Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Surgical Management of Diabetic Foot Ulcers with Platelet Rich Plasma

Nepesh Kacker[1]

[1]Assistant Professor, General Surgery, World College of Medical Sciences and Research Hospital, Jhajjar, Haryana.

Received: October 2020
Accepted: October 2020

ABSTRACT

Background: Diabetic neuropathy and peripheral vascular disease are 2 major factors causing diabetic foot ulcers (DFUs). the foremost difficulty of DFUs is non-healing for a protracted time. the most reason is said to loss of balance between metalloproteinases (MMPs) and MMP inhibitors. This status is enhanced to become serious when combining with ischemia and vascular disease. Vascular injury and ischemia reduced the oxygen and nutrients to the wound. The aim and Objectives is to evaluate the efficacy and safety of the autologous PRP for a diabetic foot ulcers. **Methods:** The PRP group or the platelet-poor plasma (PPP) group by receiving the subsequent available consecutive randomization number and type of dressing in keeping with the randomization schedule. In both groups, surgical debridement of the injuries was done to freshen the wound bed and take away all necrotic tissue debris. The wound site, sizes (length, width, and depth), and grade were documented. Type 1 or 2 diabetes is controlled by either medication or insulin, presence of a foot ulcer for a minimum of 4 weeks to be considered chronic. **Results:** The ulcer's initial length ranged from 2.1 to 6.2 cm, the initial width ranged from 1.2 to 3.1 cm, the surface area ranged from 3 to 9.2 cm^2 with an average of 7.3 cm^2, and the volume ranged from 1.1 to 3.1 cm^3 in the PRP group. The ulcer's initial length ranged from 2 to 6.1 cm, the initial width ranged from 1.2 to 3.2 cm, the surface area ranged from 4.1 to 9.2 cm^2, and the volume ranged from 1.4 to 3 cm^3. **Conclusion:** PRP is effective and safe for the treatment of diabetic foot ulcers and it significantly accelerates the healing of diabetic foot ulcers and safe where it does not make significant changes in blood hematology or blood chemistry in the patients.

Keywords: Vascular Injury, Ischemia, Tendons, Ligaments, Cytokine.

INTRODUCTION

Diabetic foot ulcer may be a major complication of diabetes and is that the major component of the diabetic foot. This medical condition affects fifteen of all patients with diabetes. A recent study showed that up to 88% of all lower leg amputations associated with a diabetic foot ulcers.[1] Diabetic neuropathy and peripheral vascular disease are 2 major factors causing diabetic foot ulcers (DFUs).[2] the foremost difficulty of DFUs is non-healing for a protracted time. The most reason is said to loss of balance between metalloproteinases (MMPs) and MMP inhibitors.[3] This status is enhanced to become serious when combining with ischemia and vascular disease. Vascular injury and ischemia reduced the oxygen and nutrients to the wound. therefore the wound healing mechanism cannot perform as within the non-diabetic patients. Lack of oxygen and nutrients, epithelial cells at wound can't express essential factors for healing like VEGF and PDGF; almost of the cells at wound changed metabolism and activity.[4] These changes in the structure and functions of cells and a few factors at DFUs delayed the healing process and broke the traditional healing process. Hence, when diabetic Mellitus patients got DFUs, almost DFUs can't be healed, and eventually, patients must be faced with lower leg amputation. DFU treatment also remains a challenge.[5] Over the recent years, great progress has been made within the techniques of wound healing, among which autologous platelet-rich gel has attracted the foremost substantial attention.[6] Platelets are known to begin the wound healing process through the discharge of locally active growth factors.[7–10] the expansion factors are ready to produce connective tissue and to induce epithelialization by the assembly of neovessels, the attraction of fibroblasts and mesenchymal cells, secretion of collagen fibers, and by a proliferation of keratinocytes.[11–14] Platelet-rich plasma (PRP) might also curb inflammation by suppressing cytokine release.[15] The aim of the study was to judge the efficacy and safety of the autologous PRP for a diabetic foot ulcers.

Name & Address of Corresponding Author
Dr. Nepesh Kacker
Assistant Professor,
General Surgery
World College of Medical Sciences and Research Hospital
Jhajjar, Haryana.

MATERIALS AND METHODS

This prospective, randomized, controlled study was wiped out the Surgery Department of a non-public institution which was approved by the moral committee of the institution. Procedures were explained to the patients and also the written informed consent was obtained. This study was performed on 40 patients. All eligible patients were randomized into two groups in step with the randomization schedule which was done by using

the SPSS program. The amount and therefore the form of dressing is provided to every vascular center once the eligible case present there. Each eligible study participant was assigned to 1 of the treatment groups:-

- The PRP group or the platelet-poor plasma (PPP) group by receiving the subsequent available consecutive randomization number
- Type of dressing in keeping with the randomization schedule. In both groups, surgical debridement of the injuries was done to freshen the wound bed and take away all necrotic tissue debris. The wound site, sizes (length, width, and depth), and grade were documented. Type 1 or 2 diabetes controlled by either medication or insulin, presence of a foot ulcer for a minimum of 4 weeks to be considered chronic, Patients with ischemia with ankle-brachial index (ABI) of greater than or adequate to 0.6 were included into the study while patients with noncompressible blood vessels for ABI testing, ABI of but 0.6, Evidence of gangrene in ulcer or on any a part of the foot, History of peripheral vascular repair within 30 days of randomization, patient has radiographic evidence in step with diagnosis of acute Charcot foot, patient has known or suspected osteomyelitis, Ulcer size area(length–width) of but 2cm, Diabetic foot ulcers that are clinically infected, Patients having symptoms or signs suggesting general infection (fever, foot pain, hotness, and redness round the ulcer), Ulcers that had exposed tendons, ligaments, or bone, Patient who is currently receiving or has received radiation or chemotherapy within 3 months of randomization, Screening albumin level of but 2.5g/dl, Screening hemoglobin (Hb) of but 10.5mg/dl, Screening platelet count of but 100×109/l, Patient undergoing renal dialysis, has known immune insufficiency, disease, active cancer, nutritional, hematologic, collagen vascular disease, rheumatic disease, or bleeding disorders, patient having inadequate venous access for blood draw were excluded from the study.

PRP Preparation

20 mL of peripheral blood was wont to prepare PRP and PPP in step with the rule of New-PRP Pro-Kit (Geneworld Ltd., HCM, VN). Briefly, blood was centrifuged at 1.500 rpm in 5 min to get plasma. Then, this plasma was centrifuged at 3.500 rpm in 5 min to gather platelets as a pellet at the underside of the centrifuge tube. Pellet was diluted in 3 mL plasma and was considered as PRP, and the remaining plasma was considered as PPP. Both PRP and PPP were activated to release protein by salt. When salt was added into PRP, fibrin gel was formed, and this gel was an accustomed to dress on the wound and activated PPP was stored at -200C for using within the next days. Data were analyzed using Student's t-test to check the mean of two groups and the paired t-test was accustomed to compare data before and after producers in each group. Qualitative data were presented as number and percentage and compared using either $\chi 2$-test or Fisher's exact test. The P-value was considered significant when it had been but 0.05.

RESULTS

The baseline characteristics of diabetic foot ulcers are shown in [Table 2]. The ulcer's initial length ranged from 2.1 to 6.2 cm, the initial width ranged from 1.2 to 3.1 cm, the surface area ranged from 3 to 9.2 cm^2 with an average of 7.3 cm^2, and the volume ranged from 1.1 to 3.1 cm^3 in the PRP group. The ulcer's initial length ranged from 2 to 6.1 cm, the initial width ranged from 1.2 to 3.2 cm, the surface area ranged from 4.1 to 9.2 cm^2, and the volume ranged from 1.4 to 3 cm^3 with an in the control group [Table 1]. There were no statistically significant differences between the two groups regarding average length, width, surface area, and volume control group regarding the ulcer healing rate per week [Table 2]. There was a statistically significant difference between the PRP group and the control group regarding the rate of completely healed ulcer at 10^{th} and 12^{th} weeks; however, the difference was insignificant values were found at the eighth week [Tables 3 & 4]

Table 1 Baseline criteria of diabetic foot ulcers

		PRP group			Control group		P-value
	Mean±SD	Minimum	Maximum	Mean±SD	Minimum	Maximum	
Length	3.414±1.1 cm	2.1 cm	6.2 cm	3.68±0.85 cm	2.0 cm	6.1 cm	0.81**
Width	1.82±0.36 cm	1.2 cm	3.1 cm	1.68±0.35 cm	1.2 cm	3.2 cm	0.28**
Area	7.2±1.4 cm2	3 cm2	9.2 cm2	7.051±1.22 cm2	4.1 cm2	9.2 cm2	0.46**
Volume	1.833±0.65 cm	1.1 cm3	3.1cm3	1.80±0.45 cm3	1.4 cm3	3 cm3	0.61**

Table 2: Comparison between the two groups according to the healing area over time

Time	PRP group	Control group	P-value
First week	0.6348±0.004	0.3831±0.008	<0.0001*
Fourth week	2.5545±0.032	1.8348±0.030	<0.0001*
Sixth week	3.6134±0.151	2.9342±0.025	<0.0001*
Eighth week	5.1023±0.061	3.8246±0.026	<0.0001*
10th week	6.2736±0.032	4.842±0.074	<0.0001*
12th week	7.1±0	5.45±0.11	<0.0001*
Ulcer healing rate per week	0.46±0.02	0.29±0.01	<0.0001*

Table 3: Comparison between the two groups according to the rate of complete healed ulcer over time

Time	PRP group [%]	Control group [%]	P-value
First week	0	0	
Fourth week	0	0	
Sixth week	0	0	
Eighth week	14.00	0	0.22**
10th week	46.00	3.9	0.001*
12th week	85.00	53	0.22*

Table 4: Comparison of the laboratory investigation between the PRP group and the control group from the baseline to the endpoint

PRP group			P-value	Control group		P-value
	Baseline	Endpoint		Baseline	Endpoint	
HbA1c	8.40±1.02	8.62±0.36	0.44	8.29±1.27	8.39±0.45	1.00**
Blood picture						
Hb	12.36±1.04	12.28±0.47	0.75	11.09±1.06	11.15±0.89	0.53**
Platelet count	248.40±30.22	245.00±15.22	0.35	240.00±22.88	241.30±40.47	0.80**
Blood chemistry						
Albumin	3.44±0.040	3.44±0.14	0.24	3.69±0.05	3.69±0.05	0.50**

DISCUSSION

In this study, the bulk of wound sizes within the PRP group and therefore the control was within the range of but or up to 7.0 cm^2 in area and fewer than or adequate 2 cm3 in volume. The remaining six cases, four within the PRP group and two within the PPP group, had areas of greater than 7 cm^2 and a volume greater than 2cm^3. The results of assorted studies suggest that a wound size of but 7.0 cm^2 is commonest the common baseline area within the majority of wounds was the same as that reported in many works of literature.[16–18] Driver et al.[4] reported that the bulk of wounds (35 out of 40) met the standards of wound area of but or capable 7.0 cm2 and volume of but or up to 2.0 cm^3. Lipkin et al.[19] reported in a very tissue-engineered product study in healing of diabetic foot ulcer that ~70% of the ulcers were but 6 cm 2. Another tissue-engineered product study in healing diabetic foot ulcer was done by Veves et al.[20] Veves et al.[20] reported that the common wound size area within the graft skin group that included 112 patients was 2.97±3.10 and within the control group that included 96 patients was 2.83± 2.45. In a large study that was done by Margolis et al.[21] during this study, the ulcer healing rate within the PRP-treated wound group is significantly faster than that within the control group. This result's the same as that reported in many pieces of literatures. Saad Setta et al.[22] reported in a very randomized trial on the utilization of PRP on chronic diabetic foot ulcers on 24 patients that the healing of ulcer by PRP is significantly faster than by control. Kakagia et al.[23] reported during a randomized trial on chronic diabetic foot ulcers of 51 patients that the speed of healing for the mixture of PRP and protease modulating matrix statistical is higher compared with the protease-modulating matrix alone. In 2001, a retrospective controlled study by Margolis et al.[24] on the employment of platelet released on diabetic foot ulcer of 26 599 patients showed a statistically significant higher rate of healing at 20th week after treatment by platelet released (50 vs. 41%; P<0.05). In 2010, a scientific review and meta-analysis of Villela and Santos 25 showed that there's scientific evidence regarding favorable outcomes especially the healing rate with the PRP group that reflects the effectiveness of the utilization of PRP for the treatment of diabetic ulcers.

CONCLUSION

The present study concludes that PRP is effective and safe for the treatment of diabetic foot ulcers and it significantly accelerates the healing of diabetic foot ulcers and safe where it does not make significant changes in blood hematology or blood chemistry in the patients.

REFERENCES

1. Kontopodis N, Tavlas E, Papadopoulos G, Pantidis D, Kafetzakis A, Chalkiadakis G, Ioannou C. Effectiveness of platelet-rich plasma to enhance healing of diabetic foot ulcers in patients with concomitant peripheral arterial disease and critical limb ischemia. Int J Low Extrem Wounds 2016; 15:45–51.
2. TranT,LeP,PhamP.Diabeticfootulcertreatmentbyactivatedplateletrich plasma: a clinical study. Biomed Res Ther 2014; 1:37–42.
3. Alvarsson A, Sandgren B, Wendel C, Alvarsson M, Brismar K. A retrospective analysis of amputation rates in diabetic patients: can lower extremity amputations be further prevented? Cardiovasc Diabetol 2012; 11:18.
4. Driver V, Hanft J, Fylling C, Beriou J, and the AutoloGelTM Diabetic Foot Ulcer Study Group. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers. Ostomy Wound Manag 2006; 52:68–87.
5. Frykberg RG, Armstrong DG, GiuriniJ, Edwards A, Kravette M, Kravitz S, et al. Diabetic foot disorders: a clinical practice guideline. Park Ridge, IL: American College of Foot and Ankle Surgeons; 2000.

6. Yang L, Gao L, Yang LV, Wang J. Autologous platelet-rich gel for lower-extremity ischemic ulcers in patients with type 2 diabetes. Int J Clin Exp Med. 2017; 10:13796–13801.
7. Lacci MK, Dardik A. Platelet-rich plasma: support for its use in wound healing. Yale J Biol Med 2010; 83:1e9.
8. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent 2001; 10:225e8.
9. Kevy SV, Jacobson MS. Preparation of growth factor enriched autologous platelet gel. Presented at the 27th Annual Meeting of the Society for Biomaterials. St. Paul, MN. 26 April 2001.
10. Everts PA, BrownMahoney C, Hoffmann JJ, Schönberger JP, Box HA, van Zundert A, Knape JT. Platelet-rich plasma preparation using three devices: implications for platelet activation and platelet growth factor release. Growth Factors 2006; 24:165e71
11. Yang HS, Shin J, Bhang SH, Shin JY, Park J, Im GI, et al. Enhanced skin wound healing by a sustained release of growth factors contained in platelet-rich plasma. Exp Mol Med 2011; 43:622–629.
12. Pietramaggiori G, Scherer SS, Mathews JC, Gennaoui T, Lancerotto L, Ragno G, et al. Quiescent platelets stimulate angiogenesis and diabetic wound repair. J Surg Res 2010; 160:169–177.
13. Pietramaggiori G, Scherer SS, Mathews JC, Alperovich M, Yang H-J., NeuwalderJ,etal.Healingmodulationinducedbyfreeze-driedplatelet-rich plasma and micronizedallogenicdermisina diabetic wound model. Wound Repair Regen 2008; 16:218–225.
14. Argolo Neto NM, Del Carlo RJ, Monteiro BS, Nardi NB, Chagastelles PC, de Brito AFS, et al. Role of autologous mesenchymal stem cells associated with platelet-rich plasma on healing of cutaneous wounds in diabetic mice. Clin Exp Dermatol 2012; 37:544–553.
15. Mishra A, Woodall JJr, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. Clin Sports Med 2009; 8:113e2
16. Margolis DJ, Kantor J, Berlin J. Healing of diabetic neuropathic foot ulcers receiving standard treatment. Diabetes Care 1999; 22:692–695.
17. Lee ET. Statistical methods for survival data analysis. Belmont, CA: Lifetime Learning Publications, Wadsworth, Inc; 1980.
18. Kalbfleisch JD, Prentice RL. The statistical analysis of failure time data. New York, NY: John Wiley and Sons; 1980.
19. Lipkin S, Chaikof E, Isseroff Z, Silverstein P. Effectiveness of bilayered cellular matrix in healing of neuropathic diabetic foot ulcers: results of a multicenter pilot trial. Wounds 2003; 15:230–236
20. VevesA, Falanga V, Armstrong DG, Sabolinski M. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers. Diabetes Care 2001; 24:290–295.
21. Margolis DJ, Gelfand JM, Hoffstad O, Berlin J. Surroga teendpoints for the treatment of diabetic neuropathic foot ulcers. Diabetes Care 2003; 26:1696–1700.
22. Saad Setta H, Elshahat A, Elsherbiny K, Massoud K, Safe I. Platelet-rich plasma versus platelet-poor plasma in the management ofchronic diabetic foot ulcers: a comparative study. Int Wound J 2011; 8:307–312.
23. Kakagia DD, Kazakos KJ, Xarchas KC, Karanikas M, Georgiadis GS, Tripsiannis G, et al. Synergistic action of protease-modulating matrix and autologous growth factors in healing of diabetic foot ulcers. A prospective randomized trial. J Diabetes Complications 2007; 21: 387–391.
24. Margolis D, Kantor J, Santanna J, Strom B, Berlin J. Effectiveness of platelet releasate for the treatment of diabetic neuropathic foot ulcers. Diabetes Care 2001; 24:483–488.
25. Villela DL, Santos VLCG. Evidence on the use of plateletrich plasma for diabetic ulcer: a systematic review. Growth Factors 2010; 28: 111–116.

How to cite this article: Kacker N. Surgical Management of Diabetic Foot Ulcers with Platelet Rich Plasma. Ann. Int. Med. Den. Res. 2020; 6(6):SG01-SG04.

Source of Support: Nil, **Conflict of Interest:** None declared