

Assessing the Safety and Efficacy of PRP in the Management of Diabetic Foot Ulcers

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Abstract:

Background and Aim: Diabetic foot ulcers remain a critical concern worldwide, even with the progress achieved in diabetes management. Diabetic foot ulcers remain a critical global challenge, even with the progress achieved in diabetes management.

Material and Methods: This study, designed as a prospective comparative analysis, focused on patients suffering from diabetic foot ulcers who were admitted to the surgical department over the course of one year. In this study, participants were categorised into two distinct groups: Group A, which was treated with conventional ordinary dressing (n=40), and Group B, which received Platelet-Rich Plasma (PRP) dressing (n=40, %). The average duration of follow-up was 6 weeks.

Results: The findings from our study indicated that participants treated with PRP experienced a wound contraction rate of 22.50%, surpassing that of the group receiving conventional treatment alone. The findings were statistically significant, indicating that PRP may improve wound healing in diabetic wounds. The time needed for wound contraction in the case group was significantly shorter than that observed in the control group ($p < 0.05$).

Conclusion: The wounds of subjects receiving PRP dressing exhibited greater contraction compared to those in the non-treated group. This finding suggests that PRP dressing serves as an effective method to enhance wound contraction in diabetic patients and can be utilised alongside traditional treatment approaches for the healing of diabetic wounds.

Keywords: Diabetic foot ulcers, Dressing, Platelet-Rich Plasma, Wound Contraction.

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Introduction

The prevalence of diabetes mellitus, marked by ongoing high blood sugar levels and metabolic disturbances, has escalated to epidemic levels worldwide, placing a significant strain on healthcare systems. Recent epidemiological data reveal a concerning upward trend in diabetes prevalence, with forecasts indicating an additional rise in the years ahead. [1] The underlying issue may stem from either a deficiency in insulin secretion, a reduction in insulin action, or a combination of both factors. In 1921, researchers Banting, Best, and Macleod revealed that pancreatic extracts have the ability to reduce blood sugar levels.

Diabetic foot ulcers (DFU) represent a prevalent and concerning complication of diabetes, with the potential to lead to significant disability and, in severe cases, mortality. [2] The prevalence of diabetes-related morbidity and mortality continues to rise. The prevalence of diabetes and its

associated complications continues to escalate, with individuals diagnosed with diabetes facing a staggering 150-fold increased risk of lower extremity amputations compared to those without the condition. [3] Skin ulcers are characterized by the loss of tissue that encompasses both the epidermis and the dermis, with potential involvement of the adipose tissue and muscle fascia.

In addition to traditional methods for promoting wound healing, innovative strategies are gaining traction, including cellular therapies like platelet-rich plasma (PRP) and collagen-based dressings. This may serve as a complementary component within a structured, high-quality treatment strategy. [4,5] Platelets are known to release a variety of specific growth factors from their alpha granules, which are found in the thrombocyte cell membrane. These growth factors include platelet-derived growth factor (PDGF), epidermal growth factor

(EGF), platelet-derived angiogenesis factor, and platelet factor. [6] The local action of these factors significantly accelerates the healing process of the wound. Research has demonstrated that platelet extract can be effective in promoting the healing of chronic non-healing ulcers, showcasing promising outcomes in various studies. Given the financial constraints faced by many patients regarding commercially available recombinant platelet gel for dressing, trials have explored the use of platelet extract derived from the patients' own blood in the treatment of diabetic wounds.

A recent prospective study involving 80 patients with diabetic foot ulcers examined the efficacy of platelet-rich plasma (PRP). The findings indicated notable advancements in complete healing, a decrease in wound volume, and a reduction in the duration of the healing process. [7] A recent clinical study found that patients with non-healing diabetic foot ulcers experienced accelerated wound healing following the administration of PRP injections over a period of 7 weeks. [8] Exhibit demonstrates additional benefits, including antibacterial and analgesic properties, which play a significant role in enhancing the healing process of diabetic foot ulcers. [9-11] PRP contains a comprehensive array of growth factors essential for the healing process. It demonstrated two significant functions in the process of wound healing. Firstly, a fibrin gel creates a barrier that helps prevent bacterial contamination. Additionally, the growth factors activated the process of wound healing. This study aims to illustrate the potential therapeutic benefits of PRP in the treatment of diabetic foot ulcers. This study sought to evaluate the impacts and benefits of platelet-rich plasma (PRP) in treating diabetic foot ulcers.

Material and Methods

This study, designed as a prospective comparative analysis, focused on patients suffering from diabetic foot ulcers who were admitted to the surgical department over the course of one year. Individuals aged 40 to 65, regardless of gender, who are experiencing diabetic foot ulcers—encompassing both type 1 and type 2 diabetes mellitus—were included in this study. The participants had controlled blood sugar levels but were dealing with non-healing ulcers on their feet, with wound sizes measuring between 4 and 7 cm. Individuals with a history of recurrent ulcers at the same location, those who smoke, or who have recently undergone anticoagulant or immunosuppressive treatment were not included in the study.

A sample of 80 patients was conveniently included in the study. Following the acquisition of informed consent, patients were categorised into two groups: one receiving conventional dressing and the other,

the study group, treated with PRP. Data from their follow-up was gathered. Participants were randomly divided into two groups: Group A, which served as the experimental group with 40 individuals, and Group B, the control group, also consisting of 40 individuals. Over a span of 7 weeks, researchers examined two distinct groups. All patients underwent an ulcer examination, during which the characteristics of the wounds were assessed and documented through photography. The dimensions of the wound were evaluated by measuring the longest edges with a metre scale.

In both experimental groups, sufficient wound debridement was performed, and local infections were managed through the application of antiseptics and the use of systemic antibiotic therapy. In the conventional group, regular applications of normal saline dressing were performed.

During each dressing, freshly prepared PRP was injected, with approximately 2 ml administered about 3/4 cm from the wound margin using a 26 G insulin syringe. The dressing included a pad and roller bandage. The dressing was altered every four days in both groups. Before its application, PRP underwent screening for all standard blood-transmitted diseases to mitigate the risk of contamination with serious viral infections. Ulcers were assessed by measuring their length and width with metric tape. The results were assessed by comparing the extent of wound reduction observed in both groups.

Statistical Analysis: The collected data was organised and input into a spreadsheet application (Microsoft Excel 2019) before being exported to the data editor interface of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were characterised using means and standard deviations or medians and interquartile ranges, depending on their distribution patterns. Qualitative variables were reported in terms of counts and percentages. The confidence level for all tests was established at 95%, while the level of significance was set at 5%.

Results

A study was conducted involving eighty patients suffering from diabetic foot ulcers. The participants were organised into two distinct groups, each consisting of 40 individuals. One group was administered PRP, while the control group underwent conventional therapy as their treatment. A comparative analysis was conducted between the two groups to assess the percentage area of wound reduction. The study population comprised individuals aged 45 to 60 years, with a higher prevalence observed among females compared to males. Traumatic onset accounted for 66.25% of

the ulcers observed. The plantar aspect emerged as the most prevalent site, accounting for 65.00% of cases. A significant majority of the patients, 70%, were utilising insulin, while 30% were relying on oral hypoglycaemic agents. In our study, we found that participants who received PRP exhibited a wound contraction rate of 22.50%, surpassing the outcomes of those who underwent conventional treatment alone. The findings were statistically significant, indicating that PRP may improve

wound healing in diabetic wounds. The time needed for wound contraction in the case group was significantly shorter than that observed in the control group ($p < 0.05$). PRP dressing therapy has demonstrated greater effectiveness and safety in the treatment of diabetic foot ulcers, promoting wound healing. Therefore, it can be recommended as an adjunct to conventional treatment methods for these ulcers.

Table 1: Patients characteristics

Variable	Cases Number (%)	Control Number (%)
Age group (in years)		
<50	8 (20)	11 (27.5)
51-60	22 (55)	20 (50)
>60	10 (25)	9 (22.5)
Gender		
Male	18 (55)	21 (52.5)
Female	22 (45)	19 (47.5)
Onset		
Spontaneous	16 (40)	11 (27.5)
Traumatic	24 (60)	29 (72.5)
Site		
Dorsum	16 (40)	12 (30)
Plantar	24 (60)	28 (70)
DM treatment		
1	12 (30)	12 (30)
0	28 (70)	28 (70)

Table 2: Wound contraction

IA-FA=CA	Cases Number (%)	Control Number (%)
<5.0	0	1 (2.5)
5.1-15.0	8 (20)	34 (85)
15.1-25.0	31 (77.5)	0
>25	1 (2.5)	0
Total	40 (100)	40 (100)

Table 3: Wound contraction

% of the area of reduction	Cases Number (%)	Control Number (%)
<16	0	39 (97.5)
16.1-26.0	3 (7.5)	1 (2.5)
>26	37 (92.5)	0
Total	40 (100)	40 (100)

Discussion

In recent years, the spotlight has increasingly turned to emerging cellular therapies like PRP therapy, which are gaining traction for their promising applications in regenerative medicine. These therapies are being explored as therapeutic agents for various chronic conditions and may serve as valuable adjuncts in a comprehensive, quality treatment strategy.

The healing potential of PRP is attributed to the presence of platelets, which serve as a natural reservoir of numerous growth factors that play a crucial role in tissue regeneration⁴ PRP contains a comprehensive array of growth factors essential for

the healing process. It plays two crucial roles in the process of wound healing. Initially, gel fibrin establishes a protective barrier that helps to thwart bacterial contamination. Additionally, the growth factors derived from platelets play a crucial role in the wound healing process. Platelets play a crucial role in the secretion of biologically active proteins, which encompass growth factors like PDGF, transforming growth factor (TGF)- β , TGF- β 2, and EGF. The introduction of these growth factors into the wound may foster a more favourable environment for tissue repair, potentially speeding up the healing process following surgery. [12,13] The function of PRP as a localized dressing is to deliver essential growth factors directly to the

wound site. This role is proposed to be advantageous due to the deficiency of growth factors in DFUs. [14] A recent meta-analysis examining the application of PRP therapy in skin wounds revealed that, in comparison to standard wound care, PRP significantly enhanced the healing process, leading to notable improvements in small, difficult-to-treat acute and chronic ulcers. [15]

The current research indicates that the occurrence of diabetic foot ulcers is more prevalent among females compared to males. It is crucial to acknowledge that these differences may stem from our concentration on a particular demographic, rather than accurately representing the overall prevalence of diabetes or diabetic foot ulcers in a wider context. Diabetic foot ulcers predominantly occur in individuals during their fifth and sixth decades of life, with the sixth decade being the next most prevalent age group affected. A mere 27.5% of the patients fell under the age of 50 years. As patients age, the likelihood of developing a diabetic foot ulcer increases significantly. The incidence of diagnosed diabetes rises with advancing age, particularly concerning the diabetic foot. Saad et al conducted a study involving 24 patients suffering from chronic ulcers, aged between 40 and 60 years. Their findings indicated that both sex and age do not significantly correlate with the healing rates of these ulcers. [16] Although research presents differing average ages, our results align with existing literature indicating that diabetic foot ulcers predominantly impact individuals in their fifties or older. [10,12]

The findings indicate that 66.25% of the ulcers were of traumatic origin, with trauma identified as the secondary triggering factor related to neuropathy. One-third of the cases were found to be spontaneous in nature, resulting from either blister rupture or minor, often unnoticed, trauma. Other studies have reported similar findings. [16,17] A significant majority of patients, specifically 65.00%, presented with ulcers located on the plantar surface of the forefoot, while the remaining 35.00% exhibited ulcers on the dorsum of the foot. Research carried out by Edmonds and colleagues in 1986 revealed a higher incidence of foot ulcers located on the plantar and forefoot regions. [18]

Our research indicates that participants treated with PRP dressing experienced a wound contraction rate of 22.50%. The duration for achieving this contraction in the study group was observed to be between 4 to 5 weeks among 35 patients. The control group exhibited a duration of 6 to 7 weeks for a total of 35 patients. In a comparison with the group treated solely with conventional dressing (normal saline dressing), which exhibited a mean wound contraction of 12.50%, the results were

statistically significant. This indicates that PRP dressing may play a beneficial role in enhancing wound healing for diabetic wounds.

Following the second week, our research indicated that PRP demonstrated greater efficacy compared to traditional dressing methods. The phenomenon can be attributed to the activation of platelets by collagen, which are subsequently released into the bloodstream as a response to endothelial injury during the process of wound healing. Following aggregation, platelets generated intercellular mediators and cytokines from their cytoplasmic pool and subsequently released the contents of their granules. Over 800 unique proteins have been emitted into the environment, exerting a paracrine effect on a range of cells. For a minimum of seven more days, platelets persisted in releasing further cytokines and growth factors derived from their mRNA reserves. Gui-Qiu and colleagues recruited 21 participants suffering from refractory diabetic lower limb ulcers, all of whom had not responded to conventional treatments, and administered homologous PRP to them. [19] The research revealed that homologous PRP significantly enhanced and expedited the healing process in diabetic lower limb wounds. Several studies have reported differing results concerning the effectiveness of PRP in treating non-healing diabetic foot ulcers. Abdel hafez and colleagues documented a remarkable 96% success rate in attaining complete healing through the use of PRP injections for diabetic foot ulcers. [20] In a related study, Salem and colleagues reported an impressive success rate of 97.6% in achieving complete healing through the use of PRP injections for diabetic foot ulcers. [21] The study presents certain limitations, notably a small sample size. Cost-effective wound care solutions are crucial, highlighting the need for thorough research and standardised methodologies in economic evaluations.

Conclusion

The wounds in subjects treated with PRP dressing contracted more than the wounds in the non-treated group, which indicates PRP dressing is an effective modality to facilitate wound contraction in patients who have diabetes and can be used as an adjunct to the conventional mode of treatment for healing of diabetic wounds. Future research should aim to further validate these findings through larger, standardized studies, enhancing PRP's clinical application and efficacy in diabetic wound care.

References

1. Abouzid MR, Ali K, Elkhawas I, Elshafei SM: An overview of diabetes mellitus in Egypt and the significance of integrating preventive cardiology in diabetes management. *Cureus*. 2022, 14:e27066.

2. Buitinga M, Cohrs CM, Eter WA, Claessens-Joosten L, Frielink C, Bos D, et al. Standards of care in diabetes – 2023. *J Clin Appl Res Educ* 2020; 69(11):2246–52.
3. Pickwell K, Siersma V, Kars M, Apelqvist J, Bakker K, Edmonds M, et al. Predictors of lower-extremity amputation in patients with an infected diabetic foot ulcer. *Diabetes Care*. 2015; 38(5):852-7.
4. Sebastian KMS, Lobato I, Hernandez I, BurgosAlonso N, Gomez-Fernandez MC, López JL, et al. Efficacy and safety of autologous platelet rich plasma for the treatment of vascular ulcers in primary care: phase III study. *BMC FAM Pract*. 2014; 15:211.
5. Suthar M, Gupta S, Bukhari S, Ponemone V. Treatment of chronic non-healing ulcers using autologous platelet rich plasma: a case series. *J Biomed Sci*. 2017; 24(1):1-0.
6. Pavlovic V, Ciric M, Jovanovic V, Stojanovic P. Platelet Rich Plasma: a short overview of certain bioactive components. *Open Med (Wars)*. 2016; 11(1):242-7.
7. Dasari N, Jiang A, Skochdopole A, Chung J, Reece EM, Vorstenbosch J, et al. Updates in diabetic wound healing, inflammation, and scarring. *Semin Plast Surg* 2021; 35(3):153–8.
8. Tran TD-X, Le PT-B, Van Pham P. Diabetic foot ulcer treatment by activated platelet rich plasma: a clinical study. *Biomed Res Ther* 2014; 1(2):37–42.
9. Cieslik-Bielecka A, Bold T, Zio»kowski G, Piercha»a M, Krolikowska A, Reichert P. Antibacterial activity of leukocyte- and platelet-rich plasma: an in vitro study. *Biomed Res Int* 2018; 2018:9471723.
10. Smith OJ, Wicaksana A, Davidson D, Spratt D, Mosahebi A. An evaluation of the bacteriostatic effect of platelet-rich plasma.pdf. *Int Wound J* 2021; 18:448–56.
11. Lai C, Li T, Hei K, Lam S, Chou Y. The long-term analgesic effectiveness of plateletrich plasma injection for carpal tunnel syndrome: a cross-sectional cohort study. *Pain Med*. 2022; 23(7):1249–58.
12. Mastrogiacomo M, Nardini M, Collina MC, Di Campli C, Filaci G, Cancedda R, Odorisio T: Innovative cell and platelet rich plasma therapies for diabetic foot ulcer treatment: the allogeneic approach. *Front Bioeng Biotechnol*. 2022, 10:869408. 10.3389/fbioe.2022.869408
13. He M, Chen T, Lv Y, et al.: The role of allogeneic platelet-rich plasma in patients with diabetic foot ulcer: current perspectives and future challenges. *Front Bioeng Biotechnol*. 2022, 10:993436. 10.3389/fbioe.2022.993436
14. Russo S, Landi S: Cost-Effectiveness Analysis for the Treatment of Diabetic Foot Ulcer in France: PRP vs Standard of Care. Department of Management, Università Ca'Foscari Venezia, Venice; 2020. 10.2139/ssrn.3681369
15. Meznerics FA, Fehérvári P, Dembrowszky F, et al.: Platelet-rich plasma in chronic wound management: a systematic review and meta-analysis of randomized clinical trials. *J Clin Med*. 2022, 11:7532. 10.3390/jcm11247532
16. Saad H, Elshahat A, Elsherbiny K, Massoud K, Safe I. Platelet-rich plasma versus platelet-poor plasma in the management of chronic diabetic foot ulcers: a comparative study. *Int Wound J*. 2011; 8(3):307-12.
17. Alsousou J, Thompson M, Hulley P, Noble A, Willett K. The biology of platelet-rich plasma and its application in trauma and orthopaedic surgery: a review of the literature. *J Bone Joint Surg Br*. 2009; 91(8):987-96.
18. Edmonds ME, Blundell MP, Morris ME, Thomas EM, Cotton LT, Watkins PJ. Improved survival of the diabetic foot: the role of a specialised foot clinic. *Q J Med*. 1986; 60(2):763-71.
19. Gui-Qiu S, Zhang B, Jing M, Yan-Hui L, Da-Ming Z, Jin-Lang Q, et al. Evaluation of the effects of
20. Abdelhafez AA, Ragab A, Younes HE, Nasser M, Khereba W: Effects of intra-lesional injection of platelet rich plasma (PRP) on healing of diabetic foot ulcers. *Int Inven J Med Medical Sci*. 2016, 3:136-42.
21. Salem A, Tawfik AM: Role of platelet rich plasma in treatment of diabetic foot ulcers. *Surg Sci*. 2016, 7(6):272. 10.4236/ss.2016.76038.