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The Significance of Polymorphism of Genes Involved in the Stages of Pharmacokinetics of Drugs Used for the Treatment of Peptic Ulcer Disease

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Abstract: *The article notes that pharmacotherapy taking into account the patient's genotype is a young direction that contributes to improving the safety and effectiveness of treatment with proton pump inhibitors. Determination of the patient's genetic affiliation by polymorphisms of the MDR-1 and CYP2C19 genes allows us to initially determine the tactics of treatment with proton pump inhibitors in patients with acid-dependent diseases.*

Keywords: *pharmacotherapy, chronic gastritis, H. pylori, CYP2C19 gene, genotypes, personification of pharmacotherapy.*

INTRODUCTION. The effectiveness of therapy depends not only on the knowledge of the doctor, his treatment tactics, not excluding the interaction of drugs, their pharmacokinetics and pharmacodynamics, but also on the adherence of patients, the characteristics of their genetic apparatus, which is not a little important in achieving the effect of the applied pharmacotherapy [2, 5, 9].

It is known that in the complex therapy of chronic gastritis, the diet occupies one of the most important places [1, 3,15], therefore, in chronic gastritis with secretory insufficiency, diet No. 2 is selected, which consists of dishes sparing the mucous membranes of the stomach and stimulating gastric secretion [4, 6, 11]. Depending on the main clinical manifestations, therapeutic nutrition is selected individually.

Pharmacotherapy chronic gastritis is selected depending on the form of the disease, where the main role is played by the etiology, pathogenesis, clinical morphological picture of the disease [10]. The tactics of treatment of chronic gastritis associated with H.pylori and non-associated are significantly different, but in both cases pharmacotherapy is selected based on the severity and activity of the pathological process with gastric mucosa, intestinal condition, as well as the activity of compensatory capabilities of the liver, pancreas and hepatobiliary system [5, 7, 8].

The principles of pharmacotherapy for chronic gastritis may be standard, but the treatment of the disease cannot be the same for all patients, it must be personalized. This approach is based on the genetic characteristics of the patient.

Based on the above, it should be noted that the effectiveness of HG pharmacotherapy is directly influenced by the intensity of metabolism of first-line drugs - proton pump inhibitors, where the genetic feature of the patient plays an important role as a source of interindividual differences in the metabolic processes of pharmacological substances[12, 13, 14].

A number of studies are being conducted in the world aimed at studying the features and influence of polymorphisms of the CYP2C19 gene on the course and effectiveness of treatment of a number of diseases where this gene plays a particularly important role [6, 17]. In this regard, the main tasks of this direction are an in-depth analysis of the occurrence of genotypes of this gene, the peculiarities of the course of diseases depending on the genetic affiliation of the patient, their impact on the results and effectiveness of treatment and, depending on this, the improvement of pharmacotherapy[16].

The purpose of the study The aim is to evaluate the effectiveness of treatment and determine the possibilities of personal pharmacotherapy by identifying the features of the occurrence of variants of the CYP2C19 gene genotype in patients with chronic gastritis.

Material and Methods. In accordance with the objectives of the dissertation, a comprehensive examination was carried out in the scientific and genetic laboratory at the Olympic Committee of Uzbekistan, 80 unrelated patients with HG who were on inpatient treatment and observation at the Regional Multidisciplinary Clinical Hospital of the city of Bukhara and at Mohi Hossa. These patients made up the main comparison group.

The control group consisted of 20 healthy unrelated and without a history of gastrointestinal pathology persons who corresponded by gender and age to the examined group of patients with HG.

The age of patients with HG ranged from 15 to 79 years, men were 27 (33.8%), women – 53 (66.2%), that is, women significantly prevailed among patients with HG.

To achieve the goal and fulfill the tasks set, the following methods were used: general clinical examination of patients, laboratory-instrumental, molecular-genetic research methods, as well as methods of statistical processing of the data obtained.

Results it is known that the pharmacotherapy of HG varies depending on the form of the course and type of the disease, which serves to restore the structure and function of the stomach. However, the result of treatment may not always be what we would like. As a result of the selected pharmacotherapy by types of HG, the following results were obtained (Fig. 1):

HG type A - recovery – 57%, improvement – 43%, without improvement, deterioration and complications were not observed;

HG type B - recovery – 41%, improvement – 33%, without improvement – 10%, deterioration – 10%, complications - 5%;.

HG type C - recovery – 33%, improvement – 33%, without improvement – 20%, deterioration – 7%, complications - 7%.

Thus, the pharmacotherapy of HG has different effects depending on the type of HG. Thus, HG type is treatable and there were no worsening and complications of the disease; whereas after pharmacotherapy, HG type C is effective only in 1/3 of patients and it should be noted that there are cases of complications and worsening of the disease. Adequate efficacy of pharmacotherapy was not observed in the type of HG. After this therapy, 1/10 of the patients' condition worsened and 1/20 of the patients had complications of the disease.

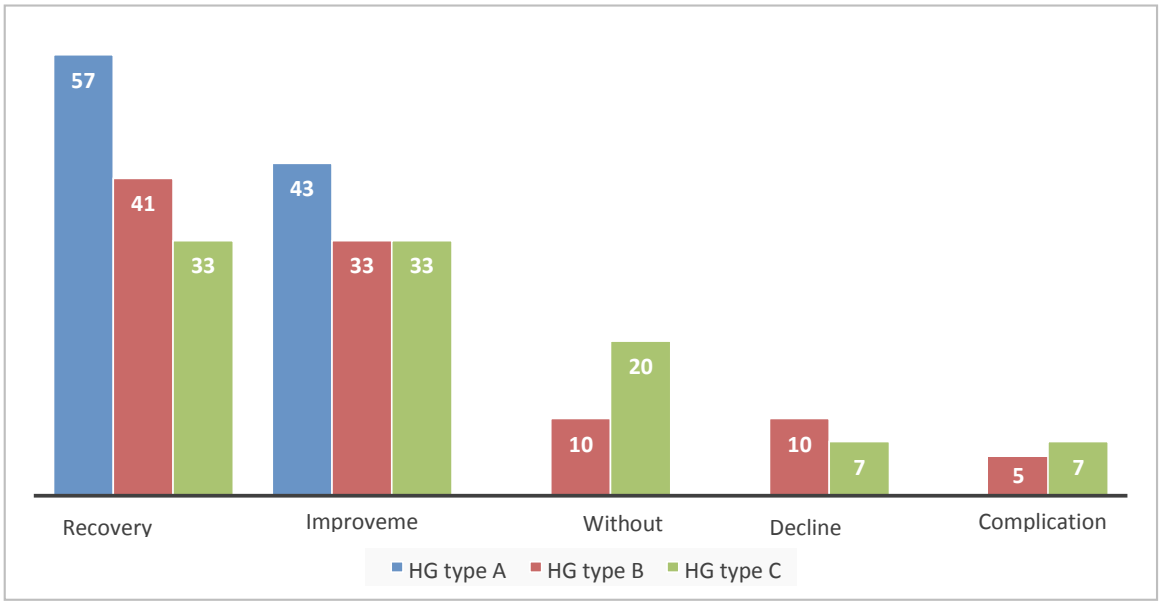

Figure 1. Treatment results depending on the type of chronic gastritis (%)

In the selected group of patients with HG, regardless of the type of disease, the frequency of occurrence of variants of the genotypes of the CYP2C19 (G681A) gene was studied by gender division, the results of which showed that the homozygous "wild" allelic genotype GG (CYP2C19*1/*1) the CYP2C19 (G681A) gene is found in more than 66% of women with HG, whereas in men with a similar diagnosis, this variant of the genotype is 2 times less common (Table 1).

Table 1.Gender characteristics of the frequency of genotype distribution of the allele variant G681A of the gene CYP2C19 in patients with HG

The studied genes	Variants of genotypes	Study groups							
		Control (n=20)				Experience (n=80)			
		Man		Woman		Man		Woman	
		n	%	n	%	n	%	n	%
CYP 2C19G681A	A/A	-		-		-		2	100,0
	G/G	7	43,75	9	56,25	18	33,33	36	66,67
	G/A	2	50,00	2	50,00	9	37,50	15	62,50

Heterozygous "wild" and "mutant" GA allelic genotype (CYP2C19*1/*2) it was detected in more than 62% of women with HG, but in male patients this variant of the genotype occurs in 37% of cases. It should be noted that the "mutant" allele genotype AA (CYP2C19*2/*2) among all variants of the genotypes of the CYP2C19 gene, it is rare – only in women with HG, and it has not been detected in male patients. The same genotype was not determined in healthy men and women from the control group.

DISCUSSION. Thus, chronic gastritis is 1.5 times more common in women, as well as the "mutant" allele genotype AA (CYP2C19*2/*2) the CYP2C19(G681A) gene does not occur in male patients. Determination of the genotypic affiliation of patients with HG makes it possible to personalize pharmacotherapy.

CONCLUSIONS. Therefore, a personalized approach to each patient in the selection of drugs for treatment is the most optimal pharmacotherapy tactic. Such an individual approach should be based on the genetic characteristics of the patient according to the drugs selected for treatment. Methods of genotyping patients provides an increase in the effectiveness and safety of pharmacotherapy, which is the main task of clinical pharmacology, therapy and medicine in general.

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