THE EFFECTIVENESS OF PLATELET - RICH PLASMA (PRP) ON THE CHRONIC WOUND HEALING PROCESS: A DESCRIPTIVE LONGITUDINAL STUDY AT THE WOUND HEALING CENTER OF NATIONAL BURN HOSPITAL.

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ABSTRACT

Objective: *We aimed to characterize the chronic wound response to Platelet-rich Plasma therapy (PRP).*

Subjects and methods*: We performed a descriptive longitudinal study at the Wound Healing Center of National Burn Hospital, from May 2019 to May 2020. Thirty patients with 33 chronic wounds were was injected subcutaneously inside and around the periphery of the chronic wound. We assessed the wound bed, wound size at the time of PRP injection and the first, second and third week of follow-up.*

Results*: After PRP treatment, the wound size reduced significantly compared to before the experiment, wound beds were cleaner and had filled with granulation tissue. Re-epithelialization appeared at the wound edge.*

Conclusion: *In addition to PRP therapy had a beneficial effect on wound healing of the chronic wound.*

Keywords*: Chronic wound, platelet-rich plasma, granulation, epithelialization.*

1. INTRODUCTION

Chronic wounds 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 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. The normal wound healing process is dynamic and complex having three phases: inflammation, tissue formation and tissue remodeling. However, if the normal healing process is interrupted, a wound can become chronic due to a lack of growth factors and cytokines which delay the healing process [3].

The goal of chronic wound treatment is to obtain wound closure as expeditiously as possible. Conventional treatment for chronic wounds include wound cleansing, necrotic tissue debridement, prevention, diagnosis, and, if necessary, treatment of infection, mechanical off-loading, management of blood glucose levels and local ulcer care with dressing application [2, 4, 5]. Cellular therapy for the treatment of chronic wounds has been a breakthrough.

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Autologous PRP is a platelet suspension in plasma derived from whole blood that is increasingly being used in clinical practice for the treatment of chronic ulcers. The concentration of platelets in PRP is 2 - 6 folds higher than that of whole blood [1, 6]. 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 [7]. The purpose of this study was to evaluate the efficacy of autologous PRP in chronic wound treatment.

2. SUBJECTS AND METHODS

2.1. Patient selection criteria

In this case series study, 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) who were admitted to Wound Healing Center, National Burn Hospital and were treated with autologous PRP from May 2019 to May 2020.

Inclusion criteria: Infected (infection was diagnosed through clinical signs and symptoms rather than culture results) and full-thickness without exposure of bone, muscle, ligaments, or tendons. Individuals with systemic disease or a history of anticoagulant, immunosuppressive were excluded. Additionally, pregnant women, patients with severe cardiovascular disorder and patients with a bleeding disorder and uncontrolled sugar levels were excluded.

2.2. Preparation of Platelet Rich Plasma (PRP)

PRP was prepared using an advanced rapid point-of-care technology, the New-PRP^{pro} Kit (Genne World Corp., Vietnam) at the patient's bedside. 28ml Blood and anticoagulant were thoroughly mixed before transferring to the processing device, to prevent the formation of blood clots.

The aspirated whole blood was then processed using the New-PRP^{pro} Kit processing device at the patient's bedside. The device works by separating peripheral blood into three distinct layers; Erythrocytes settle at the substratum, above that the plasma layer containing a rich concentrate of platelets (PRP) and platelet-poor plasma (PPP) as the top layer. After centrifugation, 7 - 8ml of PRP was harvested from the processing device using an aseptic technique.

2.3. 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, the PRP solution was injected subcutaneously inside and around the periphery of the chronic wound. An antiseptic agent dressing was used to cover the wound area (Betablast Silver, Aquacel Ag...). The dressing was changed on day 2 - 3 post-treatment. Following which the autologous PRP injection was frequently performed once a week and for 3 weeks. We assessed the wound edge and wound bed changes at the time before PRP treatment and at the first, second and third weeks of studied progress. Wound size was calculated at every visit. This assessment was supported by photography.

2.4. Statistical Analysis

The results before and after the experiment were recorded and compared by using SPSS 22-64Bit. The value of $p \leq 0.05$ was considered statistically significant.

3. RESULTS

Thirty patients were treated with PRP injections around the wound periphery. Among the included patients, 21 (70%) were males and 9 (30%) were females with a mean age of 49.52 ± 12.38 years old. These patients had 33 wounds and their positions were extremities (10 (30.3%)), sacrum (21(63.63%)), head (1 (3.03%)) and back (1 (3.03%)). Wound size mean was 55.62 ± 29.81cm^2 (Min-max: 25 - 108) (Table 1). Additionally, among the ulcers treated, there were 3(10%) venous ulcers, 5 (16.67%) diabetic ulcers, 20 (66.67%) pressure ulcers and 2 (6.67) others. The duration of the chronic wounds presented by the patients' pre-treatment ranged from 4 to 12 weeks with a mean duration of 6 weeks (Table 1). The mean healing time was found to be almost 8.2 ± 1.9 weeks. After 1 week of PRP treatment, wound size decreased by 30.38% and increased to 53.93% in the 2nd week and 71.5% in the 3rd week (Fig. 1).

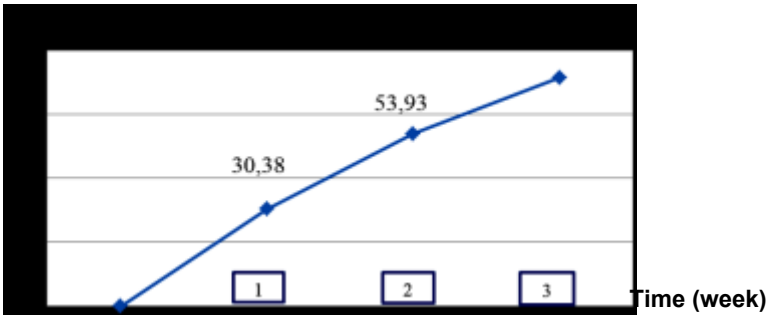

Fig 1. Distribution of cumulative wound healing time following PRP

Table 1. Duration of the wound persisted before PRP treatment wound position and wound size

Duration (weeks)	No. of Patients (n)	Percentage (%)
4 - 6	10	33.33
7 - 9	17	56.67
9 - 12	3	10
Wound position		
Extremities	10	30.3
Sacrum	21	63.63
Back	1	3.03
Head	1	3.03
Wound size (n = 33)	X±SD	Min-max
	55.62 ± 29.81cm^2	25 - 108

All the patients showed healing of the wound where 20 - 40% reduction in wound size was observed in 17 (51.51%) patients, followed by < 20% reduction in wound size in 14 (42.42%) patients over the 24 weeks follow-up post-PRP application (Table 2). Overall, a significant reduction in wound size was observed in all the treated patients.

Table 2. Percentage Improvement in Wound Healing after PRP treatment

Reduction in ulcer size at the end of follow-up	No. of Wound	Percentage (%)
< 20%	14	42.42
20 - 30%	17	51.51
30 - 40%	2	6.06
Total	33	100

After PRP treatment, the wounds were markedly improved as the treatment progressed. The proportion of wounds with epithelialization at the wound edge and granulation tissue increased significantly compared to before autologous PRP treatment (76.52% of wounds at week 2 and 82.25% at week 3 had epithelialization, 61.33% of wounds at week 2 and 74.31% at week 3 had granulation tissue). The wound sizes were significantly different at the second and third weeks after starting treatment (week 2: 45.58 ± 23.45cm^2 , $p < 0.05$; week 3: 40.33 ± 21.73cm^2 $p < 0.001$) (Table 3).

Table 3. Wound characteristics before and after PRP treatment

Wound characteristics	Week 0 (n = 33)		Week 1 (n = 33)		Week 2 (n =33)		Week 3 (n = 33)	
	n	%	n	%	n	%	n	%
Wound bed Granulation								
- Pink or red	1	3.03	9	27.27	20	60.60	21	63.63
- Hypergranulation	3	9.09	8	24.24	8	24.24	12	36.36
Soft Tissue	29	87.87	15	45.45	5	15.15	-	-
Wound size (cm^2)	$\overline{X} \pm SD$ (Min-Max)							
	(n = 33)		**(n = 33)**		**(n = 25)**		**(n = 18)**	
	55.62 ± 29.81 (25 - 108)		50.62 ± 25.39 (23 - 106)		45.58 ± 23.45 (23 - 100)		40.33 ± 21.73 (20 - 85)	
P	$P_{0-1} > 0.05$; $P_{0-2} < 0.05$; $P_{0-3} < 0.05$ $P_{1-2} > 0.05$; $P_{1-3} < 0.05$; $P_{2-3} > 0.05$							

Week 0 Week 1 Week 2 Week 3

Figure 2. Venous ulcer of the lower extremity was treated by PRP

4. DISCUSSION

Chronic wounds come with significant cost and morbidity for the patients and society as a whole. These chronic wounds a result of peripheral neuropathy, ischemia, or trauma and are often difficult to treat [8].

The main goal of any treatment modality is to obtain wound closure expeditiously. The conventional treatment includes adequate debridement, control of infection, revascularization 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 [9].

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 the healing of chronic cutaneous ulcers [10].

Platelets contain a large number of growth factors and cytokines that play key roles in inflammation and tissue repair, by contributing towards hemostasis at sites of vascular injury. These characteristics of platelets have led to the idea of using platelet-rich plasma as a therapeutic tool to promote wound healing, particularly in patients whose tissue repair is significantly impaired or delayed [11, 12].

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-β (TGF-β), 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 [11, 12]. Platelets initiate the wound healing process through the 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 33 wounds were treated with subcutaneous injections of autologous PRP in and around the wound periphery. All the patients showed healing of the wound with a reduction in wound size, and the meantime to the healing of the ulcers was 5.23 ± 2.01 weeks. The results demonstrated the safety and efficacy of autologous PRP in treating chronic non-healing ulcers.

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 ulcers with autologous PRP, among which three ulcers healed completely within 4 weeks and epithelialization of wound occurred within 6.6 weeks on average [12].

The results from our case series were concurrent with previously published studies in terms of healing time.

5. CONCLUSION

In conclusion, the results from our case series showed that PRP is a safe and effective treatment modality for chronic wounds. Using PRP to treat chronic wounds may enhance healing.

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