Specific IgE for Aero and Food Allergens in Adult Chronic Urticaria Patients Without Other Allergic Diseases

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Abstract: Chronic Urticaria (CU) is a disease characterized by occurrence of spontaneous wheals observed by the patient for more than 6 weeks duration. The prevalence of CU varies from 0.5-5% in adult population. This is a disease of complex etiologies with more areas to be explored by researches. The aim of the study was to detect the Prevalence of allergen sensitizations among adult chronic urticaria patients without other allergic diseases. This study is a cross-sectional case control study. 70 patients with CU without evident cause and 50 healthy control individuals were included in the study. Patients with any other allergic diseases (such as Asthma, allergic Rhinitis, Allergic Conjunctivitis, Drug Allergy, atopic Dermatitis, Anaphylaxis…), patients with other chronic or systemic Diseases (such as Cardiac, respiratory, renal, hepatic, hematological, thyroid or other skin Diseases, etc….) and smokers were excluded from the study. Each patient and control individual was subjected to full medical history, complete medical examination and routine lab test. Determination of allergen-specific IgE (for 20 separate food and 20 aeroallergens) in serum for the patients was done by using EUROLINE Atopy Screen. Each of the patients and control groups were comparable according to age and gender. There was a significant difference between the CU patients and the control group as regard the prevalence of any allergen sensitization (65.7% for CU patients and 18% in control group) p<0.05. There was also a significant difference between the sensitized individual in each group as regard the number of allergens per each individual; for sensitized CU patients the mean was 3 allergens and interquartile range was (2-4), for the sensitized control individuals the mean was 2 and interquartile range was (1-2) with p= 0.014. The mostly frequent allergens were found in the CU sensitized patients was the house dust mite allergens (34.8% of the sensitized CU patients were sensitized to one or more of the two types of mites; dermatophagoidespteronyssinus and or dermatophagoides farinae). The study concluded that; a great prevalence of CU patients proved to be sensitized to common allergens which open the door to start a trials to examine the value of environmental control, food avoidance and specific allergen immunotherapy in this group of patients.

Keywords: Chronic Urticaria, Allergen-Specific IgE, Aero-Allergens, Food Allergy

1. Introduction

Chronic Urticaria (CU) is a disease characterized by the appearance of spontaneous wheals with or without angioedema for more than 6 weeks duration [1]. The prevalence of CU estimated to be 1% in the general population [2]. Also CU is associated with high rate of psychological consequences as poor sleep, anxiety and depression [3].

The mast cell known to be the most important effector cell in CU through releasing of its mediators; From them the histamine with its inflammatory action, stimulation of peripheral nerves and increasing vascular permeability. Also other mediators such as leukotriene, tryptase and heparin sharing in the pathogenesis of CU [4].

The role of IgE in the activation of mast cell is well known also its role in CU as part of activation of mast cell in this disease [5]. Moreover a significant higher total serum IgE level in CU patients (34%) than the healthy control (8.6%) with a significant correlation between elevated level of serum total IgE (above 175 U/ml) with CU symptoms severity [6] were found.
On the other hand treatment with anti-IgE monoclonal antibody (Omalizumab) now known to be effective in the treatment of CU and reduction of its symptoms even in cases not responding to Anti-histamine [7-8], and decreases the need of oral corticosteroids with up to 12 months of Omalizumab use [9]. The relation between Atopic Dermatitis in early childhood (below age of 2 years) and the development of other atopic diseases has been studied and showing that there were increase incidence of developing CU in those children with ratio of proportion 2.04 (CI 1.80-2.31) [10].

There is a limited data about the cause of IgE sensitization in CU patients without any known history of other atopic diseases, this study was conducted to explore the association between IgE sensitization and CU in these type of patients.

2. Patients’ Selection

This study is a cross-sectional case control study. Patients were selected from Ain Shams University Hospital; Allergy and Clinical Immunology outpatient clinic during the period from 1st of March 2017 till the end of December 2017.

Inclusion Criteria: patients with CU complaining of spontaneous wheels without evident cause observed by the patient for more than 6 weeks duration.

Exclusion criteria:
1- Patients with vasculitic Urticaria (the single wheal duration more than 24 hours which resolves with skin pigmentation)
2- Patients with any other allergic diseases (such as Asthma, allergic Rhinitis, Allergic Conjunctivitis, Drug Allergy, atopic Dermatitis, Anaphylaxis…..)
3- Patients with other chronic or systemic Diseases (such as Cardiac, respiratory, renal, hepatic, hematological, thyroid or other skin Diseases, etc….)
4- Smokers

50 healthy individuals matched for the age and sex to the patients are selected as control group

3. Methods

Each patient and control individual was subjected to full medical history, complete medical examination and routine lab test (CBC, renal functions, liver functions, thyroid functions…..) and any patient confirmed to have one or more of exclusion criterion was omitted.

Determination of allergen-specific IgE (for 20 separate food and 20 aeroallergens) in serum for the patients was done by using EUROLINE Atopy Screen (EUROIMMUNE-Medizinische Labordiagnostika AG; Germany).

The aeroallergen panel included (dermatophagoides fariniae, dermatophagoides pteronyssinus, alternaria alternata, aspergillus fumigatus, candida albicans, cladosporium herbarum, penicillium notatum, sweet vernal grass, timothy grass, cultivated rye, alder, birch, oak, common ragweed, mugwort, orchard grass, cat, dog, cockroach and hamster)

The food panel included (egg white, egg yolk, cow milk, chocolate, wheat flour, soybean, Baker yeast, hazelnut, peanut, orange, strawberry, banana, mango, tomato, carrot, onion, chicken, lamb’s meat, codfish, and shrimp)

The patients were further classified in two groups:
- Group 1 (sensitized patients with specific IgE positive to any of the allergens examined) and group 2 (non-sensitized patients with –ve results for all the examined allergens)

The control subjects were classified also in two groups:
- Group 3 (sensitized control subjects with specific IgE positive to any of the allergens examined) and group 4 (non-sensitized patients with –ve results for all the examined allergens)

Statistical methods: the author used mean and standard deviation for describing numerical data, number and percent for describing prevalence, student t test for calculating significance between numerical variables in two groups, ANOVA for calculating significance between numerical variables in more than two groups, Chi square for difference in Nonparametric data between two groups and Mann-Whitney test for calculating significance between Nonparametric variables in more than two groups.

4. Results

70 patients with CU and 50 healthy control individuals were included in the study, table 1 shows a statistical significant difference in the prevalence of allergen sensitization by the specific IgE in-between the patients group and the control group.

Table 1. Prevalence of allergen sensitization in-between the patients group and the control group.

|               | Sensitized | Non-sensitized | total |
|---------------|------------|----------------|-------|
| CU no. (%)    | 46 (65.7)  | 24(34.3)       | 70    |
| Control no. (%)| \(\frac{9}{18}\) | 41 (82) | 50 |
| Significance  | \(p<0.05\) x²=26.75 |

Chi-square for calculation of statistical significance between the CU patients and the control

Table 2 shows the distribution of gender of the four groups denoting non-significant differences between the groups.

Table 2. Gender distribution in the four groups.

|               | Female | Male | total |
|---------------|--------|------|-------|
| Group 1 (no.) | 29     | 17   | 46    |
| Group 2 (no.) | 14     | 10   | 24    |
| Group 3 (no.) | 6      | 4    | 10    |
| Group 4 (no.) | 13     | 17   | 40    |
| total         | 72     | 84   | 120   |
| Significance  | x²=0.3095. The p-value is 0.958236 § |

Chi-square for calculation of statistical significance between the 4 groups according to gender and the control

Table 3 shows that the ages were comparable through the 4 groups without any significant differences.
5. Discussion

CU is a common dermatological disease which encounters many physical and psychological burden on the patients [11], nevertheless the etiology of CU is still unclear, even after the successful control of CU symptoms by Anti-IgE antibody (Omalizumab) which was designed primary to treat IgE mediated Asthma [12-13], the role of IgE sensitization to common aero and food allergens was not thoroughly investigated.

In the current study the author found that there was a significant difference between the patients and the control regarding the prevalence of allergen sensitization with 65.7% sensitization in the patients with CU versus 18% of control group(\(P<0.05, \chi^2=26.75\)), a lower incidence was observed in CU patients in study conducted by Zuberbier et al. 2010 who found sensitization of 39.1% of those patients by using Skin Prick Test (SPT) only and the researches in this study only performed the SPT on selected cases (69.7% of the study population) whose presented with active disease during the study time [2], in contrast the current study used the specific IgE instead of SPT to avoid the false –ve results especially in patients with active CU who couldn’t stop the anti-histaminic which alter the results of the SPT even for week after stoppage of its intake [14], Caliskaner et al. also found a rate of allergen sensitization by SPT was 27.4% in CU patients after the stoppage of its intake [14], Caliskaner et al. also found a rate of allergen sensitization by SPT was 27.4% in CU patients after the stoppage of its intake [14], Caliskaner et al. also found a rate of allergen sensitization by SPT was 27.4% in CU patients after the stoppage of its intake [14], Caliskaner et al. also found a rate of allergen sensitization by SPT was 27.4% in CU patients after the stoppage of its intake [14], Caliskaner et al. also found a rate of allergen sensitization by SPT was 27.4% in CU patients after the stoppage of its intake [14].

The prevalence of individual allergens sensitization shown in table 5 with the most prevalent allergens are the house dust mite allergens (Dermatophagoides farinae & Dermatophagoides pteronyssinus).

The no. of patients with sensitization of one or more of house dust mite allergens was 16 (34.8%) in Group 1, and the control was 3 (33.3%) \(p=0.933\) (non-significant) \(\chi^2=0.007\).

### Table 3. Ages were comparable through the 4 groups.

|           | Group 1 | Group 2 | Group 3 | Group 4 |
|-----------|---------|---------|---------|---------|
| Mean(SD*) | (15.4)  | (13.8)  | (13.7)  | (13.2)  |
| Significance | \(p=0.69\) § |

*SD= Standard Deviation
Analysis by ANOVA: ANalysis Of VAriance between groups
§ Non-significant difference

Table 4 shows the comparison between the number of allergen specific IgE in each of sensitized groups of the CU patients and the control individuals denoting a statistically significant difference between the two groups with higher number of allergens per each patient in CU group than the control group.

### Table 4. Number of allergens in each patient of the sensitized groups (group 1 and group 3).

| No. of allergens | Group 1 | Group 3 |
|------------------|---------|---------|
| Mean             | 3       | 2       |
| Inter-quartile range | 2-4    | 1-2    |

Comparison by Mann-Whitney test
‡ Significant difference

### Table 5. Number of individual allergen sensitization in each sensitized group.

| Aeroallergens | no. | Group 1 | Group 3 |
|--------------|-----|---------|---------|
| Dermatophagoides farinae | 8  | 2       |
| Dermatophagoides pteronyssinus | 12 | 2       |
| Alternaria alternata | 6  | 0       |
| Aspergillus fumigatus | 9  | 1       |
| Candida albicans | 4  | 0       |
| Cladosporium herbarum | 4  | 0       |
| Penicillium notatum | 7  | 1       |
| Sweet vernal grass | 4  | 0       |
| Timothy grass | 6  | 3       |
| Cultivated rye | 6  | 0       |
| Alder | 3  | 0       |
| Birch | 10 | 1       |
| Oak | 3  | 0       |
| Common ragweed | 3  | 1       |
| Mugwort | 8  | 2       |
| Orchard grass | 1  | 0       |
| Cat | 7  | 0       |
| Dog | 4  | 0       |
| Cockroach | 0  | 0       |
| Hamster | 0  | 0       |

| Food allergen | no. | Group 1 | Group 3 |
|--------------|-----|---------|---------|
| Egg white | 3  | 0       |
| Egg yolk | 0  | 0       |
| Cow milk | 6  | 1       |
| Chocolate | 1  | 0       |
| Wheat flour | 4  | 1       |
| Soybean | 4  | 1       |
| Baker yeast | 0  | 0       |
| Hazelnut | 1  | 1       |
| Peanut | 1  | 0       |
| Orange | 3  | 0       |
| Strawberry | 3  | 1       |
| Banana | 2  | 0       |
| Mango | 3  | 0       |
| Tomato | 0  | 0       |
| Carrot | 1  | 0       |
| Onion | 1  | 0       |
| Chicken | 0  | 0       |
| Lamb’s meat | 0  | 0       |
| codfish | 0  | 0       |
| shrimp | 2  | 0       |

Table 5. Number of allergens in each patient of the sensitized groups (group 1 and group 3).

| Number of allergens | Group 1 | Group 3 |
|---------------------|---------|---------|
| Mean                | 3       | 2       |
| Inter-quartile range | 2-4    | 1-2    |

Comparison by Mann-Whitney test
‡ Significant difference
aeroallergens also the used method was specific IgE not SPT, also Liu et al. found a positive SPT in 51.7% of 91 CU patients to 17 aeroallergens [18], a higher percent of Allergen sensitization was found by Yi Zhou et al. who found a sensitization of 95.83% of children with CU aged 4-10 years when examining 34 allergens by specific IgE [19]. Furthermore Mahesh et al. found a higher prevalence of sensitization of House Dust Mite by SPT (64%) of 122 CU patients [16], which is higher than the current study (34.8% of the sensitized patients in this study had positive specific IgE Ab to one or more of the House Dust Mite allergens; Dermatophagoides farinae and/or Dermatophagoides pteronyssinus), it was verified that the House Dust Mite allergen can induce skin manifestations either by introduction of the allergen through the respiratory route or direct contact with the allergen in the Atopic dermatitis model [20].

Food allergy is a common cause of Acute Urticaria (urticaria last less than 6 weeks) and the diagnosis often simple by history of appearance of urticaria symptoms after ingestion of certain type of food, also can be diagnosed by SPT and serum specific IgE levels to food allergens, but the relation between food allergy and CU is not clear [21], in the current study the author found the prevalence of food allergy by specific IgE for milk allergen was 8.6%, soy and wheat 5.7% for each and minor percent for other major food allergens.

Furthermore in a recent study on pediatric the authors found a positive allergen sensitization in 92 of the 95 children with CU; with the house dust mite, flour mite, egg yolk and egg white as the most prevalent allergens [22].

In the current study the number of allergens per individual were higher in the sensitized CU patients (3 allergens) than the sensitized control (2 allergens) with P= 0.014, z= 2.45, the allergen sensitization by specific IgE in healthy individual was noticed before in rate of 9.2% in 4 years old children, 14.5% at 8 years and 21.8% at 16 years old children when they examined for the presence of specific IgE for cat and dog allergens and the sensitization was a good predictor of the development of allergy symptoms on the follow up years [23].

6. Conclusions

The current cross-sectional case control study revealed a significantly higher prevalence of specific aero-allergen and food allergen sensitization in CU patients than the healthy control. That may open the door to more researches to examine the value of environmental control, food avoidance and specific allergen immunotherapy in CU patients in the future.

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