The Effect of Platelet Rich Plasma (PRP) Injection to the Wound Compared to PRP Jel Local Application Compared to Classic Dressing on Diabetic Foot Healing Ulcer

Hassan Awas Saad*, Ahmed M Yehia and Gamal Osman

Assistant professor, zagazig university, Egypt.

***Correspondence:**

Hassan Awas Saad, Assistant professor, Zagazig University, Egypt.

ABSTRACT

Background: *The goal of our work-study was to detect the net result and potency of of PRP local jnj. Dressings compared to PRP in jel to the wound for DFU healing compared to a control therapy of traditional classic dressing (PRP) also to decrease the recurrence (DFUs). Diabetic foot is a more famous and face any surgeon in his clinic or hospital. It has a new promise therapy of diabetic foot ulceration (DFU), with cellular and tissue regeneration, because of several methods in wound care management. All hope to attain good healing and hope to decrease recurrent rate.*

Patients and Methods: *Forty-five patients with DFU were matched and grouped for (PRP) local injection dressings (n = 15), PRP jel to wound edges (n = 15), or classic dressing (n = 15) from August 2019 to March 2021. There were additional complications and ulcer recurrences were detected Ulcer or raw area healing and reduction were the primary objectives at 1; 3, 6, and 12 months. The study comprised 36 (80.0%) males and 9 (20.0%) females between the ages of 30 and 65 who had DFU for 1 to 10 years.*

Results: *Local PRP injections improved healing 12/15 (80%) greater than local PRP jel dressings 10/15 (66.7%) and classic dressings 7/15(46.7%). However, PRP wound injection increase the healing of diabetic ulcers raw area more than PRP local jel or traditional classic dressing the healing period following local PRP injection was much shorter. At all follow-up visits, the in all the groups had similar rates of recurrence and complications. All of them had similar recurrence and variant safety.*

Conclusions: *PRP injection is a more potent technique for treating DFU than local PRP jel administration and classic wound dressings, with slight the same recurrence. Less Amputation rates, infection rates, and discharges are all reduced with PRP injection than PRP jel than classic treatment.*

Keywords

Diabetic foot ulcer, Platelet-Rich plasma injection, Jel, Classic dressing.

Introduction

"Loss of skin and or subcutaneous tissue (raw area) on the leg or foot according to the depth of the lesion that takes more than 2 months to heal" called a chronic leg ulcer or unhealed ulcer.

Chronic non-healing ulcers are deficient in growth factors (GFs) and nutrients, and so do not heal goid. The Food and Drug Administration (FDA) has authorized conventional recombinant GF products, such as becaplermin (recombinant platelet-derived GF), for the treatment of chronic wound ulceration. Chronic ulceration of the lower leg, including the foot, is a common problem that causes pain, social discomfort with a recorded prevalence of

1%. [1]. However, because the drug is in a liquid form, it vanished quickly after being applied to a raw area or ulcer. Furthermore, the medications are costly ulcers [2].

It has had a significant impact on bone and soft tissue healing stimulation and repair. Platelet-rich plasma (PRP) improves chronic wound healing by promoting mesenchymal cell recruitment, optimal proliferation, and extracellular matrix formation during the healing process [3]. Autologous PRP is a highly safe, simple, straightforward, and cost-effective technique for treating persistent diabetic leg or foot [4].

Patients and Methods
Our clinical research was done between August 2019 and March 2021. It included 45 patients with DFU who were referred to the surgical department at Zagazig University Hospitals' outpatient clinic and treated with the help of the vascular surgery department.

Sample Size
The 45 patients were classified to three groups: PRP local wound injection to the wound edge dressing (group A); n = 15, PRP jel local surface ulcer application (group B); n = 15, or classic dressing therapy (group C); n = 15.

Study Endpoints
After 1; 3 ;4; and 6 months and 1 year, the aim was the 1_ rate of ulcer complete healing and the percentage of reduction of ulcer raw area in size, whereas the 2_secondary points were treatment-related to complications early and the decrease ulcer recurrence after complete healing process within 1 year of follow.

Patients Assessment
All patients with non-healing lesions on their feet had a history taking and examination inquiry to discover the risk factors and treatment options for diabetic foot problems, so 'improving outcomes and reducing the risk of lower extremity amputation.

All patients had their medical histories obtained and were checked both all to confirm the diagnosis of diabetic ulcer by local and general examination. By analyzing demographic data such as age, gender, smoking, hypertension, and body mass index (BMI), diabetes mellitus was found to be linked. Pulse palpation, ankle brachial index measurement, peripheral neuropathy, and ulcer character location, size, shape, margins, and depth were all part of the local assessment.

Complete blood count, fasting and postprandial blood sugar, (HB1AC1) concentration, routine investigation, A venous duplex was also done, as well as a plain X-ray or bone computed tomography if necessary.

Ulcers Assessment
The length of the present ulcer, as size its laterality, edge, margin, form, and floor, as well as the necessity or need for antibiotic with all types if needed.

Technique
Debridement
Before any therapy, Debridement's goal was to turn a chronic or highly infected wound from chronic to acutely healthy by eliminating nonviable tissue that might cause excessive inflammation and ultimately bacterial overgrowth. Any history of complete raw are or ulcer healing, as well as the length of the wound prior to the healing before. Also, the design to check for metaplasia or malignant changes or a particular or underlying disease, a culture swab and a four-quadrant biopsy that may be acquired to open the contaminated region, simple wound incisions were performed, and deed un healthy ulcer tissues was excised as deeply as necessary until the patient wound was healthy.

Patients in Group C were treated with standard dressings; surgical removal of dead tissues was performed for all unhealthy tissues, if necessary, pus was drained, and the dressing was done by suitable materials. The wound was repeated washed by normal saline, and a dressing was chosen by using suitable qualities to controller of the exudates (dry or moist wound), then the wound was packed.

The traditional classic dressing is done twice a day with regular saline and antiseptic diluted to 50% povidone-iodine.

Any callus tissue that has formed around the area should be removed. Always let wounds exposed for 3-4 days and check them was used to treat Group A patients. Local PRP injection treatment we injected PRP around 2-3cm from the edge of the wound after it was prepared (within half an hour of preparation) to avoid loss from the close edge injection location. Because most of the tissue reformation takes place or is gathered to the base of the ulcer, the needle is directed downwards and towards the center of the base (45 degrees), followed by wet saline gauze that rechanged every three days. This regimen was followed for up to eight weeks. Depending on the extent of the ulcer, the patient required 6 to 8 doses. The patient's own blood was used to make PRP (autologous PRP). To avoid platelet activation and degranulation, 20 mL of venous blood was collected in a syringe and combined with an anticoagulant. At 23°C, the entire blood was centrifuged for 5 minutes at 3200 RPM. The initial centrifugation was known as a 'soft spin,' and it allow the blood to be separated into2 layers: the deep layer contained RBCs, while the upper layer contained platelet rich plasma. Using a pipette, the plasma was separated to sterilized tube without anticoagulant. A 'hard spin' was performed on this tube after 2nd cycle of separation at 5000 RPM for 10 minutes. The plasma is divided into platelet poor plasma and platelet rich plasma after the second spin, along with a few RBCs that form platelet pellets. The top two-thirds of the PPP is discarded, while the deep one-third is PRP, which is utilized for PRP therapy. The PRP is then aspirated into a 1ml syringe with a 20-24 gauge sized needle and then injected all around the circle of the ulcer as instructed.

Group B dressing by applying PRP jel and the dressing was changed every 3 days

Autologous of PRP jel preparation

PRP jel is made in the same way, but only the PRP fraction is placed into a mixing chamber and the reagents are added as previously stated. The gel was applied topically to the wound and covered with a nonabsorbent contact wet layer, a moisture dressing layer, and a secondary absorbent dressing once the PRP liquid transformed to a clear gelatinous consistency (typically within 15–30 seconds).

Follow-up

The feet be elevated to reduce edoema.

Patients informed to avoid any ulcer pressure by footwear or cast was prescribed (offloading). Throughout the therapy, the patients were seen once every 3-4 days. Exudates, necrotic tissue, infection. If necessary, culture and sensitivity done. The patients' wound healing rates. Were assessed in roughly 6-8 weeks by taking pictures and the hope of our study result was a decrease in the size of the wound raw area and decrease recurrency.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) was used to analyses the data statistically (version 17). percent mean SD Qualitative that provided as percent and numbers, and second Fisher's exact tests were used to examine it 50. The difference between the groups was measured using the difference of analysis of vary of (ANOVA) examination test. Significant that defined as a P-value of less than 0.05The T-test was used to compare quantity and a variables parametric data that were provided as SD and mean.

The ulcer area measured at 1 ;3 or 4 and 6, then 12 months after treatment in every group, as well as calculating the number of ulcers with full closure among the all groups at the same duration.

Results
Baseline patient's criteria

The research comprised 45 patients, with men (80.0%) and females (20.0%) ranging in age from 30 to 65 years and BMIs ranging from 19 - 37 kg/m2. with randomization strategy ended in the inclusions of similar affected patients in each of the 3 groups, without significant changes in baseline criteria for patients or ulcers (Table 1).

Figure 1: Showing male patient rt. foot with DFU healed by using PRP injection after 45 days.

Figure 2: Showing female patient lt. foot with DFU healed by using PRP jel application after 50 days.

Figure 3: Showing male patient lt. foot with DFU healed by using classic dressing after 60 days.

Baseline Ulcer Criteria

Ulcers were medial in 34 (75.5%) of the patients, solitary in 39 (86.7%), and recurrent in 18 (40%) of the cases in the entire research group (Table 1).

Procedures That Are Related

Debridement was required in 18/45 (40%) of the cases studied, without statistically significant differences in between the patients' groups (Table 2).

Ulcer Area Reduction

That of the patients had similar baseline wound ulcer surface areas (P =.948), but the decreases in wound ulcer area following therapy with substantially different across the all groups at the 3 m follow-up visits (P =.015,.001, and.001, respectively) (Table 3).

Table 1: The baseline of the ulcers and the patient's characteristics.

Variable	PRP jel application n = 15	PRP injection n = 15	Classic dressing n = 15	P value
Patients' characteristics				
Age (years) mean±SD	46.2 ±9.35	44.1±14	40.90±13.3	.48
Range	25-61	25-61	23-65	
Males	13(86.7%)	11 (73.3%)	12 (80.0%)	.65
BMI (kg/m^2) mean±SD	25.2±7.4	26.6±4.1	27.9±5.6	.50
Range	16-35	20-35	18-36	
Smoking	7 (46.7%)	5 (33.3%)	6 (40.0%)	.879
Diabetes mellitus	all	all	all	100%
Ulcers' characteristics				
Medial ulcers	11 (73.3%)	11 (73.3%)	11 (73.3%)	.88
Single ulcer	12 (80.0%)	13 (86.7%)	14 (93.3%)	.56
Mean current ulcer duration (years)	6.2±3.1	5.4±2.6	6.4 ±2.8	.45
Range	2-10	1-10	2-11	
Mean previous ulcer duration (years)	11.3±3.5	9.8±4.6	10.6±4.8	.64
Range	2-10	1-9	2-11	
Recurrent ulcers after 2years	6 (40%)	7 (46.7%)	6 (33.3%)	.86

Note: P value is significant if P <.05, calculated by using the ANOVA test.
BMI, body mass index; and PRP, platelet-rich plasma.

Table 2: Ulcer healing.

P-Value	Classic Dressing No 15	PRP Local Jel No 15	PRP Local Inj Injection No 15		Variable	
.0003	2(13.3%)	5(33.3%)	7(46.7%)	Incomplete	Ulcer Healing	
.0003	13(86.7%)	1 (53%)	8(66.7%)		4 Months	
,007	7(47,6%)	10(66.7%	12(80%	Healed		
.04	6(40%)	4(26.7%)	.2(16.7%)	Incomplete	12 Months	
,326	1(6,7%)	1(6,7%)	1(6.7%)	Recurrent		
.18	7(4-12)	(3-9)6	(3-6)9	Median Range	Median Healing Time By Month	

Note: * indicates statistical significance. Data are presented as number and percentage or median and range.

Table 3: Ulcer area reduction along the study period.

Variable		Baseline	4 months	6 months	12 months					
(A) PRP injection B) PRP jel	Mean±SD	15.7±7.4	2.5±1.3	1.6±0.5	1.1±0.4					
	Mean reduction %		84%	90%	(B) PRP application	Mean±SD	16.5 ±8.2	5.8±2.1	1.3±0.6	1.2±0.5
(C) classic dressing	Mean±SD	17.8±5.4	8.5±3.3	5.5±2.7	3.8±1.5	Mean reduction %		65%	92%	92.7%
	Mean reduction %		52%	69%	78.6%					
P value		.948	.015*	.001*	<.001*					
P1 (A vs B)		.852	.016*	.079	.351					
P2 (A vs C)		.868	.361	.003*	<.001*					
P3 (B vs C)		.756	.013*	.002*	<.001*					

Note: * Significant as P value <.05, P1, comparing groups A and B; P2, comparing groups A and C; P3, comparing groups B and C. Ulcer area was measured by cm^2.

Every two groups were analyzed independently to determine the influence of each treatment on this decrease in ulcer dimension. During every follow-, PRP injection resulted in decrease in area of ulceration in ulcer area than local jel than classic method, Similarly, after 4 months, PRP injection resulted in a substantially larger ulcer area decrease than PRP jel application, than classic other than 6 or 12 months, P =.016,.079, and.351. At the end, only after 6 is P =.003 and 12 P 0.0001 months of follow-up.

Ulcer Complete Healing Rate
During the whole follow-up period, better wounds to be healed were demonstrated following PRP wound or ulcer injection, or jel application, and classic therapy (Table 2). P =.007 showed that PRP injection resulted in a substantially larger percentage of ulcers healing fully (12/15, 80%) than PRP local jel (10/15, 66.7%) or classic treatment (7/15, 46.7%) at the final follow-up. In the subgroup with healed ulcers, healing time was considerably reduced following PRP injection compared to PRP jel application and classic treatment (P =.009 and.026, respectively).

Ulcer Recurrence
There was no significant difference in the recurrence rate between the groups, P =326. Noncompliance with classic therapy was the most common cause of recurrence, which resulted in three cases,

recurred: 1in the PRP jel local used group and 1 in the injection group after 6months of healing, and 1 in the classic group after 1:3, and 6 months of treatment and healing.

Discussion

Diabetic foot wounds are a frequent complication in diabetic patients. There is a definite trend toward increasing risk of chronic wounds due to population aging and an increase in risk factors and co-morbidities such as cigarette use, obesity, hypertension, and atherosclerosis [5].

The current study included 45 patients with DFU, ranging in age from 23 to 65years old, with the bulk of the patients being men [6]. Saad et al. conducted research on 24 individuals with chronic ulcers ranging in age from 40 to 60 years old, and found that sex and age have no bearing on the rate of healing of their ulcers. [PRP is defined as a percentage of autologous blood plasma fraction with a platelet concentration above the baseline. Platelet-enriched plasma, platelet-rich concentrate, and autologous platelet-rich plasma are all terms for the same thing. Since 1985, PRP has been used to heal wounds [7].

After interpretation and recent meta-analyses review, as well as a Cochrane reports, have recommended the use of PRP not just in diabetic ulceration, but also in such wounds as venous, traumatic, and other ulcers safety [8].

All findings of Carter et al., comprehensive prospective and meta-analysis study reveal that PRP injection then jel treatment can improve raw area healing and related variables factors including pain and infection in both chronic and acute cutaneous wounds [9].

All of these factors point to the necessity for more research that avoids all or most of these flaws. As a result, we conducted this prospective randomized controlled trial with 45 chronic diabetic wounds to assess the relative efficacy of PRP local wound injection versus PRP jel local application and traditional dressing in terms of wound healing percentage, reduction rate in raw area of wound size, and raw area of wound that had been recurred after or thought 1 year, and procedure.

This study found that PRP injection resulted in a considerably greater raw area-healing rate and quicker area decrease in size than both PRP jel local application and lastly classic dressing, but PRP jel application superior to classic dressing therapy except for a similar healing duration. In terms of recurrence and complication rates, however, the three groups were equal the same our results.

Anitua (1999) [recommended a weekly application since PRP was prepared using a simple bedside process; nevertheless, manner of predation either by max. or min. of frequency of PRP treatments that were not consistent during process of examination and treatment. Because the fluid PRP frequently flows over the wound and raw area of ulcer margins or becomes attached to the further dressing, local PRP jel treatment may be less effective.

PRP injection has been used to improve wound healing for over 20 years. PRP made from a patient's blood contains cytokines, growth factors, chemokines, and a fibrin scaffold. The molecular and cellular stimulation of a normal wound-healing response, analogous to platelet activation, is thought to be the mechanism of action of PRP.

Previous research compared PRP application to traditional dressing therapy for DFU treatment, but none compared PRP injection to jel application. In two investigations, using every 2 weeks dressing in chronic leg ulcers of varied aetiology were treated with simultaneous peri-lesional ulcer injection and local administration of PRP.

We used PRP every 2-3 weeks for the first 8 weeks of therapy in the current study. The theoretical foundation for selecting PRP injection over local application in order to give enough concentrations of platelets to the wound borders and depth, as well as sustain their supply the wound by growth factors for good periods of time than PRP jel administered locally.

After the second week, PRP was found to be more effective than traditional dressing in the current investigation. At the fourth week, the same impact was reported. This might be explained by the fact that platelets that triggered by collagen and released into the circulation following endothelial damage during wound healing. Platelets produce intercellular mediators and cytokines from the cytoplasmic pool following aggregation and release their alfa–granule content. More than 800 distinct proteins are released into the environment, having a paracrine influence on various cells. For at least another 7 days, platelets continue to secrete additional cytokines and growth factors from their mRNA stores [10].

Because there is so much disagreement in the literature about the efficacy of PRP on chronic unhealed ulcers, whether diabetic, venous, or traumatic, some research agrees with our findings while others disagree. As general taking about PRP five of the PRP-treated raw area ulcer in 8 weeks vs none in the classic treatment group, with an area decrease of roughly 82 % versus 24 %, respectively, P.001. Aguirre et al. [11] assigned 23 cases to either PRP treatment types (n = 12) or by using silicone dressing (n = 11). In the PRP vs control groups, the ulcer raw area healing duration was 9.6 versus 23.7 weeks, respectively, P.001. Similarly, Somani and Rai [12] randomly assigned 15 cases to receive either PR degra., fibrin (n = 9) or saline washing dressing (n = 6), Healing was detected in 55 % of the ulcers after 4 weeks of therapy vs 0% of the ulcers after 4 weeks of treatment.

The majority of the wounds healed within the predicted period of healing (8 weeks); after the first four weeks, all of these instances exhibited more than 50% healing Gelf et al. [10] supported the findings that we notice in our study also, stating that 'it is generally believed that recovery by 12 weeks is an acceptable aim.' 30 percent healing rates at 4 weeks predict total healing rates, and a weekly area decrease of 10-15 percent indicates a good accepted prognosis.

Table 4: Initial ulcer area, duration, and ulcer complete healing in previous studies.

Study	Intervention	PRP jel. — classic dressing	Ulcer area	Ulcer duration	Follow up
The present study	PRP injection 12/15(80%)	PRP jel10/15 (66.7%) 7/15 classic (66.7%)	16.5	72 months	1 year
Stacey et al. [10]	Frozen PRP 33/42 (78.6%)	Placebo 34/44 (77.3%)	2	3 months	36 weeks
Aguirre et al. [11]	PRP 5/12 (41.7%)	Silicone dressing 0/11 (0%)	9.6	4.5 months	8 weeks
Senet et al. [15]	Frozen PRP 1/8 (12.5%)	Saline 1/7 (14.3%)	12.5	60 months	12 weeks
Somani et al. [17]	PRP 5/9 (55.5%)	Saline 0/6 (0%)	8.14	≥6 months	4 weeks
Anuita et al. [20]	PRP 1/7 (14.3%)	Saline 0/7 (0%)	5.5	17 months	8 weeks

The decrease in ulcer area was 85.5% against 42.7 %, P.001, respectively. In a randomized study of PRP local using (n = 55 ulcers) against saline washing dressing (n = 47 ulcers) for DU, Cardenosa et al. [13] found an area decrease of 67.7% versus 11.1 percent, respectively, with P =.001. In addition, Anitua et al. [5], 20 found that in the PRP vs regular therapy groups, 73 percent versus 21 percent, P.05, respectively.

Other clinical research, on the other hand, found that PRP had no differences in effect on the healing of DFU or chronic unhealed ulcers, whether venous, diabetic, or traumatic by the same effects and results in [14]. In a study by Stacey et al. [15] individuals were randomly assigned to either platelet lysate treatment (n = 42) or placebo application (n = 44). Within three months, 75 percent of ulcers in each group had healed completely.

Robson et al., [16] established that an area of less than 15 cm2 and a period of less than 18 months are the classic dressing for a better prognosis. The process of healing for raw area taking long duration period because the study comprised bigger and longer duration than these indicated values. 4th Table in these investigations, the average recovery period ranged from 1 to 4.5 months. The study by Senet et al., [17] found higher decrease in raw area of wound at 3 months in both PRP injection or jel application groups.

Similarly, Senet et al., [17] randomly found 15cases to receive either frozen platelets diluted in normal saline (n = 8) or saline (n = 7). The ulcer raw area decrease after 12 weeks was 26.2 percent against 15.2 percent, respectively, P =.94. Only one ulcer was cured in each group.

The resistant ulcers are more likely to reoccur after healing. In our study, noncompliance with compression therapy was blamed for the majority of recurrences, even after the underlying disease had been treated.

In another study PRP, compares to another method express good method with less recurrence; but our study no great or significance difference. Consequently, it is regarded a suitable adjuvant therapy to improve wound healing, with traditional dressing.

Accordingly, 15 of the studies examining PRP's efficacy on DFU healing had a less period of follow-up (4-36 weeks), in none of them, recurrence of ulceration or wound after period was used as an endpoint. However, every treatment strategy for DFU should be evaluated for ulcer recurrence rates and wound healing criteria.

Local PRP injection improves DFU healing more than local PRP jel application or traditional classic dressing treatment. All PRP methods had similar recurrence with classic dressing. PRP injection is a potent safe tool for treating chronic wounds, and it is especially promising for diabetic foot wounds than PRP jel than classic treatment; since it promotes healing while also lowering amputation rates, infection, and exudates.

Acknowledgement

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