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Research Paper

# Topical Phenytoin in Diabetic Foot Ulcers

Medical Science

KEYWORDS :

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## ABSTRACT

*Objective: The efficacy of topical phenytoin in the treatment of diabetic foot ulcers was evaluated in a controlled inpatient study.*

*Research Design and Methods: Fifty patients were treated with topical phenytoin, and 50 patients matched for age, sex, and ulcer areas, depth, chronicity, and infection were dressed with dry sterile occlusive dressing.*

*Results: Both groups improved, but the ulcers treated with topical phenytoin healed more rapidly. Mean time to complete healing was 21 days with phenytoin and 45 days with control. The differences seen were statistically significant (P < 0.05) via the 2 test.*

*Conclusions: Phenytoin appears to be useful as a topical agent in promoting the healing of diabetic foot ulcers.*

**Introduction:**

Topical phenytoin has been reported to be efficacious in the treatment of skin and soft tissue ulcers and wounds of varying etiology (1-7). Because of these encouraging results, we undertook a controlled inpatient trial of phenytoin's effectiveness in the treatment of diabetic foot ulcers.

**RESEARCH DESIGN AND METHODS**

A total of 100 non-insulin-dependent diabetic patients having foot ulcers of type 1 and 2 of Meggitt's (8) clinical classification were included in the study. Patients presenting with gross cellulitis, deep slough, or ischemic gangrene due to major vessel involvement and trophic ulcers were not included. Fifty were treated with topical phenytoin (Punett, Bombay), and 50 served as control subjects. The groups were matched for age, sex, ulcer area, depth, and chronicity . Management of diabetic status and infection was the same in both groups. Diabetes in all patients was controlled with appropriate antidiabetic therapy. Severe diabetic subjects with ketoacidosis and nephropathy were excluded from the study. In patients with clear secondary infection, systemic antibiotics appropriate to the culture and sensitivity data were administered for up to 4 days. Before initiation of phenytoin or control therapy, ulcers were meticulously debrided of all necrotic tissue and slough and cleaned with saline. In the control group, a sterile occlusive dressing was then applied. In phenytoin groups, phenytoin powder was applied in a thin uniform layer to the ulcer surface and a sterile dry dressing applied. In both groups, the same procedure was repeated daily. Assessment of the wounds, including measurement of wound area, wound severity score, overall clinical impression scale, wound culture, and biopsy of the edge

Ulcer area was determined from the transparent grid paper by planimetry. Effect of topical phenytoin and control treatment in percentage reduction of ulcer areas. and E, complete healing. The clinical evaluation of all cases was carried out by the same person. The technique used for taking wound-swab cultures was the same for all patients. Histological examinations of biopsies were done in 12 cases in each group. Biopsy tissue was prepared by standard techniques for both light- and electron-microscopic examination. The pathologist who made the observations was blind to the treatment used. The parameters evaluated included overall assessment of wound repair with specific attention to inflammation, edema, neovascularization, number of patent capillary profiles, connective tissue ( fibroblast, collagen), and epithelialization. Each parameter was scored 0 (none) to + + + (marked). We used the x2 test to compare the data for several variables at each of the assessment points in the phenytoin and control groups. RESULTS Both control and phenytoin-treated groups showed improvement over the study period. However, healthy granulation tissue appeared earlier in the phenytoin group. On day 7, 21 of the phenytoin group showed healthy granulation compared to only 9 control wounds ($P < 0.001$). In addition, we noted that wound discharge ceased much earlier with phenytoin. Wound cultures also become negative earlier. On day 28 in the phenytoin group, 76% of the cultures were negative, whereas in the control group only 48% were negative ($P < 0.005$). This trend continued even at day 35 (88% of phenytoin cultures were negative vs. 60% in the control group, $P < 0.005$). The overall percentage reduction of ulcer area was also greater in the phenytoin group

Again, the differences between the phenytoin and control groups were significant at $P < 0.05$. Finally, we noted that the quality of the scar formation was better in the phenytoin group. Our preliminary light- and electron-microscopic observations indicated that phenytoin decreases inflammation, increases fibroblast formation and wound collagen content, and stimulates neovascularization. We observed formation of excess granulation tissue in 18 patients in the phenytoin group. However, the response was controlled after cessation of topical phenytoin. No other local or systemic adverse reaction to phenytoin therapy was observed.

**CONCLUSIONS**

This prospectively controlled trial, the first to deal exclusively with diabetic foot ulcers, indicates that the use of phenytoin to promote healing of diabetic ulcers is both effective and safe. Its use reduced patient morbidity and hospitalization time. The hypergranulation tissue response noted in 18 patients is not only correctable but also avoidable by reducing or stopping application of powder as soon as granulation base covers the entire wound. Given phenytoin's evident effectiveness in the promotion of wound healing, as well as its availability, low cost, ease of use, and safety, we strongly recommend its use as a treatment for diabetic ulcers. Phenytoin should prove especially useful in rural areas where daily attendance at the clinic or hospital is not possible.

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