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ANTI-PARIETAL CELL ANTIBODIES SEROCONVERSION IN PATIENTS WITH AUTOIMMUNE ATROPHIC GASTRITIS: A PROSPECTIVE STUDY

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◆ ***The purpose of the study*** was to evaluate the atrophic changes of body and antrum gastric mucosa, the occurrence of *Helicobacter pylori* infection and the possibility of seroconversion in patients with autoimmune gastritis throughout 10 years.

Material and methods. 203 Chernobyl nuclear power plant accident recovery workers were included in the prospective study. Blood levels of anti-parietal cell antibodies, basal gastrin-17, pepsinogens I and II were evaluated in all the patients to diagnose autoimmune gastritis and to assess gastric mucosa non-invasively.

Results. Anti-parietal cell antibodies were found in 34.5% of the patients. Eradication rates were low (32.8–50.0%) in the patients with atrophy of gastric mucosa in the first 3 years of observation. Statistically significant decrease in pepsinogen I and gastrin-17 serum levels was observed in the patients with *H. pylori*-associated autoimmune gastritis throughout first 4–6 years. In the next 7–10 years pepsinogen I and gastrin-17 serum levels were increasing possibly due to positive effect of *H. pylori* eradication therapy. Successful eradication leads to disappearance of anti-parietal cell antibodies in 33.4% of the patients by the 10th year of the observation.

Conclusion. The obtained results show that *H. pylori* eradication therapy is effective in reducing atrophic changes of gastric mucosa in the patients with autoimmune gastritis. Against the background of successful treatment the levels of pepsinogen I and gastrin-17, the markers of body and antrum gastric mucosa atrophy, were increasing. In the patients with autoimmune gastritis but without *H. pylori* infection the following trend was not noticed.

◆ **Keywords:** Chernobyl nuclear power plant; emergency responder; atrophic gastritis; autoimmune gastritis; anti-parietal cell antibodies; eradication therapy; prospective study; *H. pylori*; eradication efficacy; GastroPanel.

СЕРОКОНВЕРСИЯ АНТИТЕЛ К ПАРИЕТАЛЬНЫМ КЛЕТКАМ ПРИ АУТОИММУННОМ АТРОФИЧЕСКОМ ГАСТРИТЕ: ПРОСПЕКТИВНОЕ ИССЛЕДОВАНИЕ

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◆ ***Цель работы*** — оценить выраженность атрофических изменений слизистой тела и антрального отдела желудка, распространенность *Helicobacter pylori* и возможность сероконверсии антител к париетальным клеткам у пациентов с аутоиммунном гастритом при длительном наблюдении (10 лет).

Материал и методы. В проспективное исследование вошли 203 ликвидатора последствий аварии на Чернобыльской атомной электростанции. Для диагностики аутоиммунного гастрита и неинвазивной оценки слизистой оболочки желудка у всех пациентов определяли в крови уровни антител к париетальным клеткам, гастрина-17 базального, пепсиногенов I и II.

Результаты. Антитела к париетальным клеткам выявлены у 34,5 % обследованных. У пациентов с атрофией слизистой оболочки желудка эрадикационная терапия оказалась успешной в 32,8–50,0 % случаев в первые три года наблюдения. При аутоиммунном гастрите, ассоциированном с инфекцией *H. pylori*, в первые 4–6 лет наблюдалось достоверное снижение сывороточного уровня пепсиногена I и гастрина-17. В последу-

ющие 7–10 лет наблюдения сывороточные уровни пепсиногена I и гастрина-17 повышались, что, возможно, является положительным эффектом эрадикационной терапии *H. pylori*. Успешная эрадикация *H. pylori* привела к исчезновению антител к париетальным клеткам у 33,4 % пациентов к десятому году наблюдения.

Заключение. Результаты исследования демонстрируют эффективность эрадикации *H. pylori* у пациентов с аутоиммунным гастритом для уменьшения атрофических изменений слизистой желудка. При успешном лечении наблюдалось повышение уровней пепсиногена I и гастрина-17 базального, маркеров атрофии слизистой оболочки тела и антрального отдела желудка. У пациентов с аутоиммунным гастритом без инфекции *H. pylori* подобная динамика маркеров атрофии не отмечена.

◆ **Ключевые слова:** Чернобыльская атомная электростанция; ликвидаторы последствий аварии; атрофический гастрит; аутоиммунный гастрит; антитела к париетальным клеткам; эрадикационная терапия; проспективное исследование; *H. pylori*; эффективность эрадикации; ГастроПанель.

Introduction

The pathogenesis of autoimmune gastritis (AIG) is caused by cellular and humoral immune responses to the parietal cells of the stomach, which results in chronic inflammation and atrophy of the gastric body mucosa. Parietal cells are epithelial cells located in the glands of the body and fundus of the stomach, producing hydrochloric acid and internal factors.

When the disease progresses, patients manifest anacidity, iron deficiency, and pernicious anemia. There are difficulties in the diagnostics of AIG; therefore, the data on its prevalence depend on the diagnostic methods. The main diagnostic test of AIG is the determination of antibodies against parietal cells that interact with the hydrogen-potassium ATPase (H^+/K^+-ATPase). Antibodies against parietal cells react with the alpha and beta subunits of H^+/K^+-ATPase inhibitors, with the alpha subunit being the main antigen that activates $CD4^+$ T lymphocytes.

Antibodies against parietal cells circulating in blood serum can be detected using the immunofluorescence method, enzyme-linked immunosorbent assay (ELISA; currently, the most common), and radioimmune (most accurate) analysis. The 4A H^+/K^+-ATPase subunit is optimized as a molecular-specific antigen probe. Antibodies against parietal cells can be found in 85%–90% of patients with pernicious anemia. Their presence does not always indicate the diagnosis of AIG since they are revealed in the blood in 7.8%–19.5% of healthy adult population and in patients with type I diabetes mellitus, autoimmune thyroid gland diseases, vitiligo, and coeliac disease [1].

The prevalence of AIG varies in different populations and patient groups and depends on the diagnostic method [2, 3]. According to various estimates, its prevalence in the general population is from 2% to 5% [4]. In the Japanese population, AIG occurs in 0.5% cases (0.7% in women and 0.4% in men) [5]. According to our data, the incidence of AIG in patients with gastric dyspepsia symptoms is 6.4%, and along with *Helicobacter pylori* infection, it is 25.1% [6].

In some cases, AIG characterizes the presence of immunocrossreactivity, which is manifested along with other autoimmune diseases.

In most studies, *H. pylori* is considered a trigger in the AIG pathogenesis based on convincing data on molecular mimicry between bacterial antigens and gastric H^+/K^+-ATPase [7–9]. However, according to other studies, the role of *H. pylori* in the AIG pathogenesis remains unclear. Thus, Zhang et al. [10] revealed that the association between antibodies against parietal cells and atrophic gastritis was stronger among *H. pylori*-negative (odds ratio 11.3; 95% confidence interval 7–17) than *H. pylori*-positive (odds ratio 2.6; 95% confidence interval 2–3) patients.

Our prospective study aimed to analyse the severity of atrophic changes in the body mucosa and the antrum, the prevalence of *H. pylori*, and the possibility of seroconversion of antibodies against parietal cells in AIG patients under long-term follow-up (10 years).

Materials and methods

The study included 203 emergency responders (ERs) at the Chernobyl nuclear power plant (NPP), including 58 patients with chronic *H. pylori*-associated AIG and 12 patients with atrophic AIG. The mean age of the patients examined was 57.2 ± 9.23 years. Examination and treatment of patients were performed within the framework of federal target programs of the Union State (Russia–Belarus).

All patients underwent endoscopic biopsy, histological biopsy examination, and *H. pylori* infection diagnostics [rapid urease test and immunoglobulins G (IgG) detection for *H. pylori*]. Antibodies against parietal cells were determined (by ELISA using the ELISA test system, Orgentec, Germany). For a noninvasive assessment of the gastric mucosa (GM), the functional activity markers of inflammation and atrophy of the gastroduodenal mucosa were studied by determining the blood serum level of basal gastrin-17, pepsinogen I, and pepsinogen II (by ELISA using the GastroPanel® test system, Biohit, Finland).

To detect *H. pylori* in the GM, the presence of IgG for this bacterium was determined. The choice of this method was because, under conditions of anacidity with AIG, a urease test, *H. pylori* antigen determination in feces, and a respiratory isotope test can give a false-negative result due to the low bacterial concentration in the GM [13].

The GastroPanel® test system according to the biomarker profile evaluates five possible diagnostic categories characterizing the morphological state of the stomach:

- normal mucous membrane;
- nonatrophic gastritis;
- atrophic fundal gastritis;
- atrophic antral gastritis;
- atrophic pangastritis [11].

GastroPanel® is optimized for diagnostics of chronic gastritis, included in the endoscopic and histological classification of the updated Sydney system in 1996 [12]. In addition, GastroPanel®

The GastroPanel® biomarker profiles and their diagnostic equivalents (adapted from [13])
Профили биомаркеров ГастроПанель® и их диагностические эквиваленты (адаптировано из [13])

Biomarker profiles	PG I [30–160 μg/L][a]	PG II [3–15 μg/L]	Ratio of PG I/PG II [3–20]	Basal gastrin-17 [1–7 pmol/L]	Stimulated gastrin-17 [3–30 pmol/L]	IgG antibodies against *H. pylori*	Interpretation
1	N	N	N	N	N	N	Healthy mucosa (without atrophy and *H. pylori* infection)
2	N	N	N	L*	N	N	Healthy mucosa. High acid production
3	N or H^	N or H^	N	H**	N	N	Healthy mucosa. Low acid production (e.g., associated with the intake of inhibitors of H^+/K^+-ATPase)
4a	N or H^	N or H^	N	N or H^	HH	H	Active untreated *H. pylori* infection
4b	N	N	N	N	HH	N or H†	Effective eradication of *H. pylori*
4c	N	H	N	H	HH	H	Ineffective *H. pylori* eradication
5	L	L	L	H	HH	N^^ or H†	Atrophic gastritis of the stomach body and fundus
6	N	N	N	L	L	H	Atrophic antral gastritis
7	L	L	L	L	L	N^^ or H†	Atrophic pangastritis
8	H	H	N	H	HH	N	Short (4–10 days) pause in long-term therapy with H^+/K^+-ATPase inhibitors. Ricochet symptom in acid production

N o t e. The values in square brackets indicate the normal range of each biomarker. [a] The boundary value of PG I 30 μg/L corresponds to moderate severity/severe atrophic gastritis. ^ May be increased because of the inflammation in the mucosa. ^^ May disappear with long-term atrophy of the mucosa. * A two-week test with H+/K+-ATPase inhibitors is indicated, after which the level of gastrin-17 should normalize. ** Discontinuation of drugs is indicated, after which the level of gastrin-17 should normalize within 2 weeks. † The level of antibodies against *H. pylori* may remain increased for several months after effective eradication. PG I, pepsinogen I; PG II, pepsinogen II; *H. pylori*, *Helicobacter pylori*; N, normal values; L, low level; H, high level; NN, no need for evaluation; H^+/K^+-ATPase, hydrogen-potassium ATPase

distinguishes three other biomarker profiles reflecting functional disorders of gastric acid production (Table).

The informational content of GastroPanel® in the diagnosis of the GM morphological state has been investigated in many studies with a large number of biopsies during gastroscopy [14–16]. These studies confirmed the accuracy of GastroPanel® in detecting the most important endpoint, namely, from moderate to severe atrophic gastritis (stage II atrophic gastritis and higher according to the Operative Link on Gastritis Assessment). Thus, the normal values of pepsinogen I, pepsinogen II, and their ratio (pepsinogen I/pepsinogen II) rule out atrophic fundal gastritis with a negative prognostic value of over 95% [14, 16]. In turn, the values of pepsinogen I, pepsinogen II, and their ratios below established levels indicate stage II and above atrophic fundal gastritis [14, 17].

When detecting *H. pylori* infection, eradication therapy was recommended to all patients, which was performed for 10–14 days following provisions of the Maastricht Consensus [18]. First-line therapy included omeprazole 40 mg/day, clarithromycin 1.0 g/day, and amoxicillin 2.0 g/day. Second-line therapy included omeprazole 40 mg/day, colloidal bismuth subcitrate 480 mg/day, tetracycline 2.0 g/day, and metronidazole 1,500 mg/day.

Statistical processing of data was performed using the Statistica 10.0 program. The Wilcoxon and Mann–Whitney tests were used to compare indicators within one group and independent groups, respectively. The differences were considered significant at $p < 0.05$.

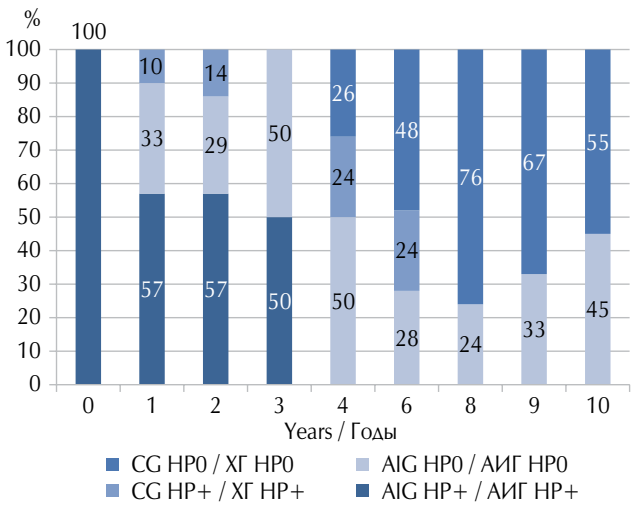

Fig. 1. Chronic *H. pylori*-associated autoimmune gastritis metamorphosis: a prospective study. GG HP0 — chronic gastritis not associated with *H. pylori*; GG HP+ — chronic *H. pylori*-associated gastritis; AIG HP0 — chronic autoimmune gastritis; AIG HP+ — chronic *H. pylori*-associated autoimmune gastritis

Рис. 1. Метаморфоз хронического *H. pylori*-ассоциированного аутоиммунного гастрита: проспективное исследование ($n = 58$). ХГ HP0 — хронический *H. pylori*-неассоциированный гастрит; ХГ HP+ — хронический *H. pylori*-ассоциированный гастрит; АИГ HP0 — хронический аутоиммунный гастрит; АИГ HP+ — хронический *H. pylori*-ассоциированный аутоиммунный гастрит

Results

Serological signs of AIG (the presence of antibodies against parietal cells in the blood serum) were noted in 34.5% of patients. Moreover, in 28.6% of cases, antibodies against parietal cells were registered in patients with *H. pylori*-associated gastritis, and in 5.9% of cases, there were no signs of this infection. In our study, the detection rate of antibodies against parietal cells in the blood was higher than in a German study in patients of a similar age group. According to a population study ($n = 9{,}684$) by Zhang et al. [10], the prevalence of antibodies against parietal cells among people aged 50 to 74 years was 19.5%.

During the eradication of *H. pylori* in ERs at the Chernobyl NPP, a rather low adherence to treatment was noted. With a high level of carcinophobia (according to the questionnaire, in 96.1%), ERs at the Chernobyl NPP underestimated the role of *H. pylori* bacteria in gastric carcinogenesis. Of patients, 38.4% did not know that, according to the main world consensus, *H. pylori* eradication reduces the risk of gastric cancer [18]. Of the Chernobyl NPP ERs, 53.2% did not adhere to the prescribed treatment because of the significant amount of previously prescribed drugs, since most patients were polymorbid.

In a year, on average, up to 30% of patients with *H. pylori*-associated AIG refused eradication therapy for various reasons, including those listed above.

According to the results of the prospective follow-up of patients with *H. pylori*-associated AIG, the effectiveness of eradication therapy in year 1 was only 32.8%, with a gradual increase by year 8 to 100% (Fig. 1). It is extremely important that after a year, antibodies against parietal cells were not detected in the presence of *H. pylori* in

the GM in 10.3% of patients. By year 4, antibodies against parietal cells and *H. pylori* infection were not detected in 25.9% of patients with an increase in this indicator to 55.2% by year 10.

Based on the analysis of the dynamics of the mean values of pepsinogen I in the blood serum of patients with *H. pylori*-associated AIG, a significant ($p < 0.05$) decrease in this indicator was noted during the first four years of the follow-up, possibly due to progression of atrophic changes in the GM (Fig. 2). A gradual increase in serum pepsinogen I from years 4 to 10 of follow-up ($p < 0.05$) is possible to have a positive effect on *H. pylori* eradication therapy due to a decrease in GM atrophy. Effective eradication therapy can decrease the severity of atrophic changes in the GM in the stomach body and antrum [18].

Analysis of variations in the mean values of basal gastrin-17 in the blood serum of patients with *H. pylori*-associated AIG revealed similar changes in time (Fig. 3). During the first 6 years, a significant ($p < 0.05$) decrease in serum gastrin-17 basal level was recorded, possibly due to the progression of atrophic changes in the antrum mucosa. The minimum values of basal gastrin-17 were noted at year 6 of follow-up. Then, from years 6 to 10 of follow-up, the gastrin-17 level increased ($p < 0.05$), which may be caused by *H. pylori* eradication therapy, which positive effect was due to a decrease in the antral atrophy.

The results of the prospective follow-up of patients with AIG are extremely interesting (Fig. 4). Seroconversion was noted in 33.3% of patients with AIG, and antibodies against parietal cells disappeared after years 8 to 10 of follow-up. Probably, to some extent, this was associated with *H. pylori* eradication therapy.

In addition, this study revealed difficulties in diagnosing *H. pylori* infection in atrophic AIG. In 50.0% of patients with AIG without signs of *H. pylori* infection, an elevated IgG antibody titre to *H. pylori* was determined by serological test as early as year 1. In year 2, elevated titre of *H. pylori* antibodies were detected in 41.7% of patients. After eradication therapy, the number of such patients decreased to 16.7% by year 10 of the study.

A very low rate of successful eradication therapy in patients with atrophic AIG of 32.8%–50.0% in the first 3 years of follow-up should be noted. This may be due to a decrease in the secretion of GM antibiotics in its atrophy. Thus, according

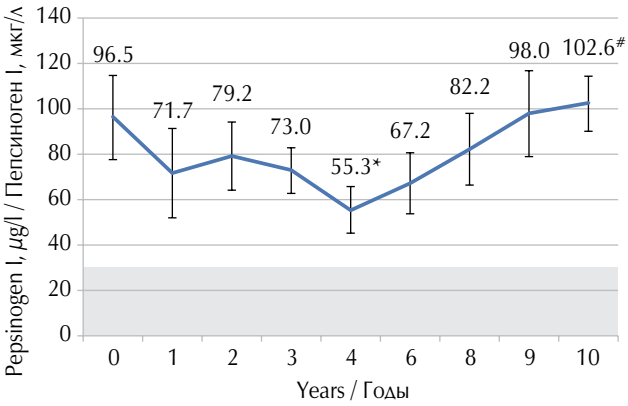

Fig. 2. Pepsinogen I serum levels ($M \pm SD$) in the patients with *H. pylori*-associated autoimmune gastritis in different years ($n = 58$). Grey colour indicates the range of values characteristic of atrophic gastritis of the stomach body. $^{*}p < 0.05$ compared to the initial value (0 year); $^{\#}p < 0.05$ compared to the indications on the 4th year of observation

Рис. 2. Пепсиноген I ($M \pm SD$) в сыворотке крови пациентов с *H. pylori*-ассоциированным аутоиммунным гастритом в различные годы наблюдения ($n = 58$). Серым выделен диапазон значений, характерный для атрофического гастрита тела желудка. $^{*}p < 0{,}05$ по сравнению с исходным значением (0 год); $^{\#}p < 0{,}05$ по сравнению со значением на четвертый год наблюдения

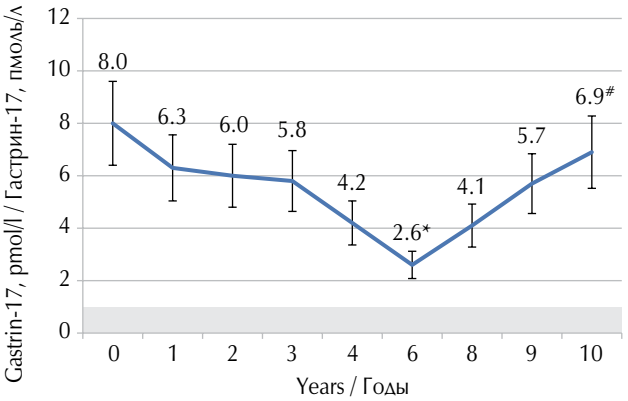

Fig. 3. Gastrin-17 basal serum levels ($M \pm SD$) in patients with *H. pylori*-associated autoimmune gastritis in different years ($n = 58$). Grey colour indicates the range of values characteristic of atrophic gastritis of the antrum. $^{*}p < 0.05$ compared to the initial value (0 year); $^{\#}p < 0.05$ compared to the indications on the 6th year of the observation

Рис. 3. Гастрин-17 базальный ($M \pm SD$) в сыворотке крови пациентов с *H. pylori*-ассоциированным аутоиммунным гастритом в различные годы наблюдения ($n = 58$). Серым выделен диапазон значений, характерный для атрофического гастрита антрального отдела желудка. $^{*}p < 0{,}05$ по сравнению с исходным значением (0 год); $^{\#}p < 0{,}05$ по сравнению со значением на шестой год наблюдения

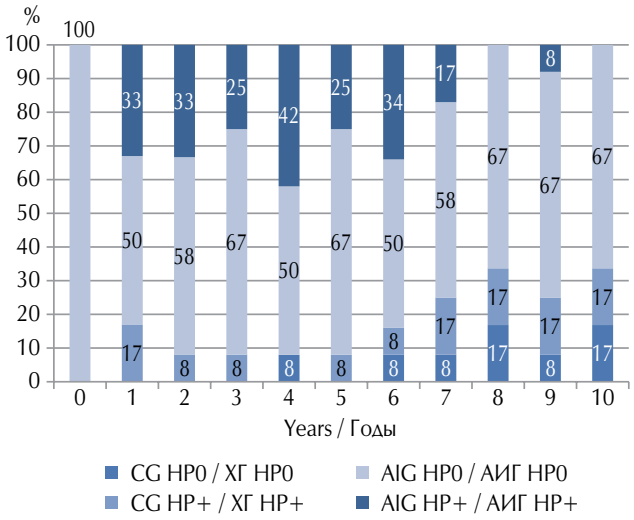

Fig. 4. Chronic autoimmune gastritis metamorphosis: a prospective study. GG HP0 — chronic gastritis not associated with *H. pylori*; GG HP+ — chronic *H. pylori*-associated gastritis; AIG HP0 — chronic autoimmune gastritis; AIG HP+ — chronic *H. pylori*-associated autoimmune gastritis

Рис. 4. Метаморфоз хронического аутоиммунного гастрита: проспективное исследование ($n = 12$). ХГ HP0 — хронический *H. pylori*-неассоциированный гастрит; ХГ HP+ — хронический *H. pylori*-ассоциированный гастрит; АИГ HP0 — хронический аутоиммунный гастрит; АИГ HP+ — хронический *H. pylori*-ассоциированный аутоиммунный гастрит

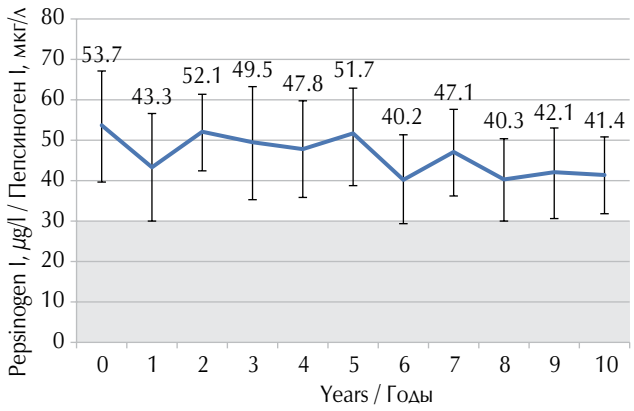

Fig. 5. Pepsinogen I serum levels ($M \pm SD$) in the patients with autoimmune gastritis in different years ($n = 12$). Grey colour indicates the range of values characteristic of atrophic gastritis of the stomach body

Рис. 5. Пепсиноген I ($M \pm SD$) в сыворотке крови пациентов с аутоиммунным гастритом в различные годы наблюдения ($n = 12$). Серым выделен диапазон значений, характерный для атрофического гастрита тела желудка

to some studies, the effectiveness of eradication therapy of *H. pylori* infection in patients with GM atrophy is low [19], but according to others, the use of nonsteroidal anti-inflammatory drugs increases the antibacterial drug concentration in gastric secretion with active inflammation in the GM [20, 21].

When studying the average values of pepsinogen I in the blood serum of patients with AIG, no significant variations in this indicator were detected, although there was a tendency ($p > 0.05$) to slightly decrease (Fig. 5). Similar dynamics were also typical for basal gastrin-17, a marker of the antrum atrophy in AIG patients without signs of helicobacteriosis.

Discussion

The study results demonstrate the effectiveness of eradication therapy of *H. pylori* infection in AIG patients to reduce atrophic changes in the GM. With successful treatment, the pepsinogen I and basal gastrin-17 levels and mucous membrane atrophy markers of the stomach body and antrum increased from years 4 to 8 of follow-up. In patients with AIG without *H. pylori* infection, no similar changes in atrophy markers were registered.

The etiological treatment of AIG remains one of the unsolved problems of modern gastroenterology. Symptomatic treatment of AIG is characterized by certain aspects associated with the inappropriateness of the use of antisecretory drugs, which aggravate the malabsorption of trace elements and vitamins (calcium, iron, magnesium, vitamin B_{12}, etc.), inherent in these patients.

One of the promising treatment areas for patients with atrophic gastritis is the use of the herbal combination drug Pepsan-R® containing guaiazulene, a derivative of azulene (chamomile extract), and dimethicone. The pharmacological effects of guaiazulene include antibacterial, anti-inflammatory, and antispasmodic effects. Dimethicone reduces gas formation and has an antifoam effect [22]. Pepsan-P® arrests the symptoms of dyspepsia, protects the mucosa of the gastroduodenal region, and improves visualization with endoscopy, sonography, computed tomography, and magnetic resonance imaging [23, 24].

Current guidelines recommend discontinuing H^+/K^+-ATPase inhibitors 14 days before the *H. pylori* test. Unlike antisecretory drugs, the use

of Pepsan-P® does not distort the results of the initial diagnosis of *H. pylori*.

To evaluate the effectiveness of the symptomatic treatment of patients with atrophic AIG, a comparative randomized study was conducted, where 116 patients with AIG were randomized into two groups. Group 1 included 61 patients who received omeprazole 20 mg/day, and Group 2 included 55 patients who received Pepsan-R® 3 capsules/day. Patients in both groups were comparable in age and severity of clinical manifestations of gastric dyspepsia, which were evaluated on a five-point scale.

Pepsan-P® treatment was more effective in patients with AIG (Fig. 6). When patients with atrophic AIG took Pepsan-R®, the most common symptoms, such as epigastric heaviness and bloating, were arrested significantly more often ($p < 0.05$). At the same time, pain in epigastrium, which was much less common in patients (25% of cases) than heaviness in this area (70% of cases), was removed significantly more often ($p < 0.05$) while taking omeprazole.

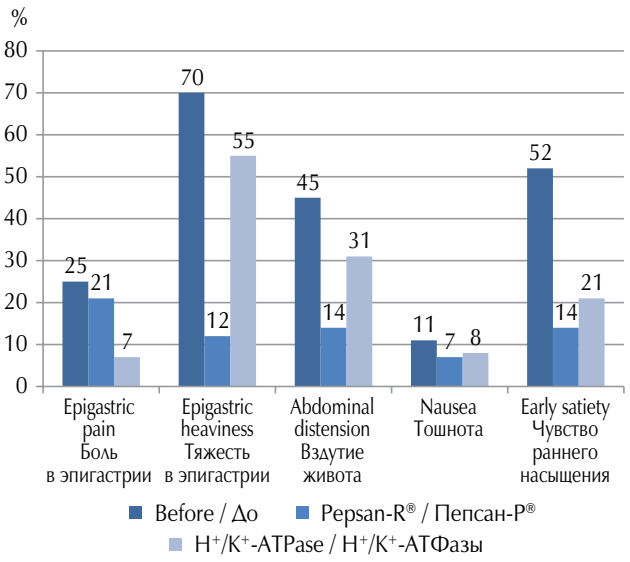

Fig. 6. Symptoms dynamics in the patients with autoimmune gastritis receiving 14-days treatment with 20 mg/day omeprazole and Pepsan-R®. * $p < 0,05$ compared to the patients receiving H^+/K^+-ATPase inhibitors

Рис. 6. Динамика симптомов на фоне 14-дневного лечения пациентов с аутоиммунным гастритом омепразолом в дозе 20 мг/сут и препаратом Пепсан-P®. * $p < 0,05$ по сравнению с пациентами, которые принимали ингибитор H^+/K^+-АТФазы

Conclusion

Thus, as a result of the study, the following conclusions can be made.

1. In patients with GM atrophy, eradication therapy was ineffective, as a positive result was achieved only in 32.8%–50.0% of cases in the first three years of the follow-up.
2. With AIG associated with *H. pylori* infection, in the first years of follow-up (4–6 years), serum levels of pepsinogen I and gastrin-17 decreased significantly, possibly due to the progression of atrophic changes in the GM. Subsequently, from years 7 to 10 of follow-up, serum levels of pepsinogen I and gastrin-17 increased, which was probably the result of *H. pylori* eradication therapy decreasing antral atrophy.
3. As a result of *H. pylori* eradication therapy, antibodies against parietal cells disappeared in 33.4% of patients by year 10 of follow-up.
4. While taking Pepsan-R®, in patients with atrophic AIG, the most common symptoms, such as epigastric heaviness and bloating, were arrested significantly more often ($p < 0.05$), compared with patients who received omeprazole.

Conflict of interest. The authors declare no conflict of interest.

References

1. Rusak E, Chobot A, Krzywicka A, Wenzlau J. Anti-parietal cell antibodies — diagnostic significance. *Adv Med Sci*. 2016;61(2):175-179. https://doi.org/10.1016/j.advms.2015.12.004.
2. Toh BH. Diagnosis and classification of autoimmune gastritis. *Autoimmun Rev*. 2014;13(4-5):459-62. https://doi.org/10.1016/j.autrev.2014.01.048.
3. Kulnigg-Dabsch S. Autoimmune gastritis. *Wien Med Wochenschr*. 2016;166(13-14):424-430. https://doi.org/10.1007/s10354-016-0515-5.
4. Massironi S, Cavalcoli F, Rossi RE, et al. Chronic autoimmune atrophic gastritis associated with primary hyperparathyroidism: a transversal prospective study. *Eur J Endocrinol*. 2013;168(5):755-61. https://doi.org/10.1530/EJE-12-1067.
5. Notsu T, Adachi K, Mishiro T, et al. Prevalence of autoimmune gastritis in individuals undergoing medical checkups in Japan. *Intern Med*. 2019;58(13):1817-1823. https://doi.org/10.2169/internalmedicine.2292-18.
6. Саблина А.О., Гвинтовкина Т.О. Аутоиммунные ассоциации, возможности диагностики и лечения аутоиммунного гастрита // Совершенствование методологии познания в целях развития науки: Сборник статей по итогам Международной научно-практической конференции; июнь 30, 2017; Самара. [Sablina AO, Gvintovkina TO. Autoimmunnye associacii, vozmozhnosti di-

agnostiki i lechenija autoimmunnogo gastrita. (Conference proceedings) Sovershenstvovanie metodologii poznanija v celjah razvitija nauki; 2017 jun 30; Samara. (In Russ.)]

7. Claeys D, Faller G, Appelmelk BJ, et al. The gastric H^+/K^+-ATPase is a major autoantigen in chronic *Helicobacter pylori* gastritis with body mucosa atrophy. *Gastroenterology*. 1998;115(2):340-7. https://doi.org/10.1016/s0016-5085(98)70200-8.
8. Bergman MP, Faller G, D'Elios MM, et al. Gastric automminity. In: Bergman MP, Faller G, D'Elios MM, et al. *Helicobacter pylori:* Physiology and Genetics. Washington (DC): ASM Press; 2001. Chapter 36.
9. Toh BH, Chan J, Kyaw T, Alderuccio F. Cutting edge issues in autoimmune gastritis. *Clin Rev Allergy Immunol*. 2012;42(3):269-78. https://doi.org/10.1007/s12016-010-8218-y.
10. Zhang Y, Weck MN, Schöttker B, et al. Gastric parietal cell antibodies, *Helicobacter pylori* infection, and chronic atrophic gastritis: evidence from a large population-based study in Germany. *Cancer Epidemiol Biomarkers Prev*. 2013;22(5):821-6. https://doi.org/10.1158/1055-9965.EPI-12-1343.
11. Suovaniemi O. State of the art GastroPanel® and Actium® innovations for the unmet need. *Terveyspalvelut*. 2011;3-4:57-59.
12. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and Grading of Gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis Houston 1994. *Am J Surg Pathol*. 1996;20(10):1161-81. https://doi.org/10.1097/00000478-199610000-00001.
13. Syrjänen K, Eskelinen M, Peetsalu A, et al. GastroPanel® biomarker assay: the most comprehensive test for *Helicobacter pylori* infection and its clinical sequelae. A critical review. *Anticancer Res*. 2019;39(3):1091-1104. https://doi.org/10.21873/anticanres.13218.
14. Väänänen H, Vauhkonen M, Helske T, et al. Non-endoscopic diagnosis of atrophic gastritis with a blood test. Correlation between gastric histology and serum levels of gastrin-17 and pepsinogen I: a multi-centre study. *Eur J Gastroenterol Hepatol*. 2003;15(8):885-91. https://doi.org/10.1097/00042737-200308000-00009.
15. Telaranta-Keerie A, Kara R, Paloheimo L, et al. Prevalence of undiagnosed advanced atrophic corpus gastritis in Finland: An observational study among 4,256 volunteers without specific complaints. *Scand J Gastroenterol*. 2010;45(9):1036-41. https://doi.org/10.3109/00365521.2010.487918.
16. Storskrubb T, Aro P, Ronkainen J, et al. Serum biomarkers provide an accurate method for diagnosis of atrophic gastritis in a general population: The Kalixanda study. *Scand J Gastroenterol*. 2008;43(12):1448-55. https://doi.org/10.1080/00365520802273025.
17. Syrjänen K. A Panel of serum biomarkers (GastroPanel®) in non-invasivediagnosis of atrophic gastritis. Systematic review and meta-analysis. *Anticancer Res*. 2016;36(10):5133-5144. https://doi.org/10.21873/anticanres.11083.
18. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection – the Maastricht V/Florence Consensus Report. *Gut*. 2017;66(1):6-30. https://doi.org/10.1136/gutjnl-2016-312288.
19. Денисов Н.Л., Ивашкин В.Т., Лобзин Ю.В., Голофеевский В.Ю. Эффективность эрадикации *Helicobacter pylori* в зависимости от уровня продукции секреторного иммуноглобулина А и морфологических изменений слизистой оболочки желудка // Российский журнал гастроэнтерологии, гепатологии, колопроктологии. – 2007. – № 3. – С. 41–45. [Denisov NL, Ivashkin VT, Lobzin JuV, Golofeevskij VJu. Jeffektivnost' jeradikacii Helicobacter pylori v zavisimosti ot urovnja produkcii sekretornogo immunoglobulina A i morfologicheskih izmenenij slizistoj obolochki zheludka. *Rossijskij zhurnal gastrojenterologii, gepatologii, koloproktologii*. 2007;(3):41-45. (In Russ.)]
20. Sherwood PV, Wibawa JI, Atherton JC, et al. Impact of gastric secretion, gastritis, and mucus thickness on gastric transfer of antibiotics in rats. *Gut*. 2002;51(4):490-5. https://doi.org/10.1136/gut.51.4.490.
21. Stern AI, Hogan DL, Isenberg JI. A new method for quantification of ion fluxes across in vivo human gastric mucosa: effect of aspirin, acetaminophen, ethanol and hyperosmolar solutions. *Gastroenterology*. 1984;86(1):60-70. https://doi.org/10.1016/0016-5085(84)90590-0.
22. Маев И.В., Дичева Д.Т., Лебедева Е.Г. Возможности антацидов в лечении хронического гастрита // Экспериментальная и клиническая гастроэнтерология. – 2010. – № 10. – С. 87–92. [Maev IV, Dicheva DT, Lebedeva EG. Vozmozhnosti antatsidov v lechenii khronicheskogo gastrita. *Eksperimental'naya i klinicheskaya gastroenterologiya*. 2010;(10):87-92. (In Russ.)]
23. Asl SM, Sivandzadeh GR. Efficacy of premedication with activated Dimethicone or N-acetylcysteine in improving visibility during upper endoscopy. *World J Gastroenterol*. 2011;17(37):4213-7. https://doi.org/10.3748/wjg.v17.i37.4213.
24. de la Portilla F, Ynfante I, Fernández A, et al. Improved quality of anorectal endoluminal ultrasonography using emulsion of dimethicone. *Dis Colon Rectum*. 2003;46(10):1436-7. https://doi.org/10.1007/s10350-004-6765-0.

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