

Double-blind placebo-controlled house dust mite control measures in adult patients with atopic dermatitis

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Summary

Background Avoidance of allergens has been shown to be of benefit in patients with atopic asthma sensitized to indoor allergens. In atopic dermatitis, there is so far little information about the effect of house dust mite elimination strategies.

Objectives We therefore performed a randomized controlled study of house dust mite control in patients with this disease.

Methods Twenty adult patients with moderate to severe atopic dermatitis were included. Inclusion criteria were a positive RAST to house dust mite antigen (CAP class > 3) and a concentration of > 2 µg g⁻¹ of the house dust mite antigen Der p1 in the patient's mattress dust. Patients were randomized to either the active treatment group (allergen-impermeable mattress encasing, acaricide spray containing tannic acid and benzylbenzoate) or a control group (allergen-permeable encasing, spray containing water and traces of ethanol). Severity of disease was estimated every 2 months by an established score (SCORAD), and eosinophil cationic protein (ECP) in the serum was determined by enzyme-linked immunosorbent assay. Furthermore, the use of topical steroids was quantified. Patients assessed daytime pruritus and pruritus-induced sleeplessness weekly on a visual analogue scale. The study lasted 1 year.

Results At the end of the study, the active treatment group showed a statistically significant reduction in Der p1 exposure as compared with the control group. However, when comparing the change from the start to the end of the study, there was no statistically significant difference between active treatment and control groups as measured by the SCORAD score and by ECP levels in the serum. Some patients in the active treatment group reported less pruritus-induced sleeplessness, but there was no statistically significant difference between the two treatment groups.

Conclusions For adult patients with atopic dermatitis it was shown that 1 year of house dust mite avoidance reduced the allergen exposure, but an improvement of overall disease activity was not demonstrated.

Key words: acaricides, atopic dermatitis, clinical trial, house dust mite, mattress encasing

House dust mite control measures have been introduced into the therapy of atopic disease in recent years. The benefit of antigen elimination procedures, although still controversial,¹ has been repeatedly demonstrated in patients sensitized to dust mites who presented with asthma and allergic rhinoconjunctivitis.^{2,3} Specific sensitization to mite antigen is also thought to play a major pathogenetic role in atopic dermatitis. It has

been shown that mite antigens are able to penetrate the epidermis and to elicit a specific immune response in the skin of affected patients, leading to an eczematous skin reaction.^{4–7} However, there is only limited evidence that eliminating house dust mites reduces the severity of skin symptoms. Only a few controlled trials^{8–10} have been published so far, and have yielded conflicting results. Tan *et al.*⁸ and Sanda *et al.*⁹ have observed a beneficial effect of house dust mite control measures. Only Tan *et al.* have used encasing of the bed mattress,⁸ and at the end of a 6-month study period the

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authors observed a significant clinical improvement. In the other study,⁹ clean room therapy with highly effective air filtration was used for dust mite elimination. In contrast, a third study,¹⁰ using an acaricide and a vacuum cleaner, did not demonstrate a correlation between the elimination of mites and improvement of the clinical score. These conflicting results prompted us to perform another house dust mite control study with the following characteristics: homogeneous age of study population (young adults only), documented sensitization to the house dust mite antigen Der p1, significant individual exposure to dust mite (Der p1 $> 2 \mu\text{g g}^{-1}$ mattress dust) prior to study entry, a study period of 1 year (to exclude seasonal variations of antigen exposure as a confounding variable) and the measurement of Der p1 levels throughout the study.

Materials and methods

Twenty patients aged 18–30 years (11 women and nine men) with moderate to severe atopic dermatitis and sensitization to the house dust mite *Dermatophagoides pteronyssinus* (specific IgE antibodies with a RAST class > 3 , CAP-FEIA method; Pharmacia, Freiburg, Germany) were enrolled. Patients with pets were excluded. The patients were randomized to a 1-year period of either placebo [allergen-permeable cotton bed covers (Bencard; Smith Kline Beecham, Munich, Germany) and a water spray containing traces of ethanol] or active treatment [allergen-impermeable polyurethane encasings (Bencase; Puttkammer, Dormagen, Germany) and an acaricide spray consisting of tannic acid and benzylbenzoate (Tresan, Innovall, Ratingen, Germany)]. The patient's mattress dust was collected by one of us in a standardized fashion. Dust samples were analysed for Der p1 by a commercial enzyme-linked immunosorbent assay (Dustscreen; ADL, Freiburg, Germany). Only patients with a significant Der p1 antigen load on their mattress ($> 2 \mu\text{g g}^{-1}$ dust) were included in the study. Disease severity was evaluated every 2 months by using an established skin evaluation score, SCORAD.¹¹ This score evaluates the extent and intensity of skin lesions and the patient's itch and sleeplessness. Throughout the study, the evaluating physician was unaware of the patient's randomization status. As a laboratory parameter for disease severity, eosinophil cationic protein (ECP) was measured in the serum by a commercial fluorescence enzyme immunoassay (CAP-System; Pharmacia). Patients were instructed to document the

following parameters weekly on a visual analogue scale: daytime pruritus, pruritus-induced sleeplessness and subjective judgement of their skin status. In addition, the amount of topical steroids needed (hydrocortisone and triamcinolone) was documented by weighing the ointment tubes. Only topical therapies were allowed. Lubrication of skin was *ad libitum* in both groups. Statistical analysis was performed by non-parametric tests for repeated measures designs,^{12,13} which can be applied for metric data as well as for data measured on grading scales. In this set-up treatment effects correspond to different time profiles of observations; this is the interaction between treatment and time. For statistical analysis only the time points 'study start' (baseline) and 'study end' were selected. The time points in between were only used for the description of study results.

Results

All patients completed the study. The active treatment group experienced a reduction in antigen exposure. As shown in Figure 1, this was a significantly larger reduction in Der p1 exposure compared with the control group ($P = 0.008$). Both groups experienced a temporary improvement of their disease (Fig. 2). However, regarding the whole study period, the profiles of the SCORAD score did not differ significantly

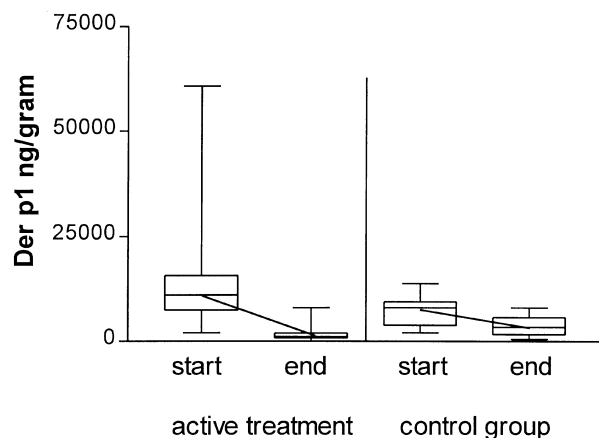


Figure 1. Der p1 exposure: effectiveness of house dust mite avoidance. Patients' mattress dust was collected in a standardized fashion. Dust samples were analysed for Der p1 by a commercial enzyme-linked immunosorbent assay. Results in the active treatment and control groups at the start (baseline) and end of the study are shown. The active treatment group experienced a significantly larger reduction in Der p1 exposure compared with the control group. Boxes show 25–75% percentile range and median; bars show range of values observed.

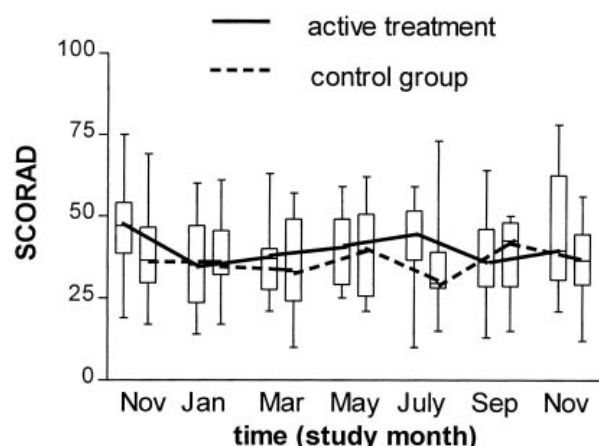


Figure 2. Time course of SCORAD scores. Disease severity was evaluated every 2 months by using the SCORAD score. Throughout the study, the evaluating physician was unaware of the patient's randomization status. Boxes show 25–75% percentile range and median; bars show range of values observed. Statistical analysis^{12,13} is shown in Figure 3(a).

between the active treatment and the control groups ($P = 0.901$, Fig. 3a). Moreover, the profiles of the ECP serum concentrations and specific IgE did not differ significantly ($P = 0.453$, Fig. 3b; $P = 0.941$, Fig. 3c). At the end, both groups had used comparable total amounts of topical steroids ($P = 0.642$, exact Wilcoxon test).

Regarding the subjective parameters, some patients in the active treatment group experienced an improvement of their pruritus-induced sleeplessness. However, there was no statistically significant difference ($P = 0.399$, Fig. 4) in the reduction of pruritus-induced sleeplessness between the active treatment and control groups. The same was true when comparing the other subjective parameters of daytime pruritus ($P = 0.799$) and subjective impression of skin status ($P = 0.583$).

There was no statistically significant difference in total IgE values between the active and control groups or in either group between the start and end of the study (data not shown).

Discussion

When comparing the active treatment and the control group, this study confirmed the efficacy of encasing and acaricides in the control of house dust mites. A significantly larger reduction in Der p1 levels was achieved for the active treatment group. However, such an effect was not seen for the objective markers of

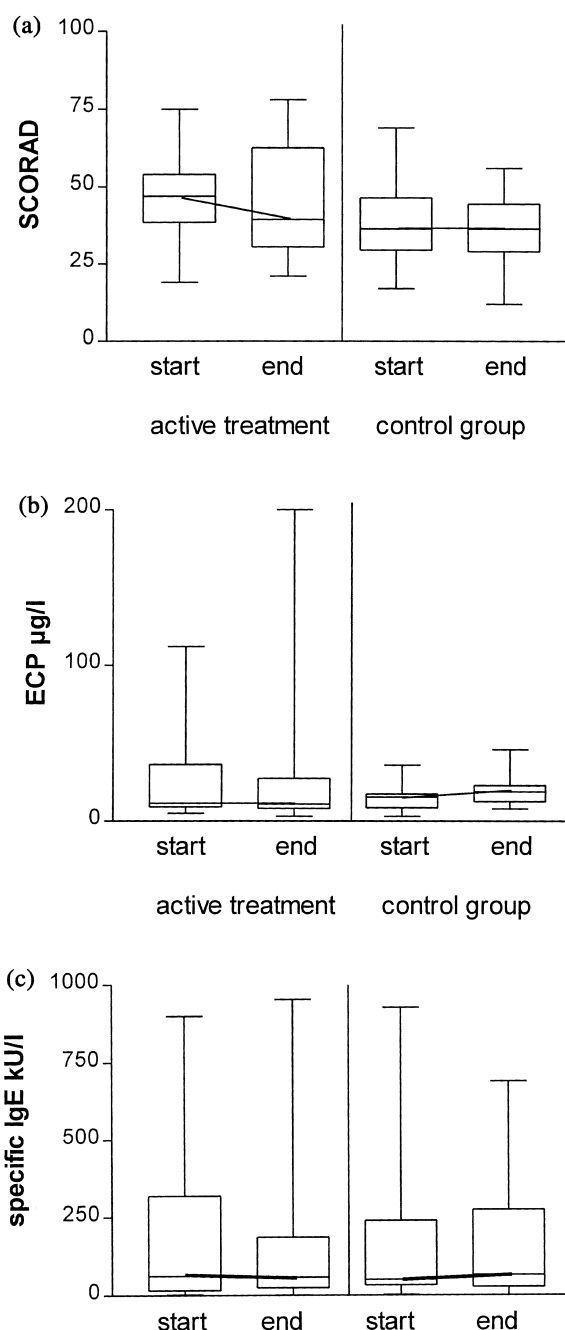


Figure 3. Objective parameters SCORAD, eosinophil cationic protein (ECP) and specific IgE: ineffectiveness of house dust mite avoidance. Disease severity was evaluated by using the SCORAD (a). ECP (b) and specific IgE (c) were measured in the serum by a commercial fluorescence enzyme immunoassay. Results in the active treatment and control groups at the beginning and end of the study are shown. The profiles of the SCORAD score, ECP and specific IgE did not differ significantly between the active treatment and control groups. Boxes show 25–75% percentile range and median; whiskers show range of values observed.

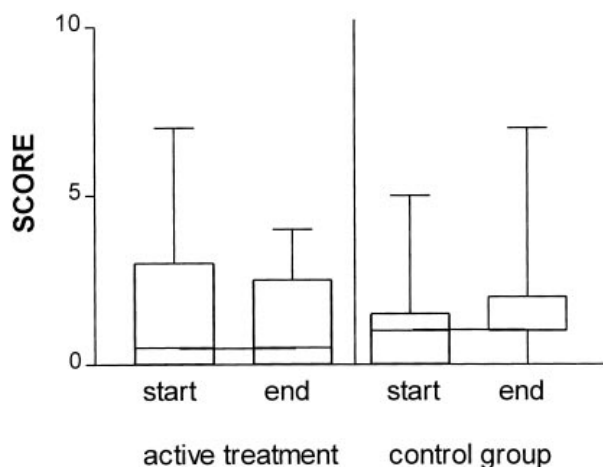


Figure 4. Subjective parameter: pruritus-induced sleeplessness. Patients were instructed to document their pruritus-induced sleeplessness on a visual analogue scale every week. Results in the active treatment and control groups at the beginning and end of the study are shown. There was no statistically significant difference when comparing the active treatment and control groups. Boxes show 25–75% percentile range and median; bars show range of values observed.

disease activity (SCORAD, ECP, usage of topical steroids) or for total IgE levels. In the present longitudinal study we confirm our results from a previous cross-sectional investigation¹⁴ in which we were also unable to demonstrate a correlation between disease severity, serum concentration of specific IgE and individual house dust mite antigen exposure in 92 mite-sensitized adults with atopic dermatitis. Our data also confirm the negative results of two other longitudinal trials reported previously:^{10,15} using natamycin or placebo spray with or without vacuuming in 20 patients (age 12–47 years) characterized by positive RAST and prick tests to house dust mite, the authors¹⁰ were unable to show a positive correlation between improvement in clinical score and reduced number of mites. Another longitudinal study¹⁵ failed to demonstrate a positive correlation between house dust mite exposure and clinical skin status in children with atopic dermatitis.

In contrast, there are two studies dealing with house dust mite control measures in atopic dermatitis that disagree with the above-mentioned findings. One controlled trial showed induction of an itch-free period in 30 atopic dermatitis patients characterized by positive mite RAST tests after they had been kept for 3–4 weeks in a 'clean room',⁹ while control patients did not improve. However, antigen levels were not reported in this study. The second study, published by Tan *et al.*,⁸ demonstrated positive results of antigen

elimination measures in a randomized double-blind placebo-controlled trial involving 48 patients (24 children and 24 adults). The effect of Gore-tex bed covers, benzyl tannate spray and high filtration vacuuming was compared with cotton bed covers, placebo spray and conventional vacuum cleaning.⁷ In this study, there was a significantly greater reduction in eczema severity score after 6 months in the active group, and this was associated with a 98% reduction in mean mattress dust load. One possible criticism of this study is that specific IgE was not assessed and thus sensitization to house dust mite antigens was not formally proven. Also, although the design of this study was very similar to the study presented here, the authors included 50% children, and stressed that they observed a more pronounced effect of antigen reduction on the clinical status of the children. A beneficial effect on the skin status was also seen in a recent controlled house dust mite avoidance study.¹⁶

In contrast to children, adults with long-standing disease often are polysensitized, and elimination of one single allergen may have an only limited impact on disease activity. Our study exclusively involved adults, which may be one explanation for its negative outcome. It is possible that concentrating on bed coverings may omit treatment of mites elsewhere in the home environment, but previous studies have identified this as the most important factor.^{8,16,17}

Until now, no subjective parameters in house dust mite control measures for patients with atopic dermatitis have been assessed. Some patients in the active treatment group reported less pruritus-induced sleeplessness even though no effect was seen regarding the objective parameters. Thus, reduction of allergen exposure during the night may reduce the symptom of nocturnal pruritus, but does not seem to be able to improve the overall disease activity as described by the SCORAD score and the ECP levels in the serum. A reason for this may be that patients continue to have contact with irritants and allergens other than house dust mites.

However, regarding the subjective parameters in the whole patient group, no statistically significant effect could be demonstrated. For future studies it would be desirable to obtain objective metric data instead of subjective measurements, e.g. by quantifying the amount of scratching with an infrared camera system¹⁸ in order to improve the accuracy of the measurements.

We conclude that in house dust mite-sensitized adult patients with atopic dermatitis, a reduction of allergen

exposure during the night does not seem to be able to improve the overall disease activity.

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