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Comparison Of the Topical Insulin Versus Topical Phenytoin in Healing of Diabetic Foot Ulcers

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ABSTRACT

Background: Diabetic foot ulcers represent a major complication of diabetes mellitus, leading to significant morbidity, prolonged hospitalization, and risk of amputation. Impaired wound healing due to neuropathy, ischemia, and infection necessitates effective therapeutic strategies. Topical agents such as insulin and phenytoin have shown potential in enhancing wound healing through different mechanisms, including promotion of granulation tissue and cellular proliferation, but comparative evidence remains limited.
Aims: To compare the efficacy of topical insulin versus topical phenytoin in promoting healing of diabetic foot ulcers.
Materials and Methods: This prospective comparative study was conducted over a period of 10 months and included 80 patients with diabetic foot ulcers. Patients were randomly divided into two groups of 40 each. Group I received topical insulin dressing, while Group II received topical phenytoin dressing. Ulcers were assessed at regular intervals for reduction in ulcer size, development of granulation tissue, time to healing, and infection control. Standard diabetic care, including glycemic control and debridement, was provided to all patients. Statistical analysis was performed using appropriate tests, with $p < 0.05$ considered significant.
Results: The mean reduction in ulcer size was significantly greater in the topical insulin group compared to the phenytoin group ($p < 0.05$). Early appearance of healthy granulation tissue was observed in Group I, with a higher percentage of patients showing satisfactory wound healing within a shorter duration. Infection control was comparable between the two groups. The mean duration of healing was significantly shorter in the insulin group, indicating faster wound resolution. No major adverse effects were noted in either group.
Conclusion: Topical insulin was found to be more effective than topical phenytoin in promoting faster and better healing of diabetic foot ulcers. Its ability to enhance granulation tissue formation and accelerate wound contraction makes it a promising, cost-effective therapeutic option. Incorporating topical insulin into routine wound care may improve clinical outcomes and reduce complications associated with diabetic foot ulcers.

Keywords*: Diabetic foot ulcer, diabetes mellitus, granulation tissue, topical insulin, topical phenytoin, wound healing.*

INTRODUCTION

Diabetes mellitus is a global health concern with rapidly increasing prevalence, particularly in developing countries.[1] Among its numerous complications, diabetic foot ulcers (DFUs) represent one of the most challenging and debilitating conditions, contributing significantly to morbidity, prolonged hospital stay, and healthcare burden.[2] It is estimated that nearly 15–25% of individuals with diabetes will develop a foot ulcer during their lifetime, with a substantial proportion progressing to infection, gangrene, and eventual amputation. The pathogenesis of DFUs is multifactorial, involving

peripheral neuropathy, peripheral vascular disease, immunological impairment, and repeated trauma, all of which contribute to delayed wound healing.[4]

Wound healing in diabetic patients is often impaired due to poor glycemic control, reduced growth factor activity, diminished angiogenesis, and defective collagen synthesis. These factors result in chronic, non-healing ulcers that are prone to secondary infections.[5] Conventional management includes glycemic control, debridement, infection management, pressure offloading, and appropriate wound dressings. However, despite advances in wound care, achieving rapid and complete healing remains a significant challenge, necessitating the exploration of newer therapeutic modalities that can enhance the healing process.[6,7]

Topical agents have gained increasing attention in recent years due to their ability to act directly at the wound site with minimal systemic side effects. Among these, topical insulin has emerged as a promising option due to its anabolic and growth-promoting effects.[8] Insulin enhances cellular proliferation, promotes protein synthesis, stimulates angiogenesis, and accelerates granulation tissue formation, thereby facilitating faster wound healing. Several studies have demonstrated that topical insulin can significantly reduce wound size and improve healing rates in chronic ulcers.[9]

Phenytoin, a well-known anticonvulsant drug, has also been repurposed for wound healing due to its observed side effect of gingival hyperplasia, which reflects its capacity to stimulate fibroblast proliferation and collagen deposition.[10] Topical phenytoin has been shown to enhance granulation tissue formation, reduce bacterial load, and promote wound contraction. Its low cost and ease of application make it an attractive alternative, particularly in resource-limited settings.[11]

Despite the documented benefits of both topical insulin and phenytoin, there is limited comparative evidence evaluating their relative efficacy in the management of diabetic foot ulcers. Given the high burden of diabetic foot ulcers and the limitations of existing treatment strategies, there is a need to identify effective, economical, and easily applicable topical agents that can accelerate wound healing. Both insulin and phenytoin have shown encouraging results individually, but direct comparison is necessary to establish their relative effectiveness in clinical practice. By evaluating parameters such as ulcer size reduction, granulation tissue formation, and healing duration, the study seeks to generate evidence that can guide clinicians in selecting the most effective topical therapy for improved patient outcomes

AIMS AND OBJECTIVES

- To compare the efficacy of topical insulin versus topical phenytoin in promoting healing of diabetic foot ulcers.

MATERIALS AND METHODS

The present prospective comparative study was conducted over a period of 10 months from February 2025 to November 2025 in department of General Surgery at Sree Mookambika Institute of Medical Sciences. A total of 80 patients with diabetic foot ulcers attending the Department of General Surgery were included in the study after obtaining informed written consent. Patients aged above 18 years with clinically diagnosed diabetic foot ulcers of Wagner grade 1 to 4 were considered eligible for inclusion. Patients with critical limb ischemia, osteomyelitis, malignant ulcers, severe systemic illness, or known hypersensitivity to insulin or phenytoin were excluded from the study.

The selected patients were randomly allocated into two groups of 40 each.

- Group I patients received topical insulin dressing
- Group II patients received topical phenytoin dressing

A detailed clinical evaluation was performed for all patients, including history, general and local examination, and relevant laboratory investigations such as fasting and postprandial blood glucose, HbA1c, complete blood count, and renal function tests. Ulcer characteristics including size, site, duration, and grade were documented at baseline.

All patients received standard wound care protocols, including surgical debridement, appropriate antibiotic therapy based on culture sensitivity, and strict glycemic control using insulin or oral hypoglycemic agents. In Group I, regular insulin diluted in normal saline was applied topically over the ulcer surface and covered with sterile dressing. In Group II, topical phenytoin solution prepared from injectable phenytoin was applied in a similar manner. Dressings were performed daily under aseptic precautions.

Patients were followed up at regular intervals, and wound assessment was carried out weekly. The primary outcome measures included reduction in ulcer size, rate of granulation tissue formation, and time taken for complete healing. Secondary outcomes included infection control and need for surgical intervention. Ulcer size was measured using standardized techniques, and percentage reduction was calculated over time.

All collected data were systematically recorded and analyzed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages. Statistical analysis was performed using Student's t-test and chi-square test, with a p value of less than 0.05 considered statistically significant.

OBSERVATION AND RESULTS

Most patients belonged to the 51–60 years age group, indicating higher prevalence of diabetic foot ulcers in middle-aged and elderly individuals. The age distribution between the two groups was comparable (p = 0.62). (Table 1)

Table 1: Age Distribution

Age (Years)	Group I n (%)	Group II n (%)	Total n (%)
30–40	4 (10.0)	5 (12.5)	9 (11.25)
41–50	9 (22.5)	10 (25.0)	19 (23.75)
51–60	15 (37.5)	13 (32.5)	28 (35.0)
61–70	8 (20.0)	9 (22.5)	17 (21.25)
>70	4 (10.0)	3 (7.5)	7 (8.75)
Total	40 (100)	40 (100)	80 (100)

There was a clear male predominance in both groups, reflecting higher susceptibility or exposure to risk factors among males. (p = 0.81). (Table 2)

Table 2: Gender Distribution

Gender	Group I n (%)	Group II n (%)	Total n (%)
Male	25 (62.5)	24 (60.0)	49 (61.25)
Female	15 (37.5)	16 (40.0)	31 (38.75)
Total	40 (100)	40 (100)	80 (100)

Baseline ulcer size was similar in both groups, indicating uniform disease severity at presentation. The absence of statistical significance confirms that both groups were comparable before intervention. Group I showed significantly greater reduction in ulcer size at all follow-up intervals. The progressive and consistent improvement highlights the superior wound-healing efficacy of topical insulin. This difference was highly statistically significant, confirming a strong treatment effect. (Table 3).

Table 3: Reduction in Ulcer Size (%)

Week	Group I (Mean ± SD)	Group II (Mean ± SD)	p value
Base line	24.5 ± 6.2	25.1 ± 5.9	0.68
Week 1	18.2 ± 4.1	12.5 ± 3.8	0.001*
Week 2	36.4 ± 5.2	25.3 ± 4.6	<0.001*
Week 3	58.6 ± 6.8	42.1 ± 5.9	<0.001*
Week 4	78.3 ± 7.1	60.2 ± 6.3	<0.001*

Early and enhanced granulation tissue formation was observed in the insulin group compared to the phenytoin group. The difference was statistically significant at all time points, indicating faster wound bed preparation. This suggests improved tissue regeneration with insulin therapy. (Table 4)

Table 4: Granulation Tissue Formation

Week	Group I n (%)	Group II n (%)	p value
Week 1	22 (55.0)	13 (32.5)	0.02*
Week 2	32 (80.0)	23 (57.5)	0.01*
Week 3	37 (92.5)	30 (75.0)	0.03*

Ulcer healing decreased significantly with increasing duration of diabetes. Patients with longer disease duration showed reduced response to treatment. (Table 5).

Table 5: Duration of Diabetes vs Ulcer Size Reduction

Duration of DM	Patients n (%)	Mean Reduction (%)	p value
<5 years	18 (22.5)	68.5 ± 6.2	**0.01***

5–10 years	32 (40.0)	59.2 ± 5.8	
>10 years	30 (37.5)	48.3 ± 5.1	

Poor glycemic control was associated with significantly reduced wound healing. Patients with higher HbA1c levels demonstrated slower ulcer size reduction. (Table 6)

Table 6: HbA1c vs Ulcer Healing

HbA1c (%)	Patients n (%)	Reduction (%)	p value
<7	20 (25.0)	75.2 ± 6.4	
7–9	34 (42.5)	60.1 ± 5.9	
>9	26 (32.5)	45.3 ± 6.2	**<0.001***

The mean healing time was significantly shorter in Group I, indicating faster wound resolution. The highly significant p value confirms the clinical advantage of insulin over phenytoin. (Table 7).

Table 7: Time to Complete Healing

Parameter	Group I (Mean ± SD)	Group II (Mean ± SD)	p value
Healing time (days)	24.6 ± 5.3	32.8 ± 6.1	<0.001*

DISCUSSION

he majority of patients in the present study were in the 51–60 years age group (28; 35.0%), followed by 41–50 years (19; 23.75%), while elderly patients above 60 years constituted 24 (30.0%) cases. Age distribution was comparable between the groups (p = 0.62), and male predominance was noted in 49 (61.25%) patients, reflecting potential gender-based vulnerability, with no significant difference between groups (p = 0.81). Baseline ulcer size was similar in both groups (Group I: 24.5 ± 6.2%; Group II: 25.1 ± 5.9%; p = 0.68), confirming homogeneity before intervention.

The demographic trends in this study, including male predominance and higher prevalence in middle-aged to elderly patients, were comparable to those reported by Madishetty R et al.[12] reflecting both biological susceptibility and behavioral factors influencing diabetic foot ulcer incidence.

Present study observed that topical insulin demonstrated significantly faster and greater ulcer size reduction and enhanced granulation tissue formation compared to topical phenytoin. Healing was influenced by both diabetes duration and glycemic control, with better outcomes in patients with shorter disease duration and well-controlled HbA1c. The mean healing time was also shorter in the insulin group, indicating superior efficacy in promoting wound closure.

These findings are consistent with those of Nagaraj J et al.[13] who reported statistically significant improvements in wound size and depth with insulin dressings compared to phenytoin and normal saline. The accelerated healing and early granulation observed in the current study align with their findings, confirming the beneficial effect of local insulin therapy. Similarly, Biradar D et al.[14] noted that insulin dressings led to greater surface area reduction and faster granulation tissue formation than saline dressings, highlighting the advantage of insulin in enhancing tissue regeneration, comparable to our results.

Bhittani MK et al.[15] reported that phenytoin dressings also resulted in faster healing than conventional dressings, though the extent of ulcer reduction and granulation was less pronounced than observed with insulin in our study. This suggests that while phenytoin improves wound healing compared to conventional therapy, insulin provides superior outcomes. Our observations regarding glycemic control influencing healing are in agreement with Madishetty R et al.[12] and Iqbal S et al.[16] who emphasized that poorly controlled diabetes and longer disease duration adversely affect wound healing, reinforcing the importance of systemic management alongside local therapy.

Furthermore, Stergioti A et al.[17] demonstrated that insulin-treated ulcers had significantly faster reductions in area, length, width, and depth, with shorter median healing times, findings which directly parallel the accelerated healing and early granulation observed in the current study. Across these studies, topical insulin consistently shows faster wound closure, improved granulation, and shorter healing times compared to phenytoin or saline, confirming its efficacy as a local therapeutic agent in diabetic foot ulcers.

CONCLUSION

Topical insulin demonstrated superior efficacy over topical phenytoin in promoting diabetic foot ulcer healing, as evidenced by faster reduction in ulcer size, earlier granulation tissue formation, and shorter healing time. Patients in the insulin group showed consistently better outcomes across all follow-up periods. Additionally, ulcer healing was significantly influenced by duration of diabetes and glycemic control, with poorer outcomes observed in long-standing and uncontrolled diabetes.

These findings highlight the importance of metabolic optimization alongside local wound care. Topical insulin appears to be a safe, effective, and promising therapeutic option for enhancing wound healing in diabetic foot ulcer management.

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Conflicts Of Interest: There are no conflicts of interest.

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