Temperature-controlled laminar airflow in adult atopic dermatitis patients – an observational study

To the Editor

Atopic dermatitis (AD) patients are commonly sensitized to house dust mites (HDM). The current consensus-based European guideline underlines the impact of allergens inducing AD flares and the importance of allergen reduction in AD patients.[1,2] With regard to preventive measures in patients with AD, the use of mattress encasings aiming to reduce skin contacts to mite allergens in bed may be considered in HDM-sensitized patients. Thus far, however, a successful approach to reducing indoor allergen aerogenic exposure is lacking. The technology of 'nocturnal temperature-controlled laminar airflow' (TLA) has been developed to reduce allergen exposure by filtering the surrounding atmosphere, particularly of the head-neck region, during sleep. While effects of the use of this technology in patients with allergic asthma were shown, AD in adults including in-vitro analyses has not been addressed yet.[3–5]

We conducted a three-month observational study investigating the effect of an add-on treatment with TLA in 10 HDM-IgE-sensitized patients with moderate-to-severe AD and a history of clinically relevant HDM allergy (see Fig. 1a). In an extension phase, patients were advised to use the device for additional 9 months to complete a whole year of application. The study was in accordance with the principles of the Declaration of Helsinki and good clinical practice guidelines and approved by the ethics committee of Hannover Medical School (No. 7231).

After 3 months of intervention, Scoring Atopic Dermatitis (SCORAD) (41.96 ± 9.78 vs. 34.15 ± 9.69, $P = 0.037$), local eczema intensity (local SCORAD) of the head-neck region (8.0 ± 1.7 vs. 6.4 ± 2.5, $P = 0.037$), and Eczema Area Severity Index (EASI; 10.01 ± 3.94 vs 8.41 ± 3.76, $P = 0.038$) improved significantly (Fig. 1b,c). The physician global assessment (PGA: 0 = clear (100% improvement), 1 = almost clear (90%–99%), 2 = significant improvement (50%–89%), 3 = moderate improvement (<50%), 4 = no improvement, 5 = worsening) displayed an improvement in seven of ten patients (Fig. 1c). Patient-assessed Dermatology Life Quality Index (DLQI) (12.55 ± 4.78 vs. 7.45 ± 4.66, $P = 0.001$) and subjective SCORAD symptoms (8.58 ± 4.47 vs. 4.86 ± 4.01, $P = 0.038$), including sleeplessness (3.52 ± 2.86 vs. 1.37 ± 2.16, $P = 0.038$), were also significantly ameliorated (Fig. 1d).

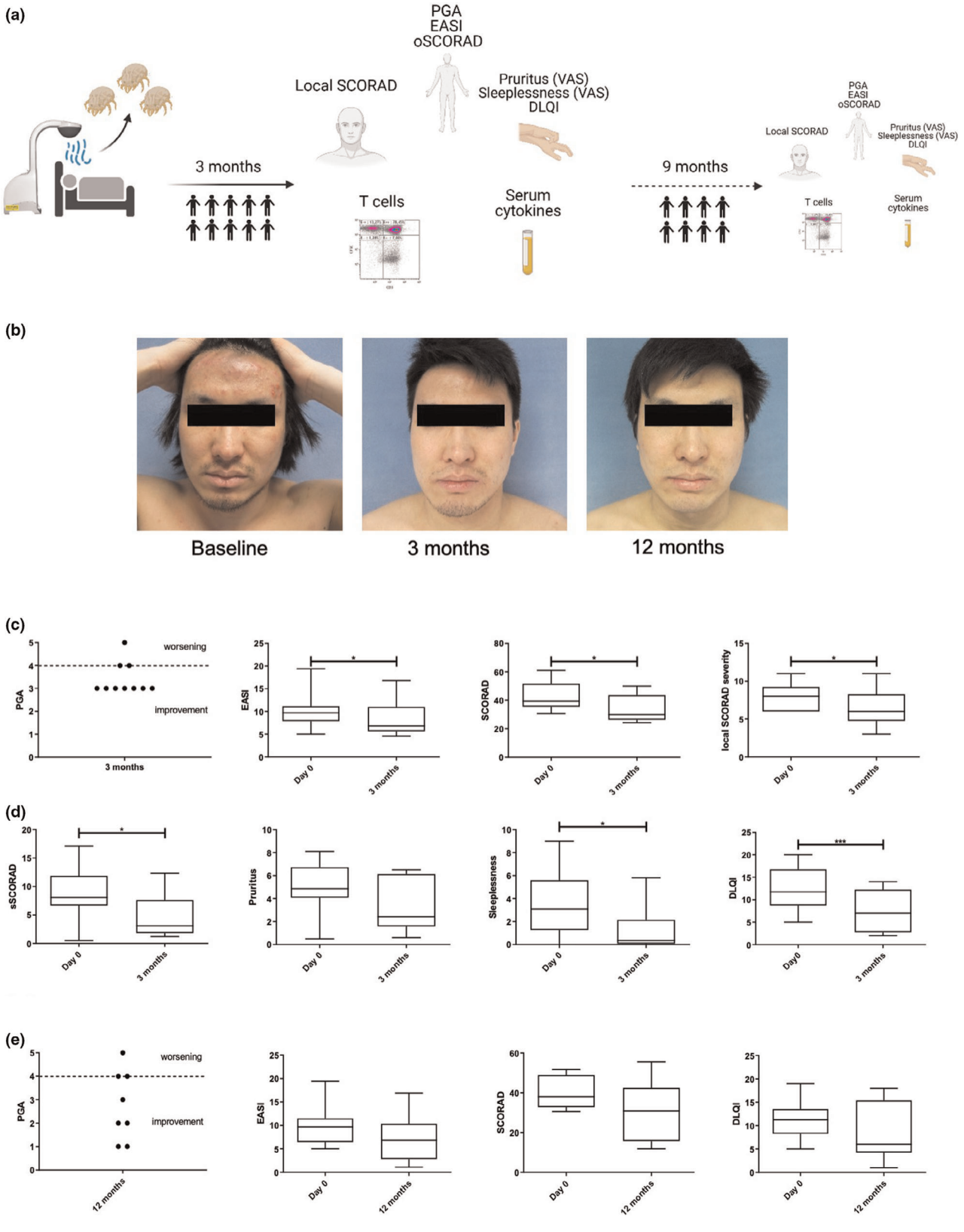
After 12 months, five of eight patients showed an improvement measured by PGA, four even with an improvement of over 50% (Fig. 1e).

In order to investigate the concomitant cellular immune response, peripheral blood mononuclear cells (PBMC) were stimulated in vitro with HDM extract. Proliferative responses of total T cells ($P = 0.002$), $CD4^+$ T cells ($P < 0.001$), skin-homing $CD4^+$ T cells ($P = 0.018$) and $CD8^+$ T cells ($P = 0.037$), measured by carboxyfluorescein succinimidyl ester (CFSE), were significantly decreased after 3 months of TLA usage (Fig. 2a). Furthermore, we investigated HDM-specific T helper cells, defined by upregulation of CD154 (CD40L) after HDM antigen stimulation.[6] Parallel staining of surface marker antigens allowed subgrouping into the polarization subtypes Th1 ($CXCR3^+$/$CCR4^-$/$CCR6^-$/$CCR10^-$), Th2 ($CXCR3^-$/$CCR4^+$/$CCR6^-$/$CCR10^-$) and Th17 cells ($CXCR3^-$/$CCR4^+$/$CCR6^+$/$CCR10^-$).[7] By this, HDM-specific Th1 ($P = 0.014$) and Th17 cells ($P = 0.039$) were detected in significantly reduced extent in the circulation after 12 months (Fig. 2b). At this time point, the effect regarding the proliferation of total T cells ($P = 0.455$), $CD4^+$ T cells ($P = 0.453$), skin-homing $CD4^+$ T cells ($P = 0.391$), and $CD8^+$ T cells ($P = 0.383$) was less pronounced compared with the measurement after 3 months, and the differences did not reach significance (data not shown). Cytokines were measured at both time points in serum by multiplex bead-based immunoassays. IL-9, hypothesized to be involved in allergic inflammation,[8] was significantly reduced after 12 months compared with baseline ($P = 0.039$; Fig. 2c).

Together, the findings of this proof-of-concept study indicate improvement of disease severity in HDM-sensitized adult AD patients during the add-on treatment with a TLA device.

In conclusion, this study is the first to suggest beneficial effects of TLA in HDM-sensitized adult AD patients regarding objective, subjective and in vitro parameters. Of note, our data are preliminary evidence and further randomized-controlled studies on the use of the TLA technology are needed to verify these promising data for adult AD patients, especially concerning better disease control and long-term effects.

Figure 1 Improvement of disease signs and symptoms after 3 and 12 months of add-on use of TLA in HDM-sensitized adult patients with AD. (a) Study design. (b) Photograph documentation of the head neck region of a study patient at day 0 and at 3 and 12 months of add-on TLA use. (c) Improvement of physician global assessment (PGA), Eczema Area Severity Index (EASI), Scoring Atopic Dermatitis (SCORAD) index, and local SCORAD of the head and neck area after three months. (d) The subjective SCORAD and the reported insomnia in particular (lower left) showed a significant improvement after 3 months of TLA. There was also a profound improvement in the Dermatology Life Quality Index (DLQI). No significant difference was seen for the reported pruritus. (e) Improvement in 5 of 8 patients regarding the physician global assessment (PGA) was revealed. A trend towards an improvement was observed for EASI, SCORAD, and DLQI. *$P < 0.05$, **$P < 001$, ***$P < 0001$.



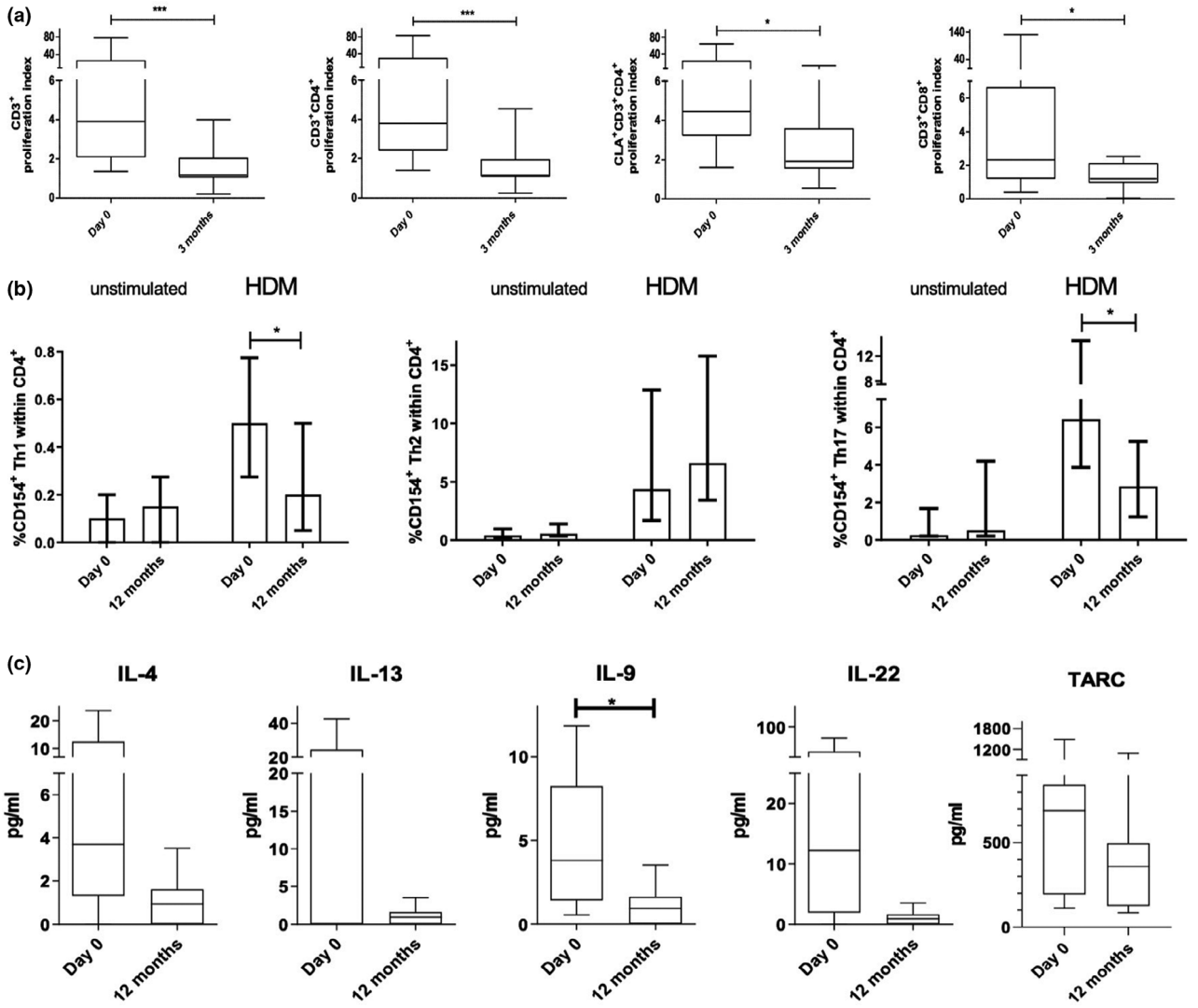


Figure 2 In vitro analysis results underpinning the clinical results of 3 and 12 months usage of TLA. (a) Proliferation of CD3+ T cells, $CD3^+/CD4^+$ T helper cells, $CD3^+/CD4^+/CLA^+$ skin-homing T helper cells and $CD3^+/CD8^+$ T cells in response to HDM extract stimulation was detected by CFSE staining. Proliferation index was calculated by dividing the frequency of stimulated cells by the frequency of unstimulated cells. (b) After in vitro stimulation with low-endotoxin D. pteronyssinus extract (HDM), reactive T cells were identified by expression of surface CD154, enriched by magnetic separation and further grouped into $CXCR1^+/CCR4^-/CCR6^-/CCR10^-$ (Th1), $CXCR1^-/CCR4^+/CCR6^-/CCR10^-$ (Th2) and $CXCR1^-/CCR4^+/CCR6^+/CCR10^-$ (Th17) fractions. Percentages refer to total $CD4^+$. (c) Serum cytokines at day 0 and after 12 months of intervention measured by LEGENDplex. *$P < 005$, **$P < 001$, ***$P < 0001$.

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The patients in this manuscript have given written informed consent to the publication of their case details. Figure 1a was created with biorender.com.

Conflict of interest

Dr. Traidl received consultancy fees from Leo Pharma, Lilly and La Roche-Posay outside the submitted work. Dr. Roesner reports grants and personal fees from Novartis outside the submitted work. Mrs Kienlin, Mrs Begemann and Dr. Schreiber have nothing to disclose. Dr. Werfel reports grants and personal fees from Novartis, personal fees from Sanofi-Regeneron, grants and personal fees from LEO, personal fees from Galderma, personal fees from Lilly, grants and personal fees from AbbVie, grants from Pfizer, outside the submitted work. Dr. Heratizadeh received personal fees from Leo Pharma, Novartis, Pierre Fabre, Sanofi-Genzyme, Beiersdorf, Hans Karrer, Nutricia, Meda, Lilly, as well as grants from Janssen outside the submitted work.

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National trends in psoriasis readmissions: a longitudinal study of the nationwide readmission database from 2010 to 2018

Dear Editor,

Psoriasis is a chronic inflammatory, immune-mediated disease affecting the skin, nails, and joints, with a 3% prevalence in the United States (US).[1] Readmission account for approximately 2/3 of total inpatient costs of patients hospitalized primarily for psoriasis.[2] Decreased hospitalization rates paralleling the introduction of biological drugs has been reported.[3] Nevertheless, data on trends of psoriasis readmission are scarce, a relevant matter in the era of high-value care. Studies have reported biologic use for psoriasis increased from 2001–2005 to 2011–2015 period.[4] Our study aims to study longitudinal trends of 30-day readmissions of psoriasis patients in the US from 2010 to 2018, to see if increased biologic usage in more recent times has any effect on rates and outcomes of psoriasis readmissions.

Data were obtained from the Nationwide Readmission Database (NRD). NRD includes nested and weighted discharge data stratified in clusters to produce national estimates. We performed a retrospective 9-year longitudinal trend analysis of NRD 2010–2018 databases. Every other year was sampled during the study period since we were interested in trends over time. We searched for index hospitalizations for patients aged ≥18 years with a 'principal' or 'secondary' diagnosis of psoriasis using ICD codes for the corresponding year. The 30-day readmissions were defined as repeat hospitalization for any reason within 30 days following index hospitalization. Elective and traumatic readmissions were excluded. The 10 most common principal diagnoses or reasons for readmissions for each sampled year were highlighted. Multivariate logistic and linear regression analyses were used to calculate an adjusted *P*-trend for categorical and continuous outcomes, respectively. We adjusted for change in demographics and Charlson Comorbidity Index score (CCI) over the years. Analysis was performed using STATA, 16 (StataCorp LLC, College Station, TX, USA).

The decrease in the 30-day readmission rate was steeper for patients hospitalized with a 'principal' diagnosis of psoriasis (16.7% in 2010 to 10.2% in 2018, adjusted *P*-trend = 0.001) than patients hospitalized with either a 'principal' or 'secondary' diagnosis of psoriasis (12.2% in 2010 to 10.4% in 2018, adjusted *P*-trend < 0.0001). See Fig. 1. Inpatient mortality of psoriasis readmissions decreased from 4.4% in 2010 to 4.2% in 2018 (adjusted *P*-trend = 0.004). The mean hospital length of stay (LOS) of psoriasis readmissions decreased from 6.3 days in 2010 to 5.8 days in 2018 (adjusted *P*-trend = 0.003). Proportion of readmitted psoriasis patients with CCI ≥3 increased from 38.8% in 2010 to 51.6% in 2018 (adjusted *P*-trend < 0.0001). Sepsis was the most common reason for readmission across all years (Table 1).

In the US more than one in three patients with psoriasis requiring hospitalization are readmitted within a year.[2] However, our study shows decreasing readmission rates and inpatient mortality over time. This is in contrast with an earlier study which showed increasing psoriasis readmissions between 2012 and 2014.[2] Our finding may be due to increased usage of biologic therapies in more recent times.[4] As previously reported,[2] infectious complications remain a frequent reason for readmission of psoriasis patients.

