ORIGINAL RESEARCH PAPER

Dermatology

EVALUATION OF EFFICACY OF ACTIVATED PLATELET RICH PLASMA (APRP) IN TREATMENT OF DIABETIC FOOT ULCER

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ABSTRACT

Diabetic foot ulcer is a major complication of diabetes mellitus affecting 15% of all patients with diabetes mellitus. Diabetic neuropathy and peripheral vascular disease are 2 major factors causing diabetic foot ulcers. Due to deficiency of oxygen and nutrients, epithelial cells at wound cannot express essential factors for healing such as VEGF and PDGF resulting in chronic non-healing ulcer. To date, the outcome of management of diabetic foot ulcer is poor. In almost therapies, management of diabetic foot ulcer relates to debridement of the wound, revascularization, off-loading of the ulcer, antibacterial actions, stimulating granulation, epidermisation and angiogenesis. As the therapeutic role of PRP in wound healing has not been clearly addressed previously and as there are not many randomized clinical trials addressing this issue, an attempt has been made in this study to know the therapeutic efficacy of PRP in wound healing while comparing it with the conventional dressing (Normal saline).

INTRODUCTION

Diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period.1 Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications.2

Diabetic foot ulcer is a major skin complication of diabetes mellitus. Foot ulcers affect the quality of life in diabetic patients .There is an increased risk of infection and poor wound healing due to a series of mechanisms which include decreased cell and growth factor response, diminished peripheral blood flow and decreased local angiogenesis.[3] Unfortunately, many of these patients will require amputation within the foot or above the ankle as a consequence of severe infection or peripheral ischemia. Neuropathy is often a predisposing factor to ulceration and amputation. Samson et al. found 'The University of Texas Wound classification system' to be better predictor of outcome.[4]

Conventional therapies such as dressings, surgical debridement and even skin grafting cannot provide satisfactory healing since these treatments are not able to provide necessary growth factors that can modulate the healing process.

Normal saline dressing acts as an osmotic dressing, with time the concentration of the saline increases due to evaporation altering it from an isotonic to hypertonic dressing which in turn decreases the fluid from the wound keeping it moist.[5] Wound heals quicker in moist environment and dressing are used to absorb excess fluid or retain fluid in an otherwise, dry wound in order to achieve a moist wound environment.[6]

Platelet-rich plasma (PRP) is defined as a portion of the plasma fraction of autologous blood having a platelet concentration above baseline.[7] PRP serves as a growth factor agonist and has both mitogenic and chemotactic properties.[8] Autologous platelet-rich plasma (PRP) is an inexpensive method used in treating non-healing ulcers as it provides growth factors which enhance healing.

Case study
Type of study: Prospective Randomized Controlled Study

MATERIAL AND METHODS :

Our study enrolled 60 Diabetic mellitus patients type 2 having DFUs with grade 1 or 2 and non-healing for at least 4 weeks attending DVL opd of a teritiary care hospital for a period of 18 months. They are divided into two groups as 30 patients received Autologous plate rich plasma (PRP gel) i.e., Group-A and 30 patients received conventional methods (wet normal saline dressing) i.e., Group-B.

Physical examination and treatment

Detailed history was taken in all cases regarding the diabetes & Ulcer duration, mode of onset, progression, and associated symptoms. Ulcers examinations was done in all this patients and wound was assessed of its   characteristics and photographed. Ulcer was assessed at the beginning of the study and at the end of the study. Ulcer were classified into grades according to Wagners Grading System. Random Blood Sugar, Platelet count, Doppler ultrasound scan of the both legs, X-ray of the foot and HbA1c levels were done.

PRP preparation

20 mL of peripheral blood will be used to prepare PRP and PPP. Briefly, blood is centrifuged at 1.500 rpm in 5 min to obtain plasma. Then, this plasma is centrifuged at 3.500 rpm in 5 min to collect platelets as a pellet at the bottom of the centrifuge tube. Pellet is diluted in 3 mL plasma and is considered as PRP. PRP is activated to release growth factor by Calcium chloride. When calcium chloride is added into PRP, fibrin gel is formed, and this gel is   immediately applied to the wound. A contact layer dressing is applied over the gel. A foam dressing (non-absorbent side) is placed over the contact dressing layer so the PRP gel is not absorbed. This is covered with the absorbent side of a foam dressing (to absorb any leaking wound exudates) and secured.

Dressing technique:

Among divided groups following procedure was performed.
For Group-A (autologous platelet gel):
Autologous platelet gel was prepared from patients own blood and placed over the ulcer bed after cleaning with 0.9% saline and dressing done using pad and roller bandage.

For Group-B (conventional dressing):
A chronic ulcer with no active pus discharge and slough was

cleaned with the 0.9% saline solution and was covered with pad and roller bandage.

During the treatment, diabetic mellitus patients advised to use antibiotics, NSAID, and vitamin. After 2 weeks if the wound showing no signs of healing, patients will be continued to be repeat this procedure. DFUs are examined for 12 weeks with a gap of 2 weeks and any improvement in ulcer is recorded each time .These findings are compared with control group for whom saline dressings will be applied.

In Both the groups, dressing was changed every 3rd day; similarly dressings done after every sitting to all the patients in both the groups and the outcome is assessed on day 0(1st sitting), at every sitting and on final day 84(12th week).

Outcome is measured between the two groups. Data were tabulated and the 2 groups were compared with reference to initial and final area, area of reduction of wound size.

Statistics

A total of 60 patients satisfied the selection criteria, the collected data was analysed with SPSS 16.0 version. To describe about the data descriptive statistics mean and S.D were used. To find the significance difference between the bivariate samples in Paired groups (Initial & Final area) Paired sample t-test was used & for Independent groups (PRP & NS) the Independent sample t-test was used. To find significant of homogenicity between the cases and control in gender, pearson's chi-square was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

Observation and discussion

Area of Ulcer on Day-0 Area of ulcer calculated using length and width of ulcer on Day-0 showed In Group-A patients, area of ulcer minimum measuring $2.25cm^2$ and maximum measuring $20cm^2$. Mean ulcer area was $8.50cm^2$ with Standard deviation +/- $4.83cm^2$.

In Group-B patients, area of ulcer minimum measuring $2.25cm^2$ and maximum measuring $20cm^2$. Mean ulcer area was $8.75cm^2$ with Standard deviation +/- $4.56cm^2$.

Mean ulcer area was almost same in both the groups. Response to Treatment in Group-A and Group-B at end of 12th week In both the groups, 3patients lost to follow-up in each group.

In Group-A, out of remaining 27patients at the end of 12th week, 13 patients showed 100% response i.e., healed totally, 5patients showed 90% improvement, 4patients showed 80% improvement and 5patients showed 70% improvement.

In Group-B, out of remaining 27patients at the end of 12th week, 3 patients showed 100% improvement i.e., healed totally, 4patients showed 90% improvement, 4patients showed 80% improvement, 3patients showed 70% improvement, 6patients showed 60% improvement and 7patients showed 50% improvement.

Of the 13patients who showed 100% improvement, 3patients ulcer healed 100% in 8weeks, another 3patients in 10weeks and 7patients by 12weeks.

Whereas in Group-B, only 3patients showed 100% improvement, of which 2patients improved 100% by 8weeks and 1 by 10weeks.

Area of Ulcer on 12th week i.e., Day-84 In Group-A patients, area of ulcer minimum measuring $0cm^2$ and maximum measuring $8cm^2$. Mean ulcer area on 12th week was $1.39cm^2$ with Standard deviation +/- $2.11cm^2$. In Group-B patients, area of ulcer minimum measuring $0cm^2$ and maximum measuring $10cm^2$. Mean ulcer area on 12th week was $3.13cm^2$ with

Standard deviation +/- $2.83cm^2$.

Among both the groups at the end of study on 12th week the difference in mean ulcer area was significant i.e., p-value was 0.0134 (<0.05).

Table 1: Comparison Of Initial & Final Mean Ulcer Area In Both Groups With P-value

Comparison	Initial		Final		p-value
	Mean	SD	Mean	SD	
Group-A	8.50	4.83	1.39	2.11	0.0001
Group-B	8.75	4.56	3.13	2.83	0.0001

Table 2: Percentage Improvement Of Ulcer In Comparison With Other Studies

Study	Percentage of improvement with PRP	Percentage of improvement with NS or Other Placebo	p-value (if calculated)
Present Study	75.17 +/- 24.12%	58.17 +/- 12.31%	0.002
Jeong et al100	96.3 +/- 7.8%	81.6 +/- 19.7%	<0.05
Saldalamacchia et al101	71.9 +/- 22.5%	9.2 +/- 67.8%	0.039
Kumar N et al102	63.2%	34.8%	<0.05
Marwa Ahmed et al103	86%	68%	____
Steed et al85	98.8%	82.1%	____
Holloway et al99	63%	29%	____
Driver et al65	68.4%	42.9%	____

Overall this study shows that PRP is a safe and effective in treating Diabetic ulcers. This study was conducted only for short duration, without any adverse reactions or recurrences. Zhao et al, to suggested that growth factors may need to be used with supplemental hyperbaric oxygen to achieve optimal benefit in ischemic wounds.

Group A Patient Images 12 , 2, 8 Weeks Respectively

Group-B Patient images at 2,8 and 12 weeks respectively

CONCLUSION

With the use of autologous Platelet Rich Plasma (PRP) dressings in comparison with the control group (normal saline group) for the treatment of Diabetic Ulcers, the following conclusions were derived, PRP showed faster and better healing rates compared the NS group.

Area reduction and percentage reduction was better in PRP group.

There were no adverse effects or reactions seen when autologous PRP was applied over the ulcer.

In our study the results confirm that, the use of PRP increases ulcer healing rate. These results provided a promising method for ulcers treatment.

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