

Factors affecting urticaria control in patients with chronic urticaria

Ozge Kangalli Boyacioglu^{1*}, Suna Asilsoy¹, Serdar Al¹, Ozge Atay¹, Gizem Atakul¹, Nevin Uzuner¹

¹ Dept. of Pediatric Allergy and Clinical Immunology, Dokuz Eylul University Faculty of Medicine, Izmir, TR

* Corresponding Author: Ozge Kangalli Boyacioglu | E-mail: ozgekangalli@gmail.com

ABSTRACT

Objective: Urticaria is a condition characterized by the development of blisters (hives), angioedema, or both. Acute urticaria is the appearance of rashes lasting 6 weeks or less, angioedema, or both. It is recommended to use the urticaria control test to evaluate disease control in patients with CSU. This study aimed to evaluate the factors affecting urticaria control in patients followed up with the diagnosis of chronic spontaneous urticaria.

Material and Methods: Urticaria control results of children diagnosed with chronic urticaria were evaluated retrospectively and factors that could affect urticaria control were investigated.

Results: Relationships between the urticaria control test and age, gender, onset time of the complaint, family history of atopy, and laboratory values such as anti-nuclear antibody (ANA) and c4 were examined.

Conclusion: Although chronic urticaria has a mild course in children, parameters such as gender, age, and ANA positivity may affect the control of the disease.

Keywords: Pediatrics, chronic urticaria, urticaria control test

INTRODUCTION

Urticaria is a condition characterized by the development of wheals, angioedema, or both. The wheals are sharply circumscribed, of varying size and shape, often surrounded by erythema, accompanied by itching or sometimes a burning sensation, and the skin returns to its normal appearance, usually within 30 min to 24 h. Angioedema may accompany urticaria in some patients. Urticaria is classified as acute or chronic according to its duration and as inducible or spontaneous according to the role of the triggers. Acute urticaria is defined as the appearance of rashes lasting 6 weeks or less, angioedema, or both. Chronic urticaria (CU) is defined as the appearance of swelling, angioedema, or both, lasting more than 6 weeks. CU may present with signs and symptoms daily or nearly every day or with an intermittent/recurrent course. CU may recur a month or year after complete remission. Urticaria can occur in all age groups, including infants and children. It is recommended to use the urticaria control test to evaluate disease control in patients with CU. Our study evaluated the factors affecting urticaria control in patients followed up with the diagnosis of CU.

MATERIAL AND METHODS

In our study, urticaria control tests of children diagnosed with CU who cured in the Dokuz Eylul Medical Faculty Pediatric Allergy and Immunology Clinic (2018-2021) were evaluated retrospectively and factors that could affect urticaria control were investigated. Although no underlying cause could be found in chronic urticaria disease, we investigated whether there is an underlying cause in chronic urticaria that is recurrent and resistant to treatment. Liver and kidney function tests, complete urinalysis, viral serology, sedimentation and CRP, total IgE, complete blood count, total eosinophilia values, skin prick tests, thyroid autoantibodies, ANA (anti-nuclear antibody), C3-C4 complement levels obtained from each patient diagnosed with chronic urticaria results were evaluated. In the skin prick test, 3 mm or more was considered positive. Additional allergic diseases of the patients and the atopy status of the families were recorded. The angioedema was not observed in any of our patients. Urticaria control test (UCT) scores of the patients were recorded in the outpatient clinic controls. UCT is a questionnaire consisting of 4 questions. The patients are questioned about the physical symptoms of urticaria, their quality of life, the need for antihistamines, and the level of subjective control with the disease.

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Each question contains 5 answer options ranging from 0 to 4, with 0 meaning "too much" and 4 points "not at all". Accordingly, if the score was 12 and above, the disease was considered under control, and if it was 11 and below, it was considered as uncontrolled. The families of patients answered the urticaria control test under the age of 5.

Ethics committee approval (IRB)

Approval was obtained from the ethics committee of Dokuz Eylül University Faculty of Medicine (7193-GOA)

Statistical Analysis

The relationships between the UCT and the factors that may affect this scoring were examined with the multiple linear regression model. The regression model was estimated using the ordinary least squares error method in Stata 13.0. The statistical significance of the explanatory variables included in the model can be analyzed according to their p values. The confidence interval was determined as 95%. Based on the adjusted R2 value, all explanatory variables in the model explain approximately 90% of the changes in the patient's urticaria control.

RESULTS

In our study; In the 2-21 age range (median 10 years), 88 (3.52%) of the 2500 patients who applied to our outpatient clinic with the complaints of urticaria were evaluated as chronic urticaria. 59.1% of patients were girls, and 41.9% were boys. The median time of onset of the patients' complaints of urticaria was 8 years (1-18 years). Liver and kidney function tests, complete urinalysis, viral serology, sedimentation, and CRP results were normal. Total IgE level was 112.5 mg/dl (2-1166 mg/dl), eosinophil level was 200 10^3 (100-1700 10^3). Thyroid autoantibody elevation was found in 10.2% of the patients, and anti-nuclear antibody positivity was found in 39.8% of the patients. Anti-DFS 70 positivity was detected in 12.5% of the patients. While the complement levels of 85.2% of the patients were normal, low C3 was found in 5.7% of the patients and low C4 in 9.1% of the patients.

The skin prick test was negative in 81.8% of patients, 6.8% food, 4.5% grass pollen, 5.7% dust, 1.1% animal sensitivity. There was atopy in the families of 37.5% of the patients. No concomitant disease was detected in 76.1%. Asthma was found in 10.2%, Hashimoto hypothyroidism in 5.7%, atopic dermatitis in 3.4%, allergic rhinitis in 3.4%, and epilepsy in 1.1%.

Relationships between the urticaria control test and age, gender, onset time of the complaint, family history of atopy, and laboratory values such as mother and c4 were examined. Accordingly, the effect of gender on the urticaria control test result is as follows: Being male increases the ability to control urticaria by 52.97% compared with women. Up to 5-6 years of age, urticaria control of patients increases by 31%, and the best control is found in this age range, but until the age of 9, the ability to control urticaria decreases by 1.2%. In the 10-15 age group, it decreases by 6.8%. This situation can be evaluated as a factor that makes it difficult to control the disease. Although urticaria control continues to decrease as age progresses after the age of 15, the rate of decrease slows down (graph 1). The presence of individuals with atopy in their family increases the ability to control urticaria by approximately 35.25%. Other factors affecting urticaria control are laboratory values such as ANA and c4. Normal and positive main values increase the controllability of urticaria by approximately 97.27% and 48.96%, respectively. Low C4 increases the controllability of urticaria by 71.44%. Finally, a one-unit increase in the total IgE value reduces the controllability of urticaria by 0.056 (table 1).

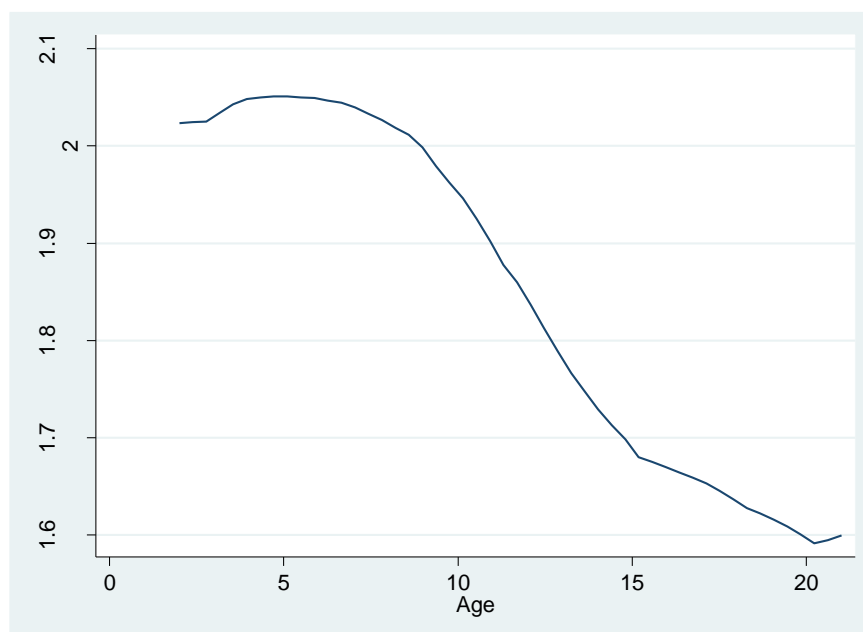
As a result, the first three variables most effective in urticaria control are Ana positivity, low C4 and male gender, respectively. Other variables (eosinophil level, thyroid autoantibodies, other comorbidities, DPT) included in the dataset and not included in the model did not significantly affect urticaria control.

Table 1: Factors Affecting Urticaria Control

| Dependent Variable | Coefficient | 95% Conf. Interval | | p |
|-----------------------|-------------|--------------------|---------|-------|
| Age | 31% | 0.211 | 0.406 | 0.000 |
| Age ² | -1.1% | -0.015 | -0.007 | 0.000 |
| Gender | 52.97% | 0.156 | 0.694 | 0.006 |
| Time_common_complaint | -7.2% | -0.130 | -0.014 | 0.024 |
| Familial Atopy | 35.25% | 0.043 | 0.561 | 0.061 |
| ANA_Normal | 97.27% | 0.337 | 1.021 | 0.00 |
| ANA_Positive | 48.96% | -0.007 | 0.805 | 0.038 |
| C4_low | 71.44% | -0.035 | 1.114 | 0.092 |
| Total IgE | -5.6% | -0.001 | 0.00004 | 0.067 |

Adjusted R2: 0.9024, F (8,80) =102.70, p=0,000, Observation 88

The statistical significance of the explanatory variables included in the model can be analyzed according to their p values. The confidence interval was determined as 95%. Based on the adjusted R2 value, all explanatory variables in the model explain approximately 90% of the changes in the patient's urticaria control.



Graph 1: Graph Of The Relationship Between Urticaria Control Test And Age:

DISCUSSION

Urticaria is a skin disease characterized by plaques that are accompanied by severe itching and develop in less than 24 h, significantly affecting the quality of life and tending to turn into a chronic disease.

Chronic urticaria lasts longer than 6 weeks and although it has been shown to be associated with some other chronic infections, such as *Helicobacter pylori* infection, rheumatological diseases, and parasitic infections, an underlying cause could not be identified in most of patients. CU treatment aims to avoid triggering factors, control urticaria symptoms and minimize treatment-related side effects (1). The urticaria control test (UCT) has 4-item questionnaire about physical symptoms, quality of life, treatment effects, and urticaria control over the previous 4 weeks (2). In this study, it was evaluated the factors affecting the 4-question urticaria control test (UCT). In our study; among 2500 patients aged 2-21 years (median 10 years) who applied to our outpatient clinic with complaints of urticaria, 88 (3.52%) patients were evaluated as having chronic spontaneous urticaria, 59.1% were female and 41.9% were male. The median time of onset of the patients' complaints was 8 years (1-18 years). Similarly, previous studies have found that CU is more common in schoolchildren (3,4). In our study, CU was observed slightly more frequently in girls than in boys, and its incidence in other studies with children varied between 44% and 54% (5). This finding suggests that the incidence of CU in childhood is similar in both genders. The age range of 5-6 is the age range where urticaria control can be the best. After the age of 9, as the child gets older, urticaria control begins to decrease rapidly until the age of 15. Although urticaria control continues to decrease as age progresses after the age of 15, the rate of decrease slows down. C-reactive protein, sedimentation and *helicobacter pylori* infection, parasitic infection results were evaluated as normal in all patients. Our patients did not have angioedema complaints.

Angioedema may be less common in children with CU. Physicians reported that 5% to 14% of their pediatric patients with CU had angioedema (6). The fact that it was not found in our patients may be due to the low number of patients. A one-unit increase in the total IgE value reduced the controllability of urticaria by 0.056, and the effect of eosinophil level on disease control was not detected. A relationship has been shown between pediatric CU and atopic diseases, including asthma, allergic rhinitis (AR), atopic dermatitis (AD), and food allergy (7,8,9). In our study, although the skin prick test was negative in 81.8% of the patients, other observed factors were 6.8% food, 4.5% grass pollen, 5.7% dust, 1.1% animal sensitivity. However, no significant relationship was found between the skin prick test and disease control. It has been shown that the coexistence of atopic diseases has no effect on the probability of recurrence or the duration of CU (10). In our study, 10.2% of the patients with CU had asthma, 5.7% had Hashimoto hypothyroidism, 3.4% had atopic dermatitis, 3.4% had allergic rhinitis, and 1.1% had epilepsy. However, no significant relationship was found between the UCT score and the comorbidities. In other studies, the frequency of comorbid diseases in patients with CU ranged from 4.3% to 23% (11). There was no data on the causal relationship between patients' comorbidities and CU. It was observed that 35.25% more disease was under control compared with UCT in those with atopy in their family. Autoimmune disorders such as hypothyroidism, hyperthyroidism, celiac disease, Sjögren's syndrome, systemic lupus erythematosus, rheumatoid arthritis, and type 1 diabetes mellitus are more common in patients with CU (12). In some patients, an autoimmune mechanism may be present. This concept is supported by the fact that autoimmune diseases that mostly affect the thyroid gland often accompany CU in adults (13). Due to urticaria can be a precursor of rheumatological diseases; The effect of laboratory values such as main and C4, thyroid autoantibodies

related to the rheumatological status of patients on urticaria control was investigated. Normal and positive ANA values increase the urticaria control score by approximately 97.27% and 48.96%, respectively. However, high thyroid autoantibodies were not considered as a factor complicating the control of the disease. Anti DFS 70 positivity was observed in 12.5% of the patients with the main positivity, and it was not found to be significant in terms of the development of rheumatological disease. It has been shown that the presence of autoantibodies in children does not affect the prognosis of the disease, unlike adult patients, where the presence of autoantibodies is associated with a longer duration of the disease, a more severe prognosis, and more intensive treatment methods (14). It is thought that chronic urticaria in children has a more positive outcome than adults (15). Based on demographic data and studies, clear predictors of disease remission could not be determined (16). The most important limitation of our study is that it is a retrospective study based on the examination of patient files.

CONCLUSION

Although chronic urticaria has a mild course in children, parameters such as gender, age, and ANA positivity may affect the control of the disease. Abnormal laboratory values are not common in patients with chronic urticaria, therefore, extensive investigations may not be necessary. However, larger studies are needed to evaluate the factors affecting disease control.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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