



## COMPARATIVE STUDY BETWEEN PALETELET RICH PLASMA VS CONVENTIONAL DRESSING IN HEALING OF CHRONIC FOOT ULCER IN DIABETIC PATIENTS – A PROSPECTIVE RANDOMIZED CONTROL TRIAL

### General Surgery

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### ABSTRACT

**Background :** Chronic non healing ulcer has become a great challenge in diabetic patients. platelet rich plasma is used as it is enriched with growth factors to enhance healing of these chronic wounds in diabetic patients and its efficacy is compared with conventional dressing.

**Methods:** This study was conducted in Indira Gandhi Medical College and hospital, pondicherry from august 2019 to October 2019. A total of 72 diabetic patients admitted for non healing foot ulcer was taken up for this study. 36 patients was treated with conventional dressing and 36 patients was treated with platelet rich plasma dressing (PRP). Size of wound , duration and cost were compared between these two groups.

**Results:** Healing was better in patients who were given PRP dressing compared to conventional dressing based on reduction in size of the wound by 6 weeks.

**Conclusion :** Autologous PRP is effective and safe in diabetic patients with chronic non healing foot ulcer

### KEYWORDS

PRP , conventional dressing , diabetic foot ulcer

### INTRODUCTION:

Chronic wounds develop in 15% of diabetic patients. Amputation of foot is done in 25% of these patients having chronic wound(1,2). Chronic wounds develop in diabetic patients due to many reasons of which one of the main cause is deficiency of growth factors. Among the blood products, platelets has a rich source of growth factors . Various platelet formulations are experimented in these conditions of which US Food and Drug Administration have approved only Becaplermin, a recombinant human platelet-derived growth factor-BB (3) for the treatment of chronic wound in diabetic patients. Other than the platelet derivatives , cell containing tissue engineered skin products are used to treat difficult wounds in diabetic patients. Currently Apligraf and Dermagraft are the two cell containing tissue engineered products approved(4). Both becaplermin and the cell containing tissue engineered products needs frequent administration , have shorter half life and are expensive. Alternate to these preparations is the platelet rich plasma (PRP). Plasma is said to be platelet rich when the platelet concentration is above the baseline values(5,6)

PRP was discovered in early 1990s and currently it is used extensively in various fields including chronic wound, dentistry, orthopaedics , orofacial maxillary surgeries(7). Various growth factors such as platelet derived growth factor, transforming growth factor- $\beta$ , fibroblast growth factor, insulin-like growth factor-1, vascular endothelial growth factor, epidermal growth factor, and also some cytokines contribute to the therapeutic efficacy of the platelet rich plasma(8,9). PRP also enhances wound healing by providing barrier effect to prevent bacterial invasion.

PRP can be acquired either from patients own blood or allogenic source of which former is preferred because of more acceptability and also reduces transmission of infections(10). There are two steps in the preparation of platelet rich plasma. First patients blood is centrifuged to separate plasma and red blood cells. Further centrifugation will separate platelet rich plasma from platelet poor plasma. Minimum of one million platelet per microliter has to be present for the clinical efficiency of the PRP(11).

### Aims and objective :

The aim of the study is to compare the effectiveness of platelet rich plasma (PRP) vs conventional dressing in the healing of chronic wound in diabetic patients.

### Types of interventions:

- Conventional dressing
- Platelet rich plasma dressing

### Types of outcome measures:

- Size of the wound
- Time of healing

- Cost effectiveness.

### MATERIALS AND METHODS:

- This study was conducted in department of general surgery , Indira Gandhi medical college and hospitals- Pondicherry from august 2019 to October 2019.
- Patients will be selected from those admitted to Department of General Surgery, Indira Gandhi medical college and hospitals- Pondicherry for chronic diabetic foot ulcer.

### Inclusion criteria:

- Age >18 year
- Patient and/or his/her legal representative has read and signed the approved Informed Consent form before treatment
- Diabetic Patient with good glycemic control.
- Ulcer: without any active infection confirmed by pus culture sensitivity or treated with antibiotic therapy.
- Circulation status: with palpable pulses.

### Exclusion criteria:

- patients with uncontrolled DM, DKA
- Active malignancy.
- Being treated with immunosuppressant drugs.
- Patient received biological treatment(s) within 30 days.
- Active infection - if osteomyelitis has been diagnosed.

Sample Size- Number of patients studied are 72. Statistical Analysis of my study will be by standard- 't' test, chi-square method.

### Methodology:

Approval from the Ethical committee , Indira Gandhi medical college and hospitals has been obtained (12/193/IEC25/pp/2019) and the same was submitted to CTRI (reg.no:2019/08/020959). Informed and written consent was obtained from both group of patients. The benefits, risks , possible complication of both the modalities were explained to the patients participating in the study.

This randomized case control study is conducted on 72 diabetic patients with chronic non healing foot ulcer. These 72 patients were divided into two groups based on odd and even admissions. Patients in Group A are subjected to conventional dressing (n=36) and the patients in Group B are subjected to PRP dressing (n=36).

Group A patients were treated by conventional dressing which includes debridement of the ulcer with excision of all necrotic tissues and Irrigation of the wound with saline followed by saline dressing. This dressing is done once or twice everyday.

Group B patients were subjected to PRP therapy. 20 ml of patients own blood was withdrawn in citrate coated tube and sent for two step

centrifugation. First soft spin centrifugation done (3000 RPM for 5 min) which separated RBC from plasma. The plasma is transferred to another tube which is further centrifuged at 4500 RPM for 5 min (hard spin). After this the plasma was separated into platelet poor and platelet rich plasma. The upper third of the tube comprised the platelet poor plasma and the lower third comprised platelet rich plasma. This PRP was aspirated in 1 ml syringe and injected all around the ulcer within 1 cm from the margin. Following which sterile dressing done. This was repeated once a week for 3 to 4 consecutive weeks based on the ulcer size.

Patients were given appropriate off-loading footwear post procedure and advised elevation of the foot while sitting. The patients ulcer were seen once in 4 days. Evaluation of the patients done based on the rate of wound healing every week and also the cost effectiveness of both procedures were evaluated.

**Observation :**

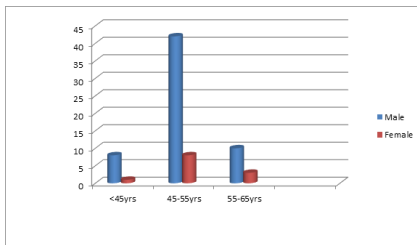
Seventy two patients with chronic diabetic foot ulcer were taken up for the study at Indira Gandhi medical college and hospitals, Pondicherry during the period of August 2019 to October 2019.

**Age and sex distribution:**

**Table :1**

Age in yrs	Male	Percentage	Female	Percentage	Total	Percentage
<45 years	8	13.3%	1	8.3%	9	12.5%
45-55 years	42	70%	8	66.67	50	69.44%
55-65 years	10	16.7%	3	25%	13	18.05%
Total	60	100%	12	100%	72	100%

**Graph :1**

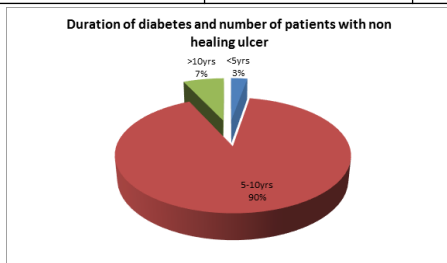


Below 45 years there were 8 males and one female, between 46 - 55 years there were 42 males and 8 females, between 55-65 years there were 10 males and 3 females. In this study, the peak incidence of chronic non healing ulcer in diabetic patients was between 45-55 years. Out of 72 cases under study 83% were males and 17% were females, incidence of 5:1 (M:F) showing male predominance.

**Duration of diabetes mellitus**

**Table :2**

Duration of diabetes mellitus	Number of patients with non healing ulcer	Percentage
< 5years	2	2.7%
5-10 years	65	90.3%
>10 years	5	6.93%
Total	72	100%

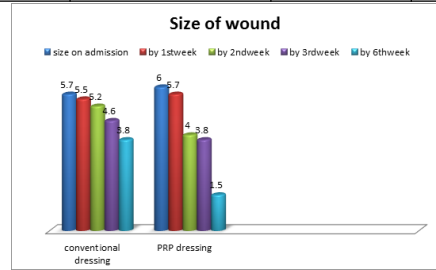


Among the 72 patients with chronic non healing ulcer under study, 90% of them had diabetes for a duration of 5-10 years with mean duration of 8.57 ± 1.23 years.

**Table : 3 Size Of Wound**

Size of wound (mean±SD)cm	Conventional dressing Group A	PRP dressing Group B	P value
On admission	5.7 ± 0.42	6 ± 0.56	< 0.0001 (significant)
1st week	5.5 ± 0.2	5.7 ± 0.1	
2nd week	5.2 ± 0.15	4 ± 0.23	
3rd week	4.6 ± 0.46	3.8 ± 0.21	
6th week	3.8 ± 0.41	1.5 ± 0.12	

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3rd week	4.6 ± 0.46	3.8 ± 0.21
6th week	3.8 ± 0.41	1.5 ± 0.12



**Graph :3**

The mean size of the wound was 5.7 to 6.56. PRP has shown significant reduction in size of the wound (P<0.0001) in 2<sup>nd</sup>, 3<sup>rd</sup> and by 6 weeks.



**PRP therapy admission wound size at 6 weeks size**

**Cost of procedure:**

As the PRP was obtained from patients own blood and the entire study was conducted in Indira Gandhi medical college which is a Puducherry government institute, everything necessary for the study purpose was free of cost.

**DISCUSSION:**

Diabetes is a common clinical condition. Chronic wounds develop in 15% of diabetic patient due to various factors including increase in age, tobacco use, obesity, hypertension, atherosclerosis, social and economic effects (12). For the past 20 years, the PRP has been used to promote wound healing as it contains cytokines, growth factors, chemokine, and fibrin scaffold.

In our study, we have conducted a randomised controlled trial in Department of General Surgery, Indira Gandhi medical college and hospital, puducherry from August 2019 to October 2019 among 72 diabetic patients who were admitted for chronic non healing ulcer to see the effectiveness of PRP in promoting healing of diabetic foot wounds, preventing infection, and reducing exudates when compared to conventional dressing. Carter et al had shown PRP therapy can positively impact wound healing and associated factors such as pain and infection in both chronic and acute cutaneous wounds(13).

**Age and Sex Distribution**

According to the observation based on table 1 and Graph 1, the peak age incidence of chronic non healing ulcer in diabetic patients was observed between 45-55 years. A total of 60 males and 12 females were considered for study and the male-to-female ratio in this study is 5:1. Saad et al carried out study on 24 patients with chronic ulcers ranging in age from 40 to 60 years, they concluded that sex and age are insignificant in correlation with the rate of healing of their ulcers.(14)

**Site of ulcer and duration of diabetes:**

In the present study, the site of diabetic feet wounds was generally the sole of the foot. The duration of diabetes ranged between 5 - 10 years, it was observed that as the duration of diabetes increases, the incidence of developing chronic non healing ulcer increases significantly.

**Size of wound:**

In our study the size of wound ranged between 5.7 - 6.56 cm. It was observed that in patients receiving PRP dressing for diabetic foot ulcer, the rate of healing was significantly (P<0.001) better than in patients who received conventional dressing after three settings. The number of PRP injections for the patient was determined based on the size of the ulcer. Many trials concluded that the larger the ulcer, the longer the duration required for treatment and the greater the number of

injections(15.16). In our study, site of the ulcer had no impact in the rate of healing. Gui-Qiu et al studied the effect of PRP on healing of chronic ulcer concluded that 'there was no significant difference between type and site of ulcers in correlation with rate of healing'(17). Various studies like Martinez-Zapata et al, reported that the percentage of total healing in PRP- treated wounds increased compared with the controls. In a meta-analysis of chronic wound studies, Carter et al, confirmed that the use of PRP treatment promotes complete healing compared with control care. Villela et al, also reached the same conclusions(18).

Most of the wounds healed within the estimated time of healing (6 weeks); all these cases showed more than 50% healing after the first 4 weeks. These results were confirmed by Gelf et al, who stated that 'it is generally accepted that a reasonable goal is healing by 12 weeks.'(19) Healing rates at 4 weeks predict overall healing rates, and a 10-15% area reduction weekly suggests an excellent prognosis'.

#### Summary :

72 diabetic patients with chronic non healing ulcer were divided into two groups , one receiving conventional dressing and the other PRP dressing at Department of general Surgery, Indira Gandhi Medical College and Hospitals, puducherry. The study was prospective, randomised control trial from august 2019 to october 2019. Rate of healing of the ulcer was observed on both group of patients and the data recorded. In our study, the male-to-female ratio was 5:1 with male predominance. The peak age incidence in our study was between 45-55 yrs. The average duration of diabetes was 5-10 years. 3-4 PRP injections was given based on the wound size. The rate of healing was significantly better in patients receiving PRP dressing compared to the conventional group from 2<sup>nd</sup> week of dressing. The average sum of money spent by both group was same.

#### CONCLUSION:

The study ends with the conclusion that, use of Platelet rich plasma significantly increases the rate of healing of chronic wound in diabetic patients and also reduces the rate of amputation.

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