Original Article

# Comparison of Efficacy of Autologous Platelet-rich Fibrin versus Saline Dressing in Chronic Venous Leg Ulcers: A Randomised Controlled Trial

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## Abstract

**Background:** Venous leg ulcer is a chronic condition, and various treatment modalities are available. Platelet-rich fibrin (PRF) is one of the newer modalities and it contains fibroblast growth factor (GF), vascular endothelial GF, angiopoitin and platelet-derived GF which enhances the wound healing. Hence, we conducted a randomised controlled trial to compare the efficacy of PRF versus saline dressing in chronic venous leg ulcers. **Aim:** This study aims to compare the efficacy of autologous PRF with saline dressing in patients with chronic venous leg ulcer and to compare the mean reduction in ulcer area at the end of 4 weeks. **Materials and Methods:** Fifteen patients with chronic venous leg ulcers of >6 months duration having an ulcer area of 1 cm × 1 cm to 5 cm × 5 cm were taken into the study and were randomly divided into two groups. Group 1: Patients received PRF dressing. Ten millilitres of patient's blood was taken and centrifuged at 3000 rpm for 15 min. A fibrin clot obtained in the middle of the tube was removed and used for dressing over the wound surface. It was repeated every week for 4 weeks. Group 2: Patients received saline dressings once a week for 4 weeks. The assessment of the ulcer size was done with the help of photographs, and ulcer area was measured. **Results:** The mean reduction in the area of the ulcer size in PRF group was 85.51%, and the mean reduction in the area of the ulcer size in Saline group was 42.74% which was statistically significant with a $P < 0.001$ and $t = 4.11$. **Conclusion:** We conclude that PRF dressing can be used as it is effective, inexpensive, safe and an outpatient procedure.

**Keywords:** Platelet-rich fibrin, saline, venous ulcers

## Introduction

Various modalities of treatment for venous ulcers include compression stockings, good wound care and sometimes surgical therapies. The treatment is often difficult and is generally associated with high recurrence rate.[1-3] Dressings play a major role in healing of these ulcers. Moist occlusive dressings with saline are known to improve wound healing. Platelet concentrates have been widely used in regenerative medicine to promote wound healing as they contain transforming growth factor (GF) *F*, platelet-derived GF, vascular-endothelial GF, platelet derived epidermal GF, insulin-like GF-I and basic fibroblast GF. Hence, we conducted a study to compare the efficacy of autologous platelet rich fibrin (PRF) over saline dressing in chronic venous leg ulcers.

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## Materials and Methods

### Selection and description of participants

A total of 15 patients were randomly divided into two groups on the basis of inclusion and exclusion criteria.

#### *Inclusion criteria*

Patients suffering from chronic venous ulcers of the lower extremity for more than 6 months, with an ulcer area varying from 1 × 1 cm to 5 × 5 cm attending the out-patient Department of Dermatology Venereology and Leprosy were included.

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### *Exclusion criteria*

Ulcers of >6 months duration, size less than 1 sq cm or more than 5 sq cm and neuropathic, arterial, diabetic or vasculitic ulcers vasculitis. Patients with infected ulcers, osteomyelitis affecting the area of the ulcer , ulcers with exposed tendons or bones Ulcers with exposed tendons or bones.Patients receiving anticoagulants/antiplatelet drugs/bleeding diathesis were also excluded from the study.

## Materials and Methods

The patients were divided into two groups; Group 1: Nine patients with chronic venous ulcer receiving PRF dressing weekly for 4 weeks. Group 2: Patients with chronic venous ulcer receiving saline dressings weekly for 4 weeks.

## Preparation of platelet rich fibrin

### *Procedure*

After obtaining consent, 10 ml of the patient's own blood was withdrawn into the vacutainer without any anticoagulant and immediately centrifuged (to prevent blood from clotting) at 3000 rotations per minute for 15 min. After 15 min, a fibrin gel appears in the centre of the vacutainer [Figure 1], in between the red blood cells (RBCs) which are settled at the base and acellular plasma above. The PRF obtained was removed with the help of a toothed forceps and was placed on the ulcer after removing the adherent RBC's [Figure 2]. On an average, 10 ml of whole blood yields about 2.5 ml of clot.

### *Dressing procedure*

Group 1: The measurements of the ulcer were taken. After 15 min, the vacutainer was removed from the centrifuge machine. A sterile non-toothed forceps was used to remove the PRF gel. With the help of an 11 number blade, the RBC clot adhering to the PRF gel was scraped off. The PRF gel was then placed on the ulcer floor and covered with a sterile gauze piece (primary dressing), which was, in turn, was covered with a sterile gauze pad (secondary dressing) held in place with a sterile roller bandage. The dressing was removed after 1 week. The PRF remnants were removed with water and sterile gauze. This treatment was repeated every week for 4 weeks.

Group 2: The measurement of the ulcer was taken. The ulcer was covered with a sterile gauze soaked in saline (primary dressing), which was in turn covered with a sterile gauze pad (secondary dressing) and was covered with a sterile roller bandage. This dressing was left in place for 1 week. This treatment was repeated every week for 4 weeks.

## Measurements documentation

The greatest length and the greatest breadth were measured using a thread and a scale (the clock face method). This was done before starting the treatment, and before repeating the treatment each time at weekly intervals and after the treatment was completed (the final measurement). Digital photographs were taken before starting the treatment, before repeating the treatment each time at weekly intervals and after the treatment was completed.

# Results

A total of 15 patients meeting the inclusion and exclusion criteria were enrolled in the study. All the patients were suffering from chronic venous ulcers. The result was assessed on the basis of ulcer area reduction. The mean ulcer area reduction after 1 week in the PRF group was 26.27%, after 2 weeks it was 46.25%, at 3 weeks it was 77.08% and after 4 weeks it was 85.51% [Table 1]. Whereas in the saline group, it was 14.55%, 23.24%, 34.78% and 42.74%, respectively [Table 2]. The overall mean reduction in the ulcer area was 85.51% in the patients with PRF dressing compared to 42.74% in the patients treated with saline dressing [Bar Diagram 1]. There was a complete closure of the ulcer in five patients (55.55%) in the PRF group [Figures 3-6]. There was no case of complete closure of the ulcer in the saline group [Figures 7-10].

Statistical analysis showed a significant reduction in the ulcer size in the PRF group compared to the saline group [Table 3].

# Discussion

PRF is an autologous platelet and leucocyte-rich fibrin material and is an important advancement in regenerative medicine. It

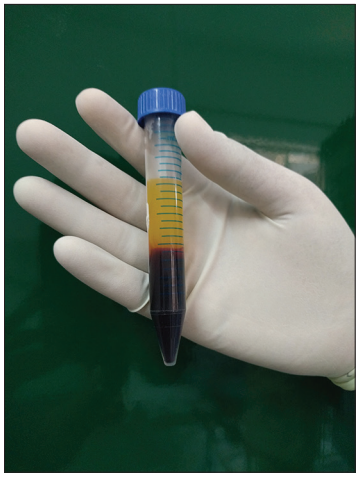
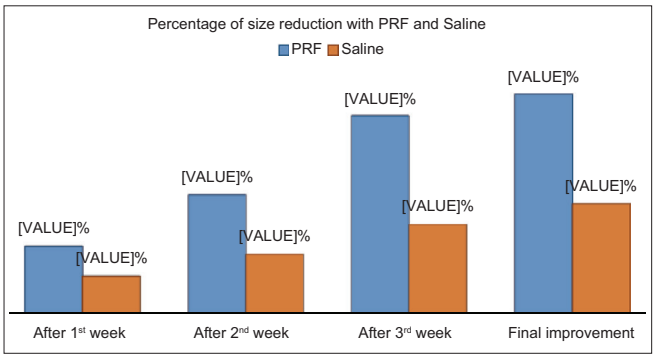


**Figure 1:** Vacutainer with platelet-rich fibrin clot

**Figure 2:** Platelet-rich fibrin placed on the ulcer

forms an organised network where the platelets and leucocytes are concentrated leading to the sustained release of various GFs, resulting in wound healing. Hence, it can also be used for the treatment of venous ulcers.[4]

A study conducted by Margolis *et al*. which included 26,599 patients, concluded that patients who were treated with products derived from platelets, tend to heal faster than patients who were treated without the products derived from platelets. He also concluded that even though the ulcers that were treated with these derivatives were bigger and deeper than the other groups these showed better improvement at the end of 12 weeks.[5] Our study showed similar results where ulcers treated with PRF showed better and faster improvement when compared to saline dressing.




**Bar Diagram 1:** The bar diagram above shows the comparison of the mean improvement in PRF group and Saline group after every week and also after the treatment for 4 weeks

In another study, Anitua *et al*. showed that healing increased significantly with the help of PRF. She also concluded that it not only helps in supplying the required GFs but also by forming fibrin matrix which helps in cell migration, it also helps in neo-vascularisation.[6] In this study, there was a mean reduction of ulcer size of 85.51% in the group treated with PRF at the end of 4 weeks.

In another study Mazzucco *et al*. concluded that healing is improved and is much faster when the wound is treated with platelet-rich gel. He stated that this also helps to reduce the hospital stay. In his study, he demonstrated that in patients who were treated with platelet-rich gel the wound healed in 3.5 weeks and the wounds which were not treated with platelet-rich gel took 6 weeks.[7] In our study, 55.55% of patients treated with PRF had complete closure at the end of 4 weeks, whereas no patient treated with saline had complete closure.

In another conducted by Saldalamacchia *et al*., it was concluded that the use of PRF had significant effectiveness in the treatment of ulcers. He stated that the use of PRF had better reduction of area of ulcer when compared with the basic wound care without the use of PRF. He concluded that though in his study he treated the patients with PRF for a short time it showed good improvement.[8] Similarly, in our study, we found mean reduction

**Table 1: Patients treated with platelet rich fibrin dressing**

| Patient number | Initial measurement in $cm^2$ | Measurement after 1st week | Measurement in $cm^2$ after 2nd week | Measurement in $cm^2$ after 3rd week | Final measurement in $cm^2$ | Percentage of improvement |
|---|---|---|---|---|---|---|
| 1 | 3.5 | 2.64 | 2.64 | 1.0 | 1.0 | 71.42 |
| 2 | 4 | 3.24 | 1.96 | 0.0 | 0 | 100 |
| 3 | 15.2 | 9.92 | 7.29 | 5.94 | 0 | 100 |
| 4 | 6.16 | 3.57 | 0 | 0 | 0 | 100 |
| 5 | 16.96 | 16.64 | 13.92 | 11.44 | 9.43 | 44.39 |
| 6 | 5.06 | 3.80 | 2.24 | 0.0 | 0 | 100 |
| 7 | 2.0 | 1.6 | 1.6 | 0.0 | 0 | 100 |
| 8 | 11.47 | 10.8 | 10.08 | 6.82 | 3.96 | 65.47 |
| 9 | 8.91 | 3.25 | 1.52 | 1.04 | 1.04 | 88.32 |
| Mean percentage of improvement | 0 | 26.27 | 46.25 | 77.08 | 85.51 | 85.51 |

**Table 2: Patients treated with saline dressing**

| Patient number | Initial measurement in $cm^2$ | Measurement after 1st week | Measurement in $cm^2$ after 2nd week | Measurement in $cm^2$ after 3rd week | Final measurement in $cm^2$ | Percentage of improvement |
|---|---|---|---|---|---|---|
| 1 | 1.4 | 1.3 | 1.2 | 0.99 | 0.99 | 29.28 |
| 2 | 5.7 | 4.86 | 4.25 | 4.08 | 3.3 | 42.10 |
| 3 | 13.8 | 12.6 | 12.6 | 12.0 | 12.0 | 13.04 |
| 4 | 3.6 | 2.64 | 2.4 | 1.87 | 1.6 | 55.55 |
| 5 | 3.68 | 2.94 | 2.66 | 2.21 | 1.6 | 56.52 |
| 6 | 1.0 | 0.9 | 0.7 | 0.5 | 0.4 | 60.00 |
| Mean percentage of improvement | 0 | 14.55 | 23.24 | 34.78 | 42.74 | 42.74 |

**Figure 3:** Patient 1 before treatment with platelet-rich fibrin dressing

**Figure 4:** Patient 1 after 4 weeks of treatment with platelet-rich fibrin dressing

**Figure 5:** Patient 2 before treatment with platelet-rich fibrin dressing

**Figure 6:** Patient 2 after 4 weeks of treatment with platelet-rich fibrin dressing

**Figure 7:** Patient 3 before treatment with saline dressing

**Figure 8:** Patient 3 after 4 weeks of treatment with saline dressing

of 85.51% in ulcer area at the end of 4 weeks in patients treated with PRF which is faster when compared to saline group.

A study carried out by O'Connell *et al.*, concluded that the treatment of venous and non-venous ulcers had different outcomes. He showed that the patients who had venous ulcers and were treated with PRF membrane had a total closure of wound in 66.7% of patients. Whereas patients with ulcers of non-venous

**Figure 9:** Patient 4 before treatment with saline dressing

**Figure 10:** Patient 4 after 4 weeks of treatment with Saline dressing

**Table 3: Group statistics**

| Variables | Number of patients | Mean | SD | *t* | *P* |
|---|---|---|---|---|---|
| Saline | 6 | 42.74 | 18.52 | 4.11 | <0.001 |
| PRF | 9 | 85.51 | 20.45 | | |

The study was statistically significant with the *P*<0.001. SD: Standard deviation, PRF: Platelet rich fibrin

origin had total closure in only 44% of patients. Hence, he proved that PRF was very efficacious in the treatment of venous ulcers.[4]

In many studies, there was no significant improvement in the ulcers treated with saline dressing.[5,7-9] Our study showed 42.74% reduction in ulcer size when treated with saline dressing, however, this was less when compared to the 85.51% ulcer area reduction in the PRF dressing group.

Although we had good reduction in the ulcer size in the patients treated with PRF, we need to validate the results with a larger sample size.

## Conclusion

This procedure is simple, patient-friendly, cost-effective, painless and can be performed as an outpatient procedure. We would like to conclude that the use of PRF dressings as an adjuvant therapy in the treatment of chronic venous ulcer shows great potential to achieve complete closure of ulcers and can successfully be used as a routine procedure in the management.

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## Conflicts of interest

There are no conflicts of interest.

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