

Differential effect of mattress covers on the level of Der p 1 and Der f 1 in dust

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Summary

Background Exposure to house dust mite (HDM) allergens can lead to the development of allergic complaints. Mattress covers seem to be an obvious option for lowering allergen exposure in sensitized individuals. Previous studies have shown that *Dermatophagoides pteronissinus* was the most prevalent HDM species in the Netherlands.

Objective In the present study, we investigated the effect of mattress covers on Der p 1 and Der f 1 concentrations in dust samples in three areas in the Netherlands; Groningen, Utrecht and Rotterdam.

Methods Dust was obtained from mattresses of 277 patients at the beginning of the study and after 12 months of the placebo-controlled intervention. It was analysed for allergen content by immunoassay. The differential effect of the intervention on Der p 1 vs. Der f 1 was analysed in a subgroup with Der p 1 + Der f 1 > 1 µg/g dust ($N = 161$). It was tested whether the intervention caused a significant change in the Der f 1/Der p 1 ratio.

Results At $t = 0$ we found very similar levels of the group 1 allergens of both species. The relatively high prevalence of *D. farinae* in our study was geographically restricted: the median Der f 1/Der p 1 ratio was 11.1 in the Rotterdam area compared with 1.32 in the Utrecht area and 0.33 in the Groningen area. Analysis of our data showed that the favourable intervention effect found for the combined allergen data (reduction factor = 2.9, $P < 0.001$) is essentially due to a favourable effect of the intervention on the Der f 1 levels only (reduction factor = 3.6, $P < 0.001$). The effect on the Der p 1 level was remarkably small (reduction factor: 1.2, $P = 0.48$). In the intervention group, the Der f 1/Der p 1 ratio decreased after 12 months by a factor 2.0, whereas in the placebo group it increased (probability of the intervention effect: $P < 0.005$).

Conclusion Mite-impermeable covers are more effective in reducing the level of Der f 1 than that of Der p 1.

Keywords allergen avoidance, Der f 1, Der p 1, house dust mite, mattress cover

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Introduction

Mattress covers seem to be an obvious option for lowering allergen exposure of mite-allergic patients. Their efficacy remains, however, unproven. In a placebo-controlled multicentre study ($N = 277$) we were unable to demonstrate clinical benefit in mite-allergic patients [1, 2]. In order to exclude that the lack of efficacy was due to an insufficient effect on mite allergen levels in mattress dust, we performed immunochemical analyses in the dust collected from the mattresses. As marker allergens we measured the content of two major mite allergens (Der p 1 and Der f 1, from *Dermatophagoides pteronyssinus* and *D. farinae*, respectively). For the main

statistical analyses, we used the summed values of these two allergens. A significantly higher reduction factor (2.81) was found with mite-impermeable mattress covers compared with placebo covers (1.01), corresponding to an intervention effect of a factor 2.77 (95% confidence interval, 1.72–4.47, $P < 0.001$).

As a post-test analysis, we checked whether the intervention-induced changes were similar for Der p 1 and Der f 1. Unexpectedly, significant differences were found.

Materials and methods

Patients

Three hundred and twenty-five house dust mite (HDM) allergic patients took part in the Dutch Mite Avoidance Study (DUMAS) regarding efficacy of the allergen-impermeable encasings [1, 2]. All the patients suffered from asthma

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and/or eczema and/or rhinitis. All patients were between 8 and 50 years, had a positive skin-prick test to *D. pteronyssinus* (ALK-ABELLO, Horsholm, Denmark, 30 BU/mL), and specific IgE to *D. pteronyssinus* (RAST ≥ 0.7 kU/L). Of 325 patients, dust data were available from 277 patients at the end of this 12-month study. Of these, 161 patients had Der p 1 + Der f 1 > 1 $\mu\text{g/g}$ dust. Participating centres were the Allergy Departments of the University Hospitals of Groningen and Rotterdam, and the Dermatology Department of the University Hospital, Utrecht. Patients were recruited through general practitioners, by contacting research staff after reading the articles about the 'DUMAS' in the media or from the three above-mentioned outpatient hospital clinics. The study protocol was approved by the Medical Ethics Committees of all participating clinical centres. Written informed consent was obtained from all the patients.

Study design

The patients were part of a randomized, placebo-controlled, double-blind, multi-centre trial which aimed to measure the effect of encasing of mattresses, pillows and duvets on complaints of allergic asthma, eczema and/or rhinitis. The follow-up lasted 1 year.

Mite avoidance measures

The active treatment consisted of Goratex bedding system (HAL, Haarlem, the Netherlands). The placebo group received cotton encasings (HAL). Encasings were applied to the mattress, duvets and pillows on all beds in the patients' room.

Dust collection, extraction and group 1 allergen assessment

Dust samples were collected by a 'blinded' study technician. Dust was subsequently sampled for 5 min from 1 m² square metre area with a vacuum cleaner (1200 W) containing a 20- μm filter paper in a filter chamber (ALK-ABELLO). Dust was sampled before treatment, at 4 months and at 12 months from the mattress, bedroom and the living room floor in the patient's house. Dust samples were weighed and stored at 4 °C until extracted. Der p 1 and Der f 1 concentrations were measured by immunoassays as previously described [1, 2].

Parameters

Changes in the HDM concentration per gram dust were measured. Unless stated otherwise, the results reported in this paper refer to mattress dust.

Study centres

Patients were recruited from three different areas in the Netherlands. The Groningen area is the northern part of the country, the Utrecht area in the middle and the Rotterdam area in the south-western part of the country.

Statistical analysis

Statistical tests were performed with SPSS 10.0 as two-tailed tests on log-transformed data. In the graphs, the box plots are shown with 10-, 25-, 50-, 75- and 90-percentile values. For the median value also the standard error of the median is indicated. This standard error of the median was calculated according to Campbell and Gardner [3].

Results

Traditionally, the predominant species of HDM in the Netherlands has been assumed to be *D. pteronyssinus* [4]. However, in the present study we found very similar levels of the group 1 allergens of both species (Fig. 1).

This relatively high prevalence of *D. farinae* was found to be geographically restricted: it was much more common in the Rotterdam area than in the Groningen area (Fig. 2).

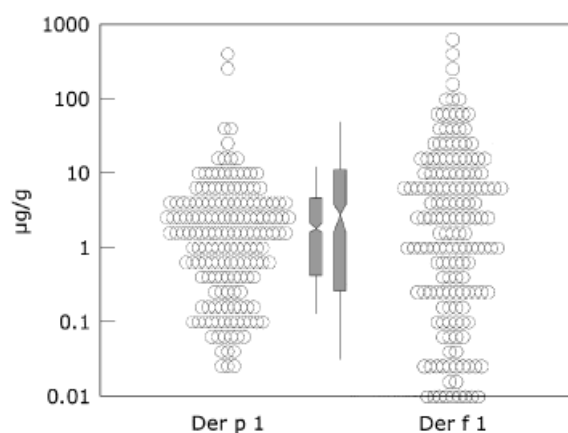


Fig. 1. The concentration at $t = 0$ of Der p 1 (left) and Der f 1 (right), expressed in $\mu\text{g/g}$ dust. The median values are indicated with the standard error of the median. In paired analysis, the difference between the two allergen levels was not statistically significant (both by Student's t -test and by Wilcoxon's signed ranks test).

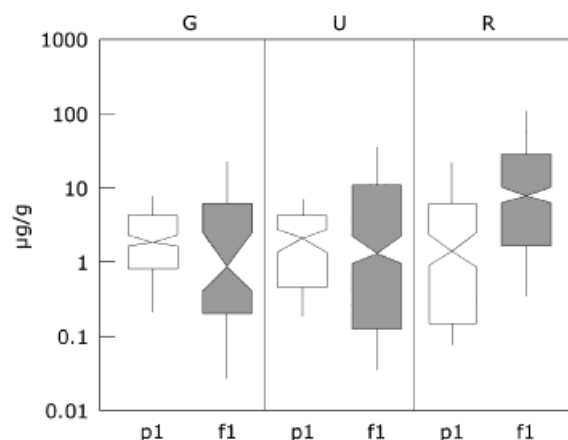


Fig. 2. Comparison between the mite allergen levels in the three study locations: G, Groningen; U, Utrecht; R, Rotterdam. By ANOVA, no significant difference was found for the Der p 1 levels. In contrast, the levels were significantly different for Der f 1: it was much more common in the Rotterdam area than in the Groningen area. ANOVA of the ratio of Der f 1/Der p 1 indicated that the difference between Der p 1 and Der f 1 was significant ($P = 0.002$).

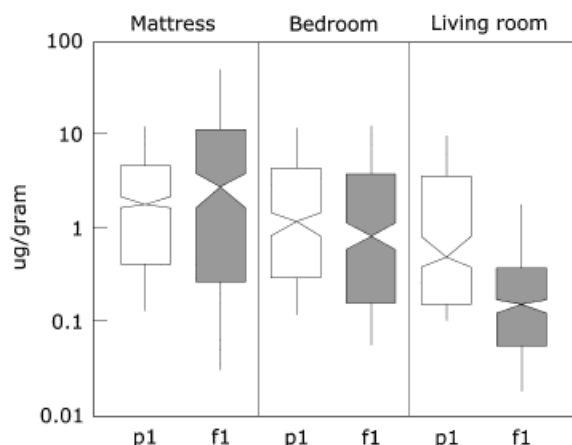


Fig. 3. Comparison between locations in the home. The contribution of Der f 1 is particularly relevant in the mattresses and much less so in dust from the living room.

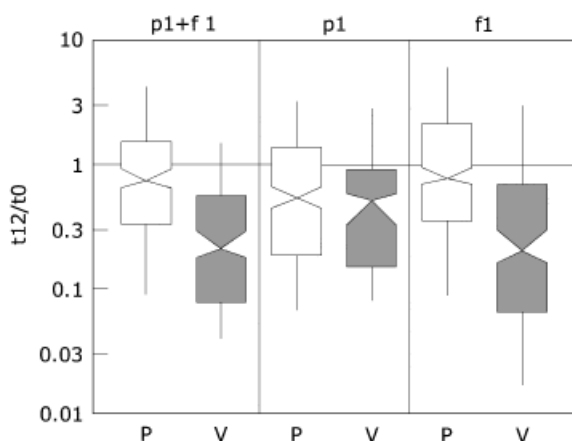


Fig. 4. Changes in the levels of Der p 1 and Der f 1 after the intervention (P, placebo; V, verum). The results are expressed as ratio ($t = 12$ months)/($t = 0$ months). The difference in the change found between placebo and verum for Der p 1+Der f 1 (left panel) reflects the effect on Der f 1 levels (right panel) rather than that of the Der p 1 levels (middle panel).

In addition to the geographical differences, we found differences within the home, with more *D. farinae* in the mattresses, compared with the floor dust of bedroom or living room (Fig. 3).

Since the present analysis is focused on the effect of the intervention on the ratio between the two allergens, we restricted this analysis to dust samples with a total allergen level (i.e. Der p 1+Der f 1) of more than $1 \mu\text{g/g}$ dust at $t = 0$ ($N = 161$, of which 71 were in the treatment group; 59 were from Groningen, 51 from Utrecht and 51 from Rotterdam). The geometric mean value for Der p 1+Der f 1 was $8.3 \mu\text{g/g}$. The results of the intervention are shown as box plots in Fig. 4.

As can be seen from this figure, the favourable intervention effect found for the combined allergen data is essentially due to a favourable effect of the intervention on the Der f 1 levels only. To investigate this more directly, we analysed the effect of the intervention on the ratio of Der f 1 to Der p 1 (Fig. 5). Statistical analysis showed a highly significant decrease in the f1/p1 ratio by a factor 3.4 (95% confidence interval: 1.5–7.8).

To exclude that the apparently selective effect of the intervention reflected differences in recruitment sites, we

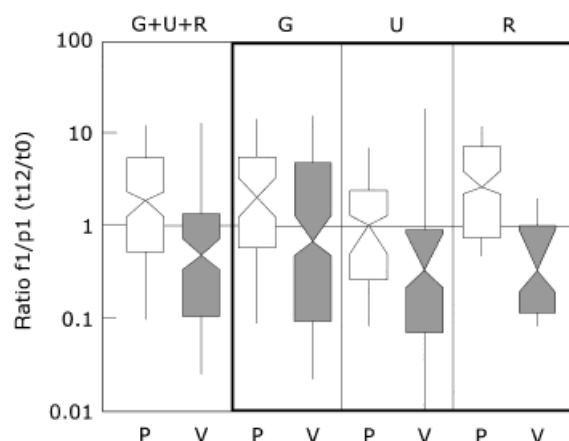


Fig. 5. Analysis of the effect of the intervention on the change (t_{12}/t_0) of the Der f 1/Der p 1 ratio; P, placebo; V, verum; G, groningen; U, utrecht; R, rotterdam. In the first panel on the left, the total study population is shown: Groningen+Utrecht+Rotterdam. In the next three panels, the results for the separate recruitment locations are shown. The conclusion is that the intervention selectively decreases the Der f 1 levels in mattress dust.

performed the same statistical analysis after stratification for the recruitment site. In Groningen, the f1/p1 ratio decreased by a factor 2.7, in Utrecht by a factor 2.3 and in Rotterdam by a factor 5.4 (Fig. 5). A detailed ANOVA confirmed a highly significant interaction between intervention effect and mite species, but no interaction between intervention effect and recruitment area.

Discussion

A high prevalence of *D. farinae* in Northern Europe has been reported in other studies, such as in Germany [5, 6] and Denmark [7]. Our data support the conclusion that, unless assays for both species are performed, mite exposure can be significantly underestimated.

The substantial variation over small distances in the relative prevalence of the two species (Fig. 2) is intriguing. Demographic as well as geologic differences might be involved. Rotterdam and Groningen are both close to the sea, but despite the short distance (250 km) between these two cities, the small climatic differences may be relevant as well. Studies by Arlian et al. [8] indicated for *D. pteronyssinus* a faster growth at optimal humidity, but a shorter half-life for desiccation.

The most unexpected result of our study is the selective effect of mite-impermeable covers on one species (*D. farinae*). This effect was also found if we calculated the allergen levels per mattress rather than per gram of dust. Perhaps the most pressing question is: how the level of *D. pteronyssinus* allergen is maintained despite the covers and why our results are different from those reported in a number of other studies [9–12], where a decrease in *D. pteronyssinus* allergen level was found. Re-colonization of mattresses from carpets and upholstered furniture is the most likely explanation. It is reported to be a rapid process [13]. We do not know whether the two mite species differ in this respect.

Our results raise another issue: are the clinical effects of the allergens produced by these two mite species quantitatively comparable? If *D. pteronyssinus* would have more

pronounced clinical effects than *D. farinae* this might contribute to an explanation of the lack of clinical effect in this intervention study [1]. However, this is not likely because the association between exposure levels and symptoms was better for Der f 1 than for Der p 1 in the Indoor Factors and genetics in Asthma (INGA) study [6].

A more detailed biological and clinical comparison between the prevalent dust mite species is eagerly awaited.

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References

- Oosting AJ, Bruin-Weller MS, Terreehorst I et al. Effect of mattress encasings on atopic dermatitis outcome measures in a double-blind, placebo-controlled study: the Dutch mite avoidance study. *J Allergy Clin Immunol* 2002; 110:500–6.
- Terreehorst I, Hak E, Oosting AJ et al. Evaluation of impermeable covers for bedding in patients with allergic rhinitis. *N Engl J Med* 2003; 349:237–46.
- Campbell MJ, Gardner Calculating confidence intervals for some non-parametric analyses. *Br Med J* 1988; 296:1454–6.
- Voorhorst R, Spijksma FT, Varekamp H. House-dust atopy and the house-dust mite. Leiden: Stafleu, 1969.
- Gross I, Heinrich J, Fahlbusch B, Jager L, Bischof W, Wichmann HE. Indoor determinants of Der p 1 and Der f 1 concentrations in house dust are different. *Clin Exp Allergy* 2000; 30:376–82.
- Gehring U, Heinrich J, Jacob B. et al. Respiratory symptoms in relation to indoor exposure to mite and cat allergens and endotoxins. Indoor Factors and Genetics in Asthma (INGA) Study Group. *Eur Respir J* 2001; 18:555–63.
- Sidenius KE, Hallas TE, Brygge T, Poulsen LK, Mosbech H. House dust mites and their allergens at selected locations in the homes of house dust mite-allergic patients. *Clin Exp Allergy* 2002; 32:1299–304.
- Arlian LG, Confer PD, Rapp CM, Vyszynski-Moher DL, Chang JC. Population dynamics of the house dust mites *Dermatophagoides farinae*, *D. pteronyssinus*, and *Euroglyphus maynei* (Acari: Pyroglyphidae) at specific relative humidities. *J Med Entomol* 1998; 35:46–53.
- Nishioka K, Yasueda H, Saito H. Preventive effect of bedding encasement with microfine fibers on mite sensitization. *J Allergy Clin Immunol* 1998; 101:28–32.
- Frederick JM, Warner JO, Jessop WJ, Enander I, Warner JA. Effect of a bed covering system in children with asthma and house dust mite sensitivity. *Eur Resp J* 1997; 10:361–6.
- Sporik R, Hill DJ, Thompson PJ et al. The Melbourne house dust mite study: long-term efficacy of house dust mite reduction strategies. *J Allergy Clin Immunol* 1998; 101:451–6.
- Warner JA. Controlling indoor allergens. *Pediatr Allergy Immunol* 2000; 11:208–19.
- De Blay F, Birnbaum J, Charpin D et al. Comparative study of surface group 1 mite allergen buildup on 10 different bedding covers. *J Allergy Clin Immunology* 1997; 99 (1 Part 2):S161.