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Double-blind controlled trial of effect of housedust-mite allergen avoidance on atopic dermatitis

Boon B Tan, Dawn Weald, Ian Strickland, Peter S Friedmann

Summary

Background The role of housedust-mite (HDM) allergen (Der p1) in the pathogenesis of atopic dermatitis is controversial. We tested the hypothesis that atopic dermatitis improves if amounts of HDM allergen in the home are reduced.

Methods Active treatment comprised Goretex bedcovers (placebo, cotton covers), benzyltannate spray (placebo, water), and a high-filtration vacuum cleaner (placebo, a conventional domestic vacuum cleaner). Dust was sampled monthly from the mattress covers and bedroom and living-room carpets. 48 patients (24 adults [mean age 30] and 24 children [mean age 10]) completed the 6-month study. 28 were in the active treatment group and 20 in the placebo group.

Findings The weight of dust collected from Goretex-covered mattresses had fallen by 98% at 1 month (from 386 to 9 mg/m²) with no change thereafter. Placebo covers caused a smaller reduction in dust load (361 to 269 mg/m²); the difference between active and placebo covers at 6 months was highly significant ($p=0.002$). Both active and placebo treatments caused significant reductions in Der p1 concentrations in bedroom and living-room carpets and the

differences between the treatments were not significant. The severity of eczema decreased in both groups, but the active group showed significantly greater improvements in severity score (difference between mean final scores 4.3 units, $p=0.006$) and area affected (difference between mean final areas 10%, $p=0.006$) in analysis of covariance with initial mattress dust weights and bedroom carpet Der p1 load as covariates. Reported analysis with final values for the covariates showed that most of the treatment effect was due to the reduction in mattress dust and carpet Der p1.

Interpretation The activity of atopic dermatitis can be greatly reduced by effective HDM avoidance. Methods to identify individuals who will benefit most from such measures are needed.

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Introduction

Atopic dermatitis affects up to one in ten children. Although the disorder spontaneously remits in most, it can persist into adult life and it greatly impairs quality of life.¹ Affected patients require long-term treatment with topical steroids and some need systemic immunosuppression. An alternative approach is to identify and eliminate provoking factors from the patients' environment.

Dermatophagoides pteronyssinus, the housedust mite (HDM), is widely suspected to be an important factor in the pathogenesis of atopic dermatitis. Epicutaneous challenge with HDM allergen in patients with atopic

Department of Dermatology, University of Liverpool, PO Box 147, Liverpool L69 3BX, UK (B B Tan MRCP, D Weald RGN, I Strickland BSc, Prof P S Friedmann FRCP)

Correspondence to: Prof Peter S Friedmann

dermatitis results in an eczematous reaction in which allergen-specific CD4 T cells are found.²⁻⁶ Patients usually improve when they are admitted to hospital, where levels of HDM allergens are low.⁷

HDM are found in all homes, and there is evidence that homes of patients with atopic dermatitis have higher numbers than normal.⁸ The major antigen of HDM (Der p1) is found in the mites' faecal pellets. There have been many attempts to eradicate HDM and other antigens by the use of preparations that kill mites or denature their antigens, barrier bedding systems, vacuum cleaning, and ventilation.⁹ Several studies have looked at the effects of acaricides on mite antigen load, but not in a clinical setting.¹⁰⁻¹² Others examined clinical consequences of anti-HDM measures in asthma.¹³⁻¹⁵ Some of these investigations did not monitor the effects on HDM antigen. Marks et al¹⁶ reported that the combination of impermeable bedcovers and a spray that killed mites and denatured their antigen did not reduce the Der p1 level in the home sufficiently or for long enough to benefit asthma patients. Ehnert et al¹⁷ found that killing mites with benzyl benzoate did not reduce Der p1 levels, although polyurethane bed bags greatly decreased the antigen concentration on the bed surface. This effect was associated with a significant reduction in bronchial hyperreactivity.

The question of whether anti-HDM measures can benefit patients with atopic dermatitis has received little attention. Roberts¹⁸ and August¹⁹ found improvement in atopic dermatitis after combinations of the use of plastic covers, vacuum cleaning, and removal of carpets. However, no studies have related clinical effects of atopic dermatitis to changes in Der p1 levels.

We have tested the hypothesis that the activity of atopic dermatitis is related to the domestic Der p1 load. We examined a combination of anti-dustmite measures that could easily be used in normal homes, for effects on both Der p1 load and the clinical activity of atopic dermatitis. Active treatment comprised microporous Goretex bedding, a benzyltannate (acaricide/allergen denaturant) spray for carpets, and a high-filtration vacuum cleaner.

Patients and methods

Patients with atopic dermatitis aged between 7 and 65 years were recruited from the dermatology outpatient department between November, 1993, and April, 1994. We defined patients younger than 17 years as children. Patients younger than 7 years were excluded to reduce the effect of spontaneous remission. All patients were defined as atopic on the basis of at least one positive immediate (15 min) response to prick-test challenge with a range of aeroallergens (Der p1, cat, or grass mix; Bencard, UK). Tests were considered positive when the wheal was at least 2 mm greater than that obtained with the diluent control. The volunteers had not previously taken HDM avoidance measures or had systemic treatment for their dermatitis in the previous 6 weeks. Pets were strictly forbidden.

In this double-blind, placebo-controlled trial of 6 months duration, the active treatment consisted of a Goretex bedding system (Intervent, W L Gore, Woking, Surrey, UK), benzyltannate complex spray (DMS Allersearch, Granville, NSW, Australia) for carpets, and a high-filtration vacuum cleaner (Nilfisk, BSE, Suffolk, UK). The spray is an alcohol-based solution containing benzyl alcohol to kill mites and 3% tannic acid to denature their allergens; its acaricidal and denaturing efficacy has been demonstrated.¹² The placebo group were given light cotton bedcovers (supplied by W L Gore), water with a trace of alcohol to spray on carpets in the same way as the active spray, and a standard upright vacuum cleaner with a poor

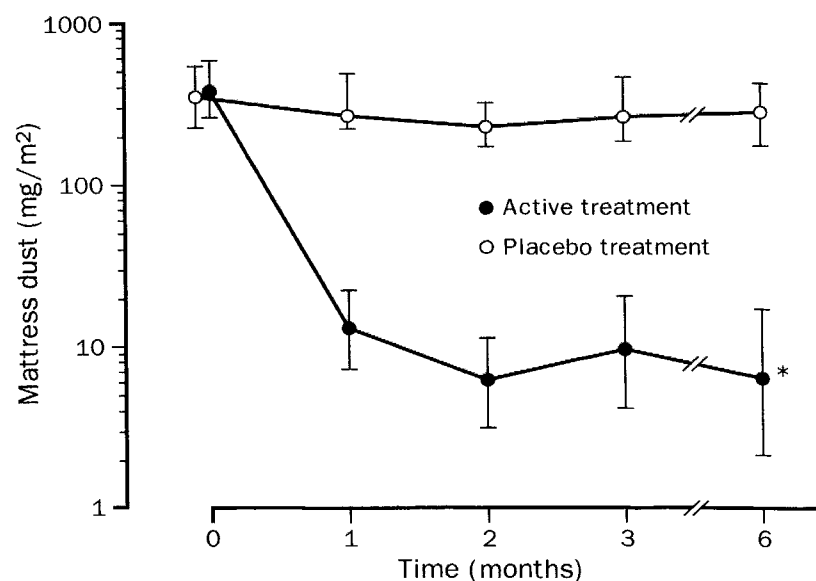


Figure 1: Change in mattress dust weight with time

Points=geometric mean values with 95% CI for all mattress dust weights (n=28 for active group, n=20 for placebo group) except at *, where n=8.

filtration performance. To standardise treatment, a trained nurse applied the bedcovers and the spray in all households. Bedcovers were applied to the mattress, duvet, and pillows on all beds in the patient's bedroom. The bedroom and living-room carpets were sprayed at a rate of 50 mL/m² once every 3 months, although the manufacturers' recommended spraying interval is 6 months. The patients were instructed to vacuum the treated carpets daily and the rest of the house two to three times a week. Soft toys were excluded from bedrooms. Patients were allowed to use their normal range of treatments.

Dust samples were collected over 2 min from a 1 m² area with a handheld vacuum cleaner (Hoover dustette) containing a 20 µm filter paper in a filter chamber (ALK, Denmark). Dust was sampled before treatment and monthly thereafter from the carpet beside the head of the bed, in front of the settee in the living room, and the whole surface of the mattress cover.

Dust samples were weighed, then extracted overnight in phosphate-buffered saline, pH 7.6, containing 0.2% (weight/volume) bovine serum albumin (Sigma, UK). In many dust samples loose fibres and hair interfered with elution of small volumes and in general, dust loads of at least 50 mg were required for effective extraction of Der p1. The supernatants were aspirated, passed through a microfilter (0.45 µm, Millipore), and stored at -20°C until assay for Der p1 by ELISA (ALK, Denmark).

One physician unaware of treatment group allocation examined all patients monthly throughout the study. The body surface area affected (rule of nines)²⁰ and severity of dermatitis (six-area, total-body severity assessment; maximum score 108)²⁰ were assessed.

The distributions of dust data (weights and Der p1 concentrations) were normalised by logarithmic transformation, and Student's *t* test (unpaired) was used for comparison between treatment groups. Differences in final eczema severity scores, change in severity scores, and surface areas affected were assessed by analysis of covariance with initial severity or surface area and log of initial mattress dust weights as covariates to control for baseline differences between the groups.

Results

60 patients (30 adults, 30 children) were randomly allocated to active or placebo treatment groups. Ten patients (one active group, nine placebo group) withdrew after randomisation but before starting treatment because they moved house, acquired pets, or changed carpets. Two patients (one in each group) were excluded after the start of the study for breaking the protocol (the actively treated patient moved house and the placebo-treated patient took Chinese herbs because of lack of efficacy of

	Geometric mean (range) Der P1 concentration in ng/m ²	
	Bedroom carpet	Living-room carpet
Active treatment group		
At baseline	3669 (16–42 014)	1321 (0–30 130)
At 6 months	249 (0–15 625)	271 (0–4270)
Placebo treatment group		
At baseline	2161 (32–36 756)	913 (54–22 391)
At 6 months	225 (0–18 063)	271 (7–6726)

Table: Concentration of Der p1 in bedroom and living-room carpets

study treatment). 48 patients (24 adults, mean age 30; and 24 children, mean age 10) completed the 6 months of treatment. 28 patients were in the active group and 20 in the placebo group. The groups were well matched for sex (active nine male, placebo eight male) and age (mean ages 21.0 and 22.5 years, respectively).

The initial geometric mean dust load in mattresses was 386 (95% CI 277–690) mg/m² in the active treatment group and 361 (243–534) mg/m² in the placebo group (figure 1). The dust load recovered from mattresses with Goretex covers fell by 98% within the first month and there was no further reduction; the geometric mean load at 3 months was 9 mg/m² (95% CI 4–20 mg/m²). Because only eight of the 28 beds contained sufficient dust for extraction and assay of Der p1, dust weights are given, and after 3 months sampling was not performed on all beds. The placebo covers also caused a small but significant ($p=0.01$) reduction in the dust load (figure 1), which did not change significantly after 2 months. At 6 months the geometric mean dust weight had fallen by 16% to 269 (193–375) mg/m². At 6 months, the difference between the active and placebo treatment groups was highly significant ($p=0.002$).

In all homes, the concentration of Der p1 was higher in bedroom carpets than in living-room carpets (table). Both active and placebo treatments significantly reduced Der p1 concentrations. The median reductions with active and placebo treatment, respectively, were 91% and 89% for bedroom carpets ($p=0.94$; U test) and 76% and 38% for living-room carpets ($p=0.27$; U test).

Both study groups showed significant reductions in the severity and area affected by eczema (figure 2). The mean fall in severity score was 12.6 units in the active treatment group and 4.2 units in the placebo treatment group. By analysis of covariance with initial eczema score and logs of initial mattress dust weight and bedroom carpet Der p1 concentration as covariates, the change of eczema severity score was significantly greater in the active treatment than in the placebo group (mean difference 4.2 [95% CI 1.7–6.7] units, $p=0.008$).

We also compared differences in final eczema severity scores between the groups by analysis of covariance with initial severity and logs of initial mattress dust weights and bedroom carpet Der p1 load as covariates. The difference between the groups was highly significant (4.3 units lower in active treatment group [1.3–7.3]; $p=0.006$). To examine the contribution of dust reduction in the bedroom to the difference between the groups, the analysis of covariance was repeated with the logs of the final mattress dust weight and carpet Der p1 load as covariates. This approach reduced the mean difference to only 1.9 (–3.0 to 6.4; $p=0.406$); thus, much of the treatment effect is indeed mediated by the changes in mattress and carpet dust in the bedroom.

The area affected by eczema also decreased in both groups (figure 2). The mean final area affected was 10%

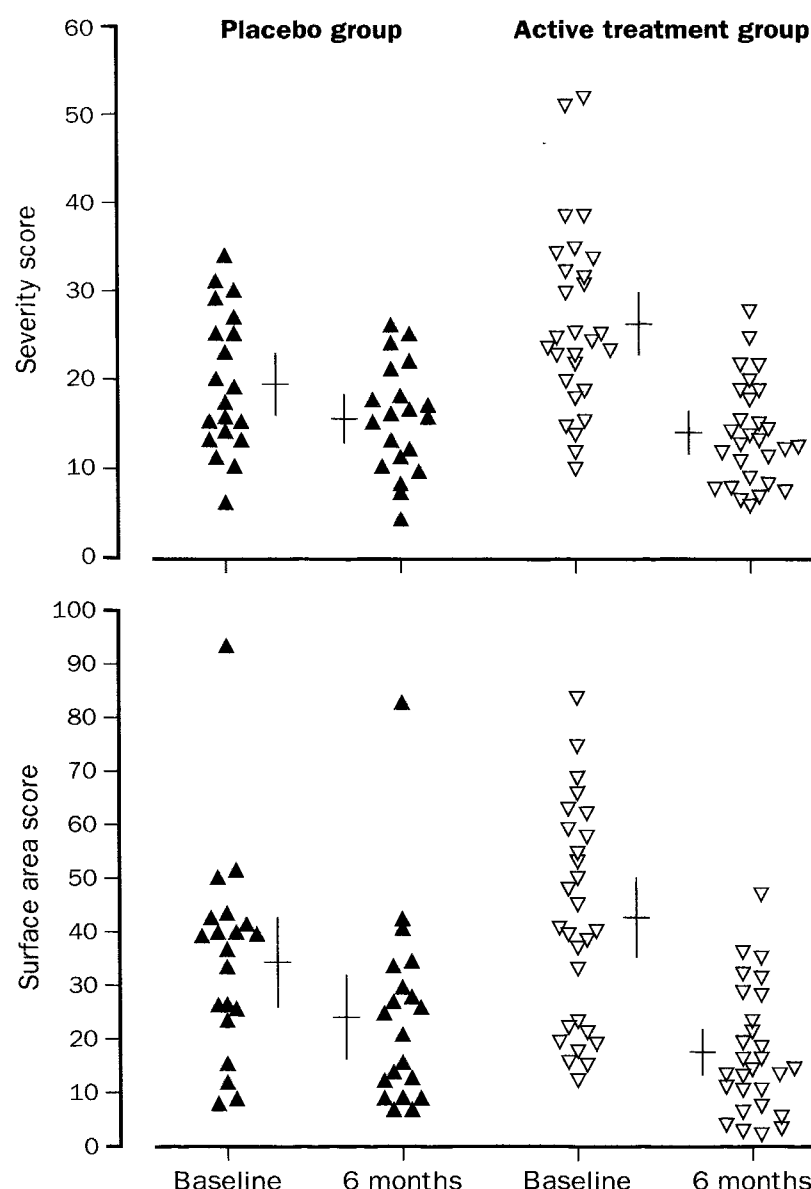


Figure 2: Effect of HDM avoidance measures on severity score and area affected by atopic dermatitis
Bars are arithmetic means with 95% CI.

greater in the placebo group than in the active treatment group (3–17, $p=0.006$, analysis of covariance). Again, analysis of covariance with the logs of the final mattress dust weight and carpet Der p1 as additional covariates reduced the size of the treatment effect to a mean difference of 8.3 (2.5–19.1, $p=0.13$), which suggests that part of the treatment effect is mediated by a change in the bedroom dust content of Der p1.

Children's and adults' responses to HDM eradication measures were analysed separately to see if they differed. Among children, those receiving active treatment had significantly lower final eczema severity than the placebo group (mean difference 11.1 [–3.1 to 25.3], $p=0.019$). Among adults the mean difference in final eczema severities was only 3 (–6.0 to 21, $p=0.28$).

We found no correlation between the initial dust or Der p1 values and eczema severity or between final dust loads and eczema severity in either group. Also, there was no clear relation between clinical improvement and the presence of positive prick-test responses to Der p1 (data not shown).

Discussion

The contribution of HDM allergy to the aetiology of atopic dermatitis is accepted as certain in the lay press, debated among allergists, and viewed with scepticism among dermatologists. Although allergic reactivity to HDM antigens can be detected by prick-test challenge in virtually all patients and by patch-test challenge in about

85%, the clinical significance of these responses is unclear.

In this study, we used a combination of anti-HDM measures to obtain the maximum possible effect. The bedding system has been associated with an improvement of asthma, rhinitis, and eczema symptoms,^{21,22} the spray used kills live mites and denatures Der p1,^{12,23,24} and the high-filtration vacuum cleaner prevents dispersion of Der p1 into the air, as occurs after conventional vacuum-cleaning.²⁵ We found that the Goretex bedding bags greatly reduced the quantities of dust in beds such that we could not retrieve sufficient dust to measure Der p1 concentrations in 68% of beds after 1 month. Treatment of carpets with the combination of the spray and a high-filtration vacuum cleaner reduced Der p1 concentrations significantly but the placebo treatment—a standard vacuum cleaner with a poor performance in tests reported by the UK Consumers Association—had a similar effect. We cannot draw conclusions about the relative contributions of the spray and the high-filtration vacuum cleaner. The final Der p1 concentrations in the carpets were similar in the two treatment groups (table), which suggests that more complete elimination of Der p1 from carpets is not possible. Upholstered furniture forms an additional reservoir for HDM.

Although the patients were randomly assigned the treatments, by chance more patients with severe eczema were assigned active treatment. Because volunteers were randomised sequentially and the clinical observer was unaware of treatment allocation, no provision was made to scrutinise the groups or to stratify them for severity. There could be an important placebo effect from the disturbance of monthly visits by a nurse to sample dust, put bags on the bedding, and spray the house. The significant improvements in the placebo group are, however, partly due to the partial efficacy of the placebo treatment, reflected by reductions of Der p1 in the carpets and dust in the mattresses.

Overall, the patients receiving active treatment showed significantly greater clinical improvement than those in the placebo group. In some individuals the amelioration was dramatic, with a substantial improvement in quality of life. The greatest benefits seemed to occur in children, but a formal study would be required to test for real differences between responses of adults and children.

Our hypothesis was that the clinical benefit derived from anti-HDM measures should be related to the reduction in Der p1 concentration in some parts of the domestic environment. Analysis of covariance suggested that a significant component of the treatment effect was related to the changes in dust and Der p1 in mattresses and bedroom carpets. However, there were no simple correlations between eczema severity and either initial dust or final dust.

We have shown that Goretex bedcovers effectively prevent contact with Der p1 in beds, but we detected no differences in efficacy of high-filtration or normal vacuum cleaners. Anti-HDM measures were associated with highly significant improvements in eczema severity. The heterogeneity of responses clearly indicates, however, that for some individuals other factors are important. Methods are needed to identify those patients who will benefit most

from these measures, and to identify the provoking factors for those who do not so benefit.

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