Urticaria is one of the most difficult problems of modern allergology. This is due to the high prevalence rate of this pathology, mainly in active working age, with a high incidence of idiopathic forms (for acute urticaria 50 %, for chronic urticaria - 95 %), a frank decrease in the life quality of patients and frequent failure of diagnostic and remedial measures.

Urticaria — is a common disease characterized by appearance of pruriginous wheals on the skin. The wheal is formed as a result of papillary dermis hydrops and has the next defining characteristics: is an unstriped element, rises above the skin surface, turns pale when pressed and passes away traceless during the day.

Chronic urticaria affects the general health and everyday life of patients. The main complaint of patients with chronic urticaria is pruritus that is significantly frank in most patients (82 %). Every fourth patient has a sleep disturbance because of pruritus. Persistent symptoms of chronic urticaria are reflected on the psychological well-being of patients, particularly those with long-term course of the disease. Patients are suffering a constant internal stress due to the unpredictable nature of exacerbations.

Thus, chronic urticaria appears to be an important medical and social problem taking into account the high prevalence and long-term course of the disease, active working age of patients and a significant reduction in their quality of life.

In most patients the cause of chronic urticaria remains unknown. According to various authors proportion of chronic and idiopathic urticaria accounts for 80-95 %. However combination of chronic urticaria with certain chronic diseases is well known.

Chronic urticaria in the setting of gastrointestinal diseases (GID) was described by Hippocrates. So it is therefore extremely important to examine patients with chronic urticaria for gastrointestinal pathology (fibrogastroduodenoscopy, seeding feces for detection of intestinal dysbiosis). This examination method is extremely important, because with intestinal dysbiosis the histaminase (inactivating histamine enzyme) generating process is interrupted.

Histamine is a key mediator in the urticaria pathogenesis as evidenced by:
- reproduction of urticarial rash with intradermal histamine release;
- Local release of gistamine in the skin in patients with urticaria;
- Clinical efficacy of antihistamines.

Skin reaction to histamine is characterized by a Lewis triad: pruritus, wheal, reflex hyperemia, but the effectiveness of antihistamines is preferably 75 %. Therefore it is extremely important to find a complex of remedial measures that allow completely to relieve the symptoms of chronic urticaria and improve the life quality of patients.

In view of the above the purpose of the present study was to examine the effectiveness of a therapeutic complex that includes antihistamines, antileukotriene agents and dietary supplements.

Materials and methods.
We observed 44 patients with chronic urticaria, aged from 18 to 65 years (mean age 46,1 ± 2,0 years), 13 (29.5 %) of them were men and 31 (70.5 %) - women.

The study design was conducted in parallel groups. All patients were randomised into three clinical groups according to treatment regimens:
Group I (basic) - 16 patients were treated with last generation antihistamines (desloratadine in dosage 5 mg 1 tablet in the morning), montelukast sodium 10 mg 1 tablet in the evening (antileukotriene agent), Bionorm 1 tablet 2 times per day.
Group II (basic) - 16 patients were treated with H1-blockers and montelukast sodium in the same way, the agent-probiotic containing Lactobacillus reuteri Protectis - 1 treca 2 times per day.

Modern approaches to pathogenetic treatment of chronic urticaria

Key words: rash, pruritus, urticaria, histamine, disbiosis, intestinal tract.
Group III (control) - 12 patients who received only a combination of antihistamines and antileukotriene agents. The duration of treatment was 3 weeks.

All groups were comparable in age and sex of patients (p > 0.05).

Product Bionorm that was appointed to the patients of first group appeared to be a combination of activated lignin, lactulose and cellulose microcrystalline. Bionorm – is an original combination (which has no analogues) of 2 types of dietary fibers and lactulose with severe prebiotic and sorption effect to optimize the functioning of intestinal tract. Sorption strength is in 10-20 times greater than conventional sorbents have (based on activated carbon). It operates in a complex, combining sorption and prebiotic effect, without damaging the intestinal tract. Lignin, having extremely high sorption capacity, fixes various microorganisms, their metabolic products, toxins of exogenous and endogenous nature, allergens, xenobiotics, heavy metals, radioactive isotopes, ammonia, divalent cations and promotes their excretion through the gastrointestinal tract. It also compensates the lack of natural dietary fiber (especially prebiotic) in the diet; optimizes the composition of the the large intestine microflora; normalizes nonspecific immunity.

Microcrystalline cellulose absorbs on their surface and removes from the the body heavy metals, free radicals, microbial toxins, tissue decomposition products, and also fixes bile acids in the intestinal tract, bilirubin, cholesterol, stimulating their elimination.

Lactulose leads to excessive excretion of bile acids in the feces and, as a result, to enhanced formation of them in the liver from cholesterol. It also inhibits the production and absorption of ammonia and provides its rapid excretion in the feces.

Prebiotic agent tablet (group II) contains at least 100 teleorganic bacteria Lactobacillus reuteri Protectis, which increase the natural defense of the digestive system, create favorable conditions for the formation of the normal intestinal microbiocenosis, have immunostimulatory effects.

For all patients the histamine level in the blood plasma has become the trend (p <0,10).

As can be seen from the table, a significant (p <0.001) reduction of histamine in serum was noted in the main patients groups who were treated with combination of H1-blocker and antileukotriene agents with dietary supplement Bionorm or probiotic preparation. In the control group decrease in production of histamine was not significant (p > 0.05).

Comparative analysis of the effect of different treatment regimens on the dynamics of the histamine level in serum of patients with chronic urticaria has showed a high degree of correlation (r = 0.68; p <0.001) between the decrease rate of histamine production after treatment with a complex of therapeutic interventions (including the therapy with BAA (biologically active additives)). When statistically comparable baseline levels of the neurotransmitter in patients of all groups (p > 0.05) in 3 weeks after completion of therapy, the differences between the main group I and control group have become statistically significant with p <0.05 (Fig. 1).

Under the influence of the treatment histamine production was normalized in 14 (87.5 %) and 9 (56.3 %) patients of the main groups and in 5 (41.7 %) patients in the control group. In the group of patients with chronic urticaria who were treated with probiotic agent, on completion of the therapeutic course differences in the average histamine levels in blood in comparison with the control group and the main group I have become the trend (p <0,10).

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>The observation period (M ± м)</th>
<th>Dynamics</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>before treatment</td>
<td>after treatment</td>
<td>D</td>
</tr>
<tr>
<td>Main group I (n=16)</td>
<td>2.21±0.24</td>
<td>0.56±0.08</td>
<td>-74.7 %</td>
</tr>
<tr>
<td>Main group II (n=16)</td>
<td>2.61±0.30</td>
<td>0.98±0.19</td>
<td>-62.5 %</td>
</tr>
<tr>
<td>Control group (n=12)</td>
<td>1.70±0.31</td>
<td>1.62±0.33</td>
<td>-4.7 %</td>
</tr>
</tbody>
</table>

Note. * - Significant difference of indexes in the group by Student’s t test for dependent samples.
Analysis of the therapeutic effectiveness of intestinal dysbiosis in patients with chronic urticaria (Table 2) has shown a significant improvement of the intestinal microflora in the main group of patients (p < 0.01). Normalization of qualitative and quantitative composition of microflora was observed in 13 (81.3 %) patients treated with Bionorm and in 11 (68.8 %) patients treated with the probiotic. Intestinal dysbiosis has remained in the majority of patients in the control group (75.0 %). Dependence of the results of treatment of intestinal dysbiosis from the treatment regimens has been confirmed also with correlation analysis data - r = 0.44 (P < 0.01). In this case, the best results were observed in patients who have been treated with Bionorm.

The results has shown that normalization of histamine production in the blood plasma and the restoration of intestinal microflora in patients with chronic urticaria in case of adding to treatment complex Bionorm agent and probiotic product leads to a significant improvement of the main clinical symptoms of the disease (Table 3, Fig. 2, Fig. 3).

The best dynamics of clinical parameters was observed in the main group I when adding Bionorm agent, where all patients before treatment had strongly expressed pruritus and rashes (Me = 3 points). During the first week of therapy intensity of symptoms was significantly reduced to 2 points (p < 0.001), after 2 weeks – to 1 point (p < 0.001), and after the end of treatment only the one patient has complained of a little itchy.

In patients of main group II who have received the probiotic agent containing Lactobacillus reuteri Protectis the severity of clinical symptoms was significantly decreased after 10 days of treatment (p < 0.01), reaching the complete disappearance of rash in 11 (68.8 %) patients, pruritus – in 5 (31.2 %) to the end of treatment.

### Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>The observation period (abs., %)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>before treatment</td>
<td>after treatment</td>
</tr>
<tr>
<td>Main group I (n=16)</td>
<td>16 (100,0 %)</td>
<td>3 (18,7 %)</td>
</tr>
<tr>
<td>Main group II (n=16)</td>
<td>15 (93,8 %)</td>
<td>5 (31,2 %)</td>
</tr>
<tr>
<td>Control group (n=12)</td>
<td>11 (91,7 %)</td>
<td>9 (75,0 %)</td>
</tr>
</tbody>
</table>

Note. * - Significant difference in the group by the McNemar test

### Table 3

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Main group I (n=16)</th>
<th>Main group II (n=16)</th>
<th>Control group (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>before treatment</td>
<td>after treatment</td>
<td>before treatment</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3,0±0,0 (3)</td>
<td>0,06±0,06 (0)</td>
<td>2,94±0,06 (3)</td>
</tr>
<tr>
<td>Rash</td>
<td>3,0±0,0 (3)</td>
<td>0 (0)</td>
<td>2,94±0,06 (3)</td>
</tr>
</tbody>
</table>

Note. The dynamics of indexes is statistically significant at p < 0.001 with Student’s t and Wilcoxon tests in all groups.
In patients of the control group who have received only a combination of antihistamines and antileukotriene agents the clinical manifestations of the disease after completion of treatment have not entirely disappeared, but their intensity is decreased (see. Table 3).

Comparative analysis of the severity of clinical symptoms in all groups showed its close correlation with the method of treatment: the correlation coefficients for the intensity of pruritus were \( r = 0.86 \) (P <0.001), for a rash - \( r = 0.78 \) (P <0.001). At the same time, significant differences (from p <0.05 to p <0.001) of the clinical effect of therapy with Bionorm and probiotic agent that containing Lactobacillus reuteri Protectis, have been observed from 5th (rash) and 7th (pruritus) day of therapy (see . Fig. 2 and 3).

Conclusions:

1. In order to achieve a clinical effect in patients with chronic urticaria the therapeutic complex which affects to all parts of pathogenesis of the disease in this patient should be prescribed.

2. Inclusion in the complex of treatment regimens of patients with chronic urticaria Bionorm agent and probiotics which are containing L. reuteri Protectis BioGaia allows more significantly to reduce the histamine levels in the blood plasma in comparison with the appointment of only antihistamine and antileukotriene agents, as confirmed by the identified correlation (\( r = 0.68 \)) between the indexes and methods of treatment.

3. Inclusion of Bionorm agent into a treatment complex can significantly improve the qualitative and quantitative composition of microflora, leading to a decrease of clinical symptoms, because the histaminase production process inactivating histamine is reverted.

4. In case of treatment with Bionorm agent a significant decrease in the intensity of pruritus and rashes is marked to the end of the first week of therapy with the complete reduction of clinical symptoms after the finishing the course of treatment.

5. Urticaria has different forms and variants of the clinical course, so it is necessary to use the appropriate approaches to the diagnosis and treatment of this disease.

References

1. Горячкина, Л. А. Острая и хроническая крапивница . и ангио-невротический отек. Учебное пособие / Л. А. Горячкина, Н. М. Ненашева, Е. Ю. Борзова. – М., 2003. – С. 47.


Fig. 2. Dynamics of average value (M) of severity of pruritus in patients with chronic urticaria for different treatment regimens

Fig. 3. Dynamics of the average value (М) the severity of rash in patients with chronic urticaria for different treatment regimens
СУЧАСНІ ПІДХОДИ ДО ПАТОГЕНЕТИЧНОГО ЛІКУВАННЯ ХРОНІЧНОЇ КРОПИВ’ЯНКИ

Є. М. Дитятковська, І. А. Родкіна, Л. В. Грибанова, М. А. Євтушенко, Ю. В. Бендецька

Резюме

В ході дослідження під нашим спостереженням знаходилися 44 хворих на хронічну кропив’янику віком від 18 до 65 років (середній вік 46,1 ± 2,0 років), із них 13 (29,5 %) чоловіків і 31 (70,5 %) жінка.

Дослідження проводилося в дизайні паралельних груп. Всі пацієнти були рандомізовані на три клінічні групи залежно від схеми лікування.

Порівняльний аналіз впливу різних схем лікування на динаміку рівня гістаміну в сироватці крові хворих на хронічну кропив’янику показав високий ступінь кореляції (r = 0,68; p < 0,001) темпів зниження продукції гістаміну після лікування з комплексом лікувальних заходів (включення в терапію препарату Біонорм). Аналіз ефективності терапії дисбіозу кишечника у хворих на хронічну кропив’янику показав істотне поліпшення стану мікрофлори кишечника в основних групах пацієнтів (р < 0,01). Нормалізація якісного і кількісного складу мікрофлори спостерігалась у 13 (81,3 %) пацієнтів, які отримували Біонорм, і у 11 (68,8 %) пацієнтів, які отримували пробіотик.

Результати дослідження показали, що нормалізація продукції гістаміну в плазмі крові та відновлення мікрофлори кишечника у хворих на хронічну кропив’янику при включення в терапевтичний комплекс препарату Біонорм і пробіотика зумовлює істотне поліпшення основних клінічних симптомів захворювання.

Доведено, що існує кореляційний зв’язок між зниженням рівня гістаміну в плазмі крові та методом лікування.

Ключові слова: висип, свербіж, кропив’яника, гістамін, дисбіоз, кишечник.

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