Platelet-rich plasma versus conventional dressing: does this really affect diabetic foot wound-healing outcomes?

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Purpose
This study aimed to compare platelet-rich plasma (PRP) versus conventional ordinary dressing in the management of diabetic foot wounds.
Background
Diabetic foot wound treatment poses a considerable burden on the medical system, with long waiting times for healing in the public hospital system. PRP enables efficient treatment of many patients with hemostatic, anti-inflammatory, and analgesic substances.
Patients and methods
This prospective study was focused on 80 diabetic feet wounds. Patients were divided into two groups: group A received conventional ordinary dressing (*N*=40, 50%) and group B received PRP dressing (*N*=40, 50%). The mean follow-up period was 12 weeks.
Results
The estimated time of wound healing was 12 weeks for 82.5% of the patients in group A and 97.5% of the patients in group B; the PRP group was found to be more effective with fewer complications, less infection, exudates, pain, and failed healing: 17.5, 12.5, 32.5, and 2.5% versus 27.5, 42.5, 62.5, and 17.5% in group B, respectively (*P*=0.001). The highest healing rate was observed for both groups at the fourth week, but it was better for the PRP group (group B): 0.89±0.13 versus 0.49±0.11 cm^2/week in group A.
Conclusion
There have been considerable advancements in the use of PRP in therapeutic processes in recent years in tissue regeneration therapy. PRP is a powerful tool for the treatment of chronic wounds and very promising for diabetic foot wounds; PRP enables healing, and reduces infection rates and exudates.

Keywords:
conventional ordinary dressing, diabetic foot wounds, healing outcomes, platelet-rich plasma

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Introduction

One of the most common causes of chronic wounds is growth factor abnormality. Platelets are considered a rich source of growth factors. Platelet-rich plasma (PRP) enhances wound healing by either the barrier effect to prevent bacterial invasion into the wound or the growth factors stimulate wound healing [1].

About 15% of diabetic patients will develop chronic wounds and about 25% of these patients will have to undergo foot amputation. The healing process is impaired in part because of deficiency of growth factors [2,3]. Becaplermin, a recombinant human platelet-derived growth factor-BB, is the only growth factor preparation approved by the US Food and Drug Administration for the treatment of diabetes mellitus (DM) wounds, but it requires daily applications for weeks to months [4].

Cell therapy and cell-containing tissue-engineered skin represent a significant advancement in the treatment of difficult to treat wounds. Currently, there are two cell-containing tissue-engineered skin products with US Food and Drug Administration approval available for use in the treatment of wounds. Apligraf (a bilayered bicellular product containing keratinocytes and fibroblasts in a bovine collagen matrix) and Dermagraft (fibroblast on a polyglactin matrix) accelerate wound healing, but also require frequent (weekly) applications, have a short shelf-life, and are expensive [5].

The use of adenovirus encoding human platelet-derived growth factor formulated in bovine collagen gel (GAM501) for the treatment of small nonhealing diabetic foot wounds has been reported. Despite these advanced researches, a more practical and effective

therapy for nonhealing diabetic wounds is clinically needed [6,7].

Plasma samples with platelet concentration above baseline values are referred to as PRP [8,9]. The clinical efficacy of the PRP was discovered in the early 1990s when new 'biological glues' were being discovered. They are at present used extensively in many clinical and surgical fields requiring tissue regeneration such as orthopedics, dentistry, wound healing, and maxillofacial surgeries [10].

The therapeutic effect of PRP is attributed to the abundance of various growth factors such as platelet-derived growth factor, transforming growth factor-β, fibroblast growth factor, insulin-like growth factor-1, insulin-like growth factor-2, vascular endothelial growth factor, epidermal growth factor, and also some cytokines primarily stored in alpha granules [11,12].

PRP can be prepared either from an autologous or an allogenic source. The majority of studies documented have used autologous platelet preparations as they are more acceptable by the patient and have a lower risk of transmission of viral infections [13].

PRP is easy to produce, with minimal effort. In a two-step process, whole blood from the patient is first centrifuged to separate plasma from packed red blood cells (RBCs) and then further centrifuged to separate PRP from platelet-poor plasma (PPP). This concentrate is then activated with the addition of thrombin or calcium, resulting in a gelatinous platelet gel. Clinically valuable PRP contains at least one million platelets per microliter [14].

Lower concentrations cannot be used to enhance healing and higher concentrations have not been shown to increase healing [15]. Blinded, multicentric, randomized-controlled studies with large sample sizes are urgently needed to establish their therapeutic efficacy. There are no universally established standards for the collection, quality control, and administration of the product [16,17].

Patients and methods

After receiving approval from the local ethical committee of Benha University and obtaining written fully informed consent from patients on the two methods of dressing and their benefits, risks, alternative interventions, and possible complications, the current study was carried out at the Vascular Unit, General Surgery Department, Benha University Hospitals, from October 2015 to July 2017, to allow a 12-week follow-up period for the last patient dressed on. This prospective randomized-controlled study was carried out on 80 diabetic patients with nonhealing feet wounds. Patients were allocated randomly using a computer-generated random number table into two groups according to the dressing method used: group A received conventional ordinary dressing (N=40, 50%) and group B received PRP dressing (N=40, 50%).

Patients included in this study had nonhealing feet wounds and fulfilled the following criteria: patients aged between 31 and 66 years, diabetic patients, both type I diabetes (insulin dependent) and type II diabetes (noninsulin dependent), with controlled blood sugar levels with nonhealing wounds on their feet, persistent wound for 3–6 months, wound size of the foot ranging from 6.5 to 8.5 cm^2, transcutaneous oxygen tension more than 30 mmHg, patients awaiting revascularization surgery, patients who had a normal peripheral platelet count ($>150\ 000/mm^3$), and patients with screening serum albumin level of more than 2.5 g/dl or hemoglobin more than 10.5 g/dl.

Pregnant women, patients with ischemic changes of the foot (transcutaneous oxygen tension$<$30), patients with radiological evidence of chronic osteomyelitis, patients not awaiting revascularization surgery, patients with severe cardiovascular disorders, patients who had received conventional skin grafting in the past, critically ill patients with immunological disturbances, and patients who were receiving or had received radiotherapy or chemotherapy within 3 months before the study were excluded.

All patients with nonhealing wounds on their feet were subjected to a formal assessment and investigations to determine the risk factors and treatment of diabetic foot disorders that required the expertise of a specialized practitioner to diagnose, manage, treat, and counsel the patient. Integration of knowledge and experience through a multidisciplinary team approach promoted more effective treatment, thereby improving outcomes and limiting the risk of lower extremity amputation.

Intervention

Sharp debridement of heavily infected wounds or nonhealing wounds was performed using a scalpel, curette, and scissors. Debridement converted a chronic or a heavily infected wound to one that was acute by removing nonviable tissue that could stimulate excessive inflammation and bacterial growth. Simple

incisions were used to open the infected area. Excision of necrotic tissue was extended as deeply and proximally as necessary until healthy, bleeding soft tissue and bone were encountered.

Any callus tissue surrounding the wound was removed. Evidence of pus on tendon sheaths indicated the need for more extensive debridement. Tendons were cut under tension to allow them to retract away from the open wound. The wounds should always be left open and inspected at 24–36 h.

Further debridement was carried out as necessary until the wound was clean and healing was underway. In the presence of an adequate arterial supply, rapid healing could occur following a thorough debridement. If healing did not occur, this was usually because of failure to drain all areas of infection or unrecognized ischemia. The decision on whether a foot could or could not be saved was made by the experienced surgeon. In case of doubt, all dead tissues were excised and the wounds were left open.

Postintervention dressing

Group A

This group of patients was treated by conventional ordinary dressing; surgical debridement was carried out for all necrotic tissues, and pus loculi were drained as discussed before and the dressing material used was prepared. Irrigation of the wound was performed with saline, and a dressing was selected by matching the properties of the dressing (such as control of exudates) with the characteristics of the wound and the patient, followed by packing of the wound. Appropriate dressing types were determined on the basis of wound location, depth, amount of slough present, amount of exudates, condition of the wound margins, and presence of infection. In general, betadine ointment with or without glycerin were used as wound-dressing materials. This dressing was performed every day and sometimes twice per day (Fig. 1).

Group B

This group of patients were treated by PRP therapy. The dressing protocol of these patients included PRP. PRP was applied to the diabetic foot after being prepared (within half an hour after preparation), followed by Vaseline gauze and then a dressing. The dressing was changed once weekly. This protocol was performed up to 12 weeks or stopped whenever healing occurred.

Each patient was sprayed with PRP around the wound edges (subdermal) and the floor (if deep). PRP was prepared from the patients' own blood (autologous PRP). Venous blood samples were drawn into 5 ml sterile tubes containing an anticoagulant (citrate dextrose – 3.2% sodium citrate) to avoid platelet activation and degranulation (10 ml). Whole blood was centrifuged at ×300*g* for 5 min at 18°C. The first centrifugation was called a 'soft spin' (×100*g*), which enabled the separation of blood into three layers: the bottommost layer comprised RBCs (55% of the total volume), the topmost layer comprised cellular plasma called PPP (40% of the total volume), and an intermediate PRP layer (5% of the total volume) called the 'buffy coat'. The upper fraction (PRP1) was separated, without disturbing the buffy coat, and was transferred into a sterile tube; this was done using a sterile syringe. The PPP, PRP, and some RBCs (i.e. the upper two layers and a very minimal 'unavoidable' amount of the bottom layer) were transferred into another tube without an anticoagulant. This tube was subjected to a second round of centrifugation (×447*g*) and was called a 'hard spin'.

This enabled the platelets (PRP) to settle at the bottom of the tube with very few RBCs. The cellular plasma, PPP (80% of the volume), was found on the top. Most of the PPP was removed with a syringe and the remaining PRP was shaken well. PRP1 was centrifuged at ×700*g* for 17 min at 18°C. The platelet pellet obtained from PRP1 was resuspended in 1 ml PPP (PRP2). Platelet activation was performed immediately by adding 0.5 ml $CaCl_2$. Application was performed immediately after the activation of wound edges and floor. Dressing was performed and lifted for 1 week until a follow-up session. Reinjection was performed after 2 weeks. However, for large wounds, more than 5.5 cm, reinjection was performed every week during a follow-up session and dressing was performed twice weekly – that is, every 3–4 days (Fig. 2).

Follow-up

The patients were advised to avoid pressure on the wound area. A special shoe with a molded insole was used. Elevation of the feet was recommended when sitting or lying down to decrease edema. The patients were seen once or twice weekly throughout the course of treatment and a clinical evaluation was performed once weekly. Clinical laboratory tests were performed every 4 weeks for all treatment groups – that is, complete blood count, random blood sugar, and serum albumin.

The patients were evaluated for the rate of wound healing in about 12 weeks and this evaluation was carried out by taking photos and measuring the wound's dimensions (length and width) using a

Figure 1

Cases of group A: conventional ordinary dressing.

metric tape at the initial visit and then every week. Characteristics of the wound such as exudates, necrotic tissue, infection, and granulation tissue were documented. The primary outcome evaluated: was reduction in the size of the wound, which was determined from photos taken every week. The secondary outcome parameters were the presence of infection, exudates, and pain.

Statistical analysis

Analysis of data was carried out using Statistical Package for Social Sciences (SPSS) (version 16; SPSS Inc., Chicago, Illinois, USA) (Bristol University, UK). Quantitative data were presented as mean and SD and were analyzed using a one-way unpaired *t*-test to compare quantitative variables as parametric data (SD<50% mean). Qualitative data were presented as numbers and percentages and were analyzed using χ^2 and Fisher's exact tests. A *P*-value of less than 0.05 was considered significant whereas a *P*-value of less than 0.01 was considered highly significant. However, a *P*-value of more than 0.05 was considered insignificant.

All these data are shown in Figs. 1, and 2.

Figure 2

Cases of group B: platelet-rich plasma (PRP) dressing.

Results

This was a prospective study that included 80 diabetic patients with nonhealed foot wounds recruited from Benha University Hospitals and were followed up for 12 weeks; patients were divided according to the dressing performed into two groups: group A included 40 patients who received conventional ordinary dressing. Group B included 40 patients who received PRP dressing. Their ages ranged from 31 to 66 years, with a mean of 49±5.06 years. All patients presented with nonhealed foot wounds and none of them presented with any other symptoms; the majority of patients were men [50 (62.5%)]. The wound was mostly present on the sole of the foot [67 (83.75%)]. The duration of diabetes in the patients ranged between 7.5 and 12.5 years, with a mean of 10.3±2.3 years, and the size of the wound ranged between 4.9 and 8.6 cm, with a mean of 7.4± 0.8 cm (Table 1 and Graph 1a and b).

Upon review of DM-related comorbidities, foot angiopathy and retinopathy, which affected wound healing and care, were observed in 15 (18.75%) and eight (10%) cases in group A versus 17 (21.25%) cases and nine (11.25%) cases in group B,

respectively. Of these diabetic patients, 64 (80%) patients were on oral hypoglycemic drugs, whereas 16 (20%) patients were on insulin injections. Other risk factors encountered were medically controlled hypertension in 31 (38.75%) patients, nephropathy in 15 (30%) patients, and smoking in 48 (60%) patients that could have impaired wound healing. There was no significant difference between both groups in terms of the presence of these risk factors (χ^2=0.104 and P=0.706) (Table 2 and Graph 2).

In terms of the previous clinical parameters, previous foot wound and minor amputations were reported in nine (11.25%) and 10 (12.5%) cases in group A versus 11 (13.75%) and 12 (15%) cases in group B, respectively. Intermittent claudication with transcutaneous O_2 tension more than 30 mmHg and foot neuropathic pain were reported in 15 (18.75%) and 25 (31.25%) cases in group A versus 17 (21.25%) and 27 (33.75%) cases in group B. Previous hyperbaric O_2 therapy was reported equally in both groups in 21 (42%) cases (P=0.736) (Table 3 and Graph 3).

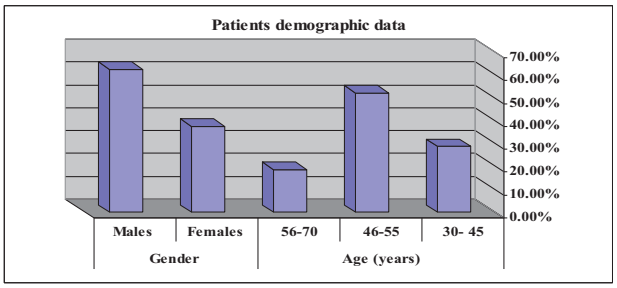
No mortality was recorded and all patients attended follow-up. PRP was shown to be more effective than conventional dressing after the second week

Table 1 Patients' demographic data

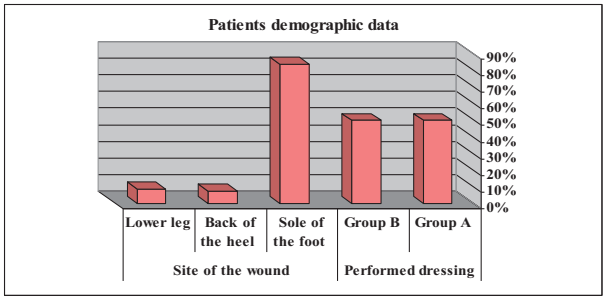
Data	Findings [*n* (%)]
Age (years)	
Strata	
31–45	23 (28.75)
46–55	42 (52.25)
56–66	15 (18.75)
Mean±SD	49±5.06
Sex	
Female	30 (37.5)
Male	50 (62.5)
Performed dressing	
Group A: conventional ordinary dressing	40 (50)
Group B: PRP dressing	40 (50)
Site of the wound	
Sole of the foot	67 (83.75)
The heel	6 (7.5)
Lower leg	7 (8.75)
Duration of diabetes [range (mean±SD)] (years)	7.5–12.5 (10.3 ±2.3)
Size of the wound [range (mean±SD)] (cm)	4.9–8.6 (6.4±0.7)

PRP, platelet-rich plasma.

Graph 1



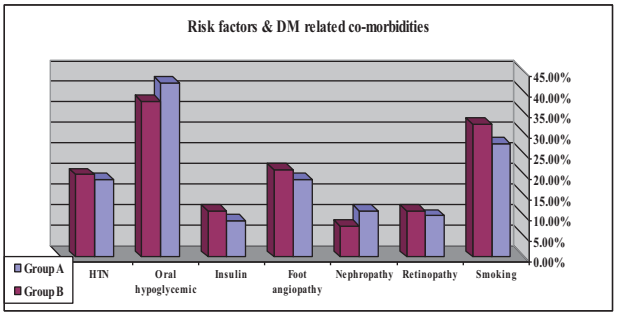
Graph. (1_A): Patients demographic data.



Graph. (1_B): Patients demographic data.

Patients' demographic data: (a) sex and age; (b) site of the wound and performed dressing.

Graph 2



Risk factors of impaired healing and diabetes mellitus-related comorbidities. HTN, hypertension.

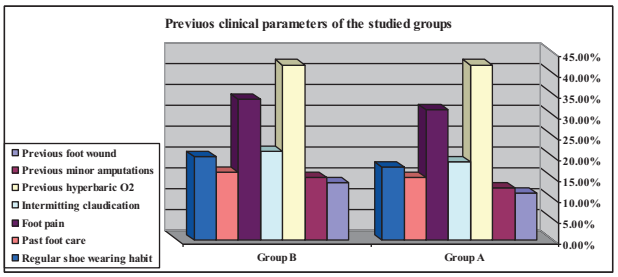
Table 2 Risk factors of impaired healing and diabetes mellitus-related comorbidities

Risk factors and DM-related comorbidities	Group A (*n*=40 patients) [*n* (%)]	Group B (*n*=40 patients) [*n* (%)]	χ^2	*P*-value
Smoking	22 (27.5)	26 (32.25)	0.104	0.706 (NS)
Retinopathy	8 (10)	9 (11.25)		
Nephropathy	9 (11.25)	6 (7.5)		
Foot angiopathy	15 (18.75)	17 (21.25)		
Insulin	7 (8.75	9 (11.25		
Oral hypoglycemic	34 (42.25)	30 (37.75)		
Hypertension	15 (18.75)	16 (20.0)		

DM, diabetes mellitus.

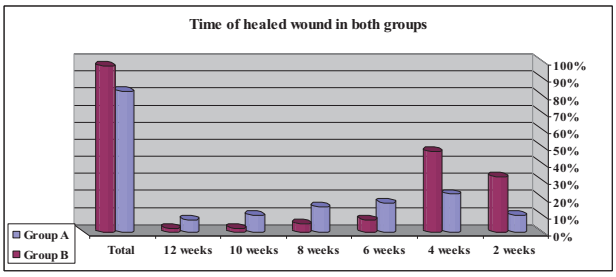
[13 (32.5%) patients vs. 4 (10%) patients, respectively]. The same result was found at the fourth week [19 (47.5%) cases versus nine (22.5%) cases, respectively]. However, subsequently, the number of healed wounds started to decline – that is, at the sixth week [three (7.5%) cases in group B versus seven (17.5%) cases in group A]. Wounds healed in 39 (97.5%) patients in group A versus 33

Graph 3



Previous clinical parameters of the studied groups.

Graph 4



Rate of healing of wound in both groups with respect to time.

Table 3 Previous clinical parameters of the studied groups

Clinical parameters	Group A (*n*=40 patients) [*n* (%)]	Group B (*n*=40 patients) [*n* (%)]	χ^2	*P*-value
Previous foot wound	9 (11.25)	11 (13.75)	0.114	0.736 (NS)
Previous minor amputations	10 (12.5)	12 (15)		
Previous hyperbaric O_2	21 (42)	21 (42)		
Intermitting claudication	15 (18.75)	17 (21.25)		
Foot pain	25 (31.25)	27 (33.75)		
Past foot care	12 (15)	13 (16.25)		
Regular shoe-wearing habit	14 (17.5)	16 (20)		

Table 4 Rate of healing of wound in both groups with respect to time

Durations	Group A (*n*=40 patients) [*n* (%)]	Group B (*n*=40 patients) [*n* (%)]	χ^2	*P*-value
2 weeks	4 (10)	5 (32.5)	21	0.001 (HS)
4 weeks	9 (22.5)	19 (47.5)		
6 weeks	7 (17.5)	3 (7.5)		
8 weeks	6 (15)	2 (5)		
10 weeks	4 (10)	1 (2.5)		
12 weeks	3 (7.5)	1 (2.5)		
Total	33 (82.5)	39 (97.5)		

HS, highly significant.

Table 5 Rate of healing (cm^2/week) in the first 8 weeks in both groups

Rates of healing	Group A (*n*=40 patients)	Group B (*n*=40 patients)	τ	*P*-value
At 2 weeks (cm^2/week)				
Mean±SD	0.41±0.20	0.80±0.21	10.9	0.001 (HS)
Range	0.21–0.61	0.59–1.01		
At 4 weeks (cm^2/week)				
Mean±SD	0.49±0.11	0.89±0.13	9.3	0.001 (HS)
Range	0.38–0.60	0.76–1.02		
At 6 weeks (cm^2/week)				
Mean±SD	0.32±0.15	0.60±0.91	10.6	0.001 (HS)
Range	0.17–0.47	0.31–1.51		
At 8 weeks (cm^2/week)				
Mean±SD	0.29±0.14	0.50±0.12	8.2	0.001 (HS)
Range	0.15–0.43	0.38–0.62		

Data are presented as ranges and mean±SD, HS, highly significant, Statistically significant difference was determined using an unpaired *t*-test (significance was towards group B).

(82.5%) patients in group B (P=0.001) (Table 4 and Graph 4).

In terms of the rate of healing (cm^2/week), after the second week, there was a higher rate of healing per week (0.80±0.21 cm^2/week in group B versus 0.41±0.20 cm^2/week in group A). At the fourth week, the highest healing rate was found for both groups, but was better for the PRP group B (0.89±0.13 vs. 0.49±0.11 cm^2/week in group A). At the sixth and eighth weeks, a higher healing rate was found for the PRP group B: 0.60±0.91, 0.50±0.12 cm^2/week vs. 0.32±0.15, 0.29±0.14 cm^2/week in group A (P=0.001) (Table 5 and Graph 5).

At 10th and 12th weeks, a higher rate of healing per week was observed (0.40±0.12, 0.39±0.11 cm^2/week in group A vs. 0.20±0.13, 0.19±0.11 cm^2/week in group B). The lowest rate of healing was reported for the PRP group at the 10th and 12th weeks. However, for the conventional group, the lowest rate of healing was reported at the eighth week (0.29±0.14 cm^2/week). There was a statistically significant difference between both groups, but towards the group B in this period of dressing, with τ of 7.1 at the 10th week and 6.9 at the 12th week (P=0.001) (Table 6 and Graph 6).

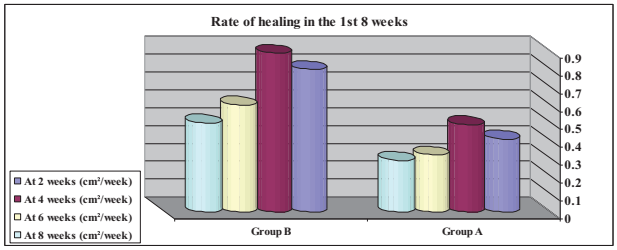
The total rate of healing (cm^2/week) was 6.8±0.54 in group A versus 7.3±0.90 in group B (Table 7 and Graph 7).

Upon review, complications occurred during the dressing period; infection, exudates, and pain were observed more in group A: 11 (27.5%) cases, 17 (42.5%) cases, and 25 (62.5%) cases, respectively, versus seven (17.5%) cases, five (12.5%) cases, and 13 (32.5%) cases, respectively, in group B. Eleven (27.5%) patients required a longer duration than the estimated time of healing (12 weeks) in group A, but this was observed in only one (2.5%) patient in group B (Table 8 and Graph 8).

Discussion

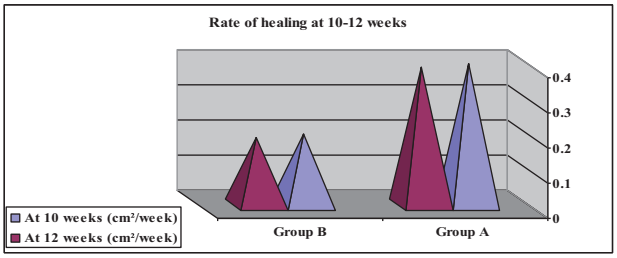
Diabetic foot wound is a common clinical problem. Because of population aging and an increase in risk factors and comorbidities such as tobacco use, obesity, hypertension, and atherosclerosis, there is a clear trend

Graph 5



Rate of healing (cm^2/week) in the first 8 weeks in both groups.

Graph 6



Rate of healing (cm^2/week) over a period of 10–12 weeks.

Table 6 Rate of healing (cm^2/week) over the period of 10–12 weeks

Rate of healing	Group A (n=40 patients)	Group B (n=40 patients)	τ	P-value
At 10 weeks (cm^2/week)				
Mean±SD	0.40±0.12	0.20±0.13	7.1	0.001 (HS)
Range	0.28–0.25	0.07–0.33		
At 12 weeks (cm^2/week)				
Mean±SD	0.39±0.11	0.19±0.11	6.9	0.001 (HS)
Range	0.29–0.50	0.08–0.30		

Data are presented as ranges and mean±SD, HS, highly significant, Statistically significant difference was determined using an unpaired t-test (significance was towards group A).

Table 7 Total rate of healing (cm^2/week) in both groups

Total rate of healing	Group A (n=40 patients)	Group B (n=40 patients)	τ	P-value
Mean±SD	6.8±0.54	7.3±0.90	4.3	0.01 (S)
Range	6.26–7.34	6.40–8.20		

HS, highly significant, Statistically significant difference was determined using an unpaired t-test (significance was towards group B).

toward increased risk of chronic wounds. The social and economic effects are inevitable [18].

PRP is defined as a proportion of the plasma fraction of autologous blood with a platelet concentration above the baseline. PRP is also known as platelet-enriched plasma, platelet-rich concentrate, and autologous platelet gel. PRP have been used to treat wounds since 1985 [19].

For more than 20 years, the PRP gel has been used to promote wound healing. Autologous PRP is composed of cytokines, growth factors, chemokine, and fibrin scaffold derived from a patient's blood. The mechanism of action of the PRP gel is believed to be the molecular and cellular induction of normal wound-healing response similar to that found with platelet activation [14].

The present study was carried out to evaluate the effectiveness of PRP in promoting healing of diabetic foot wounds, preventing infection, and reducing exudates, besides its preventive action by reducing amputation rates. There have been considerable advances in the use of PRP in therapeutic processes in recent years in tissue regeneration therapy.

On the basis of the last 10 years of research, the results of the systematic review with meta-analysis published by Carter *et al.* [20] suggest that PRP therapy can positively impact wound healing and associated factors such as pain and infection in both chronic and acute cutaneous wounds.

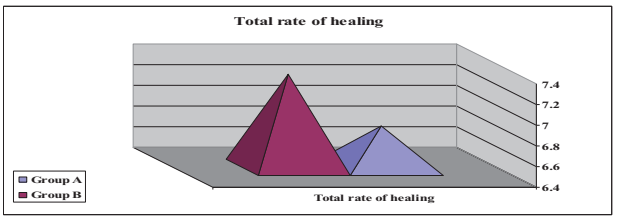
The current study was carried out on 80 patients with diabetic foot wounds; the patients' ages ranged from 31 to 66 years, with a mean of 49±5.06 years; the majority of patients were men [50 (62.5%)]. The study of Saad *et al.* [21] was carried out on 24 patients with chronic ulcers ranging in age from 40 to 60 years; they concluded that sex and age are insignificant in correlation with the rate of healing of their ulcers.

In the present study, the site of diabetic feet wounds was generally the sole of the foot [67 (83.75%)]. The duration of diabetes ranged between 7.5 and 12.5 years, with a mean of 10.3±2.3 years. It was observed that there was no correlation between the site and the rate of healing. This result was reported by Gui-Qiu *et al.* [22], who studied the effect of PRP on healing of lower extremity chronic ulcers in 21 patients; they concluded that 'there was no significant difference between type and site of ulcers in correlation with rate of healing'.

In this study, wounds varied in size and ranged between 4.9 and 8.6 cm, with a mean of 6.4±0.7 cm. It was observed that there was a significant and strong inverse correlation between the rate of healing and the size of the wounds, and there was a significant and strong proportional correlation between the size of the wounds and treatment duration (P=0.001). Also, there was a significant and strong proportional correlation between the size of the wounds and the number of injections. Many trials concluded that the larger the ulcer, the longer the duration required for treatment and the greater the number of injections [23,24].

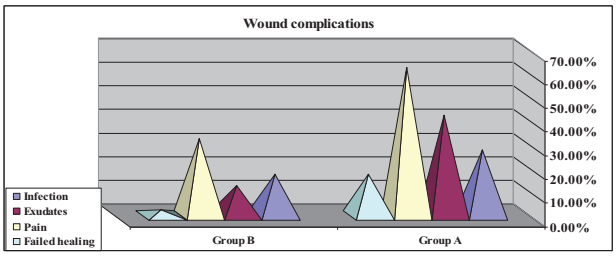
Upon review of risk factors and comorbidities, diabetes represents a worldwide public health issue, affecting ~5% of the population of the USA. Its high prevalence places this disease among one of the main pathologies

Graph 7



Total rate of healing (cm^2/week) in both groups.

Graph 8



Wound dressing complications.

Table 8 Wound dressing complications

Complications	Group A (n=40 patients) [n (%)]	Group B (n=40 patients) [n (%)]	χ^2	P-value
Infection	11 (27.5)	7 (17.5)	25	0.001 (HS)
Exudates	17 (42.5)	5 (12.5)		
Pain	25 (62.5)	13 (32.5)		
Failed healing	7 (17.5)	1 (2.5)		

HS, highly significant.

that can progress to chronic ulceration [25]. Other risk factors found in this study included DM-related comorbidities, foot angiopathy, and retinopathy, which affected wound healing and care, and smoking in 48 (60%) patients, which might have impaired wound healing directly or indirectly through vascular bad effect of smoking [26,27].

In the current study, PRP was found to be more effective than conventional dressing after the second week [13 (32.5%) vs. four (10%) patients, respectively). The same effect was reported at the fourth week [19 (47.5%) vs. nine (22.5%) cases, respectively]. This could be explained by the fact that during wound healing, platelets are activated by contact with collagen and released into the bloodstream after endothelial injury. Platelets secrete stored intercellular mediators and cytokines from the cytoplasmic pool and release their α-granule content after aggregation. More than 800 different proteins are secreted into the surrounding media, exerting a paracrine effect on different cells. This secretion is intense in the first hour and platelets continue to synthesize more cytokines and growth factors from their mRNA reserves for at least another 7 days [23].

However, after the first 4 weeks, the number of healed wounds started to decrease – that is, at the sixth week, three (7.5%) cases in group B versus seven (17.5%) cases in group A. The total number of patients in whom wounds healed was 39 (97.5%) in group A versus 33 (82.5%) in group B (P=0.001). In terms of the rate of healing, after the second week, there was a higher rate of healing per week (0.80±0.21 cm^2/week in group B vs. 0.41±0.20 cm^2/week in group A). At the fourth week, the highest healing rate was found for both groups, but was better for the PRP group B: 0.89± 0.13 vs. 0.49±0.11 cm^2/week in group A.

All systematic reviews have shown that PRP can stimulate healing of wounds. Gui-Qiu *et al.* [22] recruited 21 patients with refractory diabetic lower extremity ulcers who showed no response to conventional treatments; these patients were treated with homologous PRP. Their data indicated that homologous PRP was effective in enhancing and accelerating healing of diabetic lower extremity wounds.

Martinez-Zapata *et al.* [16] reported that the percentage of total healing in PRP-treated wounds increased compared with the controls. In a meta-analysis of chronic wound studies, Carter *et al.* [20] confirmed that the use of PRP treatment promotes complete healing compared with control care. Villela *et al.* [27] also reached the same conclusions.

All the above-mentioned studies concluded that on the basis of the meta-analysis and scientific evidence of consistent favorable outcomes, 'PRP is a treatment of choice for the topical care of wounds' [28]. This could be attributed to the fact that PRP functions as a tissue sealant and drug-delivery system, with the platelets initiating wound repair by releasing locally acting growth factors by α-granule degranulation. These growth factors aid healing by attracting undifferentiated cells to the newly formed matrix and triggering cell division and by interacting with macrophages to improve tissue healing and regeneration, promoting new capillary growth, and accelerating epithelialization in chronic wounds [29].

Seven (17.5%) patients required longer duration than the estimated time of healing (12 weeks) in group A, but this was found in only one (2.5%) patient in group B. Most of the wounds healed within the estimated time of healing (12 weeks); all these cases showed more than 50% healing after the first 4 weeks. These results were confirmed by Gelf *et al.* [30], who stated that 'It is generally accepted that a reasonable goal is healing by 12 weeks. Healing rates at 4 weeks predict overall healing rates, and a 10–15% area reduction weekly suggests an excellent prognosis'.

The use of antibiotics was more frequent in group A because of infection. Complications that developed during the dressing period were infection, exudates, and pain, which were observed more in group A: 11 (27.5%), 17 (42.5%), and 25 (62.5%), cases, respectively, versus 7 (17.5%), 5 (12.5%), and 13 (32.5%) cases, respectively, in group B. Paola *et al.* [23] reported that the fewer complications in group B could have been because of the fact that platelets exert anti-inflammatory and analgesic effects, which was confirmed by Asfaha *et al.* They reported PAR4-mediated analgesic effects *in vitro*. Also, El-Sharkawy *et al.* studied platelet secretions and their effect on macrophage cultures, concluding that 'platelet concentrates function as an anti-inflammatory agent, because of the high RANTES and LXA4 concentrations'. Also, the anti-inflammatory effect of platelets could be explained by the fact that 'PRP may suppress cytokine release and limit inflammation' [31]. On reviewing studies, the infection rate of the PRP group of the current study was higher than that stated by Anitua *et al.* [32], who reported only one patient with superinfection of his ulcer developed in PRP group.

Conclusion

There have been considerable advances in the use of PRP in therapeutic processes in recent years in tissue regeneration therapy. PRP is very promising for diabetic foot wounds as it enables healing, and reduces infection rates and exudates; in addition, it reduces amputation rates.

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Conflicts of interest

There are no conflicts of interest.

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