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Original Research Paper

General Surgery

COMPARATIVE STUDY BETWEEN EFFICACIES OF SUBCUTANEOUS PLATELET RICH PLASMA INJECTIONS WITH CONVENTIONAL DRESSING PROCEDURE IN PATIENTS WITH CHRONIC NON-HEALING ULCERS

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ABSTRACT

Background: Chronic lower limb ulcer is a chronic wound of the leg that shows no tendency to heal after 3 months of appropriate treatment or still not fully healed after 12 months. The incidence of ulceration is rising because of the ageing population and increased risk factors for atherosclerotic occlusion such as smoking, obesity, and diabetes. Chronic ulceration of the lower legs and ulcer symptoms usually include increasing pain, friable granulation tissue, and foul odor and wound breakdown instead of healing. This results in social distress and considerable healthcare and personal costs. **Aim:** To study and compare the efficacy of subcutaneous Platelet rich plasma injection with conventional dressing procedure in patients with chronic non-healing ulcers. **Study Design:** This is a comparative study done between October 2020 to September 2022, which includes 50 patients admitted in RMMCH Chidambaram detailed clinical history, examination, various investigations, appropriate treatment and follow up was done in these patients. **Results:** Patients who received subcutaneous injection of PRP around the ulcer and dressing had a faster wound healing process than the patients who received conventional wound dressing. **Conclusions:** The wounds in the subjects were treated with subcutaneous platelet rich plasma injection and dressing contracted more than the wounds in the control group (43.40% (S.D:3.74) Vs 14.03% (S.D; 3.45); P = < 0.001 Significant) which indicates platelet rich plasma dressing is an effective management to facilitate wound contraction in patients suffering from chronic non-healing ulcers and can be used as an adjunct to conventional mode of treatment (conventional dressings) for healing of chronic non-healing ulcers.

KEYWORDS : Chronic Non Healing Ulcers, PRP, Wound Dressing.

INTRODUCTION

Chronic non-healing leg ulcer (CLU) also known as chronic lower limb ulcer is a chronic wound of the leg that shows no tendency to heal after 3 months of appropriate treatment or is still not fully healed at 12 months. The incidence of ulceration is rising because of the ageing population and increased risk factors for atherosclerotic occlusion such as smoking, obesity, and diabetes[6]. Ulcers can be defined as wounds with a "full thickness depth" and a "slow healing tendency". Ulcers of skin can result in complete loss of the epidermis and often portions of the dermis and even subcutaneous fat. Chronic ulceration of the lower legs is a relatively common condition amongst adults, and ulcer symptoms usually include increasing pain, friable granulation tissue, foul odour, and wound breakdown instead of healing. This results in social distress and considerable healthcare and personal costs.[1-3] Since numerous factors lead to lower leg ulceration, it is essential that health professionals adopt an interdisciplinary approach to the systematic assessment of the individual in order to ascertain the pathogenesis, a definitive diagnosis, and optimal treatment required.[4] A correct diagnosis is essential to avoid inappropriate treatment that may delay wound healing, cause deterioration of the wound, or harm the patient.[5]

Accepted therapeutic objectives and standards of care for diabetic foot ulcers include wound debridement, pressure relief in the wound area, appropriate wound management (e.g., moist wound healing), infection management, ischemia management, medical management of co-morbidities, and surgical management as needed[7]. The TIME principle has been in studied in chronic non-healing wounds and lends itself well to the care of such patients. The portions of the TIME that address tissue debridement followed by infection control, moist balance , then edge enhancement have areas that cross over with topical wound care agents in several ways.

Apart from these conventional methods to facilitate wound healing various new methods are emerging such as cellular therapies, which include platelet-rich plasma (PRP). This can have an adjunctive role in a standardized, quality treatment plan.[8]

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 regionally on wound and augments the healing process[9]. Platelet extract has been used in many studies and has shown magnificent results in healing of chronic non-healing diabetic ulcers.[10]

Since not all patients can afford commercially available recombinant platelet gel for dressing, platelet extract from the patient's own blood has been used in trials on chronic diabetic wound.

The purpose of this study is to evaluate how autologous platelet-rich plasma (PRP) affects initial wound healing trajectories of chronic, non-healing diabetic wounds in a hospital care setting.

Hence, this study aims to demonstrate the therapeutic role of autologous platelet rich plasma in healing of chronic non-healing diabetic ulcers.

AIMS AND OBJECTIVE

- To compare the healing rate with subcutaneous injection of Platelet rich growth factors around the wound and

conventional wound management technique in chronic non-healing ulcers.
- To study incidence of chronic non healing ulcers in the diabetic and non-diabetic population
- To assess the safety of PRP injection as well as conventional dressings in patients with chronic non healing ulcers

METHODOLOGY

Study design: Single Centre, Prospective comparative study
Study period: October 2020 to September 2022
Study Population: 50 patients with chronic non-healing ulcers admitted in RMMCH Chidambaram.

Source Of Data

Study conducted among the patients who were diagnosed to have non-healing ulcers admitted in surgical ward and OPD in Rajah Muthiah Medical College Hospital, Chidambaram during the study period.

Method Of Study

This study was conducted among the inpatients and outpaients who have chronic non-healing ulcers and admitted in RMMCH during the study period. Patients will be studied in the terms of

1. Clinical History including age, sex, duration and mode of onset.
2. Examination and Appropriate investigations.
3. Post- procedure follow up to note for complications during stay in the hospital and reduction in wound surface area during subsequent follow up period.
4. Proforma
5. Informed consent

Procedure

Less than 20 ml of venous blood was drawn from the patients (depending on the wound size) into a tube containing an anticoagulant [Heparin/ EDTA] to avoid platelet activation and degranulation. Then the blood was centrifuged, the first centrifugation is called 'soft spin' (1000 rpm) for 10 min which allows the blood to separate into three distinct layers: At the bottom of the tube, the red blood corpuscles constitute 55% of total volume. At the top of the tube, the acellular plasma layer is mainly made up of circulating plasmatic molecules (in particular, fibrinogen) and is low in platelets. It is designated PPP and constitutes 40% of the total volume. Between the two, there is an intermediate PRP layer (5% of total volume) called the 'buffy coat'. Using a sterile syringe, the PPP, PRP, and some RBCs (i.e. the upper two layers and minimal 'unavoidable' amount of bottom layer) were transferred into another tube without an anticoagulant. This tube underwent a second centrifugation (3000 rpm) for 10 min called 'hard spin.' This allowed the platelets (PRP) to settle at the bottom of the tube with very few RBCs. The acellular plasma (PPP) (80% of the volume) was found on the top. Most of the PPP was taken with a syringe and the remaining PRP was left in the tube. At the time of procedure, the remaining PRP was mixed will be taken with another syringe.

Dressing Protocol

PRP group (25 patients): The PRP was injected circumferentially into the subcutaneous tissue around the ulcer followed by sterile dressing. The frequency of change of dressing will be once weekly. The dressing protocol will be performed for up to 4 weeks or stopped whenever healing occurred.

Conventional dressing method group (25 patients): wound wash was given with normal saline and betadine and excess slough to be removed and then sterile dressing will be applied. The frequency of change of dressing will be every day.

Reduction in wound surface area measured using scale and percentage reduction in wound surface area is calculated and entered.

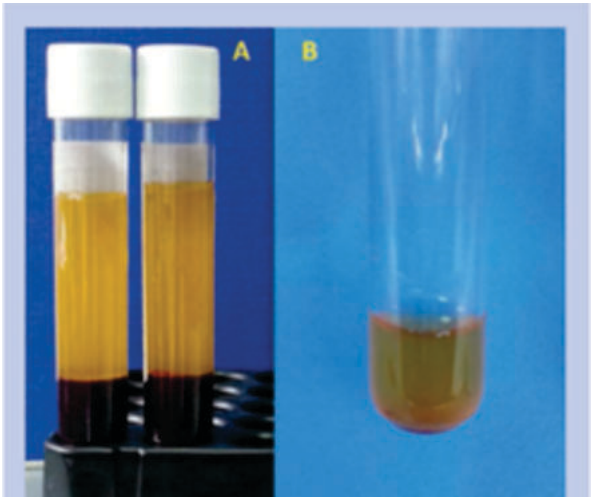

Figure – 1: Platelet Rich Plasma

Shows After the first centrifugation, 3 layers appeared. This is due to differences in the density of the blood components: the deep layer consists of red blood cells, the middle layer contains platelets and leukocytes, and the top layer is made up of platelet-poor plasma. The middle layer and top layer were collected directly by gentle aspiration with a pipette and transferred to a new, sterile centrifuge tube.

Inclusion Criteria

- Age group 20 – 60 years
- Inclusion of all types of chronic sterile ulcers.
- Ulcer size of 2-5cms in diameter.
- Presence of a foot ulcer for at least 4 weeks to be considered chronic
- Patient does not require split skin graft.

Exclusion Criteria

- Patient not willing
- Age group <20 and >60 years of age.
- Ulcers that are deep seated and has exposed tendons, ligaments, or bone. Active infection and osteomyelitis
- Burns ulcer
- Ulcer size area (length–width) of less than 2 cm or more than 6cm in diameter.

OBSERVATION AND RESULTS

Table 1. Age Distribution

Age in years	Study group		Control Group	
	No	%	No	%
<30	1	4.3	1	4.3
31-40	3	13.0	3	13.0
41-50	7	30.4	8	34.8
51-60	8	34.8	9	39.1
61-70	1	4.3	0	0.0
71-80	3	13.0	2	8.7
Total	23	100.0	23	100.0
Mean ± SD	51.78±12.29		50.48±11.58	

The mean age in the study group was 51.78 years and in control group was 50.48 years. Samples are age matched with P=0.713.

Table 2. Sex Distribution

Gender	Study group		Control Group	
	No	%	No	%
Female	10	43.5	8	34.8
Male	13	56.5	15	65.2
Total	23	100.0	23	100.0

Incidence of chronic lower limb ulcers were more in males in both the groups as compared to females.

Table 3. Onset

Onset	Study group		Control Group	
	No	%	No	%
T	14	60.9	15	65.2
S	9	39.1	8	34.8
Total	23	100.0	23	100.0

In this study, Traumatic ulcers were 60.9 % in study group and 65.2 % in control group and spontaneous ulcers were 39.1% in study group and 34.8 % in control group. It was observed traumatic ulcers were more in both the groups.

Table 4. Site

Site	Study group		Control Group	
	No	%	No	%
D	12	52.2	14	60.9
LM	2	8.7	1	4.3
MM	4	17.4	4	17.4
P	5	21.7	4	17.4
Total	23	100.0	23	100.0

Table 5. FBS

FBS	Study group		Control Group	
	No	%	No	%
<100	9	39.1	10	43.5
100-126	8	34.8	10	43.5
>126	6	26.1	3	13.0
Total	23	100.0	23	100.0
Mean ± SD	109.96±19.08		107.87±16.61	

Table 6. Comparison of Initial Area and Final Area

	Study group	Control Group	P value
Initial Area(IA)	1328.57±128.68	1338.08±131.54	0.805
Final Area(FA)	749.99±99.97	1149.84±114.74	<0.001**
CA=IA-FA	579.03±63.55	214.39±148.20	<0.001**

P=0.694, Not significant, Student t test

Table 7. Percentage % area reduction in two groups of patients

% area reduction	Study group		Control Group	
	No	%	No	%
<15	0	0.0	17	73.9
15-30	0	0.0	6	26.1
>40	23	100.0	0	0.0
Total	23	100.0	23	100.0
Mean ± SD	43.40±3.74			

Study group had better wound contraction of Mean ± SD 43.40±3.74 as compared to control group, the mean wound contraction was Mean ± SD 14.03±3.45. These were found to be statistically significant P<0.001**, significant, on Student t test

Table 8. Weeks For Complete Healing

Weeks for complete healing	Study group		Control Group	
	No	%	No	%
1 week	0	0.0	0	0.0
2 weeks	6	26.1	0	0.0
3 weeks	17	73.9	0	0.0
4 weeks	0	0.0	1	4.3
5 weeks	0	0.0	16	69.6
6 weeks	0	0.0	6	26.1
Total	23	100.0	23	100.0
Mean ± SD	2.74±0.45		5.22±0.52	

The mean time taken for complete healing of the ulcers were 2.74 weeks in study group as compared to 5.22 weeks in the control group.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Significant figures
+ Suggestive significance (P value: 0.05<P<0.10)
* Moderately significant (P value: 0.01<P 0.05)
** Strongly significant (P value: P0.01)

Statistical Software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

DISCUSSION

Chronic non-healing ulcers management remains difficult in this advanced medical era because it depends upon various factors. The idea of wound dressing to keep the wound moist, to provide the healthy environment for healing, and to prevent the wound from infection. Chronic non-healing wounds have been managed with different type of dressings.[11-14]

The present study conducted at Rajah Muthiah Medical College and Hospital. Platelet rich plasma, it has been used also in periodontal, maxillofacial surgery, orthopaedic and trauma surgery. No adverse reaction or complication has been reported. In this study, we selected chronic diabetic non-healing ulcers, used platelet rich plasma for wound dressings in study group, and compared it to conventional dressing.[17-18] 50 patients were selected in this study. Patients included in study having chronic non healing ulcers of more than 3 weeks of duration, randomized into either study group or control group using a computerized randomization chart.

In this study, Incidence of chronic diabetic lower limb ulcers were more in males in both the groups as compared to females. The mean age in the study group was 51.78 years and in control group was 50.48 years.

In this study, spontaneous ulcers were 60.9 % in study group and 65.2 % in control group and Traumatic ulcers were 39.1% in study group and 34.8 % in control group. It was observed spontaneous ulcers were more in both the groups.[15,16]

In this study dorsum of foot being most common site for ulcers in study group 52.2% and control group 60.9%. Plantar aspect study group 21.7%, control group 17.4%. Medial malleolus in both groups 17.4%, followed by lateral malleolus in study group 8.7% and in control group 4.3%.

In this study fasting blood sugar in study group mean 109.96 (SD 19.08) and in control group mean 107.87 (SD 16.61).

In our study it was observed that participants receiving Platelet rich plasma dressing had better wound contraction of 43.40% (S.D: 3.74) as compared to the control group receiving only conventional dressing (normal saline dressing) in whom the mean wound contraction was 14.03% (S.D; 3.45). These were found to be statistically significant on Student T test (p<0.001) suggesting that Platelet rich plasma enhances wound healing in chronic non-healing lower Limb ulcers.

In this study the mean time taken for complete healing of the ulcers were 2.74 weeks in study group as compared to 5.22

weeks in the control group.

Feasibility Of This Study

In the present study we have taken 50 patients suffering from chronic diabetic lower limb ulcers (>3 weeks). Patients were taken up for study based on inclusion and exclusion criteria. Out of 50 patients, 25 were study cases and 25 were control. Participants included in the study group were treated with platelet rich plasma dressing.

We have applied the following formula to calculate % reduction in area of wound after specific period in both cases and control groups.

Rate of contraction of wound after 28 days of treatment = Initial area – final area/ initial area * 100

We have found 14.03 %(S.D; 3.45) contraction of wounds in the control groups as compared to 43.40% (S.D:3.74) contraction of wounds in study group. Therefore, study groups have a better percentage of wound contraction as compared to the control group.

On applying student T test $p<0.001$ which is significant. From our study, we can say that platelet rich plasma dressing therapy facilitates wound healing in patients suffering from chronic diabetic lower limb ulcers.[19]

Summary

The present study was conducted on 50 patients to compare the efficacy of platelet rich plasma versus conventional dressing in chronic non-healing ulcers in Rajah Muthiah Medical Teaching Hospital between October 2020 to September 2022.

Patients were divided into two groups of 25 patients each and detailed history was taken and required investigations were done to rule out any focus of infection. All the 50 patients were evaluated based on many factors e.g. size of ulcer, site of ulcer, culture sensitivity from the ulcer, medical problem like Diabetes Mellitus. We found that there was significant improvement in ulcer size in group treated with platelet rich plasma. There were no complications seen in either of the group. Lower limbs were the most common site of occurrence of diabetic ulcer in the study.

CONCLUSION

The wounds in the subjects were treated with subcutaneous platelet rich plasma injection and dressing contracted more than the wounds in the control group (43.40% (S.D:3.74) Vs 14.03% (S.D; 3.45); P = <0.001 Significant) which indicates platelet rich plasma dressing is an effective management to facilitate wound contraction in patients suffering from chronic non-healing ulcers and can be used as an adjunct to conventional mode of treatment (conventional dressings) for healing of chronic non-healing ulcers.[20]

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