Allergen-Impermeable Bed Covers for Adults with Moderate to Severe Asthma and Dust Mite Allergy

Judy Nam

A. Study Purpose and Rationale

The number of persons in the United States reported to have asthma doubled between 1980 and 1996, then reached a plateau (Manino, 2002). In 2001, the Center for Disease control estimated that 20.3 million people had asthma (CDC, 2001). Asthma remains a growing concern in this country, particularly in inner-city African-American and Latino populations. While the management of asthma has improved over the past two decades, these inner-city populations showed increased rates of morbidity and mortality from asthma. African-Americans and Hispanic Americans are two to six times more likely to die from asthma than whites (Lenoir, 1999). In addition to socioeconomic issues and access to healthcare, there have been many theories put forward to explain this finding. Current theories include: exposures to allergens, pollutants and infections.

Exposure of asthma patients to irritants or allergens to which they are sensitive has been shown to increase asthma symptoms and precipitate asthma exacerbations (Cockcroft, 1979). The National Asthma Education and Prevention Program recommends that those patients with persistent asthma on daily medications be assessed for exposure and allergy to indoor perennial allergens, such as dust mite (1997). For patients with persistent asthma found to have dust mite sensitization, this panel of experts sites allergen avoidance as the most important step in the treatment. Because the bed is the most important source of dust mite exposure (Platts-Mills, 1982), the current strongest recommendations to control dust mite exposure are: encasing mattresses and bedding in allergen-impermeable covers, and to wash bedding in hot water weekly.

Although many studies have documented a decrease in mite allergen 6 or more months following a range of interventions, it remains unclear if allergen avoidance results in a clinical benefit (Woodcock, et al., 2003; Cloosterman, et al., 1999). It has been a challenge to establish whether effective allergen avoidance can be achieved through measures that are practical and cost effective and flexible enough to suit individual needs, and to determine which patients may benefit from such interventions.

This study will address whether dust mite allergen avoidance through allergen-impermeable mattress covers and bedding covers will have a clinical benefit on patients with persistent asthma and dust mite allergy.

B. Study Design and Statistical Analysis

a. Study Arms

All eligible subjects will proceed in a 4 week run-in phase, during which they will complete a diary card documenting beta-2-agonist use, morning peak expiratory flow rate (record the best-of-3 efforts [Mini-Wright flowmeter, Clement Clarke International], scores for daytime and nighttime symptoms. Those who complete the diary cards for at least 14 days will undergo stratification as moderate or severe persistent asthma by this information, then randomly assigned to receive allergen-impermeable or placebo bedding. At randomization, they will undergo complete detailed questionnaire regarding demographics, medication use, smoking exposure, time spent away from home, occupational exposures. They will also be administered the St. George Hospital Respiratory Questionnaire to assess quality of life.

The active intervention arm and the placebo arm will be asked to keep covers on their beds and bedding for one year.

b. Number of subjects to be enrolled / Methods of Statistical Analysis
Number of subjects to be enrolled in each arm = 191 subjects
This was determined by the unpaired t-test, using:
- mean of the placebo arm (frequency of beta2-agonist use) as 4 puffs/day
- mean of the active intervention arm as 3 puffs/day
- standard deviation = 3 puffs/day
- effect = 1 puff/day
- alpha = 0.05
- power = 0.90

c. Randomization
Patients will be stratified as moderate or severe asthmatic prior to randomization to achieve equal numbers of each in both arms.

C. Study Procedure

There will be a 2 year enrollment period. Each subject will participate for one year plus a one month run-in period.

a. Allergy testing
According to the National Asthma Education and Prevention Program, the patients eligible to participate in this study have indications for allergy testing. Skin prick testing will be performed once at the beginning of the study. This test is slightly uncomfortable, but is usually well tolerated and accurate, even in small children and infants. Local itch and swelling normally subsides within 1-2 hours. More prolonged or severe swelling may be treated with an oral antihistamine, topical corticosteroid cream and an ice pack. Occasional patients will experience feel dizzy or light-headed and need to lie down. Severe allergic reactions from allergy testing in asthma are very rare, and can be avoided by not testing patients during an asthma exacerbation. An allergist will administer the test and observe the patient for 1 hour after the procedure for any adverse reactions.

b. Dust Collection
The patient’s home will be visited to collect dust at the beginning of the study, at 6 months, and at 12 months. Dust mite allergen on the patient’s bed will be collected by vacuuming of a 1 m² area of the mattress for 2 minutes through a filter device. The samples will be assayed by monoclonal enzyme-linked immunosorbent assay for dust mite allergen, Der p 1 (Indoor Biotechnologies) (microgram allergen/gram of dust).

Patients will be asked to record the best of 3 Peak Expiratory Flow Rate (PEFR) daily for a total of 12 weeks through the year (increments of 4 weeks at a time). Patients will each be given a peak expiratory flow meter, a small hand-held device with a mouthpiece at one end and a scale with a moveable indicator (usually a small plastic arrow). Asthmatic patients will be familiar with the method, but will be instructed to proper use of the device. (They will be instructed to breathe in as deeply as possible, then blow into the instrument's mouthpiece as hard and fast as possible.)

D. Study Drug

N/A

E. Medical Device

Allergen-impermeable microfiber covers (Allergy Control Products) is a commercially available device which retain >99.5% of 0.4micrometer particles. (Dust mite allergens are about 10 micrometer particles.) The sham covers will be of the same material but of a conventional weave allowing 85% of
allergen to pass through. The patients will be asked to use the covers on their beds, pillows, blankets or duvets for the duration of the study, one year.

F. Study Questionnaires

Patients will be assessed with questionnaire, a 4-week diary of symptoms (see attached.) and 4-diary of daily morning best-of-3 peak expiratory flow rates. These evaluations will occur at the beginning of the study, at 6 months, and at 12 months. They will also be asked about the number of emergency department visits and unscheduled physician visits for asthma exacerbations, as well as frequency of systems steroid use in the previous 6 months period. Patients will receive a reminder phone call at months 5 and 11 to commence with the 4-week diary.

G. Study Subjects

a. Inclusion Criteria
- moderate persistent or severe persistent asthma *
- positive skin test to dust mite (at 15 minutes, wheal equal to or greater than positive control, histamine)
- ages 18-50 yrs
- resident of upper Manhattan
- The National Asthma Education and Prevention Program defines:

<table>
<thead>
<tr>
<th>Moderate Persistent Asthma as</th>
<th>Severe Persistent Asthma as</th>
</tr>
</thead>
<tbody>
<tr>
<td>symptom: daily symptoms</td>
<td>symptoms: Continual symptoms</td>
</tr>
<tr>
<td>daily use of inhaled short-acting beta-agonist</td>
<td>Limited physical activity</td>
</tr>
<tr>
<td>exacerbations affect activity</td>
<td>Frequent exacerbations</td>
</tr>
<tr>
<td>exacerbations ≥ 2/week, may last days</td>
<td>lung function: Frequent</td>
</tr>
<tr>
<td>nighttime symptoms: &gt;1/week</td>
<td>lung function: FEV1 or PEFR ≤ 60% predicted</td>
</tr>
<tr>
<td>lung function: FEV1 or PEFR&gt;60% to &lt;80% predicted</td>
<td></td>
</tr>
</tbody>
</table>

b. Exclusion Criteria
chronic systemic steroid use
- underlying chronic lung disease other than asthma
- current allergen-impermeable bed cover use
- diagnosis of CHF
- pet owner and sensitization to their pet by skin test
- pregnant
- more than one bed in the bedroom

This study is not restricted by race or gender.
No vulnerable populations will be included in this study.

H. Recruitment of Subjects
Physicians practicing in Pulmonary, Allergy, General Medicine, Asthma clinics in upper Manhattan will given study description and will agree that the patient is suitable for the study. The patient’s physician will ascertain if the patient is willing to discuss the study with the research team. Patients will be invited by phone call to discuss the study. After obtaining consent, those who qualify will be seen by an allergist who will administer the allergy skin prick test to dust mite. Those with a dog and/or cat with also be skin tested to dog and/or cat. Those found to have sensitization to dust mite allergen and not sensitized to their pet will commence with the study.

I. Confidentiality of Study Data

After randomization, the patient’s initials, date of birth, and measurements for his/her bed/bedding will be sent to the ICCR. Each patient will be assigned a research number. The bedding measurements will be sent by the ICCR to the manufacturer of the covers who will mail the boxes to the research center with only the research number as an identifier.

Data will be stored so that only researchers can access the information.

J. Potential Conflict of Interest

Neither the investigators nor the University has any propriety interest in the study device.

K. Location of Study

The intervention or placebo will take place in patients’ homes in upper Manhattan. The intervention does not involve risk to the subjects. Allergy testing and interviewing will take place at ICCR.

L. Potential Risks

The intervention, allergen-impermeable cover, is well tolerated. Previously studies utilizing these products have not reported any adverse reaction or worsening of asthma.

M. Potential Benefits

Patients may have improved asthma symptoms and quality of life.

N. Alternative Therapies

The proposed intervention is not experimental. Allergen impermeable covers are recommended by The National Asthma Education and Prevention Program and are currently routinely prescribed by physicians taking care of dust-mite allergen sensitized patients.

O. Compensation to Subjects

Patients will be compensated for any expenses incurred while traveling to and from CUMC. At the end of the study, all subjects in the placebo arm will receive allergen-impermeable covers for their beds.

P. Cost to Subjects
None.

Q. Minors as Research Subjects.

N/A

R. Radiation or Radioactive Substances

N/A

S. References


Cloosterman SGM, Shermer TRJ, et al. Effects of house dust mite avoidance measures on Der p 1 concentrations and clinical condition of mild adult house dust mite-allergic asthmatic patients, using no inhaled steroids. Clin Exp Allergy, 1999;29:1336-1346.


## Diary Card for Asthma Symptoms

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Finding</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>sleep disturbance</td>
<td>no sleep disturbance due to asthma</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>awoken once during the night for less than an hour because of asthma</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>awoken two or three times or once for more than an hour because of asthma</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>awake most of the night because of asthma</td>
<td>3</td>
</tr>
<tr>
<td>chest tightness on awakening</td>
<td>not present and didn't require extra bronchodilator during the night</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>not present but did require extra bronchodilator during the night</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>present</td>
<td>2</td>
</tr>
<tr>
<td>duration and frequency of daytime wheeze and breathlessness</td>
<td>none</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>occasional</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>frequent but not all day</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>most or all of the day</td>
<td>3</td>
</tr>
<tr>
<td>severity of daytime wheeze and breathlessness</td>
<td>none</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>mild; not incapacitating or distressing</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>moderate to severe; distressing and/or had to limit activities</td>
<td>2</td>
</tr>
<tr>
<td>cough</td>
<td>none</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>occasional</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>more than occasional</td>
<td>2</td>
</tr>
</tbody>
</table>