

Dust mite allergen avoidance in the treatment of hospitalized children with asthma

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Background: Asthma is a leading cause of hospital admission in children. The majority of children with asthma are sensitized and exposed to inhalant allergens that may contribute to chronic airway inflammation.

Objective: To evaluate the practicality and effects of dust mite (*D. farinae* and *D. pteronyssinus*) allergen avoidance in homes of children hospitalized with acute asthma.

Methods: Children 5 to 18 years of age who were admitted with asthma to a suburban Atlanta hospital were randomly assigned, without knowledge of allergen sensitization or exposure in their houses, to active (n = 13) or placebo (n = 10) treatment group. Active treatment included encasing mattress, box springs, and pillows in allergen impermeable covers; weekly hot water wash of bed linens; replacement of bedroom carpet with polished flooring; and 3% tannic acid spray to living room carpet. Placebo treatment included permeable encasings for bedding, cold water wash, and water spray for carpet. Dust samples were analyzed for dust mite, cockroach, and cat allergens, while serum samples were analyzed for IgE antibodies to the same allergens. Outcome measures included daily peak expiratory flow rates, spirometry, methacholine inhalation challenge, and hospital readmission.

Results: Children in both groups were similar by demographics, sensitization, and exposure to dust mite allergen. Allergen levels fell >3-fold in many active and placebo homes. Children in the active group had improved PEFR at 3 and 6 months after intervention ($P < .04$, $P < .05$, respectively). Six of seven children in the study who were sensitized and exposed to dust mite allergen demonstrated improved PEFR at 3 months when allergen levels fell in both bedding and bedroom floor. There was no difference in FEV₁ or methacholine challenge, although few children in either group could tolerate methacholine because of bronchial hyperreactivity. Six children (four active and two placebo) were readmitted to hospital during the study.

Conclusion: Increases in PEFR were recorded among children in the active treatment group and also among sensitized patients whose dust mite allergens fell. These results support the hypothesis that avoidance can be effective even among children admitted to hospital. The study was complicated by insufficient numbers of mite-allergic children and poor compliance with diaries and the protocol. Recruitment from the hospital resulted in participants with more severe asthma than anticipated. The results also suggest that many of the patients in this group will continue to have exacerbations triggered by upper or lower respiratory tract infections.

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INTRODUCTION

The prevalence of asthma has increased over the last 30 years and this

disease has become the leading cause of hospital admission in childhood.¹ Exposure to elevated levels of dust mite allergen early in childhood has been associated with the development of asthma in children of atopic parents.² As many as 85% of children with asthma have positive skin tests to at least one inhalant allergen. In the USA several different indoor allergens may be important in asthma. In the South-

east, dust mite allergens are of great importance.^{3,4} Significant reservoirs of allergen include mattresses, pillows, bed linens, carpet, and upholstered furniture.

Exposure to mite allergens from beds and pillows can be markedly reduced when allergen-proof encasing are used and bed linens are washed in hot (>55 °C) cycle.^{5,6} Carpet allergen levels may fall when treated with acaricides or tannic acid; however, the decreases are only modest.^{7,8} When mite-allergic patients with asthma are moved to a high altitude sanatorium or a hospital room with low levels of allergen, there is significant improvement in bronchial hyperreactivity.^{9–11} In addition, controlled trials of mite avoidance in bedrooms of patients with asthma have been successful in Berlin, Vancouver, and England.^{6,12–14}

Applying rigorous allergen reduction modifications in typical homes is difficult to achieve. Failure to follow through with mite avoidance has been explained by lack of family support, cost of modifications, and need for help in performing the changes.¹⁵ The purpose of the present study was to evaluate the practicality and effect of modifying homes of children admitted to hospital with asthma. The modifications, designed to reduce dust mite allergen, focused on the bedroom.

METHODS AND MATERIALS

Children ages 5 to 18 years who were admitted to hospital with acute asthma between January 1, 1993 and April 30, 1994 and who lived in houses in suburban Atlanta were invited to participate. While the children were hospitalized, the parent or guardian was informed about the study and if consent was given, a serum sample was drawn and frozen. Participants were

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randomly assigned without knowledge of allergen sensitization or exposure to active or placebo treatment group. A standard oral questionnaire detailing demographic information, current and past medical history, family history, and environmental characteristics was completed.

Active treatment interventions included replacing carpet in the patient's bedroom with hardwood or vinyl flooring, encasing mattress(es), box spring(s), and pillows with allergen-impermeable covers in the patient's bedroom, application of 3% tannic acid spray every 3 months to family/living room carpet, and instructions to wash all bedding in hot wash cycle weekly in laundry detergent provided by the research team. [Bedding includes mattress pad, sheets, pillow cases, and blanket/comforter.] Placebo treatment included polycotton permeable mattress, box spring and pillow encasings, placebo water spray for carpets, and instructions to wash bed linens in cold water using the detergent provided. The placebo encasings were similar in appearance to the active encasings, but lacked the urethane membrane. All encasings were kindly provided by Allergy Control Products, Inc, Danbury, CT.

Allergen sensitization was determined by RAST at conclusion of the study from serum samples collected during the study and stored at minus 20 °C. Indoor allergen exposure analysis was performed on dust samples collected at entry, 3 months, 6 months, and 12 months. Samples were obtained by standard protocol (hand vacuumed with a fitting to collect dust, 1 m² for two minutes) from bedding, bedroom floor, living/family room floor and upholstered furniture, and kitchen floor. Dust was analyzed by monoclonal antibody ELISA for house dust mite (Der p 1 and Der f 1), cat (Fel d 1), and cockroach (Bla g 2).¹⁶ At the dust sampling visits, the home was assessed for adherence to protocol, changes in furnishings, and acquisition of a pet.

Pulmonary function testing was carried out at entry, 3 and 6 months, followed by methacholine inhalation

challenge, if the child's lung function was >80% of previous best, and FEV₁, FEF_{25–75%}, or FVC were >50% predicted and provided residual volume was not elevated. Daily morning and evening peak expiratory flow rates (PEFR) were recorded on diary cards. The cards were mailed every 2 weeks to patients with a preaddressed and stamped envelope to return completed cards. The diary cards were evaluated at 12 to 16 weeks (3 months) and 24 to 28 weeks (6 months) after intervention.

Data were analyzed using paired *t* test, on SPSS, to compare mean percentage change in dust allergen levels in homes and improvement in PEFR.

RESULTS

Twenty-five children were randomized into the study (14 to active and 11 to placebo); however, one child in each group failed to participate after randomization because of family problems. One participant in the active group shared his bedroom with an identical twin with chronic asthma and both boys completed PEFR monitoring and diaries. The groups were similar by past medical history, symptom reports, medication usage, and demographics although all four African-American females were randomized to active treatment (Table 1). The children were generally full term at birth and only two experienced respiratory distress at birth. None of the children smoked tobacco, but 4/13 in the active group and 2/10 in the placebo group were exposed to passive smoke. Only a minority of participants had a history

of eczema, atopic dermatitis, or bronchiolitis. All children had previously been diagnosed with asthma and at least half had histories of "sinusitis" and "allergies" (Table 2).

Table 3 summarizes allergen sensitization and exposure to house dust mites (Der p 1 and Der f 1), cat (Fel d 1), and cockroach (Bla g 2). The majority of children (active 64% and placebo 80%) were sensitized to at least one indoor allergen. The majority of homes had elevated allergen levels in vacuumed dust. Dust mite allergen level (bedding and/or floor dust) was elevated (ie, ≥ 2 μ g group I allergen/g dust) in 9/13 active bedrooms and 7/10 placebo bedrooms. Cat allergen was elevated (≥ 8 μ g/g dust) in 3/13 active and 5/10 placebo homes. Elevated cockroach allergen (≥ 40 U/g dust) was detected in 5/13 active and 2/10 placebo homes. Six children in each group were both sensitized and exposed to elevated dust mite allergen. Sensitization and exposure to cat and cockroach allergen was less frequent in both groups.

Effect of Dust Mite Allergen Avoidance

Dust mite allergen levels were compared from entry into the study to the final visit after intervention (Fig 1). In active homes the dust mite allergen level on the bedroom floor initially ranged from <0.4 to 25 μ g/g dust. In six of the eight floors where the mite allergen level was >2 μ g, the concentration decreased, in four cases by >3-fold. In placebo homes (n = 10), seven had >2 μ g/g mite allergen on the bed-

Table 1. Demographics of Study Participants by Treatment Group

	Active (n = 13)	Placebo (n = 10)
Mean age, yr	9.8 (6–15)	8.6 (5–16)
Race, white/African-American	5/8	7/3
Sex, male/female	7/6	7/3
Housing type		
House	12	8
Apartment	1	2
Indoor tobacco smoke	4	1
Pets		
Cat indoors (outdoors)	1 (0)	2 (2)
Dog indoors (outdoors)	1 (3)	3 (2)

Table 2. Characteristics of Participants by Treatment Group

	Active n = 12	Placebo n = 10
Premature birth	2	2
Oxygen or ventilator at birth	8%	10%
Past medical history		
Asthma	100%	100%
"Sinusitis"	57%	80%
"Allergies"	75%	50%
Bronchiolitis	16%	10%
Eczema/atopic dermatitis	16%	40%
Symptom history		
Cough	25%	30%
Nasal	50%	50%
Eye	41%	10%
Rash	8%	40%
Medications at admission		
Short acting β_2 agonist	100%	100%
Cromolyn	33%	70%
Inhaled steroids	75%	40%
Theophylline	25%	—
Oral corticosteroids	16%	20%

Table 3. Sensitization* and Exposure† to Dust Mite, Cat, and Cockroach Allergens by Treatment Group

	Active n = 13	Placebo n = 10
Dust mite		
Sensitized	9	6
Sensitized and exposed	6	6
Cat		
Sensitized	1	2
Sensitized and exposed	1‡	1
Cockroach		
Sensitized	1	1
Sensitized and exposed	1‡	1

* IgE $\geq$ 40 U.† Der p 1 and Der f 1 $\geq$ 2 μ g/g, Fel d 1 $\geq$ 8 μ g/g, Bla g 2 $\geq$ 40 U/g dust.

‡ Also sensitized and exposed to house dust mite.

room floor and of these, five fell more than 3-fold. Dust mite allergen collected from bedding in active homes before intervention ranged from <0.4 to 33.5 μ g/g. Six of 11 active beds had greater than 2 μ g/g dust mite allergen; levels fell >3-fold in five of the six homes. Allergen level in the other bed fell from 5.5 to 2.9 μ g/g after intervention. In seven of 12 beds with active

covers, mite allergen levels generally remained >2 μ g/g. In active homes where there was an increase in mite allergen level in bedding (n = 2), the allergen-proof encasings had been removed from the bed at the time of the visit to collect samples. Among the placebo homes, bedding allergen levels ranged from 0.4 to 122 μ g/g. Four of the ten had >2 μ g/g initially; the levels decreased in all four, although three remained >2 μ g/g (3.9, 11.2, 20.7 μ g/g).

Objective Measures of Asthma

Changes in PEFR measurements are presented in Table 4. There was significant improvement in the active group at both 3 and 6 months ($P < .04$ and $P < .05$, respectively) after intervention as compared with placebo. Two children in the active group who were sensitized to dust mites, exposed to elevated allergen levels at entry and whose allergen levels fell at least 3-fold during the study improved from 10.5% to 48.8%. Among the children in the placebo group (n = 5) who were both sensitized and whose dust mite allergen levels decreased during the study, the PEFR varied from an improvement of 9.2% to a decrease of 22% as compared with entry PEFR.

Two of these children were also sensitized and exposed to another elevated indoor allergen: one each to cat and cockroach. Overall, six of seven children enrolled in the study, who were both sensitized and exposed to mite allergen and where allergen levels decreased, improved their PEFR at 3 months as compared with entry PEFR.

Spirometry was performed after hospital discharge and stabilization of asthma and prior to intervention. Initial FEV₁ measurements were slightly higher in the placebo group (range 61% to 105% predicted, mean 86% predicted) as compared with the active group (range 59% to 109% predicted, mean 80% predicted). Six months after intervention there was a nonsignificant improvement in the active group (range 61% to 105% predicted, mean 83% predicted) while the placebo group's FEV₁ remained the same (range 75% to 94% predicted, mean 86% predicted). The results of methacholine challenge testing are presented in Table 5. Children were excluded on a case-by-case basis from methacholine challenge if pulmonary function testing was less than 80% of the child's best baseline or showed increased residual volume or low FEV₁, FVC, or FEF₂₅₋₇₅. Children in the active group less frequently were able to perform a methacholine challenge or tolerate the initial dose of methacholine.

Four children in the active group and two in the placebo group were hospitalized after intervention. None of those in the active group were both sensitized and exposed to elevated dust mite allergen levels. One hospital admission was directly from school and was thought to be precipitated by cat allergen exposure at school. The other admissions were associated with an apparent respiratory infection. One child in the placebo group, who was both sensitized and exposed to elevated dust mite allergen, was hospitalized following onset of respiratory tract symptoms.

DISCUSSION

The present study was designed as a placebo-controlled trial of allergen

avoidance in the treatment of asthma in children who had required hospital admission. The study had several novel elements. First, the patients were not skin tested initially so that their sensitization was not known to the medical staff taking care of them or to their parents. Second, the main avoidance measures in the children's bedrooms were carried out by the study team. Third, we attempted true placebo control using placebo bedding encasings, cold water wash and detergent, and an inactive spray to the bedroom carpet. The active intervention produced significant improvement in PEFR; however, the study was only partially successful. This was in part because of insufficient numbers enrolled but also because of specific problems with the protocol that are highly relevant to the design of future studies. The main issues were related to the detailed methods of avoidance, population chosen for enrollment, and monitoring of the clinical response.

The results of intervention for dust mite allergen in the bedroom were mixed. Huss reported that the cost of dust mite avoidance, lack of family support, and the lack of assistance to complete changes were deterrents to adults completing environmental control.¹⁵ To avoid problems in the present study, the research team provided and installed the encasings onto the mattresses, box springs, and pillows, arranged for the installation of the polished floor in active homes, sprayed the living room carpet at the first visit, and provided written washing instructions and detergent. While 8/11 active homes had elevated floor dust mite allergen levels initially, only 6/8 had reduced allergen levels below 2 $\mu\text{g/g}$ after the carpet was replaced with vinyl linoleum or hardwood flooring. In five of six homes where the initial bedding dust mite allergen level was elevated, the levels fell following application of the encasings and hot water washing. In two active homes with very low allergen levels at entry, an increase in allergen levels was associated with either removal of the encasings because of enuresis or use of cold water wash.

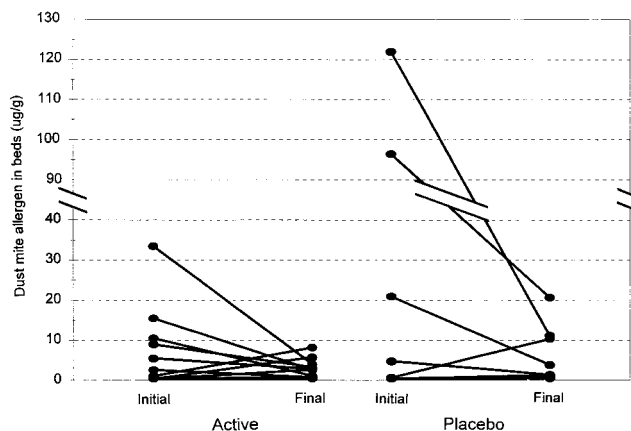


Figure 1. Change in dust mite allergen levels in bedding at initial and final visits by treatment group. The active group included 11 houses of which two had $<0.4 \mu\text{g/g}$ at initial and final visit. The placebo group includes nine houses of which two had $<0.8 \mu\text{g/g}$ at initial visit and follow-up.

Table 4. Percent Change in Peak Expiratory Flow Rate (PEFR) (L/min) at 3 and 6 Months after Intervention by Treatment Group

	Active (n = 11)		Placebo (n = 9)	
	Initial	End	Initial	End
3 Months				
PEFR mean, L/min ($\pm\text{SD}^*$)	274 (± 87)	306 (± 86)	295 (± 108)	289 (± 110)
Mean % change ($\pm\text{SE}^\dagger$)		+13.4 (± 13) $\ddagger$		-1.2 (± 13)
Range % change		+37.7 to -10.3		+13.0 to -6.0
6 Months				
PEFR mean, L/min ($\pm\text{SD}$)	295 (± 84)	328 (± 62)	288 (± 117)	266 (± 102)
Mean % change ($\pm\text{SE}$)		+15.1 (± 14) $\S$		-4.4 (± 15)
Range % change		+48.8 to -8.2		+8.6 to -22.0

$\dagger$ SE = standard error

* SD = standard deviation

$\ddagger$ $P < .04$.

$\S$ $P < .05$.

Table 5. Methacholine Challenge Testing by Treatment Group

	3 months		6 months		12 months	
	Active	Placebo	Active	Placebo	Active	Placebo
	n = 7	n = 6	n = 14	n = 10	n = 9	n = 8
None*	2	0	8	3	6	1
5 CDU $\dagger$	4	4	5	5	3	6
25 CDU $\dagger$	1	2	1	2	0	0
50 CDU $\ddagger$	0	0	0	0	0	3

* No methacholine challenge because of unsatisfactory spirometry.

$\dagger$ Methacholine concentration 5 mg/mL; 1 breath = 5 cumulative dose units (CDU).

$\ddagger$ Methacholine concentration 25 mg/mL; 1 breath = 25 cumulative dose units (CDU).

Allergen levels decreased in some placebo homes as well. A 3-fold fall in carpet allergen in 5/7 placebo homes with initially elevated level and a similar reduction in bedding allergen were

unexpected. These findings may be explained by heightened concern about the home environment, such as more frequent cleaning and washing, after hospitalization and enrollment in the

study.¹⁷ Several placebo families admitted washing bedding in hot water, and the poly-cotton encasings probably had some barrier function; thus a major problem with the protocol was that a true placebo group was not achieved. In order to compare active interventions with placebo controls, further research is needed. The extent to which allergen permeable encasings reduce collection of allergen should be evaluated. Miller reported that drying bedding in a dryer reduced dust mite level. Since most Americans dry their wash in a dryer, the effect of frequent cool water wash and heated drying needs evaluating.¹⁸

In the present study, exposure to dust mite and other allergens was evaluated by measuring the concentration of major allergens in the dust, as $\mu\text{g/g}$ dust. This method has been recommended by three international workshops and has been used in several previous successful trials.^{6,12-14,19} Some of the physical measures used, eg, replacing carpets and covering mattresses and pillows, may have more effect in decreasing the quantity of dust. Indeed, a recent report on the treatment of atopic dermatitis reported that the intervention produced highly significant decreases in the quantity of dust without a significant decrease in concentration of allergens.²⁰

Diaries detailing PEFs, medications and missed school days were sent to the families every 2 weeks along with self-addressed and stamped envelopes. Data analysis was performed at 3 and 6 months after intervention because after this time, there was poor compliance with diaries. While there was significant improvement in PEF at both 3 and 6 months among children in the active group as compared with the placebo group, spirometry demonstrated that the children continued to have significant obstructive disease, which precluded performance of methacholine challenge in many of the children.

Four children in the active group and two in the placebo group were hospitalized for asthma during the study. Children in the active group

who were hospitalized and were sensitized to dust mites were not exposed to elevated allergen levels at the time of hospitalization. The children in the placebo group were both sensitized and exposed to elevated allergen levels in the bedding.

Parents implicated a concurrent respiratory infection in four of the six children who were hospitalized. It seems likely that regular spirometry and some measurement of inflammation in the respiratory tract in addition to PEF would provide better monitoring of patients involved in studies designed to reduce exposure. On the other hand it is possible that there is a minority of children with severe asthma whose disease exacerbations are dominated by respiratory infections and who require only minimal allergen exposure to maintain inflammation in the respiratory tract.²¹

The study had been intended to enroll children with moderate asthma. A pilot study preceding the controlled study suggested that many children with moderate asthma were admitted to this hospital. In the interim between the pilot and present study, there was a change in admission policy for asthma, such that the number of children admitted decreased and most of the children who were hospitalized had more severe asthma. The children with severe asthma may require interventions in addition to allergen avoidance alone to substantially improve their asthma. Our results strongly suggest that it would be easier to establish the principle of allergen avoidance enrolling outpatients with moderate asthma.

It is difficult to enroll patients unless their routine clinical care is being carried out by members of the study team. The present study was carried out on a population of children who were cared for by several physicians using a part-time research assistant in Atlanta as the primary local liaison with the patients and their families. The results suggest that a full time local study coordinator is essential.

The findings suggest that employing proven methods to reduce dust mite allergen (allergen-proof encasings, hot

water wash, polished flooring) can be accomplished in American homes and can result in improved peak expiratory flow rate. In contrast, improvement in spirometry and bronchial hyperreactivity by methacholine challenge was not demonstrated. Issues in adherence continue to be a concern even when asthmatic children are the focus of interventions. Overall it is clear that further information about practical methods for avoidance is needed, that many houses contain more than one allergen source, and that it is extremely difficult to establish a true placebo for allergen avoidance.

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