

ROLE OF EFFECTIVENESS OF AUTOLOGOUS PLATELET-RICH PLASMA IN HEALING OF CHRONIC ULCER

R Lakshmi Devi¹, FR Jenitta Little Sophy¹, S Nambirajan¹, A Arun Raja²

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Corresponding Author:
Dr. FR Jenitta Little Sophy,
Email: jenittasophydr@gmail.com
ORCID: 0000-0003-0536-5319

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¹Assistant Professor, Department of General Surgery, Tirunelveli medical college hospital, Tamilnadu, India

²Postgraduate, Department of General Surgery, Tirunelveli medical college hospital, Tamilnadu, India

Abstract

Background: Chronic ulcers are wounds that have both a "slow healing tendency" and a "full thickness depth." Chronic ulcers of the skin can cause the epidermis, dermis, and even subcutaneous fat to completely disappear. Hence the study aims to evaluate the role of the effectiveness of autologous platelet-rich plasma in the healing of chronic ulcers. **Materials and Methods:** This observational study comprised 51 patients with chronic leg ulcers who met the inclusion criteria. Ulcers were treated with PRP therapy. The effectiveness of PRP in ulcer treatment was assessed while considering the co-morbidities.

Result: The gender distribution of non-healing ulcers among the 51 patients examined was as follows: 35 were male (68.62%) and 16 were female (31.37%). There is no significant difference in age ($p=0.543$). The maximum number of male patients affected with ulcers was between 40 to 70 years. The maximum number of female patients affected with ulcers was between 50 to 70 years. The etiology for chronic ulcers was diabetes in 86 %, and venous causes in 12 % of the patients. **Conclusion:** PRP is a highly effective treatment modality in chronic ulcer management.

INTRODUCTION

Chronic ulcers are wounds that have both a "slow healing tendency" and a "full thickness depth." Chronic ulcers of the skin can cause the epidermis, dermis, and even subcutaneous fat to completely disappear.^[1] Chronic ulcer often arise in the lower limbs and may not react to early therapy or persist despite sufficient care, and do not move toward healing with an underlying pathophysiology that may be connected with systemic illness or localized problems within a certain time frame.^[2,3]

Non-healing ulcers come in a variety of forms, including venous, arterial, diabetic, pressure, and traumatic ulcers. Normal wound healing is a dynamic and complicated process that consists of three phases: inflammation, tissue creation, and tissue remodeling. If the normal healing process is disrupted, an ulcer can become chronic owing to a lack of growth hormones and cytokines, which delay the healing process.^[3]

Lower extremity ulcers account for a significant fraction of chronic ulcers, particularly those caused by venous illness, diabetes, or arterial disease.^[4]

The objective of ulcer therapy is to have the wound closed as soon as possible. Conventional therapy for non-healing ulcers comprises wound cleansing,

necrotic tissue debridement, infection prevention, diagnosis, and treatment, mechanical off-loading, blood glucose control, and local ulcer care with dressing application.^[4]

However, several risk factors that regularly impact and contribute to the poor healing process include:^[3]

- Local causes, such as the presence of debris or necrotic tissue, infection in the ulcer, tissue hypoxia, and repeated trauma;
- Systemic diseases, such as diabetes mellitus, immunodeficiency, or malnutrition; and
- Medications, such as corticosteroids

Chronic non-healing ulcers do not heal adequately because they lack the required growth factors (GFs).^[5]

Standard ulcer treatments that are currently available address these problems and offer adequate local ulcer therapy, pressure relief for the wound area, antibiotic infection control, antiseptics, topical antibacterial agents, ischemic management, and co-morbidity medical management. Necrotic tissue debridement and moist wound healing settings are also provided. Hyperbaric oxygen therapy and skin grafting are two examples of the numerous cutting-edge non-healing ulcer therapies. Because they linger for months or years and/or recur after healing, most chronic ulcers do not heal or need more sophisticated wound care

therapy for optimal healing. Because of their potential utility in regenerative medicine, novel cell treatments such as platelet-rich plasma (PRP) therapy have received a lot of interest in the last 20 years.^[6,7] Platelets collect initially throughout the damage process and form a plug, resulting in hemostasis. Platelet membranes are then depolarised by thrombin, allowing platelet granules rich in growth factors such as PDGF, PGR, FGF, and interleukins to be released. These growth factors contribute to wound healing by laying collagen matrix, fibroblast proliferation, and early collagen maturation. Based on this foundation, autologous platelet growth factors in the form of platelet-rich plasma have been used to treat chronic leg ulcers, with mixed but encouraging outcomes.^[8]

Autologous PRP is a platelet suspension in plasma generated from whole blood that is increasingly being employed in clinical practice to treat chronic ulcers. PRP has 2-6 times more platelets than whole blood.^[9] PRP's curative capabilities are based on the fact that platelets are a physiological reservoir of a wide range of growth factors, with healing functions that play an active part in tissue regeneration.^[10]

To elucidate the effectiveness of the use of PRP in chronic ulcers, we conducted this research which had 2 aims & objectives; To study the role of the effectiveness of autologous platelet-rich plasma in the healing of chronic ulcers and to study the percentage of reduction of area of the ulcer every week for 4 weeks.

MATERIALS AND METHODS

The observational study was conducted at Tirunelveli Medical College Hospital from December 2017 to June 2019. In this study, 51 patients between the age group 18–80 years, with chronic or non-healing ulcers of various aetiologies (such as pressure ulcers, venous ulcers, arterial ulcers, or diabetic foot ulcers) who were treated with autologous PRP under compassionate use were included. Patients with a history of anticoagulants, immunosuppressive drugs, severe cardiovascular disorder, bleeding disorder,

peripheral vascular diseases, and severe anemia were excluded from the study.

The research investigator described the complete treatment and follow-up protocol to those patients who satisfied the inclusion criteria, and only after gaining voluntarily informed permission from the patients for the treatment method, they were medicated with PRP and their follow-up data was recorded.

Preparation of Platelet Rich Plasma (PRP): Patients were extensively examined, and the dimensions of the ulcers (length and breadth) were measured. Under aseptic conditions, 20 ml of venous blood was collected and placed in a test tube containing EDTA before being centrifuged at 3000 rpm for 15 minutes to separate red blood cells from platelets and plasma. The supernatant and buffy coat, which consisted of platelets and plasma, were collected and centrifuged again for 5-10 minutes at 2000 rpm. A sample of roughly 5-8 mL of the lowest layer was obtained. This contains platelet-rich plasma, whereas the supernatant fluid, which is low in platelet concentrate, is discarded.

After thorough surgical debridement, the prepared PRP was administered to the wound and covered with a non-absorbent dressing (paraffin gauze). This procedure was done once a week for four weeks. Every week, the ulcer area was measured. The wound area was determined using the ellipse formula (length width 0.7854). The treatment result was defined as a percentage change in the area determined by dividing the starting measurement by the assessment day measurement divided by the original measurement. An ellipse is more like a coiled form than a square or rectangle, which can be characterized by length and breadth alone. An ellipse has been employed in RCTs in the wound healing literature to calculate wound measurement. Every week, the area of the ulcer is measured and the progress of healing is evaluated.

RESULTS

The gender distribution of non-healing ulcers among the 51 patients examined was as follows: 35 were male (68.62%) and 16 were female (31.37%).

Table 1: Distribution of gender

Gender	Frequency (%)
Male	35 (68.62%)
Female	16 (31.37%)

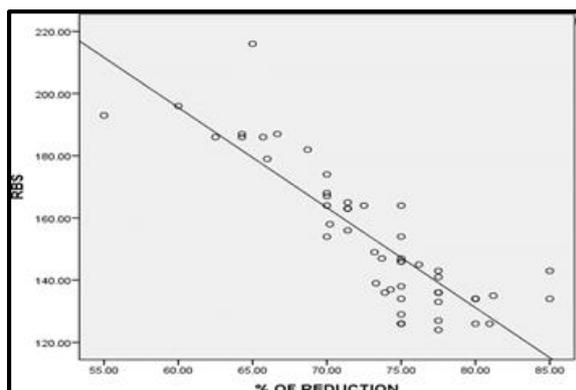
The mean age of the male patients affected was 56.26 years with a standard deviation of 11.19 years. The mean age of female patients affected was 58.19 years with a standard deviation of 8.55 years. There is no significant difference in age (p=0.543).

Table 2: Mean age and percentage of reduction

Gender		Mean and STD deviation	P-value
Age	Male	56.26 ± 11.19	0.543
	Female	58.19 ± 8.55	
% of reduction	Male	72.75 6.91	0.512
	Female	73.71 3.40	

The maximum number of male patients affected with ulcers was between 40 to 70 years. The maximum number of female patients affected with ulcers was between 50 to 70 years. The etiology for chronic ulcers was diabetes in 86 %, and venous causes in 12 % of the patients. There is no significant difference in the percentage of reduction ($p=0.512$).

The mean area of reduction of ulcers in male patients was 72.75% with a standard deviation of 6.91% The mean area of reduction of ulcers in female patients was 73.71% with a standard deviation of 3.40%. The level of random blood sugar of the patient has an inverse relationship with the percentage of reduction of the area of the ulcer.



DISCUSSION

The present study was conducted on 51 patients admitted to the surgical ward, of Tirunelveli medical college hospital from December 2017 to June 2019. Out of 51 patients, 35 patients were male (68.62%) and 16 patients were female (31.37%). Khalsa et al. found that leg ulcer was more common among males (60%) than females.^[11]

The mean age of the male patients affected was 56.26 years while the mean age of the females affected was 58.19 years. According to a study in Ireland, the prevalence was 0.12% but it was 1.03% in patients aged 70 years and over. Women were twice as likely to be affected.^[12] According to a study by Rahman et al, there were two peak periods in the age of presentation. The ages were 30–39 and 50–69 years.^[13]

Our study found that the etiology for chronic ulcers was diabetes in 86 % of the patients while venous ulcers were seen in 12 % of the patients. According to a Chinese study, the primary cause of ulceration (67%) is trauma or traumatic wounds aggravated by infection. Diabetes ulcers, venous ulcers, and pressure ulcers were responsible for 4.9%, 6.5%, and 9.2% of all ulcers, respectively. The vast majority of these injuries were sustained by farmers and other agricultural employees.^[14]

This article aimed at assessing the effectiveness of PRP in the treatment of chronic leg ulcers. The mean area of reduction of ulcers in male patients was 72.75% with a standard deviation of 6.91%

The mean area of reduction of ulcers in female patients was 73.71% with a standard deviation of 3.40%. The level of random blood sugar of the patient has an inverse relationship with the percentage of reduction of the area of the ulcer. i.e. when the random blood glucose increases the percentage of reduction of the area of the ulcer decreases.

The mean area of the ulcer of patients at admission was 21.01 cm² The mean area of the ulcer of patients in 1st week was 19.67 cm² The mean area of ulcer of patients in 2nd week was 13.54 cm² The mean area of the ulcer of patients at 3rd week was 8.80 cm². The mean area of ulcers of patients in the 4th week was 5.93 cm². The percentage of reduction of the area of ulcer in diabetic patients was 72.71% with a standard deviation of 5.42. The percentage of reduction of area of ulcer in venous ulcer was 73.33% in 4 weeks with a standard deviation of 9.17.

In a case study of a 57-year-old man with type 2 diabetes and a six-month-long wound, McAleer et al. discovered that the use of autologous PRP was beneficial in treating a chronic lower limb lesion. By the fourth week of PRP therapy, the ulcer had completely healed. These findings are comparable to those reported in our study.^[15]

In a study by Prabhu et al,^[16] among 104 patients treated with PRP, ulcers in 98 patients (94.23%) showed a good healing rate. The mean surface area of the ulcer was consistently reduced over five weeks. A marked decrease in pain along with healing was also noted.

CONCLUSION

Chronic ulcers have a cost and morbidity for both individuals and society. PRP is a risk-free, simple, low-cost, and biocompatible technique. PRP was proven to be beneficial in promoting wound healing in chronic ulcers in our study with no side effects. The study's mean percentage area of ulcer reduction is 73.0124%, indicating a considerable reduction in ulcer area. As a result, PRP is a successful approach to treating chronic ulcers. The study's findings suggest more research into the use of platelet-rich plasma preparations in the treatment of different wounds and ulcers.

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