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A randomized control trial exploring the efficacy of autologous platelet rich fibrin (PRF) compared to moist sterile saline dressing in the treatment of chronic venous leg ulcers

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Abstract

Background and objective: To assess the effectiveness of autologous platelet-rich fibrin (PRF) compared to saline dressing in patients suffering from chronic venous leg ulcers.

Method: A prospective randomized controlled trial was conducted using an open label approach, involving patients diagnosed with chronic venous leg ulcers, from July 2017 to June 2018. Following the acquisition of consent from the ethics committee, the current study was conducted, involving 13 patients.

Result: The patient population consisted of 5 females (27% of the total) and 8 males (73%). The group that received PRF treatment had a notable decrease in ulcer size in comparison to the saline group. At the conclusion of a four-week period, the PRF group exhibited a mean reduction in ulcer area of 87.95%, whereas the saline group had a reduction of 44.89%.

Conclusion: The findings of our research demonstrate a significant and noteworthy reduction in ulcers among individuals who were administered PRF dressings, in comparison to the cohort treated with saline, following a period of 4 weeks. The efficacy, simplicity, patient-friendliness, cost-effectiveness, painlessness, and outpatient nature of Platelet Rich Fibrin dressings make them a highly useful adjunctive therapy for the treatment of persistent venous ulcers. The technique outlined above demonstrates significant potential in achieving thorough closure of ulcers and can be successfully included as a standard procedure for the treatment of venous ulcers.

Keywords: Chronic venous leg ulcers, platelet rich fibrin, chronic venous insufficiency

Introduction

Venous ulcers are the most dreaded outcome of Chronic Venous Insufficiency (CVI). Approximately 75-78% of leg ulcers are classified as venous ulcers. An ulcer is classified as chronic when it endures for a duration beyond six weeks. It has a significant impact on the overall quality of life. The occurrence of venous ulcers can result in considerable morbidity and impairment, often underestimating their capacity to induce serious physical and psychological suffering among patients. The correlation between the occurrence of varicose veins and advancing age is an often-observed phenomenon. This observation is frequently observed among individuals afflicted with venous ulcers worldwide. There is a higher prevalence of venous ulcers observed in females compared to males. The chronic and recurrent nature of this ailment is well-documented to have significant psychological and socio-economic implications for the individual's well-being. Multiple studies indicate that individuals with venous ulcers have significantly fewer working days compared to those who are healthy. The deprivation of work days and the economic strain of ongoing medical care have a detrimental effect, not only on the individual receiving treatment, but also on their family. The management of venous ulcers is characterized by a prolonged duration and a notable propensity for recurrence. There are multiple therapy options available, the majority of which focus on addressing the root problem [1-3].

In addition to the treatment, it is important to provide the patient with counselling regarding the disease and the strategies they can employ to minimize the likelihood of the issue recurring. The primary objective of medical practitioners in the management of venous ulcers is to minimize ulcer size and mitigate the risk of ulcer recurrence.

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Given the chronic nature of this ailment, the ulcer lacks the necessary growth elements and nutrients essential for the healing process. This factor may contribute to the prolonged healing process of the ulcer. Dressings are crucial in the process of curing these ulcers. It is well-established that moist occlusive dressings enhance the process of wound healing. Platelet concentrates play a crucial role in expediting the healing process by providing essential growth factors and nutrients necessary for ulcer formation, as well as stimulating and facilitating wound healing. There exists a variety of platelet-rich concentrates, each possessing distinct applications within the field of medicine.

The utilization of blood-derived products for the purpose of wound and ulcer closure and healing commenced approximately five decades ago. The platelet concentrate utilized for the treatment of ulcers was Platelet Rich Fibrin (PRF). The efficacy of blood-derived products in promoting wound healing was initially documented by Whiteman *et al.* Subsequently, the utilization of these products has gained significant popularity during the past 15 years [4, 5, 6].

Material and Methods

A prospective randomized controlled trial with an open label design was done at Department of Dermatology, Sambhram Institute of Medical Sciences and Research, Bangalore, Karnataka, India from July 2017 to June 2018 in patients diagnosed with persistent venous leg ulcers. The present investigation was undertaken subsequent to obtaining approval from the ethics committee, encompassing a sample size of 13 patients. The participants were divided into two groups: Group 1, referred to as the Treatment Group, consisted of patients with chronic venous ulcers who were administered Platelet Rich Fibrin (PRF) dressing in addition

to a standardized routine of wound care and rest. Group 2, also known as the control group, consisted of patients diagnosed with chronic venous ulcers who were administered moist saline dressings in addition to a standardized routine of adequate wound care and rest.

Inclusion criteria

1. Patients with persistent lower extremity venous ulcers lasting over 6 months, seeking care at the Dermatology Venereology and Leprosy Outpatient Department (OPD).
2. The ulcer area ranges from 1cm x 1cm to 5cm x 5cm.

Exclusion criteria

1. Ulcers with a duration of fewer than six months.
2. There are various types of ulcers that can arise from different causes, including neuropathic ulcers, arterial ulcers, diabetic ulcers, and ulcers with underlying vasculitis.
3. Individuals suffering from osteomyelitis in the specific region of the ulcer
4. Exposed tendons or bones in the form of ulcers. 5cm x 5cm ulcers
5. Pseudomonas-infected ulcers with abundant exudate
6. Individuals undergoing treatment with anticoagulants, antiplatelet medications, or bleeding diathesis.
7. Individuals under the age of 18 or over the age of 80
8. Pregnancy
9. Lactation
10. Patient who did not give consent

Result

Table 1: Patients treated with PRF Dressing

Patients treated with PRF Dressing						
S. No. of patient	Initial measurement in cm ²	Measurement after 1 st week	Measurement in cm ² after 2 nd week	Measurement in cm ² after 3 rd week	Final measurement in cm ²	Percentage of improvement
1.	3.7	1.99	3.0	1.6	2.6	7.5%
2.	4.1	2.98	2.5	0.0	0.0	100%
3.	14.9	10.26	8.15	6.98	0.0	100%
4.	7.0	4.6	1.0	0.0	0.0	100%
5.	16.23	15.96	14.12	10.96	10.21	46.54%
6.	4.98	4.3	1.65	0.0	0.0	100%
7.	1.9	1.6	2.9	0.0	0.0	100%
8.	10.98	10.8	9.98	7.9	4.25	67.65%
Mean percentage of improvement	0%	26.27%	46.25%	77.08%	85.51%	88.21%

Table 2: Patients treated with Saline Dressing

Patients treated with Saline Dressing						
S. No. of patient	Initial measurement in cm ²	Measurement after 1 st week	Measurement in cm ² after 2 nd week	Measurement in cm ² after 3 rd week	Final measurement in cm ²	Percentage of improvement
1	2.1	2.1	2.5	0.99	0.99	29.28%
2	6.1	5.89	5.96	4.08	3.3	42.10%
3	14.1	13.5	13.4	12.0	12.0	14.65%
4	4.1	3.18	3.5	1.87	1.6	58.95%
5	4.3	3.6	3.9	2.21	1.6	58.65%
Mean percentage of improvement	0%	15.96%	28.29%	38.95%	45.89%	49.86%

Table 3: Group Statistics

Group Statistics					
Variables	No of Patients	Mean	Std. Deviation	t value	P value
Saline	5	44.56	15.64	6.24	<0.001
PRF	8	83.65	22.35		

Discussion

The tissue's ability to regenerate forms the basis for surgical intervention. The skin serves a dual function within the human body, functioning as one of the five sensory modalities. Its primary role is to detect tactile inputs, while also serving as a protective barrier to secure the body. The compromise or duration of this condition could potentially lead to the exposure of vital structures within the body, which may result in disease and impairment due to injury, infection, and, in certain instances, mortality. Acute wounds, which are characterized as wounds that have not exceeded a duration of 6 weeks, undergo a multifaceted and methodical process of molecular and physiological reconstruction. Nevertheless, the healing process varies in wounds that exceed a duration of 6 weeks, and these wounds are commonly known as chronic wounds. In contrast to acute wounds, the healing process in chronic wounds appears to be impeded by numerous local and systemic variables. In such cases, the healing process necessitates further stimulation, which is accomplished by administering platelet-rich fibrin. This includes numerous growth factors that are essential in initiating and promoting wound healing. These components are released in a progressive manner as necessary to facilitate expeditious and effective recovery [7-9].

In the current study, a cohort of 15 individuals was enlisted and subsequently divided into two independent cohorts. A total of nine patients were assigned to Group 1, where they were administered a weekly PRF dressing for a period of four weeks. A total of six patients were assigned to Group 2, who underwent a weekly saline dressing treatment for a period of four weeks. The cohort that had PRF treatment exhibited a significant reduction in ulcer size as compared to the group that received saline treatment. Based on Callam MJ's research, it has been observed that women have a greater incidence of varicose veins and venous ulcers as compared to men. The study revealed that the incidence of venous ulcers was 27% among females and 73% among males. The small sample size in our study may be linked to the cause behind this. In a study conducted by David J. Margolis *et al.*, a total of 26,599 individuals were examined. The findings revealed that patients who underwent therapy with platelet-derived products demonstrated a more rapid healing process in comparison to those who did not receive such products. Furthermore, he concluded that although these derivatives treated larger and deeper ulcers compared to the other groups, they demonstrated improved recovery after 12 weeks. Our study's findings suggest that ulcers treated with PRF showed more significant and faster recovery compared to saline dressing [10-12].

Sean M. O Connell's study reveals that the treatment of venous and non-venous ulcers has different outcomes. The researcher provided evidence indicating that a total of 66.7% of individuals diagnosed with venous ulcers who underwent treatment including platelet rich fibrin membrane achieved full wound healing. On the other hand, only 44% of patients diagnosed with non-venous ulcers were able to achieve full closure. Consequently, he provided evidence to

support the efficacy of PRF in the treatment of venous ulcers. In a distinct study, Anita E *et al.* shown a significant improvement in the healing process with the application of PRF. Furthermore, the researcher arrived at the determination that it not only enables the supply of essential growth factors (GFs), but also plays a role in the development of a fibrin matrix that assists in cellular migration and stimulates the production of new blood vessels. In our investigation, it was revealed that the group subjected to PRF treatment had an average reduction in ulcer size of 85.51% over a period of 4 weeks. Mazzucco *et al.* conducted an independent study and arrived at the finding that the use of platelet-rich gel on wounds results in improved healing and expedited recuperation. Furthermore, he posited that this also contributes to reducing the length of hospital stays. The findings of the study indicate that individuals who underwent platelet rich gel therapy exhibited wound healing after a duration of 3.5 weeks, but those who did not receive such treatment required a longer period of 6 weeks.

According to our study, 55.55% of patients who underwent PRF treatment successfully achieved full closure within a 4-week timeframe. Full closure was not accomplished by any of the patients who underwent saline therapy [13-15].

A distinct study conducted by G. Saldalamacchia revealed that the application of platelet-rich fibrin shown significant effectiveness in the treatment of ulcers. The individual claimed that the incorporation of platelet-rich fibrin led to a more pronounced reduction in ulcer area in comparison to the traditional wound care approach that did not involve the use of platelet-rich fibrin. Furthermore, he asserted that although the patients received PRF for a short period, it led to substantial enhancement. Similarly, our study found that patients who had PRF treatment experienced an average decrease of 85.51% in ulcer area after a period of 4 weeks. On the other hand, individuals who were administered saline dressing demonstrated a decrease of merely 42.74% in the region impacted by the ulcer. The study conducted by Hany Saad Setta *et al.* aimed to evaluate the efficacy of platelet rich plasma and platelet poor plasma in the treatment of diabetic ulcers by a comparative analysis. The present investigation effectively established that the period of wound healing for ulcers treated with platelet-rich plasma was notably reduced as compared to ulcers treated with platelet-poor plasma [16-18].

In a separate investigation carried out by Bernuzzi *et al.*, the efficacy of the platelet-rich gel in diminishing the time of the healing process was revealed. The individual exhibited a significant influence on the multiplication of cells, hence considerably enhancing the process of wound healing. Furthermore, he claimed that this impact depended on the dosage. Steed DL *et al.* conducted a randomized trial to examine the efficacy of activated platelet supernatant in the treatment of diabetic ulcers. The study found that the use of activated platelet supernatant resulted in significantly better outcomes in terms of complete ulcer healing and closure compared to a placebo administered solely with saline solution. During his trial, he achieved a closure and healing

rate of 94% at the end of 20 weeks using the platelet supernatant, while the placebo group only achieved a closure rate of 73%. The researcher concluded that the platelet supernatant exhibited use in reducing the duration of treatment required for chronic ulcers.⁶⁶ In the conducted study, it was observed that among the five patients who exhibited complete closure using PRF dressing, one patient reached closure within a two-week period, three patients achieved closure after three weeks, and one patient achieved closure after four weeks. Multiple investigations have yielded inconclusive results about the efficacy of saline dressing in improving ulcers. Our investigation also yielded similar results^[19-21].

Conclusion

The results of our study indicate a notable and statistically significant decrease in ulcers among patients who received PRF dressings, as compared to the group treated with saline, after a duration of 4 weeks. The application of Platelet Rich Fibrin dressings as an additional therapy for chronic venous ulcer treatment is extremely effective due to its efficacy, simplicity, patient-friendliness, cost-effectiveness, painlessness, and outpatient nature. The aforementioned technique exhibits considerable promise in attaining comprehensive ulcer closure and can be effectively integrated as a standard process for the management of venous ulcers.

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Conflict of interest

None.

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