

# Effectiveness of autologous PRP therapy in chronic nonhealing ulcer: A 2-year retrospective descriptive study

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## ABSTRACT

**Context:** Chronic nonhealing ulcer is a troublesome condition in patients especially with diabetes. Autologous PRP therapy can safely and effectively heal a chronic nonhealing ulcer in such patients. **Aims:** To study the effectiveness of autologous PRP therapy in a chronic nonhealing ulcer. **Settings and Design:** A retrospective descriptive study from previous case records of chronic nonhealing ulcer patients who were treated with autologous PRP therapy at a specialty orthopedic hospital from September 2017 to August 2019. **Methods and Materials:** Data on patients who presented with chronic nonhealing ulcers of >4 weeks duration who were treated with autologous PRP therapy and followed up for 20 weeks. **Statistical Analysis Used:** Statistical Package for the Social Sciences (SPSS) version 20 was used to calculate mean. Microsoft Excel was used for preparing the chart. **Results:** The mean age of patients treated with autologous PRP therapy was 61.24 years, and the follow-up period was 20 weeks. The mean duration of ulcer healing following PRP therapy was 11.25 weeks, 80% of the patient showed ulcer size reduction of >75% following therapy. **Conclusions:** In this retrospective descriptive study, it has demonstrated the effectiveness and safety of autologous PRP therapy in the healing of chronic nonhealing ulcers.

**Keywords:** Autologous PRP, chronic nonhealing ulcer, growth factors, phases of wound healing

## Introduction

A chronic nonhealing ulcer is defined as traumatic or spontaneous lesions that are not responsive to initial therapy or that persist despite appropriate standard treatment.

Mostly chronic ulcers occur in the lower limb and usually associated with diabetes and other comorbidities. The incidence of chronic ulcers increases as age advances.

In this context, autologous PRP<sup>[1-7]</sup> therapy is a promising method for the healing of chronic ulcers which outweigh other treatment modalities.

Hence we thought it was worthwhile to carry out a 2-year retrospective study on patients presented with a chronic ulcer from our institution who were treated with autologous PRP therapy.

## Subjects and Methods

### Study design

A retrospective descriptive study.

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## Study subjects

In this study, 20 patients aged between 40–75 years with chronic or nonhealing ulcers who were treated with autologous PRP therapy from our institution from September 2017 to August 2019 were included after getting institutional ethical clearance and permission from the head of our hospital to use the records.

## Method

Data on age, sex, size of the chronic ulcer of at least 4 weeks of duration who were treated with autologous PRP therapy were collected from previous case records. Autologous PRP prepared from patient's blood centrifuged at a rate of 10,000 rpm for 10 min and then again centrifuged at 5000 rpm for 5 min and patients who were on antiplatelet therapy were advised to stop antiplatelet medication 1 day before the procedure. After centrifugation, 6 mL of PRP was harvested from a device using an aseptic technique.

## Treatment procedure

The chronic ulcer was first debrided for removing infected and dead tissues, then wound was cleaned with normal saline and betadine solution, and the size of the ulcer (length, width, depth) and appearance of granulation tissue were noted. Then autologous PRP was applied to the chronic ulcer depends upon the size of the wound and kept it undisturbed for 10–20 s. Then the ulcer was covered with a sterile nonabsorbent dressing. The dressing was changed 4 days after treatment, and then weekly. Patients were followed up for 20 weeks and at the time of dressing wound were inspected for evidence of infection and size were measured for comparison from the previous size. The patient was advised to stick on medications of comorbid conditions including diabetes, hypertension, and atherosclerosis.

## Results

Each of the 20 patients who had a history of chronic ulcer of various etiologies were included in our study and were treated with autologous PRP therapy. Out of 20 patients, 12 were males (60%) and 8 were females (40%) [Table 1] and the mean age was 61.24 years. Out of 20 patients, 50% was below 60 years and 50% was above 60 years [Figure 1].

In the 20 study subjects, 14 of them were diabetic (70%), 4 of them had the peripheral arterial disease (20%), and 2 of them had venous insufficiency (10%) [Table 2 and Figure 2]. Out of 20 subjects, 16 of the patient's ulcer was in the lower limb (80%) and rest had ulcers in the upper limb.

The mean area and volume of ulcer at the beginning of PRP therapy was 13.72 cm<sup>2</sup> and 20.17 cm<sup>3</sup>, respectively. Mean area and volume after completion of PRP therapy was 1.98 cm<sup>2</sup> and 2.92 cm<sup>3</sup>, respectively.

The duration of ulcer in study subjects before PRP therapy was ranging from 4–12 weeks [Table 3 and Figure 3]. Chronic ulcer

healing was started from within 3 weeks of PRP therapy. Out of 20 subjects, ten of them showed healing of >90% of ulcer and six subjects showed >76% healing [Table 4 and Figure 4]. The mean time duration of ulcer healing was 11.25 weeks [Table 5 and Figure 5].

Out of 20 study subjects, three of them were experienced discharge from ulcer and was due to infection attributed to poor glycemic control and they were treated with antibiotics apart from hypoglycemic medications.

## Discussion

Ulcers are classified as acute and chronic based on duration. Chronic ulcers are associated with significant morbidity to the patients. Most of the chronic ulcer in our study population was in the lower limb and is associated with underlying diabetes mellitus. Other factors which contribute to the chronicity of ulcer include malnutrition, peripheral arterial disease, and infection.

The normal process of wound healing involves four phases<sup>[12]</sup> namely,

1. Hemostasis phase: In this phase, platelets in blood stick to

**Table 1: Age and sex profile of study group**

| Age         | Number of males | Number of females |
|-------------|-----------------|-------------------|
| 45-60 years | 5               | 5                 |
| 61-75 years | 7               | 3                 |

**Table 2: Cause of chronic ulcer in study population**

| Cause                       | Number of patients |
|-----------------------------|--------------------|
| Diabetes mellitus           | 14                 |
| Peripheral arterial disease | 4                  |
| Venous insufficiency        | 2                  |

**Table 3: Duration of ulcer before autologous PRP therapy**

| Ulcer duration in weeks | Number of patients |
|-------------------------|--------------------|
| 4-6                     | 5                  |
| 7-9                     | 9                  |
| 10-12                   | 6                  |

**Table 4: Improvement of ulcer size at the end of 20 weeks**

| Size reduced after 20 weeks | Number of Ulcers |
|-----------------------------|------------------|
| <60%                        | 1                |
| 60-75%                      | 3                |
| 76-90%                      | 6                |
| >90%                        | 10               |

**Table 5: Duration of ulcer healing following PRP therapy**

| Duration of ulcer healing | Number of patients |
|---------------------------|--------------------|
| 6-10 weeks                | 10                 |
| 11-15 weeks               | 8                  |
| 16-20 weeks               | 2                  |

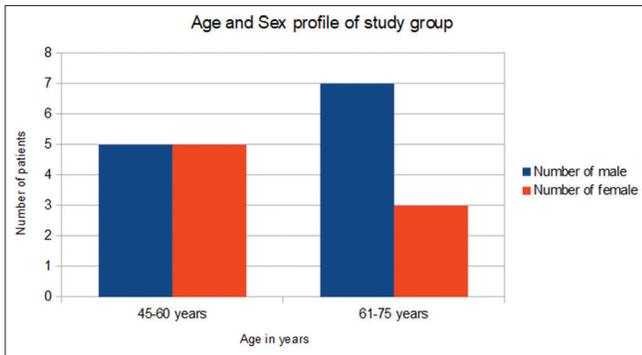


Figure 1: Age and sex profile of study group

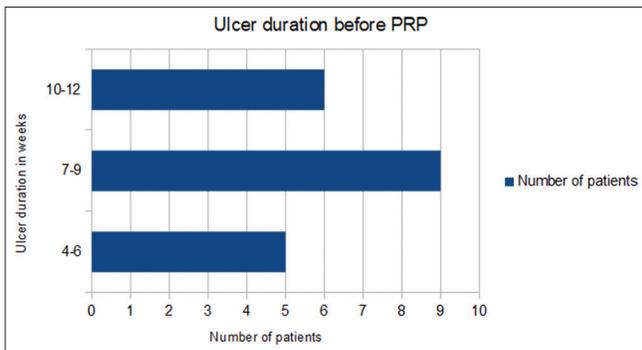


Figure 3: Ulcer duration before PRP therapy

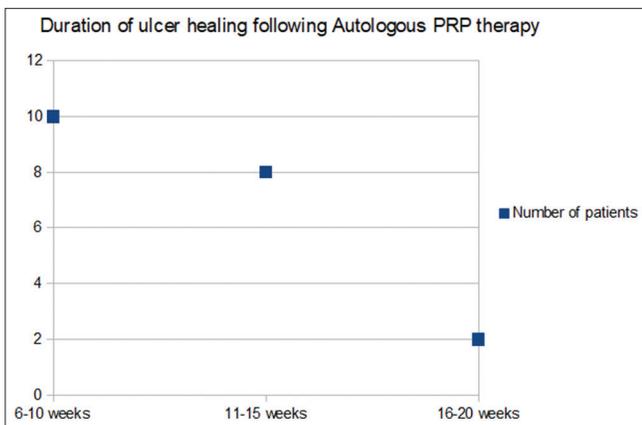


Figure 5: Duration of ulcer healing following autologous PRP therapy

- injure site and platelet activation occurs and they release chemical signals which leads to fibrin activation and forms a mesh and binds platelets to each other
2. Inflammatory phase: During this phase damaged and dead cells cleared out along with organisms via phagocytosis and PDGF are released into the wound that causes cell migration and division during the proliferative phase
  3. Proliferative phase: In this phase, angiogenesis, collagen deposition, granulation tissue formation, epithelialization, and wound contraction occurs
  4. Maturation phase: In this phase, remodeling occurs, and collagen is realigned along tension lines and cell that is no longer needed undergoes apoptosis

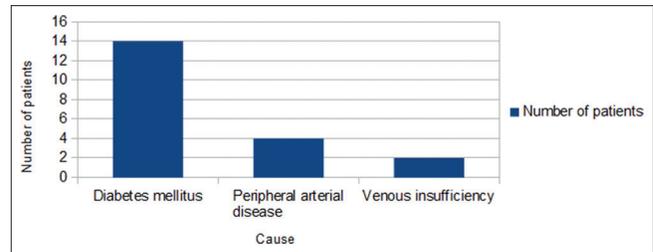


Figure 2: Cause of ulcer in study population

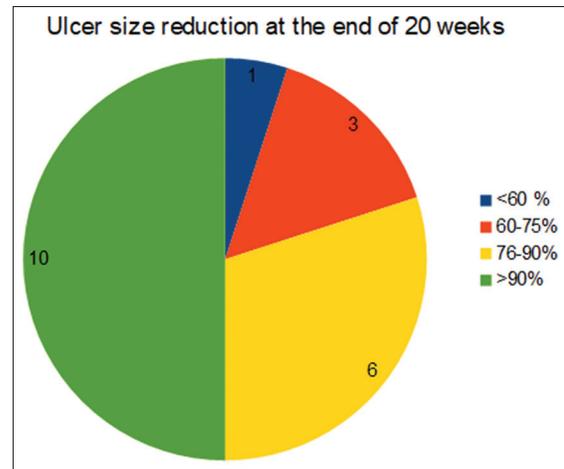


Figure 4: Ulcer size reduction at the end of 20 weeks

A wound becomes chronic or nonhealing if there is any impedance in the phases mentioned above. Factors such as malnutrition, infection, a systemic illness like diabetes mellitus, local factors such as arterial disease and venous insufficiency also delay the process of wound healing.

PRP is a complex mixture of platelets,<sup>[13]</sup> cytokines, and various growth factors<sup>[14]</sup> like EGF (epithelial growth factor); which stimulates fibroblast proliferation, TGF (transforming growth factor); which is mitogenic, chemotactic, promotes collagen production, VEGF (vascular endothelial growth factor); aid in angiogenesis, and PDGF (platelet-derived growth factor); helps to enhance macrophage and fibroblast migration. Besides, the platelet also releases various other factors such as fibronectin, vitronectin, and sphingosine 1-phosphate. Moreover, it has an advantage from the use of a single recombinant GF release is the availability of multiple GF as mentioned above. These factors aid in the healing of chronic ulcers. In this context, autologous PRP therapy plays a promising role in healing chronic ulcers.

In the setting of primary care, PRP therapy can be effectively done because they need less sophisticated methods and it is cost-effective. When comparing to other methods like VAC (vacuum-assisted closure), skin grafting, etc., which needs sophisticated methods and can be done only in the setting of tertiary or specialty centers and need admission to hospital. In the case of autologous PRP therapy, it can be done as an outpatient or daycare procedure, and there is no risk of hypersensitivity. And

**Table 6: Studies on effectiveness of PRP in chronic non healing ulcer**

| Study                                 | Type  | Ulcer etiology   | Number of patients  |
|---------------------------------------|---|--|---|
| Knighton <i>et al.</i> <sup>[8]</sup> | Randomized double-blind placebo-controlled crossover trial, | Ten venous diseases, nine diabetics, four occlusive peripheral vascular diseases, one vasculitis | 24 patients analyzed (32 included): Experimental 13, control 11 |
| Senet <i>et al.</i> <sup>[9]</sup>    | The randomized double-blind placebo-controlled trial,       | Venous ulcers  | 15 patients: Experimental eight, control seven                  |
| Kakagia <i>et al.</i> <sup>[10]</sup> | Randomized controlled trial                                 | Diabetic   | 34 patients: Experimental 17, control 17                        |
| Ahmed <i>et al.</i> <sup>[11]</sup>   | A randomized controlled trial,                              | Diabetic foot  | 58 patients: Experimental 28, control 28                        |

there is no need for frequent follow-up when compared to other therapies. The chance of infections is also lesser, hence it does not require prolonged antibiotic therapy. Hence, PRP therapy is a promising tool for primary care physicians.

Autologous PRP was prepared by double centrifugation<sup>[15]</sup> of the patient's blood since a single spin cannot adequately concentrate platelets due to interference of RBC. One of the main advantages of autologous PRP therapy is the absence of hypersensitivity reaction and infection and is found to be superior to other modalities such as ordinary wound dressing and antibiotics, vacuum-assisted closure (VAC), revascularization techniques, skin grafting, etc.

In 1986, Knighton *et al.*,<sup>[8]</sup> [Table 6] was the first one who showed that the use of autologous PRP accelerated epithelialization of granulation tissue which leads to the healing of the chronic ulcer. This was the first clinical study about local factors played a promising role in wound healing. In our study, we also proved that autologous PRP therapy is effective in healing chronic nonhealing ulcers.

Furthermore, a study conducted by Frykberg *et al.*<sup>[16]</sup> on 49 patients with 65 nonhealing ulcers who were treated with PRP therapy showed that 63 of 65 ulcers responded with a reduction in area, volume, and undermining of the ulcers. In our study, 80% of patients responded with >75% healing of the chronic ulcer.

Similarly, in a study conducted by Kakagia *et al.*<sup>[10]</sup> and Ahmed *et al.*<sup>[11]</sup> revealed that one of the common etiology<sup>[17]</sup> for chronic nonhealing ulcers was diabetes mellitus. In our study, 70% of study subjects were diabetic and they showed promising results in the healing of the chronic ulcers. However, the main challenge in diabetic patients in our study population was the control of infection and adequate glycemetic control, and 3 of them had an infection due to poor glycemetic control and they were monitored more frequently than others for adequate glycemetic control. In our study subjects, 80% of patients showed near-complete wound healing.

Kontopodis *et al.*<sup>[5]</sup> has done a study based on the effectiveness of PRP in the healing of the diabetic ulcer, and it included 72 patients with an ulcer on the lower limb. In our study, 80% of the subject had an ulcer in the lower limb.

In a study conducted by Mohamed *et al.*<sup>[18]</sup> it showed PRP therapy helps in healing chronic ulcers with a significant reduction in

morbidity to patients and improved quality of life. In our study also, there was a significant reduction in morbidity and improved quality of life in most of the patients.

Studies conducted by Hersant *et al.*<sup>[19]</sup> Damiá-Giménez *et al.*<sup>[20]</sup> Zhang *et al.*<sup>[21]</sup> showed promising results of PRP therapy in chronic ulcer healing, and our study results were also showed a similar effect.

### Limitations

The main limitation of our study was its retrospective in nature and the information collected was based on case sheet data entered by different doctors in our hospital. Moreover, the number of patients in the study group was only 20. Despite these limitations, we were able to gather information on the effectiveness of autologous PRP therapy in the healing of chronic ulcers.

### Conclusion

In our study, it is found that autologous PRP therapy is a safe and efficacious method in the healing of chronic ulcers especially in diabetic patients, most of the diabetic patients in the study population responded well to PRP therapy. The main advantage of PRP therapy is that there is no risk of hypersensitivity, none of the study subjects showed any sort of hypersensitivity reaction. Besides, there was a reduction in the morbidity of patients. The cost of preparing PRP is also lesser when compared to other modalities and can be prepared more easily with the help of centrifuge.

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### Conflicts of interest

There are no conflicts of interest.

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