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ORIGINAL PAPER

Frequency of contact allergy to house dust mites in children with atopic dermatitis

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ABSTRACT

Introduction: Frequency of contact allergy to house dust mites (HDM) in children with atopic dermatitis (AD) in terms of selected demographic factors: age, gender, and place of residence, showing the relationship between the severity of AD and the coexistence of contact allergy to HDM

Material and methods: Patients were divided into 3 groups. The study involved 85 children with AD up to the age of 5 years, in whom no elevated total IgE concentration was found and HDM IgE allergy was excluded. Comparative group I consisted of healthy children in the same age group, without a history of atopy ($n = 25$). Comparative group II included children with AD up to age of 5 years who had an elevated concentration of tot. IgE and/or sIgE against HDM ($n = 37$)

Results: Contact allergy to HDM was significantly more frequent in the study group than in comparative group I ($p < 0.05$). Contact allergy to HDM was more frequent in patients from the comparative group than in the study group. However, the difference did not turn out to be statistically significant ($p > 0.05$). Contact allergy to HDM was significantly more frequent in comparative group II than in group I. The difference was statistically significant ($p < 0.01$). The frequency of contact allergy to HDM in children does not depend on selected demographic factors such as sex, age, and place of residence. A statistically significant correlation was found between the occurrence of contact allergy to HDM and the severity of the disease assessed using the SCORAD scale. This relationship was found both in the study group and in the second comparative group.

Conclusions: Contact allergy to HDM in children with atopic dermatitis affects the severity of the disease. Patch tests with HDM should be recommended in all children with AD.

KEY WORDS:

atopic dermatitis, contact allergy, children, house dust mite.

INTRODUCTION

Atopic dermatitis (AD) is a chronic, recurrent dermatosis with severe itching, dry skin, typical morphology and localization of skin lesions, and often a positive family history of atopic disease [1]. Atopic dermatitis is a common disease in children. Symptoms often begin in early childhood, and so the onset of changes is observed in 49% of children before 6 months of age, in 75% before 3 years of age, and in 82.9% of patients up to 5 years of age [2 –4]. 40–80% of sick children tend to regress before the age of 5 years.

The prevalence of AD in children is estimated at 4.7–9.2%, and in adults this number is much lower at 0.9–1.4% [5, 6]. The location of skin lesions depends on age.

The basis of development of AD is a defect in the epidermal barrier. The mechanical, microbiological, and immunological barriers are impaired, and the composition and function of lipids in the intercellular spaces of the

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stratum corneum are disturbed, including a decrease in the level of ceramides. This contributes to a greater loss of transepidermal water and increased skin dryness [7–10]. Moreover, the skin without a proper epidermal barrier is more susceptible to the penetration of harmful external factors such as allergens, bacteria, viruses, and fungi. Atopic dermatitis is often associated with IgE-mediated allergy [11]. More than 60% of children with AD in childhood will develop symptoms of bronchial asthma and/or allergic rhinitis later [12]. Atopic dermatitis is an extremely heterogeneous disease, and genetic, immunological, environmental, neurological, and psychological factors are involved in the pathomechanism of this disease [13].

The skin structure of newborns and toddlers is significantly different from that of adults. It is thinner and more slender. Less elastin and collagen fibre is observed. The stratum corneum is with a much looser arrangement of cells. Additionally, there is immaturity of the sebaceous and sweat glands. All this makes the skin of young children very sensitive, prone to microtrauma, and easily permeable to external factors. Skin maturation occurs in the first 2 years of life [14–20].

Allergic contact eczema is an inflammation of the skin caused by an allergen in direct contact with the skin. Contact allergens in patients with AD have an impact on the course of the disease. Patients with AD are often unaware of a concomitant contact allergy. Previously, contact allergy among children was considered as a minor problem. Currently, there is a significant increase in contact allergy also in the youngest children. In the population of healthy children, contact allergy is estimated at 13–24%, while in children with eczema skin lesions the frequency of contact allergy reaches up to 66% [21]. The Wohrl study from 2003 showed that out of 2776 examined patients aged 2–89 years, the highest cases of contact allergy were reported in patients up to 10 years of age [22].

There are few clinical trials available to clearly answer the question of whether contact allergy is more common in children with AD. It is known that the coexistence of contact allergy contributes to a worse course of the underlying disease, more frequent exacerbations, and shorter periods of remission. Constant exposure to contact allergens, despite appropriate topical treatment and/or elimination diet, contributes to poor disease control.

In the population of children with AD, contact allergy is estimated at 28.8–55% [23, 24]. A defect in the epidermal barrier may allow the penetration of haptens of different lipophilicity and particles larger than 500D. Roul *et al*. examined 337 French children aged 1–15 years with suspected contact dermatitis; 257 children suffered also from atopic dermatitis [25]. On the other hand, Foti *et al*. demonstrated the presence of at least one positive patch test result in 10 out of 71 AD patients aged 5–12 years [26]. Giordano-Labadie *et al*. [27] found the frequency of contact allergy at the level of 43% among 137 children aged 4 months to 16 years with AD. A similar result of 55% was obtained by Stoðkutë *et al*. [24] examining 94 children with AD, aged 3–17 years. A study by Czarnobilska *et al*. showed that in patients with confirmed eczema and a history of atopy, atopic eczema was diagnosed in 37% of children, and allergic contact eczema was diagnosed in 20% of 7-8-year-olds; interestingly, these diseases coexisted in 18% of children [28]. The same research showed that these proportions changed in adolescents, of whom atopic eczema was diagnosed in 8% of respondents, and in whom allergic contact eczema was diagnosed in as many as 30%. The coexistence of AD and contact eczema is underestimated. The European Academy of Allergy and Clinical Immunology recommends patch testing in children with chronic eczema [29]. Early elimination of the contact allergenic factor significantly influences the effectiveness of AD treatment.

Airborne eczema is also an underestimated problem. There are few data on airborne contact dermatitis in children. Airborne eczema (airborne contact dermatitis) is contact eczema caused by substances suspended in the air. These substances settle on the skin of the exposed areas of the body, provoking the typical image of contact eczema. Darsow *et al*. showed that 15% of AD patients showed positive epidermal birch pollen tests [30].

It has been observed that patients with atopic dermatitis may not only have exacerbations to house dust mite (HDM) allergens in the IgE-dependent mechanism, but also in the mechanism of contact allergy to HDM. Such eczema is often observed on exposed parts of the skin, with intensification during the months of the heating season.

There are few data on contact allergy to HDM, and the results are inconclusive. Ingordo *et al*. [31] compared the incidence of contact allergy to HDM in patients without a history of atopy, without eczema, and in patients with AD, confirming that AD patients showed positive epidermal tests significantly more often. A study by Benhamou *et al*. [32] showed that out of 28 children with AD, as many as 15 tested positive for HDM patch tests, including 9 with an IgE allergy to HDM. The studies by Nicola Fuiano *et al*. [33] in the group of children with atopic diseases (such as allergic rhinitis, asthma, AD) as well as studies by Zhao *et al*. [34] and Lima *et al*. [35] show the usefulness of the patch test against HDM not only in the diagnosis of people with AD, but also in people with AR and asthma who do not have skin symptoms. The research by Darsow *et al*. [30] proved that positive HDM patch tests in AD patients were positive not only in patients with mite-dependent IgE allergy.

The aim of the study was to analyse the frequency of contact allergy to HDM. The following goals were assumed:

- analysis of the frequency of contact allergy to HDM in children with AD in terms of selected demographic factors,
- analysis of the frequency of contact allergy to HDM in the group of children with atopic dermatitis with and without increased total IgE and specific IgE to HDM,

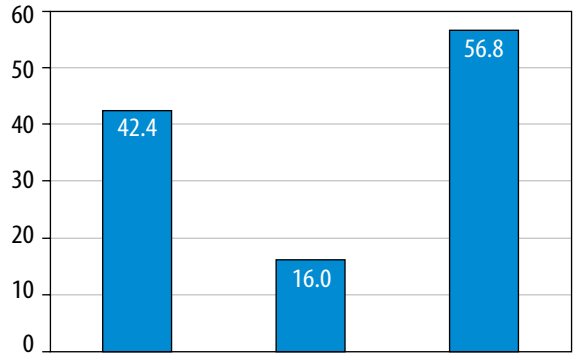

FIGURE 1. Frequency of positive patch test to house dust mite in 3 groups

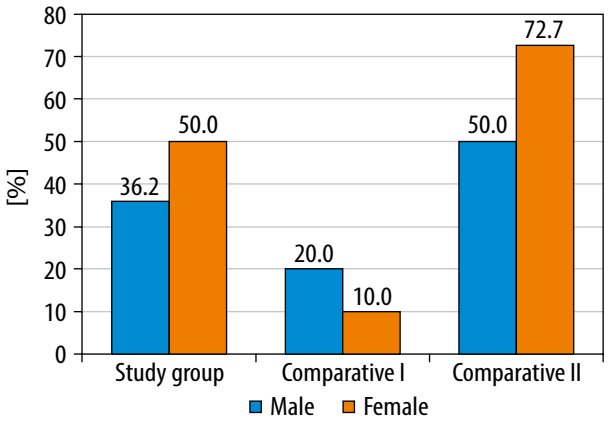

FIGURE. 2. Frequency of positive patch test to house dust mite by gender in the test group and comparative groups I and II

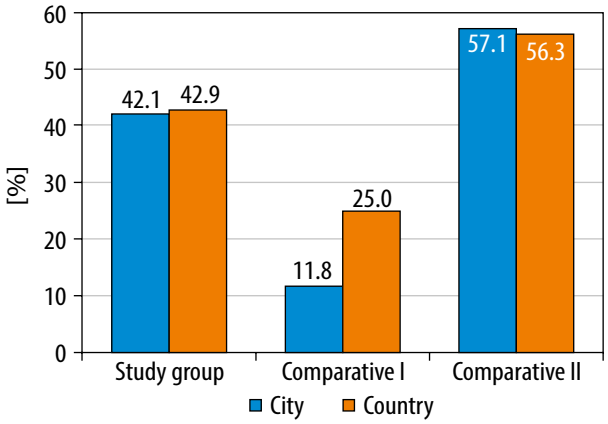

FIGURE 3. Frequency of positive patch test to house dust mite by residental place in the test group and comparative groups I and II

- determining the relationship between the severity of skin lesions in the course of atopic dermatitis and the coexistence of contact allergy to HDM in children.

MATERIAL AND METHODS

Patients were divided into 3 groups: the study group and comparative groups I and II.

The study group consisted of 85 children up to 5 years of age diagnosed with AD according to the criteria of Hanifin and Rajka. Patients with general contraindications for patch testing were excluded from the study, e.g. infectious diseases, antibiotic in the last 2 weeks, acute or generalized eczema within the last 4 weeks, back eczema (test area), topic steroid or calcinerin inhibitors at the test site, general immunosuppression, or phototherapy. The patient presented normal concentration of total IgE and no increased concentration of specific IgE for HDM, both for *D. pterynosinus* and *D. farinae*. Comparative group I consisted of 25 healthy children in the same age group, without a history of atopy. Comparative group II included 37 children with AD according to the criteria of Hanifin and Rajka, up to 5 years of age, who had an increased concentration of IgE total and/or sIgE against HDMs.

Total and specific IgE were tested using the fluoroimmunoenzymatic method of ImmunoCAP.

Children from all study groups underwent patch tests with HDM using dust mite mixtures 30% of household vases by Chemotechnique Diagnostics, catalogue number Mx-21C on IQ Ultra chamber; additional petroleum jelly was applied to the identical chamber as a negative control test. Skin tests were performed 72 hours after the application according to system of the International Contact Dermatitis Investigator Group.

RESULTS

Contact allergy to HDM in the study group occurred in 42.4% of patients and in comparative group I in 16% of patients. It transpired that contact allergy to HDM was present significantly more often in the study group than in comparative group I ($p < 0.05$).

It was shown that contact allergy to HDMs was more frequent in comparative group II than in the study group. However, the difference did not turn out to be statistically significant ($p > 0.05$). Contact allergy to HDM in comparative group I was found only in 16.0% of patients, and in comparative group II in 56.8% of patients. Contact allergy to HDM has been shown to occur significantly more often in comparative group II than in I (statistically significant $p < 0.01$) (Figure 1).

The frequency of contact allergy to HDMs in children does not depend on selected demographic factors such as gender, age, and place of residence in all study groups (Figures 2–4).

A statistically significant relationship was found between the occurrence of a contact allergy to HDM patients and the severity of the disease assessed using the SCORAD skin lesion severity scale ($p < 0.001$). It should be noted that the distribution of the results of this scale in the group of patients with positive and negative test results is completely different. SCORAD results up to 25 points were observed significantly more often in children with negative patch test: 42.9% vs. 2.8%. On the other hand, SCORAD scores of 26–50 points were

found significantly more often in children with a positive test result; the corresponding percentages are 91.7% vs. 57.1%, respectively. Similarly, results above 50 points in the SCORAD scale were significantly more often shown in patients with a positive patch test for contact allergy to HDMs: 5.5% vs. 0.0%, respectively. The first comparison group consisted of healthy children without AD (Figures 5, 6).

DISCUSSION

Coexistence of allergic contact eczema in patients with atopic dermatitis is very difficult to recognise due to the very similar nature of skin lesions in both diseases.

The coexistence of AD and contact eczema is underestimated. Giordano-Labadie *et al.* [27] showed that patients with AD in the paediatric population show as much as 43% of positive tests for contact allergens.

Czarnobilska *et al.* [36] showed 49.4% of positive patch tests for contact allergens in the population of children aged 7–16 years. Sharma *et al.* [37] examined patients aged 7–50 years, of whom 23% of respondents had positive patch test results for contact allergens. A study by Belhadjali *et al.* [38] consisted of 63 children and 24 adults – positive test results for contact allergens were found in 42.7% of the total group.

Beattie *et al.* [39] studied 114 children with AD, with an average age of 11.5 years, and found positive results in 54% of patients, while in the studies by Mortz *et al.* [40] conducted in 1146 patients with AD, contact allergy was found in 15.2% of patients.

Most of the positive results were shown for nickel, chromium, cobalt, fragrances, and lanolin.

Research in children with AD in terms of contact allergy shows that contact allergy is not uncommon in the paediatric population, especially in children with chronic eczematous skin lesions. Using of patch testing in paediatric AD patients might be helpful in diagnosis because contact allergens in these patients may cause exacerbations or persistent eczema lesions despite treatment. In 2013, the European Task Force on Atopic Dermatitis referred to the method of atopy patch test (APT) against aeroallergens and food allergens, suggesting the use of native Vaseline allergens; the allergens should be placed in a 12 mm chamber and stuck to healthy skin for 48 hours.

Numerous research results confirm that APT to aeroallergens may be a useful and valuable diagnostic method, although it is still not a routine test [41–43]. The diagnostic problem is the lack of standardization of inhaled allergens for atopy patch tests.

In 1982, Mitchell *et al.* [44] expressed the opinion that *D. pterynosinnus* may be responsible not only for immediate reactions but also for delayed skin reactions. Darsow *et al.* [45] showed that atopic patch tests with aeroallergens can be a valuable diagnostic tool in patients with AD. Ingordo *et al.* [31] compared the incidence

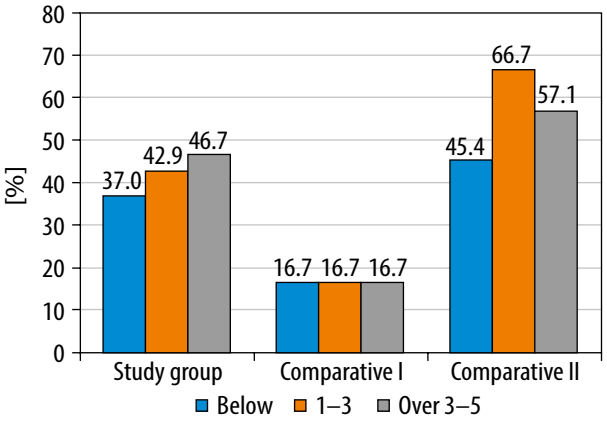

FIGURE 4. Frequency of positive patch test to house dust mite by age in the test group and comparative groups I and II

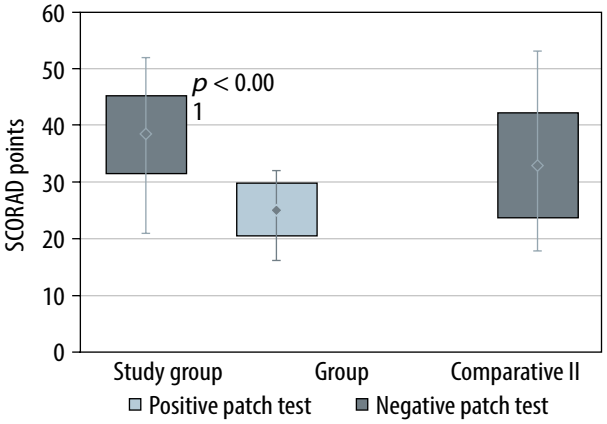

FIGURE 5. Frequency of positive patch test to house dust mite by achieved SCORAD scale in the test group and comparative group II

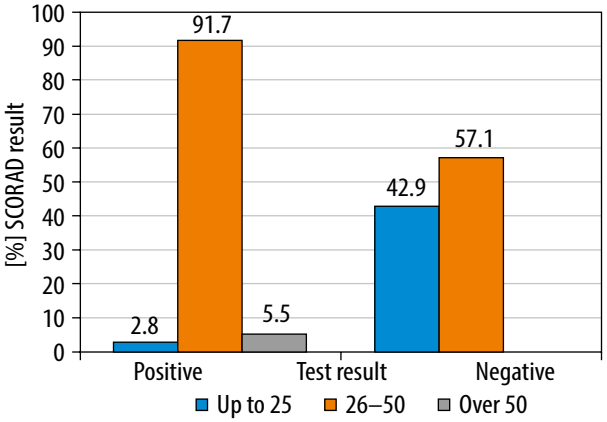

FIGURE 6. The relationship between the SCORAD result and the result of the patch test with house dust mites in the study

of contact allergy to HDMs in non-atopic patients with a history of eczema and in patients with atopic dermatitis, confirming that patients with atopic dermatitis showed positive epidermal tests significantly more often. Darsow *et al.* [30] also conducted a study on the issue of contact allergy to aeroallergens, involving 314 AD patients from 6 European countries, who underwent epidermal tests, skin tests, and sIgE with airborne allergens, where it was shown that the severity of AD was associated with con-

tact allergy to HDMs in 34% of respondents. A positive epidermal test with negative skin and sIgE test results was demonstrated in 7% of patients.

Only a few of the available studies relate only to paediatric patients. A study by Visitsunthorn *et al*. [46] from 2016 included 56 children with AD, who underwent atopic epidermal patch tests and skin tests for food and inhalation allergens, and showed that positive epidermal patch tests for *D. fariniae* and *D. pterynosinus* were seen in 33.9% and 35.8% of the respondents, and skin tests for these allergens were positive in 28.3% and 24.5%. A study by Benhamou *et al*. [47] showed that in 28 children with AD, as many as 15 were positive for HDM in patch tests, including 9 with mite-dependent IgE allergy.

The above studies confirm that contact allergy is not uncommon in patients, especially in patients with a history of chronic eczema, and should be taken into account in the differential diagnosis considerations.

The diagnostic problem is the lack of standardization of atopy patch tests against aeroallergens. Ayala *et al*. in 2002 published data on the standardization of patch tests for HDMs [48]. The reaction index was set at 0.76 for the 20% Dermatophagoides mix in petroleum jelly. Significant data were published in JEADV in 2020 by Dickel *et al*. [49], who conducted a retrospective multicentre study at the turn of 2000–2015, in a large number of patients, using standardized patch tests for aeroallergens, including HDMs (Stallerpatch by Stallergen). In a retrospective study including 3676 people with a history of atopic dermatitis, positive tests were found in 20% of patients for *D. farinae* and 22.1% for *D. pterynossinus*. The authors emphasize that patch tests with aeroallergens are an extremely valuable tool, especially in patients with AD. However, this study was performed in patients 6–80 years of age, median age 41 years.

In our own study, standardized HDM patch tests were also performed, and the patients were additionally divided into those with and without IgE sensitization to aeroallergens. The study was performed entirely in children up to 5 years of age. The authors' own research has shown that contact allergy to HDMs in paediatric patients with AD is more common than in patients without AD, and that contact allergy to HDMs in children with atopic dermatitis affects the severity of the disease. A statistically significant correlation was found between the occurrence of contact allergy to HDMs in the subjects and the severity of the disease assessed using the SCORAD skin lesion severity scale. This relationship was found both in the study group and in the second control group.

Current observations from the literature emphasize the importance of a contact allergen in the exacerbation of changes in the course of AD; however, there is no precise comparison of these data with regard to the SCORAD scale. Some studies refer to the number of exacerbation rates or the patient's quality of life scale. The SCORAD scale seems to be an objective parameter to assess the severity of AD. A statistically significant relationship was found between the presence of contact allergy to HDMs in the subjects and the severity of the disease assessed using the SCORAD skin lesion severity scale. This relationship was found both in the study group and in the second control group.

The results of our own research are difficult to compare to the data from the literature because there is no standardization of patch tests, the tests are performed in various age groups, and the severity of skin lesions in AD is not always assessed based on the available severity scales, and often on the basis of subjective questionnaires.

CONCLUSIONS

It remains to be considered whether contact allergy to HDMs in patients with atopic dermatitis is more frequent due to increased penetration of the allergen through the initially damaged skin barrier, which is related to the FLG defect and excessive activity of serine proteases. Allergens then have easier access to bind to dendritic cells of the epidermis, which are then responsible for Th2-dependent reactions.

At the same time, the authors' own research draws attention to the fact that in some patients without AD, a contact allergy to HDMs was also found. It is unclear whether patients without atopic dermatitis who have been diagnosed with a contact allergy to HDMs are patients with FLG defect but currently asymptomatic, or whether HDMs are an irritating factor.

Clinically, it is morphologically extremely difficult to distinguish between irritant eczema and allergic eczema. Such eczema is often observed on exposed parts of the skin, with intensification during the months of the heating season.

Early diagnosis of the coexistence of a contact allergy to HDMs in patients with AD can significantly improve the quality of treatment by introducing anti-mite prophylaxis methods, e.g. frequent washing of bedding, avoiding sleeping with plush toys, maintaining proper humidity, avoiding blankets etc., which can reduce the number of exacerbations and provide better disease control, which will contribute to less use of steroids and significantly improve the quality of life of patients and their families.

DISCLOSURE

The authors declare no conflict of interest.

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