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*The role of diagnostic tests in determining the factor causing chronic urticaria*

## **ABSTRACT**

### **Introduction**

Urticaria is a disease characterized by the occurrence of itchy wheals and / or angioedema. If the disease lasts for more than 6 weeks, it is called chronic urticaria (CU). CU affects about 0.5-1% of the population at all age groups, but it is much more common in middle-aged patients. The etiopathogenesis of this disease is complex and unclear. In many cases the etiology of chronic urticaria remains unknown despite significant progress in identifying the causes, triggers and pathomechanisms involved in the development of clinical symptoms of the disease. The disease has a significant impact on the patients' quality of life and the treatment is long and often unsatisfactory. Therefore, the discovery of the etiological factor in patients with CU seems to be the most important element. However, it usually takes a lot of time and money to diagnose CU, and in addition, the range of possible etiological factors is wide, which also means that the number of tests that can be performed on patients is very large. Although the international guidelines help in planning the diagnostic process, it is not always successful. That is why, we wonder if our diagnosis is sufficient and whether we should not extend it, especially when a patient, who is not particularly satisfied with the recognition of spontaneous urticaria of unknown cause, puts some pressure on a doctor.

### **Aim**

The main task was to assess if the extended diagnostics in case of chronic urticaria on the basis of a comparison of positive test results and additional tests in the group with extended and targeted diagnostics make sense.

The occurrence of contact allergy and dependent IgE in patients with CU were also pointed out. The coexistence of autoimmune urticaria with other autoimmune disorders and with other forms of chronic urticaria was analyzed. Another point was the assessment of usefulness of the oral aspirin exposure test and an attempt to analyze the coexistence of various types of urticaria.

### **Material and methods**

A retrospective analysis was made in 242 patients with chronic urticaria aged 12 to 82 years, treated in hospital and outpatient clinics at the Department of Dermatology, Sexually Transmitted Diseases and Clinical Immunology in 2007-2017.

All analyzed patients remained untreated, did not take antihistamines, immunosuppressants, general glucocorticosteroids, leukotriene drugs at least 2 weeks before the tests and during the diagnosis.

Out of the analyzed group, 56 patients were examined prospectively since 2016. They had all physical provocative tests, allergy tests (patch tests and spot tests), autologous serum test, oral aspirin test, ANA Hep-2 titres of antinuclear antibodies, the concentration of antithyroid antibodies, thyreotropic hormone and the total level of IgE immunoglobulin performed. Patients in this group had a consultation with a clinical psychologist and for 3 weeks prior to the diagnosis they were recommended to eliminate pseudoallergens from the diet.

The remaining 186 patients were analyzed retrospectively before 2016 and had a diagnosis made after less detailed tests that seemed justified after a detailed interview, physical examination and analysis of basic laboratory tests.

The obtained results were analyzed with Microsoft Office Excel. Statistical analyzes were performed with STATISTICA13PL computer programme.

## Results

Both groups of patients with extended and targeted diagnostics were similar in terms of age, sex and duration of the disease.

In the group of 56 people who underwent an extended range of diagnostic tests, the most positive results were in patch tests - as much as 42.86%, then in the prick test - 41.07% and in the sample with autologous serum - 30.36%. The oral aspirin test was positive in 16.07% patients. In physical tests, the most positive results were obtained in a dermatographic and ice cube test - 10.71% (6 people in each trial). The load test was positive in 3 people (5.37%), and the exertion test in 2 people (3.57%) and one person had a positive vibration test (1.79%). None of the tested subjects in this group had positive light tests or thermal tests.

Positive patch results, for at least one allergen, were obtained in 24 (42.86%) patients, including 18 women (32.14%) and 6 men (10.71%). Among contact allergens, the highest percentage of allergies was to metals. 21.43% of subjects were sensitized to nickel, 8.93% to cobalt and palladium and to chromium - 5.36%. For other allergens, patients with chronic urticaria were allergic to less than 5%.

Positive prick tests were obtained in 23 people (41.07%). In this group, 20 people (35.71%) had positive reactions to aeroallergens and 10 people to food ones (17.85%).

A positive test result with its own serum was obtained in 17 subjects (30.30%). More positive ASST trials were reported in women (11 patients), while in men a positive result was observed in 6 patients, but it did not have statistical significance. The analysis did not show any statistically significant connection between ASST trial and the presence of antithyroid antibodies, coexistence of thyroid diseases or the presence of antibodies against the ANAHep-2 cell nucleus components.

Positive DTE results with ASA were obtained in 9 subjects -16.07%. Women were twice as likely to have positive aspirin tests than men, but it did not have statistical significance. The analysis of the coexistence of DTE with ASA and the ASST sample also did not show statistical significance. However, in the group with the positive DTE ASA (n = 9) as many as 5 patients (55.55%) had a positive test with autologous serum.

The results of allergy tests, provocative physical tests, DTE ASA and autologous serum test in two groups with extended and targeted diagnostics showed a statistically significant

difference in the oral aspirin test. More positive results were obtained in the group with targeted diagnostics than in the group with extended diagnostics. On the other hand, more positive dermatographic outcomes were obtained in the group with extended diagnostics. Differences in the remaining results of tests and trials in both groups were statistically insignificant.

In our material, ANA Hep-2 antibody titers were much more frequently out of range in the group of patients with extended diagnostics (58.93%) than in the group with targeted diagnostics (37.04%), although it did not have statistical significance. In the group with extended diagnosis, elevated antibody titres were observed in a total of 33 patients, including 23 women and 10 men. Such a distribution of results would suggest that routine determination of the titres of these antibodies would be desirable. However, no antibodies of clinical relevance were found in the ANA Immunoblot quality assay. None of these patients were also diagnosed with connective tissue disease.

The analysis of the co-occurrence of different types of urticaria shows that quite often different factors play an important role in one patient.

A psychological consultation and a 3-week pseudoallergens elimination diet prior to the tests proved to be helpful in the diagnosis of CU, which seems to enable some patients to have this diagnosis.

## **Conclusions**

- 1.** The most important element in the discovery of etiological factors in chronic urticaria is accurate medical history and diagnostics performed according to this interview. The extended range of tests seems not to be necessary in the diagnosis of chronic urticaria.
- 2.** Contact allergy is more common in people with chronic urticaria than in the general population. The most common contact allergens in CU are metals (nickel, palladium cobalt and chromium). It seems that patch tests may be helpful in determining the causative factors of this disease, although according to international guidelines, they are not recommended in routine diagnosis of CU.
- 3.** A significant percentage of patients with chronic urticaria had positive prick tests, although it is generally believed that type I hypersensitivity according to Gell and Coombs is rarely associated with CU. Among airborne allergens, house dust mites and grass pollen were the most common and among food allergens the most positive results were connected with egg allergens.
- 4.** ANA Hep-2 antibody titres in chronic urticaria are often elevated, however, it is difficult to unequivocally assess their actual importance in the pathogenesis of urticaria.
- 5.** Hypersensitivity to aspirin is quite common in the course of chronic urticaria. Indications for conducting this test should result from a detailed interview.
- 6.** Co-morbidity of different forms of chronic urticaria is common, especially in women. The most frequent was the coexistence of contact allergy with dependent IgE allergy, but also the coexistence of autoreactivity with hypersensitivity to aspirin.