

ATOPY AND URTICARIA-SENSITIZATION TO INHALANT AND FOOD ALLERGENS IN PATIENTS WITH URTICARIA

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Abstract

Urticaria, also known as Hives, is a prevalent skin condition characterized by the activation of mast cells and basophils. Currently, anti-IgE therapy is one of the most effective and utilized treatments for managing the disease. The relation between skin atopy and cross-reactivity to various antigens in urticaria is still unclear and requires elucidation. This study investigates the relationship between food and aeroallergic sensitization (cross-reactivity) in patients with chronic immediate urticaria who do not have other clinically apparent allergic diseases. Serological tests were conducted on 54 antigens using the immunoblot method in 80 patients with ongoing CU, comprising 60% women and 40% men, with an average age of 29.3 years for women and 34.89 years for men. Sixty percent of the individuals in the studied group tested positive for food and/or inhalant allergens. A strong correlation ($r = 0.891$; $p = 0.01$) was established between the quantitative values of specific IgE to g12 and IgE antibodies for food allergens in the sensitized patients. The correlation coefficients for specific groups were as follows: $r = 0.93$ ($p = 0.01$) for group g3, $r = 0.77$ ($p = 0.01$) for group g1, and $r = 0.91$ ($p = 0.01$) for group g6.

Key words: chronic urticaria, sensitization to inhalant allergens, sensitization to food allergens, specific IgE, cross-reactivity

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Introduction. Urticaria is a common disease with an incidence rate ranging from 0.5% to 20% in the global population, depending on different sources [1–5]. The potential role of immediate hypersensitivity in chronic urticaria (CU) pathogenesis is scantily addressed in scientific research. Furthermore, evaluating immediate-type hypersensitivity via skin tests or serological tests for food or other allergies is not recommended as routine practice in urticaria [1]. The cross-reactivity between different proteins could explain the activation of mast cells in the skin or the mucosa in the gut [4].

The study aims to investigate the link between aeroallergen and food sensitivity (cross-reactivity) in patients with chronic spontaneous urticaria (CU) who do not have a concomitant, clinically pronounced allergic reaction.

Materials and methods. Patients. Eighty patients were tested, unaffected by ambulatory antihistamine treatment for a period exceeding six weeks, meeting the following criteria:

1. Age: Over 18 years.
2. Persistent lack of control of the condition for more than six weeks.
3. Absence of concomitant autoimmune or other chronic inflammatory diseases.
4. No clinically significant inhalant allergies, including allergic rhinitis and/or bronchial asthma.

Serological analysis. Serological analyses of specific IgE to 54 antigens were conducted using the immunoblot method with the Euroimmune Euroline system (Germany). The following set of allergens was tested: Atopy screen (d1 Dermatophagoides pter., d2 Dermatophagoides farinae, i1 Honey bee venom, i3 Common wasp venom, i6 Cockroach German, h1 House dust (Greer), e1 Cat, e2 Dog, e3 Horse, m1 Penicillium notatum, m2 Cladosporium herbarum, m3 Aspergillus fumigatus, m6 Alternaria alternata, g1 Sweet vernal grass, g3 Orchard grass, g6 Timothy grass, g12 Cultivated rye, t2 Alder, t3 Birch, t4 Hazel, t7 Oak, t23 Cypress, w1 Common ragweed, w6 Mugwort, w9 English plantain, u85 Latex, f25 Tomato, f31 Carrot, f35 Potato, f85 Celery, f1 Egg white, f75 Egg yolk, f2 Cow's milk, f3 Codfish, f23 Crab, f24 Shrimp/Prawn, e204 Bovine serum albumin (BSA), f76 Alpha-Lactalbumin, f77 Beta-Lactalbumin, f78 Casein, f27 Beef, f88 Mutton/Lamb, f45 Baker's yeast, f4 Wheat flour, f5 Rye flour, f9 Rice, f14 Soybean, f10 Sesame, f13 Peanut, f17 Hazelnut, f20 Almond, f49 Apple, f84 Kiwi, f237 Apricot, CCD cross-reactive carbohydrate determinants).

Statistical analysis. The statistical calculations of the obtained data were done by the Microsoft Office Excel 365 program and IBM SPSS Statistics 19.

Descriptive methods and methods. Descriptive methods and methods for evaluations were applied for:

1. Frequency analysis of the qualitative variables – relative frequencies (in percentages);
2. Graphical images;
3. Correlation analysis – Coefficient of linear correlation – Correlation depen-

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The results were evaluated according to the following scale for IgE concentration in the blood, expressed in kilounits per liter (kU/L)

Concentration (kU/L)	Class	Explanation
$0 \leq \text{sIgE} < 0.35$	0	No specific antibodies detected.
$0.35 \leq \text{sIgE} < 0.7$	1	Very weak antibody detection, often no clinical symptoms with an existing sensitization.
$0.7 \leq \text{sIgE} < 3.5$	2	Weak antibody detection, existing sensitization, often with clinical symptoms in upper levels.
$3.5 \leq \text{sIgE} < 17.5$	3	Definite antibody detection, clinical symptoms are often present.
$17.5 \leq \text{sIgE} < 50$	4	Strong antibody detection, almost always with existing symptoms.
$50 \leq \text{sIgE} < 100$	5	Very high antibody titer.
$\text{sIgE} \geq 100$	6	Very high antibody titer.
Band	Band information	
Grass mix 2	Contains Timothy grass, Cultivated rye	

dence is classified by the degree of dependence (strength) in the following 82 ways: extremely large with coefficient – $r > 0.9$; large – $0.7 \leq r \leq 0.9$, significant – $0.5 \leq r \leq 0.7$, moderate – $0.3 \leq r \leq 0.5$, weak – $r < 0.3$.

Results and discussion. Eighty patients were tested, among which 48 women (60%) and 32 men (40%) (Fig. 1A). The average age was 29.3 for the women and 34.98 for the men (Fig. 1C). Among the tested individuals, 16 (20%) had negative serological tests, whereas 64 (60%) tested positive for food or/and inhalant allergies (Fig. 1B).

In the sensitized group (64 patients), the following sensitizations were detected (allergen – n number of individuals with established sensitization to the allergen): d1 ($n = 15$), d2 ($n = 12$), I1 ($n = 11$), i3 ($n = 8$), i6 ($n = 5$), h1 ($n = 9$), e1 ($n = 8$), e2 ($n = 2$), e3 ($n = 0$), m1 ($n = 0$), m3 ($n = 0$), m6 ($n = 7$), g1 ($n = 31$), g3 ($n = 32$), g6 ($n = 31$), g12 ($n = 31$), t2 ($n = 14$), t3 ($n = 13$), t4 ($n = 10$), t7 ($n = 10$), t23 ($n = 2$), w1 ($n = 12$), w6 ($n = 10$), w9 ($n = 6$), u85 ($n = 8$), f25 ($n = 3$), f31 ($n = 1$), f35 ($n = 8$), f85 ($n = 9$), f1 ($n = 2$), f75 ($n = 0$), f2 ($n = 0$), f3 ($n = 0$), f23 ($n = 11$), f24 ($n = 4$), e204 ($n = 0$), f76 ($n = 4$), f77 ($n = 5$), f78 ($n = 0$), f27 ($n = 0$), f88 ($n = 6$), f45 ($n = 3$), f4 ($n = 2$), f5 ($n = 7$), f9 ($n = 5$), f14 ($n = 5$), f10 ($n = 6$), f13 ($n = 3$), f17 ($n = 3$), f20 ($n = 5$), f49 ($n = 7$), f84 ($n = 2$), f237 ($n = 1$).

Thirty-four patients were sensitized to both inhalant and food allergens and thirty patients were sensitized to only inhalant allergens (Fig. 2). Sensitization to house dust (Dpt), to d1 (Dermatophagoides pter.), and food allergens were found in 15 patients. Sensitization to only inhalant allergens was established in 10

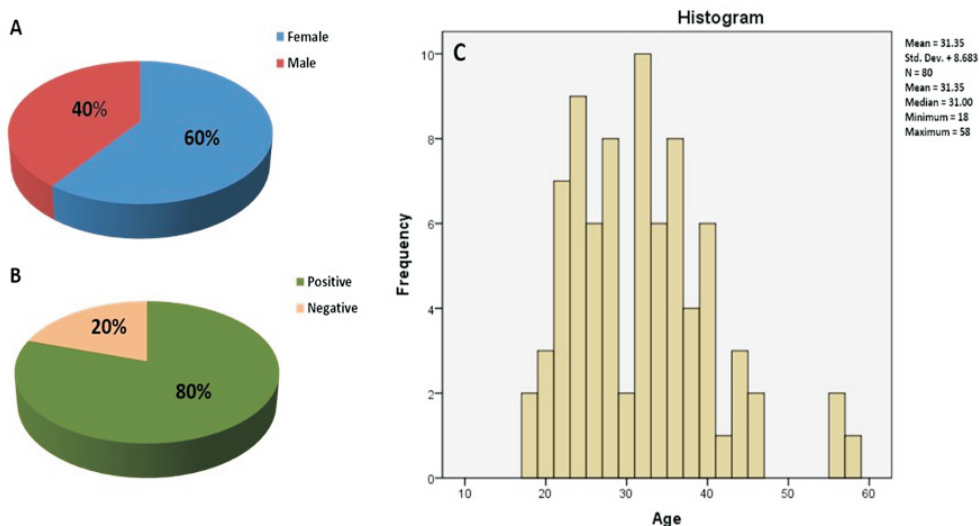


Fig. 1. Demographic characteristics of the tested patients. A) Gender distribution of patients with CU; B) Presence or absence of sensitization to inhalant and/or food allergens in patients with CU; C) Age distribution of patients with CU

patients. For w1 (Wormwood), 12 patients had concomitant food sensitization and 3 showed no possible cross-reactivity. With t2 (birch pollen), 14 had concomitant food sensitization, and 5 – no food sensitization. For g3 (grass pollen), 32 had concomitant food sensitization and 14 were without food allergen sensitization.

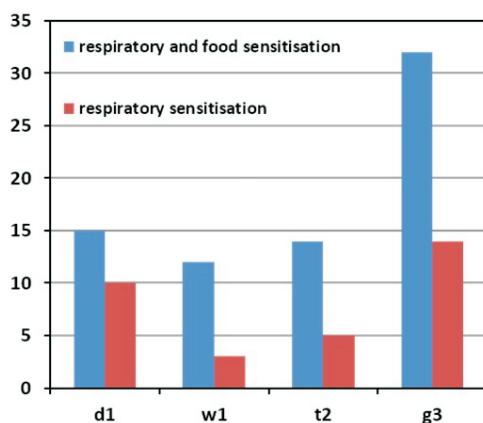


Fig. 2. Distribution of sensitization to inhalant and both inhalant and food allergens among patients with chronic urticaria

Quantitative assessment of specific IgE (kU/L) in the two studied groups of patients, divided according to criteria Group 1 inhalant sensitization and Group 2 inhalant and food sensitization showed a strong correlation between the amount

of IgE and concomitant sensitization to food allergens, possibly related to manifestations of cross-reactivity with food allergens. Graphically, the result is shown in Fig. 3 for allergen g12.

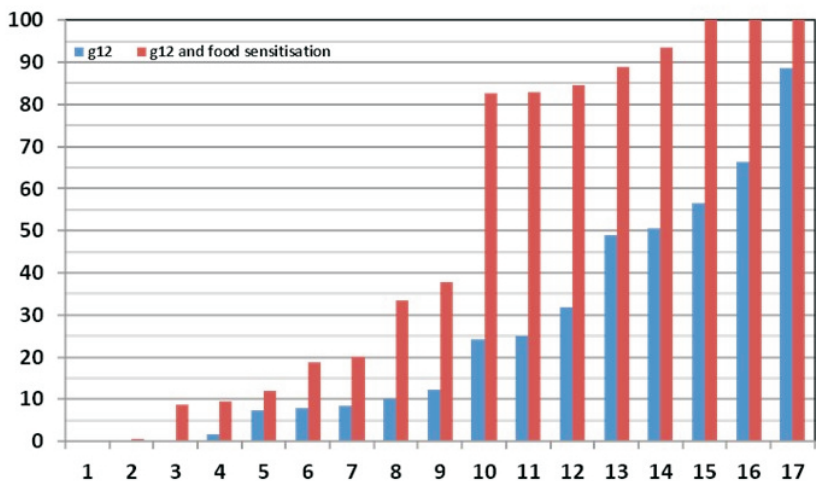


Fig. 3. Quantitative assessment of specific IgE (kU/L) in individuals with chronic urticaria with accompanying sensitization to food allergens

The graph shows a strong correlational dependency ($r = 0.891$) between the quantitative value of specific IgE to g12 and the presence of cross-reactivity to food allergens. Regarding the remaining inhalant allergens, the results are as follows: $r = 0.93$ in the groups of g3, $r = 0.77$ in the groups of g1, and $r = 0.91$ in the groups of g6. For the remaining inhalant allergens, a similar analysis was not performed given the small number of patients included in the paired groups.

Cross-reactivity occurs when IgE antibodies targeted at a specific antigen bind to another allergen from a different allergenic source, resulting in B-cell epitopes of homologous proteins. A minimum of 50–70% homology between allergens is required. This is typical for proteins from taxonomically linked sources [6–8]. This reactivity between proteins can be ascribed to the common protein sequences and common carbohydrate structures (cross-reacting carbohydrate determinants – CCD). Additionally, the shared cross-reactive T-cell epitopes could partly explain the existence of tolerance to food allergens after successful pollen immunotherapy [8]. The cross-reactivity of IgE can be clinically apparent or irrelevant. It is described as an immunological phenomenon characterized by the relation between a single IgE bind between an antibody and two or more allergen sources [8]. Consequently, later exposure to food allergen sources containing homologues proteins/allergens via ingestion, inhalation, or contact after already synthesized allergen-specific IgE antibodies, they recognize secondary allergens via cross-reactive epitopes, followed by cross-linking of basophils and mast cells, which in turn leads to clinical manifestation of allergy symptoms [8].

LIANG et al. [9] stated that patients with high levels of HDM-sIgE (≥ 3.5 kU/L) with chronic spontaneous urticaria have higher basophil expression of CD63 and Fc ϵ RI α in the peripheral blood. This research showed a strong correlational dependency ($r = 0.891$; $p = 0.01$) between the quantitative value of specific IgE g12 and the concomitant presence of IgE antibodies to food allergens, probably related to cross-reactivity to food allergens. Regarding the other inhalant allergens, the results are as follows: $r = 0.93$ ($p = 0.01$) in g3 groups, $r = 0.77$ ($p = 0.01$) in g1 groups, $r = 0.91$ ($p = 0.01$) in g6 groups.

A recent study demonstrated that the serum-free IgE level measured by IgE-TRAP protein has a better prognostic value than the total IgE level in the context of the atopic status of patients. Patients with chronic spontaneous urticaria and atopy showed significantly higher serum levels of free and total IgE than non-atopic group [3]. Other studies indicate a higher rate of positive prick tests for aeroallergens compared to control groups [1, 2]. However, the relationship is still unclear. WONG and KEITH [1] finding a high incidence of sensitization to wormwood in patients with chronic spontaneous urticaria, suggested that cross-reactivity to foods and spices may influence the course of urticaria.

In our studied groups, 34 patients with CU had sensitization to inhalant allergens, whereas 30 had sensitization to only inhalant allergens. Fifteen patients had sensitization to domestic dust (Dpt), to d1, and food allergens. Ten patients showed sensitization to inhalant allergens. For wormwood w1, 12 had concomitant sensitization to food, whereas three were without possible cross-reactivity. With birch pollen t2, 14 had concomitant food sensitization, and five had no food sensitization. For grass pollen g3, 32 had concomitant food sensitization, and 14 were without food allergen sensitization.

Conclusions. Urticaria is a common condition that can affect individuals at various stages of life, from childhood to adulthood, accentuating the clinical and social importance of the disease. Fortunately, a growing body of data is addressing the relationship between urticaria and the atopic status of affected patients, which sheds light on future possible resolutions in managing this disease. The results from this study significantly contribute to the enrichment of clinical investigation. A strong correlation was found between the quantity of IgE and sensitization to food allergens, likely due to cross-reactivity with these allergens. However, this study faces some important limitations, particularly the insufficient number of patients.

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