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Original Research Article

Safety and efficacy of platelet rich plasma in the management of diabetic foot ulcer

Raju Rani, Kathirvel Priyanka*

Department of General Surgery, Madurai Medical College, Madurai, Tamil Nadu, India

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***Correspondence:**
Dr. Kathirvel Priyanka,
E-mail: priyankakathirvel2@gmail.com

ABSTRACT

Background: Diabetic foot ulcers continue to pose a significant global issue despite the advances made in the management of diabetes. It causes major foot complications if they are not addressed properly. While several advancements have taken place in wound care management, platelet-rich plasma (PRP) promises to offer new hope in its management, aiding in cellular and tissue regeneration. Hence the present study was carried out to determine the safety and effectiveness of PRP in the management of diabetic foot ulcers in comparison to conventional dressing.
Methods: This prospective study was focused on 50 diabetic foot ulcers, carried out in a surgical unit of Onsite Hospital, Chennai, Tamil Nadu from November 2018 to November 2019. Patients were divided into two groups group A received conventional ordinary dressing (n=25, 50%) and group B received PRP dressing (n=25, 50%). The mean follow up period was 6 weeks.
Results: The present study observed that participants receiving PRP showed better wound contraction of 33.74% than the group receiving only conventional treatment with a mean wound contraction of was 12.82%. In addition, the duration required for wound contraction in the PRP group was short (mean value 4.488 cm) compared to the conventional dressing group (mean value 6.188 cm). The PRP group was found to be more effective in wound healing with fewer complications, less infection, exudates and pain.
Conclusions: PRP is a powerful tool for the treatment of chronic wounds and very promising for diabetic foot wounds and it enables healing and reduces amputation rates, infection and exudates.

Keywords: Diabetic foot ulcer, Diabetic foot, Platelet-rich plasma, Platelet, Foot ulcer

INTRODUCTION

Diabetic foot ulcers are a major health challenge. The goal of wound care in diabetic foot ulcers is to facilitate healing using standardized wound care protocols. Diabetes mellitus is a term for heterogenous disturbances of metabolism in which the main finding is chronic hyperglycemia. The cause is either impaired insulin secretion or impaired insulin action or both. In 1921, Banting, Best and Macleod demonstrated pancreatic extracts lower blood sugars. In 1936, Antanio discovered oral hypoglycemic agents. Jordan described an association of diabetes with foot lesions.[1] The incidence of diabetes and its complications are on the rise, the risk of lower extremity amputations is 150 fold higher in people with diabetes than non-diabetics.[2] Skin ulcers are defined by the loss of tissue that includes the epidermis and the dermis, affecting the adipose tissue and the muscle fascia. Apart from these conventional methods to facilitate wound healing, various new approaches such as cellular therapies that include PRP and collagen-based wound dressing are emerging. This can have an adjunctive role in a standardized, quality treatment plan.[3,4] Platelets release specific growth factors from alpha granules which are located in the thrombocyte cell membrane, which include platelet-derived growth factor

(PDGF), epidermal growth factor (EGF), platelet-derived angiogenesis factor and platelet factor.[5] These factors act locally on the wound and hasten the healing process. Platelet extract has been used in many studies and has shown impressive results in healing chronic non-healing ulcers. Since not all patients can afford commercially available recombinant platelet gel for dressing, platelet extract from the patients' blood has been used in trials on diabetic wounds. In the pathophysiology of diabetic foot is the triad of neuropathy, ischemia and infections commonly are considered the most important. The lack as well as malfunction of some growth factors, broke the natural healing process. PRP provide almost all of the growth factors for healing. It exhibited two important roles for wound healing. Firstly if forms a fibrin gel forms a barrier to prevent bacterial contamination. Secondly, the growth factors triggered wound healing. Hence, this study intends to demonstrate the therapeutic role of PRP in healing diabetic foot ulcers.

Aims

The aim was to determine the effects and advantages of PRP in the management of diabetic foot ulcers.

METHODS

This prospective comparative study was conducted in patients with diabetic foot ulcers admitted to the department of surgery from November 2018 to November 2019.

Inclusion criteria

Patients with 40-65 years of age group in both sexes presenting with diabetic ulcer foot; both type 1 and type 2 diabetes mellitus; patients with controlled blood sugar with non-healing ulcers in their foot, wound size ranging from 4-7 cm were included. Patients were given informed consent for the study. Haemoglobin should be more than 10 gm; patients with platelet count more than 2 lakhs; and patients with an ankle-brachial index of more than 0.7 were also included.

Exclusion criteria

Patients with severe cardiac disease, hepatitis, HIV, critically ill patients; patients with known or suspected osteomyelitis; patients who underwent conventional skin grafting in the past with the ulcer less than 2 cm in size were excluded in the study.

Convenient sample of 50 patients were included. After obtaining proper informed consent, patients were divided into two groups one treated with conventional dressing and the study group treated with PRP. Their follow up data was collected. Two groups were randomly assigned as the cases A (experimental group, n=25) and B (control group, n=25). Two groups were studied for 6 weeks. Ulcer examination was done in all these patients and the wound was assessed of its characteristics and photographed. The size of the wound was assessed by placing a meter scale from the edges of the wound in their longest dimensions.

Conventional dressing

In both experimental groups, adequate wound debridement done and local infection controlled by the local antiseptic application and systemic antibiotic therapy. In the conventional group, normal saline dressing was done regularly.

PRP dressing

Freshly prepared PRP was injected during each dressing, PRP of about 2 ml was injected in about 3/4th cm from wound margin using insulin syringe (26 G) and dressing did use pad and roller bandage. The dressing was changed every 4th day in both groups. PRP was screened for all routine blood transmitted diseases before its use to prevent contamination with dreadful viral infections.

Ulcers were measured (length and width, using metric tape). The outcome was measured in terms of wound reduction between the two groups.

Data were presented as frequency, percentage, mean and standard deviation. Continuable variables were analyzed using the Pearson Chi square test. SPSS version 21 was used for analysis.

RESULTS

Fifty patients with diabetic foot ulcers were studied. They were divided into two groups of 25 each. One group received PRP and the control group received treatment in the form of conventional therapy. A comparative study was done between both groups regarding percentage area wound reduction. Patients were between 45-60 years of age and males were more affected than females. 56.00% males versus 44.00% females. 56.00% of the ulcers were traumatic in onset. Plantar aspect (60.00%) was the most common site. Most of the patients were on insulin (60.00%) compared to the oral hypoglycaemic agents (40.00%). All patients in the study underwent an X-ray of the affected foot; patients with stress fractures and osteomyelitis were excluded. Our study observed that participants receiving PRP had better wound contraction of 33.74% than the group receiving only conventional treatment in whom the mean wound contraction was 12.82%; these were found to be statistically significant, suggesting that PRP enhanced wound healing in diabetic wounds. Duration required for wound contraction in the case group was short (mean value 4.488) compared to the control group (mean value 6.188) $p<0.001$ significant. Thus, 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.

Table 1: Patients characteristics.

Patients characteristics		Case	%	Control	%
Age group (in years)	<50	4	16.0	8	32.0
	51-60	14	56.0	12	48.0
	>60	7	28.0	5	20.0
Gender	Male	14	56.0	16	64.0
	Female	11	44.0	9	36.0
Onset	Spontaneous	11	44.0	9	36.0
	Traumatic	14	56.0	16	64.0
Site	Dorsum	10	40.0	8	32.0
	Plantar	15	60.0	17	68.0
DM treatment	I	15	60.0	15	60.0
	O	10	40.0	10	40.0

Table 2: Wound culture sensitivity.

Wound c/s	Case	%	Control	%	P value
EC	1	4	1	4	0.766
NOGC	14	56	18	72	
PA	2	8	1	4	
PM	2	8	2	8	
SA	6	24	3	12	
Total	25	100	25	100	

Table 3: Wound contraction.

IA-FA=CA	Case	%	Control	%	P value
<5.0	0	0	1	4	<0.0001
5.1-15.0	5	20	24	96	
15.1-25.0	19	76	0	0	
>25	1	4	0	0	
Total	25	100	25	100	

Table 4: Wound contraction.

% of the area of reduction	Case	%	Control	%	P value
<16.0	0	0	24	96	<0.0001
16.1-26.0	2	8	1	4	
>26.0	23	92	0	0	
Total	25	100	25	100	

Table 5: Duration of wound contraction.

Duration of wound contraction (weeks)	Case	%	Control	%	P value
4 to 5	22	88	1	4	<0.0001
5 to 6	3	12	2	8	
6 to 7	0	0	22	88	
Total	25	100	25	100	

DISCUSSION

Every surgeon desired that after dressing the wound, it should heal without any complications. Successful wound dressing should keep the damage moist and be devoid of any adverse reactions such as infection, maceration and allergy.[1] Diabetic foot ulcers were chronic wounds stuck in the inflammation phase and showed a cessation of epidermal growth.[4] In the present study, it was seen that the incidence of diabetic foot ulcers was higher in males (56.00%) than in females (44.00%). Diabetic foot ulcers were most commonly seen in the 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 years of age. The older the patient more the chances of having a diabetic foot ulcer. The prevalence of diagnosed diabetics increased with age (the diabetic foot). However, Saad et al carried out their study on 24 patients with chronic ulcers ranging in age from 40 to 60 years, concluded that sex and age are insignificant in correlation with the rate of healing of their ulcers.[6]

In this study, patients with osteomyelitis were excluded; 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. Similar findings have also been reported by other studies.[7]

More than half (60.00%) of the patients had an ulcer on the plantar surface of the forefoot and the remaining (40.00%) had on the dorsum of the foot. The study conducted by Edmonds et al in 1986 showed more foot ulcers were on plantar and forefoot areas.[8] They can be prevented by appropriate sized footwear. However, in our study, ulcers over the plantar aspect of the foot were not as high as postulated by Edmonds et al.

Most of the patients (60.00%) were on insulin for control of sugar, whereas only 40.00% were on oral hypoglycaemic agents. In contrast, Prabhu et al 2018 observed that more patients (66.6 per cent) were using oral hypoglycemic medication and fewer patients (33.3 per cent) were taking insulin in their research.[9]

In our study, participants receiving PRP dressing had better wound contraction of 33.74% (SD=3.96) and the duration required for wound contraction in the study group was 4 to 5 weeks for 22 patients. In the control group duration required was 6 to 7 weeks for 22 patients. Compared to the group receiving only conventional dressing (normal saline dressing) in whom the mean wound contraction was 12.92% (SD=1.91), these were found to be statistically significant, suggesting that PRP dressing enhances wound healing in diabetic wounds.

After the second week, PRP was shown to be more effective than traditional dressing in our research. This might be explained by the fact that platelets are triggered by collagen and released into the circulation following endothelial damage during wound healing. Platelets produced intercellular mediators and cytokines from the cytoplasmic pool following aggregation and released their granule content. More than 800 distinct proteins were released into the environment, having a paracrine influence on various cells. For atleast another 7 days, platelets continued to secrete additional cytokines and growth factors from their mRNA stores.[10] PRP had been shown to stimulate wound healing in all systematic reviews. Gui-Qiu et al enlisted 21 individuals with refractory diabetic lower limb ulcers who had failed to respond to standard therapies and was given homologous PRP.[11] Their findings showed that homologous PRP improved and accelerated wound healing in diabetic lower limb lesions. Martinez-Zapata et al found that when PRP was used to treat wounds, the percentage of overall healing rose when compared to controls.[12] De-Leon et al demonstrated in a meta-analysis of chronic wound studies that the use of PRP therapy enhanced full healing when compared to standard care.[13]

Limitations

The limitation was that the large samples with multicentre trials may provide more accurate results.

CONCLUSION

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.

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