

Vitamin D and Vitamin D-binding Protein in Psoriasis and Effects of Treatment

Akademisk avhandling

Som för avläggande av Medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, den 8 oktober, klockan 9:00.

av Maria Siekkeri Vandikas, leg. läkare

Fakultetsopponent:

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Avhandlingen baseras på följande delarbeten

- I. **Vandikas MS**, Hellström E, Malmberg P, Osmancevic A. Imaging of vitamin D in psoriatic skin using time-of-flight secondary ion mass spectrometry (ToF-SIMS): A pilot case study. *The Journal of Steroid Biochemistry and Molecular Biology*. 2019;189:154-60.
- II. **Vandikas MS**, Landin-Wilhelmsen K, Holmäng A, Gillstedt M, Osmancevic A. High levels of serum vitamin D-binding protein in patients with psoriasis: A case-control study and effects of ultraviolet B phototherapy. *The Journal of Steroid Biochemistry and Molecular Biology*. 2021;211:105895.
- III. **Vandikas MS**, Landin-Wilhelmsen K, Polesie S, Gillstedt M, Osmancevic A. Impact of etanercept on vitamin D status and vitamin D-binding protein in bio-naïve patients with psoriasis. *Acta Dermato-Venereologica*, in press, 2021.
- IV. **Vandikas MS**, Landin-Wilhelmsen K, Gillstedt M, Osmancevic A. Vitamin D-binding protein and the free vitamin D hormone hypothesis in bio-naïve patients with psoriasis. Submitted. 2021.

SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER



Vitamin D and Vitamin D-binding Protein in Psoriasis and Effects of Treatment

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Abstract

Background: Topical vitamin D analogues constitute an established treatment for psoriasis but the role of vitamin D in the pathogenesis of the disease remains controversial. The *in loco* production and immunomodulatory effects of vitamin D need to be elucidated. Recently, the discussion about the role of vitamin D-binding protein (DBP) in inflammation and its impact on vitamin D physiology has surged.

Aims: To try to map the distribution of vitamin D metabolites in psoriatic skin using time-of-flight secondary ion mass spectrometry (ToF-SIMS) before and after ultraviolet B (UVB) phototherapy (Paper I). To compare the serum levels of DBP in psoriasis with population-based controls (Paper II) and to study the effect of phototherapy (Paper II) and etanercept (Paper III) on vitamin D status and DBP levels. To test the free hormone hypothesis for vitamin D in psoriasis (Paper IV).

Methods: Skin biopsies from a patient with psoriasis, before and after UVB phototherapy were analyzed with ToF-SIMS. A case control study including 68 patients with psoriasis who were studied before and after UVB phototherapy and compared to 105 population-based controls. Twenty bio-naïve patients with moderate to severe psoriasis were treated with etanercept for 24 weeks and 15 matched healthy controls were followed in parallel. A cross-sectional study evaluating vitamin D status in 40 bio-naïve patients with psoriasis.

Results: Vitamin D metabolites were depicted in the skin with ToF-SIMS and information about the morphology of the skin and distribution and quantity of the metabolites in the skin was obtained simultaneously. DBP serum levels were higher in patients with psoriasis compared to population-based controls. DBP levels were higher in those subjects with self-reported arthropathy compared to those without. UVB phototherapy did not affect serum DBP levels while serum DBP decreased during etanercept treatment. Patients with adequate vitamin D levels improved most in their disease on etanercept treatment. Total 25(OH)D was a reliable measure for vitamin D status.

Conclusions: ToF-SIMS is a potentially powerful tool to be used for the investigation of the vitamin D pathway in psoriatic skin and its possible local immunomodulatory effects in the inflammatory process. DBP might be a new inflammatory biomarker in psoriasis. There seems to be a synergic treatment effect between vitamin D and etanercept in psoriasis. Measurement of total 25(OH)D reflected well vitamin D status in bio-naïve patients with psoriasis.

Keywords: Psoriasis, vitamin D, vitamin D-binding protein, phototherapy, tumor necrosis factor α inhibitor.