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Original Research Article

A clinical study on efficacy of peri-lesional autologous platelet-rich plasma in non-healing ulcers

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ABSTRACT

Background: Non-healing ulcers are a major health problem worldwide and have a great impact at personal, professional, and social levels. They are a major cause of non-traumatic lower limb amputations. The application of autologous Platelet Rich Plasma (PRP) has been a breakthrough in the treatment of non-healing ulcers, as it is an easy and cost-effective procedure, and provides the necessary growth factors that enhance tissue healing. The aim and objective of the study was to test the effectiveness of peri-ulcer autologous platelet-rich plasma injection in chronic non-healing ulcers and to assess the time taken for wound closure.
Methods: This study was conducted on 50 patients during the period of November 2020 to October 2021 from the in-patients of the surgical unit in Dr. PSIMS and RF. Autologous PRP was prepared from whole blood utilizing a rapid, point-of-care system that works on the principle of density gradient centrifugation. Fifty (50) patients with non-healing ulcers of different etiologies, who met the inclusion criteria, were treated with peri-ulcer autologous PRP injections once weekly.
Results: Of the 50 cases 29 were male and 21 were female, the mean age of the patients is 54.48±10.79 years. All the patients showed signs of wound healing with a reduction in wound size, and the mean time duration of ulcer healing was 6.75±1.47 weeks.
Conclusions: This prospective study has demonstrated the potential safety and efficacy of autologous platelet-rich plasma injection for the treatment of chronic non-healing ulcers.

Keywords: Platelet-rich plasma, PRP, Non-healing ulcers, Venous ulcers

INTRODUCTION

Non-healing ulcers are defined as spontaneous or traumatic lesions, that are physiologically impaired due to disruption of the wound healing process as a result of impaired angiogenesis, innervation, or cellular migration and are typically in lower extremities. They are unresponsive to initial therapy or persist despite appropriate care and do not proceed towards healing in a defined time period.[1,2] Although there is no specific time frame that differentiates an acute from a chronic ulcer, some suggest that the lack of approximately 15% reduction weekly or approximately 50% reduction of the surface area of the wound over one month indicates a chronic state.[3] The Wound Healing Society classifies chronic wounds into 4 categories: Diabetic ulcers, Pressure ulcers, Arterial ulcers, and Venous Ulcers. Lower extremity ulcers comprise a substantial proportion of chronic ulcers, especially those attributed to venous disease, diabetes, or arterial disease.[4] According to Gupta

et al, the prevalence in India was 4.5 per 1000 and the dominant etiology was found to be neglected traumatic wounds. The goal of ulcer treatment is to achieve complete wound closure as quickly as feasible. Conventional therapy for non-healing ulcers includes wound cleansing, debridement, preventing and treatment of infection, managing blood glucose levels, and local care with dressing.[5-7] A variety of advanced treatments for non-healing ulcers include hyperbaric oxygen therapy, skin grafting, VAC dressing, and revascularization procedures such as angioplasty and reconstructive surgery.[8-10] Cellular therapies like Platelet-rich plasma (PRP) have gathered attention for their potential for use in many chronic ulcer cases as platelets are a physiological reservoir of a variety of growth factors which are crucial elements in process of tissue repair and hence this was chosen for study.

METHODS

The aim of this study was to test the effectiveness of peri-ulcer autologous platelet-rich plasma injection in chronic non-healing ulcers. This was a nonrandomized, uncontrolled prospective observational study conducted at Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation for a period of one year from November 2020 to October 2021. A total of 50 patients with non-healing ulcers of various etiologies were included in this study. The inclusion criteria were patients in the age group of 18 to 70 years with long-standing non-healing ulcers (>4 weeks duration), ulcer >15 cm2 in size, Hb >10 gm%. Patients with platelet count <1,00,000/µL, known or suspected osteomyelitis, S. creatinine >1.5 mg/dL, severe infection (presence of visible pus or copious wound exudates), presence of cellulitis, acute ischemia or gangrene, malignant ulcers were excluded from the study. Detailed history including the name, age, sex, address, contact number, occupation, and history of medication was noted. Patients were thoroughly examined and ulcer size was measured. The treatment option with platelet-rich plasma injections was explained to the patients and their consent was taken. 20-40 ml of whole blood was collected from the patient into vacutainers containing acid citrate dextrose- a solution, which is an anticoagulant solution. The tubes were centrifuged at 900 g (2290 rpm) for 5 minutes to form three layers in each tube- bottom RBCs, middle buffy coat, and upper plasma. Buffy coat and plasma layers were transferred to empty sterile conical bottom tubes and were centrifuged at 1000 g (2410 rpm) for 10 min after which platelet pellets with few RBCs were collected at bottom of test tubes and the upper 2/3rd content of each test tubes was discarded and platelet pellets were thoroughly mixed into lower 1/3rd volume by gently shaking tubes. The product obtained was platelet-rich plasma, which was then drawn into sterile syringes and injected around the ulcer once in a week for a maximum period of 7 to 8 weeks. Wounds were assessed using Bates Jensen wound assessment tool. Wound area was measured and progress was recorded. Ethical clearance certificate was obtained from the Institutional Ethical Clearance Committee. Functions present in numbers software (Apple Inc, Cupertino CA) and online resources were used.

RESULTS

Fifty patients with nonhealing ulcers of various etiologies were treated with PRP at weekly intervals for a maximum of 6 treatments.

Table 1: Age incidence.

Age group (in years)	Number of patients	Percentage
18-30	1	2
31-40	3	6
41-50	15	30
51-60	17	34
61-70	11	22
71-80	3	6

Table 2: Sex distribution.

Gender	Cases	Percentage
Male	29	58
Female	21	42

In this study, the most common age group was in the 6th decade (Table 1) and the incidence of non-healing ulcers is more common in males than in females (Table 2).

Table 3: Distribution of ulcer presentation.

Duration	Cases	Percentage
1-3 months	32	64
3-6 months	12	24
6-9 months	4	8
9-12 months	2	4

Table 4: Area of ulcer presentation.

Area of the ulcer (in cm^2)	Cases	Percentage
20-40	20	40
41-60	16	32
61-80	6	12
>80	8	16

The duration of ulcer at the time of presentation was 1-3 months in 32 cases (Table 3). The minimum area of ulcer at presentation was 20 cm2and the maximum area was 110 cm2. The area of the ulcer at presentation was 20-40 cm2 in 20 cases followed by 41-60 cm2 in 16 cases (Table 4). The most common etiology was found to be diabetic ulcer (Table 5). Number of PRP injections

required for complete wound closure is 3 to 4 in 41.8% of cases followed by 5 to 6 in 35.2% of cases (Table 6).

Table 5: Etiology of ulcer at presentation.

Etiology	Cases	Percentage
Diabetic ulcer	32	64
Post-cellulitis ulcer	7	14
Post-traumatic ulcer	5	10
Venous ulcer	5	10
Non-Specific ulcer	1	2

Table 6: PRP injection for complete wound closure.

Number of PRP injections	Cases	Percentage
3-4	18	41.86
5-6	16	37.20
7-8	9	20.93

Table 7: Complete wound closure by etiology of ulcer.

Etiology	Cases	Percentage
Diabetic ulcer	30	93.75
Post-cellulitis ulcer	7	100
Post-traumatic ulcer	5	100
Venous ulcer	0	0
Non-specific ulcer	1	100
Total	43	

Of the 50 patients in this study, complete wound closure was achieved in 43 patients. Complete wound closure was seen in 18 patients in 3-4 weeks, 16 patients in 5-6 weeks, 9 patients in 7-8 weeks. Wound closure was achieved in 100% of patients with post-traumatic ulcers, post cellulitis ulcers, non-specific ulcers, and 93.75% of patients with diabetic ulcers. Complete wound closure was not achieved in venous ulcers (Table 7). The ulcers were assessed at each presentation using the Bates-Jensen wound assessment tool. There were a total of 214 wound assessment instances, excluding the wound assessment at the first PRP injection and after wound closure. The wound score improved in 194 instances and did not improve in 20 instances. The maximum percentage of instances of wound score assessment where the score did not improve by wound etiology was found with venous ulcers.

DISCUSSION

The present study was conducted with the aim of testing the effectiveness of peri-ulcer autologous platelet-rich plasma injection in chronic non-healing ulcers and assessing the time taken for complete wound closure in 50 cases of non-healing ulcer admitted to Dr. PSIMS and RF. In this study, the Mean (SD) value for the age of the population was 54.48±10.79 years which is comparable to studies like Li et al (61.4±13.1), and Ahmed et al (43.2±18.2).[11,12] The gender distribution of non-healing ulcers, i.e., non-healing ulcers in men is slightly greater than in women. The male to female ratio overall is around 4:3. This is consistent with the male preponderance seen in other studies like Sakata et al (77/23), Li et al (62.5/37.5), Ahmed et al (71/29), Yilmaz et al14 (84/16).[11-13] The mean duration of the ulcer at presentation is 3.61±2.48 months which is similar to that in studies by Sakata et al (3.3±3.6 months) and Stacey et al.[13,15] (3 months). The mean area of the ulcers at the time of presentation is 54.6±25.76 cm2 comparable to that in study by Crovetti et al (67.4 cm2).[16] The most common etiology in the present study is diabetic ulcer followed by post-cellulitis ulcer. The complete wound closure was achieved in 86% of cases this is comparable to that seen in the studies of Sakata et al (83%), Li et al (89.3%), and Ahmed et al (85.7%).[11-13] The time for complete wound closure was 6.75±1.47 weeks in the present study and is comparable to that seen in studies of Yilmaz et al (4.82±2.16), Crovetti et al (10), and Ahmed et al (3.87±2.13).[12,14,16] In a small number of instances patients complained of mild pain during intra-lesional PRP injections.

The limitations of the present study are that it is a single center study with limited sample size (n=50) and it doesn't compare the efficacy of PRP injections with other standardized treatment modalities for non-healing ulcers. Further research is needed in this field with large sample size, using standardized protocols for ulcer size assessment and for every aspect of preparation of PRP injections.

CONCLUSION

In this prospective study, the wound score improved in most instances of wound assessment, but for the cases of venous ulcers where the healing was not satisfactory. No significant adverse effects were observed. Peri ulcer autologous Platelet Rich Plasma injections are safe for use and beneficial in the healing of chronic non-healing ulcers, especially chronic diabetic ulcers, post-traumatic ulcers, post-cellulitis ulcers, and non-specific ulcers, and promote complete wound closure.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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