

A Comparative Study of Platelet-Rich Fibrin (PRF) in Treating Diabetic Foot Ulcers

Soundarya Mariappan¹, Shaikh Afzal Ruby², Akash Selvathangam³, Vimal Kumar Govindan⁴

Author's Affiliation: ¹Senior Resident, Department of Surgery, Vinayaka Mission's Kirupananda Variyar Medical College & Hospital, Salem, Tamil Nadu 636308, India. ²Associate Professor ³Senior Resident ⁴Professor, Department of Surgery, PSG Institute of Medical Sciences & Research, Peelamedu, Coimbatore, Tamil Nadu 641004, India.

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Abstract

Aim: To compare the efficacy of autologous platelet-rich fibrin (PRF) over moist sterile saline/povidone-iodine dressing in diabetic foot ulcers.

Objective: To compare the mean reduction in ulcer area at the end of 4 weeks of dressings.

Methodology: 60 diabetic patients with foot ulcers from the department of general surgery, general medicine, endocrinology, and cardiology were prospectively studied. Detailed clinical history was obtained, the ulcer was evaluated and the presence of wound infection was assessed for all the patients. Patients were randomised into two groups of 30 patients each. While one group received PRF dressings, the other received saline/povidone-iodine dressings. The wound healing was then compared in the two groups. The efficacy of platelet-rich fibrin dressing over moist saline/povidone-iodine dressings was assessed by comparing the percentage reduction of the ulcer area, at the end of four weeks, using chi-square test and A NOVA test.

Results: It was found that there was a better reduction in the area of the ulcer at the end of four weeks in patients who received platelet-rich fibrin dressings than in moist saline/povidone-iodine dressings.

Conclusion: PRF dressing was superior to moist saline/povidone-iodine dressings.

Keywords: Diabetes; Foot ulcer; PRF.

Introduction

Foot ulcer is a devastating complication of diabetes mellitus, particularly in the elderly. The majority of diabetic foot ulcers may heal, whereas a smaller percentage will remain active and finally lead to gangrene and amputation of the limb.^{1,2} With increasing duration of the ulcer and the increasing age of the patient, the risk of amputation also rises. Thus early prevention plays a vital role.

Wound dressings constitute a major part of the management of diabetic foot ulceration. An ideal dressing will have to reduce the symptoms, give adequate protection of the wound and promote good healing. Platelet-rich fibrin (PRF) prepared from the patient's own blood is used in the fields of orthopedics and dentistry to promote wound healing. PRF transfers growth factors to the wound surface. The use of autologous preparation reduces the risk of allergic reactions. There are very few studies comparing the efficacy of PRF with other dressing materials. This study compares the efficacy of PRF dressing with moist saline/povidone-iodine dressing in diabetic foot ulcers.

Materials and Methods

The period of study was between February 2015 and February 2016. It was an open-labeled

Corresponding Author: Shaikh Afzal Ruby, Associate Professor, Department of Surgery, PSG Institute of Medical Sciences & Research, Peelamedu, Coimbatore, Tamil Nadu 641004, India.

E-mail: drsoundarya.m@gmail.com

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prospective randomised control trial. 60 diabetic foot ulcer patients were randomised into two groups of 30 each. While the study group (Group 1) received PRF dressings, the control group (Group 2) received saline/povidone-iodine dressings. The wound healing was then compared in the two groups by comparing the percentage reduction of the ulcer area, at the end of four weeks.

Ulcers in patients of 18 years or older, having an area of 1 cm × 1 cm to 5 cm × 5 cm were included in the study, after obtaining an informed consent. Ulcers of other etiology (ischaemic ulcers, venous ulcers and ulcers with underlying vasculitis), patients with osteomyelitis affecting the area of the ulcer, and ulcers with exposure of tendons or bones, were excluded. Also excluded were pregnant and lactating patients, and those with a platelet count less than 1,50,000/mm³.



Fig. 1: Following centrifugation sample separates to form fibrin clot & RBCs.

Dressing procedure: PRF was applied over the wound surface in a thin layer and covered with a sterile saline gauze (primary dressing) followed by cotton pad and roller bandage (secondary dressing), as shown in (Fig. 3). The dressing was left in place for 1 week. After 1 week, all PRF remnants were

Detailed clinical history and other relevant data were collected. Each patient was followed up to the end of four weeks, with ulcer area measured at the end of each week. The ulcer area was calculated by multiplying the greatest length by the greatest breadth. Digital photography taken at the beginning and end of treatment. Wound swabs were obtained prior to first dressing and the patient was started on culture-sensitive antibiotics.

Preparation of platelet-rich fibrin (PRF): 10 to 15 ml of patient's blood was collected in sterile containers without any anticoagulant, which was then centrifuged at 3000 rpm for about 10 minutes. This resulted in a lower part with red blood cells and the upper part with plasma. Between the 2 layers was the fibrin clot, with trapped platelets. (Figs. 1 & 2)



Fig. 2: Separated PR for application.

removed with water and sterile gauze. Following this, the next PRF treatment was instituted. A total of four PRF treatments at weekly intervals were given for a total duration of 4 weeks. Group 2 received only sterile saline-soaked gauze dressing with povidone-iodine, which were changed daily.



Fig. 3: Dressing procedure.

The data was analyzed using STATA. The test variables were compared using the chi-square test for two-sided independent samples to compare means across dichotomous variables. The one way ANOVA test was done for comparison of means across multilevel variables. Simple calculations like percentages, proportions and mean values were derived. A Type I error of 0.05 was considered in all Analyzis. *p*-value of less than 0.1 was considered to be statistically significant.

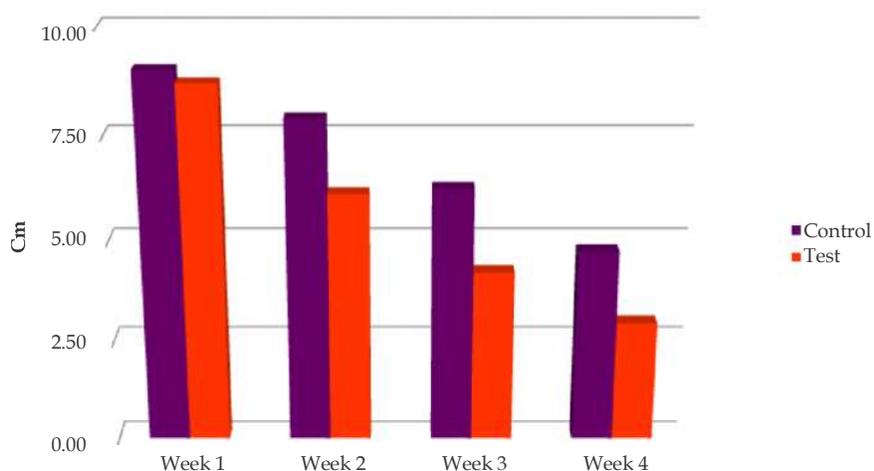
Results

The two groups were found to be matched in terms of the age and gender of the patient, and also the presence of co-morbid factors.

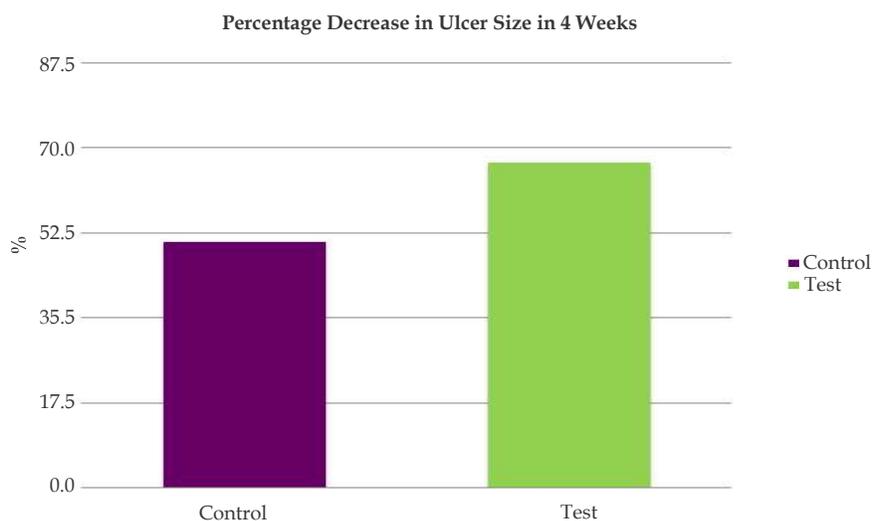
The weekly reduction in ulcer area was compared between control and test groups, as well as the percentage reduction in area.

Table 1: Reduction in ulcer area at the end of 4 weeks

% reduction of ulcer area at the end of 4 weeks	Saline		PRF		<i>P</i> -Value
	Mean	SD	Mean	SD	
	50.5	17.4	66.9	18.2	<0.01



Graph. 1: Weekly Reduction in Ulcer Area.



Graph. 2: Reduction in ulcer area at the end of 4 weeks.

Discussion

It has been well established that diabetic foot ulcers increase the morbidity and, consequently, the financial toll on the society. Therefore, early prevention of diabetic foot ulcers is of paramount importance. Once an ulcer has formed, proper care should be instituted at the earliest to prevent it from progressing to produce extensive damage and possible need for an amputation.

Ulcer care involves the choice of an ideal dressing to aid in satisfactory healing of wounds. Of the many dressing materials available, platelet-rich fibrin, a platelet aggregate prepared from the patient's own blood, has been the subject of research.

PRF preparations yield a platelet concentrate that aggregates on to a fibrin membrane that favors wound healing. It has abundant growth factors, which are released when platelets are activated on application over the wound.³ Activated platelets release growth factors that help in the repair of tissue by the process of angiogenesis, collagen production, formation of granulation tissue and re-epithelialisation.⁴ It also initiates tissue regeneration and response. 60 biologically active substances are found in platelets that are helpful in repair mechanisms including cell proliferation, intracellular matrix deposition, chemotaxis, immune modulation, antimicrobial response, angiogenesis and remodelling.⁴⁻⁷

PRF is better than Platelet Rich Plasma (PRP),⁶⁻⁹ because it is easy to prepare and cost-effective. Bovine thrombin, which has toxic effects on the cells, is required to convert fibrinogen to fibrin while preparing PRP. The conversion of fibrinogen to fibrin, in PRF, happens slowly with the naturally available thrombin that is present in the patient's own blood sample collected, thus rendering a physiological environment that is favourable for wound healing. A better cell proliferation and migration takes place that is led by the naturally formed fibrin matrix.⁶⁻¹⁰ It can release platelet cytokines during the remodelling phase of the healing process.⁶⁻¹² Growth factors concentration in platelet-rich fibrin is three times more than in platelet-rich plasma (Yazawa et al.). The release of growth factors is slower from PRF than from PRP and there is better healing with the use of platelet-rich fibrin.¹¹

Valbonesi et al. conducted a study of its use on non-healing ulcers, wherein the results were found to favorable in 11 out of 14 non-healing ulcers that were treated with platelet-rich fibrin dressings. It

was also found that growth factors had a controlled release over a period of one week when the dressing was kept intact.

Findings in our study show that there is a significant reduction in ulcer area at the end of 4 weeks, in PRF treated diabetic ulcers (66.9%) than in the saline/povidone-iodine group (50.5%), which was statistically significant (p -value <0.01). Thus, it was concluded that PRF dressings produce better healing than saline/povidone-iodine dressings. It may also be noted that the use of PRF dressings in diabetic ulcers can minimize the exhaustion of dressing materials, as it is done only once a week. The ease of preparation of PRF also makes it convenient for dressings. Its application, is thus, very useful in bedridden patients, since they can be provided better wound care.

Conclusion

Foot ulcers pose a real threat to diabetic patients in terms of morbidity and expense. Dressing materials and techniques should be tailored according to the needs of the patient. Platelet Rich Fibrin (PRF), when used for dressing in diabetic foot ulcers, had better and faster healing in comparison with saline/povidone-iodine dressing. PRF is easy to prepare. Being an autologous preparation, it has the least adverse reactions. PRF has its best effect when left undisturbed for a week since it has the property of slow release of growth factors. PRF dressing is ideal for bedridden patients.

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