

Original Research Article

COMPARISON OF WOUND HEALING EFFICACY BETWEEN TOPICAL PHENYTOIN AND POVIDONE-IODINE IN LOWER LIMB ULCERS

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ABSTRACT

Background: Chronic lower limb ulcers provide a substantial clinical challenge owing to protracted healing, elevated recurrence rates, and socioeconomic impact. Topical treatments are essential for facilitating wound healing and preventing infection. Povidone-iodine, a standard antiseptic, provides extensive antibacterial protection, whereas topical phenytoin, typically an anticonvulsant, has demonstrated potential in promoting wound healing by enhancing fibroblast proliferation and collagen synthesis. **Aims:** The study aims to evaluate and compare the efficacy of topical phenytoin and povidone-iodine dressings in patients with lower limb ulcers.

Materials and Methods: A prospective comparative study was conducted over 9 months on 60 patients with lower limb ulcers admitted to the Department of General Surgery. Patients were randomly assigned into two groups of 30 each. Group A received topical phenytoin dressings once daily. Group B received povidone-iodine dressings once daily. Baseline wound dimensions, discharge, pain score, and granulation tissue appearance were recorded on day 0, and reassessed weekly for up to 6 weeks or until complete healing. Exclusion criteria included malignant ulcers, osteomyelitis, immunocompromised states, and uncontrolled diabetes. Data were statistically analyzed using Student's t-test and Chi-square test, with $p < 0.05$ considered significant.

Results: The mean percentage reduction in ulcer area after 4 weeks was substantially greater in the phenytoin group (78.4%) than in the povidone-iodine group (59.2%) ($p < 0.01$). By the second week, 80% of patients in Group A exhibited early formation of healthy granulation tissue, compared to 50% in Group B. Topical phenytoin had higher efficacy in pain relief and discharge control. No notable detrimental effects were observed in either cohort. The average length of complete healing was 24 days in the phenytoin group compared to 33 days in the povidone-iodine group.

Conclusion: Topical phenytoin dressing markedly accelerates healing, improves granulation tissue development, and diminishes pain and exudate in lower limb ulcers compared to povidone-iodine dressing. Integrating it with conventional wound treatment regimens can enhance outcomes and decrease hospital duration.

Keywords: Chronic ulcers, Granulation tissue, Povidone-iodine, Topical phenytoin, Wound healing.

INTRODUCTION

In the field of surgery and wound care, chronic lower leg ulcers are one of the most difficult and

persistent conditions to deal with.^[1] They constitute a substantial public health issue, especially in developing nations, because to their high

prevalence, extended healing duration, and considerable effect on quality of life.^[2]

Lower limb ulcers originate from multiple causes, including trauma, diabetes mellitus, venous insufficiency, peripheral artery disease, and infections.^[3] The persistence of these ulcers frequently arises from compromised local circulation, neuropathy, recurrent infections, and protracted cellular healing processes. Consequently, effective wound treatment is crucial for enhancing functional outcomes and minimizing morbidity.^[4]

The wound healing process is intricate, encompassing inflammation, granulation tissue creation, angiogenesis, collagen deposition, and epithelialization. Any disruption in this cycle may lead to persistent non-healing ulcers.^[5] Conventional wound treatment techniques include infection control, sustaining a moist wound environment, and facilitating granulation tissue development.^[6]

Povidone-iodine is often utilized as an antiseptic owing to its extensive antibacterial range and accessibility among the different topical agents available. It diminishes bacterial burden and inhibits wound infection. Nonetheless, although it is efficient in infection control, research indicates that extended use of povidone-iodine may hinder fibroblast function and postpone wound healing due to its cytotoxic impact on regenerating tissues.^[7,8]

Phenytoin, initially developed as an anticonvulsant medication, has recently garnered interest for its wound-healing capabilities. Numerous clinical and experimental research have shown that the topical use of phenytoin accelerates granulation tissue formation, improves collagen production, stimulates fibroblast proliferation, and promotes neovascularization.^[9]

Moreover, phenytoin exhibits slight antimicrobial properties and diminishes local inflammation, facilitating expedited wound healing. Its affordability, extensive accessibility, and few adverse effects render it a potentially significant agent in wound management, particularly in resource-limited healthcare environments.^[10]

Despite accumulating evidence endorsing the wound-healing efficacy of topical phenytoin, its application has not yet been standardized in clinical practice. Numerous wound care procedures persist in utilizing traditional antiseptics such as povidone-iodine, which may not consistently enhance healing rates. Identifying the agent that yields optimal healing results, expedited pain alleviation, and enhanced granulation tissue production is essential for formulating economical and successful wound care strategies. This study seeks to provide evidence that may impact future wound management practices and enhance healing results for patients with lower leg ulcers by directly comparing two accessible topical medicines in a controlled environment.

Aims and Objectives

- To evaluate and compare the efficacy of topical phenytoin and povidone-iodine dressings in patients with lower limb ulcers.

MATERIALS AND METHODS

The present prospective comparative study was conducted in the Department of General Surgery, Sree Mookamika Institute of Medical sciences, over a period of 9 months. A total of 60 patients presenting with lower limb ulcers of various etiologies were included in the study and informed written consent from all participants.

Patients of both sexes, aged between 18 and 70 years, with chronic or non-healing ulcers of the lower limb were eligible for inclusion. Exclusion criteria comprised patients with malignant ulcers, vasculitic ulcers, osteomyelitis, immunocompromised states, or those with uncontrolled diabetes and peripheral arterial disease. Patients with known hypersensitivity to either phenytoin or povidone-iodine were also excluded from the study.

After a detailed clinical history and examination, relevant investigations such as complete blood count, fasting blood sugar, renal function tests, and wound swab culture were performed. The ulcers were measured in terms of length, breadth, and depth, and the area was calculated using the formula: length × breadth × 0.785 for irregular wounds. The initial wound size was recorded on day 0, and subsequent measurements were made weekly for comparison.

Patients were randomly allocated into two groups of 30 each using a simple random sampling method. Group A received topical phenytoin dressing, and Group B received povidone-iodine dressing. In Group A, commercially available phenytoin sodium powder (100 mg) was sprinkled evenly over the wound surface after proper cleaning with normal saline. The wound was then covered with sterile gauze and secured with a bandage. In Group B, the wound was cleaned with normal saline and then dressed with 5% povidone-iodine solution applied to sterile gauze before bandaging. Dressings were changed once daily under aseptic precautions in both groups.

Patients were evaluated weekly for up to six weeks or until complete wound healing occurred, whichever was earlier. The parameters assessed included reduction in ulcer size, development of healthy granulation tissue, amount of discharge, degree of pain using a visual analogue scale, and presence of infection. Wound cultures were repeated if there were clinical signs of infection. Healing was defined as complete epithelialization of the ulcer surface without discharge or necrotic tissue.

All data were recorded systematically and entered into a predesigned proforma. Statistical analysis was performed using appropriate software. Continuous

variables such as wound area reduction were expressed as mean $\pm$ standard deviation, and comparison between groups was done using Student's t-test. Categorical variables such as presence of granulation tissue and infection control were analyzed using the Chi-square test. A p-value less than 0.05 was considered statistically significant.

RESULTS

Both groups were comparable at baseline in terms of demographic distribution and wound characteristics. There was no statistically significant difference between groups regarding age, sex, ulcer duration, or initial ulcer size, confirming baseline comparability ($p > 0.05$). (Table 1)

Table 1: Demographic Distribution of Patients

Parameter	Group A (Phenytoin) (n=30)	Group B (Povidone-Iodine) (n=30)	p value
Mean Age (years $\pm$ SD)	49.3 $\pm$ 10.6	50.7 $\pm$ 9.8	0.61
Male : Female Ratio	19 : 11	18 : 12	0.79
Mean Ulcer Duration (weeks)	6.2 $\pm$ 2.4	6.5 $\pm$ 2.6	0.64
Mean Ulcer Area (cm ²)	12.4 $\pm$ 3.2	12.1 $\pm$ 3.4	0.78

Topical phenytoin demonstrated a significantly faster rate of ulcer area reduction at each time point compared with povidone-iodine ($p < 0.01$). Most phenytoin-treated ulcers achieved near-complete healing by the fourth to fifth week. (Table 2)

Table 2: Mean Percentage Reduction in Ulcer Area over Time

Duration	Group A (Phenytoin) Mean $\pm$ SD (%)	Group B (Povidone-Iodine) Mean $\pm$ SD (%)	p value
Week 1	22.5 $\pm$ 5.4	14.2 $\pm$ 4.9	0.001 **
Week 2	47.3 $\pm$ 8.6	32.1 $\pm$ 7.5	0.001 **
Week 4	78.4 $\pm$ 10.1	59.2 $\pm$ 9.6	0.001 **
Week 6 / Healing Completion	96.7 $\pm$ 4.2	84.8 $\pm$ 6.3	0.001 **

In both groups, longer ulcer duration was associated with delayed healing. However, phenytoin consistently shortened healing time across all duration categories, indicating a positive correlation between phenytoin use and accelerated wound closure ($p < 0.001$). (Table 3)

Table 3: Correlation between Ulcer Duration and Healing Time

Ulcer Duration at Presentation	Mean Healing Time (Group A) (days)	Mean Healing Time (Group B) (days)	p value
< 4 weeks	20.8 $\pm$ 3.1	29.2 $\pm$ 4.8	0.002 **
4 – 8 weeks	24.5 $\pm$ 4.2	33.4 $\pm$ 5.1	0.001 **
> 8 weeks	28.7 $\pm$ 5.6	37.1 $\pm$ 5.9	0.004 **

Phenytoin-treated ulcers exhibited earlier and more extensive granulation tissue formation, which was statistically significant from the second week onward ($p < 0.05$). (Table 4)

Table 4: Comparison of Granulation Tissue Formation

Week	Healthy Granulation Present – Group A n (%)	Healthy Granulation Present – Group B n (%)	p value
Week 1	14 (46.7%)	8 (26.7%)	0.09
Week 2	24 (80.0%)	15 (50.0%)	0.02 *
Week 3	28 (93.3%)	20 (66.7%)	0.01 *

Phenytoin resulted in significant pain reduction and discharge control compared with povidone-iodine, enhancing patient comfort and compliance ($p < 0.01$). (Table 5)

Table 5: Pain and Discharge Score Comparison

Parameter	Group A (Mean $\pm$ SD)	Group B (Mean $\pm$ SD)	p value
Pain Score (VAS) at Week 2	3.1 $\pm$ 0.9	4.5 $\pm$ 1.1	0.001 **
Discharge Score (0–3 scale) at Week 2	0.8 $\pm$ 0.5	1.6 $\pm$ 0.7	0.003 **

At the end of six weeks, a significantly higher proportion of patients in the phenytoin group achieved complete ulcer healing compared with the

povidone-iodine group ($p < 0.05$). No major complications or adverse reactions were reported in either group. (Table 6)

Table 6: Descriptive analysis of final Outcome

Outcome	Group A (Phenytoin) n (%)	Group B (Povidone-Iodine) n (%)	p value
Complete Healing within 6 weeks	27 (90.0%)	19 (63.3%)	0.02 *
Partial Healing	3 (10.0%)	8 (26.7%)	0.04 *
Persistent Infection	0 (0%)	3 (10.0%)	0.08

DISCUSSION

The current study demonstrated that both groups were comparable at baseline for age, sex distribution, ulcer size, and length, thereby providing consistency in outcome interpretation. The mean age of participants was almost 50 years, with males representing roughly 63% of cases, aligning with the elevated prevalence of lower leg ulcers observed in this cohort.

Topical phenytoin shown significant superiority compared to povidone-iodine in facilitating wound healing. At four weeks, the average percentage decrease in ulcer area was 78.4% in the phenytoin group, in contrast to 59.2% in the povidone-iodine group ($p < 0.001$). By six weeks, full epithelialization was observed in 90% of patients administered phenytoin, whereas only 63.3% of those treated with povidone-iodine had complete healing. These findings are corroborated by Sonker SK et al.^[11] who observed a more significant reduction in ulcer size, enhanced microbiological clearance, and a decreased duration of hospitalization in diabetic ulcers treated with phenytoin.

Phenytoin therapy resulted in earlier and more extensive formation of granulation tissue. By the second week, 80% of patients in the phenytoin cohort exhibited healthy granulation tissue, in contrast to 50% in the povidone-iodine group ($p = 0.02$). By the third week, 93.3% of ulcers treated with phenytoin had well-formed granulation tissue, indicating expedited wound bed preparation. Sandhu DK et al.^[12] also observed a greater percentage of granulation tissue on day 9 in the phenytoin group ($84.36 \pm 10.53\%$) compared to the traditional dressing group ($74.93 \pm 12.0\%$). Vijayendra P et al.^[13] also documented enhanced granulation tissue rates in the phenytoin group.

Phenytoin dressing provided further advantages of pain alleviation and decreased discharge. At two weeks, the average pain score was markedly reduced in the phenytoin group (3.1 ± 0.9) in comparison to the povidone-iodine group (4.5 ± 1.1 ; $p = 0.001$). Discharge ratings were significantly diminished (0.8 ± 0.5 vs. 1.6 ± 0.7 ; $p = 0.003$). These findings align with the results of Ranaivoarijaona GS et al.^[14] who exhibited significantly reduced VAS pain scores on days 7 and 14 in the phenytoin group relative to the povidone-iodine group.

Healing time and ulcer duration were associated; nevertheless, phenytoin sped up recovery in every subgroup. Ulcers aged under four weeks healed in 20.8 ± 3.1 days with phenytoin compared to $29.2 \pm$

4.8 days with povidone-iodine ($p = 0.002$). In ulcers exceeding eight weeks in duration, healing transpired in 28.7 ± 5.6 days inside the phenytoin group, in contrast to 37.1 ± 5.9 days ($p = 0.004$). A robust negative correlation ($r = -0.72$, $p < 0.001$) indicates that phenytoin promotes healing regardless of ulcer chronicity. Singhal P et al.^[15] reported markedly increased granulation tissue production by day 14 in wounds treated with phenytoin compared to those dressed with povidone-iodine.

Both medications were well tolerated, and no significant side effects were seen. Infrequent and temporary small responses, such as irritation or mild burning, occurred sometimes. In contrast to the current study, Singhal P et al.^[15] reported that adverse effects, including skin irritation and pruritus, occurred in only 1 patient (3.3%) within the conventional povidone-iodine group, while mild reactions such as burning sensation and erythema were noted in 2 patients (6.7%) in the topical phenytoin combined with conventional 5% povidone-iodine dressing group.

Furthermore, the results of the current study aligned with those of Sadiq K et al.^[16] who analyzed various studies and reported improved wound healing in 71%, increased granulation tissue in 90%, analgesic benefits in 54%, and antibacterial effects in 75% of studies evaluating phenytoin, with negligible adverse effects. Additionally, Manohar TM et al.^[17] observed a considerably greater reduction in wound surface area, an increased proportion of granulation tissue, and improved pain levels by day 14, as well as a markedly shorter healing duration in the phenytoin group.

The results of this study confirm that topical phenytoin is an effective, safe, and cost-efficient treatment for lower limb ulcers. Its capacity to facilitate quick granulation, diminish ulcer size, alleviate symptoms, and expedite total healing duration renders it a significant therapeutic alternative, particularly in resource-limited healthcare environments.

CONCLUSION

Topical phenytoin dressing markedly improved wound healing relative to povidone-iodine in lower limb ulcers. Patients administered phenytoin exhibited a more rapid decrease in ulcer area, quicker and more robust granulation tissue development, improved pain management and discharge, and a reduced overall healing time. Complete recovery was attained in 90% of individuals with phenytoin, as contrast to 63.3% with povidone-iodine. No negative reactions were

noted. Topical phenytoin is a safe, cost-effective, and efficient option for managing lower limb ulcers, particularly in resource-constrained environments.

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