LOW-DOSE CALCIPOTRIOL AS A THERAPEUTIC OPTION TO IMPROVE WOUND HEALING IN EPIDERMOLYSIS BULLOSA

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Introduction

Patients with dystrophic epidermolysis bullosa (DEB) suffer from chronic open wounds, predisposing them to microbial infections which contribute to delayed wound healing and ongoing inflammation, both of which promote the development of an aggressive squamous cell carcinoma. Thus, local wound care including antimicrobial defense is critical in EB wound management. An often overlooked factor important to wound healing is vitamin D3 (VD3). The skin possesses the entire enzymatic machinery required to produce active VD3 (calcitriol), underscoring its importance to proper skin function. Skin injury enhances calcitriol production, inducing the expression of VD3-target genes including the antimicrobial peptide cathelicidin (hCAP18).

Methodology/Results

Our pre-clinical experiments suggesting a beneficial effect of the VD3 analogue calcipotriol (100 nM) by inducing hCAP18 expression in recessive dystrophic EB (RDEB) keratinocytes, improving antimicrobial defense against a common wound colonizer in EB, and accelerating wound closure. Furthermore, calcipotriol exhibited significant anti-neoplastic effects, suppressing clonogenicity and proliferation of RDEB tumor cells. These data formed the basis for evaluating the topical application of a low dose calcipotriol-containing ointment in a two arm, double-blind, randomized, cross-over phase II clinical trial. 15 DEB patients are being recruited to compare topical calcipotriol therapy with placebo. The primary objective is to achieve a 40% reduction of wound area in the calcipotriol treatment group compared to placebo after 4 weeks treatment. As secondary aims we use metagenomic analysis to compare wound microbiota in calcipotriol-treated versus placebo-treated wounds and evaluate impact of treatment on quality of life (pruritus/pain).