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Role of Autologous Platelet Rich Plasma in Timely Healing of Chronic Diabetic Foot Ulcer

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ABSTRACT

Objective: To evaluate the efficacy of platelet-rich plasma in treating chronic non-healing diabetic foot ulcers, in comparison to conventional dressings.

Study Design: Quasi-experimental study.

Place and Duration of Study: General Surgery Department of Combined Military Hospital Rawalpindi, Pakistan from Jun-Dec 2023.

Methodology: A comparative study was conducted on patients with persistent non-healing diabetic foot ulcers. The study participants were split up into two groups. In Group-A, platelet-rich plasma was injected into the ulcer's base and the wound's borders. In Group-B, the ulcer was treated with saline-soaked moist dressings. Every patient underwent two months of follow-up, with planned follow-up visits on 7th, 14th, 30th, 45th, and 60th days. Autologous PRP's effectiveness in treating chronic diabetic foot ulcers was compared with conventional dressings.

Results: Mean age of 120 patients was 55.98±9.71 years. 108(90%) were males and 12(10%) were females. At the end of two months, 53(88.8%) patients from Group-A showed a significant reduction in wound grade as compared to 28(46%) patients from Group-B (p=<0.001). Furthermore, 48(80%) patients from Group-A experienced complete wound healing after 02 months as compared to 14(23.3%%) patients from Group-B (p=<0.001)

Conclusion: Treating chronic non-healing diabetic foot ulcers with Autologous Platelet-Rich Plasma is associated with better and expedited wound healing.

Keywords: Diabetic foot ulcers, Platelet-rich plasma, Wound healing

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INTRODUCTION

Diabetes Mellitus is a serious metabolic disorder characterized by elevated blood glucose levels.[1] It is a chronic disease, and its long-term presence results in various health-related disorders, including nephropathy, retinopathy, neuropathy, dermopathy, and angiopathy.[2] Because of the persistent nature of the disease and the multiple associated dreadful complications, it is a source of great economic burden on affected individuals and families and also on our health care systems.[3] As per the global data, in 2021 Diabetes Mellitus affected 10.5% of the world's population.[4] The most common complication of Diabetes Mellitus encountered by surgeons in the Outpatient Departments (OPDs) and Emergency settings is Diabetic Foot Ulcer (DFU). 19%-34% of all diabetic patients have a lifetime risk of developing diabetic foot ulcers.[5] Angiopathy, neuropathy, arthropathy, and increased vulnerability to develop infections due to chronic hyperglycemic state play an important role in the development of chronic non-healing foot ulcers in these patients.[6] Significant risk factors for DFUs and associated sequelae comprise advanced age, male gender, smoking, increased BMI, and elevated glycated hemoglobin.[7] If left untreated, these DFUs can result in infection, gangrene, sepsis, multiorgan failure, and even death.[8] The risk of lower extremity amputations associated with DFUs is high, and it significantly adds up to the socioeconomic burden of the patients and their families.

Various grading systems have been designed to assess the severity of DFUs. The Wegner classification system is a crucial tool to grade the DFU, and helps the clinicians to develop a management plan for specific grade.[9] Grade I and Grade II of the Wegner classification indicate the presence of superficial and deep ulcers, respectively, and surgeons have been treating them with conventional bandages done with saline-soaked surgical gauze. Nevertheless, the process of wound healing with this traditional approach is usually slow, and patients may land up in developing several complications over time. It has encouraged surgeons to study and evaluate modern techniques to promote the early healing of DFUs and deliver better clinical outcomes. This search for better

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treatment options for chronic non-healing DFUs has led researchers to study and evaluate the use of autologous Platelet-Rich Plasma (PRP) to promote wound healing.

PRP is a plasma, derived from the patient's own blood that is enriched with platelets and contains abundant potent growth factors to promote early tissue regeneration and wound healing.[10] Few globally conducted studies are available in the current literature that provide evidence for the beneficial role of PRP in promoting early healing of chronic DFUs. However, still there is a paucity of local data in our country comparing the use of autologous PRP with conventional dressings. Many surgeons in our country are still accustomed to the use of conventional dressings for treating DFUs.

Hence, it is imperative to conduct a study comparing the efficacy of autologous PRP with conventional dressings to treat chronic non-healing DFUs with a special focus on our local adult population.

METHODOLOGY

This Quasi-experimental study was conducted at the General Surgery Department of Combined Military Hospital Rawalpindi Pakistan from June 2023 to December 2023 after obtaining approval by the ethical review committee of the hospital (Serial no #: 506). For the calculation of sample size, the WHO sample size calculator was used with statistics of 80% of wound reduction with PRP injection, and 46.25% of wound reduction with conventional dressings.[11] Based on these, the calculated sample size was 120 patients which were equally divided into two groups (Figure).

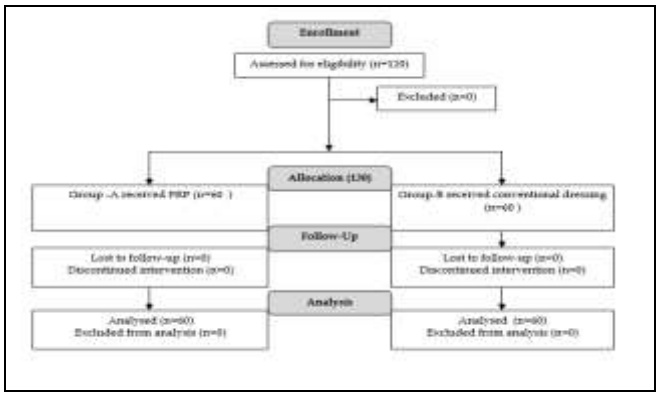

Figure: Patient Flow Diagram

Inclusion Criteria: Patients having Diabetes Mellitus for a duration exceeding more than 10 years, aged between 30-70 years, either of the male or female genders, compliant with anti-glycemic medication and reported to Surgical OPD with chronic non-healing DFU of Wegner Grade I and II, for more than last 03 months were included in the study.

Exclusion Criteria: Patients who presented to emergency with DFU with Wegner Grade > II. Patients taking chronic steroid therapy, had chronic liver disease, end-stage kidney disease, malignancy, were non-compliant with anti-glycemic medication, significantly malnourished, or had significant peripheral vascular disease were excluded from the study.

Patients were selected through non-probability consecutive sampling and divided into two equal groups using the paper lottery method. Group-A (PRP group) was treated using Autologous PRP injections, and Group-B (conventional dressing) was treated with conventional dressings. Baseline characteristics, including age and gender, were recorded. Patients were queried about their current smoking habits and the Body Mass Index (BMI) of all patients was documented to assess their obesity status (BMI ≥30). Each patient underwent comprehensive clinical examination. Bilateral distal lower limb pulses were palpated. The neurological status of bilateral lower limbs was assessed by evaluating fine touch sensations, proprioception, and vibration sensation using a 128-Hz tuning fork. The size of the ulcer was measured. In a few cases of suspected underlying bone involvement, plain X-ray film with two views was obtained. On their initial visit, the hemoglobin, platelet count, and HBA1C levels of each patient were checked and documented. Patients and attendees were educated in detail about foot care and wound management. The Endocrinologist and dietician were involved for optimum control of the patient's blood sugar levels. All data was entered in a form designed specifically for this research study. Group-A was administered autologous PRP as a primary treatment modality, and Group-B was treated using conventional moist dressings. Treatment was done by the surgeons of the same team, staying compliant with standardized treatment protocols for this specific study. For Group-A patients, autologous PRP was formed and injected in the OPD's Procedure Room. A sterile venous blood sample of 15 cc was obtained from the patient using a disposable syringe. Blood was then subsequently transferred into four plain sample collection bottles. These vials were then centrifuged for 20 minutes at the speed of 3000 rpm (Centrifuge

Machine Model: LAB-O-CHECK ITALIANO 80-1 ELECTRONIC CENTRIFUGE, last calibrated on Apr 23 from 502 EME workshop). PRP from the vial was then transferred to a sterile syringe. Patient's wound was thoroughly cleaned, and PRP was injected (1ml for 1 cm2 of the ulcer) into the ulcer's base and the wound's edges. The wound was covered with paraffin gauze, and an aseptic dressing with surgical gauze was done. For Group-B patients, moist aseptic dressing using sterile surgical gauze soaked in 0.9% normal saline solution was used and covered with crepe bandage. Furthermore, patients were advised and educated to apply similar dressings over the wound once daily. Follow-up visits were planned on 7th, 14th, 30th, 45th, and 60th days. For Group-A patients, PRP injection was repeated on day 7th, 14th, 30th, 45th days. All patients were followed for 60 days, and after that, the efficacy of treatment was assessed which was defined as Reduction in the ulcer grade as per Wegner's classification. Both groups were also compared in terms of the development of any local ulcer complication (increase in Wegner grade during the course of treatment), complete ulcer healing, and overall patient satisfaction with the treatment.

"The Statistical Package for Social Sciences (SPSS) version 23 software was used for statistical data analysis. Quantitative variables were represented using Mean±Sd deviation (SD). Frequency and percentages of categorical variables were calculated. The Chi-Square test was used to compare categorical variables, and the Independent Samples T-Test was used for quantitative variables. A *p*-value of ≤ 0.05 was considered significant".

RESULTS

One hundred and twenty patients (n=120) patients were included in the study and divided into two groups of 60 patients each. In Group-A (PRP group), autologous PRP injections were used to treat DFU. In Group-B (conventional dressing), conventional saline-soaked moist dressings were used. The comparison of baseline characters and clinical profiles between the two groups is tabulated below in Table-I:Biochemical evaluation of all patients was done on their first visit which is tabulated below in Table-II:

Autologous PRP showed better results than conventional dressings in terms of reduction in wound grade. PRP was also a superior treatment modality as compared to conventional dressings in terms of the development of local ulcer complications (increase in Wegner grade), complete wound healing, and overall patient satisfaction. Results are statistically significant ($p \leq 0.05$). This comparison is tabulated below in Table-III.

Table-I: Comparison of Baseline Characters and Clinical Profiles (n = 120)

Variables	Group-A (PRP Group) (n = 60)		Group-B (conventional dressing)(n = 60)		*p*-value
Gender	Male	52(86.6%)	Male	56(93.3%)	0.22
	Female	8(13.3%)	Female	4(6.6%)	
Mean age (years)	54.6±9.5		57.3±9.7		0.13
Obesity (BMI ≥30)	13(21.6%)		20(33.3%)		0.10
Smoking	12(20%)		17(28.3%)		0.28

Table-II: Comparison of Biochemical Profile (n = 120)

Variables	Group-A (PRP Group)(n = 60)	Group-B (conventional dressing) (n = 60)	*p*-value
Hemoglobin (g/dl)	10.9±1.8	10.9±1.9	0.97
Platelet count (x109/L)	221.6±105.6	202.4±96.8	0.30
HBA1C (%)	8.8±0.8	8.9±1.1	0.75

Table-III: Comparison of Ulcer Complication, Wound reduction/healing, and patient satisfaction between Group A and Group B (n = 120)

Variables	Group A (PRP Group) (n = 60)	Group B (conventional dressing) (n=60)	*p*-value
Local ulcer complication	4(6.6%)	16(26.6%)	0.003
Reduction in wound grade	53(88.8%)	28(46%)	<0.001
Complete wound healing	48(80%)	14(23.3%)	<0.001
Patient's satisfaction	53(88.3%)	28(46.6%)	<0.001

DISCUSSION

In this study, we evaluated the efficacy of autologous PRP versus traditional methods for treating DFUs. Autologous PRP was formed and injected into the DFUs in the OPD, and its effectiveness in promoting wound healing was assessed in each subsequent follow-up visit. We found out the Autologous PRP was more effective than conventional dressings in treating DFUs, and this difference was statistically significant.

Diabetes Mellitus is a chronic metabolic disorder that is characterized by abnormally raised blood sugar

levels in the patient's blood. It can be either due to insufficient production of insulin from the pancreas or resistance of body cells against the available insulin in the blood.[12] Long-term complications of the disease can be seen in the form of angiopathy, neuropathy, retinopathy, nephropathy, and dermopathy. The number of newly diagnosed cases of Diabetes Mellitus and the development of complications in the already known cases are consistently on the rise. Diabetic Foot Ulcers (DFUs) are a well-known consequence of Diabetes Mellitus that Surgeons have to deal with very frequently in outpatient departments (OPDs) and also in emergency settings. According to a meta-analysis consisting of twelve studies, the pooled prevalence of DFU in Pakistan was 12.16%.[13] As per international data available in the literature, 5% of the patients with Diabetes Mellitus develop DFU, and 1% of them have to undergo amputation. Because of associated angiopathy, neuropathy, and increased risk of developing infections, DFUs are hard to treat, and if left untreated, they result in a number of complications, including superficial or deep wound infections, abscess formation, osteomyelitis, dry or wet gangrene, sepsis, and multi-organ failure. Most people with these complications have to ultimately go through limb amputation, which is itself associated with poor socioeconomic and psychological outcomes.

The conventional way of treating these DFUs includes debridement and moist dressings. However, due to poor blood supply and insufficient supply of adequate growth factors to the wound, these DFUs show poor healing potential and become hard to treat.[14] Many treatment strategies and new interventions have been studied and recommended by various researchers from time to time, all directed towards a single goal of early and effective treatment of DFU. Autologous PRP is a form of regenerative medicine that has gained much popularity in the last decade due to its magical property of stimulating early healing. PRP is widely been used nowadays to treat tendons, ligaments, and bone injuries. Furthermore, its role in stimulating the growth of hair follicles to cure male pattern baldness is also been well established. Proposing the use of PRP to treat chronic non-healing DFUs effectively is one of the major advancements in managing DFUs. PRP is formed by collecting a small sample of the patient's own blood and centrifuging it at high speed for a few minutes. This will separate out the plasma portion of blood containing high concentrations of platelets. This PRP is enriched with multiple potent growth factors, that, if delivered locally into the wound, will trigger cell reproduction and tissue regeneration, ultimately resulting in early and effective wound healing.[15]

The same result was observed by Abbas *et al*., who studied the effectiveness of Autologous PRP in treating DFUs and other chronic wounds in the local population of Pakistan.[16] Ahmed *et al*., Khunder *et al*., and Singh *et al*., also concluded in their internationally conducted research studies that Autologous PRP promotes early and effective healing of DFUs.[17-19] Furthermore, Hu *et al*., in his research analysis concluded that the use of Autologous PRP for treating DFU is not associated with any significant side effects or complications.[20]

The shortcomings in the current study include a relatively small sample size and single-center study, yet it is sufficient to draw the inference. The current study's findings lend credence to the idea that the Autologous PRP is a safe and effective modality to treat chronic non-healing DFUs. More large-scale prospective randomized controlled studies with extended follow-up are needed and recommended to corroborate the present study's findings.

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LIMITATION OF STUDY

"Single center study, limited follow up period and limited sample size were few limitations of this study."

CONCLUSION

When compared to conventional dressings, autologous PRP facilitates the early and efficient healing of chronic non-healing DFUs.

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Author's contribution

Following authors have made substantial contributions to the manuscript as under:

MFUM & WAK: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

MI & WU: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

ZMUD & NM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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