RESEARCH ARTICLE

Efficacy of platelet rich plasma for acceleration of healing in chronic wounds

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Abstract

Objective: To compare the standard dressing with normal saline with platelet-rich plasma for acceleration of healing in patients with chronic wounds.

Method: The study was conducted at the Department of Plastic and Reconstructive Surgery, Dow University of Health Sciences and Dr K.M. Ruth Pfau Civil Hospital, Karachi, from April 1, 2019, to March 31, 2020, and comprised patients of either gender aged 18-60 years with arterial ulcers on the lower limb with dimension of wound <10 cm^2, haemoglobin >10g/dl and platelet count >150x10^9/L. The patients were randomised into control group A, which received conventional treatment of dressing with normal saline, and intervention group B, which received daily dressings with normal saline and weekly application of platelet-rich plasma. The procedure was repeated every week for 3 weeks. Bates Jensen wound assessment tool was used to assess the final outcome. Data was analysed using SPSS 20.

Results: Of the 98 patients, with mean age 41.68±11.03 years, there were 49(50%) in group A; 45(91.8%) males and 4(8.2%) females with overall mean age 40.10±10.8 years. The other 49(50%) patients were in group B; 39(79.6%) males and 10(20.4%) females with overall mean age 43.27±11.1 years (p>0.05). Mean wound assessment score of group B patients decreased significantly compared to group A (p=0.002).

Conclusion: Platelet-rich plasma treatment showed better performance in accelerating healing of chronic arterial wounds compared to the standard treatment of daily dressing with normal saline.

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Introduction

Chronic wounds is a term used for wounds that do not heal within 4-6 weeks[1] which usually happens due to interruptions in the inflammatory phase throughout the process of normal wound healing and due to the lack of growth factors within the wound.[2] Chronic wounds are categorised as venous or arterial ulcers, diabetic ulcers and pressure ulcers.

Conventionally, chronic wounds have been treated with leg elevation, compression, local wound care, various antiseptic dressings, oral antibiotics, irrigation and debridement.[3,4] Platelet-rich plasma (PRP) is a new biotechnology in the field of tissue-engineering that is safe, simple and cost-effective. PRP has more components responsible for growth and structural proteins that stimulate collagen and the extracellular matrix creation that encourage repairing of tissues, and which stimulate neovascularisation and regeneration of tissues and helps in wound healing.[5,6] PRP also decreases the bacterial load, levels of C-reactive proteins (CRPs) and pro-inflammatory cytokines, and promotes re-epithelisation.[7]

In Pakistan, chronic wounds are common as a result of late referrals of the patients and the vastly underdeveloped healthcare system.[8,9]

The current study was planned to evaluate the efficacy of PRP in the acceleration of healing in patients with chronic arterial ulcers compared to the conventional treatment of daily dressings with normal saline.

Patients and Methods

The study was conducted at the Department of Plastic and Reconstructive Surgery, Dow University of Health Sciences and Dr K.M. Ruth Pfau Civil Hospital, Karachi, from April 1, 2019, to March 31, 2020. After approval from the institutional ethics review board, the sample size was calculated using OpenEpi 3 in the light of literature with 4.92±11.92cm^2 mean change in PRP group and 0.13±0.27cm^2 in the control group[10] at 95% confidence interval (CI) and 80% power.

The sample was raised using non-probability purposive sampling technique from among those visiting the Plastic and Reconstructive Surgery outpatient department (OPD). Those included were patients of either gender aged 18-60 years with arterial ulcers on the lower limb with dimension of wound <10 cm^2, haemoglobin (Hb) >10g/dl and platelet count >150x10^9/L. Patients who were psychologically unfit, had infected wounds, had history of radiation therapy were excluded, and so pregnant women and lactating mothers.

The patients were randomised using randomization plan in Microsoft Excel by generating random numbers into two groups, control group A, which received conventional treatment of dressing with normal saline, and intervention

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group B, which received daily dressings with normal saline and weekly application of PRP. In both the groups, the treatment lasted 3 weeks. Consent was taken from patients in both groups and then the data collection procedure was started.

For group B, 10cc venous blood was drawn and collected in a single gel tube containing citrate as an anticoagulant. The blood was centrifuged at 1500rpm for 10 minutes. The sample was separated into three layers: bottom layer of red blood cells (RBCs), middle layer of PRP called the buffy coat, and the topmost layer of platelet-poor plasma (PPP). The PRP and PPP layers were collected in a separate tube. This tube was centrifuged again at 1500rpm for 5 minutes. The sample got divided into top PPP layer and the bottom PRP layer. The PRP layer was collected in a separate tube To which 10% calcium chloride was added as an accelerating agent to activate PRP. The activated PRP was then injected circumferentially into the wound edges, and dressing was done. Group A controls were treated with conventional dressing in the standard manner.

The 13-item Bates Jensen Wound Assessment Tool (BWAT)[11] was used to assess the wound every week for 3 weeks, and included size, depth, edges, undermining, necrotic tissue type, necrotic tissue amount, exudate type, exudate amount, skin colour, oedema, induration, granulation and epithelialisation. Wound assessment was done every week for 3 weeks, and after rating all the 13 wound components, the total score was determined ranging 0-60, with higher total score indicating the wound status was severe and progressing towards wound degeneration, and lower scores meant improvement in the wound status and progression towards wound regeneration. BWAT scores at baseline and then subsequently on first, second, third and final follow-ups were calculated for each participant. Based on the total BWAT scores, the patients were categorised with respect to wound severity, with score 13-20=minimal severity, 21-30=mild severity, and 31-40=moderate severity.

Data was analysed using SPSS 20. Mean and standard deviation were used to describe continuous data, while median and interquartile range (IQR) were used when the data was not normally distributed. Frequencies and percentages were used for categorical data. Chi-square test was applied to compare between two qualitative variables, while Mann-Whitney U test was applied for comparison of scores between the groups, if the data was not normally distributed. Comparison between age means was done using student's t test. P<0.05 was considered significant.

Results

Of the 98 patients, with mean age 41.68±11.03 years, there were 49(50%) in group A; 45(91.8%) males and 4(8.2%) females with overall mean age 40.10±10.8 years. The other 49(50%) patients were in group B; 39(79.6%) males and 10(20.4%) females with overall mean age 43.27±11.1 years (p>0.05). Characteristics of patients; ulcer at baseline between the groups were noted (Table 1).

In group A, baseline mean BWAT score was 28.31±4.12 while it was 0.39±3.64 in group B. In the first, second and third follow-ups, BWAT scores in group B started showing improvement, and in the final follow up, mean score in group A was 25.55±6.42 compared to 21.14±7.17 in group B (p=0.002) (Table 2).

At baseline, 30(61.2%) patients in group A had mild and 19(38.8%) had moderate BWAT scores. In group B, 24(49%) patients had mild and 25(51%) had moderate BWAT scores (Figure-1 and 2).

At the final follow-up, group A had 14(28.6%) patients with minimal BWAT scores, 26(53.1%) with mild, and 9(18.4%) with moderate scores. In group B, 22(44.9%) patients had minimal BWAT scores, 26(53.1%) had mild, and 1(2%) had moderate score (p=0.017) (Table 3).

Table-1: Baseline clinical characteristics.

Groups Characteristics	Control n (%)	Platelet Rich Plasma n (%)	*p*-value
For how long do you have the ulcer?			<0.001
4-6 weeks	15 (30.6)	4 (8.2)	
6-10 weeks	28 (57.1)	27 (55.1)	
10-14 weeks	6 (12.2)	6 (12.2)	
More than 14 weeks	0 (0)	12 (24.5)	
What is the site of the wound?			NA
Dorsum of the feet	11 (22.4)	14 (28.6)	
Plantar surface of the foot	9 (18.4)	8 (16.3)	
Posterior leg	8 (16.3)	8 (16.3)	
Anterior leg	6 (12.2)	7 (14.3)	
Knee	2 (4.1)	4 (8.2)	
Anterior thigh	6 (12.2)	6 (12.2)	
Posterior thigh	7 (14.3)	2 (4.1)	
What is the size of the wound?			NA
1cm^2 - 3cm^2	4 (8.2)	4 (8.2)	
3.1cm^2 - 6cm^2	29 (59.2)	22 (44.9)	
6.1cm^2 - 10cm^2	16 (32.7)	23 (46.9)	

Table-2: Inter-group comparison of Bates-Jensen Wound Assessment Tool (BWAT) scores.

Groups	Control		Platelet Rich Plasma		Mann-Whitney U	
BWAT Mean Total score at	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	Statistic	p-value
Baseline	28.31±4.12	28 (6)	30.39±3.64	31 (7)	-2.646	0.010
First Follow-up	28.02±4.53	28 (7)	26.12±4.73	26 (3)	1.960	0.053
Second Follow-up	27.55±5.47	28 (7)	25.43±5.30	25 (8)	1.949	0.054
Third Follow-up	26.47±6.19	28 (9)	23.10±6.62	25 (12)	2.599	0.011
Final visit	25.55±6.42	26 (10)	21.14±7.17	25 (14)	3.203	0.002

Mann Whitney U test was used due to BWAT total score is not normal in both groups.

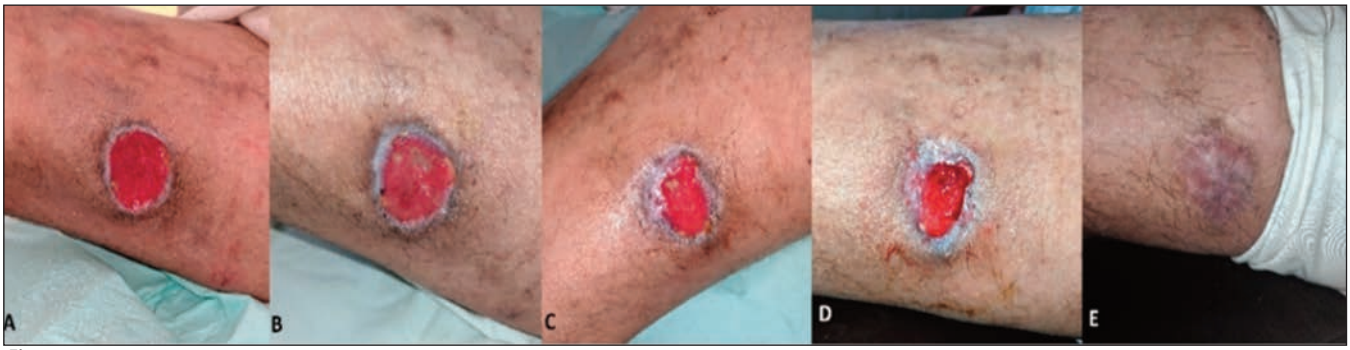

Figure-1: A 36-years-old male patient with a chronic wound over the right thigh for the preceding 6 weeks who received 3 sessions of platelet-rich plasma (PRP) therapy. A) Initial presentation showed an ulcer of approximately 5x5cm. B) At the first follow-up after the PRP procedure. C) At the second follow-up. D) At the third follow-up. E) At the final follow-up when the wound had completely healed.

Figure-2: A 27-years-old male patient with a wound over the right dorsum of the foot for the preceding 5 weeks who received 3 sessions of platelet-rich plasma (PRP) therapy. A) Initial presentation showing an ulcer of approximately 10x6cm. B) At the first follow-up after the PRP procedure. C) At the second follow-up. D) At the third follow-up. E) At the final follow-up when marked improvement in the status of the wound could be seen.

Table-3: Baseline clinical characteristics.

BWAT scores severity categories at	Control n (%)	Platelet Rich Plasma n (%)	*p*-value
Baseline			0.223
21–30 = mild severity	30 (61.2)	24 (49.0)	
31–40 = moderate severity	19 (38.8)	25 (51.0)	
First Follow-up			0.013
13–20 = minimal severity	4 (8.2)	10 (20.4)	
21–30 = mild severity	26 (53.1)	32 (65.3)	
31–40 = moderate severity	19 (38.8)	7 (14.3)	
Second Follow-up			0.214
13–20 = minimal severity	4 (8.2)	10 (20.4)	
21–30 = mild severity	31 (63.3)	28 (57.1)	
31–40 = moderate severity	14 (28.6)	11 (22.4)	
Third Follow-up			0.007
13–20 = minimal severity	9 (18.4)	22 (44.9)	
21–30 = mild severity	26 (53.1)	22 (44.9)	
31–40 = moderate severity	14 (28.6)	5 (10.2)	
Final visit			0.017
13–20 = Minimal severity	14 (28.6)	22 (44.9)	
21–30 = Mild severity	26 (53.1)	26 (53.1)	
31–40 = moderate severity	9 (18.4)	1 (2.0)	

p-value was obtained by Chi square test

Discussion

Chronic wound management with conventional treatment involves expensive resources with negligible benefits.[4] Arterial ulcers, which are also known as ischemic ulcers, occur because of reduced arterial blood supply to the lower limb. Among various causes, the commonest cause is atherosclerotic disease of the arteries. Trauma or localised pressure, diabetes, vasculitis, thromboangitis and thalassemia are considered the other causes for arterial ulcers.

In the wound recovery phase, build-up of an appropriate wound matrix after debridement of chronic wounds is the key challenge.[10,12] Burn wounds treated by conventional wound-care method take a long time to cure, resulting in substantial financial and personal costs for the patients.[13,14] Repetition of PRP application one time a week was done in the current study because the average lifetime of platelets is 7-10 days, thus decreasing local and physical wound factors that cause delay in wound healing.

In the current cases, reduction in length, width and area of the ulcer was much more with PRP compared to the conventional treatment. The mean BWAT score of PRP-treated patients continuously decreased in all follow-up assessments, and this reduction was significant in the third and final follow-ups. A systematic review pf 20 randomised controlled trials (RCTs) compared PRP to any other treatment modality for chronic wounds, and concluded that PRP was significantly effective for complete wound closure, shortening the healing time, and reducing the size of the wound in diabetic ulcers of the lower limb.[15]

However, results were variable for pressure sores and venous ulcers. Another systematic review of 29 RCTs with 2,198 wounds also concluded that PRP was effective in chronic wound management.[16]

Chronic wounds showed bright red granulation and no rejection reactions in a study on allogenic PRP in the treatment of chronic wounds.[17]

Various studies, meta-analyses and systematic reviews have documented the efficacy of PRP therapy. Such findings recommend that PRP along with standardised care was more efficacious compared to standard care alone.[18,19] A comparative study comparing PRP and conventional treatments on chronic venous leg ulcers showed that post-treatment the PRP group showed significant enhancement in the ulcers, and recovery in pain linked with the ulcer was also observed.[10]

The current study had limitations as it did not include other causes of chronic wounds, like venous ulcers. Besides, the sample size was not large enough to allow generalisation of the findings.

Despite the limitations, however, the findings suggested that PRP application for healing of wounds would assist plastic surgeons in improving the healing of chronic wounds, with shorter recovery time and less financial burden on the patients. It is recommended that the use of PRP for chronic wounds should be made a routine practice.

Conclusion

PRP therapy showed better performance in accelerating the healing of chronic arterial wounds compared to the standard treatment of daily dressing with normal saline.

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Author Contribution:

MPK: Original design, writing and data collection.
HA: Supervised the study, data collection and final approval.
SK: Data collection, revision and final approval.