

A PROSPECTIVE STUDY TO DETERMINE THE EFFICACY OF AUTOLOGOUS PLATELET RICH PLASMA VERSUS REGULAR DRESSING IN DIABETIC FOOT ULCER

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INTRODUCTION

Type 2 diabetes mellitus is becoming a global epidemic affecting the Asian population, India being the capital of diabetes. Diabetes type 2 is associated with mortality from cardiovascular disease , micro vascular complications affecting the eyes, kidneys, nerves as well as with significant co morbidities including cancer, infections. If left untreated it leads to micro vascular complications like blindness, kidney failure, foot ulcerations, amputations. Treatment of such complications of diabetes mellitus type 2 is challenging at an institutional level as well as individual level.

Most of the challenges include prolonged therapy regular follow-up, cost efficacy of the treatment , availability of health care facility, etc. though it is challenging to implement, timely management of diabetes has been proven to reduce its complications.

Diabetic foot ulcer represents a formidable clinical problem. successful treatment requires a thorough understanding of the pathological process, surgical debridement of devitalized tissue and updating various modalities of treatment . Failure to recognize the cause, pathology and associated infectious process may lead to devastating consequences, like amputation and death. The diabetic foot can be defined as a syndrome in which neuropathy, angiopathy and infection coexist leading to tissue breakdown resulting in morbidity and possible amputation.

Wagner diabetic foot ulcer grade classification system

ULCER GRADING	DESCRIPTION
Grade 0	No ulcer but high risk foot
Grade 1	Superficial ulcer
Grade 2	Deep ulcer , no bony involvement of abscess.
Grade 3	Abscess with bony involvement
Grade 4	Localized gangrene e.g. toe,heel
Grade 5	Extensive gangrene involving the whole feet

Grade 1-3 ulcers - non-gangrenous ulcer

Grade 4-5 ulcers – gangrenous ulcer

PATHOPHYSIOLOGY OF DIABETIC FOOT ULCERS

Pathogenesis

Diabetic foot ulcers have several pathological components for their tendency for non healing or chronic healing property. Those include neuropathic, vascular and immune system components which show a relationship with hyperglycemic state of diabetes mellitus. Diabetic foot ulcers are a major health challenge. The goal of wound care in diabetic foot ulcer is to facilitate healing using standard protocols of wound care practical classification of a non healing wound is one that fails to heal spontaneously within 3 months. New methods are emerging in wound healing such as cellular therapies which include platelet rich plasma (PRP) and collagen based dressing. These are adjunctive to standard quality treatment plan.

Platelets release certain growth factors from alpha granules located in thrombocyte cell membrane which include platelet derived growth factor (pdgf), epidermal growth factor (egf) and platelet derived angiogenesis factor which has its action at the local level and thereby hastens the healing process. Many studies have shown that platelet extract has shown impressive results in healing of diabetic foot ulcers. Since platelet gel is not an affordability for all patients, platelet extract from the patient's own blood has been used in trails.

The prevalence of chronic diabetic foot ulcers in the world is 1.9 to 13.1%. The incidence increases as the age increases because of risk factors like smoking and obesity in addition to diabetes. The estimated percentage of the population to develop a chronic wound is 10% in the course of a lifetime. The wound related mortality being 2.5%.

The aim of this study is to determine and evaluate how autologous platelet rich plasma affects wound healing of chronic diabetic foot ulcers in a hospital setting.

METHODS

This is a prospective case control study with simple randomization. The present study was conducted from December 2020 to December 2021 on 30 patients attending surgery opd at vinayka mission's medical and hospital karaikal.

Patients in the age group of 18 to 80 years were included with chronic non healing diabetic foot ulcers of lower limb. Duration of ulcer was 12 to 26 weeks.

Ischemic ulcers, ulcers with evidence of malignancy, active infection with pus discharge, slough, evidence of gangrene in the ulcer or on any other part of limb were excluded from the study

After obtaining permission from the ethics committee 30 patients were chosen and two groups were randomly assigned as the cases A (test group , n=15) and controls B (control group n=15).

The study involved getting consent for investigating and treating the patient as a part of the study. it also involved thorough clinical examination as per standard proforma. Routine blood investigations and viral markers were tested. Glycemic status assessed and controlled. Patient was maintained on normoglycemia throughout the study (fasting blood sugar ≤ 110 mg % and post prandial sugar ≤ 140 mg%). Anemia and hypoalbuminemia were corrected(baseline hemoglobin >10 gm% and serum albumin .3gm%. size of the wound was assessed by placing a meter scale from the edges in their longest dimension(length , breadth and depth) after removing the fibrous margin. Initial areas varied from 9 to 12 cm². APRP or conventional dressing was done as per their groups after randomization.

Technique for conventional dressing

The ulcer was cleaned with 0.9% saline solution and was covered with a pad and a roller bandage

Technique for APRP dressing

Platelet rich plasma was prepared by collecting 20 ml blood from the patient and centrifuging it. This was applied during each dressing after cleaning with 0.9% saline and dressing done using pad and roller bandage. 5ml of PRP(maximum) was used in one sitting and was used uniformly over the ulcer . the dressing was kept in place for 2 days and then consecutive conventional dressing was applied for following days. The PRP treatment was repeated every week.

The end point of the study was taken as the area of wound contraction at the end of 4 weeks or complete closure or end of follow up. Size of the wound was measured

after this period. Mean,difference in means and statistical significance was calculated using MEDCALC statistical software

RESULTS

In this study end result was established by calculating the percentage area of wound reduction after 4 weeks or complete epithelisation of wound within the time period.

A total of 30 patients were studied with overall age range from 18 to 80 years. Age ranged from 29 to 80 years in test group (A) and 18 to 79 by years in control group (B). Age wise division of patients in both groups is compared in Table 1

Table 1 : Age ranges compared among test and control groups.

Age range (years)	No of patients in test group	No of patients in control group
<30	2	2
30-50	3	4
50-70	5	5
>70	5	4

Duration of wound ranged from 12 to 26 weeks.

the wound duration comparison between the two groups is depicted in table 2

Table 2 :duration of wound compared among test and control groups.

Duration of wound in weeks	No of patients in test group	No of patients in control group
12-16	4	6
17-21	5	5
22-26	6	4

Initial wound sizes ranged from 9 to 12 cm² in both groups. The initial and final wound sizes and percentage reduction in wound sizes is compared between the two groups in table 3

Table 3 : wound sizes compared among test and control groups (before and after treatment)

Patient no	Test group A			Control group B		
	Initial area cm	Final area	% of area reduced	Initial area cm	Final area cm	% of area reduced
1	9	2	77.77	9	7	22.2
2	9	2	66.66	9	7	22.2
3	9	1	88.88	9	8	11.1
4	9	2	77.7	9	7	22.2
5	9	2.3	73.3	9	6	33.3
6	9	2	77.7	10	8	20
7	9	2	77.7	10	8	20
8	11.2	2	73.3	10	8	20
9	11.5	1	90	10	7	30
10	12	3	75	12	7.5	37.5
11	12	2	83	12	9	25
12	12	0.7	93.7	12	9	25
13	12	0	100	12	9	25
14	12	2	83.3	12	9	25
15	12	2	83.3	12	9	25

The highest wound reduction was 100% as in group A and as low as 11.11% as in group B. The patient in group A with complete epithelisation was a 59 year old male patient with ulcer duration of 23 weeks and an initial area of about 12 cm. even though the patient had bigger surface area of wound and old age because of APRP dressing he had complete wound healing.

The mean reduction in test group (A) where APRP dressing were done was 81.58% and that in control group (B) with conventional dressing was 24.4%

Difference in means was 57.34. standard error was 2.78. 95% CI was 51.607 to 63.07, t-statistic was 20.49 and significance level $p < 0.0001$.

DISCUSSION

Chronic diabetic foot ulcers are a major health problem in developing countries like India. These wounds lack the necessary growth factors for healing, they are usually superadded with infections and heal in a delayed manner.

The main goal of any treatment modality is to obtain complete wound closure. The conventional treatment includes debridement, infection control, ischemic tissue

revascularization, avoidance of pressure on the wound. Though skin grafting has some efficacy, they cannot provide growth factors. Topical application of epidermal growth factors did not promote re-epithelisation¹.

In majority of the studies topical silver based dressings were used where evidence of their efficacy was lacking². The combination of standard wound care and platelet rich plasma boosts inflammatory wounds into a state of proliferation and healing by releasing multiple growth factors and cytokines which mimic natural process of healing³.

PRP contains growth factors along with high concentration of wbc's which help in preventing infection and promoting wound healing^{5,6}.

In a meta-analysis of the use of PRP therapy, it showed that PRP facilitates wound healing and the ulcers improve significantly in hard to heal ulcers⁷. In addition, platelets exert antimicrobial activity against some bacteria of the skin and clinical data shows that the presence of infection is reduced in PRP treated wounds.

Hence, the present study was done to demonstrate the therapeutic role of PRP in healing of chronic diabetic foot ulcers. The baseline characteristics such as age, sex and location of the ulcer were similar in the patients who received PRP dressing in study group in patients who received control dressing.

Till now there is no method of preparation of PRP in literature. According to Marx, the device must use a double centrifugation technique regardless of the rate of centrifugation, a single spin cannot adequately concentrate platelets, because the red blood cells will interfere with their fine separation.

Several studies have been conducted on the use of PRP for the treatment of non-healing ulcers and the results are promising. However, currently there is a paucity of critical scientific data regarding the beneficial effects of PRP in clinical procedures. That is the inspiration in doing the present study, so as to provide what all clinical supportive data is necessary, even in smaller amounts to further substantiate the usefulness of PRP over traditional dressings in chronic non healing ulcers.

CONCLUSION

Non healing diabetic foot ulcers are a growing socioeconomic problem all over the world. All the conventional treatments relating to ulcer are time consuming and expensive. Autologous platelet rich plasma dressing might prove the first line remedy for the same and should be promoted as it is safe and cost effective.

In this study PRP application had faster and better healing rates with reduction in percentage of ulcer area. There were no adverse effects or reactions seen with use of PRP.

This way of treatment has been mentioned in literature as well as used by few clinicians and hereby, we are strengthening their view with these cases as this might become the first treatment of choice in non-healing ulcer.

The results from this case series showed that PRP is a safe and effective treatment modality for chronic non-healing ulcers. Using PRP to treat chronic 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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