuscript. Qian Yang and Shaoling Wang designed the topic and assisted with the collection of data. All authors read and approved the final manuscript.

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Figures

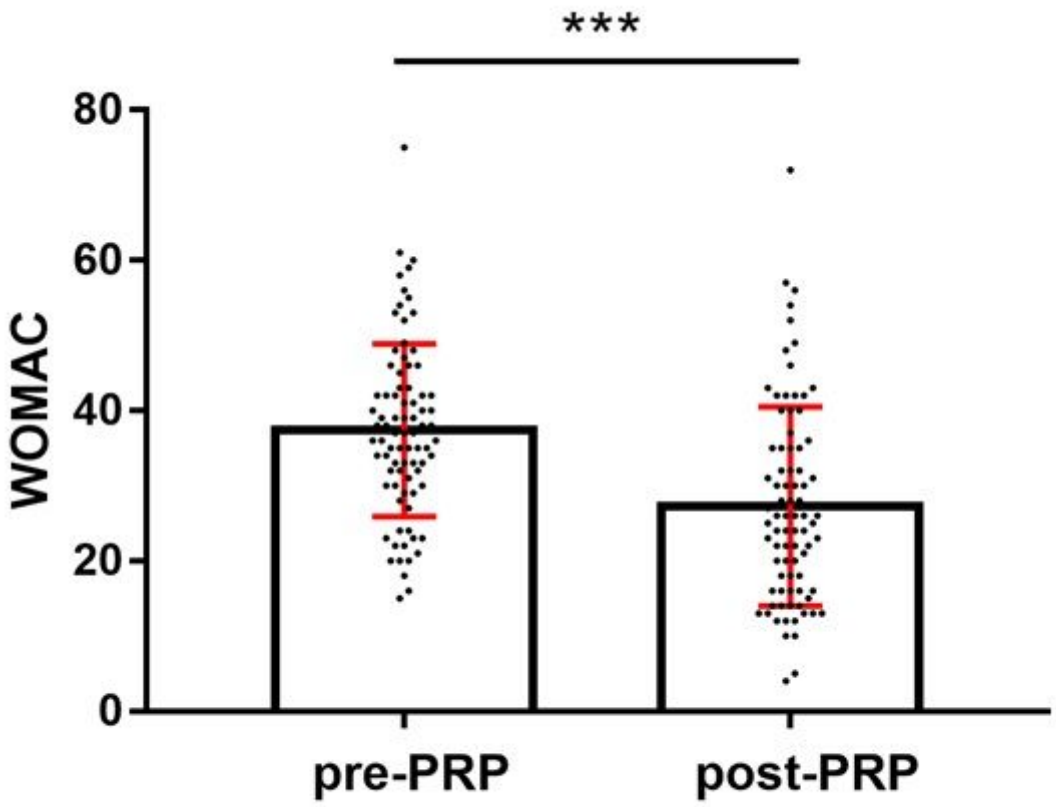
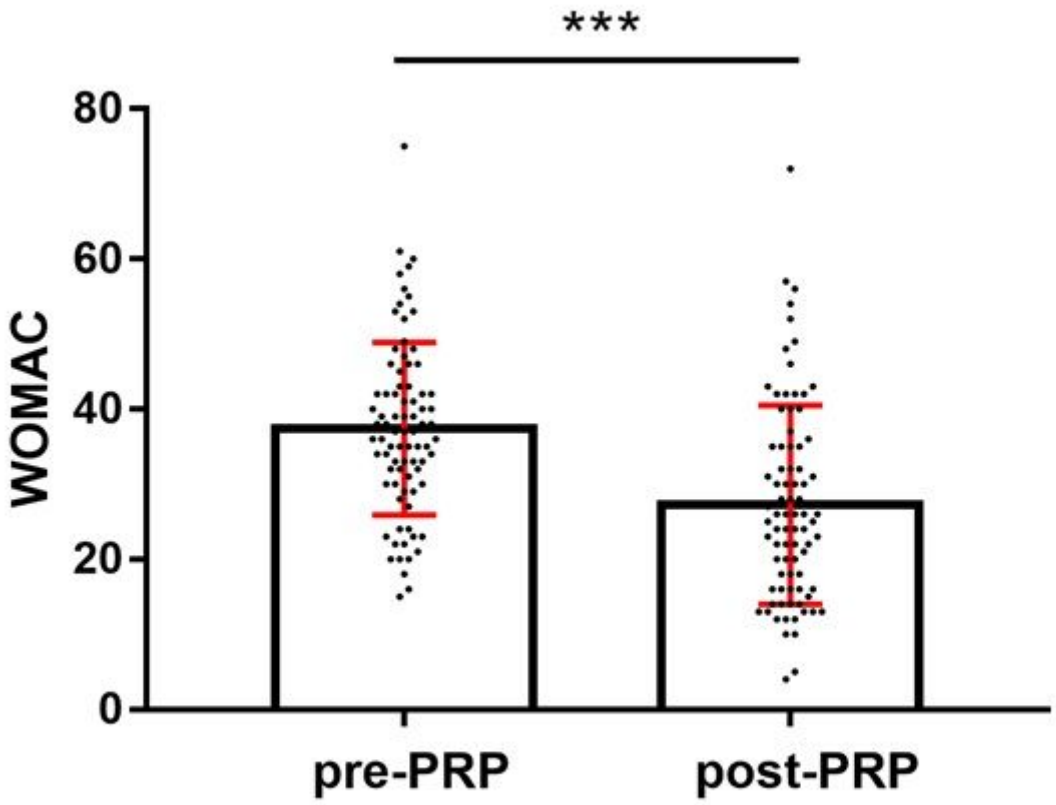


Figure 1

Change of WOMAC 6 weeks after PRP therapy. Absolute WOMAC results were compared pre PRP therapy and 6 weeks after PRP therapy. (*** P < 0.001)



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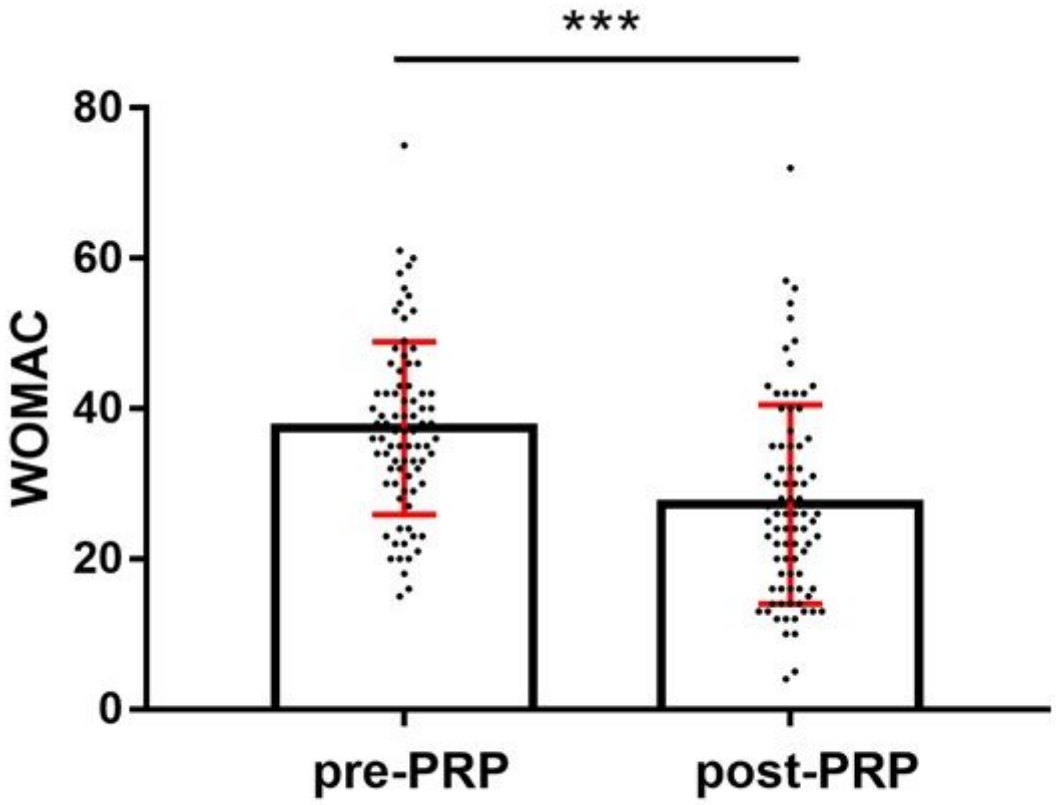

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