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The Effectiveness of Topical Insulin for Ulcer Healing: A Pilot Study

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ABSTRACT

Introduction
Chronic ulcers continue to pose a major clinical challenge, contributing to significant morbidity and mortality. These conditions are frequently associated with diabetes, venous disorders, neuropathy, and other systemic illnesses. Conventional treatments often yield suboptimal results, encouraging investigation into alternative approaches such as topical insulin. This study aims to evaluate the effectiveness and safety of topical insulin in promoting ulcer healing.

Method
A pre-post interventional pilot study was conducted at Dr. Moewardi General Hospital from September to October 2024. Seven patients aged 40-80 years with grade II-III ulcers were treated with a topical insulin solution (10 IU insulin in 1 mL saline), applied once daily for 14 days. Ulcer size was measured on days 0, 7, and 14. Adverse effects were also monitored.

Result
Out of seven participants, three showed significant improvement in ulcer size (75-100% reduction), three showed mild to moderate improvement (8-26%), and one had no response. No local or systemic adverse events, including hypoglycemia, were observed. Factors such as limited patient mobility affected follow-up adherence.

Discussion
The findings suggest topical insulin enhances ulcer healing through mechanisms involving cell proliferation, angiogenesis, and anti-inflammatory effects, consistent with prior studies. However, the small sample size and loss to follow-up limit generalizability. Further trials are required to confirm its clinical utility.

Conclusion
Topical insulin appears to be a safe and potentially effective adjunct therapy for ulcer healing in both diabetic and non-diabetic patients. Larger-scale studies with control comparisons are needed to confirm its efficacy and optimize treatment protocols.

Keywords: Topical insulin; ulcer healing; wound care

Introduction

Chronic ulcers represent a significant global health burden due to their impact on quality of life, prolonged treatment duration, and increased healthcare costs. These wounds are defined as lesions that fail to heal within approximately six weeks and may arise from various etiologies, including diabetes mellitus, vascular insufficiency, neuropathy, infection, or prolonged pressure.
[1,2] Among these, diabetic ulcers are particularly concerning, affecting a substantial proportion of diabetic patients and increasing the risk of amputation and mortality.[3] The incidence of chronic wounds continues to rise alongside increasing rates of aging, obesity, and diabetes, including in Indonesia, where they contribute to both clinical and economic challenges.[4,5]

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Delayed healing in chronic ulcers is associated with disruption of the normal wound-healing cascade, including persistent inflammation, reduced angiogenesis, and impaired extracellular matrix remodeling.[6,7] Standard management strategies such as wound cleansing, debridement, infection control, appropriate dressings, and systemic optimization remain essential but often fail to achieve satisfactory outcomes.[8] These limitations highlight the need for adjunctive therapies to accelerate wound healing and improve patient outcomes.

Insulin, beyond its metabolic role, has been shown to facilitate tissue repair by enhancing fibroblast proliferation, keratinocyte migration, angiogenesis, and collagen synthesis, while also modulating inflammatory pathways.[9,10] Several studies have reported beneficial effects of topical insulin in chronic wound healing without significant systemic side effects.[11-13] Despite these promising results, evidence in Indonesian populations remains limited. This pilot study was therefore designed to evaluate the effect of topical insulin on ulcer healing at Dr. Moewardi General Hospital, Surakarta, with the aim of providing preliminary data to support larger controlled trials.

Methods

This pilot study employed a pre-post interventional study and was conducted at Dr. Moewardi General Hospital, Surakarta, between September and October 2024. Ethical approval was obtained from the institutional review board, and all participants provided written informed consent. Eligible subjects were adults aged 20-60 years with grade II-III ulcers. Patient with active infection or uncontrolled systemic illness were excluded. A total of seven patients were recruited consecutively.

The intervention consisted of topical application of diluted insulin. A solution of 0.1 ml regular insulin (10 IU) mixed with 1 ml normal saline was prepared in a sterile spray bottle and applied once daily after wound cleansing. The ulcer was subsequently covered with Duoderm® dressing and replaced every 24 hours. Each spray bottle was replaced every two days to maintain sterility.

The primary outcome was change in ulcer size, measured at baseline (day 0), day 7, and day 14 using a transparent grid sheet and digital photography. Ulcer depth was measured clinically using a sterile disposable probe inserted gently to the deepest point of the wound and recorded in millimeters. Secondary outcomes included time to epithelialization and safety parameters. Patients were monitored for systemic effects such as hypoglycemia and local complications including infection or increased pain.

Results

Patients Characteristics

Seven patients participated in this study. The demographic and clinical characteristics are shown in **Table 1**. The majority of patients were female (57%) and aged between 60-80 years (57%). Stroke was the most frequent comorbidity (43%), followed by type 2 diabetes mellitus (29%) and psoriasis (14%). The majority of participants were non-diabetic.

Characteristic	Number (n)	Percentage (%)
Age group		
40-60 Years	3	43
60-80 Years	4	57
Sex		
Female	4	57
Male	3	43
Comorbidities		
Stroke	3	43
Type 2 diabetes	2	22
Psoriasis	1	14
None	1	14
Diabetic status		
Diabetic	2	29
Non-diabetic	5	71

Table 1. Characteristics of study participants

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Ulcer Healing Outcomes

A reduction in ulcer size from baseline to day 7 and day 14 are summarized in Table 2. Of the seven patients, two showed substantial improvement. Patient 2 achieved complete ulcer closure by day 7 (Figure 1), and Patient 7 showed a 75% reduction by day 7 (Figure 2). Patient 1 also exhibited progressive healing with callus formation and a 75% reduction by day 14. Patient 3 showed moderate improvement (26% reduction), while Patient 5 demonstrated minimal change (8%) before passing away from unrelated illness on day 10. Patients 4 and 6 were lost to follow up.

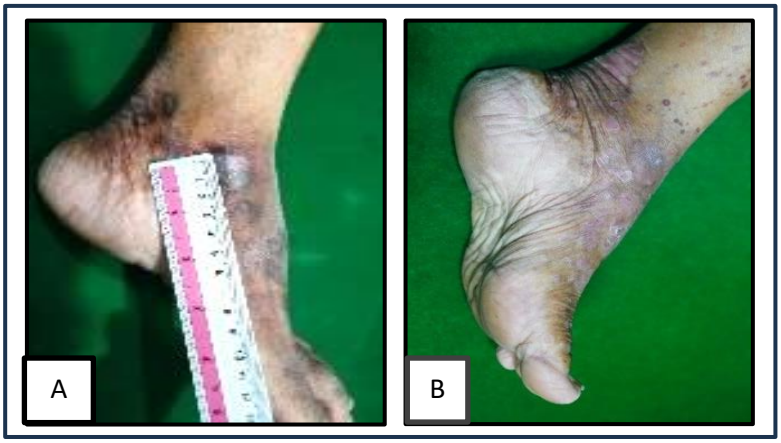

Figure 1. (A) Day 0: ulcer size 0.64 cm². **(B)** Day 7: ulcer size 0 cm², indicating complete healing

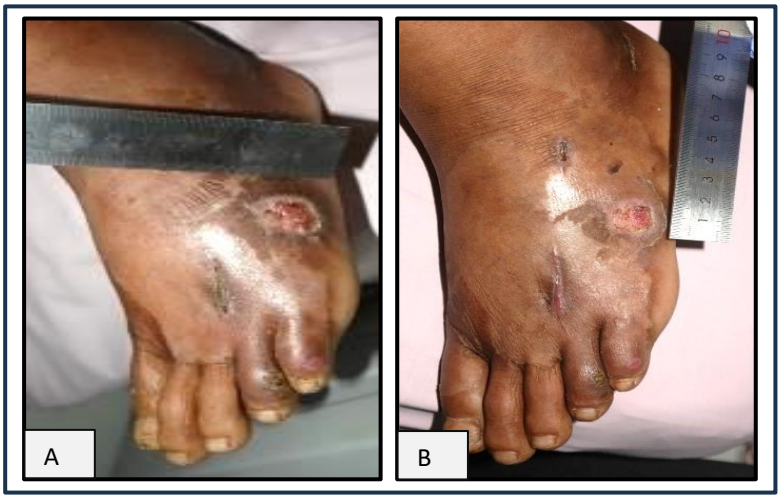

Figure 2. (A) Day 0: ulcer size 4 cm². **(B)** Day 7: ulcer size 1 cm²

Changes in ulcer size from baseline to day 7 and day 14 demonstrated an overall downward trend in the majority of patients. At baseline, ulcer size ranged from 0.64 to 35.0 cm², indicating considerable variability in wound severity among participants.

By day 7, four patients exhibited clinically meaningful reductions in ulcer size, including one patient who achieved complete wound closure. One patient showed minimal improvement, while two patients were not evaluable beyond day 7 due to loss to follow-up and death from an unrelated medical condition.

Statistical analysis using the Wilcoxon signed-rank test showed a significant reduction in ulcer size between baseline and day 7 ($p = 0.043$), supporting the observed clinical improvement **(Table 2).** However, analysis at day 14 was limited due to incomplete follow-up data.

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Variable	Baseline (Day 0) Median (IQR) cm²	Day 7 Median (IQR) cm²	p-value
Ulcer size (cm²)	4 (1–25)	2.3 (1–23)	0.043

Table 2. Comparison of ulcer size from baseline (Day 0) and Day 7

Safety Outcomes

No systemic or local adverse effects were reported. None of the patients experienced symptoms of hypoglycemia, including tremors, palpitations, sweating, confusion, or blurred vision. Local side effects such as bleeding, increased pain, or secondary infection were not observed. Pain levels remained stable as assessed by the Visual Analog Scale (VAS).

Discussion

This pilot study provides preliminary evidence supporting the potential role of topical insulin in accelerating ulcer healing. Three out of seven participants achieved marked improvement, with one showing complete healing and two demonstrating substantial reductions in ulcer size within 14 days. Importantly, no adverse systemic or local effects were observed, supporting the safety of this approach.

The observed benefits of topical insulin in this study are consistent with previous reports. Singh and Pawar (2020) demonstrated significant improvement in trophic ulcers among leprosy patients treated with topical insulin compared to saline irrigation.[1] Similarly, Thakur et al. (2020) reported faster healing of diabetic foot ulcers with topical insulin compared to conventional dressings.[2] These findings suggest that insulin may accelerate healing by modulating multiple mechanisms, including fibroblast proliferation, keratinocyte migration, angiogenesis, and regulation of inflammatory responses.[3,4]

The lack of adverse events is particularly noteworthy, as systemic insulin therapy carries the risk of hypoglycemia and electrolyte imbalance. By applying insulin directly to the wound bed, high local concentrations can be achieved without systemic absorption, thus reducing these risks.[5] This makes topical insulin an attractive adjunctive therapy, especially in patients with multiple comorbidities where systemic therapy may be limited.

However, the study has several limitations. The small sample size and pilot design restrict the generalizability of the findings. Furthermore, loss to follow-up in two patients and death in one case reduced the evaluable sample, potentially biasing outcomes. Another limitation is the lack of a control group, making it difficult to attribute improvements solely to insulin rather than natural healing or other concurrent care.

Future studies should include randomized controlled trials with larger sample sizes to compare topical insulin with standard wound care modalities. Long-term follow-up is also necessary to evaluate recurrence rates and sustained outcomes. Despite its limitations, this pilot study contributes valuable early data supporting the potential role of topical insulin as a safe, accessible, and accessible adjunctive therapy that may be associated with improvement in ulcer healing.

Conclusion

This pilot study suggests that topical insulin may be associated with improvement in chronic ulcer healing and appears to be well tolerated. A statistically significant reduction in ulcer size was observed within the first week of treatment. However, given the small sample size and absence of a control group, these findings should be interpreted cautiously. Large-scale controlled studies are necessary to validate its clinical effectiveness and establish standardized guidelines.

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