A randomized controlled trial of mite allergen-impermeable bed covers in adult mite-sensitized asthmatics

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Summary

Background Mite-allergic patients with allergic disease should benefit from avoiding mite allergens. Many physicians, however, are yet to be convinced that allergen avoidance can make a significant contribution to asthma management in these patients. Many allergen-avoidance regimes include multiple measures of allergen reduction, but as mite exposure in the home is most likely to be greatest in bed dust, bedding is usually the first target for intervention.

Objective This study selected adult patients considered to be most likely to benefit from avoiding mite allergens, namely diagnosed asthmatics, sensitized to house dust mites and exposed to mite allergen in their mattresses. Patients were randomized into a placebo-controlled trial of the use of allergen-impermeable bed covers for 12 months, without any other form of mite-reduction measures.

Methods Adults with asthma were selected from general practices and asthma clinics in south-east London. Their serum IgE to mite allergens and allergen content of mattress dust samples were measured. Those with >0.70 kU/L mite-specific IgE and >2 μg/g Der p 1 were randomized into active or placebo treatments. Information was collected on allergic symptoms and medication use and quarterly peak flow diaries were kept throughout the trial. Dog or cat allergic patients were excluded if they had a pet at home to which they were sensitized.

Results The mean decrease in μg/g Der p 1 was 25.7 (95% CI 8.9, 74.1) in the active group and 4.5 (95% CI 1.8, 11.5) in the placebo group. Der p 1 concentrations in the active and placebo groups at the end of the trial were not significantly different. There was no effect on peak flow or asthma symptoms in a simple comparison of the treatment and placebo groups.

Conclusion In this group of patients, mite allergen avoidance in the bed by the use of allergen-impermeable bedding alone cannot be recommended as an effective way of relieving asthma symptoms.

Keywords Der p 1, mite allergen avoidance, peak flow, randomized controlled trial

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Introduction

Assuming that there is a dose–response relationship between exposure and symptoms, avoidance of an allergen to which a patient is sensitized should, in theory, result in a reduction in manifestation of allergic disease. In practice, however, the evidence that allergen avoidance can play a role in disease management has yet to be provided. In the UK, the predominant indoor allergen is the house dust mite *Dermatophagoides pteronyssinus* [1, 2], and greater than 30% of the population in East Anglia are sensitized to mites [3]. In a study in Norwich, mite allergens were present in 85% of mattresses, with a geometric mean concentration of 2 μg/g; 25% of the mattresses had mite allergen concentrations greater than 10 μg/g [4]. Studies confirm that the most important source of domestic mite exposure is the bed [5]. Concentrations of greater than 10 μg/g mite allergens in the mattress are a risk factor for an increase in symptoms in sensitized individuals [6] and new mattresses quickly become infested with mites [7]. There is evidence that house dust mite allergen exposure can play a role in the aetiology of asthma [8] and that exposure to house dust mite allergens is associated with clinical activity of asthma [9]. There is also evidence that mite allergen avoidance by encasing the mattress can reduce exposure to mite allergens and improve respiratory symptoms [10, 11].

Allergen avoidance is unlikely, however, to show a positive effect in those who are not sensitized to an allergen or in those who are exposed to low doses of allergen. This implies that allergen avoidance will only be effective in a minority of asthma patients that fall into the sensitized, high-exposure category. As allergen-avoidance strategies can be costly, both in terms of materials and with patients’ time commitment, avoidance regimes undertaken by all asthmatics are unlikely
to be effective and are very unlikely to be cost effective. If patients are carefully selected, however, it is possible that this could be a welcome and useful adjunct to therapy.

Many allergen-avoidance trials use multiple interventions in order to attempt to reduce mite allergen concentrations [12]. The problem with this design is that if the regime is successful it is not possible to identify which part of the intervention worked. Trials included in a meta-analysis that have used various methods of mite avoidance alone were able to demonstrate a reduction in mite allergens. Of 13 studies that used ‘physical’ or a combination of methods, four studies demonstrated a reduction in mite allergen levels by using mattress covers [14–17].

In addition to the studies included in the meta-analysis, studies by Owen et al. [18], Wickman et al. [19], Custovic et al. [20] and Frederick et al. [21] have clearly demonstrated that mite allergen concentrations can be reduced by using mattress covers. Sporik et al. [22] have shown that the use of mattress encasings was a useful long-term strategy for mite allergen avoidance in Melbourne, where the geometric mean concentration of house dust mite is much higher than in the UK. In Japan, where the geometric mean allergen level was similar to the UK, Nishioka, Yasuoda and Saïto used Allerguard mattress covers manufactured by Beirholms Vaeverier SA (Kolding, Denmark) and obtained decreased levels of Der p 1 and Der f 1, as well as a lower rate of allergic reactions to mite allergens in atopic infants [23].

This randomized placebo-controlled trial tested a single intervention in patients who were both sensitized and exposed to mite allergen. It aimed to assess whether the use of Allerguard allergen-impermeable bed covers, as a single intervention, resulted in an improvement in allergic disease outcomes in those patients most likely to benefit from allergen avoidance.

Methods

Selection of patients

A total of 3547 adults with mild asthma, aged 18–54 years, were identified from the general practices and outpatient clinics in south-east London who agreed to take part in the study. Fig. 1 shows the flow chart for recruiting study participants. Patients with a diagnosis of asthma and at least one prescription of inhaled steroids in the previous 12 months were invited to give a blood sample for the measurement of Der p 1 using a monoclonal antibody ELISA. Patients with more than 2 μg/g Der p 1 were randomized into active or placebo groups. Inclusion and exclusion criteria are listed in Table 1. The study was approved by the Lambeth, Southwark and Lewisham and Bromley Research Ethics Committees.

Study design

Following randomization to the trial, patients were visited at home by a fieldworker blinded to their trial status. Patients and the field worker completed questionnaires on asthma symptoms and use of asthma medication. They received an electronic peak flow meter (STI Instruments, Paris, France) and a peak flow diary, which also contained questions about asthma symptoms and use of medication, and was completed daily for 7 days. Patients undertook baseline peak flow recordings twice daily for 7 days before starting to use their allocated covers for 12 months. Further 7-day peak flow diaries were then completed at 4 months, 8 months and 12 months. Patients were visited at 6 months and at 12 months for a mattress dust sample and assessment of compliance with the trial protocol. At the final visit (12 months) they repeated the asthma symptoms and medication questionnaires. They also completed a questionnaire to check that inclusion and exclusion criteria for the trial were still being met. The trial took place between January 1998 and August 2000.

Allergen-impermeable bed covers

Identical real and sham Micro fibre allergen-proof covers were provided by Allerguard. The covers were made of 0.2 denier yarn and were 75% polyester and 25% nylon, which retained >99.5% of 0.4μm particles. The sham covers were of the same material, but had a conventional weave of 5–10μm in thickness. Covers were used to encase the mattress, duvet and/or any blankets and all pillows on the bed completely. Patients were able to use their own sheets over the covers and were given no other instructions.

Assessment of Der p 1 in mattress dust

Der p 1 was measured in mattress dust taken at month 0, month 6 and month 12. Mattress surfaces were vacuumed for
2 min using a Hoover Portapower vacuum cleaner and an ALK dust sampling filter cassette (ALK, Hørsholm, Denmark). Six-month and 12-month samples were taken with the allergy-proof covers in situ. Dusts were sieved using a 300 μm sieve and a 5% extract assayed for Der p 1 using a monoclonal antibody ELISA (Indoor Biotechnologies Inc., Cardiff, UK) as previously described [24]. Where no dust could be collected from the surface of the covers, the level of house dust mite allergen was taken to be below the detection limit of the assay. Results were expressed as μg Der p 1/g dust.

Analyses

Der p 1 values were logged for the analyses. Most studies have used peak flow as an outcome measure [25] as well as improvement of asthma symptoms. In our study, peak flow was used as the primary outcome. No effect was seen on peak flow due to ‘day of the week’ or ‘diary day’; therefore unlogged mean daily peak flow measurements, defined as mean of highest morning value and highest evening value, were used for the analyses. Peak flow lability (diary maximum minus diary minimum/diary mean) and amplitude per cent mean peak flow (highest morning minus highest evening value/mean of highest morning and evening value for each day) were also analysed. Percentage change in diary days with chest tightness has been found to be a useful predictor of use of hospital services for asthma in children [26], so we also analysed diary days with chest tightness. Quality of life (QOL) at the beginning and end of the trial was assessed using the Marks Asthma Quality of Life Questionnaire [27]. Analyses were carried out using Stata 7 [28]. All analyses were adjusted for the age and sex of the participants.

Results

Following a recruitment period of over 2 years, 722/3547 (21.7%) of patients agreed to be screened for the trial and gave a blood sample for allergy testing. Subject selection following allergy testing is shown in Table 2. Thirty-nine patients (5.4%) were excluded because they were found to be allergic to their pet. Fifty-eight patients (73.4%) of those who completed the selection process agreed to take part in the trial and were randomly allocated to active or placebo groups. By the time the trial started, three of these patients no longer met the trial entry criteria and so were excluded, leaving a total of 55 patients – 30 in the active group and 25 in the placebo group. The baseline characteristics of the trial population are listed in Table 3.

From those patients randomized for the trial, 25 and 20 patients allocated to the active and placebo groups, respectively, started the trial. Geometric mean Der p 1 concentrations at the start of the trial were greater than 10 μg/g for both the active and placebo groups. Mean Der p 1 concentrations at the start of the trial and after the mid-trial and end-trial home visits for patients who started the trial are shown in Table 4. Der p 1 concentrations decreased significantly in the active group to less than 1 μg/g at 6 months and then rose slightly at 12 months. Der p 1 concentrations in the placebo group also fell and were significantly lower than baseline at 12 months. Mean Der p 1 levels fell in the active group by 25.7 μg/g (95% CI 8.9, 74.1) and in the placebo group by 4.5 μg/g (95% CI 1.8, 11.5); however, the difference between Der p 1 levels in the active and placebo group at the end of the trial was not significant. The individual Der p 1 concentrations for the patients in the two groups are presented in Fig. 2.

Table 2. Selection of mite-sensitized, mite-exposed asthmatics from 722 patients who provided blood for allergy testing

<table>
<thead>
<tr>
<th>No IgE</th>
<th>&gt; 0.7 kU/L IgE to house dust mite</th>
<th>To cat or dog if exposed</th>
<th>Home visit for dust sample</th>
<th>&gt; 2 μg/g Der p 1</th>
<th>Agreed to take part in the trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (%)</td>
<td>351</td>
<td>312</td>
<td>266</td>
<td>79</td>
<td>58</td>
</tr>
<tr>
<td>% of patients tested</td>
<td>48.6</td>
<td>43.2</td>
<td>36.8</td>
<td>10.9</td>
<td>8.0</td>
</tr>
</tbody>
</table>

Table 3. Characteristics of trial patients randomized for trial

<table>
<thead>
<tr>
<th>Mean (SD)</th>
<th>Active (n = 30)</th>
<th>Placebo (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39 (9)</td>
<td>33 (7)</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>50</td>
<td>48</td>
</tr>
<tr>
<td>Der p 1 in mattress (μg/g)</td>
<td>19.72 (5.04)</td>
<td>26.09 (5.10)</td>
</tr>
<tr>
<td>Specific IgE to house dust mite (d1) (kU/L)</td>
<td>17.37 (5.12)</td>
<td>13.80 (3.71)</td>
</tr>
<tr>
<td>Sensitized to cat (e1) (%)</td>
<td>27</td>
<td>44</td>
</tr>
<tr>
<td>Sensitized to dog (e5) (%)</td>
<td>43</td>
<td>44</td>
</tr>
<tr>
<td>Sensitized to grass (g6) (%)</td>
<td>53</td>
<td>50</td>
</tr>
<tr>
<td>Sensitized to mould (m2) (%)</td>
<td>13</td>
<td>17</td>
</tr>
</tbody>
</table>

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for the active group was 0.44 (95% CI –0.25, 1.14) and for the placebo group 0.69 (95% CI –0.04, 1.42), the difference (active–placebo) being –0.25 (95% CI –0.74, 1.23), showing a trend opposite to that predicted.

Discussion

The results of allergen-avoidance trials carried out to date remain inconsistent [29]. In Gotzsche et al.’s [13] meta-analysis of 23 trials, only five trials achieved a lowering of mite allergen levels in the intervention group and only four reported changes in morning peak flow. This study demonstrated a decrease in Der p 1 concentrations in the active group without any change in peak flow, even in carefully selected allergic asthmatic individuals who would be expected to benefit most from allergen avoidance.

The recruitment phase of the study proved to be much more difficult than anticipated. The response rate to blood testing for IgE to screen patients for mite sensitization was only 21.7%. Under half of these patients were found to be sensitized to house dust mite. Sibbald et al. [30] skin tested patients as part of asthma patient care and reported that only 22% of the patients attending clinic would have been advised to avoid mites on the basis of a positive skin test to dust mite. In our study, the per cent of patients who provided a blood sample for IgE testing who were subsequently found to be exposed to Der p 1 was only 79/722 (10.9%) or 79/351 (22.5%) of patients allergic to dust mites. If the exposure level of 10 µg/g Der p 1 had been chosen, only 41/722 (5.7%) of patients giving a blood sample for testing (or 12% of mite-allergic patients) would have been identified as potentially benefiting from mite allergen avoidance. This demonstrates the relatively low number of mild to moderate asthmatic patients, identified from general practices or allergy clinics, where allergen avoidance could be considered as part of asthma management.

Use of allergen-proof bedding in this study resulted in a decrease in Der p 1 levels measured in bed dust. This supports other studies that have found barrier methods, either used alone or in combination with other methods, successful in reducing Der p 1. It is likely that in combined allergen-avoidance regimes, it is the mattress covers that have the most effect on allergen levels [31, 22]. In this trial, use of both the
References


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