International Surgery Journal
Hemanth PA et al. Int Surg J. 2025 Nov;12(11):1924-1928
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20253448

Original Research Article

Comparative evaluation of topical phenytoin versus povidone iodine dressing in the healing of diabetic foot ulcers: a randomized controlled trial

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Received: 08 August 2025
Revised: 10 September 2025
Accepted: 30 September 2025

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ABSTRACT

Background: Diabetic foot ulcers (DFUs) are a crucial diabetes consequence that frequently leads to slow healing, infection and the need for amputation. Povidone iodine (PVP-I) is a widely used antiseptic, whereas phenytoin has lately emerged as a promising wound healing agent due to its proliferative and antibacterial effects. Hence the current study aims to compare the efficacy of topical phenytoin and povidone iodine dressings in promoting healing of diabetic foot ulcers.
Methods: A randomized controlled trial was conducted at Navodaya Medical College Hospital, Raichur among 124 patients with grade 1 or 2 diabetic foot ulcers were randomly assigned to two groups which are Group A (phenytoin dressing) and Group B (povidone iodine dressing). Ulcer area was measured at baseline and on Days 3, 5, 7, 10 and 14. Percentage reduction in ulcer area, slough clearance and granulation tissue formation was measured and subjected to statistical analysis.
Results: Both groups showed significant reduction in ulcer area by Day 14, with greater improvement in Group A (22.03±9.86%) than in Group B (13.85±5.62%) (p=0.001). Mean absolute reduction in ulcer area was higher in the phenytoin group (6.03 mm² vs. 3.99 mm², p=0.004). Slough clearance was achieved in 95.2% of patients in Group A versus 82.3% in Group B. Granulation tissue appeared earlier and was more robust in Group A. No significant adverse effects were reported.
Conclusions: Topical phenytoin dressing is significantly more effective than povidone iodine in accelerating up the healing of diabetic foot ulcers.

Keywords: Diabetic foot ulcer, Phenytoin, Povidone iodine, Wound healing

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterised by persistent hyperglycaemia due to aberrant insulin synthesis, action or both. The global burden of diabetes is steadily increasing, with the International Diabetes Federation (IDF) estimating that a new person dies every seven seconds from diabetes or its complications.[1] Diabetes impacted approximately 463 million people in 2019 and the figure is anticipated to increase to 700 million by 2045.[2] Notably, more than half of the affected population lives in low- and middle-

income countries, with many going untreated. Diabetic foot ulcers are one of the most devastating and expensive consequences of diabetes. DFUs are a substantial and growing global health concern, affecting roughly 15% of all diabetic patients over their lifetime.[3] Chronic wounds are the major cause of non-traumatic lower extremity amputations and they are associated with high morbidity, mortality and healthcare expenditures. The complex pathophysiology of DFUs, which includes peripheral neuropathy, vascular insufficiency and an increased risk of infection, sometimes leads to a lengthy healing phase, offering a significant therapeutic challenge for clinicians. Hyperglycemia also inhibits leukocyte function, lowers cytokine and growth factor production and slows angiogenesis, all of which lead to chronic, non-healing wounds.

The current standard of care for DFU management is a comprehensive strategy that includes rigorous wound debridement, pressure relief from the affected foot and strict infection control. While these strategies are beneficial, they may not always be adequate to address the underlying inadequacies in the healing process. As a result, there is a continuous need for effective adjuvant therapy, such as the use of Povidone-iodine and phenytoin, to expedite wound closure while lowering the risk of unfavourable consequences.

PVP-I is a popular broad-spectrum topical antiseptic in wound care. It is extremely efficient against a wide range of pathogens, making it an appealing option for preventing and treating infection in diabetic wounds.[4] However, there have been concerns expressed about its potential for cellular cytotoxicity, which could affect fibroblast and keratinocyte function.[5] As a result, prolonged or high-concentration use may slow wound healing. Hence the need for an alternative has been proposed. Phenytoin, a commonly used epilepsy medication, has emerged as a promising alternative for wound healing. Its significance in causing gingival hyperplasia in chronic phenytoin users highlighted its proliferative effects on connective tissues.[6]

Phenytoin promotes fibroblast proliferation, collagen synthesis, angiogenesis and granulation tissue development while also having antibacterial properties.[7] These features make topical phenytoin a desirable and cost-effective choice for encouraging wound healing, particularly in resource-constrained environments.[8]

Despite their individual strengths and widespread use, no rigorous clinical investigation has directly compared topical phenytoin to povidone-iodine dressing. A randomised controlled trial is required to give high-quality data for decision-making.

The purpose of this study was to compare the efficacy of topical phenytoin dressing to povidone iodine dressing in the healing of diabetic foot ulcers in a randomised controlled trial style. The study's goal was to analyse the reduction in ulcer size over a 14 days period utilizing each dressing technique, including granulation tissue formation, the presence of slough and overall clinical response to treatment.

METHODS

The current randomized controlled trial was conducted according to CONSORT guidelines (Figure 1) in the Department of General Surgery at Navodaya Medical College Hospital and Research Centre, Raichur, between July 2023 and December 2024. The study aimed to compare the efficacy of topical phenytoin versus povidone iodine dressings in healing diabetic foot ulcers. The study protocol was approved by the institutional ethical committee and written informed consent was obtained from all participants.

Sample size estimation

The present study was comprised of 124 patients taking insulin or oral hyperglycaemic agents suffering from diabetic foot ulcers which are not healed and for which debridement is required for healing patients divided into two groups of 62 each. Assuming an 80% healing response in the phenytoin group and 20% in the povidone iodine group with 9% margin of error, the minimum sample size was calculated to be 62 per group.

Blinding and bias control

To minimize bias, both groups received the identical antibiotic regimen. All dressings and assessments were carried out by trained staff under the direction of the primary investigator. Although blinding participants was not possible due to differences in the appearance and smell of the dressings, outcome assessors were blinded to group assignment.

Inclusion and exclusion criteria

The study comprised 124 patients with type 2 diabetes mellitus who had grade 1 or 2 diabetic foot ulcers (according to the Wagner-Meggitt classification).[9] The study also included individuals on insulin or oral hypoglycemics who had non-healing ulcers that needed to be debrided. Patients with ischaemic limb, associated osteomyelitis, cellulitis, diabetic ketoacidosis, exposed bone or haemoglobin levels less than 10 gm% are excluded from the study.

Randomization

Patients were allocated using computer-generated random numbers. Allocation concealment was ensured using the serially numbered opaque sealed envelope (SNOSE) technique. Patients were randomized into two equal groups. Group A received phenytoin dressing and Group B received povidone iodine dressing.

Intervention and follow-up

All patients underwent thorough clinical evaluation, including documentation of demographics, ulcer characteristics (site, size, base, margin, slough and discharge), comorbidities, neuropathy assessment and duration of diabetes. Routine investigations included complete blood count, HbA1c, fasting blood glucose, renal function tests, wound culture and sensitivity and imaging if necessary.

For group A, a sterile gauze soaked in a mixture of 100 mg phenytoin sodium and 5 ml normal saline was applied to the ulcer. For larger wounds, the dosage was adjusted to 150 mg for every 5 cm² increase in area. In Group B, the ulcers were dressed with sterile gauze soaked in water-soluble povidone iodine solution. Dressings were changed every alternate day or daily in case of exudative wounds.

Ulcer area measurement

Ulcer dimensions were measured using graph paper grid tracing technique on Days 0, 3, 5, 7, 10 and 14. Each traced area was quantified in mm². The mean percentage reduction in ulcer area was calculated.

Outcome measures

Primary outcome was the percentage reduction in ulcer area at 14 days. Secondary outcomes included granulation tissue formation, presence of slough, ulcer discharge and overall clinical response.

Statistical analysis

Data were entered into Microsoft Excel and analyzed using standard statistical software. Continuous variables were expressed as means and standard deviation and compared using independent or paired t-tests. Categorical variables were analyzed using chi-square or Fisher's exact test. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline demographic parameters such as age, gender, socioeconomic status, duration of diabetes, ulcer site and presence of comorbidities like hypertension and neuropathy were comparable between the two groups (p > 0.05 for all parameters).

The mean ulcer area on day 0 was similar in both groups. 35.67 mm² in Group A and 35.92 mm² in Group B (p=0.942). On day 14, the mean ulcer area was 28.83 mm² in Group A and 31.93 mm² in Group B (Figure 1). The reduction in ulcer area was statistically significant in both groups, but greater in Group A (mean reduction=6.03 mm²) compared to Group B (mean reduction=3.99 mm²) with p value 0.004). The mean percentage reduction in ulcer area was significantly higher in Group A (22.03±9.86%) than in Group B (13.85±5.62%) with p value 0.001 (Figure 2). This indicates superior healing efficacy of topical phenytoin dressing over povidone iodine.

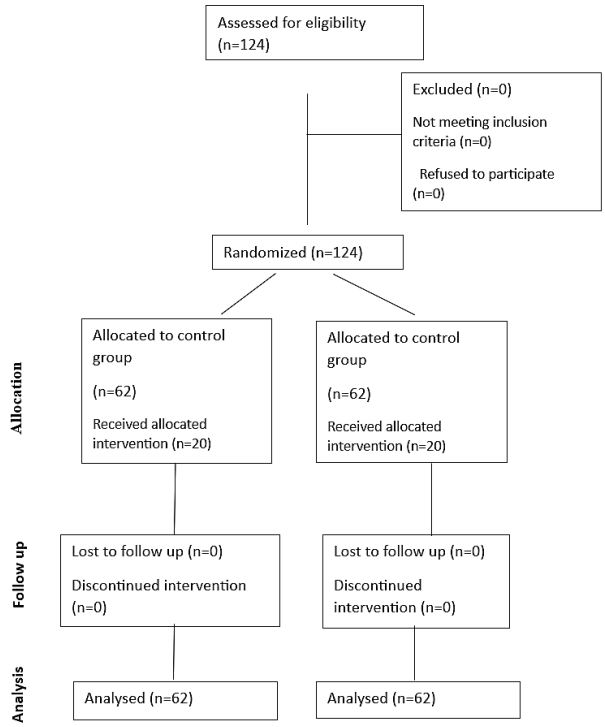

Figure 1: CONSORT flowchart.

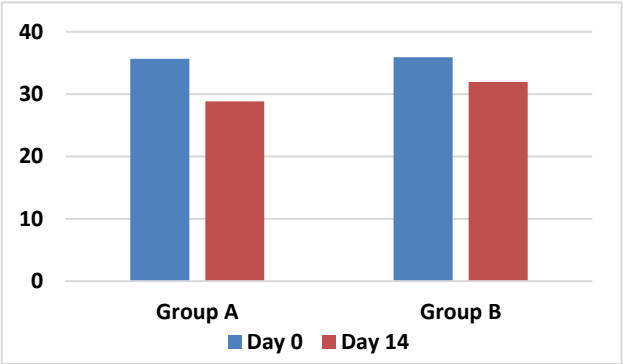

Figure 2: Comparison of Group A and Group B with mean percent reduction in area of ulcer from day 0 and day 14 by independent t test.

Regarding slough clearance, 95.2% of patients in Group A had complete slough clearance by Day 14, compared to 82.3% in Group B (Figure 3). Granulation tissue formation was more robust and appeared earlier in the phenytoin group. No significant adverse effects were reported in either group and patient compliance was high. There was no significant difference in ulcer healing based on age, gender or site of ulcer. However, factors such as presence of neuropathy, spontaneous onset and longer duration of diabetes were associated with delayed healing across both groups.

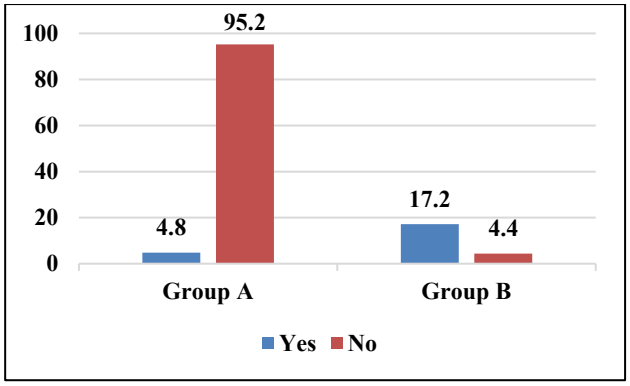

Figure 3: Comparison of mean area of ulcer on day 0 and day 14 in Group A and Group B by dependent t test.

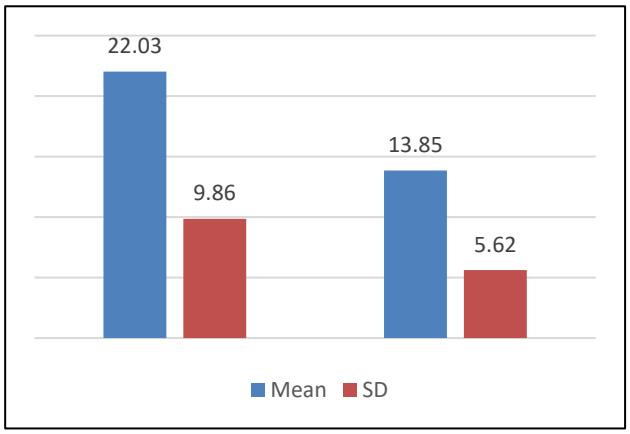

Figure 4: Comparison of Group A and Group B by status of slough at day 14.

Table 1: Baseline demographic data of study participants.

Parameter	Group A (Phenytoin) (n=62)	Group B (Povidone Iodine) (n=62)	P value
Mean age (years)	Comparable	Comparable	>0.05
Gender (M/F)	Comparable	Comparable	>0.05
Socioeconomic status	Comparable	Comparable	>0.05
Duration of diabetes	Comparable	Comparable	>0.05
Ulcer site	Comparable	Comparable	>0.05
Hypertension (%)	Comparable	Comparable	>0.05
Neuropathy (%)	Comparable	Comparable	>0.05

DISCUSSION

Diabetic foot ulcers are a major complication of diabetes mellitus, frequently requiring extended hospitalization, infection and, in extreme cases, amputation.[10] Thus, optimizing wound care procedures is critical for accelerating healing and reducing complications. Our findings showed that topical phenytoin greatly increased the healing rate of DFUs as compared to povidone iodine. The phenytoin group demonstrated a greater mean reduction in ulcer size, pace of granulation tissue formation and overall healing time. Phenytoin, which was formerly used as an anticonvulsant, has showed great potential in wound care because to its secondary pharmacological effects.[11] It is thought to stimulate neovascularization and epithelialization, which are critical steps for tissue regeneration.[12] The anti-inflammatory and antibacterial properties of phenytoin contribute to a healing environment. Furthermore, phenytoin's antibacterial effects against common wound infections like *Staphylococcus aureus* and Pseudomonas species support its use in infected ulcers.[13]

Phenytoin lowers exudate development, as demonstrated in our study, where wounds treated with phenytoin had less slough and exudate than wounds treated with povidone iodine. Our findings are consistent with studies by Rhodes et al, which demonstrated faster healing times and better granulation tissue in wounds treated with topical phenytoin.[14] A study by El-Nahas et al concluded that topical phenytoin will amplify wound healing in diabetics with foot ulcers due to neuropathy and it is safe which is as same as our study.[15] And also, A randomized control study conducted by Gunasekaran et al on the efficacy of phenytoin dressing in healing of diabetic ulcer stated that phenytoin group had superior rate of formation of granulation tissue.[16]

Povidone iodine, on the other hand, is a popular antiseptic due to its broad-spectrum antibacterial properties.[17] However, its cytotoxic effects on fibroblasts and keratinocytes may inhibit wound healing, particularly in chronic ulcers such as DFUs.[18] In our investigation, povidone iodine provided acceptable microbiological control, but epithelial regeneration and granulation tissue formation were slower. This is consistent with other results, which suggest that while povidone iodine may be useful in infected wounds, long-term use can impair tissue regeneration. Importantly, no significant adverse effects were noted in either group, indicating that both dressings are safe for topical use. However, the patients treated with phenytoin reported greater satisfaction due to faster pain relief and visible improvements in wound condition.

Limitations include the short duration of the study, which may not capture long-term outcomes or recurrence rates. Additionally, the open-label nature of the intervention could introduce bias, although efforts were made to blind the outcome assessor. Further multicentric studies with longer follow-up, cost-effectiveness analysis and quality-of-life assessments are warranted to confirm these findings and establish standardized protocols for phenytoin use in wound care.

CONCLUSION

When compared to standard povidone iodine dressing, topical phenytoin treatment accelerates healing in diabetic foot ulcers. It improves granulation tissue production, lowers wound area more effectively and is well tolerated by patients. Phenytoin is a useful addition to diabetic wound care procedures due to its low cost, convenience of availability and few side effects.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Hemanth PA, Ramappa K, Bhalki N, Rao PT, Revanth PA, Patil SP, et al. Comparative evaluation of topical phenytoin versus povidone iodine dressing in the healing of diabetic foot ulcers: a randomized controlled trial. Int Surg J 2025;12:1924-8.