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Key Words

platelet-rich plasma, diabetic foot ulcers, wound healing, conventional treatment

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Received: 22 November 2023

Accepted: 31 December 2023

Published: 5 January 2024

Citation: K.A. Malar Vannan and A. Sivapriya, 2024. Clinical Study of Therapeutic Role of Platelet Rich Plasma in Healing of Diabetic Foot Ulcers. Res. J. Med. Sci., 18: 83-87, doi: 10.59218/makrjms.2024.4.83.87

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Clinical Study of Therapeutic Role of Platelet Rich Plasma in Healing of Diabetic Foot Ulcers

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ABSTRACT

The incidence of diabetes and its complications are on a rise the risk of lower extremity amputations is 15 fold higher in diabetics as compared to non-diabetics. Apart from conventional methods to facilitate wound healing various new methods are emerging such as cellular therapies which include platelet-rich plasma (PRP), collagen based wound dressing. Present study was aimed to study therapeutic role of platelet rich plasma in healing of diabetic foot ulcers. Present study was single-center, prospective, comparative study, conducted patients with 40-65 years age, both sexes presenting with diabetic ulcer foot, type 1 or type 2 diabetes mellitus. Fifty patients were randomly assigned to two groups as study group (freshly prepared platelet rich plasma dressing) and control group (normal saline dressing). Mean age, gender, ulcer onset, site of ulcer and anti-diabetic drugs were comparable in both groups & difference was not significant statistically ($p > 0.05$). Among majority of cases had 15-25% of wound contraction (76%), while controls had 5-15% of wound contraction (96%) and difference was statistically significant ($p < 0.001$). Mean% of area reduction was higher in study Group (33.746 ± 3.968) compared to control group (12.822 ± 1.916) and difference was statistically significant ($p < 0.001$). Among cases mean duration of wound contraction was 4.488 ± 0.409 weeks, which was lesser than controls (6.188 ± 0.391 weeks) and difference was statistically significant ($p < 0.001$). Platelet Rich Plasma showed faster and better healing rates among the study group. Ulcer area reduction and percentage reduction of ulcer size was better in Platelet Rich Plasma group.

INTRODUCTION

Diabetes Mellitus is a term for heterogeneous disturbances of metabolism in which main finding is chronic hyperglycemia, the cause is either impaired insulin secretion or impaired insulin action or both. The incidence of diabetes and its complications are on a rise the risk of lower extremity amputations is 15 fold higher in diabetics as compared to non-diabetics^[1,2]. Diabetic foot ulcers are a major health challenge. The goal of wound care in diabetic foot ulcer is to facilitate healing using standardized protocols of wound care.

In pathophysiology of diabetic foot is the triad of neuropathy, ischemia and infections commonly is considered the most important. The lack as well as malfunction of some growth factors broke natural healing process. Apart from these conventional methods to facilitate wound healing various new methods are emerging such as cellular therapies which include platelet-rich plasma (PRP), collagen based wound dressing. This can have an adjunctive role in a standardized, quality treatment plan^[3,4].

Platelets release certain growth factors from alpha granules which are located in thrombocyte cell membrane which include platelet derived growth factor (PDGF), epidermal growth factor (EGF), platelet derived angiogenesis factor and platelet factor^[4]. These factors act locally on wound and hasten the healing process. PRP provide almost of growth factors for healing. It exhibited two important roles for wound healing. Firstly it forms a fibrin gel forms a barrier to prevent bacterial contamination. Secondly the growth factors triggered the wound healing^[5,6]. Present study was aimed to study therapeutic role of platelet rich plasma in healing of diabetic foot ulcers.

MATERIAL AND METHODS

Present study was single-center, prospective, comparative study, conducted in department of surgery, Government Ramanathapuram Medical College, Tamil nadu, India. Study duration was of 2 years (October 2021 to September 2023). Study approval was obtained from institutional ethical committee.

Inclusion criteria:

- Patients with 40-65 years age, both sexes presenting with diabetic ulcer foot, type 1 or type 2 diabetes mellitus, with controlled blood sugar with non healing foot ulcers, wound size ranging from 4-7 cm, Hemoglobin >10 gms%, platelet count >2 lakhs and ankle brachial index >0.7, willing to participate in present study

Exclusion criteria:

- Patients with severe cardiac disease
- Hepatitis, HIV, critically ill patients
- Known or suspected osteomyelitis
- Underwent conventional skin grafting in past
- Ulcer less than 2cm size

Study was explained to patients in local language and written consent was taken for participation and study. All patients underwent detailed history taking, complete clinical examination, preliminary blood investigations such as complete blood count, random blood sugar, renal function tests, viral markers, blood grouping and X-ray of diabetic foot.

Ulcer examination was done in all these patients and wound was assessed of its characteristics and photographed. Detailed Examination of ulcer was done as site of ulcer (whether in dorsum or plantar foot), shape, presence of necrotic tissue, edges, floor (clean or infected), depth of the wound, fixity to underlying structures, margins, surrounding skin edema, adjacent joint function, blood supply of the local part, presence of systemic features, regional nodal status, function of the limb/part, joint movements and sensation of affected limb. Size of the wound was assessed by placing a meter scale from the edges of the wound in their longest dimensions.

Fifty patients were randomly assigned to two groups as study group (25-patients) and control group (25-patients). After obtaining proper informed written consent patients divided in to two groups one treated with conventional dressing and the study group treated with Platelet Rich Plasma. In both experimental groups adequate wound debridement done and local infection controlled by local antiseptic application and systemic antibiotic therapy. In control group, normal saline dressing was done regularly.

In study group, freshly prepared platelet rich plasma was issued after preparation and injected during each dressing i.e. Platelet Rich Plasma of about 2ml is injected in about 3/4th cm from wound margin using insulin syringe (26 G) and dressing done using pad and roller bandage. The dressing was changed every 4th day in both the groups. Ulcers measured (length and width, using a metric tape). Outcome was measured in terms of wound reduction between the two groups. Their follow-up data was collected. Two group were studied for 6 weeks.

Data was collected and compiled using Microsoft Excel, analyzed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions

between qualitative variables were tested using chi-square test or Fisher exact test as applicable. $p > 0.5$ was considered as statistically significant.

RESULTS

In present study, majority patients were from <50 yrs age group (cases-84%, control-8%), were males (cases-56%, control-64%), had traumatic ulcer (cases-56%, control-64%), observed on plantar aspect (cases-60%, control-68%). In our study more diabetic wound patients were on insulin (60%) than oral hypoglycemic drugs(40%). Mean age, gender, ulcer onset, site of ulcer and anti-diabetic drugs were comparable in both groups and difference was not significant statistically ($p > 0.05$).

In present study, No Growth in Culture in 56% as well as controls (72%), Staph aureus is commonest in both groups Distribution of organisms were comparable among both groups and difference was not significant statistically ($p > 0.05$). In present study, among majority of cases had >26% of wound contraction 92% while controls had <16% of wound contraction 96% and difference was statistically significant ($p < 0.001$).

In our study, mean% of area reduction was higher in study Group (33.746 ± 3.968) compared to control group (12.822 ± 1.916) and difference was statistically significant ($p < 0.001$). In present study, among cases mean duration of wound contraction was 4.488 ± 0.409 weeks, which was lesser than controls (6.188 ± 0.391 weeks) and difference was statistically significant ($p < 0.001$).

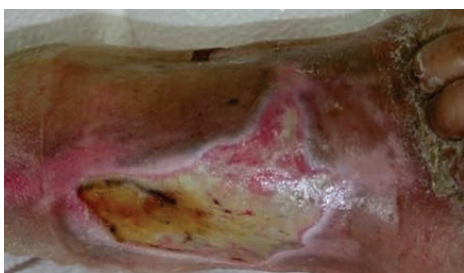


Fig.1: Before PRP



Fig. 2: After PRP dressing

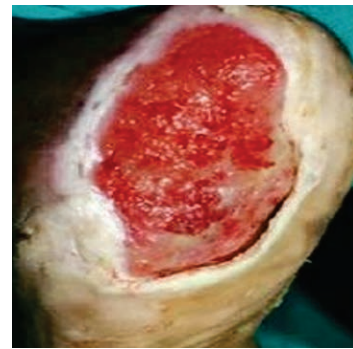


Fig.3: Before PRP



Fig. 4: After PRP dressing



Fig.5: Before PRP



Fig. 6: After PRP dressing

Table 1: General characteristics

Age groups (years)	Cases (n = 25)	Control (n = 25)	p-value
<50	4 (16%)	8 (32%)	0.23
51-60	14 (56%)	12 (48%)	
>60	7 (28%)	5 (20%)	
Mean age (mean±SD)	56.24±6.293	54.04±6.49	0.773
Gender			
Male	14 (56%)	16 (64%)	
Female	11 (44%)	9 (36%)	0.773
Onset			
Spontaneous	11 (44%)	9 (36%)	
Traumatic	14 (56%)	16 (64%)	0.768
Site			
Dorsum	10 (40%)	8 (32%)	
Plantar	15 (60%)	17 (68%)	0.773
Anti diabetic drugs			
Insulin	15 (60%)	15 (60%)	
Oral hypoglycemic drugs	10 (40%)	10 (40%)	

Table 2: Wound culture sensitivity

Organism	Cases (n = 25)	Control (n = 25)	p-value
No growth	14 (56%)	18 (72%)	0.766
Staph Aureus	6 (24%)	3 (12%)	
Proteus	2 (8%)	1 (4%)	
Pseudomonas	2 (8%)	2 (8%)	
E. Coli	1 (4%)	1 (4%)	

Table 3: Wound contraction(initial area-final area = contracted area)

Wound contraction(CA)	Cases (n = 25)	Control (n=25)	p-value
<5.0	0	1 (4%)	<0.001 Significant
5.1-15.0	5 (20%)	24 (96%)	
15.1-25.0	19 (76%)	0	
>25	1 (4%)	0	
Mean (mean±SD)	18.599±3.799	7.08±0.897	

Table 4: Percentage of area of reduction

Percentage of area of reduction	Cases (n = 25)	Control (n = 25)	p-value
<16.0	0	24 (96%)	<0.001 Significant
16.1-26.0	2 (8%)	1 (4%)	
>26.0	23 (92%)	0	
Mean (mean±SD)	33.746±3.968	12.822±1.916	

Table 5: Duration of wound contraction

Duration of wound contraction (weeks)	Cases (n = 25)	Control (n = 25)	p-value
4-5	22 (88%)	1 (4%)	<0.001 Significant
5-6	3 (12%)	2 (8%)	
6-7	0	22 (88%)	
Mean (mean±SD)	4.488±0.409	6.188±0.391	

DISCUSSIONS

It is every surgeon's desire that after dressing the wound, it should heal without any complications. Successful wound dressing should keep the wound moist and be devoid of any adverse reactions such as infection, maceration and allergy^[7]. The incidence of chronic ulcers is expected to increase as the population ages and due to increased risk factors for atherosclerotic occlusion such as diabetes, smoking^[5]. The incidence of diabetes and complications are on rise. Diabetic foot being one of the most common complications, where 15% of all diabetics develop diabetic ulcers the most common site being the foot. Diabetes has highest risk factor associated with limb threatening ischemia. Diabetic foot ulcers are chronic wounds, stuck in inflammation phase and shows cessation of epidermal growth. Trivial trauma secondary to neuropathy and distorted pedal architecture causes ulcerations. 15% of all diabetics develop foot ulcer. 20% of admissions in diabetics are for foot problems^[8,9].

In the present study it was seen that the incidence of diabetic foot ulcers were more in males (56.00%) as compared to females (44.00%). Diabetic foot ulcers are most commonly seen in 5-6th decade (56%) the next common being in the sixth decade (28%). While only 16% of the patients were in the age of <50 yrs of age. Older the patient more the chances of having diabetic foot ulcer. The prevalence of diagnosed diabetics increases with age (the diabetic foot). In this study patients with osteomyelitis were excluded. In this study, 56.00% of the ulcers were traumatic in origin, trauma being the triggering factor secondary to neuropathy. 44.00% were spontaneous in origin secondary to blister rupture or unnoticed trivial trauma.

In our study it was observed that participants receiving Platelet Rich Plasma dressing had better wound contraction of 33.74% (S.D, 3.96) and duration required for wound contraction in study group was 4-5 weeks for 22 patients. In control group duration required was 6 to 7 weeks for 22 patients. As

compared to the group receiving only conventional dressing (normal saline dressing) in whom the mean wound contraction was 12.92% (S.D 1.91) these were found to be statistically significant on unpaired Student t-test ($p < 0.001$) suggesting that Platelet Rich Plasma dressing enhances wound healing in diabetic wounds. Similar findings were noted in other studies^[10,11].

The wounds in subjects treated with PRP dressing contracted more than the wounds in the non treated group (33.74% Vs 12.82%, $p = < 0.001$ Significant) which indicates PRP dressing is an effective modality to Facilitate wound contraction in patients suffering from diabetes and can be used as an adjunct to conventional mode of treatment (conventional dressings and debridement) for healing of diabetic wounds.

A recent meta-analysis of the use of PRP therapy in cutaneous wounds showed that compared to control wound care, PRP facilitates wound healing and the ulcers improved significantly in small hard to-heal acute and chronic wounds^[11,12]. In addition, platelets exert antimicrobial activity against some bacteria of the skin, and clinical data shows that the presence of infection is reduced in PRP treated wounds^[12]. Few limitations of our study were short follow up, difficult to derive conclusion on long term healing of the ulcers and cost involved was not analyzed in this study.

CONCLUSION

Platelet Rich Plasma showed faster and better healing rates among the study group. Ulcer area reduction and percentage reduction of ulcer size was better in Platelet Rich Plasma group. PRP dressing therapy in the treatment of diabetic foot ulcers was found to be more effective, safe, promoter of wound healing, and hence can be recommended for the treatment of diabetic foot ulcers as an adjuvant to the conventional treatment.

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