SIGNS OF GENOTYPICAL FEATURES IN GASTRIC ULCER AND FEATURES OF TREATMENT

Klichova Firuza Karimovna
Bukhara State Medical Institute named after Abu Ali ibn Sino. Uzbekistan.

Annotation. The article examines the influence of the CYP2C19 gene genotype on the effectiveness of pharmacotherapy with proton pump inhibitors in a patient with peptic ulcer disease.

Key words: Genotype, CYP2C19 Gene, Proton Pump Inhibitors, Peptic Ulcer Disease, Pharmacotherapy.

Introduction. Currently, a number of measures are being carried out in Uzbekistan to prevent and eliminate various diseases, taking into account the genetic parameters of patients. The strategy of actions on five priority directions of development of the Republic of Uzbekistan in 2017-2021 defines such tasks as "... the introduction of a set of measures to improve and strengthen the health of the population, reduce morbidity rates, prevent genetic diseases and increase life expectancy ..." [1-8]. The solution of these tasks contributes to the prevention and diagnosis of various diseases, an increase in the degree of medical care, the improvement of the use of modern technologies to identify the genetic indicators of patients, and a decrease in the incidence rate.

The purpose of the study. To study individual genetic variations leading to differences in the body's response to a particular drug from the group of proton pump inhibitors in modern therapy of gastric ulcer.

Materials and research methods. A comprehensive examination of 120 patients with peptic ulcer disease who were hospitalized and monitored at the Bukhara Regional Multidisciplinary Clinical Hospital was carried out. The control group consisted of 50 healthy people with no history of pathology from the digestive tract, living in the Bukhara region, matched by gender and age to the examined group of patients with peptic ulcer disease. The age of patients with peptic ulcer disease ranged from 18 to 75 years. The initial stage of our work was the selection and optimization of the operation of the oligoprimer system for the detection of the rs4244285 polymorphism of the CYP2C19 gene by the polymorphic marker G681A. Nucleotide sequences for detecting the rs4244285 polymorphism of the CYP2C19 gene were selected using the Oligo v.6.31 program (Molecular Biology Insights Inc., USA) and synthesized at Syntol LLC and Litekh Scientific and Production Company (Moscow).

The rest of the components were purchased from the world's leading manufacturers - Serva (Germany), Sigma (USA), Helikon NPF Litekh, Sibenzim (Russia), etc. Adaptation of primer systems for standard PCR analysis was carried out using PCR analyzers "Applied Biosystems 2720" (USA) and Rotor-Gene 6000 (Corbett Australia). For amplification, a 25 μL reaction mixture was used, which contained 2.5 μL of 1 OxTaq buffer (67 mMtris-HCl (pH 8.8), 16.6 mM (NH4) 2SO4>, 2.5 mM MgCl2, 0.01% Tween-20), 0.1 μg of genomic DNA , dNTP mixture (dATP, dGTP, dCTP, dTTP at 200 μM each), 1 unit. Termusaquaticus DNA polymerase (manufactured by Sileks, Moscow) and 5-10 pM locus-specific oligonucleotide primers. Temperature-time parameters were changed depending on the pairs of oligoprimers.

For the detection of rs4244285 of the CYP2C19 gene, preliminary denaturation is 940C (1 min. 1 cycle), 35 amplification cycles: 930C (10 sec) - denaturation, 640C (10 sec) - primer annealing, 720C (20 sec) - elongation, and final synthesis 720C (1 min. 1-cycle), 10 min storage.

Polymorphic regions of the CYP2C19 gene were identified using the PCR-SSP method. The specificity and the number of amplified fragments were checked by agarose gel electrophoresis.

The results were statistically processed.

Results and its discussion. Individual variability of the drug response is one of the main problems in modern clinical practice. Genetic variability of genes encoding these enzymes, the patient's genotype play an important role in the manifestation of individual sensitivity to drugs.

It is known that one of the variants of the CYP2C19 * 2 (rs4244285) gene we are investigating consists in replacing guanine (G) with adenine (A) in position 681 (681G-A) in exon 5. Using a modified detection method, we investigated the polymorphism of the G681A gene CYP2C19, which has variants of genotypes A / A, GG, G / A.

In the study group, the genotype of patients by the CYP2C19 gene with gastric ulcer, living in the Bukhara region, was determined. It should be noted that, in the structure of the group of patients with gastric ulcer studied by us, it was revealed that carriers of the "wild type" allele CYP2C19 GG accounted for more than 67% (Fig. 1), carriers of the heterozygous allele CYP2C19 G / A accounted for 30%, carriers of the homozygous allele CYP2C19 A / A accounted for 2.5%. Thus, the frequency of the G allele corresponded to 82%, while the frequency of the A allele was about 17% of patients with gastric ulcer. It is interesting to note that in the population sample of patients with gastric ulcer, the frequency of occurrence of genotype variants of the CYP2C19 gene by gender was studied, the results of which showed that the homozygous G / G genotype occurs in more than 66% of women with gastric ulcer, while in men with with a similar diagnosis, this variant of the genotype is 2 times less common. Heterozygous genotype G / A was found in more than 62% of women with gastric ulcer, but in male patients this variant of the genotype occurs in 37% of cases. It should be noted that the A / A genotype is rare among all variants of the genotypes of the CYP2C19 gene - only in women with gastric ulcer, and in male patients it has not been detected.

The CYP2C19 gene determines the metabolic activity of proton pump inhibitors, which are the main drugs in the treatment of gastric ulcer. In our opinion, the patient's genotype may affect the effectiveness of disease therapy, especially for the allelic variant G681A, which is determined in the largest number of patients. So, if in 50% of patients with genotype A / A after pharmacotherapy, there is a recovery from gastric ulcer, then in the rest of the contingent of patients (50%) there is a deterioration.

Also, in 37% of patients with the G / G genotype, pharmacotherapy ends with recovery, but in 22% of patients with a similar genotype, treatment only improves the condition of the patients; and in 26% of patients, pharmacotherapy does not have the desired effect - without improvement, in 9% of patients with gastric ulcer, the condition worsens, and even complications may be observed (about 6%).

Conclusions. Thus, statistical studies show that up to 60% of the variability in response to pharmacotherapy is due to genetic variation between individuals. The genetic affiliation of the organism has a huge impact on the effectiveness and safety of the applied pharmacotherapy. The GG genotype for the polymorphic marker G681A of the CYP2C19 gene is found in the greatest number among patients with gastric ulcer living in the Bukhara region and corresponds to the extensive type of metabolism of proton pump inhibitors. It should be especially noted that this genotype is found 2 times more in women of this region. The use of genetic information in clinical medicine will allow the development of drug protocols and surveillance methods to reduce the risk of adverse reactions and maximize the effectiveness of treatment.

Bibliography:

1. Strategiya deystviy po pyati prioritetnym napravleniyam Respubliki Uzbekistan v 2017-2021 godakh. Tashkent. -2017. – 64 s.
2. I.V. Mayev, A.A. Samsonov, N.N. Golubev, YU.A. Kucheryavyy, Ye.V. Belyavtseva, T.I. Korovina, Ye.V. Barkalova. Khelikobakter-assotsiirovannaya forma yazvennoy bolezni zheludka i dvenadtsatiperstnoy kishki: problemy terapii // Farmateka . – 2011. - № 2. – S. 10-17.
3. Stepchenko A. A. Farmakologicheskiye printsipy individualizatsii effektivnoy i bezopasnoy farmakoterapii yazvennoy bolezni zheludka i dvenadtsatiperstnoy kishki v usloviyakh funktsionirovaniya standartov i formulyarnoy sistemy lecheniya. Avtoref. diss. na soisk. uch. stepeni dok.med.nauk. Moskva. - 2011. – S. 27.

4. Elisabeth J. Shell. Pathophysiology of Peptic Ulcer Disease // Physician Assistant Clinics. – 2021. – Vol. 6. – Iss. 4. – P. 603-611. ISSN 2405-7991. ISBN 9780323794268. https://doi.org/10.1016/j.cpha.2021.05.005. (https://www.sciencedirect.com/science/article/pii/S2405799121000475)
5. Ochilov A.K., Ochilova G.S. Znacheniye gena CYP2C19 v farmakoterapii pri khronicheskikh gastritakh // Problemy biologii i meditsiny. - 2019. - №4 (113). - S. 250-252.
6. Bel'diyev S.N., Yegorova I.V., Kononova A.G. i dr. Spornyye voprosy eradikatsii Helicobacter pylori u patsiyentov, prinimayushchikh pryamyye oral'nyye antikoagulyanty // Effektivnaya farmakoterapiya. - 2020. - T. 16. - № 1. - S. 84–90.
7. Morozov, S. V. Vliyaniye polimorfizma gena CYP2C19 na effektivnost' lecheniya bol'nykh erozivnoy gastroezofagal'noy reflyuksnoy bolezn'yu ingibitorov protonovoy pompy. Avtoref. diss.… kand. med. nauk. — M. - 2005. - S. 23.
8. Ochilov A.K. Vajnost' tsitokhromov R-450 dlya gastroenterologii // Novyy den' v meditsine. – 2020. - №2 (30/2). - S. 57-59.