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Evaluate the Effectiveness of Topical Phenytoin in Promoting Healing of Diabetic Foot Ulcers

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Abstract **Background:** Diabetic foot ulcer is one challenging problem that is associated with significant morbidity and can end with amputation. There are various agents being used for treatment of diabetic foot ulcer, with varying success rates. **Objective and Study:** To evaluate the efficacy of topical phenytoin in promoting wound healing in diabetic foot ulcer. **Methods:** This is a prospective, uncontrolled case series study that was conducted on 12 patients with diabetic foot ulcer. Patients with uncontrolled diabetes, vascular impairment and grade III, IV or V ulcers according to Wagner classification were excluded. Phenytoin was applied as a suspension (crushed phenytoin tablet dissolved in normal saline). The dose of phenytoin was applied according to the surface area of the ulcer. Wound healing was assessed according to the appearance of healthy granulation tissue, reduction in wound size, decrease in exudate and a decreasing pain score. **Result:** At the end of 14 days, the presence of healthy granulation tissue was documented in all of our patients, with reduction of wound exudate and pain score. The overall reduction in ulcer size was more than 60%. For those patients who had later skin grafting, the skin graft was completely taken. **Conclusion:** Based on our study, locally applied phenytoin for diabetic foot ulcers showed promising results in promoting early wound healing, with no local or systemic adverse effects observed.

Key Words Diabetes Mellitus, Diabetic Foot Ulcer, Topical Phenytoin

INTRODUCTION

Most wounds heal without difficulty. However, some wounds are affected by factors that impede their ability to heal, causing them to become chronic and non-healing. Factors affecting wound healing may be intrinsic, extrinsic or both [1,2]. Diabetes is becoming increasingly common worldwide, with approximately 7% of the population affected [3]. About 15% of patients with diabetes will later develop diabetic foot syndrome [4].

Diabetic foot ulcers are associated with significant morbidity and mortality, a high rate of wound infection and a high risk of amputation [5]. Many preventive and therapeutic approaches have been used to manage diabetic foot ulcers. During the last two decades, numerous topical preparations have been introduced for their management. Various agents are used to promote wound healing through the formation of healthy granulation tissue. One non-conventional topical therapy proposed for diabetic foot ulcers is phenytoin [6]. Phenytoin is an anticonvulsant drug used to treat seizures. It acts by blocking sodium transport across nerve membranes, thereby decreasing the rate of conduction. Phenytoin was introduced into therapy in 1937. A common side effect of systemic phenytoin treatment is fibrous overgrowth of the gingiva, with mild skull and skin thickening [7]. In 1958, a clinical study showed that phenytoin promoted gingival wound healing compared with controls. Since then, phenytoin has been used to promote healing in different types of wounds [8]. The effectiveness of topical phenytoin in promoting wound healing in diabetic foot ulcers was evaluated in this study.

Patients and Methods

This was a prospective, uncontrolled case series study conducted in the Department of Plastic Surgery at Al-Shaheed Ghazi Al-Hariri Hospital, Baghdad Medical Complex, from December 2025 to May 2026. A total of 12 patients with diabetic foot ulcers lasting more than six weeks were included. Patients were recruited from the outpatient clinic. All patients underwent a complete medical history, focusing on ulcer duration, chronic illnesses and any

previous surgical or non-surgical interventions for the ulcer. Physical examination focused on the ulcer site and size, limb vascular status and the presence of active infection. Preoperative X-ray and Doppler studies were requested for all patients.

Diabetic foot ulcers were classified according to the Wagner classification system, which grades ulcers based on their depth and the extent of tissue involvement. The classification system is presented in Table 1.

The study focused on patients with chronic diabetic foot ulcers who had not responded to previous nonsurgical treatment and who met the study's eligibility criteria.

Of the 40 patients screened for eligibility as shown in Table 2, 12 patients met the inclusion criteria and were enrolled in the study, whereas 28 patients were excluded because of one or more exclusion criteria, including Wagner grades III-V, abscess formation, poor vascularity, hospital admission or uncontrolled diabetes mellitus (Table 2).

Diabetic foot ulcers were classified according to the Wagner grading system (grades 0-V). Patients with Wagner grades III-V were excluded. The distribution of Wagner grades among the enrolled patients is reported in Table 3.

The effectiveness of topical phenytoin was evaluated according to signs of wound healing, including the formation of new healthy granulation tissue, increased epithelialization of the surrounding skin, decreased wound discharge and reduction in the ulcer's surface area. For patients reporting pain, pain reduction was also included in the evaluation of topical phenytoin effectiveness in treating diabetic foot ulcers. Ulcer size was measured using a plastic sheet as a template to transfer the wound outline onto graph paper. Each complete square and any square more than half covered by the tracing, was counted as 1 cm^2. Squares covering less than half of their area were omitted. All measurements were performed before treatment and two weeks after treatment (Table 4).

METHODS

Written informed consent was obtained from all participants before enrollment, following an explanation of the study objectives, procedures, potential benefits and risks.

Culture and sensitivity swabs were collected and sent for microbiological examination before starting phenytoin application. Appropriate antibiotics were administered according to culture and sensitivity results and antidiabetic treatment was continued for all patients. After removal of slough and cleaning of the ulcer with normal saline, phenytoin suspension was applied. A phenytoin sodium tablet was crushed and dissolved in 5 mL of normal saline to form a suspension. Sterile gauze was then soaked in this suspension, placed over the ulcer and left for 24 hours until the next dressing change.

The dose of phenytoin depended on the surface area of the ulcer, as follows:

- Up to 5 cm^2: 100 mg
- 5-9 cm^2: 150 mg
- 9-15 cm^2: 200 mg
- More than 15 cm^2: 300 mg

Patients were followed weekly and the final wound assessment was performed 14 days after treatment. For

Table 1: Wagner-Meggitt Classification of Diabetic Foot Ulcer

Ulcer grading	Descriptions
Grade 0	No ulcer but high-risk foot
Grade 1	Superficial ulcer
Grade 2	Deep ulcer, no bony involvement or abscess
Grade 3	Abscess with bony involvement (as shown by X-ray)
Grade 4	Localized gangrene e.g. toe, heel etc.
Grade 5	Extensive gangrene involving the whole foot

Grade 1-3 ulcers are termed non-gangrenous ulcers and Grade 4 and 5 ulcers are termed gangrenous ulcers

Table 2: Patient Screening, Eligibility and Enrollment Status

Patient screening status	Number	Percentage
Patients screened for eligibility	40	100
Eligible patients enrolled in the study	12	30
Excluded patients	28	70
Total	40	100

Table 3: Exclusion Criteria and Corresponding Assessment Methods

Exclusion criteria	Assessment
Wagner grades III, IV and V	Clinical assessment and ulcer classification
Presence of an abscess	Clinical examination and relevant investigations
Poor vascularity	Doppler ultrasonography
Uncontrolled diabetes mellitus	Clinical and laboratory assessment
Hospital admission	Clinical status

Table 4: Distribution of Patients According to Wagner Grade of Diabetic Foot Ulcers

Grade of ulcer	Number of patients
Wagner grade 1	8
Wagner grade 2	4
The study was excluded Wagner grade 3,4,5	

patients with large ulcers that did not heal by secondary intention, skin grafting was performed and graft take was assessed on the fifth postoperative day.

RESULTS

The study included 12 patients with chronic diabetic foot ulcers. The mean age was 48.4±5.6 years. Males were more commonly affected than females (8 versus 4). In this study, the mean duration of

The mean duration of the ulcer was 6.3 weeks and the mean ulcer size was 10.4 cm^2. All patients had previously received non-surgical treatment, including local wound care, without response. The most common pathogen isolated from wound cultures was Staphylococcus aureus. The most common ulcer sites were the forefoot (6 patients), dorsum of the foot (3), hindfoot (2) and heel (1).

The reduction in ulcer size was more than 60% and only two patients required split-thickness skin grafts, which were completely taken. All patients showed signs of healing after 14 days of phenytoin application, including healthy granulation tissue and an epithelialized edge, with reduced wound discharge. The formation of healthy granulation tissue, epithelialization and reduction in wound discharge were assessed clinically. These findings were evaluated at the reported follow-up assessment.

The three patients who reported pain showed a reduction in pain score by the seventh day of dressing changes.

All 12 patients experienced transient burning at the application site following topical phenytoin application. The sensation was temporary and resolved spontaneously without specific treatment. No patients discontinued treatment due to this symptom.

Pain was assessed clinically; however, no standardized pain scale or numerical pain scores were documented.

DISCUSSION

The ability of phenytoin to promote wound healing when used topically was reported more than 40 years ago. Many studies have demonstrated its effect on diabetic foot ulcers and other types of ulcers [9,10]. Several studies have shown that topical phenytoin promotes the growth of blood vessels and connective tissue. Phenytoin has also been reported to reduce wound exudate and bacterial load and to promote re-epithelialization. The exact mechanism by which phenytoin induces wound healing is unknown but it may involve increased expression of the gene for platelet-derived growth factor B in macrophages and monocytes, with a net effect of collagenase inhibition [11-14].

The wound-healing effect of phenytoin is associated with minimal systemic absorption and no adverse effects, as reported by Shaw *et al.* [11]. Phenytoin has also been shown to promote wound healing through its antibacterial activity [15]. In this study, phenytoin showed promising results in the treatment of diabetic foot ulcers. All patients showed signs of ulcer healing, including reduced ulcer size, formation of granulation tissue, adequate re-epithelialization and reduced wound exudate. In 10 of the 12 patients, the ulcers healed completely without the need for skin graft coverage. Only two patients required skin grafts because their ulcers were relatively large (>15 cm^2); graft take was excellent in both patients. Pain scores also decreased among patients who reported pain. All patients reported a transient burning sensation when phenytoin was applied.

In this study, phenytoin was used as a suspension prepared by crushing a tablet and dissolving it in normal saline. Phenytoin can also be applied to wounds as a suspension, powder or cream (the latter was not available in Iraq). Some authors who used phenytoin powder reported the development of a white eschar-like coating, which was not observed in our study because we used a phenytoin suspension [16].

In the first study conducted by Simpson *et al.* [17] to evaluate the effectiveness of phenytoin in treating chronic skin ulcers, phenytoin was administered orally. We disagree with their route of administration because oral phenytoin is associated with systemic adverse effects, whereas topical application allows direct local delivery to the wound.

- Topical phenytoin allows direct access of the drug to the wound without the risk of systemic adverse effects. One possible side effect of topical phenytoin reported in two studies is hypertrophic granulation tissue; however, we did not encounter this problem in our study. One significant finding was a reduction in wound surface area after phenytoin application, consistent with Pai *et al.* [10]
- In their double-blind controlled study evaluating the effect of phenytoin on diabetic foot ulcers, a reduction in ulcer size of more than 50% was reported. Our study was consistent with the findings of Jayalal *et al.* [3], who also demonstrated a reduction of more than 50% in diabetic foot ulcer size after phenytoin application. A reduction in pain scores was also noted in our study, consistent with the findings of Jayalal *et al.* [3], who observed a significant reduction in patients' pain scores from the seventh day. Pain reduction with phenytoin may be explained by its membrane-stabilizing effect and reduction of the inflammatory response [18]
- In two of our patients, skin grafting was used to resurface the ulcers because they were large (>15 cm^2) and required graft coverage. Our results showed that the granulation tissue induced by phenytoin supported skin graft take and no cases of skin graft failure were reported. Similar findings were reported by Tauro *et al.* [19], who used topical phenytoin for diabetic foot ulcers and reported a mean graft take of up to 92.31%. A controlled trial by Muthukumaraswamy *et al.* [9], which compared topical phenytoin with a control group in 100 patients with diabetic foot ulcers, showed a mean healing time of 21 days in the phenytoin group, compared with 45 days in the control group ($p<0.05$)
- Although our study did not compare bacterial cultures before and after phenytoin application, the antibacterial effect of phenytoin has been discussed in several studies. Pendes *et al.* [4] reported that 50% of wounds

treated with phenytoin had negative cultures by the seventh day of treatment. Histopathological studies have shown increased lymphocyte infiltration and neovascularization in wounds treated with phenytoin, which may contribute to its antibacterial action [20]

A systematic review by Shaw *et al.* [12] examined the effect of phenytoin in the treatment of diabetic foot ulcers using PubMed/MEDLINE and the Cochrane database. Based on 14 randomized controlled trials, the review found that phenytoin had a moderate effect in treating not only diabetic foot ulcers but also necrotic wounds and varicose leg ulcers.

CONCLUSIONS

Topical phenytoin application for diabetic foot ulcers showed promising results in promoting wound healing and reducing ulcer surface area.

This limitation has been emphasized in the revised Discussion and further studies involving broader patient populations are warranted.

REFERENCES

[1] Grey, Joseph E. *et al.* "ABC of Wound Healing: Wound Assessment." *BMJ*, vol. 332, no. 7536, 2006, pp. 285-288.

[2] Peate, Ian and Wynne Glencross. *Wound Care at a Glance*. 1st Ed., Wiley-Blackwell, 2015.

[3] Jayalal, J.A. *et al.* "Efficiency of Topical Phenytoin on Healing in Diabetic Foot Ulcer: A Randomized Controlled Trial." *International Journal of Scientific Study*, vol. 3, no. 3, June 2015, pp. 84-89.

[4] Pendsey, S.P. "Understanding Diabetic Foot." *International Journal of Diabetes in Developing Countries*, vol. 30, no. 2, April 2010, pp. 75-79.

[5] Price, Annie *et al. ABC of Wound Healing*. 2nd Ed., Wiley-Blackwell, 2022.

[6] Mohan, Paralakshmi Bharathi *et al.* "Role of Phenytoin in Diabetic Foot Ulcer." *Journal of Cutaneous and Aesthetic Surgery*, vol. 13, no. 3, July 2020, pp. 222-225.

[7] Firmino, F. *et al.* "Scientific Production and Applicability of Phenytoin in Wound Healing." *Revista da Escola de Enfermagem da USP*, vol. 48, no. 1, February 2014, pp. 162-169.

[8] Shapiro, M. "A Correlation of Gingival Wound Healing in Non-Epileptic Patients Receiving Diphenylhydantoin Sodium." *Experimental Medicine and Surgery*, vol. 16, no. 1, March 1958, pp. 41-53.

[9] Muthukumaraswamy, M.G. *et al.* "Topical Phenytoin in Diabetic Foot Ulcer." *Diabetes Care*, vol. 14, no. 10, October 1991, pp. 909-911.

[10] Pai, M.R. *et al.* "Topical Phenytoin in Diabetic Ulcer: A Double-Blind Controlled Trial." *Indian Journal of Medical Sciences*, vol. 55, no. 11, November 2001, pp. 593-599.

[11] Shaw, J. *et al.* "The Effect of Topical Phenytoin on Healing in Diabetic Foot Ulcer: A Randomized Controlled Trial." *Diabetic Medicine*, vol. 28, no. 10, October 2011, pp. 1154-1157.

[12] Bhatia, A. and S. Prakash. "Topical Phenytoin for Wound Healing." *Dermatology Online Journal*, vol. 10, no. 1, July 2004.

[13] Carneiro, P.M. and E.T. Nyawawa. "Topical Phenytoin Versus Emsol in the Treatment of Non-Malignant Chronic Leg Ulcer." *East African Medical Journal*, vol. 80, no. 3, March 2003, pp. 124-129.

[14] Sayar, H. *et al.* "Comparison of Efficacy of Topical Phenytoin with Hypericin in Second-Degree Burn Wound Healing: An Experimental Study in Rats." *Medical Science Monitor Basic Research*, vol. 20, March 2014, pp. 36-46.

[15] Anstead, G.M. *et al.* "Phenytoin in Wound Healing." *Annals of Pharmacotherapy*, vol. 30, no. 7-8, July 1996, pp. 768-775.

[16] Kumar, C.Shyam *et al.* "Outcome of Topical Phenytoin in the Management of Traumatic Wound." *Journal of Clinical Orthopaedics and Trauma*, vol. 11, October 2020, pp. S116-S121.

[17] Simpson, G.M. *et al.* "Use of Sodium Diphenylhydantoin in the Treatment of Leg Ulcers." *New York State Journal of Medicine*, vol. 65, no. 7, April 1965, pp. 886-888.

[18] Rituraj *et al.* "Topical Phenytoin: Role in Diabetic Ulcer Care." *International Journal of Interdisciplinary and Multidisciplinary Studies*, vol. 2, no. 4, February 2015, pp. 93-97.

[19] Tauro, L.F. *et al.* "A Comparative Study of Efficacy of Topical Phenytoin vs Conventional Wound Care in Diabetic Ulcers." *International Journal of Molecular Medicine and Science*, vol. 3, no. 8, July 2013, pp. 231-237.

[20] Meena, K. *et al.* "Effect of Topical Phenytoin on Burn Wound Healing in Rats." *Journal of Pharmacy Research*, vol. 4, no. 1, January 2011, pp. 56-59.