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Original Research Article

A Comparative Study Between Topical Phenytoin Sodium Dressing vs Povidone Iodine Dressing in Diabetic Ulcer

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Conflict of interest: Nil

Abstract:

Background: Diabetic foot ulcers (DFUs) are a major complication of diabetes, often leading to infection, delayed healing, and limb amputation. Identifying effective and affordable dressing is essential to improve clinical outcomes, particularly in resource-limited settings.

Aim: To compare the effectiveness of topical Phenytoin Sodium dressing with 5% Povidone Iodine dressing in the management of diabetic ulcers.

Methodology: A randomized comparative clinical study was conducted on 100 patients with Wagner Grade I–II diabetic ulcers at IGIMS, Patna, between April 2023 and March 2025. Participants were randomly allocated into two groups: Phenytoin Sodium (n = 50) and Povidone Iodine (n = 50). Dressings were applied on alternate days, with an 8-week follow-up period. Healing progression, infection status, and time to 50% and complete wound healing were recorded. Statistical analysis was performed using SPSS version 25.0.

Results: Patients treated with Phenytoin Sodium dressing demonstrated significantly faster healing, with a shorter mean time to 50% wound reduction (11.3 vs. 14.9 days) and complete healing (25.1 vs. 31.6 days) compared to the Povidone Iodine group. A lower proportion of infections was observed in the Phenytoin group (20%) compared to the Povidone Iodine group (34%), although this difference did not reach statistical significance. Baseline demographic and clinical characteristics were comparable between the groups.

Conclusion: Topical Phenytoin Sodium dressing is more effective than Povidone Iodine in accelerating wound healing in diabetic ulcers and demonstrates a clinically favorable trend toward reduced infection, making it a useful and cost-effective option in routine clinical practice.

Keywords: Diabetic foot ulcer, Phenytoin Sodium, Povidone Iodine, wound healing, infection rate.

Introduction

Diabetic foot ulcers (DFUs) are among the most difficult and disabling complications of diabetes mellitus that play a significant role in morbidity, health care spending, and reduced quality of life (Yadwadkar et al., 2023) [12]. The worldwide risk of diabetic patients developing foot ulcers is between 15 and 25 percent, and most develop into infection, gangrene, and amputation of the lower limb until proper management is observed their clinical management is frequently complicated and long-term due to a multifactorial pathogenesis of diabetic ulcers which involves peripheral neuropathy, peripheral arterial disease, impaired wound healing, immunological dysfunction, and repeated trauma (Maji et al., 2023) [6]. With the current upward trend in diabetes prevalence in the world and particularly in developing low- and middle-income nations, health care systems have been burdened by DFUs, giving rise to the need to adopt effective and cost-effective therapeutic

measures that can help in speeding up wound healing, as well as minimizing complications (International Diabetes Federation, 2021) [5].

The wound healing process of diabetic patients is affected pathologically as hyperglycemia causes microvascular damage, impaired migration of leukocytes, decreased production of collagen, and lower angiogenesis (Brownlee, 2001; Delamaire et al., 1997) [2,3]. These impairments postpone the conventional stages of wound healing (hemostasis, inflammation, proliferation, and remodeling) to create non-healing chronic ulcers (Falanga, 2005) [4]. In addition, polymicrobial flora is commonly colonized in DFUs, which predisposes them to infection and further postpones wound healing. Therefore, the choice of an optimal dressing material is important, and it determines the level of moisture balance, microbial control, tissue granulation, and epithelialization. Povidone Iodine and Phenytoin Sodium are only some of the many topical agents available, but evidence on their comparative use as wound-modulating agents is limited, especially in resource-limited clinical environments (Qadirifard et al., 2024) [7].

Povidone iodine, a complex of iodine and an antimicrobial agent combined with a solubilizing agent, is an antiseptic dressing that has been popularly used over the decades as a broad-spectrum antimicrobial agent (Baig et al., 2022) [2]. It works well with bacteria, viruses, fungi, and protozoa; hence it finds application in infected or contaminated wounds. But there have been concerns about its possible cytotoxicity on fibroblasts and keratinocytes, which will inhibit the formation of granulation tissue and slow epithelialization in chronic wounds. In spite of these shortcomings, povidone iodine is still one of the dressing agents widely applied in the management of diabetic foot, particularly in primary and secondary care facilities, because of its low cost and simplicity of application. Its proven efficacy in reducing microbial load makes it an ideal first-line agent in the management of local infection prior to the initiation of advanced therapies.

Phenytoin (a popular anticonvulsant), in contrast, has emerged as a potential topical wound healing agent. Phenytoin was studied in the past as a proliferative agent of fibroblasts and connective tissue, although its initial use was in targeting systemic therapy and inducing gingival hyperplasia in patients (Qadirifard et al., 2024) [7]. Topical phenytoin sodium has been shown to exhibit a number of positive effects in wound healing such as amplified fibroblast growth, amplified collagen deposition, induction of granulation tissue growth and diminished inflammatory exudates. Research indicates that phenytoin could have weak antibacterial effects and also could help to reduce pain in the ulcer. These characteristics underscore its potential as a relatively cheap, easy-to-use, and safer alternative to traditional antiseptic dressings over chronic wounds, especially diabetic ulcers (Maji et al., 2023) [6]. Nevertheless, in spite of the encouraging results, there is a low penetration of phenytoin in clinical practice, mainly because there is less extensive large-scale comparative investigation and because standardized preparations are not available.

Since the increasing demand for diabetic foot activity necessitates evidence-based, cost-effective, and patient-reliant treatments for diabetic ulcers, comparative analysis of topical phenytoin sodium dressing and povidone iodine dressing becomes essential. These comparative researches are necessary to ascertain which form of modality has quicker healing, greater granulation tissue formation, lower occurrence of infection, and greater patient outcome. Besides, determining which dressing is more effective can greatly shorten the time of hospitalization, the use of antibiotics, and the possibility of amputation, which are directly related to physical, psychological, and socioeconomic morbidity in patients. This paper, therefore, aims to evaluate and compare the therapeutic effectiveness of these two popular topical agents in the treatment of diabetic ulcers with the view of shedding light on their associated strengths and weaknesses.

This is because in India, where diabetic foot ulcer is a widespread issue and access to more advanced wound care modalities is still lacking in most areas, the need to have a low-cost but effective method of treatment is especially acute. Phenytoin sodium and povidone iodine are cheap, easily obtainable, and easy to apply and thus they are the most appropriate option in terms of their universal usage in both rural and urban medical centres. Such a systematic comparison of the two might help clinicians to use the most suitable therapy based on clinical evidence other than tradition and convenience. The study also has implications on the health of the population, where better management of ulcers can be of significant benefit to the lower limb amputation rate, which, despite being lower in low- and middle-income countries, is disproportionately high among diabetic populations in the countries.

Methodology

Study Design: This study was designed as a randomized comparative clinical study conducted to evaluate the effectiveness of Topical Phenytoin Sodium Dressing versus Povidone Iodine Dressing in the management of diabetic ulcers.

Study Area: Department of General Surgery, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India.

Study Duration: The study was conducted over a two-year period, from April 2023 to March 2025,

including patient recruitment, intervention, and an 8-week postoperative follow-up for each participant.

Study Participants

Inclusion Criteria

1. Adults aged 18–70 years with confirmed Type 2 Diabetes Mellitus (controlled; HbA1c ≤ 7%).
2. Single diabetic ulcer measuring 5–15 cm in largest dimension.
3. Ulcers classified under Wagner Grade I or II.
4. Willingness to provide written informed consent.

Exclusion Criteria

1. Severe vascular insufficiency (ABI < 0.5).
2. Radiological evidence of osteomyelitis.
3. Patients receiving immunosuppressive therapy.
4. Known hypersensitivity to phenytoin or povidone iodine.
5. Pregnant or lactating women.
6. Deep infections or septic arthritis.
7. Unwillingness or inability to comply with follow-up.
8. Patients requiring advanced management for co-morbid systemic illnesses (CKD, CLD, etc.).

Sample Size: A total of 100 patients were enrolled and randomly allocated into two equal groups using a computer-generated randomization system (random.org):

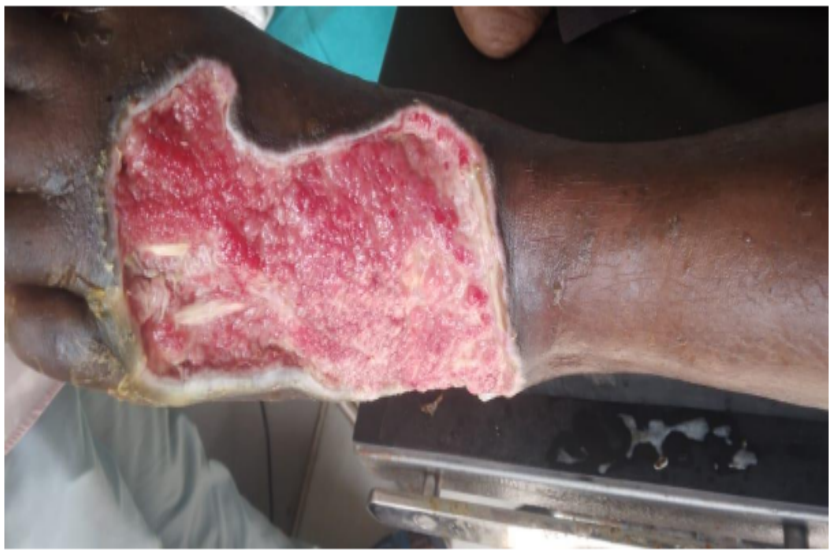
- **Group A –** Phenytoin Sodium Dressing (n = 50)
- **Group B –** 5% Povidone Iodine Dressing (n = 50**)**

Procedure: After screening based on inclusion and exclusion criteria, eligible patients were enrolled following informed consent. Detailed history-taking and clinical examination were performed, including ulcer assessment for size, location, depth, granulation, exudate, and neuropathy. Baseline investigations included CBC, fasting and postprandial blood glucose, HbA1c, LFT, KFT, PT/INR, viral markers, and X-ray evaluation. Systemic optimization was ensured through strict glycemic control, often requiring insulin therapy adjusted to daily blood glucose readings. Comorbidities such as hypertension and hyperlipidemia were managed appropriately, and nutritional support with smoking cessation counseling was provided.

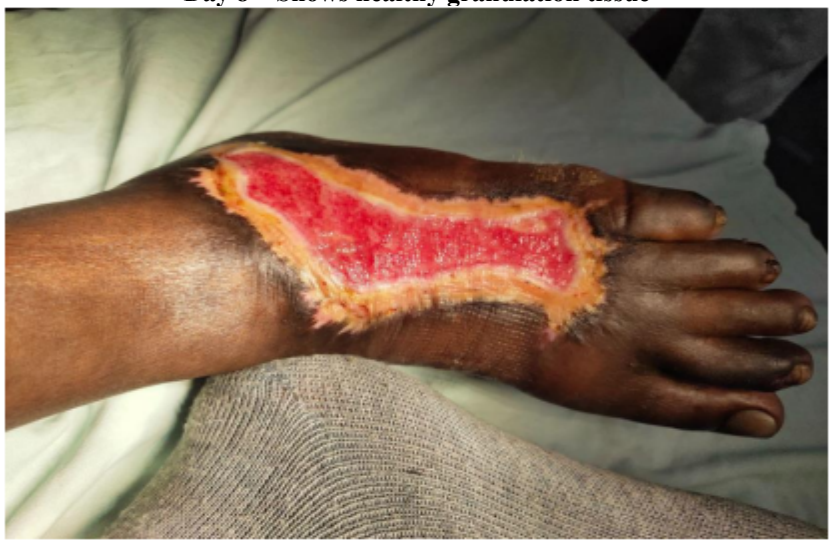
Randomization assigned patients to either the phenytoin group or the povidone iodine group. Initial wound swab cultures were taken, followed by thorough surgical debridement to remove necrotic tissue until fresh bleeding was evident.

Group A received dressing with sterile gauze soaked in Topical Phenytoin Sodium Injection, while Group B received 5% Povidone Iodine Dressing. Dressings were changed every alternate day. Wound tracing, photographs, and measurements were performed every 8 days. Repeat swab cultures were taken on Day 4 and subsequently until negative. Follow-up continued in OPD until complete wound healing or completion of the 8-week study period.

Day 1 - Post debridement dressing done with Phenytoin sodium



Day 8 – Shows healthy granulation tissue



Day 24 - >75% healthy granulation tissue formed

Note: Patient was further planned for skin grafting after swab culture was found to be sterile

Statistical Analysis: Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± SD and compared using the student's t-test. Categorical data were compared using the Chi-square test or Fisher's exact test. Healing time was analyzed using Kaplan–Meier survival curves, and logistic regression was applied to identify independent predictors of ulcer healing. A p-value < 0.05 was considered statistically significant.

Result

As demonstrated in table 1, the distribution of patients in the two dressing groups was comparable, with no significant bias in the distribution of age. The most patients in the two groups were found to be the 51–60 years group, with 22 and 19 patients respectively, after which there was the 6170 years group, with 16 and 17 patients each. The 41-50 years age group had a similar pattern with 10 patients having Phenytoin Sodium and 11 having Povidone Iodine. The least representation was in the age group of 71 to 80 years, which had 2 patients in Phenytoin Sodium group and 3 in Povidone Iodine group. In general, the table indicates the healthy balance of the age sample between the two treatment modalities.

Table 1: Association between Age Group and Dressing Type

Age Group (Years)	Phenytoin Sodium (n)	Povidone Iodine (n)
41–50	10	11
51–60	22	19
61–70	16	17
71–80	2	3

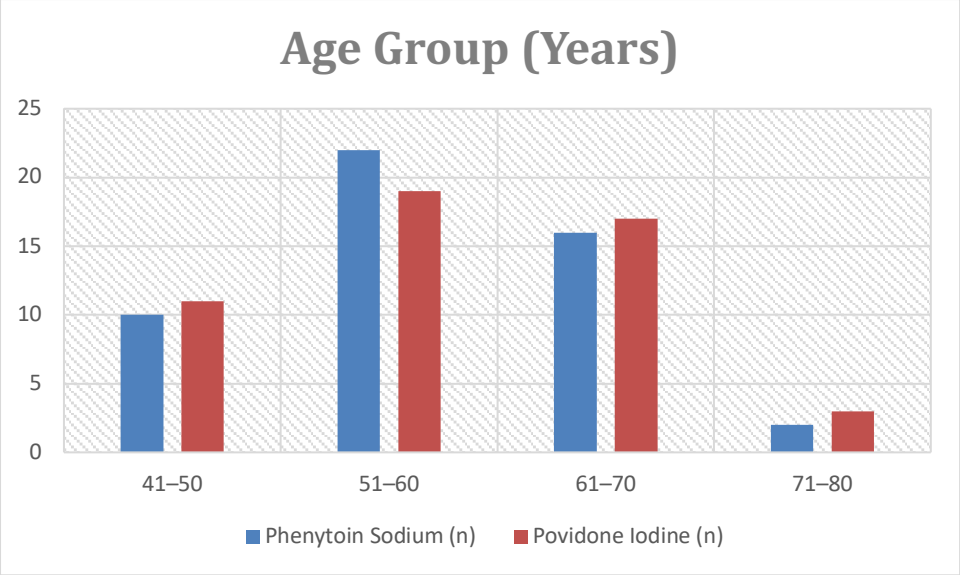


Figure 1: Age Group and Type of Dressing

As may be observed in Table 2, the distribution of the types of dressing between the genders is almost identical meaning that there is no significant preference or difference in the way the dressing is distributed among genders. In female participants, 22 were assigned to Phenytoin Sodium dressing and 21 to Povidone Iodine dressing, and this represents an equal allocation. On the same note, there were 28 males who were treated with Phenytoin Sodium and 29 males treated with Povidone Iodine, which also showed an almost equal ratio. On the whole, it can be stated that the dressing types were equally applied in all genders, which also makes the groups comparable.

Table 2: Association between Gender and Dressing Type

Gender	Phenytoin Sodium (n)	Povidone Iodine (n)
Female	22	21
Male	28	29

Table 3 presents the comorbidity rates in patient patients who had used Phenytoin Sodium and Povidone Iodine dressings, which suggests the existence of a relatively similar trend between both groups. Most patients in both groups did not have any comorbid conditions although in the Phenytoin Sodium group (25) was slightly higher compared to the Povidone Iodine group (21). The most prevalent comorbidity in either group was hypertension (HTN) with an equal percentage proportion found in all combinations (HTN with dyslipidemia, CKD, IHD, and obesity). The presence of comorbidities in individual conditions such as CKD, dyslipidemia, and IHD was similarly equal in the two dressing groups indicating that the comorbidities were not skewed to either of the two treatment modalities.

Table 3: Association between Comorbidities and Dressing Type

Comorbidity	Phenytoin Sodium (n)	Povidone Iodine (n)
CKD	2	2
Dyslipidemia	4	3
HTN	7	8
HTN, CKD	1	2
HTN, Dyslipidemia	5	5
HTN, IHD	3	5
HTN, Obesity	0	1
IHD	2	3
None	25	21
Obesity	1	0

Table 4 indicates the relationship between the status of smoking and the dressing applied in the study. In the group of non-smokers, patients treated with Phenytoin Sodium dressing (n=29) were slightly more than those dressed with Povidone Iodine dressing (n=25). The two dressing dressings were equally distributed among smokers however, with a little fewer smoker receiving Phenytoin Sodium

dressing (n=21). On the whole, the table shows that the frequency of dressing types in smoking categories is quite equal, and there are no significant differences in the dressing styles that are used by smokers and non-smokers.

Table 4: Association between Smoking Status and Dressing Type		
Smoking Status	**Phenytoin Sodium (n)**	**Povidone Iodine (n)**
Non-Smoker	29	25
Smoker	21	25

Table 5 indicates that the wound treated with Phenytoin Sodium recovered much more rapidly than the wound treated with Povidone Iodine in either of the endpoints measured. The average days taken to reach 50 percent healing were significantly lower in the Phenytoin group (11.3 ± 2.3 days) than in the Povidone Iodine group (14.9 ± 2.9 days), with a highly significant p-value of 0.001. Equally, the mean time to heal was lower in Phenytoin group (25.1 ± 3.9 days) as compared to Povidone Iodine group (31.6 ± 4.5 days) with a statistically significant p-value of 0.002. These results suggest that Phenytoin Sodium is significantly more useful in the process of accelerating wound healing.

Table 5: Healing Endpoints			
Healing Parameter	**Povidone Iodine (n=50)**	**Phenytoin Sodium (n=50)**	**p-value**
Mean Days to 50% Healing	14.9 ± 2.9	11.3 ± 2.3	0.001 **
Mean Days to Complete Healing	31.6 ± 4.5	25.1 ± 3.9	0.002 **

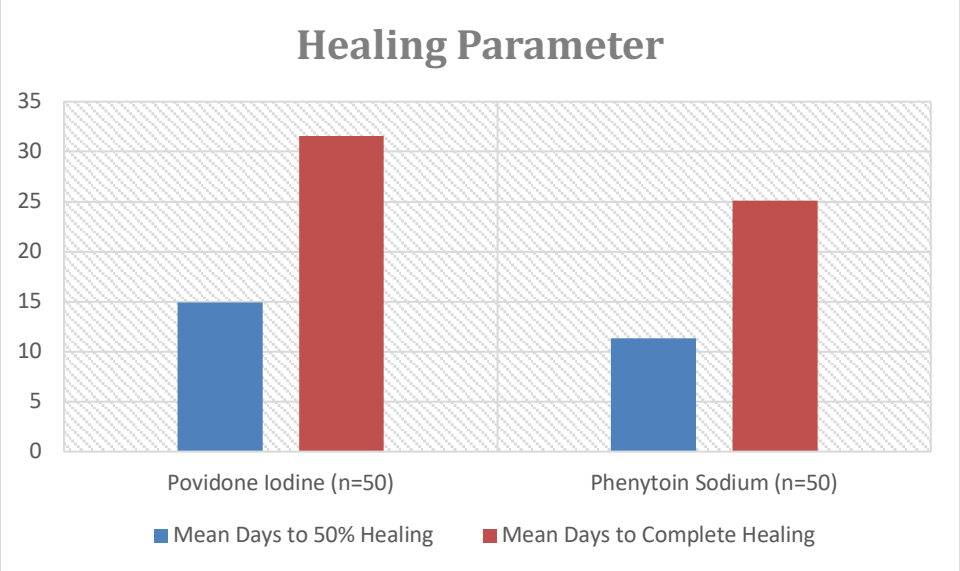


Figure 2: column chart of "mean days to 50% healing" and "mean time to complete healing," with error bars (± standard deviation).

Table 6 indicates that the Povidone Iodine group had a higher rate of infection compared to the Phenytoin Sodium group. Infection was observed in 34% (17 out of 50) of patients treated with Povidone Iodine, whereas only 20% (10 out of 50) of patients in the Phenytoin Sodium group developed infection. Conversely, a higher proportion of patients in the Phenytoin Sodium group remained infection-free (80%, 40 out of 50) compared to the Povidone Iodine group (66%, 33 out of 50). On Chi-square analysis, this difference did not reach statistical significance ($\chi^2 = 1.83$, $p = 0.17$); however, a clinically relevant trend toward reduced infection was observed in patients treated with Phenytoin Sodium dressing.

Table 6: Infection Rate			
Infection Status	**Povidone Iodine (n = 50)**	**Phenytoin Sodium (n = 50)**	**p-value**
Yes	34% (17/50)	20% (10/50)	0.17
No	66% (33/50)	80% (40/50)	

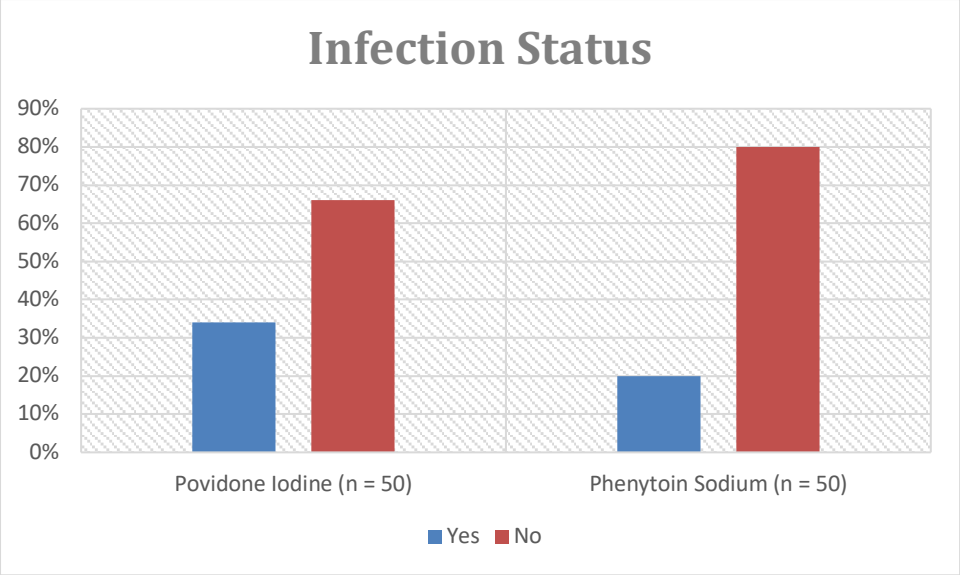


Figure 3: Infection rates in types of dressings

Discussion

The present study compared the effectiveness of topical Phenytoin Sodium dressing and Povidone Iodine dressing in the management of diabetic ulcers, with emphasis on healing kinetics, granulation tissue formation, infection control, and overall clinical outcomes. As both groups were demographically and clinically comparable with respect to age distribution, gender, comorbidities, smoking status, and Wagner ulcer grading, the observed differences in outcomes can be largely attributed to the therapeutic effects of the dressing modalities rather than baseline disparities.

The findings of this study demonstrate that topical Phenytoin Sodium significantly enhanced key wound-healing parameters, including earlier granulation tissue formation, faster 50% wound size reduction, and shorter overall healing duration. The mean time to appearance of healthy granulation tissue was significantly shorter in the Phenytoin group (7.54 ± 2.30 days) compared to the Povidone Iodine group (9.94 ± 2.35 days). These results are consistent with the observations of Tabana et al. (2024) [10], who reported 8 days earlier onset of granulation tissue in Phenytoin-treated ulcers compared to conventional dressings. The beneficial effects of Phenytoin may be attributed to its ability to stimulate fibroblast proliferation, collagen synthesis, and neovascularization, thereby optimizing the early phases of wound healing.

In addition, Phenytoin demonstrated superior performance in terms of wound size reduction and complete healing time. In the present study, 50% wound reduction was achieved significantly earlier in the Phenytoin group (11.36 ± 2.78 days) than in the Povidone Iodine group (14.18 ± 2.95 days), and complete healing occurred sooner in the Phenytoin group (25.26 ± 4.78 days vs. 30.92 ± 5.15 days). These findings are in agreement with Adana et al. (2025) [1], who reported greater wound area reduction in Phenytoin-treated patients, and with Singhal et al. (2025) [8], who observed improved granulation coverage when Phenytoin was used alongside conventional dressings. Such consistency across studies reinforces the role of Phenytoin as an effective wound-healing adjunct.

Infection control remains a critical determinant of prognosis in diabetic ulcers. In the present study, a lower proportion of infections was observed in the Phenytoin group (20%; 10/50) compared to the Povidone Iodine group (34%; 17/50). However, on Chi-square analysis, this difference did not reach statistical significance ($p = 0.17$). Despite the lack of statistical significance, a clinically favorable trend toward reduced infection was evident in the Phenytoin group. Similar trends have been reported by Sonker et al. (2024) [9], who observed a greater reduction in positive wound cultures with Phenytoin dressing compared to Betadine. The reduced infection rates associated with Phenytoin may be indirectly related to accelerated granulation and epithelialization, which limit the duration of tissue exposure and bacterial colonization. In contrast, prolonged use of Povidone Iodine, despite its broad antimicrobial action, has been associated with cytotoxic effects on fibroblasts and keratinocytes, potentially delaying granulation and epithelialization.

The findings of the present study are further supported by reports from Vijayendra et al. (2024) [11] and Maji et al. (2023) [6], who documented faster healing rates, shorter dressing duration, and improved clinical outcomes with topical Phenytoin compared to conventional wound care. The reproducibility of these findings across diverse clinical settings strengthens the evidence supporting

the therapeutic value of Phenytoin in diabetic ulcer management.

One potential limitation of the present study was the slightly smaller baseline ulcer size observed in the Phenytoin group (1.66 ± 0.46 cm) compared to the Povidone Iodine group (1.98 ± 0.50 cm). Nevertheless, Wagner grade distribution was comparable between groups, reducing the likelihood that baseline severity significantly influenced the observed outcomes. Moreover, the magnitude of difference in healing duration, particularly the reduction of overall healing time by more than six days, suggests a true therapeutic advantage rather than an effect attributable solely to baseline variation.

Additionally, lower pain scores observed in the Phenytoin group (5.48 ± 1.03) compared to the Povidone Iodine group (6.28 ± 1.16) may have contributed to improved patient comfort and compliance. Reduced pain is often associated with decreased inflammation and accelerated epithelial healing, which is particularly relevant in outpatient and ambulatory care settings.

The cost-effectiveness, ease of application, and wide availability of Phenytoin further enhance its clinical utility, especially in resource-limited settings where advanced wound care options may not be accessible. Previous studies, including those by Adana et al. (2025) [1], have similarly highlighted the favorable risk-benefit profile of Phenytoin. In contrast, while Povidone Iodine remains useful for initial infection control, its prolonged use may adversely affect cellular processes essential for wound healing.

Overall, the present study aligns with existing national and international evidence, demonstrating that topical Phenytoin Sodium dressing offers advantages over Povidone Iodine in terms of faster healing, enhanced granulation tissue formation, improved patient comfort, and a trend toward lower infection rates. These findings support the use of Phenytoin Sodium as a clinically effective, affordable, and practical dressing option for the management of diabetic ulcers.

Conclusion

The present comparative study demonstrates that topical Phenytoin Sodium dressing is more effective than Povidone Iodine in promoting the healing of diabetic foot ulcers. Both treatment groups were comparable with respect to age, gender, comorbidities, and smoking status, ensuring a balanced assessment of outcomes. Phenytoin consistently showed faster healing, achieving earlier 50% ulcer reduction, quicker granulation tissue formation, and earlier complete wound closure. Although the proportion of infections was lower in the Phenytoin group, this difference did not reach statistical significance; however, a clinically favorable trend toward reduced infection was observed. These benefits may be attributed to Phenytoin's ability to enhance fibroblast activity, collagen synthesis, and tissue regeneration. Given its superior healing profile, affordability, ease of application, and favorable clinical performance, Phenytoin Sodium emerges as an effective and practical dressing option for the management of diabetic ulcers, particularly in resource-limited settings.

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