Effects of Narrow-band Ultraviolet B and Solar Radiation on Vitamin D Synthesis and of Empowering Heliotherapy on Quality of Life in Dermatological Patients

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Toni Karppinen, MD, defended his PhD thesis on January 27th, 2017 in Department of Dermatology and Venereology, University of Tampere and Tampere University Hospital. Opponent was Docent Leena Koulu, MD, PhD, Department of Dermatology and Venereology, University of Turku and Turku University Hospital and supervisors were Professor Erna Snellman, MD, PhD, Department of Dermatology and Venereology, University of Tampere and Tampere University Hospital, and Professor Emeritus Timo Reunala, MD, PhD, Department of Dermatology and Venereology, University of Tampere and Tampere University Hospital. The thesis book is available at: http://urn.fi/URN:ISBN:978-952-03-0335-8.

Narrow-band ultraviolet B (NB-UVB) phototherapy is used to treat dermatoses such as psoriasis and atopic dermatitis (AD), diseases having a negative impact on the health-related quality of life (HRQoL). NB-UVB can also raise serum 25-hydroxyvitamin D [S-25(OH)D] levels. Since solar ultraviolet radiation (UVR) is not capable of inducing cutaneous vitamin D synthesis in winter, we set out to determine whether NB-UVB exposure can enhance S-25(OH)D levels in subjects receiving cholecalciferol supplementation, and whether NB-UVB can be used to sustain post-summer S-25(OH)D levels during the winter. We also studied whether vernal solar UVR can raise S-25(OH)D levels during outdoor activities in a snow-covered landscape, and what would be the effects of empowering heliotherapy (EHT) on HRQoL and disease severity in psoriasis and AD patients.

The psoriasis patients and healthy subjects described in paper I were receiving daily oral cholecalciferol supplements of 20 µg prior to the study and during it. Psoriasis patients received 18 NB-UVB exposures and the healthy subjects received 9. After 9 exposures each, their mean S-25(OH)D levels had increased by 13 and 17 nmol l^{-1} ($p<0.001$), respectively, while after the 18th exposure S-25(OH)D in the psoriasis patients had increased by 49 nmol l^{-1}. One month later the S-25(OH)D level was still 30 nmol l^{-1} above the baseline in the psoriasis patients and 18 nmol l^{-1} above in the healthy subjects. Baseline CYP27A1 and

Toni Karppinen (middle), defended his PhD thesis on January 27th, 2017. Opponent was Docent Leena Koulu (first towards right) and Professor Erna Snellman (first towards left) and Professor Emeritus Timo Reunala (second towards left) served as Supervisors.

CYP27B1 levels were significantly lower in the psoriasis lesions than in the skin of the healthy subjects ($p<0.001$). Cathelicidin levels were similar in both, whereas human beta defensin 2 levels were significantly higher in the psoriasis lesions ($p<0.001$). NB-UVB did not alter the CYP27A1, CYP27B1 and cathelicidin levels in the psoriasis patients, but their average human beta defensin 2 level decreased significantly ($p<0.002$). The NB-UVB exposures significantly reduced CYP27A1, CYP27B1 and cathelicidin levels in the healthy subjects. To conclude, NB-UVB radiation is effective in raising S-25(OH)D levels even in subjects receiving supplementations. The vitamin D hydroxylating enzymes in healthy skin react more actively to NB-UVB than those in psoriasis lesions. Human beta defensin 2 seems to have a role in the pathogenesis of psoriasis. The difference in the expression of vitamin D-hydroxylating enzymes between psoriasis lesions and healthy skin, and the role of cutaneously synthesized vitamin D in the healing of psoriasis, are subjects which require further investigation since the roles of these effects remain unclear.

The healthy subjects studied in paper II were randomized into an intervention group receiving NB-UVB exposures every other week from October to April, or a control group. One standard erythema dose (SED) was administered on the first occasion and 2 SED on all subsequent occasions. Two weeks after the last irradiation the S-25(OH)D in the intervention group had increased by 12 nmol l^{-1} ($p<0.029$) whereas that in the control group had decreased by 11 nmol l^{-1} ($p<0.022$). In summary, suberythemal NB-UVB exposures maintained and even increased the S-25(OH)D levels in winter. These could be used to maintain S-25(OH)D levels in haemodialysis patients, who typically respond slowly to oral cholecalciferol.

The healthy subjects in paper III were exposed to vernal solar UVR in March and April either during their late winter holiday, or at noon on working days. They received a mean cumulative ultraviolet B (UVB) radiation dose of 12 SED on the face and hands, i.e. 7% of the total body surface area, over a mean period of 12 h spent out of doors. Those whose baseline S-25(OH)D concentrations were below 90 nmol l^{-1} showed significant increases of 6 nmol l^{-1} $p<0.001$), while those with a baseline over 90 nmol l^{-1} showed a decrease of 7 nmol l^{-1} ($p<0.01$). In summary, the 'vitamin D winter' in Finland lasts only until March, encouraging people to engage in vernal outdoor activities.

Papers IV and V assess the effects of two-week EHT courses on the HRQoL and disease severity in psoriasis and AD patients. The mean Dermatology Life Quality Index (DLQI) decreased significantly by 5 and 8 units ($p<0.001$) in these two groups, respectively, after EHT, and remained decreased by 3 and 5 units ($p<0.001$), respectively, after 3 months. The Self-Administered Psoriasis Area and Severity Index (SAPASI) decreased by 5.0 units from an initial 7.4 units and was still 2.6 units below the initial level 3 months after EHT ($p<0.001$). The Patient-Oriented Scoring of Atopic Dermatitis (PO-SCORAD) index decreased by 24.0 units from an initial figure of 36.7, and was still 14.6 units below the initial figure ($p<0.001$) 3 months after EHT. The RAND-36 physical and mental component summary scores decreased significantly during EHT and remained decreased 3 months after EHT in both groups. In summary, EHT improves the HRQoL and alleviates disease severity in psoriasis and AD patients.

To conclude, NB-UVB exposures are effective in raising and maintaining S-25(OH)D levels in psoriasis patients and healthy subjects. Vernal solar UVR can elevate S-25(OH)D in subjects with a baseline level below 90 nmol l^{-1}. Two-week EHT courses improve the HRQoL and alleviate disease severity in psoriasis and AD patients for at least 3 months.

List of original publications:

I. Ala-Houhala MJ, Karppinen T, Vähävihu K, Kautiainen H, Dombrowski Y, Snellman E, et al. Narrow-band UVB treatment boosts serum 25-hydroxyvitamin D in psoriasis patients on oral vitamin D supplementation. Acta Derm Venereol 2014; 94: 146–151.

II. Karppinen T, Ala-Houhala MJ, Ylianttila L, Kautiainen H, Viljakainen H, Reunala T, Snellman E. Narrowband ultraviolet B exposures maintain vitamin D levels during winter: a randomized controlled trial. Acta Derm Venereol 2016; 96: 490–493.

III. Karppinen T, Ala-Houhala MJ, Ylianttila L, Kautiainen H, Lakkala K, Hannula H-R, et al. The effect of vernal solar UV radiation on serum 25-hydroxyvitamin D concentration depends on the baseline level: observations from a high latitude in Finland. Int J Circumpolar Health 2017; 76: 1272790.

IV. Karppinen T, Ylianttila L, Kautiainen H, Reunala T, Snellman E. Empowering heliotherapy improves clinical outcome and quality of life of psoriasis and atopic dermatitis patients. Acta Derm Venereol 2015; 95: 579–582.

V. Karppinen T, Laine J-P, Kautiainen H, Pasternack R, Reunala T, Snellman E. Empowering heliotherapy in psoriasis and atopic dermatitis: an observational study of 186 subjects. Acta Derm Venereol 2017; 97: 255–257.