International Journal Dental and Medical Sciences Research
Volume 3, Issue 5, Sep-Oct 2021 pp 274-278 www.ijdmsrjournal.com ISSN: 2582-6018

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

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Submitted: 01-09-2021 Revised: 09-09-2021 Accepted: 12-09-2021

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 excellent results. 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 20 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 20 wounds. Healing of the ulcers with full re-epithelialization was seen in 8 cases (40%). Of the remaining ulcers, 12 (60%) were taken up for skin grafting once the ulcer has granulated well. In these cases of skin grafting, 10 ulcers have healed completely with 2 case of graft failure Time taken for the wounds to heal completely by re-epithelization ranged from 6 weeks (2 venous ulcer) to 16 weeks (2 diabetic foot ulcer). Of the ulcers (n=12, 60%) which underwent skin grafting, 10 (83.33%),healed completely, with 2 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

I. 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.

II. MATERIAL AND METHODS

A prospective study of 20 cases of chronic leg ulcers who presented to the General surgery department at Narayan Medical College & Hospital, Sasaram from January 2021 to April2021 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 were selected. 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 dressing was on 5th day which was then followed by alternate saline dressing. Based on the response of ulcer to the first procedure /application decision was 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 autologous platelets

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Volume 3, Issue 5, Sep-Oct 2021 pp 274-278 www.ijdmsrjournal.com ISSN: 2582-6018

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, number of times application, skin grafting, time taken for complete healing.

III. RESULTS

In this study a total of 20 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 cm2 to 1 Ox8. At the end of 2nd week, ulcer size had reduced by an average of 21.87% (range O%- 60%) in 20 wounds. 12 wounds were clinically assessed as improved, and 8 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 4 ulcerswere covered with split thickness skin graft. After the end of 6th week, the 4 wounds which underwent skin grafting have healed completely and 2 ulcer re-epithelialized. The remaining ulcers (N=8) were again measured and the ulcer sizes were found to have reduced by an average of 67.52% (range 40%-90%).Reductioninwoundsizebyweeks:-

woundswerealsolooked into in the aspect of granulation tissue clinically andalltheulcers were found to have a healthy granulationtissueandthe edges showedsignsof healing.

NumberofPRPapplication:-

Thenumberoftreatmentswithplateletrichplasmavaried from2-6applications[average 2.9applicationperulcer](figure-1).

Healingoftheulcerswithfullre-epithelializationwasseenin 8 cases (40%). Of the remaining ulcers, 12 (60%) were takenup for skin grafting once the ulcer has granulated well. Inthesecasesofskingrafting,10 ulcershavehealedcompletelywith2 case ofgraft failure (figure-2).

Timetakenforthewoundstohealcompletelybyre-epithelization ranged from 6 weeks (2 venous ulcer) to 16weeks(2diabeticfootulcer).Oftheulcers(n=12 ,60%)whichunderwentskingrafting,10(83.33%),healedcompletely,with2 case of graft failure.

Duration of Ulcer (weeks)	No. of Patients (n)	Percentage (%)
9–12	4	20
13–16	14	70
17–20	2	10
21–24	2	10

Table 1: Duration the ulcer 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

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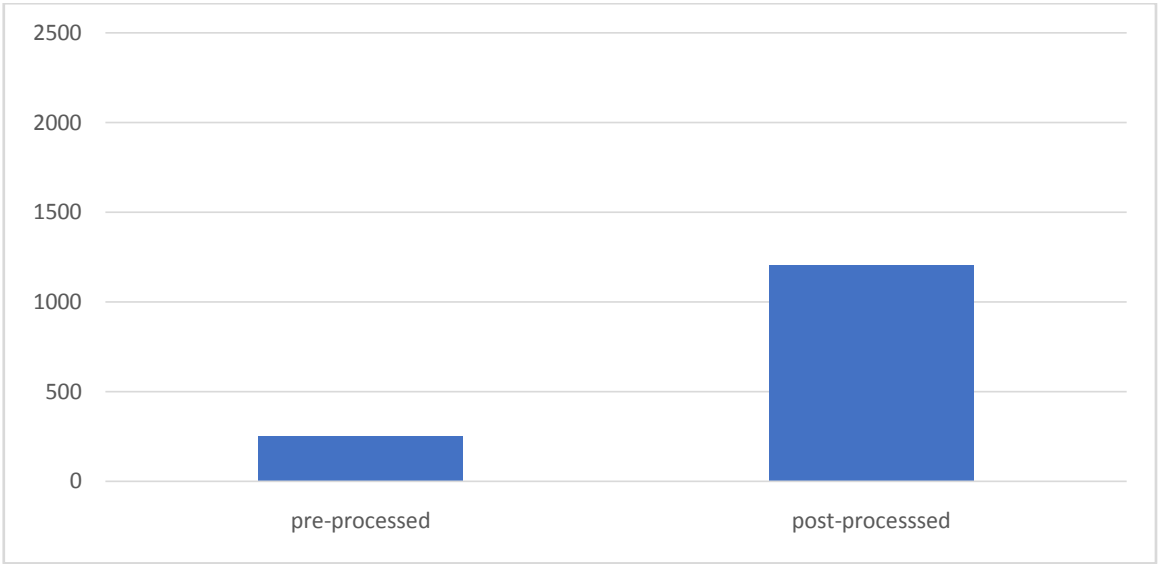

Platelet count (*10.3/µ/L)
Distribution of Platelet counts at pre- and post- processing (*p < 0.05)

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

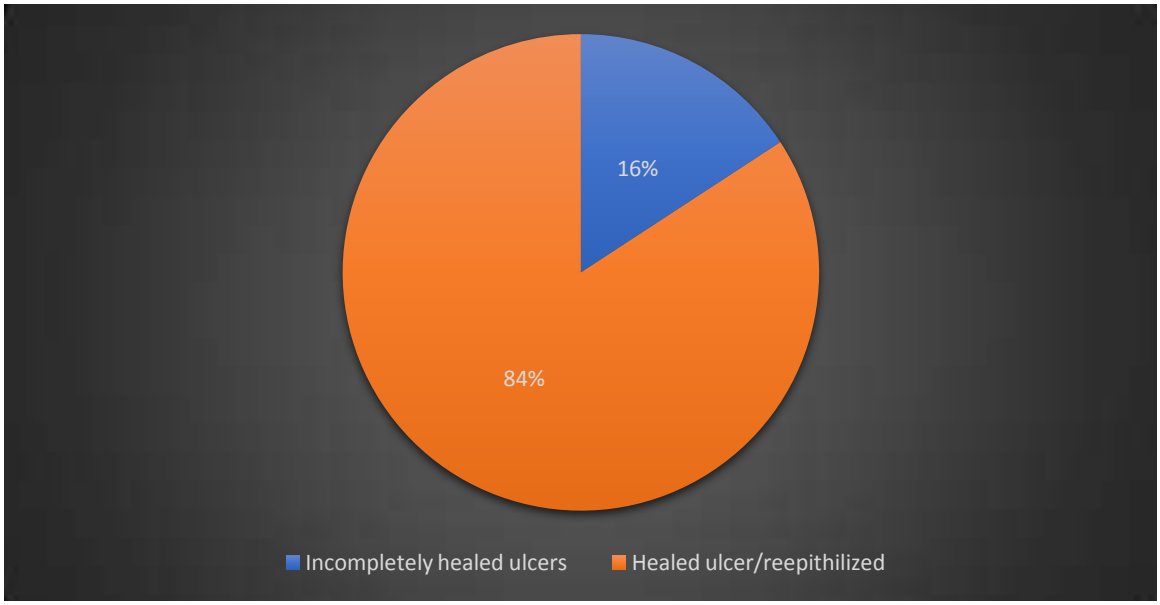

Figure-2: Wound response to PRP.

Variables	Crovetiet al[3]	Driveretal[4]	O'Connelletal[5]	Presentstudy
Age	NA	18-95	18-85	18-60
No.ofulcers	24	40(prp-19,saline-21)	30(venous-17,non-venous-13)	20
Etiology	Alltypesofchronic ulcers	NA	venous andnonvenous	venous anddiabetic
No.ofPRPapplications	1/wk-12weeks	NA	Averageof2applica-tions perpatient	1applicationevery 2 weeks

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DecreaseinWoundsize	NA	NA	NA	2weeks- 21.87% 4weeks-59.43% 6weeks-67.52%
Woundre-epitheliza-tion	9ulcers	68.4% in PRPgroup42.9% in salinegroup	66. 7%invenous ulcergroup 44% innonve-nousulcergroupby 12 weeks	8ulcers
SSG	NA	NA	NA	12ulcers
Unhealed/partial response	partial-9 stopped-4	NA	NA	NA

Table-3: Comparisonofpreviousstudiesinrelationtothepresentstudyisgiven

IV. DISCUSSION

Wound healing is a complex process that is regulated byinteractionsbetweenalargenumberofcelltypes,extracellularmatrix proteins and mediators such as cytokines and growthfactors.Lackofbalance betweentheseinteractions mayresult in a chronic wound. One possible cause of imbalanceinthewoundhealingprocessishighbacterial countsleadingtoaprolongedinflammatoryresponsewithhighlevelsof cytokines. This leads to increased production of matrixmetalloproteases.Highmatrixmetalloprotease activityresults in uncontrolled breakdown of extracellular matrixand growth factors. This leads to a chronic wound whichfails to heal. Chronic foot ulceration is an epidemiologicallywidely prevalent disease in India as well as in the worldleading to huge wastage in work hours of the people. It alsoimpacts the quality of life of the people affected.

Plateletsplayamajorroleintheprocessofwoundhealingthroughtherelease of various growth factors from the granules presentinthem.Plateletrichplasmawithitsconstituent highplateletconcentration and growth factors, help in the recreation ofidealenvironment for woundhealing.

Crovetti et al.[3] published a prospective non-blinded studyregardingtheefficacyofplateletgel(PG)inhealingcutaneous chronic wounds. The wounds of the 24 patientsenrolledinthisstudyvariedinorigin,andetiologiesincludeddiabetes- related, vascular insufficiency, infectious disease,post-traumatic,NEUROPATHIC,andvasculitis-related.Theprotocolforthisstudyconsistedofonce-weeklyplateletgel (PG) applications of either autologous or homologousorigin.Atthetimeofthestudypublication, ninepatientshadhealed completely, two went on to receive cutaneous grafts,fourhadstoppedtreatment,andninehadrespondedpartiallyand nine had responded partially and were still receivingtreatment.

Driveretal.[4]carriedoutthefirstreportedprospective,randomized, controlled multicenter trial in the United Statesregarding the use of autologous PRP for the treatment ofdiabetic foot ulcers. Participants included 72 patientswithtype1andtype2diabetesbetweentheages of18and95from14investigationsitessufferingfroman ulcerofatleastfour weeks duration. In this study, investigators comparedthe effectiveness of autologous PRP gel to that of normalsaline for 12 weeks. The primary objective of this study wasto evaluate the safety of PRP and the incidence of completewound closure, defined as 100 percent re-epithelialization,when compared to the control treatment, and a secondaryobjectivewasrateofwoundclosure.Patients wererandomizedintotwogroups-standardofcarewithPRPgelorcontrol(saline)-andwereevaluatedbiweeklyfor12 weeks. After excluding 32 patients from the final per-protocol analysis because of failure to complete treatmentand 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 thePRPgrouphealedafterameanof42.9days(SD18.3) vs.
47.4 days (SD 22.0) in the control group.

O'Connell et al[5] presented promising findings from a pilotstudy involving the treatment of chronic lower-extremityulcers with autologous platelet-rich fibrin matrix membrane(PRFM). In this present study 10 ulcers were selected, witha mean patient age of 47.6 yrs. The ulcer size varied from3x3cm2to10x8cm2.Totalno.ofPRPapplications ranged'
from2-6(average2.9),withaspaceof2weeksbetween applications. All the patients received autologous plateletrichplasma.Thewoundwerefollowedtilltheyh

ealedeitherby re- epithelization or after SSG. The decrease in size ofulcersrangedfrom0%to60%attheendof2weeks,20%to88%after4weeksand40%to90%at6weeks.Fourwoundsre-epithelized,ofwhich1ulcerby6weeks,twoulcersby8 weeks and another by 16 weeks. The remaining 6 ulcerswent on to receive skin grating of which 1 had graft failure;this was further treated with repeat PRP application leadingto complete healing.

Comparison of various studies (table-3) different rates ofhealing attained in these studies as well as others done onchroniculcerscanbeattributedtothenon-standardizationof PRP preparation technique, frequency of PRP applicationover the ulcers, etiology of the ulcers in different studies,influenceofother factorsoverthe woundhealing.

Apart from this many studies done on PRP application inpatient care some of these are McAleer et al. (2006)[6] foundthat the use of autologous PRP was successful in healing achronic lower extremity wound in a case study of a 57-year-oldman

Althoughthisstudyislimitedasacasestudyinvolving a single patient, it suggested that PRP can besuccessfulinhealingwoundsthathavefailedtohealbyothertreatmenttechniques.Salemietal.(2008)[7]wasa morerecentcase study evaluating the effectiveness of a combination ofautologousadiposetissueandPRPinalowerextremityulcerofthree years duration in a non-diabetic.[8]

V. CONCLUSION

Theuseofplateletrichplasmacanbeanoption whentreatingrecalcitrantwoundsofdifferingetiologies.Itshouldbereservedtowoundsthatdonotshowanyprogressafter6monthswithtreatmentofwoundaetiology andstandardwoundcare.

Inthisstudyaswellasinotherstudiestherewervariationsin the response of the chronic ulcers to the platelet richplasmaapplicationwhichcanbeattributedto,variationsin patient characteristics between patients with type 1 andtype2diabetesmellitus,durationofdiabetesdiagnosis,degree of control of diabetes, patient age, patient gender,initialwoundarea,wounddepth,woundduration,andwound location, which can alter the possible outcomes ofthis treatment.

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