

EDITORIAL

Anti-allergic mattress covers in asthma: to do or not to do?

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Introduction

Although early studies on mite-impermeable mattress covers suggested clinical benefit in asthma [1, 2], other double-blind placebo-controlled studies show less favourable results [3, 4]. The results of the study by Luczynska et al. [5] published in this issue of the journal lack evidence of clinical benefit in mild-to-moderate asthmatic patients, despite a decrease in allergen load. These findings seem to be in contrast to the fact that house dust mite (HDM) allergen has proved to be an important trigger in allergic asthma.

From a number of cross-sectional and longitudinal studies, it can be concluded that there is a very close association between HDM exposure and HDM sensitization [6]. In addition, HDM exposure in already sensitized individuals can trigger an exacerbation of asthma, and prolonged exposure can lead to the persistence of symptoms [7]. Asthma is usually more severe in sensitized patients who are exposed to higher allergen levels [8].

There is clear biological plausibility for the role of HDM allergens, in that the proteolytic activity of their enzymes can actively damage the airway epithelium. In effectively mite allergen-free environments, as in hospitals [9] or in high-altitude Alpine clinics [10], the condition of asthmatic patients improves both symptomatically and in terms of non-specific bronchial responsiveness. Even 1 month at high altitude can result in a reduction in airways inflammation, measured as adenosine 5'-monophosphate (AMP), bronchial hyper-responsiveness (BH), blood eosinophils and eosinophilic cationic protein (ECP) [11]. Ten weeks of high-altitude allergen avoidance in adolescent patients with persistent asthma, despite treatment with high-dose inhaled corticosteroids, resulted in improvement of asthma, assessed by clinical and inflammatory markers of disease severity. These findings indicate that short-term rigorous allergen avoidance can improve the control of severe asthma over and above what can be achieved by high doses of inhaled steroids [12].

Although it is impossible to achieve such low levels of HDM exposition at sea level as at high altitude, in the past much effort has been put in attempts to reduce HDM exposition in the home environment. Methods such as extensively vacuum cleaning, use of acaricides, air filters, ventilation, smooth floors, removing carpets and curtains, etc. have been used in order to reduce HDM exposition.

Reduction of allergen exposure in the bedroom and the bed is considered to be the primary target of avoidance measures, since the bed is the most important habitat and source of mite allergens to which we are exposed for many hours during sleep.

The most effective avoidance measure is to cover the mattress, pillows and duvets with mite allergen-impermeable

covers [1–3] and washing all bedding in hot temperature [13]. Covering the mattresses, pillows and duvets is a relatively simple method that can substantially reduce night-time HDM exposure. Its efficacy can be studied in a placebo-controlled manner. Therefore, over the past few years many studies have focused on this subject.

Anti-allergic mattress coverings: secondary prevention

In some studies, anti-allergic covers are combined with the use of acaricides. Overall, it is difficult to compare the results of the different studies because of large differences in study design, study population (children vs. adults, differences in disease severity) and outcome measures.

Part of the confusion is resolved by distinguishing clearly between two measures of effectiveness: reduction in allergen exposure (efficacy) and impact on symptomatic illness (clinical effectiveness) [14]. It is not surprising that interventions that lack efficacy are clinically ineffective. In a narrative review, Custovic et al. [15] examined 31 studies in which mattress covers, in some cases combined with acaricides, were used. However, only nine of these reported a significant reduction in mite counts and/or mite allergen level. In three of these nine studies, the period of treatment was too short (8–12 weeks). In the remaining six studies, which were controlled studies (6–12 months), a significant reduction in allergen load was accompanied by clinical improvement such as a significant improvement in lung function, symptoms, medication use and/or BH. In a quantitative meta-analysis, Gotzsche et al. [16] included 23 studies of chemical and physical methods aimed at reducing HDM exposure among asthmatic patients who were sensitive to mites. This meta-analysis focused on asthma symptoms and peak flow, and was unable to show an overall significant improvement in these clinical outcome measures. Only six of the 23 methods studied adequately reduced levels of mite allergen: these methods concerned physical (encasings) or combined physical and chemical (acaricides). In the subgroup of trials that reported a successful reduction in the population of mites, the results were similar to the overall results. This meta-analysis only looked at the asthma symptom scores and peak flow rates, although these were not the primary outcomes of the successful studies.

In 2001, the Cochrane Review on HDM control measures for asthma was published [17]. The objective of this review was to assess the effects of reducing exposure to HDM antigens in the homes of mite-sensitive asthmatics, assessing chemical and physical methods separately and together. Randomized trials of mite-control measures vs. placebo or

no treatment in asthmatic patients sensitized to HDM in the period 1973–1999 were searched.

Twenty-nine trials (939 patients in the analyses) were included. Nine trials assessed chemical methods alone, 15 physical methods alone and five a combination of chemical and physical methods. Overall, there was no statistically significant difference in improvement of asthma, asthma symptom scores, medication usage or peak flow in the morning between the intervention and control group. For chemical methods used alone, there was a statistically significant adverse effect on symptoms ($P = 0.03$) compared with placebo, whereas for physical methods used alone, as evaluated in parallel group trials, there was a statistically significant beneficial effect ($P = 0.02$).

Looking at the 20 trials using physical methods (with or without chemical methods), only seven trials showed a significant reduction in HDM exposition.

The authors conclude that overall, the trials of current chemical and physical methods aimed at reducing exposure to HDM allergens failed to show an effect on clinical outcome measures. The explanation that they find most plausible is that the methods reviewed did not adequately reduce mite antigen levels, i.e. had no efficacy. They pose that currently available evidence does not provide a secure basis for advice and policy concerning prescription of encasings.

Table 1 summarizes more recent double-blind, placebo-controlled studies in atopic patients performed after 1998. Three studies have focused on atopic dermatitis patients [18–20] showing conflicting results. In allergic rhinitis patients, Terreehorst et al. [21] could not demonstrate significant clinical improvement, despite a significant reduction in Der p 1 and Der f 1 allergens. Clinical effectiveness in asthmatic patients could not be demonstrated in most studies [22–24]; only one study reported a significant decrease in the dose of inhaled steroids in children [25].

In a recent large multi-centre study in 1122 adult asthmatic patients, allergen-impermeable bed covers as a single intervention method did not result in clinical improvement in adult patients with asthma [26]. Surprisingly, the peak expiratory flow rate significantly improved in both groups, suggesting a large placebo effect. The prevalence of HDM sensitivity in this study was only 65% in both groups; there was no difference in the pattern of improvement between the mite-sensitive patients and those who were not sensitized to mites.

Another surprising finding was that the concentration of Der p 1 in the mattress dust showed no significant difference between the active and placebo groups at 12 months. The authors suggest that the total amount of allergen recovered would more adequately reflect the effect of the intervention than the allergen concentration.

Subsample analysis was performed in two patient groups who were expected to benefit most from HDM avoidance methods: patients with high sensitivity to mite allergen and patients with a high baseline level of mite allergen in their mattress. Also, in these subgroups no significant clinical improvement could be demonstrated.

The authors concluded that dust-mite allergen-impermeable covers are clinically ineffective for routine management of adult asthma in the absence of other mite-control measures.

Primary prevention

In Berlin, a cohort of 1314 newborn babies was followed for 3 years. Children who were sensitized in the first 3 years of life were exposed to significantly higher HDM concentrations. From this study, it was concluded that avoidance measures in the domestic environment aimed at the primary prevention of allergen-driven sensitization should be introduced at the earliest possible stage, if possible during infancy [27].

The Manchester Asthma and Allergy study showed in a prospective, prenatally randomized way that it is possible to achieve and maintain a low mite allergen environment during pregnancy and the first year of life in homes of infants at risk of atopy [28].

However, evidence for indoor allergen exposure being a primary cause in the development of asthma is not so clear. Data from Germany [29] do not support the hypothesis that exposure to environmental allergens directly causes asthma in childhood, but that induction of specific IgE responses and the development of childhood asthma are determined by independent factors. Since allergic asthma seems to be a Th2 disease, immunomodulating factors such as early childhood infections, lipopolysaccharide exposure or other factors influencing gene–environment interaction and individual susceptibility seem to be relevant for the development of childhood asthma.

Apart from allergen sensitization and exposure, a number of factors are associated with increased incidence of asthma: reduced exposure to infection and to farm animals in early childhood and maternal smoking [30].

The first results of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA birth cohort study) study showed that the use of HDM-impermeable mattress covers on the child's and parents' beds reduced night cough, but not other respiratory symptoms, atopic dermatitis and atopic sensitization in the first 2 years of life [23].

Tertiary prevention

Is it possible that HDM avoidance measures, such as anti-allergic mattress coverings, prevent further deterioration of already established disease in HDM-sensitized patients?

In patients with moderate-to-severe asthma (severe hyper-responsiveness despite relatively high doses of inhaled corticosteroids), the effect of mattress encasings on allergen sensitivity in the airways was studied in the Netherlands [31]. Bronchial challenges with HDM were performed before and after 1 year of intervention. During the study period, the dose of inhaled steroid remained unchanged. In the placebo group, bronchial allergen challenge after 1 year resulted in a significant decrease in PD₂₀ allergen, indicating a significant increase in allergen sensitivity. No significant change in Der p 1 concentration in the dust collected from the mattresses was found after 1 year compared with before. In the actively treated group, the PD₂₀ allergen remained unchanged, while there was a significant decrease in Der p 1 concentration in the dust collected from the mattresses. In addition, the significant increase in blood eosinophils seen in the placebo group after 1 year compared with before was not seen in the

Table 1. Published randomized controlled trials from 1998 to 2003 looking at the effect of avoidance measure on clinical outcome variables of the atopic syndrome

Author	Study design and duration	Avoidance measures	Effect on mite/allergen	Clinical outcome
Friedman and Tan [18]	RDBP; 6 months; <i>n</i> = 48, adults, AD	Encasing, vacuum cleaning, acaricide spray	Significant reduction in dust weight	Improvement of eczema scores (<i>P</i> < 0.0006)
Gutgesell et al. [19]	RCT; 12 months; <i>n</i> = 12, adults, AD	Encasing, acaricide spray	Significant reduction in Der p 1	No effect on SCORAD (AD score) and ECP levels
Rijssenbeek-Nouwens et al. [31]	RDBP; 12 months; <i>n</i> = 27, adults, AA	Encasing	Significant reduction in Der p 1	Significant increase in HDM-induced early reaction during bronchial challenge in placebo group combined with a significant increase in number of blood eosinophils, no effect in active treatment group.
Sheikh et al. [22]	RDBP; 6 months; <i>n</i> = 47, children (5–14 years), AA	Encasing	Not measured	No effect on peak expiratory flow, asthma symptom scores, medication usage and asthma consultations
Koopman et al. [23]	RDBP; 24 months; <i>n</i> = 1282 allergic pregnant women, effect on their children (0–2 years) was measured, AA, AD	Encasing	Reduced HDM levels	No effect on respiratory symptoms, atopic dermatitis and atopic sensitization
Rijssenbeek-Nouwens et al. [24]	RDBP; 12 months; <i>n</i> = 30, adults, AA, AR	Encasing	Significant reduction in Der p 1	No effect on PC ₂₀ histamine, QoL, asthma and nasal symptom scores between the groups
Oosting et al. [20]	RDBP; 12 months; <i>n</i> = 86, adults and children (8–50 years), AD	Encasing	Significant reduction in Der p 1 + Der f 1	Improvement of nasal symptom scores in active treatment group compare with before treatment No effect on LSS (AD score)
Halcken et al. [25]	RDBP; 12 months; <i>n</i> = 60, children (6–15 years), AA	Encasing	Significant reduction in HDM allergens	Significant decrease in the dose of inhaled steroids
Brunekreef et al. [34]	RDBP; 3 years; <i>n</i> = 855, pregnant women and their children (3 years)	Encasing	Significant reduction in HDM allergens	No clinical improvement
Woodcock et al. [26]	RDBP; 12 months; <i>n</i> = 1122, adults, AA	Encasing	No significant reduction in HDM allergens	No clinical improvement (mean morning expiratory flow rates) between the groups
Terrehorst et al. [21]	RDBP; 12 months; <i>n</i> = 279, adults and children (8–50 year), AR	Encasing	Significant reduction in Der p 1 + Der f 1	No clinical improvement (nasal allergen provocation testing and rhinitis-specific visual-analogue scale, daily symptom scores)

RDBP, randomized double-blinded placebo-controlled trial; RCT, randomized controlled trial; ECP, eosinophilic cationic protein; LSS, least significant score; AA, allergic asthma; AD, atopic dermatitis; AR, allergic rhinitis; HDM, house dust mite; Der p 1, major allergen of the *Dermatophagoides pteronyssinus*; Der f 1, major allergen of the *Dermatophagoides farinae*; QoL, quality of life.

actively treated group. The only parameter that changed during the study was Der p 1 exposition.

These data suggest that anti-allergic mattress coverings may have some protective effect against further increase in airway allergen sensitivity.

Summarizing the large amount of data from the literature, it seems that the use of anti-allergic mattress covers as a solo intervention in allergic asthma does not result in clinical benefit. On the other hand, the relationship between HDM exposure and asthma severity has often been established.

How can we reconcile these observations?

Although in most studies the night-time exposure to HDM was significantly reduced, patients can still be exposed to large amounts of HDM during daytime, in other parts of the house, at work, during social events, etc. As was stated earlier, the extremely low levels of HDM exposure, as at high altitude cannot be reached at sea level. More rigorous allergen avoidance methods focused on both the home and working environments may have some clinical benefit; however, double-blind placebo-controlled studies are not possible.

In addition, in allergic asthma severity is influenced by factors other than HDM exposure, including other allergens, viruses and air pollution, which are not influenced by the avoidance measures. Furthermore, in more advanced stages of allergic asthma chronic inflammation results in structural changes in bronchial architecture [32], processes that cannot be reversed by allergen avoidance.

The question remains: anti-allergic mattress coverings: to do or not to do? What should we advise the 'workers in the field'?

First it is important that the patients receive optimal treatment for their disease, including medication, education in asthma management and instruction in how to avoid risk factors, such as smoking, emotional stress, etc [33]. When patients do not receive optimal treatment, allergen avoidance measures are useless!

Second, in HDM-allergic patients who receive optimal treatment, allergen avoidance measures should not be limited to the sleeping room alone, but should include patients' home and working environments.

Anti-allergic mattress covers may then have an additional effect on the patient's well-being, and perhaps may in part prevent further deterioration of the disease.

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