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Article

Platelet-Rich Plasma (PRP) Allogenic: A Potential Challenge for Decreasing Random Blood Glucose, Uric Acid, and Cholesterol Levels in A Preliminary Pre and Post Test Study on Adult Subjects

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Abstract. Ideally, metabolic homeostasis is maintained through stable glucose regulation, balanced lipid metabolism, and effective uric acid clearance under conditions of minimal systemic inflammation. In real clinical conditions, aging and persistent low-grade inflammation frequently disrupt this balance, leading to hyperglycemia, dyslipidemia, and elevated uric acid levels. Current pharmacological management mainly emphasizes metabolic control and may not sufficiently address underlying tissue dysfunction or inflammatory processes. Platelet-rich plasma (PRP) is a blood-derived bioregenerative product containing growth factors with anti-inflammatory and regenerative properties, offering a potential supportive approach for metabolic regulation. Nevertheless, PRP administration has predominantly relied on invasive delivery methods. Nebulization provides a non-invasive pulmonary route that enables rapid systemic absorption, representing an alternative delivery strategy. Despite its potential advantages, clinical evidence regarding the metabolic effects of PRP delivered via nebulization remains limited, creating an urgent need for preliminary clinical evaluation. Therefore, this pre–post test study aimed to assess the effects of allogeneic PRP nebulization on random blood glucose, uric acid, and total cholesterol levels. Fourteen adult subjects received PRP nebulization for five consecutive days. The intervention resulted in a significant reduction in random blood glucose levels and mild decreasing trends in uric acid and total cholesterol without serious adverse events.

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1. Introduction

Metabolic diseases such as diabetes mellitus, hyperuricemia, and dyslipidemia have become major health problems worldwide, especially among adults and the elderly [1]. According to data from the World Health Organization 2023, more than 500 million people worldwide live with diabetes, and about 60% of them are over 60 years old. Aging is associated with a gradual decline in physiological functions, including the regulation of blood glucose levels, uric acid metabolism, and cholesterol balance. As a result, older adults are more vulnerable to metabolic imbalance and chronic low-grade inflammation [2]. Recent studies have emphasized that aging-related chronic low-grade inflammation plays an important role in glucose dysregulation, dyslipidemia, and hyperuricemia, thereby increasing cardiometabolic risk in elderly populations [3]. In addition, chronic inflammation and endothelial dysfunction have been shown to contribute simultaneously to impaired glucose regulation, lipid metabolism, and uric acid homeostasis [4-5]

To date, the management of metabolic disorders still relies mainly on long-term pharmacological treatment. Although these therapies are effective in controlling metabolic parameters, long-term use may cause side effects and does not necessarily improve tissue function that has declined due to aging. Therefore, alternative or supportive approaches are needed that not only control metabolic levels but also address inflammation and tissue dysfunction [6].

One approach that has gained increasing attention is the use of Platelet-Rich Plasma (PRP), which is a blood-derived product with platelet concentrations approximately 2–12 times higher than normal blood levels. Platelets in PRP contain various growth factors, including Platelet-Derived Growth Factor (PDGF), Transforming Growth Factor-β (TGF-β), Vascular Endothelial Growth Factor (VEGF), Epidermal Growth Factor (EGF), and Insulin-like Growth Factor (IGF-1 and IGF-2). These growth factors play important roles in tissue repair, angiogenesis, and regulation of inflammatory processes [7]. Beyond tissue regeneration, PRP-derived growth factors have been reported to influence insulin signaling, endothelial function, and inflammatory modulation, which are key mechanisms involved in glucose and lipid metabolism [3], [8]

Experimental studies have shown that PRP administration may reduce blood glucose levels by enhancing pancreatic β-cell regeneration, improving insulin sensitivity, and reducing oxidative stress [9-10]. PRP has also been reported to help maintain glucose balance by regulating hepatic glycogen metabolism and increasing glucose transporter activity (GLUT2 and GLUT4) [11-12]. In addition, several studies suggest that PRP may influence lipid metabolism and uric acid–related inflammatory pathways, indicating potential systemic metabolic effects [13-14].

Most previous PRP studies have used direct injection into tissues such as muscles, skin, or joints, focusing mainly on local therapeutic effects. The use of PRP through inhalation or nebulization is still limited and considered experimental. This delivery method is of interest because the lungs have a large surface area and high vascularization, which may allow active substances in PRP to be absorbed rapidly and distributed systemically without invasive procedures [15].

However, clinical evidence regarding the effects of PRP nebulization on metabolic parameters such as blood glucose, uric acid, and cholesterol levels is still very limited. To date, most available studies focus on local PRP administration, while the systemic metabolic effects of PRP delivered via the pulmonary route remain largely unexplored [16-17].

Furthermore, it is still unclear whether PRP-derived growth factors administered by nebulization reach the systemic circulation in sufficient concentrations to produce biological effects [18]. Evidence regarding the safety of PRP administration via inhalation is also limited. Existing reports are mostly based on preliminary studies, experimental models, or small case observations. Therefore, further

investigation is required to evaluate the feasibility and short-term safety of PRP nebulization in adult subjects [17].

This lack of clinical evidence highlights an important knowledge gap regarding the feasibility, safety, and early metabolic effects of PRP delivered via nebulization. Therefore, this study aimed to evaluate the effects of acute exposure to allogeneic PRP nebulization on random blood glucose, uric acid, and total cholesterol levels in adult subjects. This study was designed as a preliminary clinical investigation to provide early evidence on the potential systemic metabolic effects of PRP administered through a non-invasive pulmonary route [19-20]. To the best of our knowledge, no previous clinical studies have evaluated the systemic metabolic effects of allogeneic PRP administered via nebulization in adult or elderly populations.

2. Methods

2.1. Research Design and Location

The study used a preliminary (pilot) clinical study design with a one-group pre–post test model without a control group. This design was applied to assess changes in random blood glucose, uric acid, and total cholesterol levels before and after the administration of allogeneic PRP nebulization. Each subject participated in the study for approximately twelve days, consisting of baseline assessment on day 0 (D0), nebulization intervention for five consecutive days (D1–D5), post-intervention evaluation on day 6 or 7 (D6/D7), and an optional safety follow-up on day 12 (D12). The study was conducted in a licensed clinic or health facility equipped with a dedicated nebulization room and a PRP processing laboratory that complied with biosafety standards and good clinical practice (GCP) principles

2.2. Research Population and Sample

The study population consisted of clinically stable adults aged 18–70 years who were able to provide written informed consent. Inclusion criteria were age between 18 and 70 years, stable general condition without acute infection, and willingness to participate in all stages of the study. Exclusion criteria included a history of severe allergy to blood products, previous severe transfusion reactions, uncontrolled pulmonary diseases such as acute asthma exacerbation or severe chronic obstructive pulmonary disease, pregnancy or breastfeeding, severe immunosuppression, active malignancy, active tuberculosis, active wounds or ulcers of the respiratory tract, and hemoptysis. Any additional condition assessed by the attending physician that could potentially compromise subject safety was also considered a reason for exclusion.

During the intervention, subjects were withdrawn if oxygen saturation decreased below 94%, bronchospasm occurred, hypersensitivity reactions developed, or post-procedural fever suspected to be related to PRP administration appeared. The planned sample size for this pilot study was 30 subjects, in accordance with preliminary feasibility objectives rather than hypothesis testing.

A total of 30 subjects were enrolled at baseline. However, only 14 subjects completed all intervention sessions and post-intervention evaluations and were included in the final per-protocol analysis. The remaining 16 subjects were excluded primarily due to non-compliance with the nebulization schedule**.** This relatively high attrition rate is acknowledged as a limitation inherent to the pilot nature of the study and the absence of a control group, which restricts causal inference.

2.3. PRP Preparation and Production

The PRP used in this study was sterile allogeneic PRP prepared by a licensed clinical laboratory in accordance with standardized laboratory protocols and biosafety regulations. PRP was obtained from healthy donors who underwent routine screening for blood-borne infectious diseases, including HIV,

hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV), and syphilis. Only donors with negative screening results were included in the PRP production process.

PRP preparation was performed aseptically using plasma separation techniques following internal laboratory procedures. The final PRP volume ranged from 2 to 4 mL per session and did not undergo chemical activation or preservative addition to maintain biological integrity. Each PRP batch was packaged in a sealed sterile container, labeled with batch identification, and visually inspected to ensure absence of hemolysis or contamination. PRP was used on the same day as preparation. All PRP production, handling, storage, and documentation processes were conducted by trained laboratory personnel under investigator supervision, with complete traceability records maintained

2.4. Intervention Procedure (PRP Nebulization)

Each subject received five consecutive daily sessions of allogeneic PRP nebulization (D1–D5). In each session, 3 mL of PRP was mixed with 1 mL of 0.9% NaCl solution and administered using a jet or closed mesh nebulizer for approximately 10–20 minutes until the solution was fully nebulized.

Prior to each session, vital signs including heart rate, respiratory rate, blood pressure, and oxygen saturation (SpO_2) were measured. Subjects were positioned sitting upright in a well-ventilated room. Continuous monitoring was conducted during nebulization to detect early symptoms such as coughing, dyspnea, chest discomfort, or dizziness. Following each session, subjects were observed for at least 30 minutes, and all findings were documented. The procedure was immediately discontinued if SpO_2 dropped below 94%, bronchospasm occurred, or acute hypersensitivity reactions developed. Subjects were instructed on post-procedure warning signs, including shortness of breath, fever, or allergic symptoms, and were required to return the following day for the next session.

2.5. Data Collection and Examination

Laboratory assessments were performed twice: at baseline (D0) and after completion of the intervention (D5). Primary outcome parameters included random blood glucose, uric acid, and total cholesterol levels. Random blood glucose measurements were obtained using the same sampling method and analytical technique at both time points to ensure consistency. Uric acid and total cholesterol were analyzed using enzymatic colorimetric assays.

Secondary outcomes included safety parameters and metabolic-related subjective complaints. Safety was assessed by monitoring adverse events (AEs) and serious adverse events (SAEs), such as bronchospasm, fever, or allergic reactions. Subjective complaints, including fatigue, gout-related joint pain, and dizziness, were assessed using a 0–10 Likert scale. Intervention adherence was calculated as the percentage of completed nebulization sessions for each participant. All data were recorded in standardized Case Report Forms (CRFs).

2.6. Confounding Factor Control

Pre- and post-intervention values for random blood glucose, uric acid, and total cholesterol were compared within subjects. Data normality was assessed using the Shapiro–Wilk test. As the data were not normally distributed, the Wilcoxon signed-rank test was applied. Results are presented as medians and interquartile ranges (IQRs) with a significance level set at $p < 0.05$. Primary analyses were conducted using a per-protocol approach, while sensitivity analyses using an intention-to-treat framework with simple imputation for missed sessions were performed to assess robustness. Safety outcomes were summarized descriptively based on incidence, severity, and relationship to the intervention, referencing adapted CTCAE criteria.

2.7. Data Analysis

Data analysis was performed by comparing pre- and post-intervention examination results for each key parameter, namely random blood glucose, uric acid, and total cholesterol. Data normality was

tested using the Shapiro–Wilk test. Results indicated that the data were not normally distributed, so analysis was continued using the Wilcoxon signed-rank test. Results are presented as medians and interquartile ranges (IQRs), with 95% confidence intervals. Additional analyses were conducted using a per-protocol and intention-to-treat approach using simple imputation for missed sessions. Safety aspects were analyzed based on the incidence of adverse events (AEs) and serious adverse events (SAEs), the severity of the events, and the relationship to the intervention, referring to the clinically adapted CTCAE criteria.

3. Results and Discussion

Table 1 shows a decrease in random blood glucose levels in almost all respondents after PRP nebulization. Most respondents shifted toward the normal random blood glucose category following the intervention, indicating an overall improvement in glycemic control.

Table 1. Frequency Distribution of Random Blood Glucose Levels Before and After PRP Nebulization (N= 14)

Category	Previous Frequency	% Before	Frequency After	% After
Normal (<140 mg/dL)	10	71.4%	13	92.8%
Impaired Glucose Tolerance (IGT) (140–199 mg/dL)	1	7.2%	0	0.0%
High (≥200 mg/dL)	3	21.4%	1	7.2%
Total	14	100%	14	100%

This study shows that allogeneic PRP nebulization has a significant effect on reducing random blood glucose. The median random blood glucose decreased from 125.50 mg/dL before intervention to 111.00 mg/dL after intervention ($p = 0.046$). In addition, the proportion of respondents with normal random blood glucose increased from 71.4% to 92.8%, while the categories of impaired glucose tolerance and high glucose levels decreased. These findings indicate improved glucose homeostasis and reduced inter-individual variability after intervention, suggesting better metabolic stability among participants.

These results are in line with research conducted by El Tahawy et al., which showed that PRP administration in diabetic rats significantly lowered blood glucose levels and improved pancreatic structure. PRP has been shown to stimulate pancreatic beta cell regeneration and increase the number of Langerhans islets, which play a role in insulin production. The growth factors in PRP, such as PDGF, IGF-1, and TGF-β, are thought to accelerate pancreatic tissue repair and increase insulin sensitivity, thereby lowering blood glucose levels more effectively [12].

The decrease in random blood glucose in this study is noteworthy because PRP was administered via a non-invasive nebulization route and over a short duration, indicating that PRP exerts systemic metabolic effects beyond local tissue regeneration. PRP contains bioactive growth factors including PDGF, IGF-1, TGF-β, and VEGF, which play important roles in modulating glucose metabolism, insulin sensitivity, and vascular endothelial function [18], [21].

The observed decrease in random blood glucose levels is consistent with experimental studies reporting that PRP can lower blood glucose levels and oxidative stress in diabetic animal models. The proposed mechanism involves increased IGF-1 levels and decreased TNF-α expression, which

suppress inflammation and improve cellular energy metabolism. PRP has also been reported to improve vascular endothelial function, thereby enhancing glucose delivery to peripheral tissues. These systemic mechanisms may explain the observed glucose-lowering effect of PRP even when administered through inhalation [22].

In addition to its anti-inflammatory effects, PRP has been reported to directly influence insulin signaling pathways. Both autologous and allogeneic PRP can accelerate tissue repair and improve metabolic regulation in diabetic conditions through the release of PDGF, TGF-β, IGF, VEGF, and FGF. These growth factors contribute to improved insulin sensitivity and reduced peripheral insulin resistance. The use of allogeneic PRP is particularly advantageous, as it does not depend on the patient's platelet quality, making it more applicable in individuals with chronic metabolic disorders [23]. This mechanism is consistent with the increased proportion of respondents with normal random blood glucose levels observed in this study.

PRP also contributes to improved glucose metabolism through enhanced vascular endothelial function and microcirculation. Recent studies report that PRP promotes angiogenesis and ameliorates endothelial dysfunction through VEGF and FGF signaling, resulting in more efficient glucose distribution to target tissues. Riskayanti et al. showed that PRP increased FGF-2 and type I collagen expression in diabetic tissues, supporting tissue regeneration and short-term metabolic stability [24]. These findings support growing evidence that PRP exerts systemic biological effects, particularly through growth factor–mediated metabolic modulation, while non-invasive delivery may reduce inflammatory reactions commonly associated with invasive PRP injections [25-26].

On the other hand, several studies suggest that PRP effects on glucose regulation are more pronounced with long-term administration or invasive delivery routes. Therefore, the effectiveness of PRP nebulization still requires further investigation [6]. Additionally, the pre–post design without a control group and the limited sample size restrict causal interpretation, and external factors such as diet and physical activity may have influenced changes in random blood glucose levels.

Nevertheless, the consistency of these findings with current experimental and clinical evidence suggests that allogeneic PRP nebulization has potential as a non-invasive adjunctive therapy for metabolic regulation. The practicality of allogeneic PRP, which is independent of patient platelet condition, further enhances its applicability in individuals with metabolic and chronic diseases [18], [21].Table 2 shows the distribution of uric acid levels before and after PRP nebulization in 14 respondents.

Table 2. Frequency Distribution of Uric Acid Levels Before and After PRP Nebulization (N= 14)

Category	Previous Frequency	% Before	Frequency After	% After
Low (<2.4 mg/dL)	1	7.2%	0	0.0%
Normal (2.4–6.0 mg/dL)	7	50.0%	8	57.2%
High (>6.0 mg/dL)	6	42.8%	6	42.8%
Total	14	100%	14	100%

Table 2 shows the distribution of uric acid levels before and after PRP nebulization in 14 respondents. After the intervention, the proportion of respondents with normal uric acid levels increased, while no participants remained in the low category. The median uric acid level decreased slightly from 5.80 mg/dL to 5.50 mg/dL ($\Delta = 0.30$ mg/dL; $p = 0.396$). Although the change was not statistically significant, the downward trend and narrowing of the interquartile range indicate a mild stabilizing effect on purine metabolism.

Previous studies have reported acute gout flare-ups following intra-articular PRP injections in patients with hyperuricemia, attributed to high local concentrations of platelet-derived proinflammatory mediators [27][28]. In contrast, PRP nebulization in this study did not trigger uric acid elevation or inflammatory symptoms, likely due to lower systemic concentrations and the non-invasive route of administration. The use of allogeneic PRP may also reduce immune-mediated platelet activation compared to autologous PRP, further minimizing inflammatory risk.[29-30].

Experimental evidence suggests that hyperuricemic PRP does not inhibit tissue regeneration but modulates inflammatory signaling, as shown by reduced IL-6 and IL-8 expression and increased collagen synthesis [14]. This mechanism may explain the absence of gout flares and the mild improvement observed in this study**.** Overall, acute exposure to allogeneic PRP nebulization appears metabolically safe with respect to uric acid regulation, providing stabilization without provoking inflammatory reactions commonly reported in invasive PRP therapies [31].

Table 3. Frequency Distribution of Total Cholesterol Levels Before and After PRP Nebulization (N= 14)

Category	Previous Frequency	% Before	Frequency After	% After
Normal (<200 mg/dL)	6	42.8%	6	42.8%
High threshold (200–239 mg/dL)	6	42.8%	7	50.0%
High (≥240 mg/dL)	2	14.4%	1	7.2%
Total	14	100%	14	100%

The median total cholesterol level decreased from 201.50 mg/dL to 198.50 mg/dL ($p = 0.279$). Although statistically insignificant, the reduction in the high cholesterol category suggests a mild stabilizing effect on lipid metabolism. Growth factors such as PDGF and TGF-β are known to improve endothelial integrity and reduce inflammation, which may indirectly support lipid homeostasis [32]. Previous studies have demonstrated that allogeneic PRP does not induce systemic inflammatory or metabolic disturbances, even after processing such as freeze-drying. Stable TGF-β1 activity suppresses proinflammatory cytokines and supports metabolic balance [33]. These mechanisms are consistent with the absence of cholesterol elevation or metabolic stress observed in this study.

Tables 4 and 5 demonstrate that all three metabolic parameters showed a downward trend after intervention, with a statistically significant reduction observed only in random blood glucose levels ($p = 0.046$)**.** Uric acid and total cholesterol levels showed non-significant decreases, indicating stabilization rather than corrective effects.

Table 4. Median Values and Interquartile Range (IQR)

Variable	Median Before (IQR)	Median After (IQR)	Δ (Changes)	Direction of Change
Blood Glucose Level (mg/dL)	125.50 (68.75)	111.00 (12.50)	□ 14.50	Reduced
Uric Acid (mg/dL)	5.80 (3.10)	5.50 (2.07)	□ 0.30	Mildly Decreased
Total Cholesterol (mg/dL)	201.50 (52.25)	198.50 (36.50)	□ 3.00	Reduced

Taken together, these findings suggest that short-term allogeneic PRP nebulization exerts selective systemic metabolic effects, with the strongest impact on glycemic regulation**,** accompanied by favorable safety and stabilization of uric acid and lipid parameters.

Table 5. Results of the Wilcoxon Signed Rank Test on Parameters of Random Blood Glucose, Uric Acid, and Total Cholesterol

Variable	Z	Asymp. Sig. (2-tailed)
Blood Glucose Level	-1.992	0.046
Uric Acid	-0.848	0.396
Total Cholesterol	-1.083	0.279

Based on the results of the Wilcoxon Signed Rank Test, the Z value for blood glucose levels was 1.992 with a significance value of 0.046 (<0.05), indicating a significant difference between before and after treatment. These results indicate that the treatment given was able to significantly reduce blood glucose levels. The Z value for uric acid levels was 0.848 with p = 0.396 and total cholesterol was 1.083 with p = 0.279, indicating that there was no significant difference between before and after treatment for both parameters. Although the direction of change indicated a decrease, the change was not strong enough to be considered statistically significant.

The results of the study show a decrease in the median value of the three parameters after treatment, namely blood glucose, uric acid, and total cholesterol. The median value of blood glucose decreased from 125.50 mg/dL to 111.00 mg/dL with a smaller difference between respondents, indicating more uniform results. This decrease was proven to be significant based on the Wilcoxon test with a p-value of 0.046, so it can be concluded that the treatment had a real effect on lowering blood glucose levels. The median uric acid level also decreased from 5.80 mg/dL to 5.50 mg/dL, while the Wilcoxon test results showed a p-value of 0.396, meaning that the change was not yet significant. The same was observed for total cholesterol, which decreased from 201.50 mg/dL to 198.50 mg/dL with a p-value of 0.279, indicating no significant difference. In general, the treatment administered was able to significantly reduce blood glucose levels, while changes in uric acid and total cholesterol levels did not show significant results.

Based on the results of the study, the total cholesterol levels of respondents showed a slight decrease after allogeneic PRP nebulization. The median total cholesterol level decreased from 201.50 mg/dL to 198.50 mg/dL, with a p-value of 0.279, indicating a statistically insignificant change. Although the decrease was not large, the direction of the change indicated an improvement in some respondents, where the proportion of those in the high cholesterol category decreased from 14.4% to 7.2%. The findings indicate that exposure to allogeneic PRP through inhalation can have a mild modulatory effect on lipid metabolism without causing adverse reactions. Growth factors such as PDGF and TGF-β in PRP are thought to help improve endothelial function and reduce inflammation, which may contribute to cholesterol stability.

4. Conclusion

The results of the study show that acute exposure to allogeneic PRP nebulization has a positive effect on the body's metabolic balance. Blood glucose levels experienced a statistically significant decrease, while uric acid and total cholesterol levels showed a slight decrease, although not significant. The downward trend in all three parameters indicates that the intervention tends to improve overall metabolic regulation. Growth factors such as PDGF, TGF-β, and IGF in PRP are thought to play a role in increasing insulin sensitivity, improving vascular endothelial function, and reducing inflammatory processes associated with metabolic dysfunction. No serious side effects were found during or after the intervention, indicating that allogeneic PRP nebulization is safe for short-term exposure. The results of the study provide preliminary indications that allogeneic PRP via inhalation

has potential as a non-invasive adjunctive therapy to help maintain metabolic balance, particularly in controlling blood glucose levels, with mild stabilizing effects on uric acid and cholesterol levels. Further studies with longer durations and larger sample sizes are needed to confirm long-term efficacy and safety. Future randomized controlled trials with larger sample sizes are required to confirm these preliminary findings.

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