

Narrowband ultraviolet B treatment improves vitamin D balance and alters antimicrobial peptide expression in skin lesions of psoriasis and atopic dermatitis

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Summary

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Conflicts of interest

None declared.

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Background Narrowband ultraviolet B (NB-UVB) is a routine treatment for psoriasis and atopic dermatitis (AD) but its effect on vitamin D balance is not well studied.

Objectives To examine whether NB-UVB treatment in winter improves vitamin D balance in psoriasis and AD, and to study the effects of NB-UVB on antimicrobial peptide and cytokine expression in the skin.

Methods Eighteen adult patients with psoriasis, 18 with AD and 15 healthy subjects received a total of 15 NB-UVB exposures on the whole body, given three times a week. Serum calcidiol (25-hydroxyvitamin D) was measured by radioimmunoassay. Antimicrobial peptide and cytokine expression in skin lesions was examined by real-time quantitative polymerase chain reaction.

Results At onset 16 (89%) patients with psoriasis, 17 (94%) patients with AD and eight (53%) healthy subjects had vitamin D insufficiency (calcidiol $< 50 \text{ nmol L}^{-1}$). NB-UVB treatment significantly increased ($P < 0.001$) serum calcidiol. The increase was 59.9 nmol L^{-1} (95% confidence interval, CI 53.5–66.9) in psoriasis, 68.2 nmol L^{-1} (95% CI 55.4–80.1) in AD and 90.7 nmol L^{-1} (95% CI 63.8–123.4) in healthy subjects. Psoriasis Area and Severity Index and SCORAD improved significantly ($P < 0.001$) but no correlation to the increase of serum calcidiol was found. Cathelicidin and human β -defensin 2 (HBD2) expression was high in skin lesions of psoriasis. After six NB-UVB treatments cathelicidin increased further while HBD2 expression decreased. A similar trend was observed in AD lesions. NB-UVB caused a marked but nonsignificant decrease of interleukin (IL)-1 β and IL-17 in psoriasis lesions.

Conclusions The present study shows that in addition to a significant improvement of psoriasis and AD, NB-UVB treatment effectively corrects vitamin D insufficiency. It also increases cathelicidin and decreases HBD2 levels in healing skin lesions of psoriasis and AD. This effect might be mediated by improved vitamin D balance and the local cytokine network.

At present vitamin D insufficiency is common worldwide.¹ In the Nordic countries and Britain this condition frequently affects people especially during winter when vitamin D synthesis induced by the sun is zero.^{2–5} The desirable concentration of serum calcidiol (25-hydroxyvitamin D), which is the best indicator of vitamin D status, is still under debate but a

concentration of $50\text{--}80 \text{ nmol L}^{-1}$ is considered to be optimal for the skeleton.^{6,7} Recently, it was shown that heliotherapy in the Canary Islands in winter significantly improved serum calcidiol both in Finnish patients with atopic dermatitis (AD) and in Swedish patients with psoriasis (PS).^{8,9} Also artificial broadband ultraviolet (UV) B irradiation has been shown to

increase serum calcidiol in postmenopausal women with PS.¹⁰ We recently showed that a short low-dose narrowband UVB (NB-UVB) course is an alternative to improve vitamin D balance in healthy women in winter.¹¹

Vitamin D is important not only for the health of the bones but also an association between vitamin D deficiency and the incidence or unfavourable prognosis of a broad variety of diseases, such as various types of cancer (e.g. colon, prostate and breast cancer), autoimmune diseases, infectious diseases and cardiovascular diseases, has been described in a number of studies.^{1,12,13} However, these associations need further studies to be confirmed. Vitamin D has long been known to affect skin inflammation and cutaneous innate or adaptive immune responses.¹⁴ In particular, calcitriol (1,25-dihydroxyvitamin D) is a major factor involved in the regulation of the antimicrobial peptide cathelicidin.¹⁵ This and another inducible cutaneous antimicrobial peptide, human β defensin 2 (HBD2), can act as proinflammatory mediators or 'alarmins' and link adaptive and innate immune responses.¹⁶ Recent studies suggest that defensins and cathelicidin have a role in the pathogenesis of skin inflammation in PS. In particular, increased gene copy numbers of the β -defensins correlate with the risk of developing this disease.¹⁷ In addition, cathelicidin peptide LL-37, which is increased in psoriatic skin, induces an autoinflammatory cascade leading to skin inflammation.^{18,19} Thus, vitamin D seems to have different functions in addition to maintaining skeletal health. However, even if the only function of vitamin D is shown to be regulation of calcium homeostasis, it should be mandatory to prevent vitamin D insufficiency worldwide.

The aim of the present study was to examine whether NB-UVB treatment for patients with PS or AD improves their vitamin D balance. As antimicrobial peptides are directly involved in the pathogenesis of inflammatory skin diseases, we also studied whether NB-UVB treatment has an effect on the expression of cathelicidin, HBD2 and various cytokines in psoriatic and atopic skin lesions.

Materials and methods

Subjects, narrowband ultraviolet B exposures and calcidiol measurements

Altogether 56 adult subjects representing Fitzpatrick skin types II and III volunteered and 51 completed the study. The ethics committee of the Tampere University Hospital approved the study protocol and all subjects gave informed consent to participate. Inclusion criteria were no phototherapy, solarium, sun holidays or vitamin D supplementation during the preceding 2 months. The study was conducted during January–March in 2008 and 2009. Eighteen patients with PS (eight women and 10 men; mean age 48 years), 18 with AD (nine women and nine men; mean age 33 years) and 15 healthy doctors, nurses or other healthcare workers (15 women; mean age 42 years) received a total of 15 NB-UVB exposures, given three times a week, on the whole body with a Waldmann UV

7001 cabin (Waldmann, Villingen-Schwenningen, Germany) equipped with 20 TL-01 tubes. The initial NB-UVB dose for all participants was 0.13 J cm^{-2} corresponding to one standard erythema dose (SED). Thereafter the dose was gradually increased up to 1.19 J cm^{-2} (9.5 SED). The mean cumulative UVB dose received after 15 NB-UVB exposures was 8.88 J cm^{-2} which corresponds to 71.5 SED. The clinical improvement was measured in PS by Psoriasis Area and Severity Index (PASI) and in AD by SCORAD. Two subjects withdrew from the study for personal reasons, two due to skin reactions (erythema or photosensitivity) and one because of pregnancy.

Blood samples for serum calcidiol measurements were taken before the first NB-UVB treatment and then 2 days after the sixth and 15th NB-UVB exposures. In addition, a follow-up sample was taken 1 month after the NB-UVB course. The serum samples were protected from light, centrifuged and then stored at -20°C . Serum calcidiol concentration was analysed in duplicate by using radioimmunoassay (Immunodiagnostic Systems, Boldon, U.K.) as in our previous study.⁸ Calcidiol concentration $< 50 \text{ nmol L}^{-1}$ was regarded as vitamin D insufficiency and $< 25 \text{ nmol L}^{-1}$ as deficiency.⁷

Skin biopsies and real-time quantitative polymerase chain reaction

Punch biopsies were taken from the same representative skin lesions from patients with PS ($n = 7$) or AD ($n = 8$) immediately before the first and seventh NB-UVB exposures. Skin biopsies from healthy subjects ($n = 7$) served as controls. The biopsies were immediately frozen and stored at -70°C before being examined.

Total RNA from biopsies was isolated using Eurozol Reagent (EuroClone, Milan, Italy). One microgram of RNA was reverse transcribed with High Capacity cDNA Reverse Transcription kit (Applied Biosystems, Foster City, CA, U.S.A.) to cDNA as previously described.²⁰ The expression of cathelicidin and HBD2 was evaluated using a LightCycler[®] 2.0 system and the corresponding human Universal Probe Library Set (Roche, Basel, Switzerland). The primers were designed by an algorithm on <http://www.universalprobelibrary.com> and hydroxymethylbilane synthase (HMBS; previously known as porphobilinogen deaminase) was used as housekeeping gene in a duplex real-time quantitative polymerase chain reaction (qPCR). HMBS was chosen because it, cathelicidin and HBD2 belong to a low-abundance class of mRNAs. Analysed genes and corresponding primers are listed in Table 1. Fold induction relative to the healthy volunteers was calculated as previously described.²¹ Results were considered significant when at least a twofold difference in expression levels was detected and statistical analysis revealed $P < 0.05$.

Real-time qPCR for various cytokines and chemokines was performed with PerfeCTa qPCR FastMix (Quanta Biosciences, Gaithersburg, MD, U.S.A.) in the ABI Prism 7700 Sequence Detector System (Applied Biosystems). PCR primers and probes for cytokines and chemokines were obtained as

Table 1 Target genes and corresponding primers for cathelicidin and human β -defensin 2 (HBD2) in real-time quantitative polymerase chain reaction

Target gene	Forward	Reverse
Cathelicidin	5'-TCGGATGCTAACCTCTACCG-3'	5'-ACAGGCTTTGGCGTGTCT-3'
HBD2	5'-TCAGCCATGAGGGTCTTGTA-3'	5'-GGATCGCTATACCACAAA-3'

predeveloped assay reagents [interleukin (IL)-1 β , IL-4, IL-10, IL-17A, interferon (IFN)- γ , transforming growth factor (TGF)- β , tumour necrosis factor (TNF)- α , CCL20 (macrophage inflammatory protein-3a, MIP-3a)] or they were self-designed [β -actin, CCL17 (thymus and activation regulated chemokine, TARC)] and ordered from Applied Biosystems.

Statistics

The changes in serum calcidiol concentration, PASI and SCORAD were analysed by a permutation test with Monte-Carlo P-value. Confidence intervals (CIs) for the changes were obtained by bootstrapping (5000 replications). Cathelicidin and HBD2 expression in PS and AD skin lesions before and after NB-UVB treatment was compared with that in healthy controls using the Mann-Whitney test. Comparison of cathelicidin and HBD2 expression in the untreated and NB-UVB-treated skin lesions was performed with the Wilcoxon matched pairs test. Statistical analysis of cytokine expression in PS skin vs. AD skin was performed with the nonparametric Mann-Whitney test.

Results

Narrowband ultraviolet B treatment and serum calcidiol

At onset the mean $\pm$ SD serum calcidiol concentration was 36.8 ± 12.45 nmol L⁻¹ in patients with PS, 32.2 ± 12.2 nmol L⁻¹ in patients with AD and 60.5 ± 21.8 nmol L⁻¹ in healthy subjects (Fig. 1). Sixteen (89%) patients with PS, 17 (94%) with AD and eight (53%) healthy controls had vitamin D insufficiency (calcidiol < 50 nmol L⁻¹). Of these subjects five with PS and seven with AD had vitamin D deficiency (calcidiol < 25 nmol L⁻¹).

The NB-UVB course significantly ($P < 0.001$) increased serum calcidiol in PS, AD and healthy subjects (Fig. 1). After 15 NB-UVB exposures serum calcidiol increased by a mean of 59.9 nmol L⁻¹ (95% CI 53.5–66.9) in PS, by 68.2 nmol L⁻¹ (95% CI 55.4–80.1) in AD and by 90.7 nmol L⁻¹ (95% CI 63.8–123.4) in healthy subjects. There was no difference in the increase of serum calcidiol between these three groups ($P = 0.21$). One month after the NB-UVB course calcidiol was nearly at the same elevated level in PS and AD but showed some decrease in the healthy subjects (Fig. 1).

The NB-UVB course improved PASI from 8.0 (range 3.5–16.1) to 3.6 (range 0.7–9.0) in PS ($P < 0.001$). The SCORAD improved from 37.1 (range 12.9–74.0) to 14.2 (range 4.8–41.2) in AD ($P < 0.001$). The clinical improvement (mean PASI reduction -4.1, mean SCORAD reduction -22.9) did not

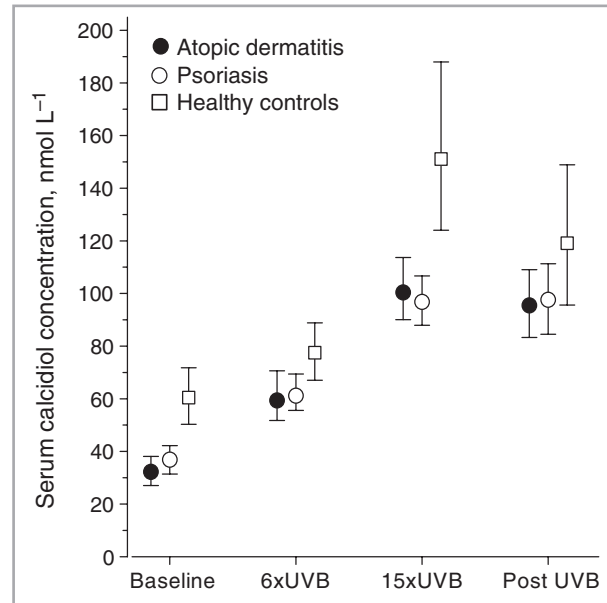


Fig 1. Effect of narrowband ultraviolet B (NB-UVB) treatment on serum calcidiol concentration. Fifteen NB-UVB exposures significantly increased serum calcidiol concentration (mean; 95% confidence intervals) in 18 patients with psoriasis, 18 patients with atopic dermatitis and 15 healthy subjects ($P < 0.001$). The serum calcidiol level was still elevated in patients and healthy subjects 1 month after the last NB-UVB exposure.

correlate to the increase of serum calcidiol either in PS [$P = 0.43$, $r = -0.20$ (95% CI -0.65 to 0.29)] or in AD [$P = 0.08$, $r = 0.42$ (95% CI -0.13 to 0.80)].

Expression of antimicrobial peptides cathelicidin and human β -defensin 2

Analysis of mRNA expression levels of cathelicidin before NB-UVB treatment revealed significantly elevated levels of cathelicidin in lesional PS skin compared with the skin of healthy subjects (Fig. 2a). In AD skin lesions cathelicidin was also expressed but the increase was not significant (Fig. 3a). After six NB-UVB treatments cathelicidin expression increased markedly in PS and slightly in AD (Figs 2a and 3a). However, neither observation reached statistical significance.

Before NB-UVB treatment HBD2 mRNA expression levels were also significantly upregulated in skin lesions of PS and AD compared with healthy controls (Figs 2b and 3b). NB-UVB treatment significantly reduced HBD2 expression in PS lesions (Fig. 2b) and also in AD lesions (Fig. 3b) but this change did not reach statistical significance.

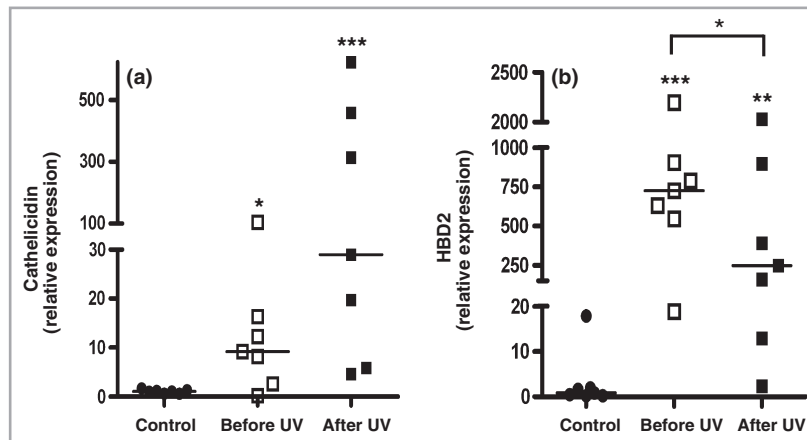


Fig 2. Expression of cathelicidin and human β -defensin 2 (HBD2) in psoriasis. Biopsies of a marker psoriatic plaque ($n = 7$) were taken before and after six narrowband ultraviolet (UV) B treatments. Total mRNA was extracted and transcript levels of cathelicidin (a) and HBD2 (b) analysed by real-time quantitative polymerase chain reaction. Statistical analysis of psoriatic skin before and after UV treatment vs. healthy (nonpsoriatic) controls ($n = 7$) was performed with the Mann–Whitney test. Comparison of treated and untreated biopsies was performed using the Wilcoxon matched pairs test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

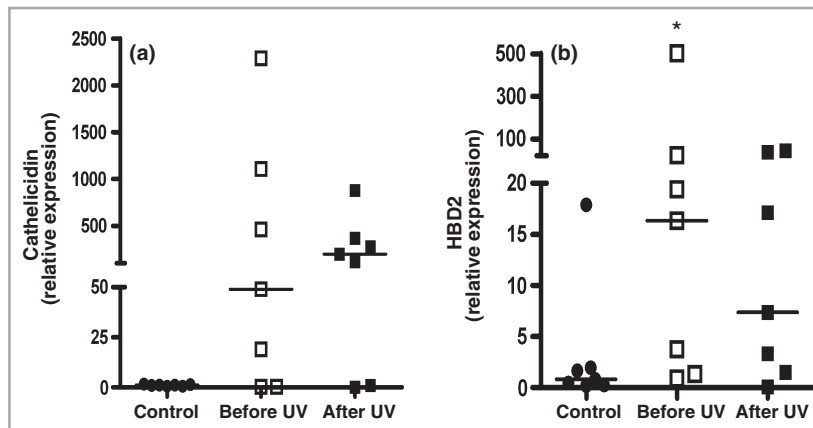


Fig 3. Expression of cathelicidin and human β -defensin 2 (HBD2) in atopic dermatitis. Biopsies of atopic dermatitis skin lesions ($n = 7$) were taken before and after six narrowband ultraviolet (UV) B treatments. Total mRNA was extracted and transcript levels of cathelicidin (a) and HBD2 (b) analysed by real-time quantitative polymerase chain reaction. Statistical analysis of atopic dermatitis skin before and after UV treatment vs. healthy controls ($n = 7$) was performed with the Mann–Whitney test. Comparison of treated and untreated biopsies was performed using the Wilcoxon matched pairs test. * $P < 0.05$.

Cytokine and chemokine expression

Before NB-UVB treatment PS lesions expressed significantly higher amounts of IL-1 β ($P < 0.01$), IL-17A ($P < 0.01$) and IFN- γ ($P < 0.05$) compared with AD lesions (Fig. 4). CCL17 (TARC) was significantly ($P < 0.05$) higher in AD lesions whereas IL-10, TGF- β 1, TNF- α and CCL20 (MIP-3a) were expressed similarly in both diseases. IL-4 expression was basically negative in PS and AD lesions.

After six NB-UVB treatments expression of IL-1 β and IL-17A was markedly reduced in PS lesions (Fig. 4). However, these changes were not significant. NB-UVB treatment did not change the expression of IL-4, IL-10, IFN- γ , TGF- β 1, TNF- α , CCL17 (TARC) or CCL20 (MIP-3a) (Fig. 4).

Discussion

The present study performed in winter showed low concentrations of serum calcidiol in patients with PS and AD. The same observation was made in our earlier heliotherapy study for AD.⁸ In the present study the subjects were consecutive patients referred for NB-UVB treatment in our department. Almost all patients had vitamin D insufficiency and some of them even had vitamin D deficiency (calcidiol $< 25 \text{ nmol L}^{-1}$). Vitamin D insufficiency was not as pronounced in the healthy subjects. They were educated doctors, nurses and other personnel from our department who have better knowledge of healthy food and vitamin D sources than people on average. However, 53% of them also had vitamin D insufficiency. These results clearly

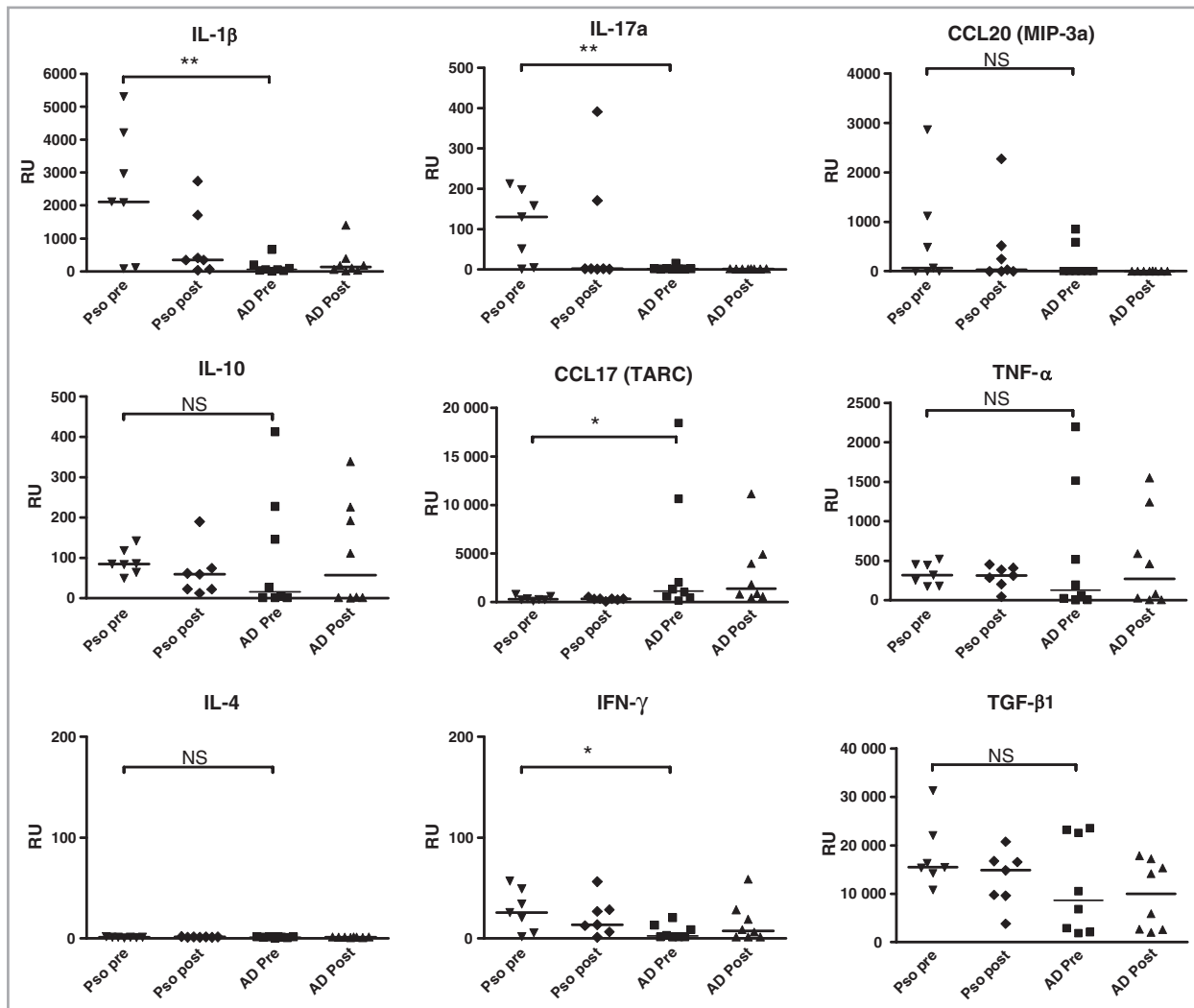


Fig 4. Expression of cytokines and chemokines in the skin lesions of psoriasis (Pso) and atopic dermatitis (AD) before and after narrowband ultraviolet B (NB-UVB) treatment. Real-time quantitative polymerase chain reaction was used to analyse the mRNA expression levels of different cytokines and chemokines in Pso ($n = 7$) and AD ($n = 8$) skin lesions before and after six NB-UVB treatments. Relative units (RU) are expressed as fold differences relative to the calibrator (β -actin). IL, interleukin; MIP, macrophage inflammatory protein; TARC, thymus and regulation activated chemokine; TNF, tumour necrosis factor; IFN, interferon; TGF, transforming growth factor. Statistical analysis of Pso skin vs. AD skin was performed with the nonparametric Mann–Whitney U-test. NS, not significant, * $P < 0.05$, ** $P < 0.01$.

show that seasonal vitamin D insufficiency or deficiency continues to be very common in Finland and that this condition also affects patients with PS and AD.^{3,22}

Fifteen NB-UVB treatments given with a similar protocol that we usually use to treat AD significantly increased serum calcidiol in all three study groups. In agreement with this, two recent studies in patients with PS have shown that NB-UVB exposures markedly increase serum calcidiol.^{23,24} In the study of Osman-covic *et al.*²⁴ the patients received a mean of 28 NB-UVB treatments. However, the calcidiol response was not as high as in the present study. The reasons for this could be differences in the patient material, rather high initial concentration of serum calcidiol, previous UVB treatments and the variable length of the treatment period. In the present study 15 NB-UVB treatments significantly improved PASI in PS and SCORAD in AD. The clinical

improvement did not, however, correlate to the increase of serum calcidiol.

The NB-UVB course increased serum calcidiol in the healthy subjects similarly to the patients with PS and AD. This confirms our previous observation that a short NB-UVB course is an efficient way to increase low serum calcidiol in winter.¹¹ In that study healthy subjects received NB-UVB exposures on seven consecutive days. However, seven exposures given on consecutive days did not increase serum calcidiol as much as six exposures in the present study although the cumulative UVB dose was nearly the same. This suggests that calcidiol synthesis is more effective when NB-UVB exposures are given every second day compared with daily exposures. More studies should be performed to confirm the most effective NB-UVB protocol.

After the NB-UVB course serum calcidiol was followed up for 1 month. At this time point, serum calcidiol was still elevated in the patients with PS and AD, as in our previous study with healthy subjects.¹¹ These results show that a short course of NB-UVB is a possible and easy way to improve vitamin D balance in winter. Fifteen suberythral NB-UVB exposures every second or third day rapidly increase serum calcidiol, and this effect is long lasting. The time to receive two SED of NB-UVB in a Waldmann 7001 cabin is short, < 1 min. Theoretically, tens of subjects could be handled during a day with one NB-UVB cabin to treat low serum calcidiol effectively during winter.

In wintertime, if no UVB exposure is available, vitamin D supplements should be used to improve vitamin D balance. In a recent Swedish study vitamin D supplements increased serum calcidiol by 11.0 nmol L^{-1} and a sun vacation by 14.5 nmol L^{-1} .⁴ In previous Finnish studies the daily dietary vitamin D intake was about $7.5 \mu\text{g}$ in winter.^{11,22} This meets the current Finnish recommendation for vitamin D intake, but it seems not to be enough to maintain a sufficient vitamin D balance. To obtain recently recommended calcidiol concentrations of $> 75 \text{ nmol L}^{-1}$ a dietary intake of vitamin D of $17\text{--}20 \mu\text{g}$ daily is required.^{25,26} This is hard to receive without supplements in winter as for only $7.5 \mu\text{g}$ per day one needs to consume, for example, fish two or three times a week together with having 6 dL of vitamin D-fortified milk daily and five or six sandwiches with vitamin D-fortified margarine. A study comparing the effects and costs of oral vitamin D substitution with a short NB-UVB course in the treatment of vitamin D insufficiency would be of importance.

Antimicrobial peptides such as cathelicidin and HBD2 can act as proinflammatory mediators or 'alarmins' in the skin and link adaptive and innate immune responses.¹⁵ Recent studies suggest a role for the defensins and cathelicidin in the pathogenesis of skin inflammation in PS and AD.^{17,27} Indeed, we found increased expression of these antimicrobial peptides in the skin lesions of PS and AD, confirming earlier results.^{17,28} We also showed that repeated treatment with NB-UVB reduced HBD2 expression in healing PS and AD skin lesions. Similar HBD2 findings have previously been reported in AD skin lesions treated by NB-UVB.^{28–30} Gläser *et al.*³¹ recently showed an increase of HBD2 after a short UV exposure to healthy skin whereas we found decreasing HBD2 levels in the NB-UVB-treated healing PS and AD lesions. At the same time we saw a significant increase in serum calcidiol, the best indicator of the hormonally active form of vitamin D (calcitriol, i.e. 1,25-dihydroxyvitamin D) which exerts potent anti-inflammatory actions through inhibition of NF κ B activation, and inhibits IL-17A-induced HBD2 in keratinocytes *in vitro*.³² NB-UVB is known to induce local synthesis of calcidiol and calcitriol in keratinocytes.³³ Both local and systemic vitamin D metabolism are triggered by the same stimulus. We propose that the effects of NB-UVB-triggered vitamin D production might outweigh the HBD2-inducing effect of short-term UVB in our study population.

In contrast to HBD2, UVB treatment does not induce cathelicidin in keratinocytes *in vitro*²¹ but induces cathelicidin hCAP18 expression in healthy skin *in vivo*.³⁴ Calcitriol is the only factor known to date which induces cathelicidin in skin epithelial cells.¹⁵ Treatment of healthy skin with active vitamin D or the application of vitamin D analogues to PS skin induces cathelicidin.³⁰ Cathelicidin expression thus correlates with local vitamin D concentrations. Cathelicidin expression, however, did not correlate with the disease activity in the present study as NB-UVB decreased skin inflammation but increased cathelicidin transcript abundance. In particular, increased cathelicidin in PS should lead to more skin inflammation as cathelicidin LL-37 has been suggested to serve as a proinflammatory signal in PS.^{18,19} LL-37 binds self-DNA and the LL-37/self-DNA complexes trigger the activation of plasmacytoid dendritic cells in the skin and an immune response in PS.¹⁸ These contrasting observations need to be further investigated in future studies. Possible explanations include anti-inflammatory activities of vitamin D, such as inhibition of T-cell recruitment or inhibition of dendritic cell activation, which might be responsible for the immunosuppressive effects of NB-UVB observed in this study.³⁵

PS and AD both cause local inflammation but their cellular mechanism and effects on the cytokine milieu are different in the skin lesions of these patients. PS consists of chronic inflammation including activation of Th1 but also Th17 cytokines whereas, depending on the stage of the disease, Th1 cytokines, Th2 cytokines and CCL17 (TARC) dominate in AD.^{36–38} Supporting the previous results, we found significantly higher amounts of IL-1 β , IFN- γ and IL-17A in psoriatic skin lesions, whereas the hallmark cytokine CCL17 (TARC) was highly expressed in AD.

This is the first study in which NB-UVB treatment has been shown to reduce expression of IL-1 β and IL-17A in psoriatic skin lesions. IL-1 β is a proinflammatory cytokine that is processed from its inactive form (pro-IL-1 β) to its active form by microbial products and metabolic stress, leading to enhanced lymphocyte activation and destruction of local tissues. In addition to the proinflammatory function, IL-1 β is suggested to be a critical mediator of the differentiation of human T cells producing IL-17.^{39,40} In turn, IL-17 is shown to enhance vitamin D₃-induced expression of the antimicrobial peptide cathelicidin.³² Although the expression of cathelicidin did not immediately decrease along with IL-17A in this study, lowered IL-17 levels may later decrease inflammation and neutrophil activation in lesional skin sites.^{41,42} Our results suggest that the interplay between cytokines and vitamin D in the regulation of antimicrobial peptides in keratinocytes of cutaneous inflammatory diseases is complex and only partly understood. As these molecules exert cytokine-like functions the analysis of their regulatory pathways in inflammatory skin disease deserves further study.

In conclusion, the present study showed that, in addition to clinical response, a short NB-UVB course effectively corrects vitamin D insufficiency in patients with PS and AD and in healthy subjects. NB-UVB treatment altered HBD2 and cathelicidin

lidicin expression in healing skin lesions, which might be mediated by improved vitamin D balance and cytokine network.

What's already known about this topic?

- Two studies in patients with psoriasis (PS) have shown that narrowband ultraviolet B (NB-UVB) exposures markedly increase serum calcidiol. We recently showed that a short low-dose NB-UVB course is an alternative to improve vitamin D balance in healthy women in winter.
- Recent studies suggest a role of the defensins and cathelicidin in the pathogenesis of skin inflammation in PS and atopic dermatitis (AD). Calcitriol is involved in the regulation of cathelicidin.

What does this study add?

- Fifteen NB-UVB treatments significantly increased serum calcidiol in patients with AD or PS and in healthy subjects. The effect persisted for at least 1 month.
- Repeated treatment with NB-UVB reduced the initially increased expression of the antimicrobial peptide human β -defensin 2 in healing PS and AD lesions. Simultaneously serum calcidiol increased significantly.
- NB-UVB treatment reduced the expression of interleukin (IL)-1 β and IL-17A in psoriatic skin lesions.

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