

Clinical effectiveness of a mite allergen-impermeable bed-covering system in asthmatic mite-sensitive patients

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Background: Exposure to allergens plays a role in the development of bronchial hyperresponsiveness and in the chronic inflammatory response seen in asthmatic patients. House dust mites (HDMs) are an important source of allergen. Reduction of these allergens might lead to better lung function and reduction of asthma symptoms.

Objective: The effect of HDM-impermeable covers on HDM allergen levels, peak flow values, and asthma symptoms were measured. Therefore a randomized clinical trial was carried out.

Methods: Fifty-two allergic asthmatic patients were randomly allocated to use the HDM-impermeable or placebo covers. During the study period, daily peak flow and asthma symptom scores were recorded. Dust samples were taken from the mattresses.

Results: We observed a significant reduction in HDM allergen levels on the mattresses after encasing them with HDM-impermeable covers (reduction of 87% of Der p 1 in micrograms per gram of dust; $P < .001$). Baseline symptoms were so low that no improvement could be established. Morning peak expiratory flow is significantly higher in the intervention group compared with that seen in the placebo group during the study period ($\beta = 20.2$; $P < .01$).

Conclusions: HDM-impermeable covers significantly decreased the level of HDM allergens. Furthermore, morning peak flow was significantly increased during the intervention period. This study indicates that HDM allergen-avoidance measures might have beneficial effects on allergen reduction and asthma outcome. (J Allergy Clin Immunol 2004;114:858-62.)

Key words: Asthma, house dust mite, allergen avoidance, peak expiratory flow

Persons spend approximately one third of their lives in bed. The microenvironment (temperature and humidity) and food supply in bed are ideal for house dust mite (HDM) growth. Consequently, mattresses,

Abbreviations used

BHR: Bronchial hyperresponsiveness

HDM: House dust mite

ICS: Inhaled corticosteroid

PEF: Peak expiratory flow

bedding, and pillows highly contribute to the total exposure to HDM.¹⁻³

Inhalation of HDM allergens can cause inflammation and bronchial hyperresponsiveness (BHR). Symptoms and BHR change in time and depend to a great extent on the level of stimulus exposure.³ Therefore reduction of allergen exposure might improve lung function and decrease symptoms in asthmatic patients.¹ HDM-impermeable covers for mattresses, bedding, and pillows can lower the exposure to HDM allergens (Der p 1 and Der f 1) in bed drastically.⁴⁻¹⁵ The effectiveness of HDM-impermeable covers on clinical parameters is under debate. On the one hand, the meta-analysis of Gøtzsche et al¹⁶ suggests no beneficial effect of HDM sanitation on clinical outcomes. Furthermore, some studies find no clinical benefit from HDM-impermeable covers.^{12,14} On the other hand, some previous research revealed that the use of HDM-impermeable covers could lead to an improvement of BHR,^{9,13} improvement in peak expiratory flow (PEF),^{5,11} improvement in symptom scores,^{5,17} and less use of inhaled corticosteroids (ICSs).¹⁵ Therefore it seems that the relationship between HDM-impermeable covers and clinical parameters is not yet clear. Further study is necessary to establish the clinical effect of using bed covers. The aim of this study was to evaluate the effectiveness of nonpolyurethane HDM-impermeable bed covers on peak flow parameters and symptom scores in asthmatic patients with HDM allergy.

METHODS

Selection and inclusion of patients

Patients with asthma between 12 and 60 years of age were recruited from general practices in The Netherlands. A RAST for HDM, grasses, trees, cats, dogs, and *Aspergillus fumigatus* was performed. Patients were considered to be allergic to HDM if they had

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TABLE I. Baseline characteristics of the study population

	Active group (n = 26)	Placebo group (n = 26)
Sex (M/F)	14/12	13/13
Age (y)	31.5	36.1
Corticosteroid use (yes/no)	11/15	10/16
Bronchodilator use (yes/no)	10/16	12/14
Smoking (yes/no)	5/21	6/20
Monoallergy (yes/no)	5/20	7/19
HDM allergy		
Level 1	6	5
Level 2	6	7
Level 3	4	4
Level 4	5	3
Level 5	0	2
Level 6	0	2
Reversibility (%)*	17.7 (11.3-24.8)	15.9 (10.7-21.2)
Morning PEF (L/min)	399.2 (356.3-442.1)	415.5 (375.9-455.1)
PC ₂₀ histamine (mg/mL)†	0.5 (0.1-1.9)	1.1 (0.5-2.2)
Overall symptom scores‡	2.1 (1.1-3.4)	2.0 (1.0-3.4)
Cough§	0.6 (0.2-1.0)	0.3 (0.1-0.6)
Breathlessness§	0.5 (0.3-0.9)	0.7 (0.4-1.2)
Wheezing§	0.3 (0.1-0.6)	0.4 (0.1-0.7)
Expectoration§	0.4 (0.2-0.7)	0.3 (0.1-0.6)
Tiredness§	0.4 (0.2-0.7)	0.5 (0.2-0.9)
Disturbed sleep§	0.3 (0.1-0.6)	0.2 (0.0-0.3)

Means and CIs or the absolute distribution (dichotomous parameters) are shown.

*Median (tested by using the Mann-Whitney *U* test) with 25th-75th percentile.

†Geometric mean with 95% CI.

‡Scale (0-60).

§Scale (0-10).

at least a level 1 HDM RAST result. Patients with HDM allergy underwent a spirometry test in a lung-function laboratory. Patients were included on the basis of reversibility ($\geq 15\%$, 15 minutes after inhalation of 800 μg of salbutamol), on the basis of BHR (PC₂₀ histamine of ≤ 8 mg/mL), or both.¹⁸ Patients were excluded if a patient met at least one of the exclusion criteria (eg, other diseases influencing lung function, use of oral steroid or cromoglycates, or being sensitive to cat and dog allergens while the animal was present in the domestic environment). Patients were included between the spring of 1998 and the summer of 1999. The Medical Ethical Committee of the University of Maastricht approved the study protocol. Informed consent of the subjects was obtained before the start of the study.

Study design

This study was a prospective, double-blind, placebo-controlled clinical trial with a baseline period of 2 weeks, followed by an intervention period of 9 weeks. Four home visits took place during the study. Subjects were randomly allocated to the allergen-avoidance group or the placebo group. The allergen-avoidance group received nonpolyurethane and moisture-permeable HDM-impermeable covers, whereas the placebo group received covers permeable to HDM. Participants received covers for mattresses, duvets, and pillows.

Dust collection and Der p 1 assessment

Dust samples were taken from mattresses at the beginning of the baseline period, 1 week after the start of the intervention period, and at the end of the intervention period. All dust samples were collected with a vacuum cleaner (Bosch activa 60, type BS6, 1300 W). The upper surface of the whole bare mattress (or, after encasing directly, on the mattress covers) was sampled in a standardized way with an intensity of 2 minutes per square meter. The amount of dust was weighed, and a 10% (wt/vol) extraction in 0.01 mol/L NH_4HCO_3 was performed by means of overnight rotation at 4°C. The samples were centrifuged, and supernatants were used for detection of Der p 1 by means of ELISA. Der p 1 was expressed as micrograms per gram of dust and micrograms per square meter of mattress surface, as recommended by Platts-Mills et al.¹⁹

Measurement of clinical parameters

Patients were asked to fill in a daily diary card during the study period of 11 weeks. Patients recorded their asthma symptom scores, 3 morning and evening PEF rates, medication use, smoking habits, and specific daily events. The following asthma symptom scores were recorded: cough, breathlessness, wheezing, expectoration, tiredness, and disturbed sleep. The symptoms were scored on a modified Borg scale (0 = no symptoms to 10 = severe symptoms).

Statistical analysis

The distributions of the concentrations of Der p 1 (in micrograms per gram and micrograms per square meter) and weighed dust (in grams) were positively skewed. These concentrations were ¹⁰log transformed to achieve a normal distribution. PC₂₀ was also transformed to obtain a normal distribution.

Data from the first week were excluded for baseline period analyses to avoid bias caused by learning effects in measuring peak flow values. An overall symptom score was calculated as the sum of the separate symptom scores of each day (on a scale from 0-60). The highest of the 3 recorded morning and evening PEF rates from the diary cards was used for the analysis. The peak flow variability was measured as follows:

$$(\text{highest PEF} - \text{lowest PEF}) / (\text{highest PEF}) \times 100.$$

Weekly means were calculated for morning PEF, PEF variability, and symptom scores. The variables had to be filled in for at least 4 days in the diary before a weekly mean was calculated.

Baseline characteristics were analyzed by using unpaired *t* tests, χ^2 tests, and the Mann-Whitney *U* test depending on the type of variable and the degree of normal distribution. Differences between the active and placebo groups for Der p 1 concentrations (in micrograms per gram and micrograms per square meter) and weighed dust (in grams) were analyzed by means of the Student unpaired *t* test. Repeated measurement was used for modeling the effects of the intervention on morning peak flow and peak flow variability. The error structure model that is used in the general linear mixed model is unstructured. Possible variables that are related to the outcome and potentially confuse the results were use of ICSs during the study period, smoking, and monoallergy-multiallergy. A correction for the baseline peak flow was added as an extra item to the model.

The resulting model was as follows:

dependent variable =

$$\begin{aligned} & \alpha + (\beta_1 \times \text{time}) + (\beta_2 \times \text{group}) + (\beta_3 \times \text{time} \times \text{group}) \\ & + (\beta_4 \times \text{ICS}) + (\beta_5 \times \text{smoking}) + (\beta_6 \times \text{monoallergy}) \\ & + (\beta_7 \times \text{baseline value dependent variable}) + \text{error.} \end{aligned}$$

Patients were taken into the analysis as long as they participated in the study (intention-to-treat analysis). *P* values used in all analyses

TABLE II. Der p 1 concentrations and total amount of dust on mattresses for the active and placebo groups

		Before intervention	After 1 week of intervention	After 9 weeks of intervention
Mean active group (n = 26)	Der p 1 ($\mu\text{g/g}$)	5.31 (2.47-11.42)	0.69† (0.26-1.83)	1.00 (0.47-2.10)
	Dust (g)	0.50 (0.36-0.68)	0.06† (0.04-0.09)	0.12† (0.09-0.16)
	Der p 1 ($\mu\text{g/m}^2$)	0.96 (0.40-2.31)	0.01† (0.00-0.04)	0.04† (0.02-0.11)
Mean placebo group (n = 26)	Der p 1 ($\mu\text{g/g}$)	3.13 (1.57-6.22)	2.69* (1.22-5.94)	2.91* (1.24-6.85)
	Dust (g)	0.60 (0.42-0.88)	0.26* (0.20-0.35)	0.42* (0.29-0.61)
	Der p 1 ($\mu\text{g/m}^2$)	0.70 (0.32-1.53)	0.26* (0.12-0.56)	0.46* (0.18-1.17)

Geometric means and 95% CIs are presented.

*One patient failed to follow-up (n = 25).

† $P < .05$.

were 2-tailed, and differences with P values of .05 or less were considered significant. For statistical analysis, SPSS (SPSS, Chicago, Ill) and SAS (SAS Institute Inc, Cary, NC) software were used.

RESULTS

Fifty-two patients started the intervention period, and after allocation, both the active group and the placebo group consisted of 26 patients. The baseline characteristics are given in Table I. No variable differed significantly between the groups ($.17 < P < .94$). The mean symptom score was 2.1 (on a scale of 0-60). In the placebo group one patient failed to fill in the diary cards and could therefore not be included in the analyses for clinical parameters. Patients in both the active and placebo groups missed days in their diary cards because of illness, vacation, or other reasons. Consequently, some weekly means were missing. No significant differences were seen between the group participants with and without some missing weekly means. Therefore data of all 51 patients were used for analysis.

Concentrations of Der p 1 and weight of dust sampled in the baseline period and after 1 and 9 weeks of intervention are summarized in Table II. During baseline, no significant difference between the active and the placebo group was seen. The level of HDM allergens and total dust was significantly lower in the active group compared with that in the placebo group after 1 week of intervention. Furthermore, Der p 1 in micrograms per meter squared and total dust remained significantly lower in the active group compared with that in the placebo group after 9 weeks of intervention. Reductions in Der p 1 in micrograms per meter squared of 98.5% ($P = .001$) and 95.4% ($P = .001$) were found in the active group after 1 and 9 weeks of intervention, respectively.

Because the baseline symptom score was very low in the research population, no analysis was done on the effect of HDM avoidance on symptom score. The average morning PEF differed significantly between the placebo and active groups during 9 weeks of follow-up ($P = .01$; Fig 1 and Table III). Repeated-measurement analysis showed no significant difference for the course in time of morning PEF between the active and placebo groups (Table III). Results of the likelihood ratio test were significant for the model ($P = .00$; $\chi^2 = 448.22$).

The use of ICSs and smoking had a significant influence on the peak flow rate in the model. The peak flow

variability did not differ significantly between the 2 treatment groups during the study period ($P = .99$).

DISCUSSION

In the present study the use of HDM-impermeable covers led to significant reductions of HDM allergens after 1 and 9 weeks of intervention compared with the use of placebo covers. Moreover, this study showed significantly higher morning peak flow in the intervention group compared with in the placebo group during follow-up. No difference for trend in time between the groups was found. Furthermore, no significant differences between the active and placebo groups were seen for PEF variability.

The effectiveness of HDM-impermeable covers for reducing HDM allergen exposure has also been suggested by other studies.⁴⁻¹⁵

Measures that lead to very large reductions in HDM allergen exposure, such as HDM-impermeable covers, can have beneficial effects in patients with HDM allergy with asthma. Several studies tried to evaluate the effect of HDM-impermeable covers on the lung-function parameters and symptoms in asthmatic patients. Some studies found clinical benefits from the use of covers.^{5,8,9,11,13,17,20} In one study patients even managed to reduce their use of ICSs by almost 50%.¹⁵ However, other studies did not find clinical effects, such as lower BHR, less symptoms, or higher PEF, when covers were used,^{6,12,14,17} although in one study each, a significant decrease in total serum IgE levels and a significantly lower eosinophil peroxidase concentration were seen in the intervention group.^{6,12}

This study showed that reducing HDM allergen levels could improve the morning peak flow in asthmatic patients by 20 L/min. Morning peak flow is an important asthma-related lung-function parameter. Morning peak flow is likely most affected by mite avoidance in the bed. Reduction of allergens during the night by using impermeable covers seems to result in beneficial effects on morning peak flow.

An improvement of 20 L/min could be seen as a clinically important outcome, especially keeping in mind that the PEF at the start of the study was approximately 400 mL/min. Furthermore, the difference between the groups is as large as the normal physical decrease in PEF in 10 years.^{21,22}

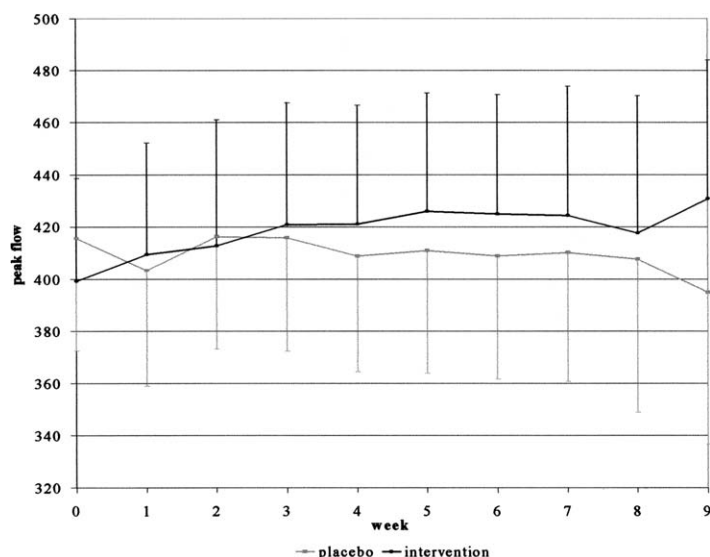


FIG 1. Morning PEF for the active and placebo groups during 9 weeks of intervention. Means and 95% CIs are given. **P* value between groups after 9 weeks of intervention on the basis of the repeated-measurements analyses reported in Table III.

TABLE III. Repeated-measurement model with morning peak flow as the dependent variable

	Estimate (β)	SE	df	t	P value
Intercept	38.41	18.20	44	2.11	.04
Code placebo vs active	-20.22	7.80	44	-2.59	.01
Week	0.27	0.68	44	0.40	.69
ICS use ($\mu\text{g}/\text{d}$)	-0.042	0.01	44	-3.43	.0
Smoking vs no smoking	-25.75	10.23	44	-2.52	.02
Monoallergy vs multiple allergy	-7.26	9.23	44	-0.79	.44
Correction baseline	1.01	0.04	44	27.46	.01

Contact with other allergens, such as grasses and animals, can also trigger an inflammatory response in sensitive persons. The inclusion period of this study was a whole year, and therefore influence on our results by allergen exposure in specific seasons is unlikely. Furthermore, active and placebo measures were randomly allocated during the whole year. It was expected that the influence of seasonal allergens on outcome was equal in both groups. Patients who had a pet and were more allergic to that specific animal than to HDM were excluded from this study. It could be expected that subjects with a monoallergy for HDM would have a more distinct benefit from the use of covers than patients with a multiallergy. In our study the repeated-measurement model was corrected for the number of allergies. Thus it is very unlikely that this factor influences the results.

Medication use and, in particular, use of ICSs can act as a confounding factor. During follow-up, the use of ICSs was significantly higher in the active than in the placebo group. It is possible that patients' symptoms were

better controlled by medication, and therefore preventive measures like covers had less effect on the decrease in peak flow variability. On the other hand, use of more ICSs can be an indicator of more severe asthma. Although the use of ICSs was higher in the intervention group, the morning peak flow value remains significantly higher in this group compared with in the placebo group after correction for ICS use.

More patients are required to find a difference between groups for PEF variability; the SD for this parameter is larger compared with the SD of morning PEF.

Because symptom scores were very low at study baseline, there was hardly any room for improvement during intervention. The instrument used for measuring symptoms has been proved sensitive in a previous study.²³ Therefore it seems likely to assume that the population was feeling rather asymptomatic. According to other studies, it seems essential to achieve and maintain a major reduction in allergen levels for many months before the effects on symptoms and pulmonary function become fully apparent.^{5,9,15} It takes some time to reverse the already developed process of inflammation.²³ Even high-altitude and hospital studies observed distinct improvement only after months.^{24,25} The follow-up of this study was probably not long enough to make conclusions on long-term benefits.

Incorporation of covers into a multisystem avoidance program might result in more distinct effects.^{23,26-29} Nevertheless, in most studies in which covers were combined with other devices, the results of HDM reduction were attributed to the effect of the covers.^{23,28,29}

In conclusion, this study shows that reducing HDM allergen levels could improve the morning peak flow in asthmatic patients by 20 L/min in 9 weeks. Research to evaluate the long-term clinical effect of avoidance

measures with a sufficient follow-up is necessary. Furthermore, the use of medication and the presence of other allergies than HDM allergy should be taken into account in other studies on the effectiveness of HDM sanitation.

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