

## Results of PRP Injection, Local Jel, and Classic Dressing on Diabetic Foot Ulcer

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### Abstract

**Background:** Diabetic foot ulcers (DFU) are a prevalent clinical issue. Platelet-rich plasma (PRP) has a new promise in treating chronic ulcers for good tissue and rapid wound healing, so; wound care still debates different methods that aid wound regeneration rate. The debate of PRP still has an essential role in wound healing without complications.

**Patients and methods:** We have 45 cases complaining of chronic diabetic ulcer divided as follows (n = 15) local jel dressing, local PRP injections (n = 15) local PRP injection, alone (n = 15) classic dressing the study from August 2019 to March 2021. In Zagazig University's surgical department, we follow the degree of healing at 4, 6, and 12 months. Also, detect any other complication or comorbidity, or recurrence. We have 36 (80.0%) males and female is 9 (20.0%), ages ranged from 35 and 65, who had diabetic ulceration long duration of ten years.

**Results:** injections of PRP (12/15, 80%) of healing more rapidly than local jel (10/15, 66.7%) and classic dressings (7/15, 46.7%). The healing duration in PRP injection is shorter than other methods but with the same recurrent rate.

**Conclusions:** PRP injection is a technique that has a more rapid healing time than local jel that injection had to mean shorter duration of wound healing than local jel, and the last (prpjel) has a shorter duration of healing than classic dressing with the same redcurrant rate or near-equal recurrence rate.

### **Keywords**

PRP diabetic foot; Injection; Local jel; Ulcer; Classic dressing

## **Introduction**

Loss of a part of the skin leaving large resistant ulcer in diabetic patients that resistant healing more than two years, called chronic diabetes foot ulcer of the lower leg and foot that occurred mainly at the sites of pressure that prevent the patient from working and self-recovery [1].

The PRP's modes of action are, in brief, as follows: The platelets take part in the clot-forming coagulation process. Collagen from the nearby connective tissue travels immediately over the circulation after the blood vessel injury and, along with other substances, triggers the accumulation of platelets and stimulation [2]. Platelet-derived growth factors, which include (PDGF), growth factor-1, an insulin-like growth factor, growth factor-2, epidermal converting growth factor-, vascular endothelial growth factor, and fibroblast growth factors, are secreted by platelets during the creation of clots [3]. The establishment of granulomatous tissue, activation of mechanisms that result in collagen creation, a gathering of fibroblasts, macrophages, and other cells, and the emergence of new tissue are all factors that PRP has been shown to get better. Although it's a great benefit, other research must verify its action [4 PRP used in our study depends on loss or deficiency of growth factor and nutrition to the wound that ends by resistant ulcer. The comparison between local jel and local injection depends on the absorption of nutrients from wound edges being more rapid than local jel.

Many local gels or creams, or points are used for rapid wound healing either depending on bactericidal effect or aid the wound by nutrition or increasing blood supply. Still, the cost is higher and needs a prolonged duration [5]. Recombinant GF products, such as becalming (platelet-derived Growth factor recombination), give good results for ulcer healing. Autologous PRP is safer, more straightforward, and cost-effective [3]. Technique for treating foot ulcerations that may reach the muscles, tendons, and bones [6].

## **Patients and Methods**

The study was done between August 2019 and March 2021 in Zagagic University's surgical department. 45 patients with DFU came to the outpatient clinic and were treated with vascular surgery sharing.

### **Inclusion Criteria**

1. Patient with good coagulation profile for injection

2. Resistant diabetic ulcer
3. Non malignant criteria

### **Exclusion Criteria**

1. Patient with a bleeding tendency not suitable for injection
2. Malignant ulcer.

### **Sample Size**

The 45 cases of DFU (group A n = 15), local jel (group B n = 15), PRP injection (group Cn = 15 classic dressing).

### **Study End Points**

The ulcer's complete healing occurred through 6-13 months, and secondary endpoints were complications related to treatment and after concomitant good healing from 6-12 months of follow-up. After four weeks, if there is no significant healing, we stop and search for the underlying. Cause.

### **Patients Assessment**

All patients resistant to healed ulcers comprehensive examination and inquiry to discover underlying risk factors to improve the outcomes and remove the risk of loss of limbs. All demographic data and patients' character, history of another disease or hypertension, ok, and BMI all data are taken into investigation, like brachial ankle index, pulse palpation, neuropathy, ulcer character, and routine investigation (lives and kidney function, CBC, fasting and postprandial blood sugar, and HBAC1A). Venous duplex, a plain X-ray, or bone CT if needed.

### **Ulcers Character**

Edge, size, shape, floor, infection, and need debridement or antibiotics were all calculated with complete healing history and duration of the ulcer healing before to previous healing. Related antibiotic coverage malignant suspicious, and culture swap.

### **Technique**

Debridement is done for the group and before any procedures of other groups. You usually listen to words about extensive debridement needed for diabetic foot ulceration. Simply debridement is done by removing all infected tissue as possible by removing any pocket of collection, leaving a packed open wound with daily or twice daily dressing if needed. The wound character and depth of infection were observed to be suitable, with regular antiseptic diluted dressing.

### **Group B**

Method of injection is essential to attain the maximum benefit of prp nutrition and Growth factor. First, don't make an injection in an infected wound as the infection interferes would healing, and the spread of infection with injection is possible to occur. Second, good wound scrape before the injection; the injection is 3-4 cm away from the edge to avoid loss if the injection locations are near. The needle was

directed 45 degrees to the center of the base, then closed, dressing with wet gauze. Revision is done every three days, injection every two weeks till 6-8. Two shots are separate.

### Preparation

They started the aspiration of about 20 ccs of blood from the visible venous source with Edita or heparin. Centrifugation of the sample 5 minutes at 3200 RPM. The aspirate, the platelet-rich upper most  $\frac{2}{3}$  was plasma; the second cycle is 5000 RPM in 10 min divided into platelet-poor plasma and RBCs. They also aspirated the injection by 1ml syringe with needle injected as the previous description.



**Figure 1:** Showing the preparation of PRP after centrifugation for local injection

### Autologous PRP Jel Preparation

PRP gel is the same after blood centrifugation; the uppermost plasma riched is aspirated and mixed with added reagents. Then applied locally in a gelatinous liquid wound closed with gauze, and the patient was seen every three days.



**Figure 2:** diabetic foot pressure ulcer baseline



**Figure 3:** the ulcer size after two weeks of injection



**Figure 4:** showing right foot ulcer good and clean granulated wound



**Figure 5:** After complete wound healing after PRP jel application

## Follow up

Any pressure on the ulcer area must be avoided, and leg off leading or casting. Following the surgery, appropriate off-loading footwear or perhaps. Patients are seen every three days. Assess the healing every 6-8 weeks by measuring the wound's dimensions (length and breadth), observation of infection, granulation tissue, pus, culture swap, and edge biopsy if needed.

## Statistical analysis

The Statistical Package for Social Sciences (SPSS) for data analysis statistics (version 17). The t-test was for quantitative variables comparison by mean and SD. Fifty percent mean SD Qualitative by Fisher's exact tests groups comparison—P-value of less than 0.05 is significant. Follow up 6-12 months.

## Baseline Patient Criteria

Cases male (80.0%) and females (20.0%) medium age 35 to 65 years and ranged BMI 15 to 35 kg/m<sup>2</sup>. Showing no significant baseline differences in (Table 1).

| Variable                             | PRP application<br>n = 15 | PRP injection n<br>= 15 | Classic dressing n =<br>15 | P value |
|--------------------------------------|---------------------------|-------------------------|----------------------------|---------|
| <b>Patients' characteristics</b>     |                           |                         |                            |         |
| Age (years) mean ± SD                | 47.2 ± 9.35               | 44.1.±16                | 40.90 ± 16.3               | 0.48    |
| Average                              | 36-65                     | 25-62                   | 36-65                      |         |
| Males/female                         | 13(86.7%)                 | 11 (73.3%)              | 12 (80.0%)                 | 0.65    |
|                                      | -                         | 4                       |                            |         |
|                                      | 2                         |                         | 3                          |         |
| BMI (kg/m2) mean ± SD                | 15.2 ± 6.4                | 26.6 ± 4.1              | 34.9 ± 5.6                 | 0.5     |
| Range                                | 16-35                     | 20-35                   | 18-36                      |         |
| Smoking                              | 7 (47.7%)                 | 5 (43.3%)               | 6 (44.0%)                  | 0.879   |
| Diabetes mellitus                    | 100%                      | 100%                    | 100%                       | 100%    |
| <b>Ulcers' characteristics</b>       |                           |                         |                            |         |
| Medial ulcers                        | 12 (73.3%)                | 12 (73.3%)              | 12 (73.3%)                 | 0.88    |
| Single ulcer                         | 13 (80.0%)                | 14 (86.7%)              | 13 (93.3%)                 | 0.56    |
| Mean recurrent ulcer/ years)         | 6.2 ± 3.2                 | 5.4 ± 2.5               | 6.4 ± 2.8.                 | 0.45    |
| Range                                | 01-Oct                    | 1.5-10                  | 02-Oct                     |         |
| Mean previous ulcer duration (years) | 11.3 ± 3.4                | 9.8 ± 4.3               | 10.6 ± 4.9                 | 0.64    |
| Range                                | 02-Oct                    | 01-Sep                  | 02-Nov                     |         |
| Recurrent ulcers                     | 7                         | 6                       | 6                          | 0.86    |
|                                      | -40%                      | -46.70%                 | -33.30%                    |         |

**Table 1:** Ulcer characters

#### Baseline ulcer criteria

Ulcers mainly near the recurrent rate (75.5%) (Table 1).

#### Procedures that are related

No, a significant difference was detected after six months (See Table 2)

| Variable                     |                   | PRP application<br>(n = 15) | PRP injection<br>(n = 15) | Classic dressing (n<br>= 15) | P value  |
|------------------------------|-------------------|-----------------------------|---------------------------|------------------------------|----------|
| Ulcer healing at four months | Healed            | 5(32.3%)                    | 7 (47.7%)                 | 2(14.3%)                     | .003*    |
|                              | Incomplete        | 11 (67.7%)                  | 7 (52.3%)                 | 15(89.7%)                    | .003*    |
| Ulcer healing at one year    | Healed            | 11(67.7%)                   | 15(85%)                   | 6 (45.7%)                    | .007*    |
|                              | Incomplete        | 5 (29.7%)                   | 1 (12.7%)                 | 7 (45%)                      | .04*     |
|                              | Recurrent         | 1(7.7%)                     | 0 (0%)                    | 2 (15.3%)                    | 0.326    |
| Healing time (months)        | Median (range cm) | 6 (5-9)                     | 5 (3-7)                   | 6 (4-9)                      | P = .18* |

|  |  |  |  |  |               |
|--|--|--|--|--|---------------|
|  |  |  |  |  | P1 =<br>.009* |
|  |  |  |  |  | P2 =<br>.395  |
|  |  |  |  |  | P3 =<br>.026* |

**Table 2:** The healing time of the ulcer

Significance. Data are presented as numbers and percentages by the Kruskal-Wallis test

### Ulcer complete healing rate

By follow-up (Table 2). P =.007 showed that PRP injection has considerably less healing duration than gel application followed by classic dressing (was linked to a faster but non-significant healing time than traditional dressing treatment.

| Variable                   |                       | Baseline   | Four months | Six months | 12 months |
|----------------------------|-----------------------|------------|-------------|------------|-----------|
| <b>(A) PRP application</b> | Mean ± SD             | 16.5 ± 8.2 | 5.8 ± 2.1   | 1.3 ± 0.6  | 1.2 ± 0.5 |
|                            | Mean reduction %      |            | 65%         | 92%        | 92.70%    |
| <b>(B) PRP injection</b>   | Mean ± SD             | 15.8 ± 8.4 | 2.4 ± 1.3   | 1.6 ± 0.5  | 1.3 ± 0.5 |
|                            | Mean reduction %      |            | 85%         | 91%        | 75%       |
| <b>Classic dressing</b>    | Mean ± SD             | 18.8 ± 5.4 | 7.5 ± 3.3   | 5.4 ± 2.7  | 3.7 ± 1.5 |
|                            | Mean size reduction % |            | 52%         | 69%        | 0.45%     |
| <b>P value</b>             |                       | 0.947      | .016*       | .001*      | <.002*    |
| <b>P1 (A vs. B)</b>        |                       | 853        | .017*       | 0.079      | 0.31      |
| <b>P2 (A vs. C)</b>        |                       | 867        | 0.362       | .003*      | <.001*    |
| <b>P3 (B vs C)</b>         |                       | 0.756      | .014*       | .001*      | <.001*    |

**Table 3:** Ulcer area decreasing

### Significant reduction by p value

P = .016, A..001 B, and..002 C, respectively. Decreasing size after PRP injection was more visible than jellocal, but at 6 or 12, decreasing but less reduction than first four months also, after one year, nonsignificant difference by p-value (Table 3).

### Discussion

Diabetic patients are usually complicated by foot ulceration that, with neglected patients, becomes chronic and deep in bones. With increasing comorbidity risk due to associated chronic diseases like hypertension and heart problems. PRP terms, Since1985, have been used to heal wounds [8]. In our study, we have 45 patients with diabetic ulceration, ranging in age from 35 to 65 years old, [7]. Had 24 diabetic foot ulcers aged 40 to 60, without sex and age difference of healing ulcers [9].

Cochrane review and recent analysis concluded that the use of PRP is not for diabetic foot wounds only but in other wounds such as venous, traumatic, and other ulcers [10]. Furthermore, we found no significant differences in recurrence between the groups. The tables appear the rate of reduction in the first six months and year that concludes the stop difference in reduction after the first year. The findings of Carter et al. found there is a significant difference between PRP injection and local jel and classic dressing but good results in fibrin injection [11].

In contrast to our procedure and line, Attitu 199 used PRP every week, but We used PRP every 2-for three weeks for six weeks. The cause of its idea and line of treatment that the weekly injection to attain enough nutrition and growth factor to the wound to improve health and healing of the area, but we found no significant differences between the results [12]. The injection may be ineffective if injection has done near the edge, which leads to spilling and loss of its effect, so we injected the wound 3-4 cm away from the edge. PRP provides the wound with molecular and cellular stimulation by cytokines, growth factors, chemokines, and fibrin [13]. Previous research, after comparing PRP application to traditional dressing therapy (injection and local), did not compare the injection and local jel in the chronic leg. [14]. After the second week and fourth weeks, PRP was good effective than traditional dressing because the platelets were triggered by collagen after endothelial damage during wound healing, by alfa protein formation by platelet. Much distinct nutrition from proteins is provided from PRP, and the platelets continue to secrete more cytokines and growth factors in the first week of injection healing, but mg is 50% in the first four weeks of the wounds healed after (8 weeks); [16] [15] supported good wound healing accepted after 3 weeks 40% healing rates at four weeks, and 97% healing, which indicates a good prognosis.

There is disagreement with the no benefit of PRP in healing in diabetic, venous, or traumatic that against our findings. Some research agrees with our results, but others disagree. Five our results in healed reduction after six months vs. that in the classic dressing group, with an area decrease of roughly 85% against 25 % respectively, P.001. Aguirre et al. had 23 patients with PRP injection treatment (n = 12) or covered silicone (n = 11). The PRP ulcer healed in 9.6 weeks vs. classic groups in 23.7 weeks, P.001. But, Somani and Rai, who had 15 patients, found healing of the ulcer is 55% in PR fibrin (n = 9) but zero in the group treated with saline dressing (n = 6), area decrease of 67.7% vs. 11.1 %, respectively, P =.001. In, Anitua et al. 20 results, the PRP vs. classic therapy groups, 73 % versus 21 %, P.05, respectively. In a study by Stacey et al., within 12 weeks [14] using platelet lysate treatment (n = 42) or placebo mode (n = 44)., 75 % of all ulcer healing was done in both groups [16].

Our conclusion agrees with this. Similarly, Senet et al. found that the more prolonged unhealed ulcer needed PRP injection or jel diluted PRP with normal saline (n = 8) or saline alone (n = 7). The ulcer is reduced in 2 months by 26.2 % vs. 15.2 %, respectively, P =.94 [17]. In VLU, Robson et al. [18] found PRP effective if the area is less than 6 cm and less than one year.

Table 4: The recovery time calculated from one month to 4.5 months. The study by Senet et al. [15] showed a high percentage of healing that occurred after 12 weeks, with 33.3 % and 46.7 % ves 12.5 % after PRP injection; it may be due to using fresh plasma rather than frozen one [18].



| Study                    | Intervention             | Control           | Ulcer area | Ulcer duration | Follow up   |
|--------------------------|--------------------------|-------------------|------------|----------------|-------------|
| <b>The present study</b> | PRP injection            | PRP application   | 16.5       | 72 months      | One year    |
|                          | 12/15(80%)               | 10/15(66.7%)      |            |                |             |
| <b>Stacey et al. 10</b>  | Frozen PRP 33/42 (78.6%) | Placebo           | 2          | Three months   | 36 weeks    |
|                          |                          | 34/44 (77.3%)     |            |                |             |
| <b>Aguirre et al. 11</b> | PREP                     | Silicone dressing | 9.6        | 4.5 months     | Eight weeks |
|                          | 5/12 (41.7%)             | 0/11 (0%)         |            |                |             |
| <b>Senet et al. 15</b>   | Frozen PRP 1/8 (12.5%)   | Saline            | 12.5       | 60 months      | 12 weeks    |
|                          |                          | 1/7 (14.3%)       |            |                |             |
| <b>Somani et al. 17</b>  | PRP                      | Saline            | 8.14       | ≥ 6 months     | Four weeks  |
|                          | 5/9(55.5%)               | 0/6(0%)           |            |                |             |
| <b>Anuita et al. 20</b>  | PREP                     | Saline            | 5.5        | 17 months      | Eight weeks |
|                          | 1/7(14.3%)               | 0/7(0%)           |            |                |             |

**Table 4:** Other studies show ulcer healing altogether and duration.

The resistance of ulcer healing occurred because of underlying causes that may be presented in group C and treated. Fifteen of the studies, none of them used the rate of recurrences as the primary endpoint. However, DFU has a different system of treatment that should evaluate the recurrence of infection and ulceration rates and wound healing. So, we prolonged allow-up to one year, don't forget there is local paint suitable to improve wound healing, but it is adjuvant, not the main line, in the dressing process.

## Conclusion

Local PRP injection is better dressing therapy in wound healing than local jel classic dressing, and the last is a shorter healing time than classic dressing. Still, all groups had the recurrence and safety. PRP injection is a potent treatment in resistant diabetic ulcers with limb saving from amputation.

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