Role of Platelet Rich Plasma [PRP] in the Treatment of Chronic Wounds

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ABSTRACT

Introduction: Chronic leg ulcers pose a formidable challenge to the surgeon necessitating various treatment modalities. Due to recurrence in wounds with conventional therapy, newer modalities of treatment with PRP showed promising results in various branches of medicine like plastic and reconstructive surgery, orthopedics, and dermatology, cardiovascular and thoracic surgery. Study aimed to record the effect of platelet rich plasma in the treatment of chronic ulcers particularly venous and diabetic leg ulcers.

Material and methods: A prospective study of 10 cases of chronic leg ulcers. Chronic leg diabetic ulcers, venous foot ulcers of more than 3 months duration both males and females with normal platelet count and activity are selected. Age group between 18ys and 60 yrs with ulcers between size varying 2x2cm 2 to 10 x10 cm2 were included.

Results: Wounds were measured on day O along their greater dimensions and were recorded, which ranged from 3x3 cm2 to 10x8. At the end of 2nd week, ulcer size had reduced by an average of 21.87% (range 0%- 60%) in 10 wounds. Healing of the ulcers with full re-epithelialization was seen in 4 cases (40%). Of the remaining ulcers, 6 (60%) were taken up for skin grafting once the ulcer has granulated well. In these cases of skin grafting, 5 ulcers have healed completely with 1 case of graft failure Time taken for the wounds to heal completely by re-epithelization ranged from 6 weeks (1 venous ulcer) to 16 weeks (1 diabetic foot ulcer). Of the ulcers (n=6, 60%) which underwent skin grafting, 5 (83.33%),healed completely, with 1 case of graft fail.

Conclusion: The use of platelet-rich plasma can be an option when treating recalcitrant wounds of differing etiologies.

Keywords: Platelet Rich Plasma, Chronic Wounds

INTRODUCTION

PRP is an autologous product derived from whole blood through the process of gradient density centrifugation, there by concentrating a large number of platelets in a small volume of plasma. Platelets play a major role in the process of hemostasis and later wound healing in any wound. During the process of injury platelets gets initially accumulated and form plug producing hemostasis. later by the action of thrombin, platelet membrane gets depolamarised and release of platelet granules which are rich in various growth factors like PDGF, PGR, FGF, interleukins.[1,2] These growth factors aid in the process of wound healing by laying collagen matrix, fibroblast proliferation and early maturation of collagen. Based on this background autologous platelet growth factors in the form of platelet rich plasma started in the management of chronic leg ulcers, with variable but encouraging results necessitating the need to continued use and further studies into its effectiveness.

MATERIAL AND METHODS

A prospective study of 10 cases of chronic leg ulcers who presented to the plastic surgery department at King George Hospital, Visakhapatnam from October 2014 to January 2016 was conducted. Chronic leg diabetic ulcers, venous foot ulcers of more than 3 months duration both males and females with normal platelet count and activity are seleted. Age group between 18ys and 60 yrs with ulcers between size varying 2x2cm 2 to 10 x10 cm2 were included.

Preparation of PRP and application:- Informed written consent was taken from all the patients after explaining the treatment protocol and other options available for them. In this study autologous PRP was prepared by centrifugation of the patient's blood at 3500rpm for 15 min in a table top centrifuge after aseptic collection from the ante cubital vein using a 16 G needle, which is then transferred to a sterile vaccutainer. Anti-coagulant was not used in this study. Once the blood has fractionated into its components the top most layer of platelet rich plasma gel was collected and cut into small pieces, based on size of ulcer and placed over the ulcer which is then covered with sterile Vaseline gauze and dressed. The first look dressing is on 5th day which is then followed by alternate saline dressing. Based on the response of ulcer to the first procedure /application decision is taken to repeat the procedure after 2nd week only and subsequent applications. If the ulcer was large and full epithelialization was not possible early then it was skin grafting when it is fit. As autoogous platelets used in the study there was no chance of spread of infectious diseases and allergic reactions.

The ulcers were followed up under the following parameters like size of ulcer [with tape], quality of granulation tissue, no of times application, skin grafting, time taken for complete healing.

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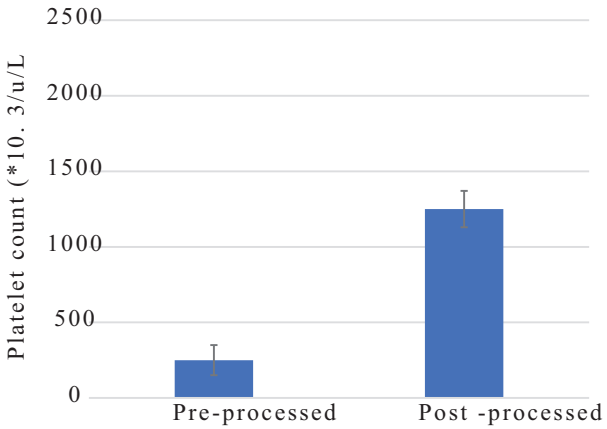
RESULTS

In this study a total of 10 ulcers were selected and taken up for the PRP application. Routine investigations as per the selected protocol were done. Once the patients were found fit for the procedure, pre procedure ulcer measurements and photographs were taken. Debridement was done for the ulcer followed by moist dressing initially avoiding chemical irritants like betadine or hydrogen peroxide. Follow-up of the ulcers was done as per the preplanned protocol. In this study the patients age ranged from 23 yrs. to 58 yr. (mean 47.6 yrs.) out of which male: female= 4:1. Most of the Ulcers are found to be in 13-16 weeks (table-1).

Wounds were measured on day O along their greater dimensions and were recorded, which ranged from 3x3 cm^2 to 1 Ox8. At the end of 2nd week, ulcer size had reduced by an average of 21.87% (range O%- 60%) in 10 wounds. 6 wounds were clinically assessed as improved, and 4 as unchanged. After the end of 4thweek the wounds were again measured and the ulcer sizes were found to have reduced by an average of 59.43% (range 20% to 88%) (table-2). All the wounds were clinically assessed as improved and 2 ulcers were covered with split thickness skin graft. After the end of 6th week, the 2 wounds which underwent skin grafting have healed completely and 1 ulcer re-epithelialized. The remaining ulcers (N=7) were again measured and the ulcer sizes were found to have reduced by an average of 67.52% (range 40%-90%).



Distribution of Platelet counts at pre- and post- processing (*p < 0.05)

Figure-1: Distribution of Platelet counts at pre- and post- processing

Duration of Ulcer (weeks)	No. of Patients (n)	Percentage (%)
9–12	2	20
13–16	7	70
17–20	1	10
21–24	1	10

Table-1: Duration the ulcers persisted

No. of weeks	Minimum decrease in size	Maximum decrease in size	Average
2 weeks	0%	60%	21.87%
4 weeks	20%	88%	59.43%
6 weeks	40%	90%	67.52%

Table-2: Reduction in wound size by weeks

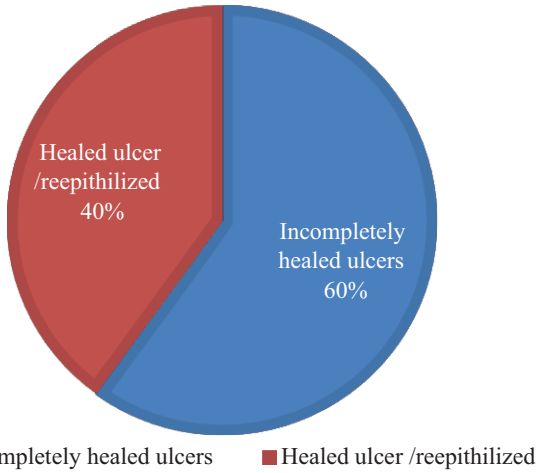


Figure-2: Wound response to PRP

Variables	Croveti et al[3]	Driver et al[4]	O'Connell et al[5]	Present study
Age	NA	18-95	18-85	18-60
No. of ulcers	24	40 (prp-19, saline-21)	30 (venous-17, non-venous-13)	10
Etiology	All types of chronic ulcers	NA	venous and non venous	venous and diabetic
No. of PRP applications	1/wk - 12 weeks	NA	Average of 2 applications per patient	1 application every 2 weeks
Decrease in Wound size	N A	NA	NA	2 weeks- 21.87% 4 weeks- 59.43% 6 weeks- 67.52%
Wound re- epithelization	9 ulcers	68.4% in PRP group 42.9% in saline group	66. 7% in venous ulcer group 44% in nonvenous ulcer group by 12 weeks	4 ulcers
SSG	NA	NA	NA	6 ulcers
Unhealed/ partial response	partial - 9 stopped - 4	NA	NA	NA

Table-3: Comparison of previous studies in relation to the present study is given

Reduction in wound size by weeks:-wounds were also looked into in the aspect of granulation tissue clinically and all the ulcers were found to have a healthy granulation tissue and the edges showed signs of healing.

Number of PRP application: -The number of treatments with platelet rich plasma varied from 2-6 applications [average 2.9 application per ulcer] (figure-1).

Healing of the ulcers with full re-epithelialization was seen in 4 cases (40%). Of the remaining ulcers, 6 (60%) were taken up for skin grafting once the ulcer has granulated well. In these cases of skin grafting, 5 ulcers have healed completely with 1 case of graft failure (figure-2).

Time taken for the wounds to heal completely by re-epithelization ranged from 6 weeks (1 venous ulcer) to 16 weeks (1 diabetic foot ulcer). Of the ulcers (n=6, 60%) which underwent skin grafting, 5 (83.33%), healed completely, with 1 case of graft fail

DISCUSSION

Wound healing is a complex process that is regulated by interactions between a large number of cell types, extracellular matrix proteins and mediators such as cytokines and growth factors. Lack of balance between these interactions may result in a chronic wound. One possible cause of imbalance in the wound healing process is high bacterial counts leading to a prolonged inflammatory response with high levels of cytokines. This leads to increased production of matrix metalloproteases. High matrix metalloprotease activity results in uncontrolled breakdown of extracellular matrix and growth factors. This leads to a chronic wound which fails to heal. Chronic foot ulceration is an epidemiologically widely prevalent disease in India as well as in the world leading to huge wastage in work hours of the people. It also impacts the quality of life of the people affected. Platelets play a major role in the process of wound healing through the release of various growth factors from the granules present in them. Platelet rich plasma with its constituent high platelet concentration and growth factors, help in the recreation of ideal environment for wound healing.

Crovetti et al.[3] published a prospective non-blinded study regarding the efficacy of platelet gel (PG) in healing cutaneous chronic wounds. The wounds of the 24 patients enrolled in this study varied in origin, and etiologies included diabetes- related, vascular insufficiency, infectious disease, post-traumatic, NEUROPATHIC, and vasculitis- related. The protocol for this study consisted of once-weekly platelet gel (PG) applications of either autologous or homologous origin. At the time of the study publication, nine patients had healed completely, two went on to receive cutaneous grafts, four had stopped treatment, and nine had responded partially and nine had responded partially and were still receiving treatment.

Driver et al.[4] carried out the first reported prospective, randomized, controlled multicenter trial in the United States regarding the use of autologous PRP for the treatment of diabetic foot ulcers. Participants included 72 patients with type 1 and type 2 diabetes between the ages of 18 and 95 from 14 investigation sites suffering from an ulcer of at least four weeks duration. In this study, investigators compared the effectiveness of autologous PRP gel to that of normal saline for 12 weeks. The primary objective of this study was to evaluate the safety of PRP and the incidence of complete wound closure, defined as 100 percent re-epithelialization, when compared to the control treatment, and a secondary objective was rate of wound closure. Patients were randomized into two groups-standard of care with PRP gel or control (saline) - and were evaluated biweekly for 12 weeks. After excluding 32 patients from the final per-protocol analysis because of failure to complete treatment and protocol violations, the authors found that 68.4 percent (13/19) of patients in the PRP group and 42.9 percent (9/21) in the control group had wounds that healed. Wounds in the PRP group heale sd after a mean of 42.9 days (SD 18.3) vs. 47.4 days (SD 22.0) in the control group.

O'Connell et al[5] presented promising findings from a pilot study involving the treatment of chronic lower-extremity ulcers with autologous platelet-rich fibrin matrix membrane (PRFM). In this present study 10 ulcers were selected, with a mean patient age of 47.6 yrs. The ulcer size varied from 3x3 cm2 to 10x8 cm2. Total no. of PRP applications ranged from 2-6 (average 2.9), with a spa ce of 2 weeks between applications. All the patients received autologous platelet rich plasma. The wound were followed till they healed either by re- epithelization or after SSG. The decrease in size of ulcers ranged from 0% to 60% at the end of 2 weeks, 20% to 88% after 4 weeks and 40% to 90% at 6 weeks. Four wounds re-epithelized, of which 1 ulcer by 6 weeks, two ulcers by 8 weeks and another by 16 weeks. The remaining 6 ulcers went on to receive skin grating of which 1 had graft failure; this was further treated with repeat PRP application leading to complete healing.

Comparison of various studies (table-3) different rates of healing attained in these studies as well as others done on chronic ulcers can be attributed to the non-standardization of PRP preparation technique, frequency of PRP application over the ulcers, etiology of the ulcers in different studies, influence of other factors over the wound healing.

Apart from this many studies done on PRP application in patient care some of these are McAleer et al. (2006)[6] found that the use of autologous PRP was successful in healing a chronic lower extremity wound in a case study of a 57-year-old man Although this study is limited as a case study involving a single patient, it suggested that PRP can be successful in healing wounds that have failed to heal by other treatment techniques. Salemi et al. (2008)[7] was a more recent case study evaluating the effectiveness of a combination of autologous adipose tissue and PRP in a lower extremity ulcer of three years duration in a non-diabetic.[8]

CONCLUSION

The use of platelet-rich plasma can be an option when treating recalcitrant wounds of differing etiologies. It should be reserved to wounds that do not show any progress after 6 months with treatment of wound aetiology and standard

wound care.

In this study as well as in other studies there were variations in the response of the chronic ulcers to the platelet rich plasma application which can be attributed to, variations in patient characteristics between patients with type 1 and type 2 diabetes mellitus, duration of diabetes diagnosis, degree of control of diabetes, patient age, patient gender, initial wound area, wound depth, wound duration, and wound location, which can alter the possible outcomes of this treatment. Other possible variables include variation in PRP characteristics between various studies i.e. preparation of PRP, growth factor content of autologous PRP can vary from patient to patient, even in patients with similar platelet counts, time gap between successive PRP applications.

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