

Efficacy and Safety of Intralesional Platelet Rich Plasma (PRP) Therapy in the Management of Chronic Non-healing Leg Ulcers in our Population

MUHAMMAD ASLAM JAVED¹, SADAF AMIN², WISHAL RAZA³, IMRAN YOUSUF⁴, KHALID JAVEED KHAN⁵

^{1,4}Department of Surgery, Pak Red Crescent Medical and Dental College, Dina Nath.

²Department of Dermatology, Punjab University Teaching Hospital/ University of Punjab, Lahore.

^{3,5}Department of Surgery, Fatima Jinnah Medical University / Sir Ganga Ram Hospital Lahore.

Correspondence to: Muhammad Aslam Javed, Email: aslamjaved0304@gmail.com, Cell: 03045713206

ABSTRACT

Background: Autologous Platelets Rich Plasma (PRP) therapy not only hastens chronic wounds and ulcers healing but also diminishes the rate of amputations of lower leg caused by non-healing recalcitrant ulcers. In this study we have demonstrated the magical results of intralesional autologous PRP in the healing of resistant to heal chronic leg ulcers.

Methods: In this metacentric study 26 patients having 30 chronic leg ulcers of more than 6 weeks duration and various etiologies, were treated with intralesional autologous PRP application on weekly basis for a duration of 8 weeks and the final results were calculated by percentage improvement in the volume and area of the ulcer/wound.

Results: In our study 26 patient with 30 chronic recalcitrant leg ulcers/wounds were treated with intralesional autologous PRP therapy on weekly basis. Mean age of the included patients was 34.5 years. 19 were male patients and 7 were female. The mean time period of the healing of chronic ulcers was 5.3 weeks. The final mean percentage improvement outcome in the volume and area of the ulcers was calculated as 86% and 88% respectively.

Conclusions: PRP therapy is safe, cost effective office based simple procedure in treating recalcitrant chronic leg ulcer/wounds.

Keywords: Non-healing, intralesional, autologous platelet rich plasma, chronic ulcers

INTRODUCTION

Non healing chronic leg ulcer is defined as spontaneous or traumatic wound that is commonly seen in lower leg and is not responding to initial conventional therapy or that remain unresponsive and show no signs of healing.¹ It might be due to an underlying etiology that may be related to systemic or localized factors.¹ Non-healing chronic leg ulcer is one of the major health issue worldwide and its prevalence ranges from 1.9 to 13.1%² and is estimated to affect around 2–6 million people in the USA alone.³

Platelet-rich plasma (PRP) therapy application has considerably shown an increased trend in a wide range of diseases in recent years and excellent satisfactory outcomes have been observed in cutaneous ulcers in numerous case series and case controlled studies.⁴

Platelet rich plasma (PRP) therapy contains various tissue growth factors like PDGF (platelet-derived growth factors), transforming tissue growth factors (TGF)- β 1, epidermal growth factors, vascular endothelial growth factor-A, insulin like growth factors.⁵ These growth factors are present in higher concentration in plasma as compared to their levels in the blood. These growth factors have numerous functions, like stimulating neovascularization, activating keratinocytes, promoting fibroblasts proliferation, expressing regenerative keratinocyte phenotype, and enhancing immunological response and phagocytosis through local accumulation of polymorph nuclear leukocytes and macrophages.⁵ The aim of this prospective metacentric study is to objectively judge the impact of intralesional PRP therapy on chronic non-healing leg ulcers by serial measurements of ulcer dimensions and margins reduction towards the center of the lesion.

METHODS

It is a multi-centric prospective study carried out in patients of chronic non-healing leg ulcers of more than six weeks duration, who presented in the Department of Surgery, PRCM & DC Dina Nath, Department of Surgery Sir Ganga Ram Hospital, Lahore, Department of Surgery Hussain Memorial Hospital, Lahore and Dermatology Department University of Punjab, Lahore during a period from January 2019 to June 2020.

In our study, 26 patients with 30 chronic non-healing leg ulcers were included. Ethical board clearance was taken before starting the study. Patients having ulcer/wounds of numerous etiologies, those lasting more than six week duration and patients who had already taken conventional oral and topical treatment for at least six weeks were included.

Patient having ulcer with active bacterial infection, coagulation disorders, uncontrolled diabetes mellitus and sapheno-femoral incompetency were excluded. Detailed history of patients was taken and thorough examination was done, including length, width and depth of ulcer was also measured.

Under strict aseptic measures at least 15 ml of blood (venous) was taken with a syringe. It was added to a test tube voil having acid citrate dextrose (blood: Acid citrate dextrose ratio was 9:1). It is then centrifuged at 1500 revolutions per minutes (slow spin) for 10 minutes to separate the RBCs from plasma. Then the superficial plasma and the buffy coat (composed of platelets) was separated. It is then centrifuged at 4000 revolutions per minutes (hard spin) for another 5 minutes. The plasma bottom layer about one-third was taken. 10% CaCl₂

(calcium chloride) was added in it as activator (0.3 ml for 1 ml of plasma). The mean platelet count was measured 3.5 lac/mm³ and mean conc. of platelets in platelets rich plasma was measured as 6.03 Lac/mm³. Then the wound was debrided and thoroughly cleaned with normal saline and PRP was injected onto the margins of the ulcer/wound. The wound was then covered with a non-absorbent gauze. The patient was advised to remove dressing after 48 hours. This procedure was carried out once a week for total of 8 weeks. Each week the volume and area of the ulcer was measured and photographed at each visit.

Area of the ulcer was measured as Length x width x 0.7854. The volume of the ulcer was assessed with the following formula: (length into width into 0.7854) x depth. The final improvement outcome was measured as a percentage reduction of volume and area of the ulcer, which was calculated on day 1 minus assessment day sizing divided by day 1 measurement.

RESULTS

26 patients with 30 non-healing chronic leg ulcers were treated with intralesional PRP therapy. There were 19 male (73.08%) and 7 female patient (26.92%). The mean age of the patients was 34.5 year. 5 (19%) patients fall in the age group 20–30 year, 16 (62%) between 30-40 year, 4 (15%) between 50-60 year and 1 (4%) between 60-70 year.

Table 1: Percentage Improvement Outcome in the Area of ulcers at the end of 8th session

| % reduction in the area | No. of Ulcers | % |
|-------------------------|---------------|-----|
| <60 | 0 | 0 |
| 61-70 | 0 | 0 |
| 71-80 | 6 | 20% |
| 81-90 | 6 | 20% |
| 91-100 | 18 | 60% |

Table 2: Percentage Improvement Outcome in the Volume of ulcers at the end of 8th session

| % reduction in the volume | No. of Ulcers | % |
|---------------------------|---------------|--------|
| <60 | 1 | 3.33% |
| 61-70 | 3 | 10% |
| 71-80 | 5 | 13.33% |
| 81-90 | 7 | 23.33% |
| 91-100 | 15 | 50% |



Figure1: Before and After Result of Intralesional PRP in Diabetic Foot Ulcer

The ulcer duration ranged from 3 months to 1 year with a mean duration of ulcer 4.25 month. The mean time taken for healing of ulcer/wounds were 5.3 weeks. 18 ulcers (60%) showed 100% improvement in the mean area of the ulcers (see Table-1), whereas 15 ulcers (50%) showed 100% improvement in the volume of the ulcer (see Table-2). Baseline mean area measurement of the ulcer was 12.5 cm² and volume was 5.45 cm³. The final calculated area of the ulcer at the end of 8 weeks was 1.50 cm² and volume of the ulcer was 0.75 cm³. The mean percentage betterment outcome in the volume and area of ulcers was calculated as 86% and 88% respectively (Figure 1). No adverse effects were noted during the study period except for transient pain while injecting PRP onto the ulcer margins. All the patients were satisfied at the end of treatment period.

DISCUSSION

Common causes of chronic non-healing cutaneous leg ulcers include diabetic ulcers, traumatic ulcers, venous leg ulcers, mixed arterio-venous ulcers, pressure ulcers, neuropathic ulcers and ulcers due to systemic disorders.⁶ Wound healing in chronic ulcers is impaired due to increase in pro-inflammatory cytokines, high metalloprotease activity, hypoxia and recurrent superadded bacterial infections thus leading to growth factors and fibrin deficit, which slows down the evolution process.⁷

PRP therapy is a novel and inexpensive office based method of treatment for non-healing chronic leg ulcers. It has got platelet concentration up to five times more than the normal plasma platelet count.² Over the past few years it has gained abundant popularity due to its ability to provide rich growth factors directly on to the wound. It can be applied either directly on to the floor of the ulcer as gel form or by sprinkling onto the wound surface and can also be given as intralesional injection on to the margins and floor of the ulcer/wound.⁸

In our study on 26 patients with 30 chronic non-healing leg ulcers, the mean time period for healing of ulcer/wounds were 5.3 weeks, while in a study by Gopinath *et al.*⁸ on 33 patient, mean duration of healing was 7.67±2.314 weeks. Another study by Bernuzzi *et al.*⁹ the mean duration of healing was 6.2 weeks. Sakata *et al.*¹⁰ carried out a study on 40 chronic non-healing ulcers and had mean duration of healing as 4.83 weeks.

Frykberg *et al.*¹¹ carried out a study on 49 patient with 65 non healing venous leg ulcers; the mean percentage reduction of volume and area were 56.1% and 43.1% respectively, with a mean treatment duration of 2.3 week. In our study, the mean percentage reduction of the volume and area was calculated to be 86% and 88%, with a mean of 5.3 week treatment, while in a study conducted by Gopinath *et al.*⁸ on 33 patient, the total improvement in the volume and area of ulcers were noted to be 90.7% and 85.7% respectively at the end of 6th week. In a study by Suryanarayanan *et al.*¹² patients having 33 ulcer were treated for 6 weeks; percentage improvement in volume and area were 95% and 91.7% respectively and is comparable with our study.

Autologous PRP has short half-life/biological activity after topical application, and thus there is a need to repeat procedure several times on weekly basis till adequate or

desirable results are achieved. The only side effect that was seen in our study was transient pain during intralesional PRP injection that subsided few hours after the procedure. The only short comings in our study were a compact sample size and little duration of study, thereby in order to define standard operating procedure, large randomized control trials should be conducted in terms of method of platelet rich plasma preparation, amount of plasma to be injected and duration of intralesional injections. While conducting such trials it is also difficult to randomize patients on the basis of various etiological factors that influence wound healing like cause of an ulcer, its size, duration and associated co-morbidities. Ulcers which are larger in size take more time to heal as compared to smaller lesions.

CONCLUSION

Conventional therapies do not provide the necessary tissue growth factors for the healing of recalcitrant chronic ulcers. PRP is an affordable, safe, biocompatible office-based procedure without any adverse effects for the treatment of recalcitrant difficult to heal ulcers.

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