Topical Phenytoin Accelerates Healing in Epidermolysis bullosa simplex

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For a few decades phenytoin (PHT) has been used as an anticonvulsant or antiarrhythmic agent. In dermatology, it has been used as a wound-healing agent in the treatment of leg ulcers and in the dystrophic form of epidermolysis bullosa. Preliminary observations suggest the efficacy of topical PHT in the management of leg ulcers. We therefore thought to assess the effect of topical PHT in the management of epidermolysis bullosa simplex (EBS).

Eight patients (2 males, 6 females) aged between 1 and 40 years suffering from localized EBS were evaluated. The diagnosis of EBS was made by the family history, the clinical presentation and the histology (1 case). The patients were treated with a PHT cream (2 or 5% in a hydrophilic base). The cream was applied twice daily at the sites of bulla formation (hand and feet) during 6-36 months. The results were evaluated clinically by regular controls and by a questionnaire filled in by the patient. The parameters assessed were: (1) the rate of wound healing of bullae and (2) the decrease in the disease activity as expressed by a decrease in the number and size of newly formed bullae. The plasma levels of PHT were determined in 2 cases. The follow-up period ranged from 6 months to 3 years.

Topical application of PHT induced, in all cases, an increase in the rate of wound healing. It was markedly faster in 3 of 8 patients. Of particular interest is the case of a 2-year-old girl who had such a severe form of EBS that she was unable to walk. The application of PHT overnight, in a thick coat under occlusion led to marked improvement and allowed a normal physical activity. We determined the plasma levels of PHT after 3 months of treatment in the 2 children. In both cases, we did not find detectable PHT levels in plasma.

In 50% of our patients, the application of PHT induced a feeling of burn during several minutes. This side effect, probably due to the NaCl content of the cream, was further avoided by a saline-free preparation of the cream.

One year after the end of the study, the 3 patients whose daily activities were largely limited by their EBS, still continue the treatment.

The results of this prospective open trial indicate that topical PHT is beneficial to patients suffering from EBS. Most of our patients reported a quicker rate of healing of their lesions and felt improved over a long period of time. Nevertheless, lacking a control group, it is not possible to conclude that the therapeutic effect we observed was due only to PHT. Therefore our observations should be confirmed by a double-blind study. Meanwhile we think that since our patients stick to the treatment even after 3 years, this therapy is beneficial to them. Also, several

previous controlled (PHT vs. excipient) studies clearly showed that topical PHT causes a significantly quicker healing of cutaneous lesions [1,2]. Such a property is substantiated by in vitro experiments showing that PHT increases fibroblast proliferation, increases the expression of epidermal growth factor receptors in fibroblasts and decreases collagenase and collagen peptidase activity [3, 4].

Although the use of topical PHT remains controversial in western countries [5], it is an inexpensive drug, which is widely used as a wound-healing agent in developing countries. In the same way, our small open trial shows that patients with a mild form of EBS do feel improved by topical PHT by a likely effect on the healing of lesions.

Further experimental studies with PHT are required, as well as a double-blind, case-controlled trial in EBS patients.

References

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