

## Clinical Study to Compare the Efficacy of Platelet Rich Plasma versus Conventional Dressing in Chronic Non-Healing Ulcers

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**Abstract:** Chronic Wounds Are A Major Health Challenge And Are A Growing Socioeconomic Problem All Over The World. The Goal Of Wound Care In Chronic Ulcers Is To Facilitate Healing Using Standardized Protocols Of Wound Care. The Main Goal Of Any Treatment Modality Is To Obtain Wound Closure Expeditiously. The Aim Of Our Study Is To Compare And Find Out Which Is Better Among Platelet-Rich Plasma Vs. Conventional Dressing. In This Study, A Total Of 50 Patients Of Chronic Non Healing Ulcers Who Presented In Our Institute Were Evaluated From December 2015 To October 2017. Patients Were Randomly Grouped Into Two Groups - PRP And Conventional Dressing Group Of 25 Patients Each. Definitely, PRP Group Showed Better Results In Term Of Healing Rate And Required Significantly Less Number Of Dressings For Wound Closure. Results From Our Research Showed That PRP Is A Safe And Effective Treatment Modality For Chronic Non-Healing Ulcers. Using PRP To Treat Chronic Wounds/Ulcers May Not Only Enhance Healing But Also Prevent Lower Extremity Amputations Caused By Non-Healing Wounds.

**Keywords:** PRP, Conventional Dressing

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Date of Submission: 24-02-2018

Date of acceptance: 12-03-2018

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### I. Introduction

Chronic Wounds Are Defined As Wounds, Which Have Failed To Proceed Through An Orderly And Timely Reparative Process To Produce Anatomic And Functional Integrity Defined Differently By Various Authors Ranging Over A Period Of 1-3 Months. The Prevalence Of Chronic Non Healing Ulcer In The World Ranges From 1.9 To 13.1%<sup>[1, 2]</sup>. The Incidence Of Chronic Ulcers Is Expected To Increase As The Population Ages And Due To Increased Risk Factors For Atherosclerotic Occlusion Such As Smoking, Obesity, And Diabetes. It Is Estimated That Almost 10% Of The Population Would Develop A Chronic Wound In The Course Of A Lifetime; With Wound-Related Mortality Rate Of 2.5%<sup>[2]</sup>

Apart From These Conventional Methods To Facilitate Wound Healing Various New Methods Are Emerging Such As Cellular Therapies Which Include Platelet-Rich Plasma (PRP), A Collagen-Based Wound Dressing. Platelets Release Certain Growth Factors From Alpha Granules Which Are Located In Thrombocyte Cell Membrane Which Include Platelet-Derived Growth Factor (PDGF), Epidermal Growth Factor (EGF), Platelet Derived Angiogenesis Factor And Platelet Factor 4. These Factors Act Locally On the Wound And Hasten The Healing Process. Platelet Extract Has Been Used In Many Studies And Has Shown Impressive Results In Healing Of Chronic Non Healing Ulcers.

The Purpose Of This Study Is To Evaluate How Platelet-Rich Plasma (PRP) Affects Initial Wound Healing Trajectories Of Chronic Non-Healing Wounds In A Hospital Care Setting. The Present Study Will Assess The Therapeutic Role Of Platelet-Rich Plasma/Allogenic Platelet Concentrate Available In The Healing Of Chronic Non-Healing Ulcers.

### Aims and Objectives

1. To Assess The Various Factors Responsible For Chronic Non Healing Ulcers.
2. To Compare The Rate And Duration Of Healing Of Chronic Non Healing Ulcers During The Study Of Experimental And Control Groups.
3. To Assess The Incidence Of Complications Using Both Methods Of Dressing In Chronic Non-Healing Ulcers

## **Material and Methods**

The Study Was Conducted On 50 Patients (Sample Size) Of Chronic Non Healing Ulcer In The Department Of Surgery, JA Group Of Hospitals And GR Medical College, Gwalior (MP) During December 2015 To October 2017 After Getting Proper Written And Informed Consent From The Patients.

### **Criteria for Selection:**

Patients With Chronic Non Healing Ulcers Attending Surgery OPD And Being Referred From Another Department To Surgery Department Or Getting Admitted In Department Of Surgery, JA GROUP OF HOSPITAL GWALIOR And Validating The Following Inclusion And Exclusion Criteria:-

### **Inclusion Criteria:**

1. Patients In The Age Group Of 15 To 80 Years With Chronic Long-Standing Non-Healing Ulcers.
2. Ulcer  $\geq$  4weeks Duration.
3. Ulcer  $\leq$  15cm<sup>2</sup> In Size.
4. Haemoglobin  $\geq$  10 G%.

### **Exclusion Criteria**

1. Screening Platelet Count  $< 100 \times 10^9/L$ . (IE1 Lakh Per Microliter )
2. Patients with Known Or Suspected Osteomyelitis.
3. Patients with Serum Creatinine  $> 1.5$  Mg/Dl.
4. Severe Infection
5. Presence of Cellulitis, Gangrene.
6. Diabetic.

## **II. Procedure Methodology:**

The Study Was Designed As A Prospective, Randomized Controlled Clinical Study. Those Patients Who Met The Inclusion Criteria Were Explained The Entire Treatment And Follow-Up Procedure By The Study Investigator, And Only After Obtaining Voluntary Written Consent From The Patients For The Treatment Procedure, They Were Treated With PRP And Normal Conventional Dressing. Their Follow-Up Data Were Collected. Two Groups Were Randomly Assigned As the Cases A (Experimental Group, N = 25) and B (Control Group, N = 25). A Detailed History Was Taken In All Cases Regarding The Duration, Mode Of Onset, Progression, And Associated Symptoms. Also, The Etiological Factor Responsible Was Elicited In The History. Ulcer Examination Was Done In All These Patients and the Wound Was Assessed For Its Characteristics and Photographed. The Ulcer Was Assessed By the Investigator at The Beginning Of The Study And At Every Dressing And Photographed For Follow Up.

**For Conventional Dressing:** A Chronic Non Healing Ulcer With No Active Pus Discharge And Slough Was Cleaned With The 0.9% Saline Solution And Was Covered With A Pad And Roller Bandage. The Conventional Treatment Includes Adequate Debridement, Control Of Infection By Local Measures Such As The Use Of Betadine Etc And Systemic Antibiotics, And Avoidance Of Undue Pressure On The Wound. <sup>(3, 4, 5)</sup>

**For Platelet Rich Plasma:** Freshly Prepared Platelet-Rich Plasma Was Issued From G.R.M.C Gwalior Blood Bank And Injected Periphery During Each Dressing I.E. PRP Was Injected At The Healing Margins Using Insulin Syringe (26 G) After Cleaning With 0.9% Saline And Dressing Done Using Pad And Roller Bandage. Maximum Of 5ml Of PRP Was Used In One Sitting And It Was Used Uniformly Over The Healing Margin Of The Ulcer And The Procedure Was Done On OPD Basis. The Dressing Was Changed Every 3rd Day in Both the Groups.

Platelet-Rich Plasma Was Screened For All Routine Blood Transmitted Diseases Prior To Its Use And The Potential Threats Associated With The Use Of Blood And Its Products Were Explained To The Patient. Ulcers Were Assessed And Measured (Length And Width Across Longest Dimension, Using A Metric Tape). The Outcome Was Measured In Terms Of Wound Reduction Between The Two Groups. Other Wound Characteristics I.E. Presence Or Absence Of Granulation Tissue, Pain, Colour, Edges, Etc. Was Documented. The Endpoint Of The Study Was Taken As The Complete Closure Or End Of Follow Up.

## **III. Observation & Results**

During The Study, 50 Patients with Chronic Non Healing Ulcers Were Randomized Into The Study (PRP) And Control (Conventional Method Of Dressing) Group In A Group Of 25 Each. These Groups Were Studied For The Effect Of Conventional Versus PRP Dressing On Epithelialization, Reduction And Complete Healing Of The Non Healing Ulcer.

**Statistical Analysis:** The Analysis Was Done By Using Students Paired‘T’ Test For Continuous Variables Within The Groups And Unpaired ‘T’ Test For Continuous Variables Between Cases And Controls.

**Age Distribution:**

In Our Study Of 50 Patients, Age Ranged From 11 To 80 Years With The Maximum Number Of Patients Between 50 – 60 Years, Followed By Age Group Of 21-30 And 41-50 Years With 12 Patients In Each Group. Out Of 50 Patients, 39 (78%) Patients Were Males and 11 (22%) Patients Were Female I.E. Our Study Shows A Male Preponderance Of Chronic Non Healing Ulcer.

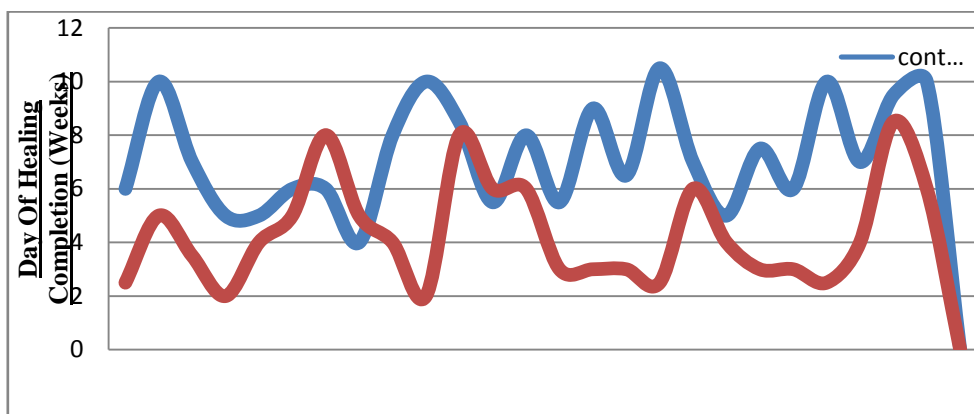
**Ulcer Characteristics:**

- **Ulcer Size:** In Our Study Of 50 Patients The Ulcer Size Ranged From 6 To 15 Cm<sup>2</sup>. The Mean Size In Control Group Was 9.48±1.91 Cm<sup>2</sup> And Among Cases 9.56 ±1.87 Cm<sup>2</sup>.
- **Ulcer Location:** In Our Study, The Most Common Location of Chronic Non Healing Ulcer Is Lower Limb 44(88%) Out Of 50 Patients Next Being Torso 4(8%) Patients and Only 2 (4%) Patients on Upper Limb.
- **Etiology of Chronic Non-Healing Ulcer:** In Our Study, 23(38%) Out Of 50 Patients Developed Chronic Non Healing Ulcer Following Trauma and 19(38%) Patients Had Venous Ulcer Followed By Trophic And Vasculitic Etiology.
- **Total Duration of Ulcer:** Out Of The 50 Patients Of Chronic Non Healing Ulcer Maximum Patients Were With The Duration Of 16-19 Weeks I.E. 22 Patients (44%) Followed By 16 Patients In 20-23 Weeks Group I.E. 32 Percent.

**Healing Profile:**

- **Day Of Healing Completion (Weeks):** In Our Study, We Observed That Healing In Cases Or Experimental Group Took Significantly Less Time When Compared With Control Group. The Mean Duration of Healing in Control Group Was 7.3 ±1.91 Weeks and Mean Duration of Healing for Cases Group Was 4.38±1.94 Weeks. The Probability Value (P-Value) Obtained After Applying Unpaired T-Test For The Above Data Comes Out To Be 0.0001 Which Is Statistically Significant.

Day Of Healing Completion (Weeks)	Groups	
	Cases	Controls
Mean	4.3800	7.3000
SD	1.9100	1.9400
N	25	25
Pvalue	0.0001	



**A chronic non healing ulcer at the anterior aspect of leg from 1 year.  
Final result following 10 PRP applications.**

- **Number Of Dressings Required For Complete Healing:** In Our Study, We Observed That Healing In Cases Or Experimental Group Took A Significantly Lesser Number Of Dressings When Compared With Control Group.
- The Mean Number of Dressings Required for Healing in Control Group Was  $12.8 \pm 1.94$ , And a Number of Dressings Required for Healing in Cases or Experimental Group Were  $7.60 \pm 2.9$ . The Probability Value (P-Value) Obtained After Applying Unpaired T-Test For The Above Data Comes Out To Be 0.0001 Which Is Statistically Significant.

### **Discussion**

Chronic Wounds Are A Major Health Problem Especially In Developing Countries Like India And They Are Often Difficult To Heal And Are Associated With Superadded Infection. The Main Goal Of Any Treatment Modality Is To Obtain Wound Closure Expeditiously. The Conventional Treatment Includes Adequate Debridement, Control Of Infection, Re-Vascularisation Of Ischemic Tissue, And Avoidance Of Undue Pressure On The Wound. Skin Grafting Has Shown Some Efficacy; However, They Are Not Capable Of Providing The Necessary Growth Factors To Modulate The Healing Process And Are Expensive.<sup>[6, 7]</sup>

An Experimental Tool Used In Combination With Standard Wound Care, Topically Applied Working Platelet Concentrate Or Plasma (PRP), May Be Used To Boost Chronic Inflammatory Wounds Into The State Of Proliferation And Healing As They Release Multiple Growth Factors And Cytokines Into The Wound Mimicking Natural Healing Conditions<sup>[8,9]</sup> PRP Contains Various Necessary Growth Factors For Wound Healing.

In Addition, The High Concentration Of WBC's Present In PRP Is Also Helpful In Preventing Infections<sup>[10]</sup> And Platelet-Rich Plasma Has Already Been Used To Treat Wounds Since 1985<sup>[11]</sup>. The Mechanism Of Action For PRP Is Thought To Be The Molecular And Cellular Induction Of Normal Wound Healing Response Similar To That Seen With Platelet Activation<sup>[12]</sup>. PRP Accelerate All Phases Of Wound Healing (Most Prominent In Angiogenesis)<sup>[12]</sup>

In Our Case Series, 25 Patients As Case And 25 As Control With One Wound/Ulcer Per Patient Were Treated With Multiple Doses Of Subcutaneous Injections Of PRP Around The Ulcer Margin. All The Patients Showed Healing Of The Wound With A Reduction In Wound Size, And The Mean Time Of Healing Of The Ulcers Was  $4.38 \pm 1.9$  Weeks. Reduction In Pain Was Observed In All The Patients Post-Treatment And Also, The Quality Of Life Of The Patients Significantly Improved. The Results Demonstrated The Safety And Efficacy Of Autologous PRP In Treating Chronic Non-Healing Ulcers

A Study Conducted By Frykberg Et Al<sup>[13]</sup> On 49 Patients With 65 Non Healing Ulcers Showed That 63 Of 65 Ulcers Responded With A Reduction In Area, The Volume Of The Ulcers In A Mean Duration Of 2.8 Weeks With 3.2 Treatments. Steenvoorde Et Al<sup>[14]</sup> Conducted A Study On 12 Patients With 13 Wounds, Showing That 7 Of 13 Wounds Required More Than 1 Application, With A Mean Number Of 2.2 Applications And A Mean Treatment Period Of 4.2 Weeks.

Kakudo Et Al.<sup>[15]</sup> Treated Five Cases Of Intractable Skin Ulcer With Autologous PRP, Among Which Three Ulcers Healed Completely Within 4 Weeks And Epithelization Of Wound Occurred Within 6.6 Weeks On Average.

A Prospective, Randomized, Controlled, Blinded Multicenter Study Conducted By Driver Et Al., Initially Included 72 Patients With Diabetic Foot Ulcers Who Were Treated With Autologous Platelet-Rich Plasma Gel Or Control (Saline Gel). However, 32 Patients Were Excluded From The Final Protocol Because Of Protocol Violations And Failure To Complete Treatment. Their Study Results Showed That Significantly More Wounds Healed In Patients Treated With Platelet-Rich Plasma Gel (13 Out Of 16 Or 81.3%) Than Patients Treated With Control Gel (Eight Out Of 19 Or 42.1%). However, The Study Had Several Limitations Including Small Sample Size, Protocol Violations Occurring During The Study Period, And High Rate Of Patient Dropouts<sup>[16]</sup>.

The Results From Our Case Series Were Concurrent With Previously Published Studies In Terms Of Healing Time. In This Study, Initial Area Of The Ulcer (In  $\text{cm}^2$ ) Was Similar Between The Two Groups. However, The Final Time And Number Of Dressing Required For Complete Closure Was Significantly Less In Those Treated With PRP As Compared To The Control Group And This Difference Was Statistically Significant

### **IV. Conclusion**

We Were Able To Derive The Following Conclusions While Application Of Platelet Rich Plasma (PRP) Dressing In Comparison With The Control Group For The Treatment Of Chronic Non Healing Ulcers:-

1. PRP Showed Faster and Better Healing Rates among the Study Group.
2. Ulcer Area Reduction And Percentage Reduction Of Ulcer Size Were Better In PRP Group.
3. Formation Of Granulation Tissue Over The Ulcer Is Better And Early With PRP Group.

4. There Were No Adverse Effects Or Reactions Seen With The Use Of PRP.

In Conclusion, The Results From Our Case Series Showed That PRP Is A Safe And Effective Treatment Modality For Chronic Non-Healing Ulcers. Using PRP To Treat Chronic Wounds/Ulcers May Not Only Enhance Healing But Also Prevent Lower Extremity Amputations Caused By Non-Healing Wounds. Therefore, Further Research And Randomized Controlled Clinical Trials On Larger Patient Population Are Necessary To Validate The Results.

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Arjit Singh "Clinical Study To Compare The Efficacy Of Platelet Rich Plasma Versus Conventional Dressing In Chronic Non-Healing Ulcers "IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 3, 2018, pp 42-46