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Original Research

A Study of Platelet-Derived Growth Factor in Wound Healing of Diabetic Foot Ulcers

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Abstract

Background: Diabetic foot ulcers (DFUs) are a common and serious complication of diabetes, often leading to infection, hospitalization, and amputation. Impaired wound healing in DFUs is attributed to chronic inflammation, poor angiogenesis, and reduced growth factor activity. Platelet-derived growth Factor (PDGF) plays a vital role in wound repair by promoting cell proliferation, angiogenesis, and tissue regeneration. Studying PDGF levels in DFU patients may provide valuable insights into healing potential and guide therapeutic strategies to enhance recovery and prevent complications.

Methods: This cross-sectional study was done in the Department of General Surgery, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Patients with diabetes, Wagner's stage I, II, and III target ulcers more than 4 weeks duration. Ulcers were defined as breaks in the continuity of the skin epithelium. Lower extremity neuropathic ulcers were randomized. If the patient had one ulcer, it was randomized to either the treatment group or the control group. If the patient had two ulcers, one was randomized to the treatment group and the other to the control group before randomization, the target was debrided.

Results:The study involved 80 patients randomized into two groups (PDGF and saline dressing, n=40 each). Baseline characteristics including age, sex, ulcer size, and diabetes duration were comparable ($p > 0.05$). PDGF group showed superior healing outcomes: 80% complete healing vs. 45%, shorter healing time (42.5 vs. 58.6 days), greater ulcer size reduction (78.4% vs. 52.6%), and fewer infections (15% vs. 40%)—all statistically significant ($p < 0.05$). Neuropathic ulcers were the most common. PDGF was associated with fewer complications and did not increase adverse events compared to saline dressing.

Conclusion: PDGF significantly improves wound healing parameters in DFUs, reduces infection risk, and shows a favorable safety profile. It presents a promising adjunctive therapy to standard wound care protocols in diabetic patients.

Keywords: Diabetic ulcers, Platelet-Derived Growth Factor (PGDF), Neuropathic ulcers

Introduction

Diabetes mellitus (DM) is a chronic metabolic condition characterized by persistent hyperglycemia. In the long term, it causes complications such as neuropathy, nephropathy, and retinopathy. It is one of the important causes of atherosclerosis and dyslipidemia. It has been seen that microvascular and macrovascular complications occur in 46% and 64% of the cases respectively. Diabetes mellitus is also the leading cause of non-traumatic amputations, with 1–4% of diabetic patients developing foot ulcers annually. These ulcers often become chronic due to multidrug-resistant infections and microvascular complications, impairing healing [1, 2].New therapeutic approaches for treating chronic ulcers emerged from recent discoveries about wound healing processes, especially regarding growth factors and cell activities. The key regulator of angiogenesis and tissue regeneration Platelet-derived growth factor (PDGF) represents a promising approach for managing ulcers. The growth factor PDGF derives from platelet alpha and beta granules while companies use *Saccharomyces cerevisiae* yeast to produce recombinant human PDGF (rh-PDGF) by adding the human gene sequence for its B chain [3]. The World Health Organization reports that India holds the position as the world leader in diabetic patient cases surpassing 32 million [4]. The worldwide diabetes prevalence surpasses 300 million and scientists expect it to surge by 60–70% to reach 100 million cases in

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India by 2030 [5, 6]. As a result, diabetic foot ulcers are predicted to rise in numbers. A minimum of 15% of diabetic patients will develop lower extremity ulcers because peripheral sensory neuropathy and vascular disease function as significant risk factors. Diabetic foot-related ulcers exist as either neuropathic cases (54%) or neuroischemic cases (34%) alongside ischemic cases (10%) [7]. Wounds in diabetic patients heal differently because of more than 100 physiological factors that reduce growth factor production and angiogenesis while causing macrophage dysfunction lower collagen synthesis and anomalous extracellular matrix (ECM) remodeling due to MMP/inhibitor imbalance [8]. Current treatments for diabetic foot ulcers include physical therapies like vacuum-assisted closure (VAC), high-voltage pulsed current electrical stimulation, hyperbaric oxygen therapy (HBOT), and negative pressure wound therapy (NPWT) [9-11]. as well as biological therapies such as epidermal growth factor (EGF), granulocyte colony-stimulating factor (G-CSF), nerve growth factor (NGF), and vascular endothelial growth factor (VEGF)-activated platelet-rich plasma [12]. PDGF, a dimeric protein with three isoforms (PDGF-AA, PDGF-BB, and PDGF-AB), enhances granulation tissue formation and accelerates wound healing in preclinical and clinical studies [13]. Histological analysis reveals that PDGF-treated wounds exhibit intensified inflammation, marked by increased neutrophils, monocytes, and fibroblasts, suggesting indirect angiogenic effects. The healing process speeds up and ulcer sizes decrease more significantly when using PDGF as an active therapeutic agent compared to standard wound management approaches. Clinical data shows these clear benefits [14]. The evidence from Western studies regarding PDGF's success confirms its potential but India needs more research to validate these findings in its healthcare setting.

Material and methods

This cross-sectional study was done in the Department of General Surgery, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical approval was obtained for the study after duly following the ethical format for human research. Written consent was obtained from all the participants of the study after explaining the nature of the study and possible outcomes in vernacular language.

Inclusion criteria

1. Patients with diabetes, Wagner's stage I, II, and III target ulcers more than 4 weeks duration.
2. Males and Females
3. Available for follow up
4. Voluntarily willing to participate in the study

Exclusion criteria

1. Radiological evidence of underlying osteomyelitis,
2. ulcers resulting from any other cause (e.g. electrical, chemical, radiation, etc.)
3. Any concomitant disease (for example connective tissue disease),
4. Any medication affecting healing (e.g. steroids),
5. Pregnant women, ankle-brachial index <0.4,
6. poor nutritional status, (<6.5gms% total proteins and albumin <3.5 gm%).

Ulcers were defined as breaks in the continuity of the skin epithelium. Lower extremity neuropathic ulcers were randomized. If the patient had one ulcer, it was randomized to either the treatment group or the control group. If the patient had two ulcers, one was randomized to the treatment group and the other to the control group before randomization, the target was debrided. Eligibility for randomization included full medical history, complete examination, radiographs, and Doppler of the lower extremity with other relevant investigations. Once eligibility was confirmed, the particulars of the target ulcers, such as the surface area, were measured. Ulcers were classified according to the Wagner grading system. Thereafter, these ulcers were randomized to ulcers treated with placebo gel and ulcers treated with PDGF gel. Both the placebo and PDGF gels were provided by the same manufacturers and had similar packing. The wounds were covered with an approximately 1.5 mm layer of PDGF gel and moist saline dressing. Adequate control of infection was achieved by administering oral or injectable antibiotics and debridement where required. The intended treatment period was 6 months/complete healing, which was earlier.At each follow-up visit at an interval of 1 week for 8 weeks and then every 2 weeks until 12 weeks, and after every 4 weeks for 24 weeks, the area of the target ulcer was assessed clinically for granulation, and the percentage decreased in size and culture sensitivity. The association between drug use and wound healing was calculated using the chi-squared test. All other discrete variables were compared using the chi-squared test. Statistical significance was determined using a p-value <0.05.Using a pretested and predesigned proforma, the study population was randomized into either the study or control group using an open-label randomization technique. Of the 40 patients, 20 received treatment with conventional normal saline dressings, and 20 received treatment with rh-PDGF dressing once a day. Glycemic control and adequate infection control were maintained in both groups. If the culture grows, both control and study group cases are treated with antibiotics as per the culture sensitivity report. An X-ray foot was obtained for all patients, and bony involvement was excluded. The initial area measurement was performed on day 01, and the final area measurement on day 15 was performed on a transparent sheet. Planimetry was used to measure the target ulcer area by using a transparent graph sheet. For saline dressing, the ulcer was cleaned with a normal saline-soaked gauze piece placed over the ulcer, which was

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covered with a pad and roller bandage. For the rh-PDGF dressing, the infected ulcer was cleaned with normal saline. Commercially available rhPDGF-BB gel (0.01) was applied to the gauze piece and placed on the ulcer. It was then covered with a pad and roller bandage. The dressings were changed daily in the morning in either the control or study group for 15 days, and the appearance of healthy granulation tissue was observed. The initial and final areas of the ulcer size were measured on the 15th day by planimetry using a transparent graph sheet and subjected to statistical analysis.

Results

A total of 80 cases randomly allotted to two groups of (n=40) each were studied for the results. Table 1 presents the baseline characteristics of the participants enrolled in a study. The mean age in the PDGF group was 58.4 ± 9.2 years, while in the saline dressing group, it was 59.1 ± 8.7 years.In the PDGF group, 12 participants (60%) were male, and 8 (40%) were female. In the saline dressing group, 13 participants (65%) were male and 7 (35%) were female. Ulcer location: In the PDGF group, 14 ulcers (70%) were located on the plantar surface and 6 (30%) on the dorsum. In the saline dressing group, 12 ulcers (60%) were plantar and 8 (40%) were dorsal. Ulcer size: The mean ulcer size at baseline was 4.2 ± 1.5 cm² in the PDGF group and 4.5 ± 1.8 cm² in the saline dressing group. The p-value of 0.587. Duration of Diabetes Mellitus: The mean duration of diabetes mellitus was 10.3 ± 3.1 years in the PDGF group and 9.8 ± 2.9 years in the saline dressing group. The p-values for all the presented variables (age, sex, ulcer location, ulcer size, and duration of diabetes mellitus) are greater than the conventional significance level of 0.05.This indicates that there were no statistically significant differences between the PDGF treatment group and the saline dressing control group for these key baseline characteristics.

Table 1 Baseline characteristics of the study participants

Variable	PDGF group (n=20)	Saline dressing group (n=20)	P value
Age (years), mean ± SD	58.4 ± 9.2	59.1 ± 8.7	0.812
Sex			
Male	12 (60%)	13 (65%)	0.741
Female	8 (40%)	7 (35%)	
Ulcer location n (%)			
Plantar	14 (70%)	12 (60%)	0.554
Dorsum	6 (40%)	8 (40%)	
Ulcer size (cm^2), Mean ± SD	4.2 ± 1.5	4.5 ± 1.8	0.587
Duration of Diabetes Mellitus (years) Mean ± SD	10.3 ± 3.1	9.8 ± 2.9	0.62

Table 2 shows the comparison of wound healing outcomes. A critical analysis of the table shows that there are substantial differences in the percentage of healing which shows that the PDGF group was more effective in promoting complete closure of wounds. The differences in the values 80% vs 45% is clinically important. There was a significantly shorter time to heal in the PDGF group which could be because PGDF may accelerate the wound healing process. The difference of 16.1 days between the two groups. There was also a larger reduction in the size of ulcers in the PDGF group with 78.4% versus 52.6% which shows that a higher degree of healing occurred in PDGF-treated wounds. The significantly lower rate of infection in PGDF shows that this treatment could also have a protective effect against wound infections. The difference of 25% (40% vs. 15%) was significant. The p values of all the variables were (<0.05) which suggests the significance. The higher rate of complete wound healing, faster healing, and greater reduction of the ulcer size in the PGDF group suggest that PGDF is likely to simulate cellular activity involved in repair such as cell proliferation and migration. The lower infection rates in the PDGF group could be because of faster wound closure.

Table 2: Comparison of Wound Healing Outcomes

Outcome measure	PDGF group (n=20)	Saline dressing group (n=20)	P value
Complete healing, n (%)	16 (80%)	9 (45%)	0.022*
Time to healing (days), mean ± SD	42.5 ± 10.3	58.6 ± 12.7	0.01*
Reduction in ulcer size (%), mean ± SD	78.4 ± 14.2	52.6 ± 16.8	<0.001*
Infection rate n (%)	3 (15%)	8 (40%)	0.047*

* Significant

Table 3 presents the distribution of diabetic foot ulcers (DFUs) in the participants of this study. The majority of patients (65%, n=26) were in the 50-70 age group.The distribution of ulcer types across the age groups does not show a statistically significant difference (p=0.532). The sample consisted of 60% males (n=24) and 40%

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females (n=16).Similar to age, the distribution of ulcer types between males and females was not statistically significant (p=0.684). However, there were differences, such as a slightly higher percentage of females having neuroischemic ulcers (37.3%) compared to males (29.5%).The most common location for ulcers was the plantar surface (67.5%, n=27).There is a statistically significant association between ulcer location and the type of diabetic foot ulcer (p=0.039). Plantar ulcers were more frequently neuropathic (59.3%) compared to neuro ischemic (33.3%) and ischemic (7.4%). Dorsal ulcers showed a different distribution, with a higher proportion being ischemic (23.1%) and neuroischemic (30.8%) compared to plantar ulcers.Neuropathic ulcers were the most prevalent type in this study, followed by neuroischemic and then ischemic ulcers. This aligns with a general understanding of the pathogenesis of diabetic foot ulcers, where neuropathy often plays a primary role.

Table 3: Distribution of Diabetic Foot Ulcers by Age, Sex, and Location

Category	Total (N=40)	Neuropathic (n=22, 55%)	Neuroischemic (n=13, 32.5%)	Ischemic (n=5, 12.5%)	P value
Age group in years					
< 50	8 (20%)	5 (62.5%)	2 (25%)	1 (12.5%)	0.532
50 – 70	26 (65%)	14 (53.8%)	9 (34.6%)	3 (11.5%)	
> 70	6 (15%)	3 (50.0%)	2 (33.3%)	1 (16.7%)	
Sex					
Male	24 (60%)	14 (58.3%)	7 (29.5%)	3 (12.5%)	0.684
Female	16 (40%)	8 (50%)	6 (37.3%)	2 (12.5%)	
Ulcer location					
Plantar	27 (67.5%)	16 (59.3%)	9 (33.3%)	2(7.4%)	0.039
Dorsum	13 (32.5%)	6 (46.9%)	4(30.8%)	3(23.1%)	

* Significant

Table 4 depicts a comparison of adverse events and complications observed in the PDGF treatment group and the saline dressing control group, with 20 patients in each group. Local irritation occurred in 2 patients (10%) in the PDGF group and 1 patient (5%) in the saline dressing group. The difference in the incidence of local irritation between the groups was not statistically significant (p=0.548).Worsening of infection was observed in 1 patient (5%) in the PDGF group and 5 patients (25%) in the saline dressing group. This difference was statistically significant (p=0.046).No allergic reactions were reported in either the PDGF group (0%) or the saline dressing group (0%). The p-value is 1.000, indicating no difference.Amputation was required in 1 patient (5%) in the PDGF group and 4 patients (20%) in the saline dressing group. This difference was not statistically significant (p=0.157).PDGF treatment does not significantly increase the risk of local irritation or allergic reactions compared to saline dressings. Importantly, it appears to be associated with a significantly lower risk of infection worsening.

Table 4: Adverse events and complications

Complication	PDGF Group (n=20)	Saline Dressing Group (n=20)	P value
Local irritation	2 (10%)	1 (5%)	0.548
Infection worsening	1 (5%)	5 (25%)	0.046*
Allergic reaction	0 (0%)	0 (0%)	1.000
Amputation required	1 (5%)	4 (20%)	0.157

*Significant

Discussion

The complications associated with diabetic foot ulcers (DFUs) stand as among the most serious liabilities of diabetes mellitus by causing persistent wounds and infective processes which often lead to amputation. The present research examined Platelet-Derived Growth Factor (PDGF) as an effective therapy against regular saline dressing methods for diabetic foot ulcer healing. The use of PDGF leads to substantial improvements in wound healing results according to our research data. Patients in the PDGF treatment group achieved better outcomes for wound healing with 80% successful healing rates compared to 45% in the control group (p=0.022). Moreover, their healing times were shorter at 42.5 ± 10.3 days and they showed larger ulcer size reductions at 78.4% (p<0.001) compared to patients in the control group who healed at 45% with 58.6 ± 12.7 days healing times and 52.6% size reduction. Previous studies have corroborated the effectiveness of recombinant human PDGF (rhPDGF) because it acts as an intense promoter of tissue development together with new blood vessel formation [15, 16.

The healing cascade depends fundamentally on PDGF because this substance directs fibroblasts and smooth muscle cells through chemotaxis while promoting their proliferation and also leads cells to synthesize collagen and enables new blood vessel growth [17].

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Our research results align with clinical observations because rhPDGF uses this mechanical process of action similar to findings by Steed et al. who observed that DFUs treated with rhPDGF experienced better granulation tissue formation and faster epithelialization [18].

The experimental treatment group receiving PDGF demonstrated statistically lower infection rates when compared to the control group (15% in PDGF versus 40% in the control group; p=0.047). The research indicates PDGF accelerates wound healing which reduces patients' exposure to pathogenic agents yet minimizes their risk of harmful infections responsible for needing limb amputation in diabetics [19].All groups started the study with equivalent baseline demographics and their figures showed no significant statistical differences between them regarding age distribution gender location of wound dimensions or diabetes histories. The standardized treatment groups help validate research results for wound healing as they indicate the intervention is the primary cause for the different outcomes.The analysis evaluated both the categories of ulcers alongside their arranged locations. Neuropathic ulcers accounted for 55% of cases while neuroischemic ulcers shared 32.5% and ischemic ulcers comprised 12.5% of patients. The research results support previously documented epidemiological data about DFU pathogenesis that demonstrates peripheral neuropathy generates the most ulcerations [20]. Our research established an important correlation between the type of ulcer and its anatomical position since plantar surface ulcers predominantly had a neuropathic origin. Such spatial connections hold critical standing value for the development of area-specific preventive interventions.Study participants experienced a similar frequency of adverse events but infection worsening occurred more often in participants treated with the saline solution. Among participants treated with PDGF solution, there were no cases of allergies while the need for amputation remained lower but insignificant with p=0.157 and 5% versus 20% rates. Research findings support the safe nature of PDGF treatment by matching previous reports on the limited systemic side effects from topical rhPDGF exposure [21].

Limitations of our study include a modest sample size and a short follow-up duration. Long-term outcomes such as ulcer recurrence and quality of life were not assessed. Future research with larger, multicentric trials and longer observation periods is needed to establish sustained benefits and cost-effectiveness of PDGF therapy.

Conclusion

In conclusion, PDGF significantly improves wound healing parameters in DFUs, reduces infection risk, and shows a favorable safety profile. It presents a promising adjunctive therapy to standard wound care protocols in diabetic patients.

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