Autologous Platelet Rich Plasma Versus Vacuum Assisted Closure Therapy in management of chronic leg ulcers

Ashraf Kamal Abdalla, M.D. [*] ***; Amr Mohamed EL Hefny, M.D.*** [*] ***;***
Khaled Ahmed Reyad, M.D. [**] ***; Noura Omar Mohamed, M.B.B.CH.*** [**] ***;***
Department of General Surgery[*], Department of Plastic and Maxillofacial Surgery[**],
Faculty of Medicine, Ain Shams University.

ABSTRACT

Background: *Chronic wound healing is a major health problem. In addition to suffering and pain, failure of healing process also had financial and social burdens. Because these wounds lack the necessary growth factors for healing, they are often difficult to heal and are frequently complicated by superinfection. Chronic non healing leg ulcer is defined as skin loss on the leg or foot for more than 6 weeks with no signs of healing. Chronic ulceration of the lower leg including the foot is a frequent condition causing pain, social discomfort, and generating considerable costs.* ***Objective:*** *to compare between the effect of autologous platelet rich plasma (PRP) and Vacuum Assisted Closure Therapy (VAC) in management of chronic leg ulcers regarding to Pressure Ulcer Scale for Healing (PUSH) including surface area of the ulcer , exudate amount and tissue type of the ulcer bed.* ***Patients and Methods:*** *Fifty two adult patients with a history of chronic leg ulcers that not healed for six weeks or more despite treatment of the underlying causes and appropriate local wound treatment. They are divided into two equal groups.* ***Results:*** *The two studied groups had shown no difference regarding age, gender and special habits according to demographic data. There were no differences between the two studied groups regarding clinical data of wound character. In healing process, the first group was shown complete healing in 16 patients by secondary intension, incomplete healing in 10 patients who need skin graft. In second group the patients were shown complete healing in 5 patient by secondary intension, incomplete healing in 21 patients who need skin graft. With a significant difference (p = 0.040).* ***Conclusion:*** *There is no appropriate dressing for all types of wounds, so assessment and continuous observation of the characteristics of the wounds should be done to decide the proper dressing required. The use of negative pressure wound therapy and platelet-rich plasma can be a tool in management of chronic wounds which had no improvement with conventional dressing. It should be reserved to wounds that do not show any progress after 3 weeks with treatment of wound etiology and standard wound care. PRP is simpler, safer, less costly, shorter time for wound healing, less painful, no hospital admission so less transmission of infection and autologous nature in the preparation had proved the superiority of PRP over VAC therapy.*

Keywords: *Vacuum assisted closure therapy, platelet rich plasma.*

INTRODUCTION

Chronic wound healing is a major health problem. In addition to suffering and pain, failure of healing process also had financial and social burdens. Because these wounds lack the necessary growth factors for healing, they are often difficult to heal and are frequently complicated by superinfection[(1)] .Chronic non healing leg ulcer is defined as skin loss on the leg or foot for more than 6 weeks with no signs of healing. It is a frequent condition causing pain, social discomfort and also generating considerable costs. Most common types of chronic leg ulcers are diabetic, Ischemic, venous, post burn and post traumatic leg ulcers[(2)]. During the acute stages of wound healing, the healing process occurs in a stepwise method starting with hemostasis then inflammation. This followed by cell proliferation then remodeling with scar formation. During the proliferative phase, both cell proliferation and migration are required for formation of granulation tissue to support epithelialization but these processes disrupted in chronic wounds [(3)]. Angiogenesis stimulated by different growth factors, cytokines, and lipid mediators produced in response to injury. Vascular endothelial growth factor (VEGF) is one of the most essential proangiogenic mediators and its sufficient level believed to be important for proper wound healing

Corresponding Author:

(4). It is recognized that effective wound management requires accurate assessment of both the patient and the wound to determine the optimal treatment plan for achieving wound care goals. Numerous wound and patient risk factors are known to potentially complicate wound healing and increase health care costs **(5).** Conventional treatments include debridement and dressing like gauze, sofra tulle, films, foam, and hydrogel but, in many cases, these treatments do not result in reliably satisfactory outcomes Consequently, there had been heightened interest in developing new advanced therapies to address the compromised wound. Specifically, in treatment of chronic wounds, platelet-rich plasma (PRP) and Vacuum assisted closure therapy (VAC) shown promising experimental and clinical results **(6).** Platelet-rich plasma (PRP) defined as a portion of fractionated plasma of autologous blood having a platelet concentration above baseline. PRP had both mitogenic and chemotactic properties and serves as a growth factors stimulator **(7).** Autologous platelet-rich plasma (PRP) is one of the promising therapies containing high levels of platelets, fibrin and growth factors as vascular endothelial growth factor (VEGF), platelet derived growth factor (PDGF) and epidermal growth factor (EGF). Also It provokes biological effects as angiogenesis, chemotaxis, cell differentiation, and proliferation; which are crucial for tissue repair and healing **(8).**Vascular endothelial growth factor (VEGF) involved in many phases of wound healing through affection of the interactions between inflammatory circulating cells and endothelial cells, facilitates formation of more mature blood vessels by alterations in production or deposition of collagen, which would be more effective in oxygen supply to the wound and increase of granulation tissue formation **(9).** Platelet rich plasma (PRP) used in the treatment of chronic wounds, ulcers of soft tissue, periodontal, oral surgery, maxillofacial, orthopedic, trauma surgery, cosmetic and plastic surgery and burns. The use of PRP is contraindicated in platelet dysfunction syndrome, thrombocytopenia, hemodynamic instability, and malignant conditions **(10).** Negative pressure wound therapy (NPWT) or vacuum assisted closure therapy (VAC) had been developed as an alternative to the basic forms of wound management, which uses the negative pressure to optimize conditions for wound healing and it requires fewer painful dressing changes **(11).** Negative pressure wound therapy (NPWT) promotes wound healing by applying a vacuum through a special sealed dressing. The vacuum draws out fluid from the wound and increases blood flow to the area. The vacuum may be applied continuously or intermittently, depending on the type of wound being treated and the clinical objectives. Typically, the dressing is changed two to three times per week. The dressings used for the technique include open-cell foam dressings and gauze, sealed with an occlusive dressing intended to contain the vacuum at the wound site **(12).** The negative pressure wound therapy pump is like a vacuum or suction machine, which attached via a tube to sterile foam interface the wound bed. The pump removes fluid away from the wound. The fluid is collected in a canister connected to the pump. NPWT promotes the process of wound healing as it stimulates both migration of the cells and blood flow to the wound **(13).**

It is recommended that the negative pressure wound therapy is used for twenty-three hours a day. The pump can be detached so patient can go to the toilet or have a shower. Depending on the type and size of the wound the dressing usually needs to be replaced every two to three days **(14)** Vcuum assisted closure therapy (VAC) can be used from two to six weeks according to the type of wound. The wound may heal spontaneously by secondary intension, but in other cases surgery as skin grafting may be indicated to finalize healing **(15).** Negative pressure wound therapy can be used in traumatic wounds, venous, diabetic, pressure ulcers, dehisced surgical wounds, flaps, skin grafts and full-thickness burns. While negative pressure wound therapy contraindicated in unstable fractures, enterocutaneous or unexplored fistulae to organs or body cavities, sinus of unknown depth or origin, wounds with malignancy, necrotic wound, untreated osteomyelitis, actively bleeding wounds, wounds with open joints and wounds with exposed blood vessels or organs **(16).** There are many mechanisms of negative pressure wound therapy. They include change in micro vascular blood flow, removal of exudates, edema reduction, stimulate granulation tissue formation, and decrease in bacterial colonization and maintenance of a moist wound healing environment**(17).**

AIM OF THE WORK

The aim of this study is to compare between the effect of autologous platelet rich plasma (PRP) and Vacuum Assisted Closure Therapy (VAC) in management of chronic leg ulcers regarding to Pressure Ulcer Scale for Healing (PUSH) including surface area of the ulcer , exudate amount and tissue type of the ulcer bed.

PATIENTS AND METHODS

This prospective interventional comparative study included fifty two adult patients presented with chronic leg ulcers admitted to Department of plastic and Maxillofacial surgery, Faculty of Medicine, Ain Shams University and department of plastic surgery, Benha Teaching Hospital. The study duration was 6 months from March 2019 till September 2019. Patients were fully informed about the procedure. Written consents were obtained. Patients were divided into 2 groups: **Group A:** 26 patients with chronic leg ulcers were treated with platelet rich plasma (PRP). **Group B:** 26 patients with chronic leg ulcers were treated with Vacuum assisted closure therapy (VAC).

Inclusion Criteria:

Patients with chronic leg ulcer, Any age, Both genders and Leg ulcers with clean floor.

Exclusion Criteria:

Infected ulcers, Ulcers with necrotic tissue, Ischemic limb, Severe sensory loss, Patients receiving medications that delay healing (Steroids,Chemotherapy,…..), Uncontrolled DM, Very bad general condition and Malignant ulcers.

Methods:

Patients were subjected to the following: History taking, Clinical examination, Explanation of the procedure to the patients, Informed consent and Investigations.

History taking: This included Personal history (name, age, occupation, special habits (smoking,..), Complaint, Present history, Past history and Family history.

Clinical examination: This included: Vital signs, General examination, Local examination: Type of ulcer (traumatic, post burn, venous or diabetic), surface area of ulcer, Site of ulcer, Infected or not, Edges and its bed.

Investigations: Routine investigations: Complete blood count, random blood glucose, coagulation profile, Kidney, Liver function tests and virology markers. Duplex was done in case of venous ulcers.

Preparation of the wound: Wound swab for culture and sensitivity. Washing the wound with normal saline.

Study Interventions:

- ***Group A (PRP group):*** Under complete aseptic conditions, 20 mL of patient's venous blood was drawn and was added to a test tube containing acid citrate dextrose in a ratio of 9:1 (blood: acid citrate dextrose). Then was centrifuged at 2000 rpm for 5 min, the red blood cells were separated from platelets and plasma.

Figure (1): Electric centrifuge used in PRP preparation.

Then the lower part of the plasma was collected and centrifuged again at 5000 rpm for 15 min.The bottom layer of about 1.5 mL was harvested, and 10% calcium chloride solution was added to activate PRP (0.3 mL for 1 mL of PRP).

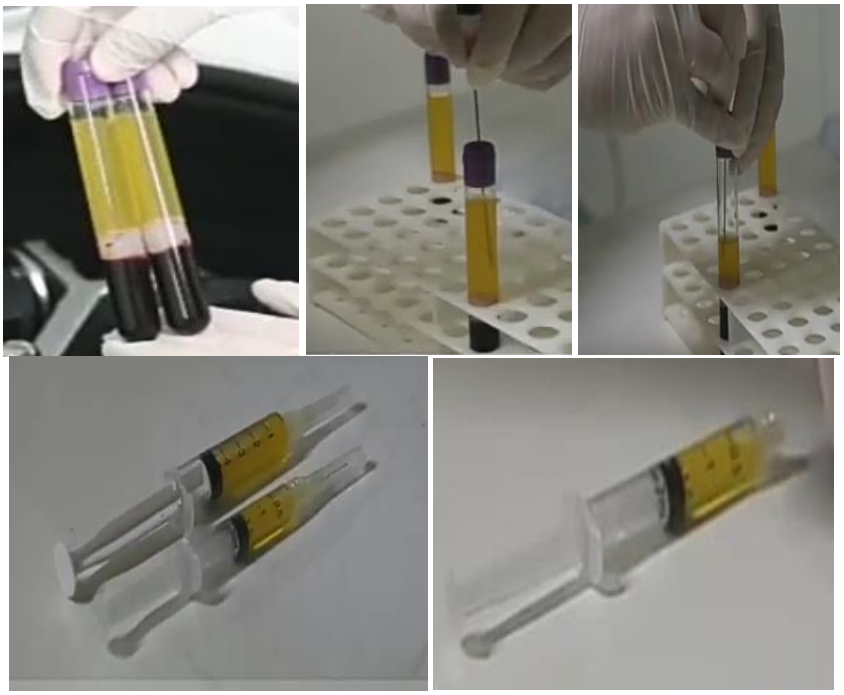

Figure (2): PRP preparation.

Activated PRP was injected in the edges and floor of the ulcer. The remaining amount of PRP was put on the surface of the ulcer with dressing by a non adhesive dressing twice weekly. PRP injection was repeated once weekly for 6 weeks. Photos were taken at first day then every week.

Figure (3): Injection of PRP at edges and floor of chronic diabetic foot ulcer.

- ***Group B (VAC group):*** General technique for Negative Pressure Wound Therapy was done as follows: "The periwound was protected by applying a skin barrier then followed by a transparent film. A dressing or filler material was fitted to the contours of a wound (which was covered with a non-adherent dressing film) and the overlying foam was then sealed with a transparent film. A drainage tube was connected to the dressing through an opening of the transparent film.

Figure (4): Vacuum assisted closure therapy (VAC) in treatment of chronic post traumatic leg ulcer.

A vacuum tube was connected through an opening in the film drape to a canister on the side of a vacuum pump or vacuum source, turning an open wound into a controlled, closed wound while removing excess fluid from the wound bed to enhance circulation and remove wound exudate. Intermittent suction pressure was used with a cycle of five minutes on -125 mmHg and two minutes stand by. Canister was monitored daily for exudate quantity and type. Canister was replaced when full (Alarm sound) and at least once a week to control odor. Dressings were changed two times per week.

Then comparison between healing in chronic leg ulcers between group A and group B according to Pressure Ulcer Scale for Healing (PUSH) which was done every week for 6 weeks.

The Pressure Ulcer Scale for Healing (PUSH) is composed of three parameters: Surface area of the wound, Exuadate amount and Tissue type of the wound bed.

Total scores range from 0 to 17 with higher scores indicating worse ulcers. Scores were also plotted on graphs to show change over time.

Table (1): Pressure ulcer scale for healing (PUSH). **(18)**

Pressure Ulcer Scale for Healing
PUSH Tool 3.0

Length X Width (in cm2)	0 0	1 < 0.3	2 0.3–0.6	3 0.7–1.0	4 1.1–2.0	5 2.1–3.0	Sub-score
		6 3.1-4.0	7 4.1-8.0	8 8.1-12.0	9 12.1–24.0	10 > 24.0	
Exudate Amount	0 None	1 Light	2 Moderate	3 Heavy			Sub-score
Tissue Type	0 closed	1 Epithelial Tissue	2 Granulation Tissue	3 Slough	4 Necrotic Tissue		Sub-score
							Total Score

Tissue type definitions:
0 – Closed, if wound completely covered with epithelium (new skin).
1 – Epithelial tissue: for superficial ulcers, new pink or shiny tissue growing from edges or as islands on ulcer surface
2 – Granlation tissue: pink or beefy red tisue with a shiny, moist granular appearance
3 – Slough: yellow or white tissue that adheres to ulcer in strings or think clumps or is mucinous
4 – Necrotic tissue (eschar): black, brown or tan tissue that adheres firmly to wound bed or under edges and may be firer or softer than surrounding skin

Adapted from www.npuap.org, © National Pressure Ulcer Advisory Panel

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The distribution of quantitative data was tested by Kolmogorov-Smirnov test of normality. So, the quantitative data were presented as mean, standard deviations and ranges when parametric while non-parametric were presented as median with inter-quartile range (IQR). Also qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using **Chi-square test** and/or **Fisher exact test** when the expected count in any cell found less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using **Independent t-test** while with non parametric distribution was done by using **Mann-Whitney test.** The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non significant (NS), P-value < 0.05: Significant (S) and P-value < 0.01: Highly significant (HS).

RESULTS

The sample of the study consisted of 52 patients with chronic leg ulcers in two groups: 26 patients were treated with platelet rich plasma (PRP) in the first group, 26 patients were treated with vacuum assisted closure therapy (VAC) in the second group.

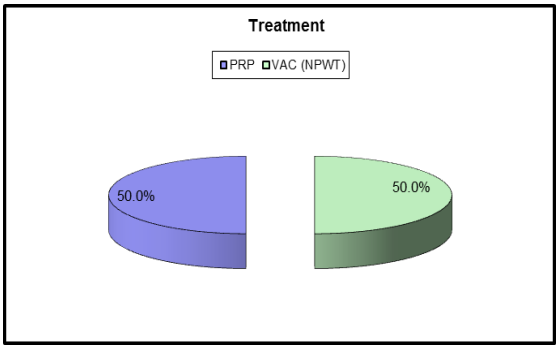

Figure (5): Distribution of cases among two studied groups.

Table (2): Demographic data of the two studied groups.

		No. = 52
Age (years)	Mean±SD Range	42.75 ± 9.63 20 – 55
Gender	Male Female	34 (65.4%) 18 (34.6%)
Special habits (smoking)	Smoker Non smoker	21 (40.4%) 31 (59.6%)

The sample of the study consisted of 52 patients in two groups: PRP group and VAC group; with a mean age of 42.75 ± 9.63 and a range of 20 to 55 years old.

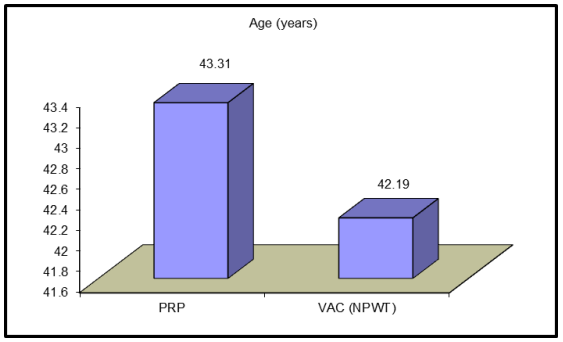

Figure (6): Comparison between PRP group and VAC group regarding age.

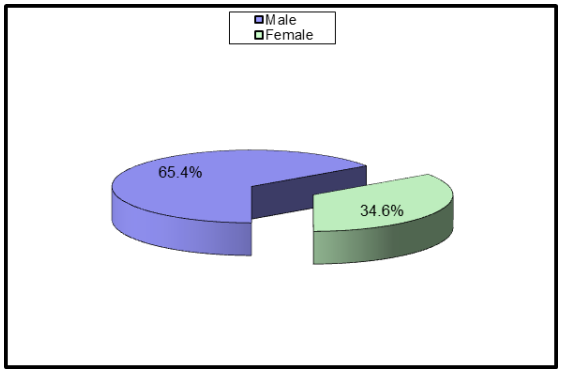

Figure (7): Gender distribution among the cases of the study in the two groups.

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This study included 52 patients; 34 patients were males (65.4%) and 18 patients were females (34.6%). 26 patients were treated with PRP; 16 patients were males (61.5%) and 10 patients were females (38.5%). The patients were treated with VAC included 26 patients; 69.2% were males (18patients) & 30.8% were females (8patients). The differences between two groups regarding gender were nonsignificant p=0.560 (NS).

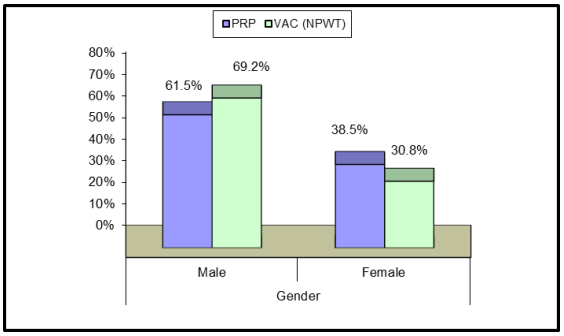

Figure (8): Comparison between PRP group and VAC group regarding gender.

In this study, 31 patients were non smoker (59.6%) and 21 patients were smokers (40.4%). 57.7% of the patients treated with PRP were non-smokers (15patients) and 42.3% were smokers (11 patients). 61.5% of the patients treated with VAC were non-smokers (16 patients) and 38.5% were smokers (10patients). The differences between PRP and VAC patients regarding special habits(Smoking) were not significant (p= 0.777).

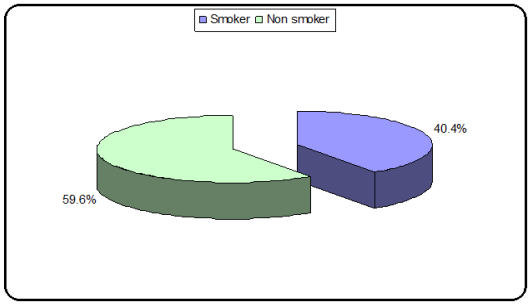

Figure (9): Percentage of Smokers and Non smokers in the total sample.

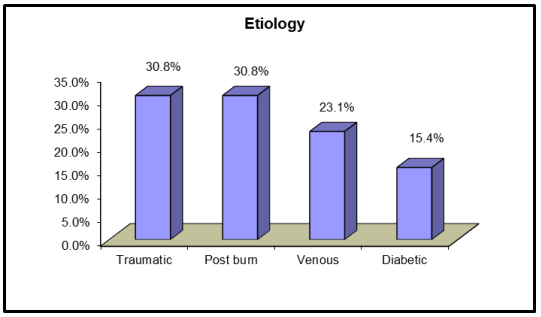

Figure (10): Etiology among the studied cases.

According to the etiology of chronic leg ulcers in patients treated with PRP and VAC; post-burn chronic leg ulcers were 30.8%, post traumatic chronic leg ulcers were 30.8%, venous chronic leg ulcers were 23.1% and diabetic chronic leg ulcers were 15.4 % (8patients).p value was 1.000 (non significant). Differences were non significant.

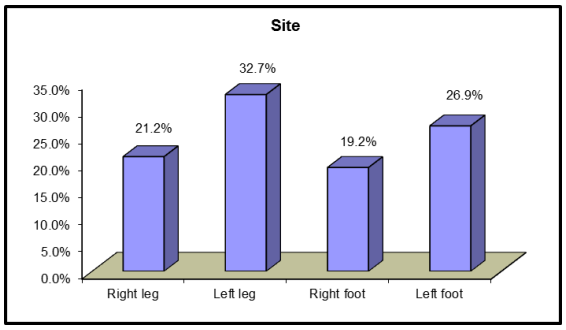

Figure (11): Site of chronic leg ulcers in two studied groups.

Regarding site of the ulcers in patients in two groups; 32.7% were in left leg, 21.2% were in right leg, 19.2% were in right foot and 26.9% were in left foot..P value was 0.728, differences between sites of ulcers were non significant.

Surface areas of ulcers in patients treated with PRP were ranged from 6 to 24 cm2 while in patients treated with VAC were ranged from 8 to 30 cm2..P value was 0.087; differences between two groups were insignificant.

Table (3): Demographic and clinical characteristics of the two studied groups **.**

		No. = 52
Gender	Male Female	34 (65.4%) 18 (34.6%)
Age (years)	Mean±SD Range	42.75 ± 9.63 20 – 55
Special habits (smoking)	Smoker Non smoker	21 (40.4%) 31 (59.6%)
Site	Right leg Left leg Right foot Left foot	11 (21.2%) 17 (32.7%) 10 (19.2%) 14 (26.9%)
Etiology	Traumatic Post burn Venous Diabetic	16 (30.8%) 16 (30.8%) 12 (23.1%) 8 (15.4%)
Surface area(cm^2)	PRP VAC (NPWT)	6-24 8-30

Table (4): Comparison between PRP group and VAC group regarding demographic and clinical characteristics.

		PRP	**VAC (NPWT)**	**Test value**	**P-value**	**Sig.**
		No. = 26	**No. = 26**			
Age (years)	Mean±SD Range	43.31±9.38 20 - 55	42.19±10.02 21 - 54	0.414•	0.680	NS
Gender	Male Female	16 (61.5%) 10 (38.5%)	18 (69.2%) 8 (30.8%)	0.340*	0.560	NS
Special habits (smoking)	Smoker Non smoker	11 (42.3%) 15 (57.7%)	10 (38.5%) 16 (61.5%)	0.080*	0.777	NS
Site	Right leg Left leg Right foot Left foot	6 (23.1%) 10 (38.5%) 4 (15.4%) 6 (23.1%)	5 (19.2%) 7 (26.9%) 6 (23.1%) 8 (30.8%)	1.306*	0.728	NS
Etiology	Traumatic Post burn Venous Diabetic	8 (30.8%) 8 (30.8%) 6 (23.1%) 4 (15.4%)	8 (30.8%) 8 (30.8%) 6 (23.1%) 4 (15.4%)	0.000*	1.000	NS

P > 0.05: Non significant; P < 0.05: Significant; P < 0.01: Highly significant.
*: Chi-square test; •: Independent t-test

Table (5): Comparison between PRP group and VAC (NPWT) group regarding Surface area of the ulcer (cm2).

Surface area of the ulcer (cm^2)		PRP No. = 26	VAC (NPWT) No. = 26	Test value≠	P-value	Sig.
Baseline	Median (IQR) Range	9 (8 – 15) 6 – 24	10 (9 – 12) 8 – 30	-1.709	0.087	NS
1st week	Median (IQR) Range	7.75 (6 – 12) 3 – 24	9 (9 – 11) 6 – 20	-2.012	0.044	S
2nd week	Median (IQR) Range	5.5 (4 – 9) 0 – 20	8 (8 – 10.5) 5 – 18	-2.546	0.011	S
3rd week	Median (IQR) Range	5 (3 – 8) 0 – 20	7.75 (7 – 10.5) 3 – 16.5	-2.711	0.007	HS
4th week	Median (IQR) Range	3.5 (0 – 8) 0 – 20	6.5 (5 – 8) 2 – 15.5	-2.011	0.044	S
5th week	Median (IQR) Range	2.5 (0 – 8) 0 – 15	6 (4.5 – 7.5) 1.5 – 14.8	-2.019	0.043	S
6th week	Median (IQR) Range	0 (0 – 7.5) 0 – 10	5.5 (4.25 – 6.75) 0 – 13.75	2.057	0.040	S
Friedman test	P-value[1]	<0.001	<0.001			
% of improvement	Median (IQR) Range	100 (75 – 100) 46.7 – 100	54.38 (42.5 – 69.44) 35.42 – 100.0	3.666	<0.001	HS

≠: Mann-Whitney test.

Surface areas of chronic leg ulcers in two groups had shown improvement but it was more rapid in patients treated with PRP, P values were significant.

Table (6): Comparison between PRP group and VAC (NPWT) group regarding exudate amount.

Exuadate amount		PRP	VAC (NPWT)	Test value*	P-value	Sig.
Baseline	None Light Moderate Heavy	0 (0.0%) 0 (0.0%) 2 (7.7%) 24 (92.3%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 26 (100.0%)	2.080	0.149	NS
1st week	None Light Moderate Heavy	0 (0.0%) 1 (3.8%) 11 (42.3%) 14 (53.8%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 26 (100.0%)	15.600	0.000	HS
2nd week	None Light Moderate Heavy	1 (3.8%) 7 (26.9%) 11 (42.3%) 7 (26.9%)	0 (0.0%) 0 (0.0%) 4 (15.4%) 22 (84.6%)	19.025	0.000	HS
3rd week	None Light Moderate Heavy	4 (15.4%) 6 (23.1%) 14 (53.8%) 2 (7.7%)	0 (0.0%) 1 (3.8%) 14 (53.8%) 11 (42.3%)	13.802	0.003	HS
4th week	None Light Moderate Heavy	7 (26.9%) 9 (34.6%) 10 (38.5%) 0 (0.0%)	0 (0.0%) 1 (3.8%) 21 (80.8%) 4 (15.4%)	21.303	0.000	HS
5th week	None Light Moderate Heavy	8 (30.8%) 8 (30.8%) 10 (38.5%) 0 (0.0%)	1 (3.8%) 4 (15.4%) 21 (80.8%) 0 (0.0%)	10.681	0.005	HS
6th week	None Light Moderate Heavy	16 (61.5%) 0 (0.0%) 10 (38.5%) 0 (0.0%)	5 (19.2%) 0 (0.0%) 21 (80.8%) 0 (0.0%)	9.665	0.002	HS
P-value[1]		< 0.001	<0.001			

*: Chi-square test.

Exuadate amounts decreased gradually in two groups but in patients treated with VAC; exuadate amounts were more than in patients treated with PRP. The differences between two groups in exuadate amounts were significant.

Table (7): Comparison between PRP group and VAC (NPWT) group regarding tissue type of the wound bed.

Tissue type of the wound bed		PRP	VAC (NPWT)	Test value*	P-value	Sig.
Baseline	Closed Epithelial tissue Granulation tissue Slough	0 (0.0%) 0 (0.0%) 0 (0.0%) 26 (100.0%)	0 (0.0%) 0 (0.0%) 0 (0.0%) 26 (100.0%)	NA	NA	NA
1st week	Closed Epithelial tissue Granulation tissue Slough	0 (0.0%) 1 (3.8%) 14 (53.8%) 11 (42.3%)	0 (0.0%) 0 (0.0%) 23 (88.5%) 3 (11.5%)	7.761	0.021	S
2nd week	Closed Epithelial tissue Granulation tissue Slough	1 (3.8%) 3 (11.5%) 21 (80.8%) 1 (3.8%)	0 (0.0%) 0 (0.0%) 26 (100.0%) 0 (0.0%)	5.532	0.137	NS
3rd week	Closed Epithelial tissue Granulation tissue Slough	4 (15.4%) 3 (11.5%) 19 (73.1%) 0 (0.0%)	0 (0.0%) 0 (0.0%) 26 (100.0%) 0 (0.0%)	8.089	0.018	S
4th week	Closed Epithelial tissue Granulation tissue Slough	7 (26.9%) 1 (3.8%) 18 (69.2%) 0 (0.0%)	0 (0.0%) 1 (3.8%) 25 (96.2%) 0 (0.0%)	8.140	0.017	S
5th week	Closed Epithelial tissue Granulation tissue Slough	8 (30.8%) 7 (26.9%) 11 (42.3%) 0 (0.0%)	1 (3.8%) 4 (15.4%) 21 (80.8%) 0 (0.0%)	9.388	0.009	HS
6th week	Closed Epithelial tissue Granulation tissue Slough	16 (61.5%) 0 (0.0%) 10 (38.5%) 0 (0.0%)	5 (19.2%) 0 (0.0%) 21 (80.8%) 0 (0.0%)	9.665	0.002	HS

*: Chi-square test.

Differences between two groups according to tissue type were significant as healing and reepithelization of chronic leg ulcers in patients treated with PRP were more rapid than patients treated with VAC.

Figure (12): Case treated with VAC therapy; (A)Female patient 54 years old with chronic post traumatic leg ulcer of 6weeks duration, (B) After two weeks of VAC therapy, (C) After 5 weeks of VAC therapy with granulation tissue formation with no reepithelization, (D) After skin grafting with well taken graft.

Table (8): Comparison between PRP group and VAC (NPWT) group regarding pressure ulcer scale for healing..

Surface area of the ulcer (cm^2)		**PRP**	**VAC (NPWT)**	**Test value≠**	**P-value**	**Sig.**
		No. = 26	**No. = 26**			
Baseline	Median (IQR) Range	9 (8 – 15) 6 – 24	10 (9 – 12) 8 – 30	-1.709	0.087	NS
1st week	Median (IQR) Range	7.75 (6 – 12) 3 – 24	9 (9 – 11) 6 – 20	-2.012	0.044	S
2nd week	Median (IQR) Range	5.5 (4 – 9) 0 – 20	8 (8 – 10.5) 5 – 18	-2.546	0.011	S
3rd week	Median (IQR) Range	5 (3 – 8) 0 – 20	7.75 (7 – 10.5) 3 – 16.5	-2.711	0.007	HS
4th week	Median (IQR) Range	3.5 (0 – 8) 0 – 20	6.5 (5 – 8) 2 – 15.5	-2.011	0.044	S
5th week	Median (IQR) Range	2.5 (0 – 8) 0 – 15	6 (4.5 – 7.5) 1.5 – 14.8	-2.019	0.043	S
6th week	Median (IQR) Range	0 (0 – 7.5) 0 – 10	5.5 (4.25 – 6.75) 0 – 13.75	2.057	0.040	S
Friedman test	P-value[1]	<0.001	<0.001			
% of improvement	Mean±SD	67.80±30.77	38.27±20.63	t=2.896	0.006	S
	Range	13.3-100	10.38 – 100			

≠: Mann-Whitney test **.**

Pressure ulcer scale for healing had shown improvement of healing in two groups, but healing in patients treated with PRP was more rapid and overcomed healing in patients treated with VAC, P value was 0.001 (significant).

Table (9): Comparison between PRP group and VAC (NPWT) group regarding healing.

Healing	PRP	VAC (NPWT)	Test value*	P-value	Sig.
	No. = 26	No. = 26			
Healed	16 (61.5%)	5 (19.2%)	9.665	0.002	HS
Non healed	10 (38.5%)	21 (80.8%)			

*: Chi-square test.

Regarding complete healing, percentage of complete healing in patients treated with PRP was 61.5% but in patients treated with VAC was 19.2 % with significant difference, P value was 0.002.

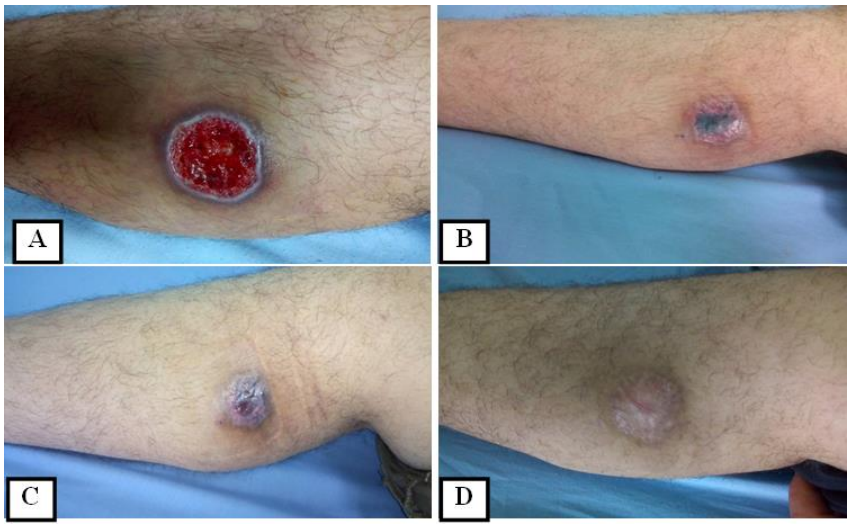

Figure (13): Case treated with PRP. (A) Male patient 38 years old with post traumatic chronic ulcer for 2 months duration he has been injected with PRP at ulcer edges and its bed, (B) Effect of PRP injection appeared only after 2 weeks with reduction size of ulcer and began to heal,(C) After one month, (D)complete healing of the ulcer after 40 days .

Clinical outcome:

In this study, there were different parameters for evaluating the clinical outcomes which included:

Percentage of improvement at the end of setting:

The percentage of improvement of the wound characters after the end of the procedure in relation to the original wound characters had been determined as in patients treated with PRP was ranged from 13.3% to 100% with Mean±SD of 67.80±30.77 . While in patients treated by VAC was ranged from 10.38 % to100% with Mean±SD of 38.27±20.63.. Regarding percentage of improvement between the two groups at the end of setting the differences had been significant (p = 0.001).

DISCUSSION

Chronic wounds had major effects in both health and economy. The most important object of any management is to gain fast closure for any wound. The conventional methods include frequent debridement, control of infection, revascularization of the affected tissues and avoidance of unnecessary pressure on the wound. **(19)**

Several studies had been shown that the application of autologous platelet factors enhanced epithelial formation by the effect of platelets in healing process. It stimulates cell division, proliferation, migration, angiogenesis and revascularization. Thus, granulation tissue formation had been promoted leading to complete repair of chronic wounds. **(20)**

Negative pressure treatment had been introduced as a component of therapy for patients with chronic wounds. It maintains a moist environment, optimizes blood flow, removes exudates and applies negative pressure to promote wound closure. These devices are able to initiate numerous factors that may be deficient in a chronic wound. Additionally, numerous studies had been shown that these devices were associated with increased rate of granulation tissue formation in these wounds. **(21)**

The aim of this work is to compare between the effects of autologous platelet rich plasma and Vacuum assisted closure therapy on improvement of healing of chronic leg ulcers.

In this study, 52 patients were included with a history of chronic leg ulcers that did not heal for six weeks or more. It had been divided into two equal groups. In the first group, 26 patients were treated by autologous platelet rich plasma. In the second group, 26 patients were treated by Vacuum assisted closure therapy. In both groups evaluation of the wounds was done using pressure ulcer scale for healing.

This study had different characters from previous trials in the type of comparison. In this study, the comparison was between the role of PRP and VAC on chronic leg ulcer healing. Previous studies had been used each type of applications separately in relation to ordinary dressings.

Other study found that most chronic ulcers healed by secondary intention after application of NPWT; 56 % of 77 patients without definitive surgical interference. On the contrary, this study had been shown that 19.2% of chronic ulcers were healed by secondary intension. **(16)**

Yao et al. (2014) Had described that healing was faster in 95% of 171 patients were treated by NPWT with different co-morbidities in the form of coronary heart disease, cerebrovascular disease, diabetes, peripheral arterial disease, chronic renal disease and congestive heart disease. In this study, all these co-morbidities had been excluded as they delayed the healing process.(22)

Previous study had been found that following NPWT, there was improvement of granulation tissue formation at the wound bed with improvement in graft survival by 90% **(23).** In this study, the patients were treated by NPWT had shown complete healing by secondary intension in 19.2% and 80,8 % healed after skin grafting.

Difference may be due to each wound had individual unique characters such as size, site, cause and type of tissue affected**.**

Platelet Rich Plasma release growth factors which are essential during the healing process in cell proliferation, angiogenesis, extracellular matrix synthesis, inflammatory regulation and aid in new tissue synthesis and remodeling.

Kakudo et al. **(2012)** used PRP in management of 5 patients with chronic ulcers in their study, they found that the average time of healing was 6.6 weeks.(24) Another study had shown complete healing of chronic ulcers when PRP was injected at subcutaneous level in and around peripheral of chronic ulcers and was combined by application of one dose of PRP gel. the mean time of ulcer healing was 8.2 weeks in twenty-four cases. **(19)** In our study, time of compete healing after injection of PRP once weekly at the edge and bed of chronic leg ulcers was 2-6 weeks and the percentage of healing was 61% of 26 patients.

Other study had described that after fifteen days the percentage of wound closure was 90% and high angiogenesis level with treatment by non-activated PRP but reached the same percent after twenty-six days in using activated PRP. In comparison between the activated and none activated platelets with thrombin in angiogenesis and complete healing in chronic diabetic ulcers. (**25)** In our study that we used activated PRP in treatment of chronic wounds but the percentage of healing was 61% with average time of 4 weeks.

Regarding PRP preparation **Sommeling et al. (2012)** concluded that no standardization in PRP preparation when they made fifteen randomized controlled trials and twenty-five case control studies in a systematic analysis.(26) In present study there was improvement of healing when we used double centrifugation technique.

Marukawa et al. (2011) noticed that there were increased about three times in platelets count and about 2 - 3 times in growth factors release from platelets with using the technique of double centrifugation for the preparation of PRP.(27) In our study we also used technique of double centrifugatuion in PRP preparation.

After PRP application and the percentage of healing was 61% in 2-6 weeks. This explains that PRP promotes formation of granulation tissue by stimulation of angiogenesis enhancing healing process.

Regarding the patients gender in this study there were 34 males and 18 females. No correlation was found between gender and the result of wound healing. This is the same as what was found in previous studies by **Suthar et al. (2017). (19)**

The method of application of PRP is another variable measure that needs to be taken into account. **Kakudo et al. (2012)** found that 8.2 ± 1.9 weeks was the mean time of healing when the greater part of PRP was applied topically on the wound site to enhance wound healing.(24) Our study had been shown that injection of PRP reduced the healing time to a mean of four weeks.

Regarding our study, we found that both VAC and PRP stimulate chronic wound healing but PRP is more favorable as there was no need to hospital stay. Ninety Hundred percent of patients treated by VAC were admitted to the hospital. Regarding the cost, VAC was more expensive than PRP. Most of the patients healed by secondary intension in PRP patients but in VAC therapy, the wound closure was done predominant by skin grafting.

CONCLUSION

There is no appropriate dressing for all types of wounds, so assessment and continuous observation of the characteristics of the wounds should be done to decide the proper dressing required. The use of negative pressure wound therapy and platelet-rich plasma can be a tool in management of chronic wounds which had no improvement with conventional dressing. It should be reserved to wounds that do not show any progress after 3 weeks with treatment of wound etiology and standard wound care. PRP is simpler, safer, less costly, shorter time for the method, less painful, no hospital stays so less transmission of infection and autologous nature in the preparation had proved the superiority of PRP over VAC therapy.

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