Section: Surgery

Original Research Article

COMPARATIVE EVALUATION OF TOPICAL PHENYTOIN VERSUS CONVENTIONAL NORMAL SALINE DRESSINGS FOR HEALING DIABETIC FOOT ULCERS: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) represent a significant challenge in clinical practice, often characterized by delayed healing and high risk of complications. While conventional dressings with normal saline are widely used, topical phenytoin has shown potential to accelerate healing due to its fibroblast-stimulating and antimicrobial properties. The objective is to compare the efficacy and safety of topical phenytoin dressings versus conventional normal saline dressings in patients with Wagner grade 1 and 2 diabetic foot ulcers.

Materials and Methods: This prospective, randomized controlled trial included 60 patients with Wagner grade 1 or 2 DFUs. Patients were randomly assigned to receive either topical phenytoin dressings (n=30) or normal saline dressings (n=30). Both groups received standard wound care including debridement, systemic antibiotics, and glycemic control. Outcomes assessed included percentage ulcer area reduction, time to granulation tissue appearance, bacterial culture conversion, and hospital stay duration.

Results: The phenytoin group exhibited a significantly greater mean percentage reduction in ulcer area (66.1% ± 4.9) compared to the saline group (35.1% ± 7.5; $p < 0.001$). Granulation tissue appeared earlier in the phenytoin group (8.8 ± 3.0 days) versus controls (12.9 ± 4.1 days; $p < 0.001$). Bacterial culture conversion by day 10 was significantly higher in the phenytoin group (76.2%) than in the saline group (22.2%; $p = 0.01$). The mean hospital stay was shorter in the phenytoin group (21.4 ± 3.5 days vs. 24.1 ± 2.8 days), though not statistically significant ($p = 0.09$). No adverse effects were reported with topical phenytoin.

Conclusion: Topical phenytoin is a safe and effective adjunctive treatment for diabetic foot ulcers, resulting in faster wound healing and improved bacterial clearance compared to conventional normal saline dressing. Larger, multi-center trials are recommended to confirm these findings.

Keywords: Diabetic Foot Ulcer, Phenytoin, Topical Dressing, Wound Healing, Randomized Controlled Trial, Normal Saline.

INTRODUCTION

Diabetic foot ulcers (DFUs) are a serious complication of diabetes mellitus, contributing significantly to morbidity, healthcare burden, and lower-limb amputations globally. These ulcers often result from peripheral neuropathy, ischemia, and immunosuppression, and are characteristically stalled in the inflammatory phase of healing.[1-3]

Conventional treatment protocols involve regular debridement, offloading, infection control, and moist wound dressings. While normal saline dressings are widely used due to their safety and affordability, they lack bioactive properties that actively promote healing.[4-6]

Phenytoin, originally an anticonvulsant, has shown promise in wound healing due to its stimulatory effect on fibroblasts, enhanced collagen formation, reduced collagenase activity, and antimicrobial action. Reports of gingival overgrowth in patients using phenytoin sparked interest in its potential tissue-proliferative effects.[7,8]

Although several studies have explored the use of topical phenytoin in wound healing, few randomized controlled trials have assessed its specific efficacy in diabetic foot ulcers, particularly in the Indian population. This study evaluates the comparative effectiveness of topical phenytoin versus normal saline in the healing of Wagner grade 1 and 2 DFUs.[9,10]

MATERIALS AND METHODS

Study Design and Setting: This prospective, randomized controlled trial was conducted between August 2024 and September 2025 in the Department of General Surgery at a tertiary care teaching hospital in India. Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was obtained from all participants.

Inclusion criteria:

- Adults aged 35–70 years with type 1 or 2 diabetes mellitus
- Presence of Wagner grade 1 or 2 foot ulcers

Exclusion criteria:

- Absent distal pulses or peripheral arterial disease
- Wagner grade 3–5 ulcers
- Severe renal impairment
- Known allergy to phenytoin
- Patients unwilling to participate

Randomization and Intervention

Participants were randomized into two equal groups (n=30 each) using a computer-generated random number sequence:

- Study Group: Received daily dressings with topical phenytoin. Phenytoin sodium tablets were crushed and mixed in 5 ml of normal saline:
  - 100 mg for 0–5 cm^2 ulcer
  - 150 mg for 5.1–9 cm^2
  - 200 mg for 9.1–15 cm^2
  - 300 mg for >15 cm^2 ulcers
- Control Group: Received daily dressings with sterile gauze soaked in normal saline.

In both groups, wounds were cleaned and debrided prior to dressing changes. All patients received standard care including glycemic control and antibiotics guided by culture sensitivity.

Outcome Measures

1. Ulcer Area: Measured weekly using length × width, and percentage area reduction calculated.
2. Granulation Tissue Appearance: Number of days until the first appearance of healthy granulation tissue.
3. Microbiological Culture: Swabs taken on Day 0 and Day 10 for culture and sensitivity.
4. Hospital Stay: Total duration of hospitalization (in days).
5. Safety: Monitoring for adverse local/systemic reactions to phenytoin.

Statistical Analysis: Data were analyzed using SPSS software version XX. Quantitative variables were expressed as mean ± standard deviation (SD) and compared using the unpaired t-test. Categorical variables were compared using the Chi-square test. A p-value <0.05 was considered statistically significant.

RESULTS

All 60 patients completed the study protocol. Baseline characteristics were comparable across both groups, except for a slightly larger mean initial ulcer area in the control group.

Table 1: Baseline Characteristics

Characteristic	Phenytoin Group (n=30)	Saline Group (n=30)	P-value
Age (years)	56.3 ± 9.3	57.8 ± 8.6	0.61
Male (%)	73.3%	83.3%	0.589
Initial ulcer area (mm^2)	2809.3 ± 1157.2	3862.3 ± 2379.5	0.035
Positive culture on Day 0	70%	60%	0.589

Table 2: Healing Outcomes

Parameter	Phenytoin Group	Saline Group	P-value
% Reduction in ulcer area	66.1% ± 4.9	35.1% ± 7.5	<0.001
Granulation tissue appearance (days)	8.8 ± 3.0	12.9 ± 4.1	<0.001
Culture conversion (Day 10)	76.2%	22.2%	0.01
Hospital stay (days)	21.4 ± 3.5	24.1 ± 2.8	0.09
Adverse effects	None reported	None reported	—

The mean percentage reduction in ulcer size and earlier appearance of granulation tissue were significantly better in the phenytoin group. Although hospital stay was shorter in the phenytoin group, the difference did not reach statistical significance.

DISCUSSION

This study demonstrates that topical phenytoin is significantly more effective than normal saline in promoting the healing of Wagner grade 1 and 2 diabetic foot ulcers. The faster reduction in ulcer area and earlier granulation suggest a multifactorial benefit—enhanced fibroblast activity, collagen synthesis, and reduced infection burden.

The significantly higher culture conversion rate by Day 10 supports the antimicrobial potential of phenytoin, likely due to both direct antibacterial action and enhanced immune function. These findings are consistent with previous studies by Muthukumar swamy et al. and Tauro et al., affirming phenytoin's role in wound healing.

The absence of adverse effects confirms its safety. Though the shorter hospital stay was not statistically significant, it may still offer practical and economic advantages.

Limitations

- Single-center design
- Modest sample size
- Short-term follow-up without long-term outcome assessment
- Initial ulcer area difference despite randomization

Future studies with blinding, multicenter recruitment, and long-term endpoints are warranted.

CONCLUSION

Topical phenytoin is a safe, inexpensive, and effective alternative to normal saline for diabetic foot ulcer management. It significantly enhances healing outcomes and microbial clearance. Integration of phenytoin dressings into DFU care protocols may improve recovery and reduce complications. Further large-scale, multicenter trials are recommended to validate these findings.

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