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Modern Approaches to the Treatment of Chronic Gastritis: Achievements and Prospects

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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: *cytochrome P450, gene polymorphism, MDR-1 gene, CYP2C19 gene, chronic gastritis, personification of pharmacotherapy.*

INTRODUCTION. Human genetics is considered a little-studied field, although it has long been the most interesting object for humanity. The principle of operation of genes is complex, but in turn highly sophisticated, and this mechanism provides and regulates every process-whether it is in the cell or in the whole body, to the final result [1, 5].

It should be mentioned that the genetic component is one of the main factors influencing the pharmacological response. This is also indicated by statistical data, according to which up to 60% of the variability of the body's response to the effects of drugs is associated with genetic variations of a patient with a particular disease [6, 9, 14]. Accordingly, the recommended introduction of the use of information about the genetic characteristics of the patient in clinical practice will allow in all areas of medicine to develop protocols for pharmacotherapy of diseases, new methods of monitoring patients, as well as reduce the risk of adverse reactions, prevent them and maximize the effectiveness, ensure the safety of pharmacotherapy. [11, 13].

It is known that the effect of drugs in the body is directly related to its therapeutic concentration, which must be created not only in the blood, but also in target cells [2, 5, 10]. The MDR1 gene (multidrug-resistance gene) is a gene of multidrug resistance, is the main gene regulating the creation of the necessary intracellular concentration of drugs [4, 8]. The MDR1 gene promotes cell binding to drugs, its entry into the cell, and/or efflux into the intercellular space [9, 10], which explains the development of cell resistance to drugs during the expression of this gene. Therefore, the MDR1 gene plays an important role in the effectiveness of pharmacotherapy of various diseases, including HG [7, 10, 12].

Such regulation of pharmacokinetic processes is often the same for many groups of drugs [4, 9], regardless of the location and form of influence, the main of which may be enzymes of the cytochrome P450 family [11] and such transport proteins as - glycoprotein P (P-gp) - the most important representative of the ABC transporter superfamily (ATP-binding cassette, subfamily B), an ATP-binding cassette protein of subfamily B involved in drug transfer [2, 4, 9].

The high–molecular membrane protein - Pgp is located in the cytoplasmic membrane of cells of many organs and tissues of the body and, in the form of an ATP-dependent pump, promotes the efflux of xenobiotics into the intercellular space [13], thereby protecting the cell from the effects of xenobiotics [3, 7, 10], which is the main function of Pgp[3, 4, 12]. This protein, located in the cell membrane, prevents the absorption of drugs in the intestine; prevents the penetration of drugs through histohematic barriers, in addition, the excretion of drugs into the bile by the liver and urine by the kidneys [6, 15]. The Pgp protein has been detected in the membrane of many organs and tissues of the body: in the liver, it is located on the surface of liver cells and it is contained by small biliary ducts of the liver on its apical surface; also found on the same surface of enteral epithelial cells and colon cells; also, in the kidneys, it is located on the membrane of proximal tubules and found on the apical surface pancreatic small ducts [2, 6].

Under the influence of many drugs, the activity of the Pgp protein can be modulated [12, 11]. Thus, drugs can inhibit the functional activity of the transporter protein or become inducers of Pgp. It is known that inhibitor drugs reduce the functional activity of the Ddr protein and often cause the development of HP [5, 13]. In this group of medicines by Marolim S. And his co-authors, (2004) include such drugs as quinidine, verapamil, carvedilol, spironolactone, as well as many antifungal drugs. It should be noted that in parallel, in this case, the concentration of drugs that are substrates of the Pgp protein increases in the body, due to an increase in absorption and slowing down the excretion of these drugs, the risk of HP increases [3, 8]. There are a lot of such drugs -substrates of the Pgp protein, they include drugs: digoxin, diltiazem, erythromycin, levofloxacin and others. But among all these groups of drugs, PPIs and clarithromycin, which are the main drugs of eradication therapy in H. pylori-associated HG, are of particular importance for the pharmacotherapy of HG.

Some drugs are inducers of Pgp, which increase the functional activity of the transporter protein, thereby simultaneously contributing to a decrease in the concentration in the blood plasma of drugs that are substrates of the Pgp protein, since Pgp at the same time inhibits the absorption of drugs and accelerates their excretion, resulting in a decrease in the effectiveness of drugs. According to Sadeque J.M. and his co-authors (2000), St. John's wort extracts, rifampicin and other drugs are considered to be Pgp protein inducers [5, 9].

The purpose of the study the analysis of types, clinical manifestations of chronic gastritis according to genotypic variants of polymorphism C3435T, G2677T and C1236T of the gene (MDR-1) transporter of xenobiotics glycoprotein P, as well as pharmacoepidemiological evaluation of the treatment process.

MATERIAL AND METHODS. The age of patients with chronic gastritis ranged from 18 to 63 years. At the same time, it should be noted that women predominated among patients with chronic gastritis.

The initial stage of our work was the selection and optimization of the system of oligoprimes for the detection of polymorphism rs1045642 of the MDR-1 gene by polymorphic marker C3435T and polymorphism rs4244285 of the CYP2C19 gene by polymorphic marker G681A, i.e. improvements in the methodological method for detecting these genetic markers. Nucleotide sequences of detection of polymorphism rs1045642 of the MDR-1 gene and polymorphism rs4244285 of the CYP2C19 gene were selected using the program "Oligo v.6.31" (Molecular Biology Insights Inc., USA) and synthesized in "Syntol" and "Litech".

RESULTS In our studies, we also determined the effect of polymorphisms C3435T, G2677T, C1236T of the MDR1 gene on the effectiveness of pharmacotherapy of HG associated with H.pylori. The results of pharmacotherapy were evaluated by the criteria of recovery, improvement, no improvement, deterioration and complications.

It is known that the polymorphism C3435T of the MDR1 gene has genotypes C/S, T/Thousand/T. After the pharmacotherapy, the following treatment results were noted depending on the genotype: in patients with the C/C genotype, recovery, without improvement, deterioration and complications

were noted in the same amounts and were 15% each, but improvement was noted in about 39% of patients with a similar genotype (Fig. 1).

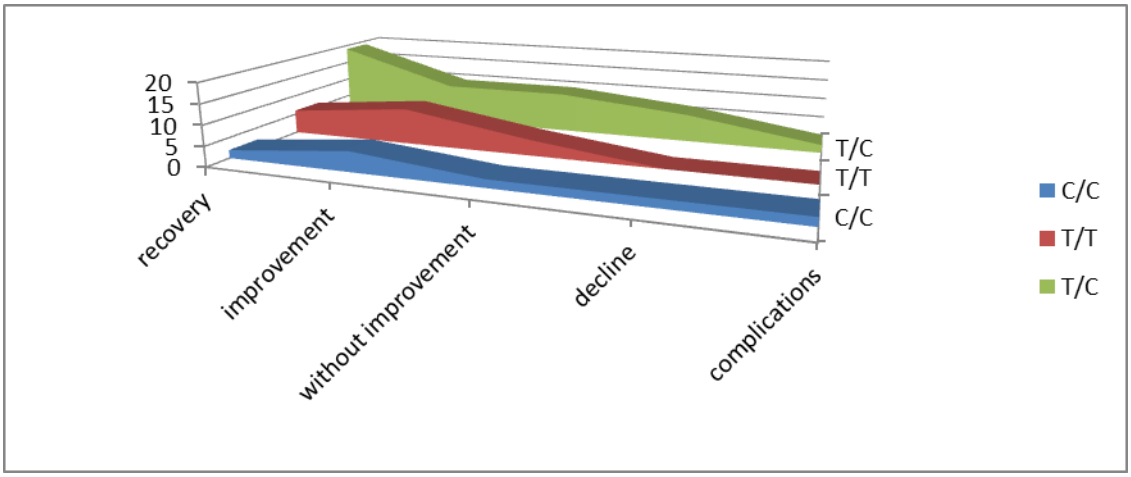

Figure 1. The results of HG treatment and their relationship with the frequency of distribution of C3435T polymorphism genotypes of the MDR1 gene

It turned out that in patients with the T/T genotype, pharmacotherapy ended in recovery and improvement in 31 and 49% of cases, but in 21% of patients, treatment was without improvement, nevertheless, in patients with a similar genotype, no deterioration and complications were noted. Patients with the C/T genotype accounted for the main number of patients and recovery occurred in about 40% of cases, but patients with and without improvement after pharmacotherapy accounted for the same number – about 29%; 9% of patients had deterioration and 2% of patients suffered from complications.

In addition, polymorphisms G2677T, C1236T of the MDR1 gene were studied. Polymorphism G2677T has genotypes G/G, TT and G/T. The results of treatment were evaluated according to the same criteria. Thus, in patients with genotypic affiliation G/G, recovery occurred in about 39% of patients, while improvements were noted in 33% of cases, 22% of patients were without improvement, deterioration was detected in about 6% of patients, but complications were not detected (Fig.2).

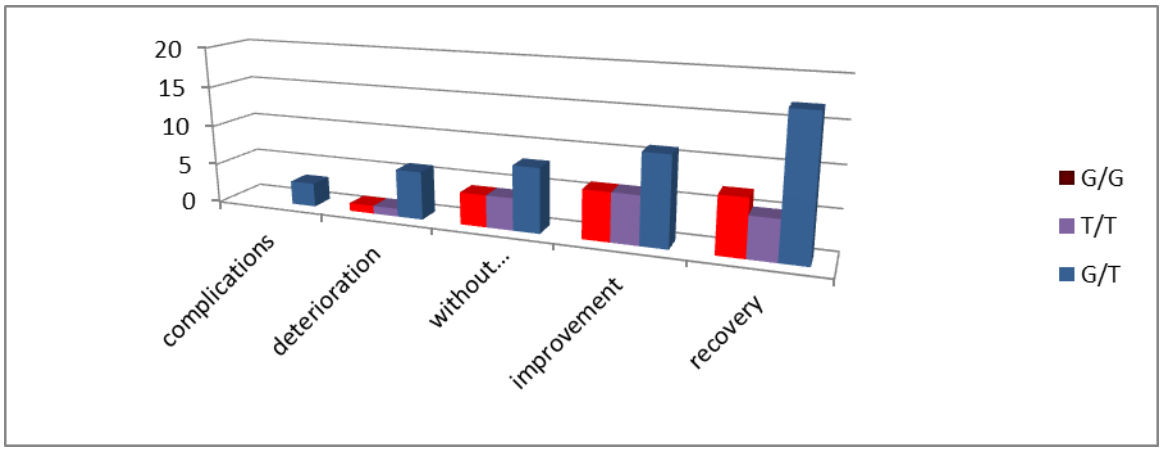

Figure 2. The results of HG treatment and their relationship with the frequency of distribution of genotypes of the G2677T polymorphism of the MDR1 gene

In patients with the T/T genotype, treatment had a high effect and recovery was noted in 31% of patients, the condition of 37.5% of patients also improved, but without improvement or even deterioration were in 25% and 6% of patients, respectively, no complications were noted.

Heterozygous genotype G/T was detected more than other genotypes of the studied polymorphism and pharmacotherapy ended with recovery in about 38% of patients, improvement was found in 24%

of patients, without improvement were about 18% of patients, while deterioration was noted in 13% of cases and complications were observed in 6.66% of patients.

Polymorphism C1236T of the MDR1 gene has genotypes C/C, T/T housand/T. Like the previous polymorphisms, the genotypes of this polymorphic variant of the studied gene were distributed according to the criteria for evaluating the results of pharmacotherapy. So, if pharmacotherapy showed good results in patients with the C/C genotype and 35% of patients had recovery from the disease and 29% of patients had improvement, then 17% of patients had no improvement, and 11% had deterioration and about 6% of patients had complications (Fig.3).

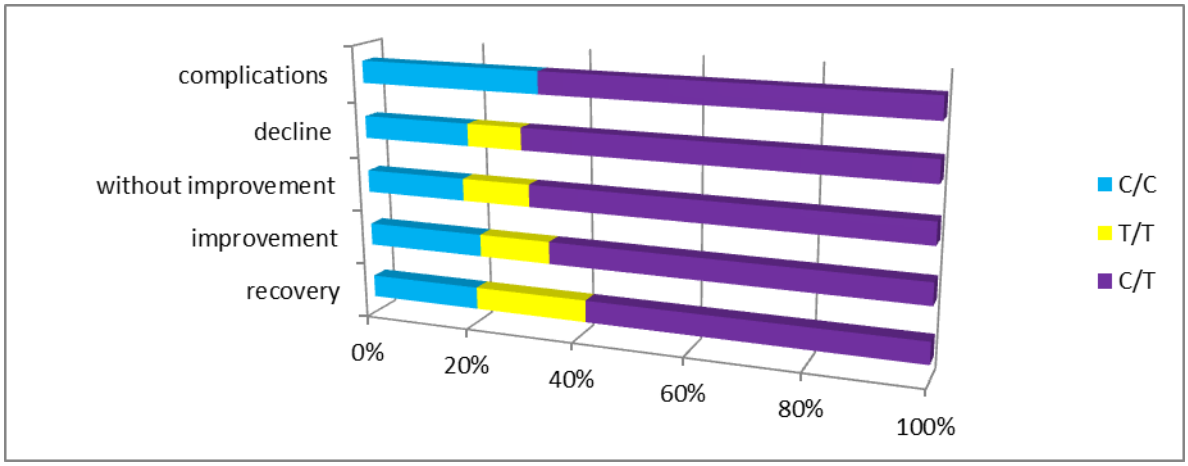

Figure 3. Results of treatment of He and their relationship with the frequency of distribution of genotypes of polymorphism C1236T of the MDR1 gene

Patients with the T/T genotype recovered in 45.5% of cases and the condition improved in 27%, but 18% of patients were without improvement and deterioration was observed in 9% of patients, but there were no complications.

DISCUSSION. Patients with genotypic affiliation with / T made up a huge part of the studied and the results according to the criteria for evaluating pharmacotherapy were as follows: recovery occurred in about 33% of patients, improvement after treatment was in about 29% of patients, but 21% of patients were without improvement, while deterioration and complications were detected in 13 and about 4% patients, respectively.

CONCLUSIONS. Thus, the research results show that in order to obtain a complete pharmacotherapeutic effect, the doctor needs to have information about the patient's genotype. Such patient data helps the doctor to optimize the chosen treatment plan and, most importantly, to select the dose and treat the patient effectively and safely.

REFERENCES:

1. Arvanitidis, K. Genetic polymorphisms of drug-metabolizing enzymes CYP2D6, CYP2C9, CYP2C19 and CYP3A5 in the Greek population // K. Arvanitidis, G. Ragia, M. Iordanidou et al.//Fundam. Clin. Pharmacol. 2007. Vol. 21 №4. P. 419 - 426.
2. Efrén Martínez-Quintana, Fayna Rodríguez-González, José María Medina-Gil, Paloma Garay-Sánchez, Antonio Tugores // Actividad de CYP2C19 y factores de riesgo cardiovascular en pacientes con síndrome coronario agudo. Medicina Clínica. Volume 149. Issue 6. 2017. Pages 235-239.
3. Kim K.A., Park P.W., Park J.Y. Effect of ABCB1 (MDR1) haplotypes derived from G2677T/C3435T on the pharmacokinetics of amlodipine in healthy subjects//Br. J. Clin.Pharmacol. 2007, Jan. Vol.63, №1. P. 53–58.
4. Kim R. Drugs as P-glycoprotein substrates, inhibitors, and inducers. Drug Metab. Rev., 2012, 34, 47-54.

5. Ochilov A.K., Musayeva D.M. "Treatment of chronic gastritis depending on allelic variants of the CYP2C19 gene" "Topical issues of medical science in the XXI century" Tashkent, 04/25/2019.
6. Ochilov A.K., G.S.Ochilova. "The value of the CYP2C19 gene in pharmacotherapy in chronic gastritis" Problems of Biology and Medicine, 2019, No. 4 (113) 250-252 p.
7. Ochilova G.S., Musaeva D.M. The effect of polymorphism of the MDR1 gene on the effectiveness of treatment of chronic gastritis. //New Day in Medicine 1 (29) 2020.309-312 s.
8. Ochilov A.K., Ochilova G.S. Clinical significance of polymorphisms of the CYP2C19 gene // University science: a look into the future. Collection of scientific papers based on the materials of the International Scientific Conference dedicated to the 85th anniversary of Kursk State Medical University (February 7, 2020) Volume I. 2020. 376-379 P.
9. Klichova F.K., Ochilova G.S. The significance of the MDR-1 gene of pharmacotherapy // Collection of abstracts of the II All-Russian scientific and practical conference with international participation "Safety of pharmacotherapy: NOLI NOCERE!" Kazan, May 16, 2019, pp. 46-47.
10. Ochilov A.K., Ochilova G.S. Clinical significance of polymorphisms of the CYP2C19 gene // Collection of scientific papers based on the materials of the International Scientific Conference "University science: a look into the future" dedicated to the 85th anniversary of Kursk State Medical University. Kursk. February 7, 2020. Volume I. pp. 376-379.
11. Ochilova G. S. Characterization of glycoprotein-P as a drug transporter protein // New day in medicine. 2020. Vol. 2. – No. 30/2. - pp. 60-53
12. Ochilova G.S. The distinguishing feature of the MDR-1 gene for personalization in pharmacotherapy // Collection of abstracts of the III All-Russian scientific and practical conference with international participation "SAFETY OF PHARMACOTHERAPY: NOLI NOCERE!" Kazan. May 21, 2020. pp. 161-162.
13. Musaeva D.M., Ochilova G.S. Personalized pharmacotherapy of chronic gastritis // Materials of the IV All-Russian remote scientific and practical conference with international participation "Pharmacology of different countries" dedicated to the 85th anniversary of Kursk State Medical University and the 75th anniversary of Victory in the Great Patriotic War 1941-1945 Kursk. September 29-30, 2020.
14. Isakov, V.A. Farmakogeneticheskiy analiz metabolizma i klinicheskoy effektivnosti ingibitorov protonnogo nasosa/ V.A.Isakov//Klin. farmakol. ter. 2003. № 1. S. 32 - 37.
15. Kuzuya T., Kobayashi T., Moriyama N., Nagasaka T., Yokoyama I., Uchida K., Nakao A., Nabeshima T. Amlodipine, but not MDR1polymorphisms, alters the pharmacokinetics of cyclosporine A in Japanese kidney transplant recipients//Transplantation. 2003. Vol.76, №5.P. 865–868.