

Efficacy and Safety of PRP in the Treatment of Diabetic Foot Ulcers**Pranav Rambhai Patel¹, Khyati Shah², Mehul Kumar K Vasaiya³, Kunal Chinubhai Modi⁴**¹Associate Professor, Department of General Surgery, GMERS Medical College and Hospital, Gandhinagar, Gujarat^{2,3}Assistant Professor, Department of General Surgery, GMERS Medical College, Himmatnagar, Gujarat⁴Associate Professor, Department of General Surgery, GMERS Medical College, Himmatnagar, Gujarat

Received: 25-07-2023 / Revised: 28-08-2023 / Accepted: 30-09-2023

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Conflict of interest: Nil

Abstract:**Background and Aim:** Autologous platelet-rich plasma (PRP) has been shown to improve wound healing. However, clinical evidence for its treatment in diabetic ulcer patients is inconclusive. The study sought to ascertain the effects and benefits of PRP in the treatment of diabetic foot ulcers.**Material and Methods:** This prospective comparative study was carried out in patients with diabetic foot ulcers admitted to the tertiary care department of surgery in India for a period of one year. The study covered 60 patients in total. Case A (experimental group, n=30) and Case B (control group, n=30) were allocated at random. To avoid contamination with deadly viral infections, PRP was checked for all normal blood transmitted diseases before usage. The length and width of the ulcers were measured with a metric tape. The difference in wound decrease between the two groups was measured.**Results:** Patients ranged in age from 45 to 60 years old, with males being more impacted than females. Furthermore, when compared to the traditional dressing group, the PRP group required less time for wound contraction. PRP was proven to be more effective in wound healing, with less problems, infection, exudates, and discomfort.**Conclusion:** DFUs have a negative impact on the quality of life of diabetic patients. The wounds in the PRP-treated subjects contracted more than the wounds in the non-treated group, indicating that PRP dressing is an effective modality for facilitating wound contraction in diabetic patients and can be used as an adjunct to the conventional mode of treatment (conventional dressings and debridement) for diabetic wound healing.**Keywords:** Debridement, Diabetic Ulcer, Platelet-rich Plasma, Wound Reduction.

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Introduction

Diabetic foot ulcer is a serious complication of diabetes mellitus and the most common component of the diabetic foot. This medical issue affects 15% of all diabetes mellitus patients. According to a recent study, diabetic foot ulcers account for up to 88% of all lower leg amputations.[1] More crucially, the number of diabetic patients is expected to rise to 439 million by 2030. Diabetic neuropathy and peripheral vascular disease are the two most common causes of diabetic foot ulcers (DFUs).[2] The most problematic aspect of DFUs is prolonged non-healing. The primary cause is an imbalance between metalloproteinases (MMPs) and MMP inhibitors.[3] When combined with ischemia and vascular disease, this condition is elevated to serious. Ischemia and vascular damage limited the amount of oxygen and nutrients available to the wound. Although standard ulcer treatments such as revascularization, debridement, antibiotic use, offloading of the affected legs, and intensive blood

glucose management have been well applied in patients with diabetic ulcers, a significant number of patients with diabetic ulcers would eventually undergo lower extremity amputation despite these treatments.[4,5] The paucity of wound healing-related growth factors in diabetic ulcer patients, such as vascular endothelial growth factor (VEGF) and platelet-derived growth factor (PDGF), has been attributed to the unsatisfactory efficacy of these conventional treatments.[6] Platelet-rich plasma (PRP) has been proposed to have higher efficacy for wound healing than traditional therapies with the advancement of regenerative medicine. PRP is a product derived from fresh whole blood that contains a high concentration of platelets, which can release a variety of highly concentrated growth factors such as PDGF, TGF- β , VEGF, EGF, fibrinogen, osteocalcin, and insulin-like growth factor (IGF). It is worth noting that these factors are required for the regulation of

critical cellular processes involved in wound healing, such as cell proliferation, chemoattractant, and cell metabolism.[7]

Because not all patients can afford commercially available recombinant platelet gel for wound dressing, platelet extract from patients' blood was employed in diabetic wound trials. The trinity of neuropathy, ischemia, and infections is usually regarded as the most critical in the pathogenesis of diabetic foot. The absence or dysfunction of some growth factors disrupted the natural healing process. PRP contains nearly all of the growth factors required for healing. It played two critical roles in wound healing. For starters, fibrin gel creates a barrier to prevent bacterial infection. Second, growth factors induced wound healing. As a result, the purpose of this study is to demonstrate the therapeutic impact of PRP in the healing of diabetic foot ulcers.

The study sought to ascertain the effects and benefits of PRP in the treatment of diabetic foot ulcers.

Material and Methods

This prospective comparative study was carried out in patients with diabetic foot ulcers admitted to the tertiary care department of surgery in India for a period of one year.

Inclusion Criteria

Patients between the ages of 40 and 65, both sexes, presenting with diabetic ulcer foot; type 1 and type 2 diabetes mellitus; patients with controlled blood sugar and non-healing ulcers in their foot, wound size ranging from 4 to 7 cm, were included. For the study, patients provided informed consent. Patients with haemoglobin levels greater than 10 gm, platelet counts greater than 2 lakhs, and an ankle-brachial index greater than 0.7 were also included.

Exclusion Criteria

Patients with severe heart illness, hepatitis, HIV, critically sick patients; patients with known or suspected osteomyelitis; and patients who had previously undergone conventional skin grafting with an ulcer less than 2 cm in size were excluded from the trial. The study covered 60 patients in total. Following the receipt of sufficient informed consent, patients were separated into two groups: one treated with traditional dressing and the other with PRP. Their follow-up information was gathered. Case A (experimental group, n=30) and Case B (control group, n=30) were allocated at random. For six weeks, two groups were studied. All of these patients had an ulcer examination, and the site was evaluated and documented. The wound's size was determined by extending a metre scale from the wound's longest measurements.

Conventional dressing

In the experimental groups, appropriate wound debridement was performed, and local infection was controlled with the use of local antiseptics and systemic antibiotic therapy. Normal saline dressing was used on a regular basis in the conventional group.

PRP dressing

Freshly made PRP was injected during each dressing; approximately 2 ml of PRP was administered in approximately 3/4th cm from the wound margin using an insulin syringe (26 G), and dressing was done with a pad and roller bandage. In both groups, the dressing was changed every fourth day. To avoid contamination with deadly viral infections, PRP was checked for all normal blood transmitted diseases before usage. The length and width of the ulcers were measured with a metric tape. The difference in wound decrease between the two groups was measured.

Statistical Analysis

The collected data was assembled and input into a spreadsheet programme (Microsoft Excel 2007) before being exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). The confidence level and level of significance for all tests were set at 95% and 5%, respectively.

Results

Sixty diabetic foot ulcer patients were investigated. They were split into two groups of 30. The experimental group received PRP, while the control group received conventional therapy. A comparison study was conducted between both groups in terms of % area wound reduction. Patients ranged in age from 45 to 60 years old, with males being more impacted than females. The onset of 56.06% of the ulcers was distressing. The most prevalent place was plantar aspect. In comparison to oral hypoglycemic medications, insulin was used by the majority of the patients. All participants in the study had their affected foot X-rayed; individuals with stress fractures and osteomyelitis were eliminated.

Our study indicated that participants who received PRP had better wound contraction than those who only received conventional treatment, where the mean wound contraction was; these differences were found to be statistically significant, implying that PRP improved wound healing in diabetic wounds. The time necessary for wound contraction in the case group was significantly shorter than in the control group (p0.001). Thus, PRP dressing therapy in the treatment of diabetic foot ulcers was proven to be more effective, safe, and a promoter

of wound healing, and can thus be recommended as an adjuvant to standard treatment.

Table 1: Demographic Distribution of study Participants

Variables	Case, N (%)	Control, N (%)
Age group (in years)		
<50	5 (16.6)	9 (30)
51-60	17 (56.6)	14 (46.6)
>60	8 (26.6)	7 (23.3)
Gender		
Male	17 (56.6)	19 (63.3)
Female	13 (43.3)	11 (36.6)

Table 2: Wound culture sensitivity

Wound c/s	Case, N (%)	Control, N (%)	P value
EC	1 (3.33)	1 (3.33)	0.23
NOGC	16 (53.3)	21 (70)	
PA	3 (10)	1	
PM	3	3	
SA	7	4	
Total	30	30	

Statistically significance at $p < 0.05$

Table 3: Wound contraction

IA-FA=CA	Case, N (%)	Control, N (%)	P value
<5.0	0	1 (3.33)	0.23
5.1-15.0	6 (20)	29 (96.6)	
15.1-25.0	22 (73.3)	0	
>25	2 (6.6)	0	
Total	30	30	

Discussion

DFUs are the outcome of a failed healing process in diabetes people. The absence or dysfunction of some growth factors disrupted the natural healing process. PRP and PPP delivered nearly all of the growth factor required for healing. In reality, all patients went to have their DFUs totally healed. Platelet-rich plasma (PRP) is plasma that has been enhanced with platelets. When calcium is activated, fibrin is produced, and platelets release growth factors. PRP had two essential roles in wound healing in this example. First, gel fibrin formed a barrier to prevent bacteria from entering the wound bed. Second, when treated with PRP, platelet growth factors activated wound healing and balanced the wound.[8] Males were shown to have a higher incidence of diabetic foot ulcers than females in the current study. Diabetic foot ulcers were most common in the fifth and sixth decades, with the seventh decade being the least common. While only 16% of the patients were beyond the age of 50. The likelihood of developing a diabetic foot ulcer increases with age. The proportion of confirmed diabetes rose with age; however, Saad et al conducted a study on 24 patients with chronic ulcers ranging in age from 40 to 60 years and reported that gender and age are negligible in connection to the rate of healing of their ulcers.[9]

PRP contains a variety of growth factors that have the ability to induce tissue regeneration and repair. PRP triggered by thrombin may release wound healing growth factors such as TGF, PDGF, IGF, VEGF, and EGF.[9-11] These growth factors are essential for cell creation, proliferation, and differentiation, as well as for increasing collagen synthesis and activating macrophages and other growth factors. The increased concentration of these growth factors in PRP can considerably boost fibroblast proliferation and type I collagen expression. Furthermore, PRP has been shown to increase granulation, angiogenesis, cell proliferation, and re-epithelialization in vivo. Furthermore, PRP may have certain additional characteristics that make it acceptable for clinical application, such as being low-cost and minimally intrusive.[12-14] More than half of the patients had an ulcer on the forefoot's plantar surface, with the remainder having an ulcer on the foot's dorsum. Edmonds et al.'s 1986 study found that plantar and forefoot ulcers were more common.15 They can be avoided by wearing appropriately sized footwear. However, in the current investigation, ulcers on the plantar part of the foot were not as common as Edmonds et al. predicted. The majority of the patients were on insulin for sugar control, with only 40.00% on oral hypoglycemic medications. In contrast, Prabhu et al 2018 discovered that more patients (66.6%) used oral hypoglycemic medicine

and fewer patients (33.3%) used insulin in their study.[16] In our study, PRP was found to be more effective than standard dressing after the second week. This could be explained by the fact that platelets are activated by collagen and released into the blood after endothelial damage occurs during wound healing. Following aggregation, platelets created intercellular mediators and cytokines from the cytoplasmic pool and discharged their granule content. More than 800 different proteins were released into the environment, each with a paracrine effect on different cells. Platelets secreted more cytokines and growth factors from their mRNA reserves for at least another 7 days.[17] When Martinez-Zapata et al employed PRP to treat wounds, the percentage of overall healing increased when compared to controls.[18]

The study's limitation was that large samples from multicenter trials may yield more reliable results.

Conclusion

DFUs seriously affected to life quality of diabetic mellitus patients. 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 (conventional dressings and debridement) for healing of diabetic wounds. PRP showed faster and better healing rates among the study group. In addition, ulcer area reduction and percentage reduction of ulcer size were better in the PRP group. More studies that report the safety outcomes and quality of life of patients with diabetic ulcers receiving PRP therapy should be conducted.

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