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Plasma or Fibrin Matrix? A Comparative Study between PRP versus PRFM Therapy in Diabetic Foot Ulcer

Ashwath Rao[1], Manikanta K. S.[2], Mir Md Noorul Hassan[3]

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Abstract

Introduction: Diabetic foot ulcer is one of the most common conditions encountered in surgical OPD. The incidence of a diabetic foot ulcer is around 15% among the diabetic population. Around 80% of non-traumatic amputation is due to chronic diabetic foot ulcer. Recent advances are made in treating wounds in which platelet-rich plasma (PRP) and platelet rich fibrin matrix (PRFM) therapy have proven beneficial.

Materials and Methods: A prospective study was conducted from February 2021 to February 2023, for a period of 2 years which included 42 patients. Group A received autologous platelet rich plasma therapy (PRP) and group B received autologous platelet rich fibrin matrix therapy (PRFM) each consisting of 21 patients.

Results: PRFM Group showed better reduction in ulcer size compared to respective PRP Group, and demonstrated statistically significant p-values. Around 47% of the subjects had complete closure of the ulcer after 5 sessions of PRP dressing while it was 90% with PRFM dressing.

Conclusion: PRFM is better modality to treat diabetic foot ulcer when compared to PRP therapy

Keywords: Platelet rich fibrin matrix therapy; Platelet rich plasma therapy; Diabetic foot ulcer.

Author Affiliation: [1]Post graduate, [2]Assistant Professor, [3]Professor, Department of General Surgery, Bangalore Medical College & Research Institute, Bangalore 560034, Karnataka, India.

Corresponding Author: Ashwath Rao, Post graduate, Department of General Surgery, Bangalore Medical College & Research Institute, Bangalore 560034, Karnataka, India.

Email: raoash1994@gmail.com

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INTRODUCTION

Diabetic foot ulcer is one of the most common conditions encountered in surgical OPD. The incidence of a diabetic foot ulcer is around 15% among the diabetic population[1] and the prevalence is 4.54%.[2] It is one of the most common causes of hospitalization and disability in diabetics.[3] Around 80% of non-traumatic amputation is due to chronic

diabetic foot ulcer.[4] Every 30 seconds a lower limb is lost somewhere in the world as a consequence of diabetes.[5] This demands prompt and early treatment to reduce the morbidity associated with the condition. Conventional dressing requires frequent visits to the hospital and the duration of the treatment is long adding to the existing financial and social burden of the patient.

Recent advances are made in treating wounds in which platelet rich plasma (PRP) and platelet rich fibrin matrix (PRFM) therapy have proven beneficial. Both therapies are done using the patient's blood and subjecting it to centrifugation and using the preparation for dressing. Various studies are available providing the data on effectiveness of each in treating chronic ulcers. But very less studies are available comparing PRP and PRFM and concluding the superiority of one over the other. Hence, in our study, we used these two modalities to understand the efficacy of the treatment modality and conclude the better option between PRP and PRFM therapy for diabetic foot ulcers.

AIMS & OBJECTIVES

To compare the effectiveness of platelet rich plasma and platelet rich fibrin matrix therapy in the treatment of diabetic foot ulcer.

MATERIALS AND METHODS

A prospective study was conducted from February 2021 to February 2023, for 2 years, at the Department of General Surgery, in the Hospitals attached to Bangalore Medical College and Research Centre, Bengaluru. The study population comprised selected outpatients with diabetic foot ulcers.

The sample size was calculated as 42, using the sample size calculation formula, (1.96) 2pq/d2, where p is the average annual diabetic foot ulcer incidence, p=2.8% 6, q=(100-p)=97.2%, and d is the maximum permissible error which was taken as 5%.

Inclusion Criteria:

1. Type 2 diabetes mellitus.
2. Well controlled blood sugar levels, with fasting blood sugar </=150mg/dL.
3. Grade 1 and Grade 2 ulcers according to Wagner classification.
4. Baseline ulcer area between </=20cm^2, rounded of to closest whole number.
5. Clean wound with minimal slough.

Exclusion Criteria

1. People who do not consent.
2. Uncontrolled diabetes, with fasting blood sugar >150 mg/dL.
3. Ulcer of grade 3 and above according to Wagner classification.
4. Poorly nourished, debilitated, bedridden patients.
5. Patients who are a known case of other chronic systemic/local diseases.

Patients were divided randomly into 2 groups of 21 participants each, using computer software. Group A received autologous platelet rich plasma therapy (PRP) and Group B received autologous platelet rich fibrin matrix therapy (PRFM). Informed written consent was obtained before the study. All participants underwent a detailed local examination before the therapy to record the baseline area (length x breadth) of the ulcer in sq. cm.

The PRP was prepared after drawing 20 mL of blood into a vacutainer containing Acid Citrate Dextrose (ACD) anticoagulant and was centrifuged at 1000 rpm for 8-10 minutes (soft spin). There were 3 layers of blood separation, the upper platelet poor plasma (PPP) and the middle buffy coat (Platelet rich plasma) were separated from the lower RBC layer and were transferred into another vacutainer without anticoagulants. This was subjected to centrifugation at 3000 rpm for 6-8 minutes (hard spin). The top layer of PPP was discarded and the lower PRP was mixed with 10% Calcium Chloride, made into a gel form, and transferred over a sterile gauze, which was gently spread over the ulcer bed and covered by non-absorbable dressing among the patients in group A.

The PRFM was prepared by centrifuging 10 mL of the patient's blood, collected in a vacutainer without anticoagulants, at 3000 rpm speed for 10 minutes. At the end of 10 minutes, there were 3 layers upper layers of straw colored acellular plasma, the lower layer of RBC, and the middle layer of PRFM. The PRFM layer was separated from the rest and transferred into sterile gauze. This was used for the ulcer dressing in patients of Group B, in a similar fashion, as was done for Group A. Both the procedures were repeated weekly for 5 weeks

in both groups.

During each follow-up, the area of the ulcer was reassessed and closure of the wound was recorded accordingly.

Data was made into a database using MS Excel and statistical analysis was done using Epi-info software.

RESULTS

Table 1: Age and gender wise distribution of study subjects

(n=42)

Age groups	PRP		PRFM		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
40-45	7	33.3	2	9.5	9	21.43
45-50	6	28.6	14	66.7	20	47.62
50-55	4	19	4	19	8	19.05
55-60	4	19	1	4.8	5	11.9
Total	**21**	**100**	**21**	**100**	**42**	**100**
Gender						
Female	5	23.8	6	28.6	11	26.19
Male	16	76.2	15	71.4	31	73.81
Total	**21**	**100**	**21**	**100**	**42**	**100**

In our study, of the 42 subjects, the majority of the patients belonged to the age group of 45-50 years and around 74% were males. (Table 1)

Of the 42 study subjects, around 40% had an ulcer size between 5–10cm^2. The minimum size of ulcer at the start of the study was 4 cm^2 and the maximum was 20 cm^2. (Fig. 1)

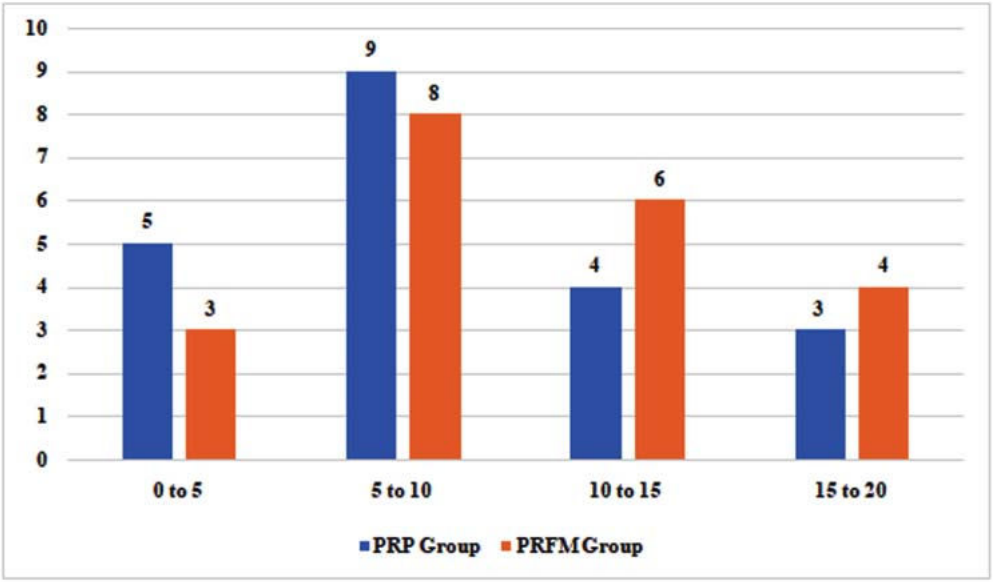

Fig. 1: Showing baseline ulcer size distribution

After the first session, there was a 32% reduction in ulcer size in the PRFM group while only a 22% reduction was observed in the PRP group. At the end of the 5th session, PRFM group showed a 96% reduction while the PRP group had only 83% reduction. (Table 2)

Table 2: Percentage reduction in ulcer size from baseline size after each session of PRP and PRFM therapy

(n=42)

-	PRP Group			PRFM Group		
	Minimum	**Maximum**	**Mean**	**Minimum**	**Maximum**	**Mean**
After 1st session	0	75	21.83	11.11	60	31.96
After 2nd session	14.29	100	46.52	27.78	100	60.51
After 3rd session	28.57	100	64.93	38.89	100	82.59
After 4th session	28.57	100	75.22	50	100	91.39
After 5th session	42.86	100	83.45	61.11	100	96.56

On independent samples T-test between PRP and PRFM ulcer dressing, after each session, the PRFM Group showed a better reduction in ulcer size compared to the respective PRP Group and demonstrated statistically significant p-values as shown in Table 3.

Table 3: Comparison of reduction in ulcer size between PRP and PRFM Groups (Independent sample T-test)

(n=42)

-	Therapy	Mean	Std. Deviation	P-value	Mean Difference
After 1st session	PRP Group	21.833	16.119	0.035	-10.123
	PRFM Group	31.956	13.856		
After 2nd session	PRP Group	46.517	23.468	0.05	-13.996
	PRFM Group	60.513	21.354		
After 3rd session	PRP Group	64.930	26.494	0.016	-17.663
	PRFM Group	82.594	18.437		
After 4th session	PRP Group	75.217	22.820	0.009	-16.176
	PRFM Group	91.394	14.429		
After 5th session	PRP Group	83.447	19.772	0.011	-13.114
	PRFM Group	96.561	10.897		

Around 47% of the subjects had complete closure of the ulcer after 5 sessions of PRP dressing while it was 90% with PRFM dressing. A chi-square test of independence showed that PRFM therapy yields better treatment outcomes compared to PRP ulcer dressing. χ^2 (1, n=42) =9.023, P=0.0026 <0.05 (Table 4 & 5).

Table 4: Patients showing complete healing of ulcer after each session between PRP and PRFM Groups

(n=42)

-	PRP Group	PRFM Group
After 1 session	0	0
After 2 sessions	1	3
After 3 sessions	5	5
After 4 sessions	1	4
After 5 sessions	3	7
Incomplete healing after 5 sessions	11	2
Total	**21**	**21**

Table 5: Therapy outcome in various treatment groups at the end of the 5th session (n=42) (Chi-square test)

-	Therapy		Total
	PRP Group	**PRFM Group**	
Complete Healing after 5 sessions	10 (47.62)	19 (90.48)	29
Incomplete Healing even after 5 sessions	11 (52.38)	2 (9.52)	13
Total	**21**	**21**	**42**

χ2 (1, n=42) =9.023, P=0.0026 <0.05

DISCUSSION

Various newer advances such as hyperbaric oxygen therapy, negative pressure wound therapy, and placental extract dressing have been described. Among these PRP and PRFM have been proven to be beneficial by many authors.

Various active molecules in platelet are beneficial in wound healing. The alpha granules of platelet contain platelet derived growth factor, transforming growth factor beta, vascular endothelial growth factor, epithelial growth factor, fibronectin, vitronectin[7-9], and delta granules contain calcium, dopamine, serotonin, histamine, and adenosine all of which act in tandem to promote wound healing.[10]

In PRFM platelets are trapped in fibrin meshwork which allows slow and sustained release of these growth factors.[11] These fibrin mesh also acts as a scaffold for cell migration, proliferation, and differentiation.[12]

Suchetha *et.al* showed that platelet concentration in PRP was higher compared to PRFM.[13] But the study by Yazawa *et.al* showed that after incorporating platelets into fibrin the mean concentration of growth factors was 3 times more than PRP along with the sustained release of them for approximately 1 week.[14] Further, a study conducted by Dohan Ehrenfest *et. al* demonstrated that there was a significant difference in biological behavior in invitro between PRP and PRFM.[15] Kochok and Surabhi described various advantages of PRFM over PRP such as no biochemical modification because of lack of anticoagulants, a long term effect due to slow release of growth factors, support cytokine enmeshmeshment and cell migration, supports and accelerates wound healing due to slow polymerization.[16]

In our study, it was observed that after 1st session there was a 31.95% reduction in ulcer size after PRFM when compared to PRP which was 21.83%. The maximum reduction in wound size was observed at the end of the 5th session of PRFM. The study conducted by Yufi Wang *et. al* showed that maximum wound reduction after PRFM occurred in 1st and 2nd sessions of treatment.[17]

In a study conducted by Sarvajnamurthy et. al mean duration for complete healing of ulcer after PRP was 5.1 weeks[18] and in the study conducted by Konchok *et. al* mean duration for complete healing after PRFM was 5 weeks.[16] A study by Vaibhav *et.al* showed 94.56% complete healing at the end of the 5th session of PRFM therapy.[19] In our study, 47.62% of PRP therapy and 90.48% of PRFM therapy showed complete healing at the end of the 5th week (Fig. 2). This data was found to be statistically significant.

In PRFM group 2 patients did not show the ulcer

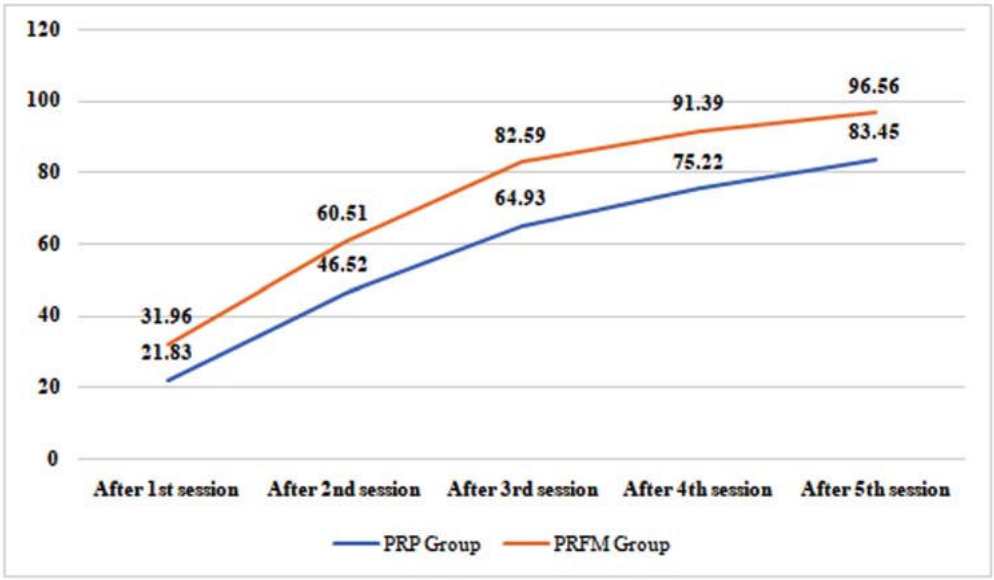

Fig. 2: Showing the percentage of reduction in ulcer size between each session of PRP and PRFM groups (n=42)

healing by the end of the 5th session and the size of the ulcer was large which required additional 2-3 sessions for complete healing. Of 11 patients in the PRP group, 4 patients showed complete healing

in additional 3-4 sessions and the rest required additional interventions.

CONCLUSION

Platelet rich fibrin matrix (PRFM) therapy is shown to be more effective in terms of reducing diabetic foot ulcer size requiring a lesser number of sessions when compared to platelet rich plasma (PRP) therapy. However large sized ulcer requires more PRFM sessions. Hence, we conclude that PRFM therapy is a better modality for treating diabetic foot ulcers.

REFERENCES

1. Ahmad J. The diabetic foot. Diabetes Metab Syndr. 2016;10:48–60.
2. Crawford F, Nicolson DJ, Amanna AE, Martin A, Gupta S, Leese GP *et.al.* Preventing foot ulceration in diabetes: systematic review and meta-analyses of RCT data. Diabetologia. 2020;63(1):49-64.
3. Government of India, Ministry of Health & Family Welfare: standard treatment guidelines - the diabetic foot - prevention and management in India - full background document (draft) [Jun;2020];http://clinicalestablishments.gov.in/WriteReadData/5381.pdf January. 2016 & Family Welfare Government of India.
4. Jeffcoate WJ, Harding KG. Diabetic foot ulcers. Lancet. 2003;361(9368):1545-51.
5. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217-28.
6. Yazdanpanah L, Shahbazian H, Nazari I, Arti HR, Ahmadi F, Mohammadianinejad SE, *et.al.* Incidence and Risk Factors of Diabetic Foot Ulcer: A Population-Based Diabetic Foot Cohort (ADFC Study)-Two-Year Follow-Up Study. Int J Endocrinol. 2018:7631659.
7. Assoian RK, Fleurdelys BE, Stevenson HC, Miller PJ, Madtes DK, Raines EW *et.al.* Expression and secretion of type beta transforming growth factor by activated human macrophages. Proc Natl Acad Sci U S A. 1987;84(17):6020-24.
8. Banks RE, Forbes MA, Kinsey SE, Stanley A, Ingham E, Walters C *et.al.* Release of the angiogenic cytokine vascular endothelial growth factor (VEGF) from platelets: significance for VEGF measurements and cancer biology. Br J Cancer. 1998;77(6):956-64.
9. Kaplan DR, Chao FC, Stiles CD, Antoniades HN, Scher CD. Platelet alpha granules contain a growth factor for fibroblasts. Blood. 1979;53(6):1043-52.
10. Liao HT, Marra KG, Rubin JP. Application of platelet-rich plasma and platelet-rich fibrin in fat grafting: basic science and literature review. Tissue Eng Part B Rev. 2014;20(4):267-76.
11. Chignon-Sicard B, Georgiou CA, Fontas E, David S, Dumas P, Ihrai T *et.al.* Efficacy of leukocyte- and platelet-rich fibrin in wound healing: a randomized controlled clinical trial. Plast Reconstr Surg. 2012;130(6):819e-29e.
12. Borie E, Oliví DG, Orsi IA, Garlet K, Weber B, Beltrán V *et.al*. Platelet-rich fibrin application in dentistry: a literature review. Int J Clin Exp Med. 2015;8(5):7922-29.
13. Suchetha A, Lakshmi P, Bhat D, Mundinamane DB, Soorya KV, Bharwani GA. Platelet concentration in platelet concentrates and periodontal regeneration-unscrambling the ambiguity. Contemp Clin Dent. 2015;6(4):510-16.
14. Yazawa M, Ogata H, Nakajima T, Mori T, Watanabe N, Handa M. Basic studies on the clinical applications of platelet-rich plasma. Cell Transplant. 2003;12(5):509-18.
15. Dohan Ehrenfest DM, Bielecki T, Jimbo R, Barbé G, Del Corso M, Inchingolo F *et.al.* Do the fibrin architecture and leukocyte content influence the growth factor release of platelet concentrates? An evidence-based answer comparing a pure platelet-rich plasma (P-PRP) gel and a leukocyte- and platelet-rich fibrin (L-PRF). Curr Pharm Biotechnol. 2012;13(7):1145-52.
16. Dorjay K, Sinha S. Platelet-rich Fibrin in Nonhealing Leg Ulcers: A Simple and Effective Therapeutic Option. J Cutan Aesthet Surg. 2021;14(2):160-65.
17. Wang Y, Wang X, Chen R, Gu L, Liu D, Ruan S, Cao H. The Role of Leukocyte-Platelet-Rich Fibrin in Promoting Wound Healing in Diabetic Foot Ulcers. Int J Low Extrem Wounds. 2021:15347346211052811.
18. Sarvajnamurthy S, Suryanarayan S, Budamakuntala L, Suresh DH. Autologous platelet rich plasma in chronic venous ulcers: study of 17 cases. J Cutan Aesthet Surg. 2013;6(2):97-9.
19. Thorat V, Khan IM, Gaikwad S. Platelet rich fibrin matrix the cost effective way to treat trophic ulcer in diabetes: A pilot study. Medical Science. 2020;24(104):2752-59.