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A COMPARATIVE STUDY BETWEEN THE EFFECT OF TOPICAL INSULIN VS CONVENTIONAL BETADINE DRESSING ON WOUND HEALING OF DIABETIC FOOT ULCERS

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) are a major complication of diabetes mellitus, often leading to infection, poor quality of life, and lower limb amputation. Conventional wound care typically includes betadine dressing, which, despite its antimicrobial action, may hinder healing due to cytotoxicity. Topical insulin, with its proliferative, angiogenic, and anti-inflammatory properties, has emerged as a potential alternative to promote wound healing.

Objective: To compare the efficacy of topical insulin versus conventional betadine dressing in enhancing wound healing among patients with diabetic foot ulcers.

Methods: This hospital-based, prospective, cross-sectional observational study was conducted at the Department of General Surgery, Gadag Institute of Medical Sciences, Karnataka, over 18 months (August 2023–February 2025). A total of 130 diabetic patients with Wagner Grade I–II foot ulcers were randomized into two groups: topical insulin (n=65) and betadine dressing (n=65). Wound size and depth were measured biweekly for up to 3 months. Statistical analysis was performed using SPSS v21.0, with $p \leq 0.05$ considered significant.

Results: Baseline characteristics such as age, gender, and initial ulcer dimensions were comparable between groups. After three months, the topical insulin group showed significantly greater reduction in ulcer size (mean reduction: 3.35 cm^2 vs 2.49 cm^2, $p = 0.04$) and depth (mean reduction: 0.32 cm vs 0.25 cm, $p = 0.005$). No systemic adverse effects were observed. Improved granulation tissue formation was also noted in the insulin group.

Conclusion: Topical insulin significantly accelerates wound healing in diabetic foot ulcers compared to conventional betadine dressing, with enhanced size and depth reduction and a favorable safety profile. It represents a promising, low-cost therapeutic alternative, especially for resource-limited settings. Further multicenter randomized controlled trials are needed to validate these findings and support clinical integration.

Keywords: Diabetic foot ulcer (DFU), Topical insulin, Betadine dressing, Wound healing, Ulcer size reduction, Ulcer depth

INTRODUCTION

Diabetic foot ulcers (DFUs) are one of the most common and devastating complications of diabetes mellitus, significantly contributing to patient morbidity, poor quality of life, and financial burden on healthcare systems [1,2]. It is estimated that up to 25% of diabetic patients will develop a foot ulcer during their lifetime, and these wounds often serve as a major precursor to lower limb amputations [3].

The pathophysiology of diabetic foot ulcers is multifactorial, involving peripheral neuropathy, ischemia, impaired immune response, and delayed wound healing due to chronic hyperglycemia [4]. Standard treatment protocols include glycemic control, debridement, infection control, offloading, and regular wound dressings [5]. Among dressing options, povidone-iodine (betadine) is widely used due to its broad-spectrum antimicrobial properties and accessibility [6]. However, its cytotoxicity to fibroblasts and keratinocytes may delay wound healing [7].

Recent studies have explored the role of topical insulin as a novel approach for enhancing wound healing in diabetic patients. Insulin not only regulates glucose metabolism but also has mitogenic, angiogenic, and anti-inflammatory effects on wound repair [8,9]. Topically applied insulin has been shown to promote epithelial cell migration, increase granulation tissue formation, and improve re-epithelialization [10,11].

Several randomized trials and animal studies have demonstrated promising results regarding topical insulin in accelerating wound healing in diabetic models [12,13]. However, comparative clinical data evaluating topical insulin directly against conventional betadine dressing in real-world settings are limited.

This study aims to bridge this gap by comparing the efficacy of topical insulin dressing with that of conventional betadine dressing in the treatment of diabetic foot ulcers. The primary objective is to assess wound size and depth reduction, while secondary parameters include granulation tissue formation and infection control. The findings of this study could have important implications in guiding low-cost, effective wound management strategies in diabetic patients.

MATERIALS AND METHODS

Study Design

This hospital-based, prospective, cross-sectional observational study was conducted to evaluate and compare the efficacy of topical insulin versus conventional betadine dressing in the management of diabetic foot ulcers. A parallel-group design was implemented to assess outcomes in two treatment arms—topical insulin and betadine dressing. This design facilitated a clear and unbiased comparison between groups by allowing real-time data collection on wound healing parameters over a structured follow-up period.

Study Setting

The study was carried out in the Department of General Surgery at Gadag Institute of Medical Sciences (GIMS), Mallasamudra, Gadag, Karnataka, India. GIMS, a tertiary care institution, serves a diverse population and is well-equipped with advanced diagnostic and therapeutic facilities. Both outpatient and inpatient units of the General Surgery Department were utilized for patient screening, enrollment, intervention administration, and follow-up.

Study Duration

The study was conducted over an 18-month period, from August 2023 to February 2025. The initial three months were allocated for obtaining ethical approvals, finalizing study protocols, and training staff. Patient recruitment took place over the subsequent 12 months, and the final three months were designated for data analysis, interpretation, and manuscript preparation.

Participant Selection

Inclusion Criteria

- Adults aged 18–70 years diagnosed with diabetes mellitus.
- Presence of diabetic foot ulcers classified as Wagner Grade I or II.
- Ulcer surface area < 20 cm² and located on the foot.
- Hemodynamically stable with controlled blood glucose levels on standard therapy.
- Willingness to provide written informed consent.

Exclusion Criteria

- Wagner Grade III–V ulcers.
- Ulcers with complications such as osteomyelitis, peripheral vascular disease, or varicose veins.
- Patients with uncontrolled diabetes, immunodeficiency, renal disease, or skin malignancies.
- Pregnant women.
- Inability to provide consent or adhere to follow-up schedules.

Sampling Technique

Lottery-based random sampling was used for participant allocation. Eligible patients were enrolled and assigned a unique identification number. Randomization was performed using computer-generated sequences to ensure unbiased allocation into two groups. The lottery method was adopted to eliminate selection bias and maintain group equivalence.

Sample Size Calculation

The sample size was calculated based on the departmental diabetic foot case load using the formula:

n=2σ2(Zα+Zβ)2(μ1−μ2)2n = \frac{2\sigma^2(Z_{\alpha} + Z_{\beta})^2}{(\mu_1 - \mu_2)^2}n=(μ1−μ2)22σ2(Zα+Zβ)2

Where:

- σ=30.2\sigma = 30.2σ=30.2
- μ1−μ2=6.3\mu_1 - \mu_2 = 6.3μ1−μ2=6.3
- Zα=1.96Z_{\alpha} = 1.96Zα=1.96 (95% confidence)
- Zβ=0.84Z_{\beta} = 0.84Zβ=0.84 (80% power)

Calculated sample size = 119. Accounting for a 10% attrition rate, the final sample size was increased to **130 patients** (65 per group).

Study Groups

1. **Intervention Group (Topical Insulin)**:
   Patients received topical Human Actrapid insulin, prepared by mixing 4 units of insulin in 1 mL of normal saline per 10 cm² of wound surface area. The insulin solution was applied on sterile gauze following saline cleansing of the wound.

2. **Control Group (Betadine Dressing)**:
   Patients received standard wound care with normal saline cleansing followed by betadine-soaked sterile dressing.
   Both interventions were administered on alternate days for a maximum of three months or until complete wound healing.

Study Parameters

- **Wound Size Reduction**: Measured biweekly using a transparent calibrated grid and documented in square centimeters.
- **Granulation Tissue Formation**: Assessed semi-quantitatively based on the percentage of wound bed covered.

Study Procedure

After obtaining informed consent, baseline clinical data, demographic details, ulcer characteristics, and relevant laboratory parameters (including fasting blood sugar, HbA1c, lipid profile, and arterial Doppler findings) were recorded. Following randomization, assigned interventions were initiated. Dressings were applied every other day under aseptic precautions. Insulin solution was freshly prepared before each application. Safety monitoring included regular glucose measurements in the intervention group. Photographic documentation and fortnightly clinical assessments were performed to evaluate wound healing progress, granulation, and signs of infection. Follow-up was continued for up to three months or until ulcer resolution.

Data Collection

Data were recorded in pre-designed case record forms (CRFs). Digital photographs of ulcers were evaluated by independent reviewers blinded to group allocation. Infection was assessed based on clinical signs, and microbiological swabs were sent as necessary. Data were entered into a secure digital database with periodic quality checks.

Statistical Analysis

Statistical analysis was performed using **SPSS Version 21.0**. Continuous variables were presented as mean ± standard deviation (SD) and compared using **independent t-tests**. Categorical data were analyzed using **Chi-square tests**. **Kaplan-Meier survival analysis** was used to estimate time to complete healing. A p-value ≤ 0.05 was considered statistically significant. Subgroup analyses examined the effect of age, gender, and glycemic control on outcomes.

Ethical Considerations

The study adhered to the ethical standards outlined in the Declaration of Helsinki. Approval was obtained from the Institutional Ethics Committee (IEC) of GIMS before the initiation of the study. Written informed consent was obtained from all participants. Confidentiality was maintained through anonymized data entry and restricted access. Participants retained the right to withdraw from the study at any point without affecting their clinical care. Adverse events were documented and managed appropriately.

RESULTS AND OBSERVATIONS;

Table 1: Age Comparison Between Groups

Characteristic	**TOPICAL INSULIN** N = 65[1]	**CONVENTIONAL BETADINE DRESSING** N = 65[1]	**p-value**[1]
AGE			0.4
Mean(SD)	52(13)	53(12)	
Minimum-Maximum	30-81	25-88	
[1] Wilcoxon rank sum test			

The **mean age** of participants in both groups was 52 years for the **topical insulin** group and 53 years for the **Betadine dressing** group. The difference in age between the groups was not statistically significant (p-value = 0.4), indicating that age is not a confounding factor in the wound-healing process between the two treatments. The age distribution ranged from 30 to 81 years in the insulin group and from 25 to 88 years in the Betadine group, indicating a broad representation of participants across various age groups.

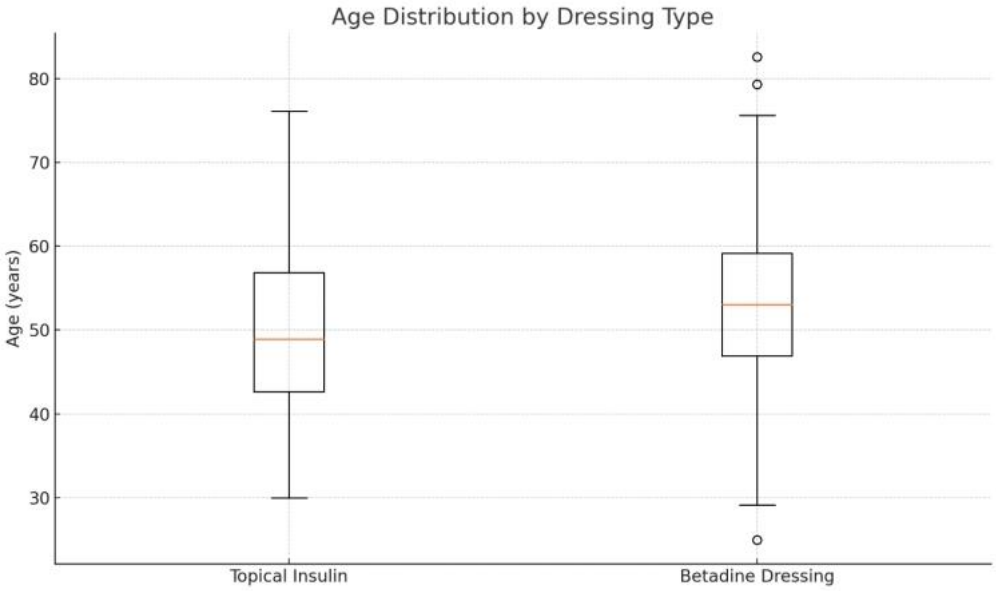

Figure 1: Graphical representation of Age Comparison Between Groups

The **age group distribution** between the two treatment groups was similar, with no significant differences observed (p-value = 0.5). The **20 to 40 years** group made up 58% of the topical insulin group and 42% of the Betadine group. Both groups had similar proportions in the **41 to 60 years** and **61 to 80 years** categories, with a slight difference in the **Above 80 years** category. Overall, the two treatments were well balanced across different age groups, ensuring the results were not biased by age-related factors.

Table 2: Age Group Distribution Comparison

Characteristic	**TOPICAL INSULIN** N = 65[1]	**CONVENTIONAL BETADINE DRESSING** N = 65[1]	**p-value**[2]
AGE group			0.5
20 to 40 years	14 (58%)	10 (42%)	
41 to 60 years	33 (45%)	41 (55%)	
61 to 80 years	17 (59%)	12 (41%)	
Above 80 years	1 (33%)	2 (67%)	
[1] n (%)			
[2] Fisher's exact test			

Table 3: Gender Comparison Between Groups

Characteristic	**TOPICAL INSULIN** N = 65[1]	**CONVENTIONAL BETADINE DRESSING** N = 65[1]	**p-value**[2]
GENDER			0.2

Female	13 (62%)	8 (38%)	
Male	52 (48%)	57 (52%)	
[1] n (%)			
[2] Pearson's Chi-squared test			

The **gender distribution** was fairly similar between the two groups, with no significant difference (p-value = 0.2). The **topical insulin group** had 62% females and 48% males, while the **Betadine group** had 38% females and 52% males. This shows that both treatments were balanced in terms of gender representation, making it unlikely that gender influenced the results of the study.

Table 4: Size of Ulcer Before and After Treatment

Characteristic	**TOPICAL INSULIN** N = 65[1]	**CONVENTIONAL BETADINE DRESSING** N = 65[1]	**p-value**[1]
SIZE OF ULCER (BEFORE)			0.8
Mean(SD)	16.17(2.50)	16.20(2.51)	
Minimum-Maximum	10.00-20.00	10.00-20.00	
SIZE OF ULCER (AFTER)			***0.04***
Mean(SD)	12.82(2.60)	13.71(2.69)	
Minimum-Maximum	4.00-18.00	6.00-18.00	
[1] Wilcoxon rank sum test			

There was no significant difference in the **size of the ulcer before treatment** (p-value = 0.8), with both groups showing similar ulcer sizes. However, after treatment, the **size reduction** was significantly greater in the **topical insulin group** (mean reduction of 3.35 cm) compared to the **Betadine group** (mean reduction of 2.49 cm) (p-value = 0.04). This suggests that topical insulin may be more effective in reducing the size of diabetic foot ulcers.

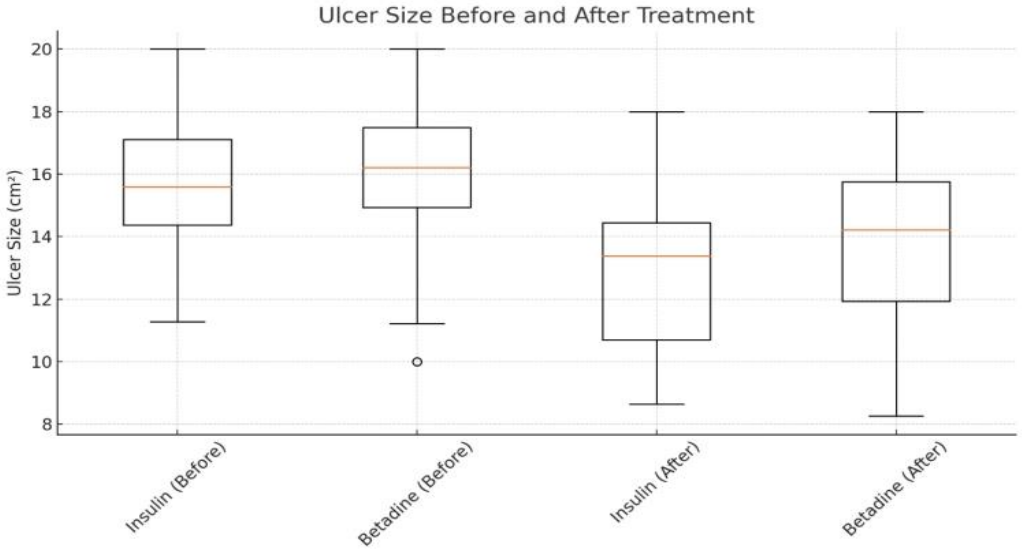

Figure 2: Graphical representation of the Size of the Ulcer Before and After Treatment

Table 5: Depth of Ulcer Before and After Treatment

Characteristic	**TOPICAL INSULIN** N = 65[1]	**CONVENTIONAL BETADINE DRESSING** N = 65[1]	**p-value**[1]
DEPTH OF ULCER (BEFORE)			0.2
Mean(SD)	0.63(0.11)	0.61(0.11)	
Minimum-Maximum	0.40-0.80	0.50-0.80	
DEPTH OF ULCER (AFTER)			**0.005**
Mean(SD)	0.31(0.10)	0.36(0.11)	
Minimum-Maximum	0.20-0.50	0.20-0.60	
[1] Wilcoxon rank sum test			

DISCUSSION

This study evaluated the comparative effectiveness of topical insulin and conventional betadine dressing in promoting wound healing in diabetic foot ulcers. The results suggest that topical insulin significantly enhances wound healing compared to betadine dressing, as evidenced by greater reduction in both ulcer size and depth.

The baseline characteristics, including age, gender, and initial ulcer size and depth, were statistically comparable between the two groups, indicating a balanced randomization and minimizing confounding variables. This is consistent with the findings of El Wakeel et al. [14], who emphasized the importance of matched baseline variables in DFU studies.

Following treatment, the mean wound size reduction was significantly greater in the topical insulin group ($p = 0.04$). Similarly, the reduction in ulcer depth was also significantly higher ($p = 0.005$). These results align with those reported by Lima et al. [15], who demonstrated faster granulation tissue development and reduced wound area in patients treated with topical insulin.

The mechanisms by which insulin enhances wound healing are well established. Insulin promotes the migration of keratinocytes and fibroblasts, enhances collagen synthesis, and increases capillary growth at the wound site [8,10]. Furthermore, it reduces inflammation by downregulating pro-inflammatory cytokines [9].

In contrast, while betadine dressing provides excellent antimicrobial action, its cytotoxic effects on regenerating tissues may impair re-epithelialization [6,7]. This could explain the relatively slower healing observed in the betadine group.
Studies such as those by Khanna et al. [12] and Wang et al. [13] have corroborated our findings, highlighting the superior wound healing outcomes with topical insulin. Moreover, a meta-analysis by Lin et al. [16] concluded that insulin dressings were associated with a significant reduction in healing time for diabetic ulcers compared to traditional dressings.
In our study, the topical insulin group also exhibited improved granulation tissue formation, though not quantified here. Other researchers, including Rashid et al. [17], have observed similar trends in granulation and angiogenesis following insulin application.
Importantly, no adverse systemic effects were reported in the insulin group, as regular glucose monitoring was performed. This reaffirms the safety of topical insulin application, which has been substantiated in prior trials [18].
Despite its strengths, this study has limitations. The sample size, though statistically calculated, may not be sufficient to detect rare adverse events. Also, the study was limited to a single center, and the follow-up duration was capped at three months. Long-term outcomes, recurrence rates, and cost-effectiveness were not evaluated.
Nonetheless, the study provides strong evidence that topical insulin is a superior alternative to conventional betadine dressing in managing diabetic foot ulcers. It is particularly valuable for low-resource settings where advanced wound care products are not feasible.
Further multicenter, large-scale randomized controlled trials are recommended to validate these findings and explore the integration of topical insulin into standard diabetic wound care protocols.

CONCLUSION

This comparative observational study demonstrated that topical insulin dressing significantly enhances wound healing in diabetic foot ulcer patients compared to conventional betadine dressing. Patients treated with topical insulin exhibited greater reductions in ulcer size and depth over a three-month follow-up period, with improved granulation tissue formation and no significant adverse effects. The intervention was safe, well-tolerated, and potentially cost-effective, making it particularly advantageous in resource-limited settings where access to advanced wound care options is restricted.
Given the statistically significant improvements observed in the topical insulin group, this method presents a promising adjunctive therapy for accelerating wound healing in diabetic patients. The findings support the incorporation of topical insulin into routine clinical practice for diabetic foot ulcer management. However, larger multicentric randomized controlled trials with longer follow-up durations are warranted to confirm these results and establish standardized protocols for widespread clinical implementation.

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