ABSTRACT

Objectives: To evaluate hypersensitivity to Dermatophagoides pteronyssinus (D. pteronyssinus) and D. farinae in pediatric patients with atopic dermatitis (AD), and to assess the therapeutic value of using acaricides with other environmental anti house dust mites (HDM) measures.

Methods: Ninety-eight children with AD were chosen randomly from the Pediatric Allergy Clinic in Al-Noor Hospital, Khalifa branch, Abu Dhabi, United Arab Emirates during the period between January 2008 to January 2009 and were evaluated for severity and chronicity. They were subjected to skin prick test (SPT) including D. pteronyssinus and D. farinae antigens and were also assessed for the therapeutic value of acaricides and environmental anti HDM measures.

Results: We found that 74.5% of patients were sensitive to one or both strains of HDM. A highly significant association was found between the severity of the symptoms of AD and its persistence with hypersensitivity to HDM (p=0.001). Acaricides and environmental anti HDM measures can improve patients with mild AD.

Conclusion: Hypersensitivity to HDM is an important factor for the more acute, more chronic, and more severe AD. Anti HDM measures including the use of acaricides can help control mild AD. We recommend SPT as a part of the work up of patients with AD. The HDM sensitive patients can benefit from anti HDM measures.


From Department of Pediatrics (Adham), Ain Shams University, Departments of Pediatrics (Tawfik), and Public Health (Abdo), Zagazig University, and Al-Noor Hospital, (Tawfik, Adham), Abu Dhabi, United Arab Emirates.

Received 1st September 2010. Accepted 3rd January 2011.

Address correspondence and reprint request to: Dr. Tamer M. Adham, Department of Pediatrics, Ain Shams University, PO Box 46713, Abu Dhabi, United Arab Emirates. Tel. +971 (50) 4110291. E-mail: drtadham@hotmail.com

Depiding on disease severity, atopic dermatitis (AD) may have a considerable adverse effect on the quality of life of affected individuals and their families and may result in significant physical, social and occupational impediment. Moreover, sleep disturbance is common, and may lead to tiredness, irritability, and lack
of concentration during the day. It may even adversely influence a child’s emotional and social development and may predispose to psychological difficulties. 1-2 In the Gulf Region, AD was the most common skin disorder (21.3%) among a pattern of skin diseases during the period 2001-2005 at the Dermatology Clinics of major tertiary hospitals. 3 The normal progression of AD is for it to resolve during childhood, but it may persist into adult life or recur in the teenage or early adult years, a late-onset disease, while unusual, has been reported. Epidemiological data indicates that the prevalence of AD in developed countries has increased substantially over the last 40 years. 4-6 Accordingly, the costs to society brought by this affliction continue to worsen. Recently, Ellis and colleagues 7 estimated the annual cost of AD in the United States to reach 3.8 billion dollars.

House dust mites (HDM) have been implicated in the etiology of AD. The European HDM, *Dermatophagoides (D)* pteronyssinus and the American HDM, *D. farinae* are the most common mites that thrive in household dust. They represent one of the major environmental aeroallergens to which AD patients are hypersensitive that can also responsible for exacerbations of the disease, either through contact with the skin or by systemic exposure by inhalation of antigens. 8,9 The HDM thrive in warmer temperatures and high humidity, and they can be found all year round. 10 As the Gulf Region is situated in a warm and humid area, the indoor climatic conditions are favorable for mites and molds. Allergic reactions to these allergens were found in clinical studies conducted in this region. 11 The HDM induce peripheral eosinophilia and elevate serum IgE levels leading to increased histamine release and elevated activity of the T helper cell mediated immune system, with the release of vascular mediators stimulating in turn pruritus and inflammatory cutaneous change. 12 With the commercial availability of HDM derived allergen mix for cutaneous hypersensitivity testing, skin prick test (SPT) has become included in the diagnostic criteria of many allergic conditions. 13 Specific immunotherapy against HDM sensitization based on SPT can be effective in atopic diseases including AD resulting in reduction of specific IgE levels against HDM allergens with concomitant increases in the serum levels of the T helper cell subsets 1 cytokines, interferon-gamma and the tolerogenic cytokine interleukin-10. 14-18 Unfortunately, specific immunotherapy is costly, takes years to complete, is not readily available and needs to be supervised by an allergologist, these are among the factors that make this treatment less popular. 14-16

There are various kinds of acaricidal substances that can be used to protect against HDM, they are either chemical or natural substances, the natural ones are the most accepted nowadays owing to their safety. Neem oil is a natural acaricide obtained from Neem seeds. The Neem tree has been described as a miracle tree in Indian writings 4,500 years ago. These seeds act in an ingeniously simple way, it spoils the basic food that mites live on (skin debris) rendering it inedible, and manipulates vital hormones that are responsible for growth, development, and reproduction of the mites leading to their lethal anti HDM action. The main active ingredient of Neem is Azadirachtin, it is non toxic to humans beings, birds, earthworms, and animals. 19

Combining acaricides with vacuum cleaning in bedrooms and other environmental anti HDM measures can reduce the HDM count and reduce patient exposure to these allergens. 20 The aim of this study was to evaluate the occurrence of HDM (D. pteronyssinus and D. farinae) hypersensitivity in pediatric patients with AD in the United Arab Emirates, and to assess the value of using acaricides (here Neem oil extract) with other environmental anti HDM measures as a therapeutic tool for AD.

**Methods.** This is experimental cross sectional study included 98 children with AD including 51 males and 47 females with a mean age of 7±2.4 years. Patients were chosen by a simple random method from the Pediatric Allergy Clinic in Al-Noor Hospital, Khalifa branch, Abu Dhabi, United Arab Emirates during the period between January 2008 to January 2009. An ethical approval was obtained prior to starting our study and a verbal consent was taken from parents of our studied patients and/or patients. We depended on the United Kingdom diagnostic criteria for AD as recent and extensively validated criteria for assessing our patients with suspected AD. 21,22

Inclusion criteria must include an itchy skin condition (or parental report of scratching or rubbing in a child), and 3 or more of the following: History of involvement of the skin creases (including cheeks in children under 10 years). A personal history of other atopic disease (or history of any atopic disease in a first degree relative in a child under 4 years). A history of a generally dry skin over the previous year. Visible flexural eczema (or eczema involving the cheeks, forehead and outer limbs in children under 4 years). Onset under the age of 2 years.

**Measures to assess clinical severity.** We adopted the SCORAD (scoring for AD) as a tested and validated scoring system to assess for the severity of AD (score less than 20 was considered as low SCORAD showing a mild disease, while a score of 20 or more was considered as high SCORAD reflecting severe AD). 23 For assessing the chronicity of the disease we considered 3 classes of skin lesions:

**Acute.** Intensely pruritic erythematous papules and vesicles overlying erythematous skin; frequently
associated with extensive excoriations and erosions accompanied by serous exudates.

Subacute. Erythema, excoriation, and scaling.

Chronic. Thickened plaques of skin, accentuated skin markings (lichenification), fibrotic papules (prurigo nodularis); possible coexistence of all 3 types of lesions in chronic AD.\textsuperscript{24}

Exclusion criteria. We excluded children with other itchy skin conditions, chronic or acute skin diseases, patients who have received antihistamines within a week prior to SPT and children on systemic steroids or immunosuppressive therapy. Patients were subjected to the following: Full history taking, including symptoms of AD (pruritus, xerosis, ichthyosis, palmar hyperlinearity, keratosis pilaris, and so forth) and a past or family history of atopy. Complete physical examination: Focusing on manifestations of AD, we noted the type of lesions present for assessing the chronicity as well as the extent of lesions. The SCORAD system was used to measure the severity of the disease through scoring.

The main 5 manifestations of AD were assessed on a scale of 3 (mild, moderate, or severe) including redness, edema, oozing rash, excoriations with itching and Lichenification. The collective score was added to the subjective assessment of the intensity of AD and sleep affection on a scale of 10 for each. Adding one for each 1% of skin surface area affected (using rule of 9s). Other forms of atopy, mainly asthma and allergic rhinitis were also taken into consideration.

Skin prick test. The test was carried out by a trained nurse under the consultants’ supervision. Using a disposable plastic one mm needle to puncture through the drop of allergen extract put on the flexor surface of forearm by a standardized dropper. The result was read after 20 minutes, it was considered positive if the induration reaction to the allergen was 3 mm above the diameter of the control induration reaction. All patients were skin tested for control and for histamine as the standard positive, saline as the standard negative as the standard positive, saline as the standard negative. Prick test solutions were supplied together with 18 allergens including \textit{D. farinae} and \textit{D. pteronyssinus} and the most common foods, epithelia, moulds, and pollens. Patients were instructed to discontinue antihistamine therapy 3-7 days before their appointment (depending on the type of antihistamine used) to avoid the suppressive effects of antihistamines on skin test results. Prick test solutions were supplied from Stallergenes, Cedex, France and were stored in a refrigerator at 2-8\degree.

The use of acaricides (Neem oil extract) and environmental anti HDM measures: Neem oil extract preparation was used as a therapeutic tool for patients with sensitivity to one or both strains of HDM as proven by SPT. The product that was used is Milbiol, a product of Hexal, Munich, Germany which contains isopropanol as well (as a solvent). Parents were instructed to use it in the patient’s vacuumed mattresses, pillows and blankets. Regarding Environmental anti HDM measures, instructions were given to parents regarding the removal of carpets and curtains from the bedrooms, avoidance of stuffed toys and hot washing of all bedding once/week.\textsuperscript{25} Follow up of the improvement of the symptoms of AD was carried out in a visit after 2 weeks. Good response was defined as resolution of symptoms among patients with mild AD, or improving of symptoms among patients with severe AD.

Statistical analysis. Statistical analysis was carried out by using the Statistical Package for the Social Sciences, version 11 (SPSS Inc., Chicago, IL, USA). Groups were compared by analysis of variance and the difference was tested by chi-square test considering \(p\)-value \(<0.05\) as significant and \(<0.001\) as highly significant, Bivariate Pearson correlations were computed to assess the associations between the size of SPT and SCORAD and also \(p\)-value \(<0.05\) was considered significant.\textsuperscript{36}

Results. The mean age of the group was 7.8±3.1 years as shown in Table 1. In Table 2, and according to the symptoms and classification of our patients, 17.3% were classified with acute AD, 11.2% with subacute AD, while 71.5% suffered chronic AD. It also shows that 76 patients (74.5%), were sensitive to one or both strains of HDM, among them 71 patients (69.6% of the studied group) were sensitive to \textit{D. pteronyssinus} while 69 patients (61.4%) were sensitive to \textit{D. farinae}, and 58 patients (56.8%) were sensitive to both strains. The significant relationship between HDM hypersensitivity and the severity of the symptoms of AD, its persistence as well as the occurrence of both acute and chronic forms of AD (but not the subacute form) is also shown in Table 2. In the scatter-plot shown in Figure 1, our study reveals that there is a significant correlation \((r=0.19, p=0.013)\) between high SCORAD, reflecting severe AD, and the maximal size of SPT hypersensitivity reaction to HDM (whether to \textit{D. pteronyssinus} and \textit{D. farinae}).

<table>
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<tr>
<th>Table 1</th>
<th>Distribution of atopic dermatitis patients according to age, gender, and nationalities.</th>
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In Table 3, our work shows a significant effect of anti HDM measures (including the use of Neem oil extract combined with other environmental measures) in improving the symptoms of mild AD ($p=0.02$), unfortunately this significant improvement did not occur among patients with severe AD.

**Discussion.** Although the United Arab Emirates is a desert country where the prevailing high temperature, negligible rainfall and scant vegetation would suggest a low prevalence of allergy, AD and other atopic diseases are quite common. With a prevalence exceeding 30% for atop in some areas, and exceeding 22% for AD in particular, the Gulf Region is considered among the areas with high prevalence of atopic diseases in the world. Several authors have described clinical improvement when mite elimination and avoidance strategies were employed.

Among our AD patients, the prevalence of the sensitization to HDM was high (74.5%), this rate of sensitization is supported by the idea that HDM are among the major environmental aeroallergens to which AD patients are hypersensitive as stated in the official list of allergens maintained and updated by the Allergen Nomenclature Committee.

High rates of positivity for HDM specific IgE antibodies against antigen of *D. pteronyssinus* (Der p 1), Der p 2, antigen of *D. farinae* (Der f 1), and Der f 2 that are the main allergens of *D. pteronyssinus* and *D. farinae*, were found among AD patients by different researchers.

Patients with allergic urticaria, as another form of skin allergy do have high rates of sensitization to HDM as well. An Indian study conducted by Mahesh et al, utilizing SPT for detecting HDM hypersensitivity found that 79% of patients with chronic urticaria associating asthma, rhinitis, or eczema. In a previous work that we conducted on patients with allergic rhinitis in the same locality, we found that 76% of our studied group was sensitive to *D. pteronyssinus*.

This shows the importance of HDM as a common global allergen among patients with AD, and even with other atopic diseases as well.

Our patients with hypersensitivity to HDM were found to be more likely to suffer acute AD, chronic AD, or to suffer a more severe form of the disease as shown in Table 2. Atopic patients with HDM hypersensitivity in the same age group and locality were found to suffer more severe and more chronic forms of their allergic rhinitis disease. The early and long term exposure to HDM allergens may be responsible for this phenomenon. The acute exacerbations, the chronicity, the aggravation of AD (and other forms of atopy as well) with HDM exposure as well as the potential merit of reducing exposure to HDM as a therapeutic tool for AD was reported by other authors as well.

Our study has shown as well that patients with a higher degree of hypersensitivity to HDM as shown by a larger SPT reaction do suffer more severe disease as reflected by a higher SCORAD as shown in Figure 1. The use of a standardized dropper in the SPT helped us...
to avoid the possibility of false size of the SPT reaction caused by variation of allergen extract drop size, as there is a dose dependent reaction size known to happen with skin tests.\textsuperscript{32} The importance of the size of the reaction in the diagnosis of atopy to be correlated with the degree of hypersensitivity and with the severity of clinical signs is agreed by other authors as well.\textsuperscript{34}

Depending on work carried out by previous investigators who mentioned that reducing HDM allergen exposure can improve atopic dermatitis\textsuperscript{33} our work has evaluated the response of using Neem oil extract as an acaricide with other anti HDM environmental measures in improving the symptoms of AD as shown in Table 3, which reveals a significant improvement only among patients with mild AD while no significant improvement occurred for patients suffering severe disease. This can be explained by the fact that some atopic patients including AD patients do suffer HDM hypersensitivity either as a major cause or just among many other allergens, so even control on HDM exposure can’t produce a constant improvement among patients of all classes of the disease due to exposure to other several implicated allergens.\textsuperscript{34-36}

Limitations of this study include the possibility that hypersensitivity to other allergens (other than HDM) might have interfered with the response to anti HDM measures, and that we cannot differentiate between the effectiveness of Neem oil extract versus other anti HDM measures.

In conclusion, hypersensitivity to \textit{D. pteronyssinus} and \textit{D. farinae} appears an important risk factor for AD especially the more acute, more chronic, and more severe forms of the disease. Anti HDM measures including the use of Neem oil extract as an acaricide can help controlling mild AD. The inadequate response among patients with severe AD motivates us to conduct further studies focusing on more effective interventions among those patients. We recommend SPT to be carried out as a part of the routine work up of patients with AD, so that those who are sensitive to HDM can undergo special measures helping to control their disease. We also recommend assessing the response to anti HDM measures among patients with AD who are solely sensitive to HDM for better evaluation of the effectiveness of such measures.

References


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