## RESEARCH PAPER

# To determine the effect of autologous platelet rich plasma vs topical insulin injections on wound healing in patient with diabetic foot ulcer

**Dr. Arun Balaji[1], Dr. Tulika Singh[2*], Prof. Dr. J. Sridhar[3], Dr. Sonvivith R[4], Dr. N. Renuka Naidu[5]**

[1]Associate Professor, ORCID: 0000-0002-4952-8522, drarunbalaji87@gmail.com
[2*]Third Year Post Graduate, ORCID: 0009-0003-9198-9239
[3]MS, FIAGES, Head Of The Department, ORCID (0000-0001-6113-0421)
[4]Third Year Post Graduate, ORCID (0009-0008-8169-7140)
[5]Second Year Post Graduate, ORCID (0009-0003-4097-3405)

[1,2,3,4,5]Department of General Surgery, Vinayaka Missions Kirupananda Variyar Medical College and Hospital, Salem, Vinayaka Missions Research Foundation

**Corresponding author:**

**Dr. Tulika Singh**

Third Year Post Graduate, Department of General Surgery, Vinayaka Missions Kirupananda Variyar Medical College and Hospital, Salem, Vinayaka Missions Research Foundation, ORCID: 0009-0003-9198-9239

**ABSTRACT**

**Background:** Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired pancreatic function, reduced insulin secretion, or insulin resistance. Diabetic foot ulcers (DFUs) occur in approximately 4–10% of diabetic patients, with the incidence increasing markedly in older adults. Chronic, non-healing ulcers necessitate cost-effective and efficient therapeutic strategies. Insulin supports wound repair through molecular pathways involving AKT and ERK activation, while platelet-rich plasma (PRP), enriched with platelets and growth factors, has demonstrated significant potential in enhancing tissue regeneration.

**Methods:** This randomized clinical trial enrolled 100 patients with post-debridement DFUs measuring <10 × 10 cm². Participants were allocated into two groups: Group A received intralesional PRP, and Group B received topical insulin therapy. Wound healing was evaluated on days 3, 7, 14, and 21, focusing on ulcer size reduction, granulation tissue development, and the requirement for additional interventions. Statistical analysis was performed using standard software, with $p < 0.05$ considered statistically significant.

**Results:** The mean age of participants was comparable between groups (PRP: 57.18 years; topical insulin: 56.28 years; $p = 0.36$). Patients treated with PRP demonstrated significantly enhanced granulation tissue formation (59.88 ± 1.30 vs. 44.48 ± 1.71 at day 21) and lower rates of re-intervention (36% vs. 62%; $p = 0.009$) compared with those receiving topical insulin.

**Conclusion:** PRP therapy showed superior clinical efficacy over topical insulin in promoting wound healing among patients with DFUs. Improved granulation response, faster ulcer reduction, shorter hospitalization, and reduced re-intervention rates underscore PRP as a more effective therapeutic option for managing chronic diabetic foot ulcers.

**Keywords:** Diabetic Foot Ulcer, Wound Healing, Platelet-Rich Plasma, Topical Insulin, Granulation Tissue, Re-intervention Rate

**How to cite this article:** Balaji A, Singh T, Sridhar J, Sonvivith R, Naidu NR. To Determine the Effect of Autologous Platelet Rich Plasma vs Topical Insulin Injections on Wound Healing in Patient with Diabetic Foot Ulcer. Int J Drug Deliv Technol. 2026;16(14s): 82-86. DOI: 10.25258/ijddt.16.14s.12

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Diabetes mellitus is a long-standing metabolic disorder marked by elevated blood glucose levels, arising from impaired pancreatic function, reduced insulin secretion, or peripheral insulin resistance.[1] Among its many complications, diabetic foot ulcers (DFUs) are particularly common, often developing following minor trauma or infection, especially in the distal extremities where vascular insufficiency is more pronounced.[2]

Between 4% and 10% of individuals with diabetes experience DFUs, with the risk increasing substantially with advancing age.[3] [4] Over a lifetime, nearly 15% of diabetic patients are expected to develop a foot ulcer, and approximately 5% present with active ulceration at any given time.[3] [4]

The management of DFUs is challenging for clinicians and financially burdensome for patients.[5] Standard care typically includes effective offloading with specialized footwear, regular dressings such as povidone-iodine or hydrocolloid preparations, and, when necessary, surgical interventions including skin grafts. A variety of topical agents have also been used to promote ulcer healing.[1] [2] [6] Despite these available options, newer modalities—such as growth factors and pluripotent cell-based therapies—remain costly, and their overall safety and long-term efficacy require further evaluation.[1] Consequently, there is a need for simpler, affordable, and clinically effective strategies for managing chronic, non-healing ulcers.

Insulin plays a substantial role in tissue repair due to its influence on metabolic regulation, protein synthesis, cellular proliferation, and tissue growth.[6] [7] It modulates key biological functions in fibroblasts, endothelial cells, and keratinocytes—enhancing their migration, proliferation, and secretory activity. At the molecular level, insulin accelerates wound healing through pathways involving AKT and ERK, both of which are central to cellular growth and differentiation. Inhibition of these signaling pathways diminishes insulin's therapeutic effects, underscoring their importance.

Two major downstream targets of AKT—endothelial nitric oxide synthase (eNOS) and glycogen synthase kinase 3β (GSK3β)—play additional roles in tissue repair. Phosphorylation of GSK3β reduces its activity, while phosphorylation of eNOS promotes nitric oxide production, which supports angiogenesis, tissue morphogenesis, enhanced perfusion, and improved cell survival even under ischemic conditions.[8]

Platelet-rich plasma (PRP) is an autologous concentrate obtained through centrifugation, separating whole blood into platelet-poor plasma, a platelet-rich layer, and erythrocytes. PRP contains platelet concentrations two to six times higher than baseline and is abundant in bioactive proteins essential for wound repair. Platelet alpha-granules harbor growth factors such as PDGF, VEGF, TGF-β, EGF, and adhesive proteins including fibronectin, fibrinogen, and vitronectin. Delta granules contain serotonin, histamine, calcium, dopamine, and adenosine, which act synergistically with growth factors to regulate healing. These biologically active components have increasingly been recognized for their potential to reduce morbidity in chronic, non-healing ulcers.[9]

The growth factors released from platelets drive key reparative processes including angiogenesis, chemotaxis, cellular proliferation, and differentiation. Multiple studies have reported favorable outcomes with PRP in managing chronic wounds.

The present study aims to compare the therapeutic efficacy of autologous platelet-rich plasma versus topical insulin application in promoting wound healing among patients with diabetic foot ulcers.

### Materials and Methods

This randomized clinical study included 100 patients presenting with post-debridement diabetic foot ulcers measuring less than 10 × 10 cm². Participants were allocated into two groups (A and B) using a simple lot randomization technique. Group A received intralesional autologous platelet-rich plasma (PRP), while Group B was treated with topical insulin. Wound healing progression was evaluated on days 3, 7, 10, 14, 18, and 21, assessing ulcer size reduction, granulation tissue formation, and the requirement for additional procedures such as repeat debridement. Mean healing time was calculated for both groups, and chi-square analysis was used to compare outcomes between the two treatment modalities.

**Preparation and Application of Platelet-Rich Plasma:** PRP was prepared by centrifuging whole blood to separate it into platelet-poor plasma, platelet-rich plasma, and an erythrocyte layer. The upper and middle fractions containing platelet-rich plasma were collected and used for treatment. Prior to PRP administration, the ulcer was thoroughly cleansed with povidone-iodine, and devitalized or infected tissue was removed. Approximately 5–6 mL of PRP (depending on wound size) was injected into the base and margins of the ulcer, followed by sterile dressing. Applications were repeated on days 3, 7, 10, 14, 18, and 21. Treatment effectiveness was evaluated based on shrinkage in ulcer dimensions, granulation tissue development, discharge, need for further intervention, and overall duration of hospitalization.

**Topical Insulin Application:** Post-debridement ulcers assigned to Group B were treated with human insulin, administered at a dose of 1 unit per 1 cm² of ulcer area. Insulin was injected into both the ulcer bed and its edges, followed by dressing. The process was performed on days 3, 7, 10, 14, 18, and 21, with regular monitoring for signs of infection or healing progress. Outcome measures included reduction in ulcer size, granulation tissue formation, presence of discharge, the need for re-intervention, and mean hospital stay.

**Inclusion criteria:** Patients older than 35 years with non-infected diabetic foot ulcers classified as Grade 2 or Grade 3, measuring between 1 cm and 10 cm in diameter, were included. Ulcers located on the dorsum of the foot, plantar surface, toes, or medial/lateral leg were eligible. Participants were required to have controlled diabetes managed with oral hypoglycemics or insulin, hemoglobin levels >9 g/dL, and willingness to undergo treatment.

Exclusion criteria: Patients were excluded if they had infected ulcers extending to tendons or bone, uncontrolled diabetes, anemia with hemoglobin <8 g/dL, or declined consent for participation.

### Statistical Analysis

Data entry was performed using Microsoft Excel 2013, and

analysis was conducted with statistical software. Qualitative variables were summarized using frequencies and percentages, while quantitative variables were presented as mean ± standard deviation. Intergroup comparisons of continuous variables were conducted using parametric tests, including unpaired and independent sample t-tests. Categorical variables were analyzed using the chi-square test. A p-value <0.05 was considered statistically significant.

**Results**

**Table- 1: Distribution based on Age and Gender**

| | PRP | | Topical Insulin | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| 31 – 40 | 2 | 4% | 3 | 6% | 5 | 5% |
| 41 – 50 | 10 | 20 % | 12 | 24 % | 22 | 22 % |
| 51 – 60 | 21 | 42 % | 15 | 30 % | 36 | 36 % |
| 61 – 70 | 13 | 26 % | 19 | 38 % | 32 | 32 % |
| 71 – 80 | 4 | 8% | 1 | 2% | 5 | 5% |
| Total | 50 | 100% | 50 | 100% | 100 | 100 % |
| Mean Age | 57.18 ± 9.83 | | 56.28 ± 9.74 | | 56.73 ± 9.75 | |
| Chi square test= 4.30, p value is 0.36, statistically no significance | | | | | | |

The age groups are divided into ranges of 10 years, from 31 to 80 years. Specifically, 42% in PRP grp and 30% in Topical Insulin grp aged 51-60 years, while 26% in PRP grp and 38% in Topical Insulin group aged 61-70 years. The mean ages are 57.18 years for PRP and 56.28 years for Topical Insulin, with an overall mean age of 56.73 years. Chi square indicated no statistical significant difference (p=0.36). The PRP group, 74% are male and 26% are female, while in the Topical Insulin group, 60% are male and 40% are female. The overall distribution shows 67% male and 33% female participants. The chi-square test result (p=0.13) suggests that the gender distribution between the two groups is not statistically significant.

**Table 2: Distribution of the study population based on side of ulcer**

| | PRP | | Topical Insulin | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Right | 29 | 58 % | 26 | 52 % | 55 | 55% |
| Left | 21 | 42 % | 24 | 48 % | 45 | 45% |
| Total | 50 | 100 % | 50 | 100 % | 100 | 100 % |
| Chi-square test= 0.36, p value 0.54, Not statistically significant | | | | | | |

The distribution of ulcer sites among participants, categorized by right or left side. In the PRP group, 58% of ulcers are on the right side and 42% on the left. For the Topical Insulin group, 52% of ulcers are on the right and 48% on the left. The overall distribution shows a nearly equal split, with 55% of ulcers on the right and 45% on the left. The chi-square test (p=0.54) indicates not significant statistically in distribution of ulcer side.

**Table 3 Distribution of the study population based on size of ulcer at admission**

| | PRP | | Topical Insulin | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| 1 – 3 $cm^2$ | 0 | 0% | 0 | 0% | 0 | 0% |
| 4 – 6 $cm^2$ | 3 | 6% | 2 | 4% | 5 | 5% |
| 7 – 9 $cm^2$ | 4 | 8% | 1 | 2% | 5 | 5% |
| >9 $cm^2$ | 43 | 86 % | 47 | 94 % | 90 | 90 % |
| Total | 50 | 100 % | 50 | 100 % | 100 | 100 % |
| Chi-square test= 2.17, p=0.33, Not statistically significant | | | | | | |

The majority of ulcers in both groups are larger than 9 $cm^2$, with 86% in PRP group & 94% in Topical Insulin group. The chi-square test (p=0.33) shows no significant statistical difference in ulcer size distribution among groups.

**Table 4: Distribution of study population based on Granulation tissue growth**

| | 3rd day | 7th day | 14th day | 21st day |
|---|---|---|---|---|
| PRP group | 7.32 ± 0.24 | 24.78 ± 0.14 | 44.87 ± 1.58 | 59.88 ± 1.30 |
| Topical Insulin group | 7.18 ± 0.14 | 18.54 ± 0.46 | 23.14 ± 1.40 | 44.48 ± 1.71 |

The growth of granulation tissue at 0, 7, 14, and 21 days. The PRP group shows progressive growth from 7.32 at day 0 to 59.88 ± 1.30 at day 21, while the Topical Insulin group shows an increase from 7.18 at day 0 to 44.48 ± 1.71 at day 21, indicating significant tissue growth in PRP group than Insulin group.

**Table 5 Need for re-intervention (Debridement) in both groups**

| | PRP | | Topical Insulin | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Yes | 18 | 36 % | 31 | 62 % | 49 | 49% |
| No | 32 | 64 % | 19 | 38 % | 41 | 41% |
| Total | 50 | 100% | 50 | 100% | 100 | 100% |
| Chi-square test= 6.69, p=0.009, statistically significant | | | | | | |

This table shows the necessity for re-intervention (debridement) among participants. In the PRP group, 36% required re-intervention compared to 62% in the Topical Insulin group. The chi-square test (p=0.009) shows a statistically significant higher need for re-intervention in the Topical Insulin group.

**Table 6: Post procedure pain at injection site in both groups according to Visual analogue scale**

| | PRP | | Topical Insulin | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| No pain | 26 | 52 % | 23 | 46 % | 49 | 49 % |
| Mild | 19 | 38 % | 20 | 40 % | 39 | 39 % |
| Moderate | 5 | 10 % | 7 | 14 % | 12 | 12 % |
| Severe | 0 | 0% | 0 | 0% | 0 | 0% |
| Excruciating | 0 | 0% | 0 | 0% | 0 | 0% |
| Total | 50 | 100% | 50 | 100% | 100 | 100 % |
| Chi-square test= 0.54, p=0.76, Not statistically significant | | | | | | |

The level of pain post-procedure using the Visual Analog Scale. In the PRP group, 52% reported no pain, 38% mild, and 10% moderate pain. Similarly, in the Topical Insulin group, 46% reported no pain, 40% mild, and 14% moderate pain. No severe or very severe pain was reported in either group. There is no discernible difference in pain levels across the groups, according to the chi-square test (p=0.76).

**Discussion**

According to the age distribution analysis of the current study, participants ranged in age from 31 to 80 years, with most of them falling between 51 and 60 years of age (i.e., 42% of the PRP group and 30% of the Topical Insulin group). The PRP group's and the Topical Insulin group's average ages were 57.18 and 56.28 years, respectively. This suggests that there was no statistically significant difference between the two groups (p=0.36). This age distribution is typical for studies on chronic wounds, where older persons are more vulnerable because of extended exposure to risk factors like diabetes and immobility. Comparatively in few studies[10,11,12] The participants' age distribution showed a similar tendency, with average age for insulin group being 53.94 ± 9.26 & saline group being 55.92 ± 7.98. The fact that the mean age of the insulin group is somewhat low from that of saline group indicates that a broad spectrum of diabetic patients are frequently candidates for topical therapies and platelets. The present study indicated that 74% of the PRP group were male, when compared to 60% in the Topical Insulin group, with an overall male representation of 67%. This distribution was not statistically significant (p=0.13). In few studies[12,13], With a 5:1 male-to-female ratios in insulin population and a 3:1 ratio in saline population, male were dominating. This gender distribution shows that men are more likely to get diabetic foot ulcers than women. Mostly due to occupational hazards and higher rates of trauma in men.

In the research conducted by few supported general effectiveness of PRP for decreasing wound size and enhancing healing outcomes, even though specific ulcer locations were not mentioned. The study's equal distribution of ulcer sites lends credence to the PRP and topical insulin therapies applicability in a variety of ulcer sites.[14,15]

PRP and topical insulin are similarly efficient regardless of the location of the ulcer, which facilitates more adaptable treatment regimens and gives patients and healthcare Professionals confidence in the treatments' adaptability. The present study makes a unique contribution to the understanding of wound management in clinical practice by providing detailed information about ulcer locations. According to the current study, PRP therapy significantly shortens healing times, which is strong evidence in favour of its application in clinical settings. The results are consistent

with previous research, supporting PRP's function in promoting wound healing and providing a beneficial therapeutic alternative for patients whose ulcers have persisted for a long time. The present study found no significance in difference of initial size of ulcers between the groups, with majority being larger than 9 $cm^2$.

Overall, results of our study on development in growth of granulation tissue are consistent with previous research and emphasize the value of cutting-edge treatments like PRP in accelerating wound healing. The thorough research bolsters the wider implementation of the PRP in the clinical practice and offers a thorough comprehension of the treatment outcomes. Potential advantages of the platelet rich plasma (PRP) in promoting granulation development and facilitating overall wound healing are supported by the comparison with relevant research.[14,15]

Comprehending how a therapy affects the length of hospital stay is essential for medical professionals and administration. PRP therapy has been shown to significantly reduce hospital stays, which implies that it may be a useful choice for managing chronic ulcers, especially in a hospital context. Better patient outcomes may result from this and the optimization of hospital resources. In the present study, a higher need for re-intervention was noted in Topical Insulin group (62%) in comparison with PRP group (36%, p=0.009). The decreased need for re-intervention in the PRP group shows its efficacy in stimulating more complete and sustained healing. Re-interventions, such as debridement or amputation can be burdensome for patients and healthcare providers. Reducing the need for these improves patient comfort and reduces healthcare expenses. The result of our study is consistent with that of a larger body of research on PRP's advantages in lowering the demand for further procedures.[15]

## Conclusion

The comprehensive analysis of the present study compared with the literature provides robust evidence for the efficacy of PRP in wound management. The findings consistently show that PRP outperforms Topical Insulin in key areas such as reducing ulcer size, promoting granulation tissue growth, need for re-intervention. These benefits translate into significant clinical advantages, including faster healing times, reduced need for re-interventions, and improved patient comfort and quality of life.

The reduced need for re-interventions with PRP treatment further demonstrate its effectiveness in creating a favourable healing environment. These findings suggest that PRP can be a valuable tool in the clinician's arsenal for managing chronic wounds, particularly in patients who have not responded well to conventional treatments. The ability to reduce wound exudate and control infection highlights PRP's role in comprehensive wound care strategies.

In summary, the present study's findings highlight PRP's potential to enhance healing outcomes, reduce treatment time, and improve patient quality of life. The significant benefits observed with PRP treatment underscore the importance of incorporating topical insulin in clinical practice to achieve optimal patient outcomes and efficient healthcare delivery.

## REFERENCES


1. Cavanagh PR, Buse JB, Frykberg RG, Gibbons GW, Lipsky BA, Pogach P, et al. Consensus development conference on diabetic foot wound care. Diabetes Care. 1999;22(8):1354–60.
2. Terashi H, Kitano I, Tsuji Y. Total management of diabetic foot ulcerations: Kobe classification as a new classification of diabetic foot wounds. Keio J Med. 2011;60(1):17–21.
3. Leone S, Pascale R, Vitale M, Esposito S. Epidemiology of diabetic foot. Infez Med. 2012;20:8–13.
4. Shahi SK, Kumar A, Kumar S, Singh SK, Gupta SK, Singh TB. Prevalence of diabetic foot ulcer and associated risk factors in diabetic patients from North India. J Diabetic Foot Complications. 2012;3:83–91.
5. Richard JL, Schuldiner S. Epidemiology of diabetic foot problems. Rev Med Interne. 2008;29:222–30.
6. Nather A, Bee CS, Huak CY, Chew JL, Lin CB, Neo S. Epidemiology of diabetic foot problems and predictive factors for limb loss. J Diabetes Complications. 2008;22:77–82.
7. Bakri FG, Allan AH, Khader YS, Younes NA, Ajlouni KM. Prevalence of diabetic foot ulcer and its associated risk factors among diabetic patients in Jordan. J Med. 2012;46:118–25.
8. Flahr D. The effect of no weight-bearing exercise and protocol adherence on diabetic foot ulcer healing: a pilot study. J Wound Manag. 2010;56(10):40–50.
9. Kaki WS. Diabetes. In: Setati S, Alwi I, Sudoyo AW, Simadibrata M, editors. Book of Science of Internal Medicine. Jakarta: Interna Publishing; 2014. p. 2367.
10. Tellechea A, Leal E, Veves A, Carvalho E. Inflammatory and angiogenic abnormalities in diabetic wound healing: role of neuropeptides and therapeutic perspectives. Open Circ Vasc J. 2010;3:43–55.
11. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376:2367–75.
12. Hobizal KB, Wukich DK. Diabetic foot infections: current concept review. Diabetic Foot Ankle. 2012;3:18409. Available from: http://dx.doi.org/10.3402/dfa.v3i0.18409
13. Hoffman AF. Evaluation of arterial blood flow in the lower extremity. Clin Podiatr Med Surg. 1992;9:19–56.
14. Boulton AJ. The diabetic foot—an update. Foot Ankle Surg. 2008;14:120–4. doi:10.1016/j.fas.2008.05.004.
15. Papanas N, Papatheodorou K, Papazoglou D, Kotsiou S, Maltezos E. Association between foot temperature and sudomotor dysfunction in type 2 diabetes. J Diabetes Sci Technol. 2010;4:803–7.