



ROLE OF PLATELET DERIVED GROWTH FACTOR DRESSINGS IN DIABETIC FOOT ULCERS

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ABSTRACT

Diabetes is a common affliction in all parts of the world. Its incidence is rising in developing countries like India.

Based on current trends, the International diabetes federation projects that 438 million individuals will have diabetes by the year 2030.

Diabetic foot ulcers, the most common cause of chronic wounds, occur approximately in 5 to 10% of diabetic patients.

The management of diabetic foot is focused primarily on avoiding amputation of lower extremities.

Platelet derived growth factor PDGF is a dimeric protein. It has been shown in pre-clinical and clinical studies to promote the formation of granulation tissue and to stimulate wound healing.

KEYWORDS : Diabetic ulcers, Platelet derived growth factor, wound healing.

INTRODUCTION

Diabetes is a common affliction in all parts of the world. Diabetic foot infections are one of the most common manifestations of the disease necessitating hospital admissions. Foot disorders such as ulceration, infection, and gangrene are the leading causes of hospitalization in them. The worldwide prevalence of diabetes mellitus has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 285 million in 2010. Based on current trends, the International diabetes federation projects that 438 million individuals will have diabetes by the year 2030. Currently, 4.0-11.6 percent of India's urban population and 3 percent of the rural population above the age of 15 has diabetes. India has been called the diabetes capital of the world, and it is estimated that 41 million Indians have the disease and Every fifth diabetes in the world is an Indian. Diabetic foot ulcers, the most common cause of chronic wounds, occur approximately in 5 to 10% of diabetic patients. Among them 1% undergo amputations at the rate of 15 times more when compared to general populations.

The management of diabetic foot is focused primarily on avoiding amputation of lower extremities. Hence early recognition and proper therapy of diabetic foot lesion may save foot and leg. Hence regular debridement of diabetic wounds are required. However the healing is often delayed leading to intense morbidity to the patients.

Numerous developments have been made in management of wounds. Initially moist gauze dressings were done which were later replaced by hydrocolloid dressings, gels, foams, hyperbaric oxygen, platelet derived growth factors, epidermal growth factors, granulocyte colony stimulating factor, vascular endothelial growth factor, platelet rich plasma and vacuum assisted closure.

Platelet-derived growth factor (PDGF) is a cationic, heat stable protein stored in the granules of circulating platelets and is released from platelets into the serum during blood clotting. PDGF is the major human serum polypeptide growth factor and is a potent mitogen for cells of mesenchymal origin, such as fibroblasts and arterial smooth muscle cells.

PDGF stimulates many metabolic processes, including general protein and collagen synthesis, collagenase activity, and chemotaxis of fibroblasts and of smooth muscle cells. Furthermore, PDGF has been shown to stimulate the production of IGF-I (insulin-like growth factor I or somatomedin C) in cultured human fibroblasts and porcine aortic smooth muscle cells. These in vitro properties suggest that PDGF, delivered from platelets at the site of injury in vivo, may play an important role in the initiation of the repair process of wounds. Subsequently, monocytes, macrophages, and injured endothelial cells may provide a local source of PDGF-like molecules for continuation of the repair process.

PDGF positively promotes angiogenesis indirectly through activities on other inflammatory cells. Recombinant DNA technology has been used to produce a recombinant human platelet-derived growth factor (rPDGF).

Aim of this study is to evaluate the efficacy of PDGF dressings in healing of diabetic ulcers of the foot, to compare and analyze the distribution of diabetic ulcers of the foot with age, sex, location of the ulcer.

MATERIALS AND METHODS

This is a prospective longitudinal study performed at Alluri Sitarama Raju Academy of Medical sciences & Hospital, Eluru, Andhra Pradesh from November 2017 to April 2019 including 50 patients.

The patients were randomly assigned into either Saline or PDGF dressing group. Hence 25 patients in each group. No cross overs were permitted. In this study no patient or physician blinding was present. All the patients were studied and clinical findings were recorded as per the case sheet, necessary investigations ordered and appropriate treatment given. All the cases were followed up to discharge and subsequently for a follow up every week till 4 weeks.

INCLUSION CRITERIA:

All cases of diabetic foot ulcers with Wagner stage 1,2 and who do not meet the exclusion criteria.

Table-1: Wagner's classification of diabetic foot ulcers.

Grade 0	High risk foot and no ulceration.
Grade 1	Superficial ulcer
Grade 2	Deep ulcer(cellulitis)
Grade 3	Osteomyelitis with ulceration or abscess
Grade 4	Gangrenous Patch. Partial foot gangrene
Grade 5	Gangrene of entire foot

EXCLUSION CRITERIA:

- Patients with recognised active charcot disease.
- Ulcers resulting from electrical, chemical or radiation burns and those with collagen vascular disease.
- Ulcers due to malignancy Untreated osteomyelitis.
- Patients with uncontrolled hyperglycemia (HBA1C > 12%).
- Patients on concomitant medication such as corticosteroids, immunosuppressives, chemotherapy.

All patients were advised Diabetic diet and oral hypoglycemic or insulin was used for medical metabolic management after physician consultation.

All wounds were debrided upon admission with an aim to achieve complete skin cover and save the limb. All ulcer areas were obtained by tracing them onto a 1mm × 1mm graph paper.

In the PDGF group, ulcer was cleaned with Normal Saline. Commercially available rh-PDGF-BB gel (0.01%) was applied on the gauze piece and put on the ulcer. It was then covered with pad and roller bandage.

The dressings were changed daily morning in both control and study group for 15 days and appearance of healthy granulation tissue is observed. The initial area and final area of the size of the ulcer are measured on 15th day by planimetry using a transparent graph sheet and subjected to statistical analysis.

The following formula was used to calculate % reduction in area of wound after 15 days period in both cases and control groups.

$$\text{Rate of contraction of wound after 15 days of treatment} = \frac{(\text{Initial area} - \text{Final Area}) \times 100}{\text{Initial Area}}$$

Appropriate wound closing with skin grafting or secondary suturing with local flaps or healing with secondary intention was allowed.

During discharge patient was advised diabetic diet to be followed, avoidance of trauma to the ulcer site, regular continuation of diabetic medication and weekly follow up every week till 4 weeks.

The demographics of the study and control group like age, sex, site of ulcer, onset of diabetic foot ulcer, type of treatment, area of the contraction was assessed.

RESULTS

The 50 patients included into the study were divided by random assignment into two groups named study group and control group.

Table-2: Age Distribution.

Age	PDGF (study)	NORMAL SALINE (control)
20-30	02	00
31-40	04	02
41-50	05	06
51-60	10	09
61-70	04	08
TOTAL	25	25
Mean	50.3	50.6

In our study mean age in PDGF group is 50 and in Normal saline group is 51

Table-3:Sex Distribution.

Sex	PDGF (study)	NORMAL SALINE (control)
Male	16	14
Female	09	11
Total	25	25

Total number of males in the study was 30(60%) and females were 20(40%).

Table-4:Site of ulcer in study

Site	No.of cases	Percentage
Plantar	28	56.00
Dorsum	22	44.00
Total	50	100

In our study it was observed that diabetic ulcers more commonly occurs on the plantar aspect (56%) of the foot as compared to the dorsal aspect (44%).

Table-5:Onset of diabetic foot ulcers

Type of onset	No.of persons	Percentage
Traumatic	32	64.00
Spontaneous	18	36.00
Total	50	100

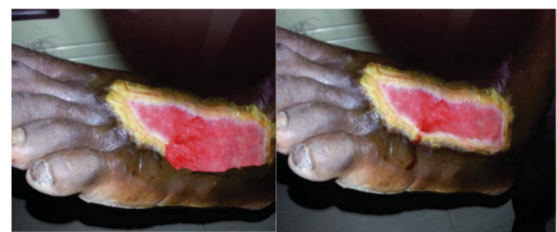
Trauma is then most common cause of diabetic foot ulcer (64%) while only 36% were spontaneous in origin.

Table-6:Wound contraction

Group	Mean Area Reduction	S.D	Median	P-Value
Study	38.95%	2.94	37.40	P<0.001
Control	13.09%	2.50	11.60	

In our study it was observed that mean % of area reduction was higher in study group (38.95%) as compared to the controls (13.09%).

Diabetic foot ulcers in the study group had better mean percentage of wound contraction of 38.95% as compared to the control group which had mean percentage of wound contraction of 13.09%, the difference in the mean 25.86% of area reduction of the two groups where studied using unpaired student t test was found to be significant (p < 0.001).



Before treatment

After 15 days of treatment

DISCUSSION

Diabetic foot ulcers are chronic wounds, with prolonged inflammation phase and shows cessation of epidermal growth. Invariably the diabetic foot ulcers are resistant to heal because of multidrug resistant organism growth and microvascular complications. The present study was conducted at Alluri Sitarama Raju Academy Of Medical Sciences(ASRAMS) from November 2017 to April 2019 to study the effect of use of PDGF in diabetic foot ulcers. In the present study it was seen that the incidence of diabetic foot ulcers were more in males as compared to females. The second national data source, NHDS documented more males suffering from diabetic foot ulcer than females. Diabetic foot ulcers are most commonly seen in 5th decade next common in the sixth

decade, 22 % of patients were in fourth decade. Older the patient more the prevalence of having diabetic foot ulcer.

Mean age which was in 5th decade in our study was almost similar to most of the studies. Majority of the patients were in the 6th decade according to Margolis et al. The lower age of the patients presenting with diabetic lower extremity ulcer can be attributed to life style changes due to urbanization which increases the risk of developing lower extremity diabetic ulcers.

Higher incidence of males over females could be due to the fact that females have a largely indoor existence in our society.

In this study patients with vascular complications such as pulse less limb and the patients with untreated osteomyelitis were excluded. In this study, 64% of the ulcers were traumatic in origin, trauma being the triggering factors secondary to neuropathy, 36% were spontaneous in origin secondary to blister rupture or unnoticed trivial trauma.

More than half (56%) of the patients had ulcer on the plantar surface of the forefoot and the remaining (44%) had on the dorsum of foot. Study conducted by Edmonds et al. showed more foot ulcers were on plantar and fore foot areas. Most of the diabetic foot ulcers are invariably due to poor foot care and due to gait abnormalities.

In our study it was observed that patients receiving rh-PDGF dressing had better wound contraction of 38.95% as compared to the group receiving only conventional dressing (normal saline dressing) in whom the mean wound contraction was 13.09% these were found to be statistically significant on unpaired student t test ($p < 0.001$) suggesting that rh-PDGF dressing enhances wound healing in diabetic wounds. PDGF is the 1st recombinant cytokine growth factor for topical applications to wounds for accelerating wound closure. At wound site PDGF results in endogenous production of the growth factor and extracellular matrix synthesis, fibroblast proliferation and eventually collagen production.

From our study, we can say that rh-PDGF dressing therapy facilitates wound healing in patients suffering from diabetes mellitus.

CONCLUSION

The aim of our study is to evaluate the efficacy of PDGF dressing in the diabetic foot ulcers when compared with normal saline dressings. The wounds in the study group treated with rh-PDGF dressing contracted more than the wounds in the control group (38.95% versus 13.09%; $P \leq 0.001$ -statistically significant) which indicates rh-PDGF dressing is an effective modality to facilitate wound contraction in patients suffering from diabetes. Rh-PDGF dressing is found to be more effective, safe promoter of wound healing and can be used as an adjunct to saline dressing for healing of diabetic wounds.

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