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Vitamin D3 supplementation in polymorphic light eruption: Randomized double-blinded placebo-controlled trial

Short title: Vitamin D supplementation in polymorphic light eruption

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Abstract

Polymorphic light eruption (PLE) is a common photodermatosis with a high prevalence of approximately 11 to 21% in the population. Similar to lupus erythematosus (LE), an UV-inducible systemic autoimmune disease, PLE has a female preponderance with a mean onset in the second to third decade of life. PLE lesions are very itchy and typically appear on sun-exposed body sites in spring or early summer. The quality of life in patients with PLE is often severely disturbed, as evidenced by high levels of anxiety and depression. For prophylaxis besides conventional sunscreens, photo(chemo)therapy is effective in many cases, when administered over several weeks for hardening in early spring before the first natural sun exposure takes place. However, because pro-longed treatment with UVB and/or photochemotherapy is potentially carcinogenic, the search for pathogenic mechanisms and new treatment options in PLE is ongoing. The exact pathogenesis of PLE is currently unknown but findings suggest an autoimmune-type background with resistance to UV-induced immune suppression and simultaneous immune reactions against skin photo-neoantigens. We have recently found that PLE patients had significantly reduced 1,25-(OH)2-vitamin D3 serum levels (13-14ng/ml) compared to the normal population (>30ng/ml). In addition, we were able to demonstrate in an intra-individual half-body trial that topical administration of an immunostimmulatory 1,25-(OH)2-vitamin-D3 analogue calcipotriol reduced PLE symptoms in an experimental study. In the proposed randomized double-blinded placebo-controlled trial we attempt to study the effect of oral vitamin D3 supplementation (40.000 IE given orally at week 0 and 2) on PLE symptoms. PLE patients will be subjected to experimental photoprovocation with solar simulated UV radiation over several days before and after vitamin D3 supplementation. Disease symptoms will be quantified with a newly established and validated PLE test score, (AA + SI + 0.4P [range, 0-12], where AA is affected area score [range, 0-4], SI is skin infiltration score [range, 0-4], and P is pruritus score on a visual analogue scale [range, 0-10]). We will also study the effect of oral vitamin D3 on abnormalities i) in levels and function of regulatory T cells, ii) chemotaxis of leucocytes, and iii) proinflammatory cytokines, i.e. alterations that we have previously linked to PLE pathogenesis. This will be done by i) FACS and co-culture T cell proliferation assays, ii) response of peripheral neutrophil leucocytes to the chemoattractants leukotriene B4 (LTB_4) and formyl-methionyl-leucyl-phenylalanin, and iii) ELISA and immuno bead assay of patient serum. The results of the project will enlighten the mechanism of PLE and may establish the base of a novel prevention strategy via the vitamin D3 pathway.

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