DOI: 10.7860/JCDR/2023/60861.17987

Original Article

Surgery Section

Comparison of the Efficacy of Autologous Platelet-Rich Plasma and Saline Dressing in Healing of Diabetic Foot Ulcer- A Randomised Control Study

S GOWSICK[1], D BALAJI[2], ARUL[3], ES UNNIKRISHNAN[4], R MANISH[5]

ABSTRACT

Introduction: According to research by the World Health Organisation (WHO), there are 347 million diabetics worldwide, and by 2030, it will overtake smoking as the seventh leading cause of death and diabetic people have a lifetime risk of up to 25% for developing a foot ulcer. Many novel techniques are emerging to fasten wound healing, including cellular therapies using Platelet-Rich Plasma (PRP) and collagen-based dressings.

Aim: To compare the efficacy between instillation of autologous PRP and conventional dressing using normal saline/povidone iodine in Diabetic Foot Ulcers (DFU).

Materials and Methods: This randomised control clinical study was conducted in the Department of General Surgery at SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India. The duration of the study was 18 months, from April 2021- September 2022. A total of 174 DFU patients were included in the study, meeting inclusion and exclusion criteria's. Patients were divided into case (n=87) and control group (n=87). For six weeks, the case group got autologous PRP, while the control groups regularly had standard dressings. Wound areas were measured using ruler scale weekly and percentage of healing was monitored for 12 weeks. The data were analysed with International Business Machines (IBM)- Statistical Package for Social Sciences (SPSS) version 21.0.

Results: In a group of 87 each, 174 patients with chronic non healing DFUs were randomly assigned to the study group (PRP) or the control group (conventional dressing method) throughout the 9 months study. The age of the patients ranged from less than 40 years to over 61 years. The age group between 51 and 60 years had the highest percentage of patients (50.6%), followed by the age group over 61 years (23.6%). About 12 weeks after the treatment, it was discovered that, the case group had a 86% reduction in wound area of 86.51±15.71 mm, whereas, the control group had a 61% reduction in wound area of 65.47±30.18 mm and 65.1% of patients from the case group showed wound healing, while 42.7% of patients from the control group showed wound healing. These findings were found to be statistically significant (p-value <0.001).

Conclusion: The use of PRP led to a higher rate of wound healing in less time when compared to traditional wound care in the therapy of chronic DFUs, as shown in the present study. For chronic DFUs, PRP was able to speed up healing, making it a potentially viable and promising treatment.

Keywords: Diabetes mellitus, Non-healing ulcer, Wound healing

INTRODUCTION

Since 1980, the prevalence of diabetes in the adult population around the world has increased from 4.7% to 8.5%. In 2012, diabetes contributed to 1.5 million fatalities. More than 2.2 million people died as a result of cardiovascular and other ailments, which were made more likely by higher than optimal blood glucose levels [1]. With over 62 million people in India, already living with diabetes, the disease is quickly assuming the position of a possible epidemic [2]. According to Wild S et al., India would see the largest growth in the number of people with diabetes worldwide, from 171 million in 2000 to 366 million in 2030. It is estimated that up to 79.4 million people in India could have diabetes mellitus by 2030 [3]. Global prevalence rates for DFUs among people with diabetes mellitus were estimated to be 6.3% [4]. The prevalence of DFU ranges from 4% to 10%, and infections, which account for 40% to 80% cases, are the most frequent cause of morbidity and mortality in DFU [5].

The PRP is plasma from the same individual that has a platelet concentration that is many times higher than the baseline amount. The prospect of utilising PRP to quicken wound healing has been researched over the past 10 years. PRP acts as a growth factor agonist by having chemotactic and mitogenic properties. All of the body's clotting and growth factors, including Vascular Endothelial Growth Factor (VEGF), endothelial growth factor, and Insulin-like Growth Factor, (IGF) are present, as well as, a high concentration of platelets. These growth factors all encourage rapid wound healing. PRP is a revolutionary advancement in the realm of wound healing. PRP reduces inflammation and supplies essential growth factors, which expedites the healing of wounds [6]. Due to its potential to promote and expedite tissue regeneration, PRP is an endogenous therapeutic technique that is gaining popularity in regenerative medicine [7]. Numerous growth factors, including Platelet-derived Growth Factor (PDGF), Epidermal Growth Factor (EGF), Fibroblast Growth Factor (FGF), Insulin-like Growth Factor-1 (IGF-1), IGF2, VEGF, Transforming Growth Factor (TGF), and Keratinocyte Growth Factor (KGF), are known to play a role in the healing of wounds [8].

Due to the high cost of the commercially available recombinant platelet gel for dressing, experiments have been conducted using platelet extract from the patient's own blood or allogenic platelet concentrate. Between 1.9% and 13.1% people worldwide, have non healing ulcers [9,10]. As the population ages and the prevalence of risk factors for atherosclerotic occlusions like smoking, obesity, and diabetes rises, chronic ulcer incidence is predicted to rise. According to estimates, at some point in their lives, people will experience chronic wounds at a rate of about 10%, with a 2.5% death rate [10]. The healing abilities of PRP are based on the physiological storage of a range of Growth Factors (GFs) with healing functions within platelets, which actively

participate in tissue regeneration [11]. These ulcers have a significant financial impact on the patient and the healthcare system. It will have an impact on the patient's quality of life and productivity. PRP speeds up the healing process and considerably reduces chronic non healing wounds. Due to antibacterial activity of the platelets, clinical data demonstrates that, infections are less common in wounds treated with PRP [12,13]. The present study aimed to assess the effects of PRP on the early wound healing trajectories of DFUs in a hospital care setting. The aim of the present study was to compare the efficacy between instillation of autologous PRP and conventional dressing using normal saline/povidone iodine in DFUs.

MATERIALS AND METHODS

This randomised control clinical study was conducted in the Department of General Surgery at SRM Medical College and Hospital and Research Centre, Kattankulathur, Tamil Nadu, India. The duration of the study was 18 months, from April 2021-September 2022. Approval of Institutional Ethics Committee was taken prior to the study (Approval number 2416/IEC/2021). CTRI registration number was CTRI/2021/06/034368.

Sample size calculation [14]: Patients were divided into two groups, 87 in each group.

Sample size was calculated using the following formula:

n=(Z1+Z2) 2 (S12+S22)/(μ1-μ2)

μ1=45. 13, μ2=18.82

S1=52.70, S2=12.50

n=20.61 (2777.29+156.25)/692.22

=60460.26/692.22

n=87

Inclusion criteria: Patients with Type 1 or Type 2 diabetes controlled by either medication or insulin, DFU of size more than 2 cm^2, all postdebridement wounds and clean ulcer bed were included in the study.

Exclusion criteria: Patients with thrombocytopenia (platelet count less than 100,000/mL or other platelet disorders), traumatic ulcer, active infection on the ulcer bed, osteomyelitis, charcot's joint and patients on current use of chemotherapy or radiotherapy were excluded in the study.

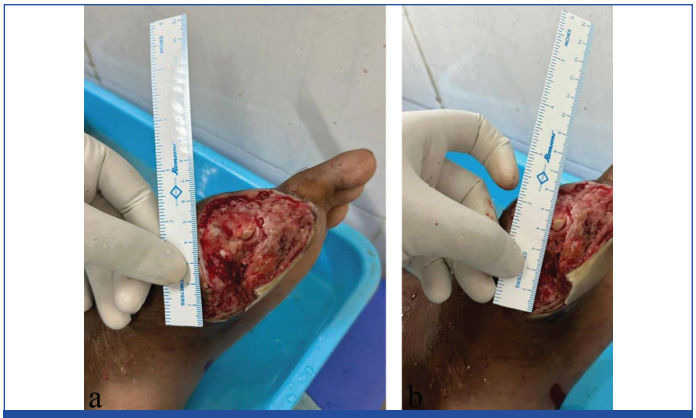
A total of 174 patients were chosen for the study, after obtaining informed and written consent. Case group (PRP group, n=87) and control group (saline dressing group, n=87) were randomised using single blinded technique. Each eligible study participant was randomly assigned to one of the treatment groups: the autologous PRP group or the control group by consecutive randomisation number. The first participating surgeon (the blinded surgeon) select the eligible patients, prepared all wounds, documented and continued to follow the wounds during the patient visits, regarding the wound size. This surgeon was blind to the type of dressing. The second surgeon (the unblinded surgeon) knew the number of the study patients and the treatment group of this patient according to a generated randomisation schedule. He also knew the type of the applied dressing and prepared dressings for the patients.

Study Procedure

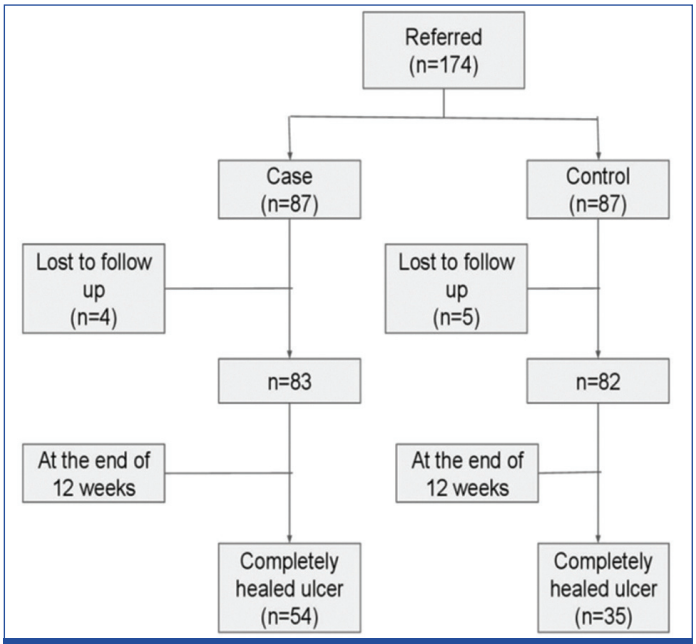
After admission, patients were taken into the study that fulfilled the inclusion criteria and written permission from those who wanted to take part. In addition, the following information was gathered: clinical history of onset, duration of ulcer, duration and treatment for diabetes mellitus and general physical examination, examination of ulcer, diagnosis, tests, and information about the last operation. Investigations include routine preoperative haematological (neutrophils, lymphocytes and platelets), biochemical (serum electrolytes, urea and creatinine), serological (Human Immunodeficiency Virus (HIV) and Hepatitis B Surface Antigen (HBsAg)), and radiological tests (foot X-rays). These tests were done to optimise the patients preoperative condition and also, before each procedure haemotological values were repeated with the normal reference range according to the hospital laboratory values.

In group A, autologous PRP was produced from the patient's peripheral blood samples and injected into the edges of the ulcers once every week for 12 weeks. In group B, patients were treated with saline dressings alone. Under rigorous aseptic conditions, autologous PRP was produced using a two fold centrifugation process. A total of 10 mL of blood was collected from the antecubital vein, and from that, 2.5 mL was split evenly between four anticoagulated (sodium citrate) tubes. The supernatant plasma was collected after five minutes of centrifugation at 1800 rpm and then transferred to two plain tubes for a second round of centrifugation at 2500 rpm. PRP, which was located in the tube's bottom layer was extracted and validated by the Department of Transfusion Medicine (blood bank). PRP was injected into the wound's margins after surgical debridement, and a non absorbent dressing was applied. After 24 hours, the patient was told to remove the bandage and clean the area thoroughly. The division repeated this procedure every week for a total of six weeks. Measurements of the wound's area and volume were taken weekly for 12 weeks using the ellipse method (length×width×0.7854 and length×breadth×depth×0.7854) cm^3. An Ellipse method is closer to a wound shape than a square or rectangle, that would be described by simple length×width. The use of an ellipse for calculating wound measurement has been used in randomised controlled trials in wound healing literature [Table/Fig-1a,b].

The distribution of cases based on the study design is explained in [Table/Fig-2].

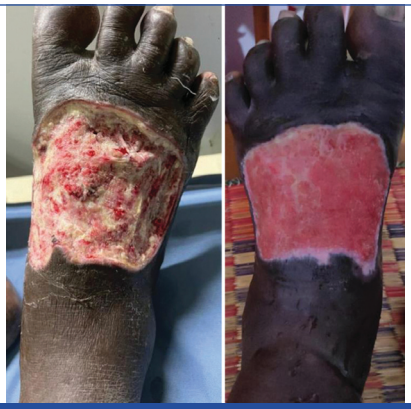


[Table/Fig-1]: Measuring the area of the ulcer using ruler scale.



[Table/Fig-2]: Consolidated Standards of Reporting Trials (CONSORT) diagram.

Follow-up was done weekly for 12 weeks. The ulcer's healing rate was measured using metric tapes measuring the dimensions (length, width, and depth) at the initial and each visit. Also, the colour of the granulation tissue [Table/Fig-3,4] was monitored, and laboratory tests (complete blood count and random blood sugar) were performed for all patients in two groups every four weeks.



[Table/Fig-3]: Ulcer bed with slough with minimal granulation.
[Table/Fig-4]: Ulcer bed with healthy granulation tissue- bright red in colour. (Images from left to right)

The endpoints of the current analysis were ulcer healing or the end of the study that occurred after week 12.

STATISTICAL ANALYSIS

Mean, standard deviation, frequency, and percentage were used to illustrate the data. To examine the differences between continuous variables, the independent sample t-test was utilised. In addition, the Pearson Chi-square test was used to compare categorical variables. The (p-value <0.05) in a two-tailed test were considered significant. The data was analysed with IBM-SPSS version 21.0.

RESULTS

Over 18 months, 174 people with chronic, non healing ulcers were randomly assigned to either a research group (plating with PRP) or a control group (traditional dressing). The effectiveness of PRP dressing compared to conventional dressing on epithelialisation, reduction, and complete healing of the non healing ulcer was investigated in both groups. In the present study, 174 patients, age ranged from less than 40 years to more than 61 years, with 88 patients between 51-60 years (50.6%), followed by 41 (23.6%) patients in age groups more than 61 years, 38 (21.8%) patients in age group 41-50 years and 7 (4.0%) patients less than 40 years. It demonstrates that most patients with chronic non healing ulcers were either older adults or those who did not respond to early therapy and whose ulcers continued to worsen despite receiving proper care. It was found that, 104 (59.8%) were males, and 70 (40.2%) were females. According to the authors research, men were more likely to get persistent, non healing ulcers [Table/Fig-5].

Out of the 174 patients with chronic non healing ulcers, the maximum number of patients were with a duration of 6-10 weeks, i.e., 82 patients (47.1%) followed by 72 patients (41.4%) in the 11-15 weeks group, 14 patients (8.0%) in more than 16 weeks and six patients (3.4%) in less than five weeks [Table/Fig-6]. It was also found that, 33 patients (37.9%) from the case group and 29 patients (33.3%) from the control group developed ulcers on the dorsum of the foot, while 54 patients (62.1%) from the case group and 58 (66.7%) from control group developed ulcers on plantar of the foot [Table/Fig-7]. Among 174 patients, 51 patients (58.6%) from the case group and 54 patients (62.1%) from the control group were taking insulin to control diabetes, while 30 patients (34.5%) from the case group and 28 patients (32.2%) from the control group were taking oral antidiabetic drugs. 6 patients (6.9%) and 5 (5.7%) from the case and control groups were taking insulin and oral antidiabetic drugs [Table/Fig-8].

Variables			Group		Total	p-value
			Case	Control		
Age group (years)	<40	Count	5	2	7	0.118
		% within group	5.7%	2.3%	4.0%	
	41-50	Count	13	25	38	
		% within group	14.9%	28.7%	21.8%	
	51-60	Count	46	42	88	
		% within group	52.9%	48.3%	50.6%	
	>61	Count	23	18	41	
		% within group	26.4%	20.7%	23.6%	
Gender	Female	Count	37	33	70	0.643
		% within group	42.5%	37.9%	40.2%	
	Male	Count	50	54	104	
		% within group	57.5%	62.1%	59.8%	

[Table/Fig-5]: Patients demographic data.

Variables			Group		Total	p-value
			Case	Control		
Duration of the ulcer (weeks)	<5	Count	4	2	6	0.56
		% within group	4.6%	2.3%	3.4%	
	6-10	Count	39	43	82	
		% within group	44.8%	49.4%	47.1%	
	11-15	Count	35	37	72	
		% within group	40.2%	42.5%	41.4%	
	>16	Count	9	5	14	
		% within group	10.3%	5.7%	8.0%	
Total		Count	87	87	174	
		% within group	100.0%	100.0%	100.0%	

[Table/Fig-6]: Total duration of the ulcer before treatment.
Chi-square test

Variables			Group		Total	p-value
			Case	Control		
Site of ulcer	Dorsum of foot	Count	33	29	62	0.527
		% within group	37.9%	33.3%	35.6%	
	Plantar of foot	Count	54	58	112	
		% within group	62.1%	66.7%	64.4%	
Total		Count	87	87	174	
		% within group	100.0%	100.0%	100.0%	

[Table/Fig-7]: Site of ulcer.
Chi-square test

Variables			Group		Total	p-value
			Case	Control		
Route of administration of antidiabetic drugs	Insulin	Count	51	54	105	0.884
		% within group	58.6%	62.1%	60.3%	
	Oral	Count	30	28	58	
		% within group	34.5%	32.2%	33.3%	
	Oral and insulin	Count	6	5	11	
		% within group	6.9%	5.7%	6.3%	
Total		Count	87	87	174	
		% within group	100.0%	100.0%	100.0%	

[Table/Fig-8]: Route of administration of antidiabetic drugs.
Chi-square test

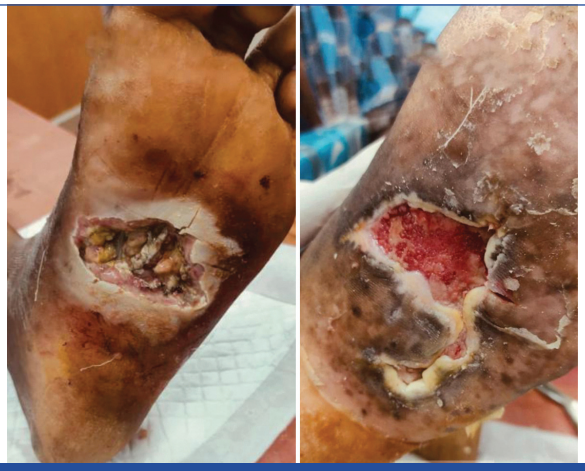
In the present study, 174 patients, the mean wound area in the initial week was found to be 51.45±8.95 mm^2 and 54.38±9.80 mm^2

in the case and control groups, respectively. However, the wound area decreased significantly in the following weeks in both groups (p-value <0.001) [Table/Fig-9].

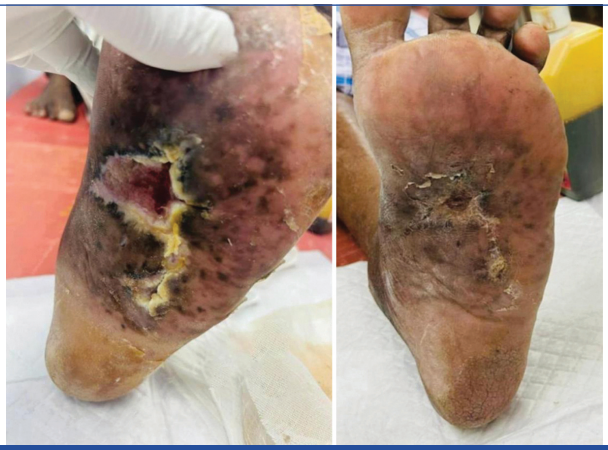
Area of wound in mm²	Group				p-value
	Case		Control		
	Mean	Standard deviation	Mean	Standard deviation	
Initial week	51.45	8.95	54.38	9.80	0.889
2nd week	36.11	7.91	45.42	12.70	<0.001
4th week	25.42	9.62	36.09	17.67	<0.001
6th week	17.65	12.38	30.46	17.17	<0.001
8th week	12.72	12.65	28.13	19.43	<0.001
10th week	10.61	11.20	25.39	18.93	<0.001
12th week	7.52	9.29	20.76	18.63	<0.001

[Table/Fig-9]: Area of wound.
Independent sample t-test

One complete case is provided with the images [Table/Fig 10-13] after PRP treatment. When the percentage reduction in wound area was compared, it was found that, 86.51±15.71 mm was observed in the case group, while 65.47±30.18 mm was observed in the control group after 12 weeks of treatment. These findings were found to be statistically significant (p-value <0.001) [Table/Fig-14].



[Table/Fig-10]: Preoperative image.
[Table/Fig-11]: Second week after autologous PRP treatment with healthy granulation. (Images from left to right)



[Table/Fig-12]: Fourth week after PRP treatment.
[Table/Fig-13]: Fifth week after PRP treatment- complete healing with epithelisation. (Images from left to right)

Among 174 study patients, 12 showed wound healing at 6 weeks, and 10 showed healing at 8 weeks, 13 at 10 weeks, and 19 at 12 weeks from the case group. None of the control group patients showed wound healing until 10 weeks in the study. A total of 15 patients in control group showed wound healing at ten weeks, while 20 patients showed wound healing at 12 weeks of treatment.

Percentage reduction in wound healing (%)	Group				p-value
	Case		Control		
	Mean	Standard deviation	Mean	Standard deviation	
2nd week% of the area of reduction	29.91	8.14	18.36	12.41	<0.001
4th week % of the area of reduction	51.41	14.11	36.79	25.04	<0.001
6th week % of the area of reduction	66.50	21.55	47.38	25.23	<0.001
8th week % of the area of reduction	76.51	21.96	51.92	30.26	<0.001
10th week % of the area of reduction	80.37	19.84	57.12	30.41	<0.001
12th week % of the area of reduction	86.51	15.71	65.47	30.18	<0.001

[Table/Fig-14]: Percentage reduction in wound healing.
Independent sample t-test

These findings were found to be statistically significant (p-value <0.001) [Table/Fig-15].

Four patients from the case group and five from the control group lost the follow-up. When wound healing was considered at the end of 12 weeks, 54 (65.1%) cases and 35 (42.7%) cases showed wound healing from the case and control groups, respectively. About 12 weeks after the treatment, it was discovered that, the case group had a 86% reduction in wound area, whereas, the control group had a 61% reduction in wound area. As p-value <0.003, these findings were found to be statistically significant [Table/Fig-16].

Variables			Group		Total	p-value
			Case	Control		
Duration of wound healing (weeks)	6	Count	12	0	12	<0.001
		% within group	22.2%	0.0%	13.5%	
	8	Count	10	0	10	
		% within group	18.5%	0.0%	11.2%	
	10	Count	13	15	28	
		% within group	24.1%	42.9%	31.5%	
	12	Count	19	20	39	
		% within group	35.2%	57.1%	43.8%	
Total		Count	54	35	89	
		% within group	100.0%	100.0%	100.0%	

[Table/Fig-15]: Duration of wound healing in weeks.
Chi-square test

Variables			Group		Total	p-value
			Case	Control		
Wound healing in 12 weeks	Yes	Count	54	35	89	0.003
		% within group	65.1%	42.7%	53.9%	
	No	Count	29	47	76	
		% within group	34.9%	57.3%	53.9%	
Total		Count	83	82	165	
		% within group	100.0%	100.0%	100.0%	

[Table/Fig-16]: Wound healing at 12 weeks.
Chi-square test

DISCUSSION

Particularly in developing nations like India, DFUs pose a severe health risk since, they lack the GFs required for healing, are frequently challenging to treat, and are frequently accompanied by super added infections. Quickly achieving wound closure is the primary objective of all treatment modalities. The standard course of treatment entails thorough wound debridement, revascularisation of ischaemic tissue, infection control, and avoidance of excessive

wound pressure. Although, skin grafting has shown some promise, it is pricey and unable to supply the GFs required to control the healing process [15]. The present research aims to see if PRP may improve the healing rates of chronic, non healing ulcers. Patients in the present trial in the PRP dressing group and the traditional dressing group were comparable at baseline regarding age, sex, and ulcer site. In the current prospective randomised controlled trial on PRP to treat chronic non healing ulcers, 174 patients were split evenly between a case group and a control group, for a total of 87. The case group received PRP, while the control group received conventional dressing. Therefore, the wound area in the case group was much less than in the control group. Statistics showed a statistically significant (p-value <0.001) decrease in wound area. The goal of the current study was, to evaluate the effectiveness of PRP to a standard dressing of normal saline in the treatment of clean, non healing DFU. Since, autologous blood was inexpensive and simple to get, the authors utilised it to make PRP. Marx RE and Elsaid A et al., also used autologous blood for preparing PRP as it has no special considerations regarding antibody formation [15,16]. Although, there are other options for treating DFU, including Vacuum Assisted Closure (VAC) therapy, biologic dressings, and oxygen therapy, the authors chose normal saline as the control group because it is inexpensive, accessible, and widely used, in contrast to the other treatment modalities, which, despite being more effective, may have restricted availability and prohibitive costs, especially in developing countries.

According to Margolis DJ et al., research that involved 26,599 individuals, patients who received platelet-derived products had a tendency to heal more quickly than patients who get other types of treatments [17]. He said that eventhough, the ulcers treated with these compounds were larger and deeper than those in the other groups, they nevertheless healed more quickly after 12 weeks. Similar findings were seen in the present study, where ulcers treated with Platelet-rich Fibrin (PRF) improved more quickly and effectively than those treated with saline dressing. Somani A et al., found similar outcomes with a p-value <0.001 and t=4.11, the mean reduction in the area of the ulcer size in the PRF group was 85.51%, while the mean reduction in the area of the ulcer size in the saline group was 42.74% [18]. In the present study, the case group recovered more patients than the control group. After 12 weeks, 65.1% of the case group's patients had healed their wounds, compared to 42.7% of the control group's patients. It was determined that, these results were statistically significant (p-value <0.001) According to Martinez-Zapata MJ et al., PRP treated wounds had a higher percentage of overall healing than the controls [19]. The same findings were drawn by Villela V et al., [20]. After the second week, PRP was shown to be more efficient than standard dressing in the study by Prakasam N et al., [21]. At the fourth week, the same result was reported. This might be explained by the fact that platelets are activated during wound healing by coming into touch with collagen and are then released into the circulation following endothelial damage. Complete healing of chronic, non healing ulcers was shown to occur with the injection of autologous platelet factors by Knighton DR et al., in 1986. This clinical research first demonstrated the fascinating potential of locally active components taken from autologous blood to speed up the healing of persistent cutaneous ulcers [22].

Oyibo SO et al., discovered that, the ulcer area in diabetic patients was connected with healing time (p-value <0.001) and was predictive of healing (p-value=0.004) in research involving 194 patients. Healing was not impacted by the patient's age, sex, or ulcer duration. A substantial link between the ulcer diameter and the healing rate was discovered by Oyibo SO et al., using traditional wound therapy (as it was in some of the current studies) [23]. In a research by Frykberg RG et al., on 49 patients who had 65 non healing ulcers, it was shown that, 63 out of 65 ulcers reacted with a decrease in area and volume of the ulcers over the course of a mean of 2.8 weeks and 3.2 treatments [24]. Five cases of intractable skin ulcers were treated by Kakudo N et al., using autologous PRP; three of the ulcers totally recovered within 4 weeks, and the wound epithelised, on average, in 6.6 weeks [25].

Any difference in the rate of wound healing in controlling blood sugars using oral hypoglycaemic drugs or insulin were not explained. Because, the pace of healing might vary between the dorsum and plantar surfaces, the ulcer's placement can be thought of as a complicating factor. In comparison to those receiving insulin, patients using oral medicines may experience slower healing times. Although, the findings of several studies using PRP to treat non healing ulcers have been encouraging, there is still a lack of important scientific information regarding the positive effects of PRP in clinical treatments [26]. The study's sample size was small to make conclusions about the general population. Additionally, the follow-up was brief in order to draw a conclusion about the use of PRP for long term ulcer healing. To firmly establish the effectiveness of PRP dressing, additional randomised controlled prospective clinical trials are required. Furthermore, a consistent protocol for the creation of PRP is required, as there is currently no standardisation of the technique in the literature. These trials should be designed with rigorous study protocols and should include larger sample sizes, diverse populations, and longer follow-up periods. This will help to ensure that, the results are reliable and can be applied to a wider range of patients.

Limitation(s)

The difference in the rate of wound healing between patients taking oral hypoglycaemic drugs and insulin is not monitored it may be difficult to determine which medication is more effective in promoting wound healing in diabetic patients. Therefore, the lack of monitoring could potentially limit the conclusions that can be drawn from the study and impact the treatment of diabetic patients with wounds. Monitoring the differences in the rate of wound healing between the dorsal and plantar aspects is important because the location of the wound can affect the rate and quality of healing. For instance, wounds on the plantar aspect of the foot (the sole) may take longer to heal due to the pressure and weight placed on the area during standing and walking. Similarly, wounds on the dorsal aspect (the back) may be exposed to different levels of friction and pressure that can impact the rate of healing.

CONCLUSION(S)

Around the world, ulcers and other persistent wounds that refuse to heal are increasingly a public health concern. The traditional methods used to treat persistent ulcers and wounds take time and money. The use of PRP led to a higher rate of wound healing in less time when compared to traditional wound care in the therapy of chronic DFUs, as shown in the present study. As a result, the person's performance should improve, and long term foot ulcer treatment costs should decrease.

REFERENCES

[1] Global report on diabetes. World Health Organization. ISBN 978 92 4 156525 7 (NLM classification: WK 810). World Health Organization 2016.
[2] Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. Australas Med J. 2014;7(1):45-48.
[3] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes-estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(3):1047-53.
[4] Abuhay HW, Yenit MK, Wolde HF. Incidence and predictor of diabetic foot ulcer and its association with change in fasting blood sugar among diabetes mellitus patients at referral hospitals in Northwest Ethiopia, 2021. Plos one. 2022;17(10):e0274754.
[5] Singh AK, Yeola M, Singh N, Damke S. A study on diabetic foot ulcers in Central rural India to formulate empiric antimicrobial therapy. Journal of Family Medicine and Primary Care. 2020;9(8):4216.
[6] Ullah A, Jawaid SI, Qureshi PNAA, Siddiqui T, Nasim K, Kumar K, et al. Effectiveness of injected platelet-rich plasma in the treatment of diabetic foot ulcer disease. Cureus. 2022;14(8):e28292. Doi:10.7759/cureus.28292.

[7] Anitua E, Alkhraisat MH, Orive G. Perspectives and challenges in regenerative medicine using plasma rich in growth factors. J. Control. Release. 2012;157(1):29-38.
[8] Chicharro-Alcántara D, Rubio-Zaragoza M, Damiá-Giménez E, Carrillo-Poveda JM, Cuervo-Serrato B, Peláez-Gorrea P, et al. Platelet rich plasma: new insights for cutaneous wound healing management. J Funct Biomater. 2018;9(1):10.
[9] Rayner R, Carville K, Keaton J, Prentice J, Santamaria N. Leg ulcers: Typical presentations and associated comorbidities. Wound Pract Res. 2009;17(4):168-85.
[10] Agale SV. Chronic leg ulcers: Epidemiology, an etiopathogenesis, and management. Ulcers. 2013;2013:413604.
[11] Andia I, Abate M. Platelet-rich plasma: Underlying biology and clinical correlates. Regen Med. 2013;8(5):645-58.
[12] Lacci MK, Dardik A. Platelet-rich plasma: Support for its use in wound healing. J Biol Med. 2010;83(1):01-09.
[13] Carter MJ, Fylling CP, Parnell LK. Use of platelet-rich plasma gel on wound healing: A systematic review and meta-analysis. Eplasty. 2011;11:e38.
[14] Tsachiridi M, Galyfos G, Andreou A, Sianou A, Sigala F, Zografos G, et al. Autologous platelet-rich plasma for nonhealing ulcers: A comparative study. Vasc Specialist Int. 2019;35(1):22-27. Doi: 10.5758/vsi.2019.35.1.22. PMID: 30993104; PMCID: PMC6453601.
[15] Marx RE. Platelet-rich plasma: Evidence to support its use. J Oral Maxillofac Surg. 2004;62(4):489-96.
[16] Elsaid A, El-Said M, Emile S, Youssef M, Khafagy W, Elshobaky A. Randomized controlled trial on autologous platelet-rich plasma versus saline dressing in treatment of non healing diabetic foot ulcers. World Journal of Surgery. 2020;44:1294-301.
[17] Margolis DJ, Kantor J, Santanna J, Strom BL, Berlin JA. Effectiveness of platelet releasate for the treatment of diabetic neuropathic foot ulcers. Diabetes Care. 2001;24:483-88.
[18] Somani A, Rai R. Comparison of efficacy of autologous platelet-rich fibrin versus saline dressing in chronic venous leg ulcers: A randomised controlled trial. Journal of Cutaneous and Aesthetic Surgery. 2017;10(1):8.
[19] Martinez-Zapata MJ, Martí-Carvajal AJ, Solà I, Expósito JA, Bolíbar I, Rodríguez L. Autologous platelet-rich plasma for treating chronic wounds. Cochrane Database Syst Rev. 2012;10:89-92.
[20] Villela V, Falanga A, Brem H, Ennis W, Wolcott R, Gould L, et al. Role of PRP and maintenance debridement in treatment of difficult-to-heal chronic wounds. Ostomy Wound Manage. 2010;6(3):2-13.
[21] Prakasam N, Prabakar MS, Reshma S, Loganathan K, Senguttuvan K. A clinical study of platelet rich plasma versus conventional dressing in management of diabetic foot ulcers. International Surgery Journal. 2018;5(10):3210-16.
[22] Knighton DR, Ciresi KF, Fiegel VD, Austin LL, Butler EL. Classification and treatment of chronic non healing wounds: Successful treatment with autologous platelet-derived wound healing factors (PDWHF). Ann Surg. 1986;204:322-30.
[23] Oyibo SO, Jude EB, Tarawneh I, Nguyen HC, Armstrong DG, Harkless LB, et al. The effects of ulcer size and site, patients age, sex and type and duration of diabetes on the outcome of diabetic foot ulcers. Diabet Med. 2001;18(2):133-38.
[24] Frykberg RG, Driver VR, Carman D, Lucero B, Borris-Hale C, Fylling CP, et al. Chronic wounds treated with a physiologically relevant concentration of platelet-rich plasma gel: A prospective case series. Ostomy Wound Manage. 2010;56:36-44.
[25] Kakudo N, Kushida S, Ogura N, Hara T, Suzuki K. The use of autologous platelet rich plasma in the treatment of intractable skin ulcer. Open J Reg Med. 2012;1:29-32.
[26] Suryanarayan S, Budamakuntla L, Khadri SI, Sarvajnamurthy S. Efficacy of autologous platelet-rich plasma in treating chronic non healing leg ulcers. Plastic and Aesthetic Research. 2014;1:65-69.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate, Department of General Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India.
2. Professor, Department of General Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India.
3. Assistant Professor, Department of General Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India.
4. Postgraduate, Department of General Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India.
5. Postgraduate, Department of General Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. D Balaji,
Professor, Department of General Surgery, SRM Medical College Hospital and Research Centre, Kattankulathur-603203, Tamil Nadu, India.
E-mail: trace.balaji@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 28, 2022
- Manual Googling: Mar 17, 2023
- iThenticate Software: Apr 19, 2023 (10%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Oct 27, 2022**
Date of Peer Review: **Dec 31, 2022**
Date of Acceptance: **Apr 26, 2023**
Date of Publishing: **May 01, 2023**