Possibilities Of Serological Diagnosis Of Atrophic Processes Of The Gastric Mucosa

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Abstract
The association between HP infection and CAH development suggested by the Correa cascade is supported by several cohort studies. To diagnose and determine the severity of atrophy at the Center, patients underwent a serological analysis by ELISA method in the clinical and biochemical laboratory of the State Institution "RSNPMCT and MR". Analyzes were taken in 69 (58.5%) patients, including 35 (50.7%) with CAH, 34 (49.3%) with CNG. Analysis of the non-invasive indicator of the level of pepsinogens in patients with CAH determined that severe atrophy was detected in 20%, moderate atrophy - 42.9%, weak atrophy - 34.3%, and no atrophy was found in 2.9% of patients. The pepsinogen parameters in patients with CNG were also as follows: PG I was within 95.4 ± 7.2 μg / L, PG II 14.5 ± 1.3 and PGI / PGII 6.6 ± 0.2. Pepsinogen values were more pronounced in patients with CAH: with a pronounced degree of atrophy, PGI was 8.7 ± 0.1 μg / l and PGI / PGII was 1.1 ± 0.1; with moderate atrophy 16.6 ± 0.9 μg / l and 1.6 ± 0.1; with mild atrophy 27.2 ± 1.5 and 2.3 ± 0.2, respectively.

Keywords: *Chronic atrophic gastritis, chronic non-atrophic gastritis, pepsinogen, helicobacter pylori, gastric mucosa.*

Introduction

Helicobacter pylori (HP) is the main etiological factor for chronic gastritis worldwide, and long-term infection can lead to progressive destruction of gastric glandular patches throughout the stomach, described as multifocal atrophic gastritis, which is characterized mainly by macular lesions of the mucous membrane of the antrum and body stomach [2, 3, 7]. The relationship between HP infection and the development of chronic atrophic gastritis (CAG), suggested by the

Correa cascade [10], is supported by several cohort studies [13] and the beneficial effect of HP eradication in body atrophy, but without intestinal metaplasia, this latter presumably went beyond the "point of no return" [12, 13].

Epidemiological data on the prevalence of CAG in different parts of the world are scarce, and the results are difficult to compare due to methodological differences between studies in terms of the definition and diagnosis of CAG and the studied populations. In studies from Asian countries, the diagnosis of CAG included all atrophic lesions, regardless of the localization of atrophy in the gastric mucosa (GM); In most of the studies conducted in Western countries, the diagnosis of CAG included only patients with atrophic corpus lesions, such as atrophic gastritis with limited corpus or multifocal atrophic gastritis. In addition, various diagnostic methods for the diagnosis of CAG, that is, surrogate serologic markers of gastric function pepsinogen I (PGI) or pepsinogen I / II ratio (PGI / PGII) or histopathology of endoscopic biopsy specimens, make common data incomparable [1, 4, 5]. Serological studies carried out in different parts of the world have shown the prevalence of CAG up to 27% [6, 8]. According to a systematic review [11], estimates of the prevalence of CAG worldwide were 23.9% and 27.0% in the general population and in individual groups, respectively, using serology, and 33.4% in the general population, and 31.6 % in selected groups based on biopsies. An increase in the prevalence of CAG with age was shown in serological studies [9, 11], which was confirmed by an extensive histological study [2, 13].

Materials and Methods

To diagnose and determine the severity of atrophy at the Center, patients underwent serological analysis by ELISA method in the clinical and biochemical laboratory of the State Institution "RSNPMCT and MR" using the ELISA apparatus Humareader HS (Human, Germany) using a set of reagents for PGI - IFA-BEST - D- 3762 and for PGII - IFA-BEST - D-3764 (Novosibirsk).

To determine the level of PGI and PGII, a fasting blood sample was taken. The blood was centrifuged at 1500 xg for ten minutes, after which the centrifugate was stored at a temperature of –20^{o}C and further analyzed in the laboratory.

According to the manufacturer's instructions, a PGI <30 μg / L was taken as a positive marker of gastric atrophy; for inflammation of the coolant, the amount of PGII was considered above 22 μg / l; a PGI to PGII ratio (PGI / PGII) less than 2.5 was considered positive for atrophy.

Results

Analyzes were taken in 69 (58.5%) patients, of which 35 (50.7%) patients with CAG, 34 (49.3%) with chronic non-atrophic gastritis (CNG). The prevalence of severe atrophic gastritis of the gastric corpus, determined by the content of PGI and the ratio of pepsinogens PGI / PGII in the blood serum, was 20% in the examined patients. For a weak atrophy of the mucous membrane of the body of the stomach, this figure was 34.3% (table 1.). No obvious fluctuations in the prevalence of atrophic gastritis in men and women were found.

The frequency of severe atrophic gastritis in the group of patients from 45 to 54 years old was 14.3%, 55-64 years old - 18.7% and over 65 years old - 25%. Moderate atrophy was diagnosed at the age of 45-54 years - 42.8%, 55-64 years old - 43.8% and over 65 years old in 41.7% of patients. Mild atrophy was detected at the age of 45-54 years - 42.9%, 55-64 years - 31.3% and over 65 years in 33.3% of patients. In total, severe atrophy was detected in 20%, moderate atrophy

- 42.9%, mild atrophy - 34.3%, and in 2.8% of patients, atrophy was not observed. Age 55 to 64 and over 65 years was a risk factor for moderate to mild atrophy of the gastric corpus. The increase in the incidence of atrophy in older age groups did not have gender differences.

Table 1

Frequency of diagnosis of coolant atrophy by serological method in patients with CAG

Age	Atrophy							
	Severe atrophy (PGI < 9 μg / L), n=7		Moderate atrophy (PGI = 19-10 μg / L), n=15		Weak atrophy (PGI = 29-20 μg / L), n=12		No atrophy (PGI > 30 μg / L), n=1	
	абс	%	абс	%	абс	%	абс	%
45-54 years old n=7	1	14,3**	3	42,9***	3	42,9***	0	0
55-64 years old n=16	3	18,8	7	43,8***	5	31,3***	1	6,3
Over 65 years old n=12	3	25.0***	5	41.7**	4	33.3***	0	0
Total (n=35)	7	20.0**	15	42.9***	12	34.3***	1	2,9

Note: * - differences relative to data without atrophy are significant (* - P <0.05, ** - P <0.01 *** - P <0.001)

We investigated the average level of PGI, PGII in the blood serum and their ratio in the examined patients with CNG (n = 34) (Table 2.). At the same time, we found almost no gender differences. Moreover, in all patients with CNG, PG I was within 95.4 ± 7.2 μg / L, PG II was 14.5 ± 1.3, and PGI / PGII was 6.6 ± 0.2.

Table 2

Serum pepsinogen levels in patients with CNG

Gender	**PGI (μg / L) M±m**	**PGII (μg / L) M±m**	**PGI / PGII M±m**
Men, n= 15 (44,1%)	98,5±7,3	15,9±1,1	6,9±0,4
Women, n=19 (55,9%)	92,7±6,1	13,2±0,9	6,2±0,3
Total, n=34 (100%)	95,8±7,2	14,5±0,1	6,7±0,1

Further analysis of the obtained data showed that the content of pepsinogens and their ratio significantly decreased in patients with atrophy of the coolant in comparison with those without atrophy (Table 3). Since the degree of atrophy was assessed by the indicators of pepsinogens, with a pronounced degree of atrophy, the PGI was 8.7 ± 0.1 μg / l and the PGI / PGII was 1.1 ± 0.1,

respectively; with moderate atrophy 16.6 ± 0.9 μg / l and 1.6 ± 0.1; with mild atrophy 27.2 ± 1.5 and 2.3 ± 0.2, respectively.

Table 3

Average level of pepsinogens in blood serum in patients with CAG.

Degree of atrophy	PGI (μg / L) M±m	PGII (μg / L) M±m	PGI / PGII M±m
1. Severe atrophy, n = 7	8,7±0,1	8,3±0,3	1,1±0,1
2. Moderate atrophy, n = 15	16,6±0,9	10,6±0,4	1,6±0,1
3. Weak atrophy, n = 12	27,2±1,5	12,1±1,1	2,3±0,2
4. No atrophy, n = 1	70,8	17,4	4

Thus, we can say that the risk factor for both severe atrophic gastritis of the gastric corpus and of a mild and moderate degree was age over 55 years.

Discussion

To date, the world has already developed a certain idea of the serological diagnosis of ARS. Studies by various authors, conducted over two decades, have confirmed that atrophic fundic gastritis can be successfully diagnosed by measuring the serum content of PGI or PGI / PGII (U. Peitz, T. Wex, M. Vieth - 2011). Recent studies show that serological screening using a set of biomarkers can serve as a reliable indicator of precancerous pathology and early noncardiac gastric cancer (NGC) (M. Rugge, 2016; F. Ikeda, 2016; S. Saito, 2017; T. Kotachi, 2017 ; H. Yoon, 2015). Thanks to the national cancer control programs adopted in Japan and mass screening, including serological methods, there is the highest survival rate for NGC in the world, at 53%. In other countries, this figure does not exceed 20%. At the same time, the proportion of detected early cancer in the general structure of NGC patients increases (Zheng, H. 2007).

In studies conducted in the world to study the early diagnosis of atrophic processes of the gastric mucosa, a number of results were obtained, including: it was found that the low PGI level and the PGI / PGII ratio are prognostically significant for the risk of NGC (Belkovets A.V., 2018) ; it was found that the method of early detection of atrophic gastritis by the level of pepsinogens allows to reliably establish the presence of atrophy of the gastric body and assess the degree of its severity (Katchieva P.Kh., 2018); it has been proven that mass screening of serological markers of gastrin - 17 and PGI makes it possible to characterize the risk of formation of coolant atrophy (Khubieva M.M., 2014); it has been shown that chronic gastritis with or without HP infection is a variable process in which mild atrophy of the mucous membrane of the body may appear or disappear, and moderate to severe atrophy rarely regresses, it has also been proven that risk factors for the development of atrophy are age and the degree of chronic inflammation of the gastric mucosa (Stefan Redéen, 2010); It has been found that the use of serum biomarkers such as IgG to HP levels, pepsinogens can reduce the cost and public health burden of screening for HNGC (Somee Jeong, 2017).

In recent years, Uzbekistan has been the subject of many scientific works in the field of gastroenterology. Among them, the prevalence and molecular genetic characteristics of HP in Uzbekistan are shown (Karimov M.M., 2019). The results of the study showed that among

patients with diseases of the gastrointestinal tract associated with HP, the degree of infection with Cag-positive strains up to 80% was found in patients with CAG and CNG.

Conclusions

Analysis of the non-invasive indicator of the level of pepsinogens in patients with CAH determined that severe atrophy was detected in 20%, moderate atrophy - 42.9%, weak atrophy - 34.3%, and no atrophy was found in 2.9% of patients. The pepsinogen parameters in patients with CNG were also as follows: PG I was within 95.4 ± 7.2 μg / L, PG II 14.5 ± 1.3 and PGI / PGII 6.6 ± 0.2. Pepsinogen values were more pronounced in patients with CAH: with a pronounced degree of atrophy, PGI was 8.7 ± 0.1 μg / l and PGI / PGII was 1.1 ± 0.1; with moderate atrophy 16.6 ± 0.9 μg / l and 1.6 ± 0.1; with mild atrophy 27.2 ± 1.5 and 2.3 ± 0.2, respectively. It was also noted that the frequency of severe atrophy is more common in persons over 65 years of age. No gender differences were found.

Thus, it must be stated that we have revealed a rather high frequency of atrophic gastritis of the gastric corpus in the examined patients. The experience of using serological diagnostics of atrophic gastritis allows us to conclude about the adequacy of the methodological level used for the task. Undoubtedly, serological studies of atrophic gastritis deserve wide application in practical medicine and can undoubtedly replace the morphological diagnosis of the GM.

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