

# Efficacy of autologous platelet - rich plasma (PRP) in chronic wound treatment

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## Abstract

**Introduction:** Chronic wounds are a global economic burden that have increased the morbidity and mortality in patients. Chronic wounds present for an extended period of time are more difficult to heal. Nowadays, the application of biotechnology in treatment of chronic wound is a popular trend. We conducted this study to evaluate the effectiveness of autologous Platelet Rich Plasma (PRP) in chronic wound treatment

**Patients and methods:** A pilot descriptive longitudinal study was conducted at the Wound Healing Center of the National Burn Hospital from November, 2021 to December, 2022. Thirty patients with 30 chronic wounds were enrolled in the study and injected the autologous PRP into the peri-wound area and wound bed every 5-7 days. We observed and assessed progress of wound bed and wound size at the time of autologous PRP injection and at the first, second and third week of follow-up.

**Results:** All the patients showed healing of the wound where 40-50% reduction in wound size was observed in 17 (56.67%) patients, followed by 50-60% reduction in wound size in 2 (6.66%) patients over the 4 weeks follow-up post-PRP application. The proportion of wounds with epithelialization at the wound edge and granulation tissue increased significantly compared to before autologous PRP application (63.33% of wounds at week 2 and 76.67% at week 3 had epithelialization, 60% of wounds at week 2 and 76.67% at week 3 had granulation tissue). The wound sizes were significantly reduced in the second and third weeks compared to before treatment (week 2:  $38.4 \pm 25.7 \text{ cm}^2$ ,  $p < 0.05$ ; week 3:  $27.1 \pm 13.6 \text{ cm}^2$ ,  $p < 0.001$ ). **Conclusion:** The local autologous PRP therapy had a beneficial effect on wound healing of the chronic wound.

**Keywords:** Chronic wound, Autologous platelet rich plasma, Granulation, Epithelialization

## Introduction

Chronic wound are defined as spontaneous or traumatic lesions that are unresponsive to initial therapy or that persist despite appropriate care and do not proceed towards healing in a defined period time with an underlying etiology that may be related to systemic disease or local disorders [1], [2]. Many types of chronic wounds may include venous, arterial, diabetic, pressure and traumatic ulcers.

Chronic wound treatment aims to obtain healing as expeditiously as possible. Conventional treatment for chronic wounds includes wound cleansing, necrotic tissue debridement and if necessary, treatment of infection, mechanical off-loading, management of blood glucose levels and local ulcer care with dressing application [2], [3], [4]. Autologous PRP is a platelet suspension in plasma derived from whole blood that is increasingly used in clinical practice to treat chronic ulcers. The concentration of platelets in PRP is 2–6 folds higher than that of whole blood [1], [5]. Platelets contain proteins, known as growth factors that trigger biological effects including directed cell migration, angiogenesis, cell proliferation and differentiation, which are key elements in the process of tissue repair and regeneration [6]. Several studies have also been published on the role of PRP for the treatment of chronic wounds with positive responses [1,3,4,5,6]. Nowadays, there are not so many reports in this issues have been published in Vietnam. The purpose of this study was to evaluate the efficacy of autologous PRP in chronic wounds treatment.

## Materials and Methods

### Patient selection criteria

In this case series, 30 patients between the age group 18–65 years old, with chronic wounds of various aetiologies (such as pressure ulcers, venous ulcers, arterial ulcers or diabetic foot ulcers, trauma injuries...) who were treated by autologous PRP from November, 2021 to December, 2022.

Exclusion criteria: Infected wound (infection

was diagnosed through clinical signs and symptoms rather than culture results) and full-thickness without exposure of bone, muscle, ligaments, or tendons.

Systemic disease or history of anticoagulant, immunosuppressive.

Pregnant women, patients with severe cardiovascular disorder and patients with a bleeding disorder and uncontrolled sugar levels.

Site of study: Wound Healing Center, National Burn Hospital

### Preparation of Platelet Rich Plasma (PRP)

PRP was prepared using an advanced rapid point-of-care technology, the New-PRP Kit (Genne World Corp., Vietnam) at the patients bed side. 28 ml blood and anticoagulant were thoroughly mixed before transferring to the processing device, to prevent formation of blood clots, which in turn facilitates higher cell recovery. At this time, 1 ml aliquot of pooled blood was segregated and later analyzed for pre-processed platelet counts and sterility. The aspirated whole blood was then processed using the New-PRP Kit processing device at the patients bedside. The device works by separating peripheral blood into three distinct layers; Erythrocytes settle at the substratum, above that the plasma layer containing rich concentrate of platelets (PRP) and platelet poor plasma (PPP) as the top layer. After centrifugation, 7 ml of PRP was harvested from the processing device using aseptic technique, of which 1 ml aliquot was separated for post-processed platelet counts and sterility analysis. The remaining 6 ml was transferred to the sterile field for subcutaneous injections and activation of platelets.

### Treatment procedure and chronic wound assessment

The chronic wounds were firstly debrided to remove any necrotic and infected tissues and the wound bed was cleaned thoroughly with betadine solution. Based on the wound size and bed, PRP solution was injected subcutaneously inside and around the peri-wound of the chronic wound. A antiseptic agent dressing was used to cover the

wound area (Betablast Siver, Aquacel Ag...). The dressing was changed on day 3 post-treatment; the wound was irrigated with normal saline and assessed for the presence of any form of infection. Following which the autologous PRP injection was frequently performed once a week and during 3 weeks. We assessed the wound edge and wound bed changes at the time of before PRP treatment (week 0) and at the first (week 1), second (week 2) and third week (week 3) of studied progress. Wound size was calculated at every visit for evaluating the percentage Improvement in Wound Healing after PRP treatment (This variable will be divided as follows: <40%; (40-50%); (50-60%))

The percentage of reduction in ulcer size at the end of follow-up =

$$\frac{\text{Wound size (week 0)} - \text{Wound size (week 3)}}{\text{Wound size (week 0)}}$$

Note: Wound size (week 3): Wound size at the third week

Wound size (week 0): Wound size at the time of before PRP treatment

#### Statistical Analysis

The results before and after experiment were recorded and compared by using Stata 12.0. All results are presented as the mean  $\pm$  SD (min-max) or percentage. Between and within group comparisons of efficacy variables were carried out using the Wilcoxon signed-rank test for paired samples. The value of  $p \leq 0.05$  was considered statistically significant.

## Results

Thirty patients were treated with PRP injections around the peri-wound area. Among the included patients, 19 (63.33%) were males and 11 (36.67%) were females with a mean age of  $55.4 \pm 16.8$  years old. These patients had 30 wounds and their locations were sacrum (60%), trochanter (23.33%), ischium (10%) and low-extremities (6.67%). Wound size mean was  $52.74 \pm 22.62$  cm<sup>2</sup> (Table 1). Additionally, among the treated chronic wounds, there were 22

(73.4%) pressure ulcers, 4 (13.3%) trauma wounds, 1 (3.3 %) venous ulcers, and 3 (10%) others.

Table 1. Wound locations and wound size before autologous PRP treatment (n=30)

Wound location	No. of Wound	Percentage (%)
Sacrum	18	60
Trochanter	7	23.33
Ischium	3	10
Low-extremities	2	6.67
Wound size (n=30)	X $\pm$ SD	Min-max
	52.74 $\pm$ 25.62 cm <sup>2</sup>	30-89

All the patients showed healing of the wound where more than 40% reduction in wound size was observed in 17 (56.67%) patients, followed by (50-60%) reduction in wound size in 2 (6.66%) patients over the 4 weeks follow-up post-PRP application (Table 2).

Overall, significant reduction in wound size was observed in all the treated patients.

Table 2. Percentage Improvement in Wound Healing after PRP treatment (n=30)

Reduction in wound size at the end of follow-up	No. of Wound	Percentage (%)
<40%	11	36.67
(40–50%)	17	56.67
(50-60%)	2	6.66
Total	30	100

After PRP treatment, the proportion of wounds with epithelialization at the wound edge and granulation tissue increased significantly compared to before autologous PRP treatment (63.33% of wounds at week 2 and 76.67% at week 3 had epithelialization, 60% of wounds at week 2 and 76.67% at week 3 had granulation tissue). The wound sizes were significantly reduced at the second and third weeks compared to before treatment (week 2:  $38.4 \pm 25.7$  cm<sup>2</sup>,  $p < 0.05$ ; week 3:  $27.1 \pm 13.6$  cm<sup>2</sup>  $p < 0.001$ ) ( Table 3).

Table 3. Wound characteristics before and after PRP treatment

Wound characteristics	Week 0 (n=30)		Week 1 (n=30)		Week 2 (n=30)		Week 3 (n=30)	
	n	%	n	%	n	%	n	%
Wound bed Granulation								
- Pink or red	-	-	9	30	18	60	23	76.67
- Hypergranulation	5	16.66	9	30	6	20	7	23.33
Soft Tissue	25	83.34	12	40	6	20	-	-
Wound size (cm <sup>2</sup> )	X±SD (min-max)							
	(n=30)		(n=30)		(n=30)		(n=30)	
	52.74 ± 25.62		49.8 ± 27.9		38.4 ± 25.7		27.1 ± 13.6	
P	P0-1>0.05; P0-2<0.05; P0-3<0.001							
(Wilcoxon signed-rank test)	P1-2< 0.05; P1-3<0.05; P2-3<0.05							

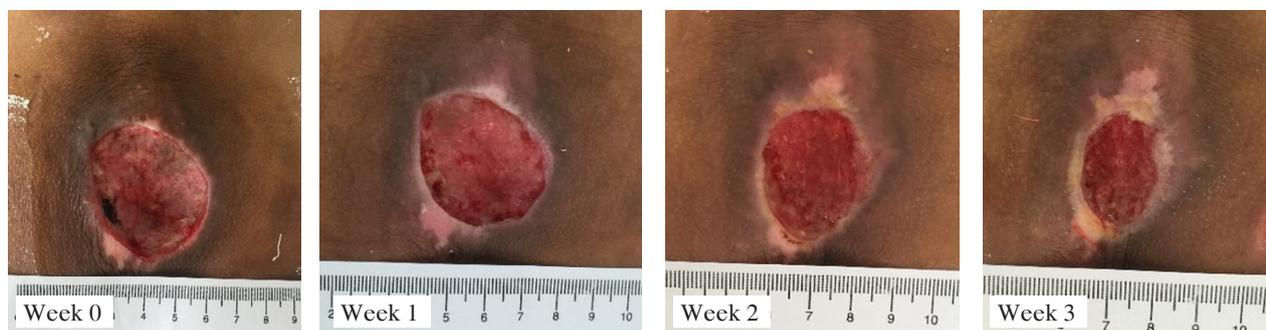


Figure 2. Sacral pressure ulcer was treated by autologous PRP

**Discussion**

Chronic wounds come with significant cost and morbidity for the patients and society as a whole. These non-healing ulcers of lower extremity develop as a result of peripheral neuropathy, ischemia, or trauma and are often difficult to treat [7]. The main goal of any treatment modality is to obtain wound closure expeditiously. The conventional treatment includes adequate debridement, control of infection, re-vascularization of ischemic tissue, and avoidance of undue pressure on the wound. Skin grafting has shown some efficacy, however they are not capable of providing the necessary growth factors to modulate the healing process and are expensive [8]. In 1986, Knighton et al. showed that the use of autologous platelet factors accelerated epithelialization of granulation tissue leading to complete repair of chronic non-

healing ulcers. This was the first clinical study that demonstrated the promising role of locally acting factors derived from autologous blood in promoting healing of chronic cutaneous ulcers [9,10]. Platelets contain a large number of growth factors and cytokines that play key roles in inflammation and tissue repair, by contributing towards haemostasis at sites of vascular injury. These characteristics of platelets have led to the idea of using PRP as a therapeutic tool to promote wound healing, particularly in patients whose tissue repair is significantly impaired or delayed [10,11]. PRP is a rich concentrate of platelets, cytokines and growth factors dispersed in a very small amount of plasma which can be prepared from a sample of centrifuged autologous blood. The α-granules of platelet rich plasma contain various growth factors primarily Platelet Derived Growth Factor

(PDGF), Vascular Endothelial Growth Factor (VEGF), Transforming Growth Factor- $\beta$  (TGF- $\beta$ ), Insulin-like Growth Factor (IGF) and Fibroblast Growth Factor (FGF) to name a few that locally attract progenitor cells to stimulate proliferative and differentiation activities and improve wound healing via autocrine and paracrine mechanisms [12]. Platelets initiate the wound healing process through release of locally active growth factors [13] that attract undifferentiated cells to the site of injury and promote their cell division. In our study, 30 patients with 30 chronic wounds were treated by subcutaneous injections of autologous PRP into the peri-wound area. All the patients showed healing of the wound with reduction in wound size, and the mean time to healing of the ulcers was  $5.23 \pm 2.01$  weeks. The results demonstrated the safety and efficacy of autologous PRP in chronic wound treatment. A study conducted by Frykberg et al., on 49 patients with 65 chronic wounds showed that 63 of 65 ulcers responded with a reduction in area, volume and undermining of the ulcers in a mean duration of 2.8 weeks with 3.2 treatments [14]. Another study by Kakudo et al., treated five cases of intractable skin ulcer with autologous PRP, among which three ulcers healed completely within 4 weeks and epithelialization of wound occurred within 6.6 weeks on average [13]. The results from our case series were concurrent with previously published studies in terms of healing time. The wound sizes were significantly reduced at the second and third weeks compared to before treatment (Table 3). In this study, among the 30 patients who were included, 26 (86.7%) patients had more than one comorbidity. Before hospitalization at our center, their chronic wounds failed to respond to presently available treatment plans that include dressings or skin graft. When these patients were admitted to our center, they were evaluated by our multidisciplinary teams to manage comorbidities, then the local autologous PRP therapy. Our study is a descriptive longitudinal case series study limited by the absence of a control group. Nevertheless, we

feel that the longitudinal nature of our study adds significance to the attractiveness of autologous PRP therapy as a supportive therapy.

### Conclusion and recommendation

In conclusion, the results from our study showed that PRP is an effective treatment modality for chronic wounds. Using PRP to treat chronic wounds may enhance healing

These observations are preliminary, and therefore not conclusive, as it was required further studies with large sample sizes allowing comparisons with a control group and evaluation of changes of bio-markers in chronic wound tissue after the autologous PRP therapy.

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