Psoriasis and vitamin D

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Thesis title: Psoriasis and vitamin D. Insights from a randomised clinical trial, a cross-sectional analysis of the Tromsø Study 2015-16 and a factorial Mendelian randomisation study using the UK Biobank and HUNT

Psoriasis is a chronic immune-mediated inflammatory skin disease. Emerging evidence has led to the current understanding of psoriasis as a systemic inflammatory disease, which is associated with overweight, metabolic syndrome, cardiovascular disease, inflammatory bowel disease and increased all-cause mortality. The exact cause of psoriasis is not known, but existing knowledge suggests an interplay between genetic susceptibility and environmental factors. The latter gives the potential for prevention. Vitamin D may represent a target for prevention, as an association between lower serum 25-hydroxyvitamin D (25[OH]D) levels and psoriasis has been found in some studies. Overweight is considered a risk factor for both psoriasis and vitamin D deficiency. Moreover, topical vitamin D analogues are routine treatment for psoriasis, but effect of per oral supplementation is not established.

This thesis aimed to enhance understanding of the link between serum 25(OH)D and psoriasis in the general population and explore the impact of overweight, and thereby increase knowledge as to whether 25(OH)D levels should be monitored in psoriasis patients. It also aimed to investigate whether vitamin D supplementation has any place in the treatment of psoriasis.

Using a cross-sectional design, we investigated the association between serum 25(OH)D and psoriasis in the seventh survey of the large population based Tromsø Study (Tromsø7) and assessed possible effect modification by overweight. We did not observe any statistically significant relationship between 25(OH)D and psoriasis, neither lifetime nor active disease. However, our analysis may have been underpowered to detect a threshold effect in the lower serum 25(OH)D spectrum, as few participants had lower serum 25(OH)D. Interaction analyses indicated that high body mass index (BMI) and vitamin D deficiency combined increase the odds of active psoriasis more than the sum of the two, with an estimated 92% higher odds for active psoriasis in subjects with BMI >27.5 kg/m2 and 25(OH)D. We suggest that providing advice to prevent vitamin D deficiency may be considered in the follow-up of overweight and obese patients with psoriasis.

We conducted a randomised, double-blind placebo-controlled trial through two winter seasons in Tromsø, to examine the effect of vitamin D supplementation on psoriasis severity in subjects with lower serum 25(OH)D. Vitamin D supplementation did not affect psoriasis severity in our study. Low baseline severity scores may explain the lack of a measurable effect, still, any large effect seems unlikely among those with mild disease (Psoriasis Area Severity Index (PASI) x (PASI) 5). Surprisingly, 25(OH)D levels in the intervention group increased less-than-expected based on previous experimental data from the same source population, and this may have affected our results. Further biological analyses investigating the vitamin D metabolism in persons with psoriasis are warranted.

To follow-up on our findings in Tromsø7, we performed a factorial Mendelian randomisation (MR) study to explore the relative excess risk for psoriasis due to interaction between genetically predicted BMI and serum 25(OH)D. Our study builds on previous MR studies investigating single effects, which have demonstrated a causal relationship between both higher BMI and lower 25(OH)D and increased risk for

psoriasis. MR studies are more robust to residual confounding and reverse causation compared to traditional observational approaches. In our study, we used cross-sectional data from two independent population-based cohorts; the UK Biobank (UKB) and the Trøndelag Health Study (HUNT). We observed no interaction between BMI and 25(OH)D on the odds for psoriasis. Specifically, the combined effect did not exceed the additive effect of the two factors. Considering the minor differences in actual BMI and 25(OH)D between the factorial groups, as well as the limited statistical power inherent in factorial MR designs, small interaction effects may have been undetected.

Papers:

Jenssen M, Furberg AS, Jorde R, et al. The association between serum 25-hydroxyvitamin D levels and psoriasis in a large population-based cohort: a cross-sectional analysis of The Tromsø Study 2015-16. Br J Dermatol. 2024 Apr 17;190(5):680-688. doi: 10.1093/bjd/ljad472. PMID: 38015798.

Jenssen M, Furberg AS, Jorde R, et al. Effect of Vitamin D Supplementation on Psoriasis Severity in Patients With Lower-Range Serum 25- Hydroxyvitamin D Levels: A Randomized Clinical Trial. JAMA Dermatol. 2023 May 1;159(5):518-525. doi: 10.1001/jamadermatol.2023.0357. PMID: 36988936; PMCID: PMC10061314.

Jenssen M, Arora N, Løset M, et al. Exploring interaction between genetically predicted body mass index and serum 25-hydroxyvitamin D levels on the odds for psoriasis in UK Biobank and the HUNT Study: A factorial Mendelian randomisation study. Submitted manuscript.