

THE PATIENT'S GENOTYPE IS THE MAIN INDICATOR FOR CHOOSING AN EFFECTIVE AND SAFE PHARMACOTHERAPY FOR CHRONIC GASTRITIS

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✓ *Resume,*

The article presents the results of a genotypic study of patients with chronic gastritis in the Bukhara region by the polymorphism rs1045642 of the MDR-1 gene by the polymorphic marker C3435T. It turned out that in the present region, patients with the CT genotype prevail and the type B of chronic gastritis prevails in terms of occurrence. When studying the effectiveness of the classical pharmacotherapy used, depending on the genotype of a patient with HCG, the disease ends with recovery mainly in patients with the SS genotype.

Key words: MDR-1 gene, polymorphism, chronic gastritis, polymorphic marker C3435T of MDR-1 gene, P-glycoprotein.

ГЕНОТИП ПАЦИЕНТА – ОСНОВНОЙ ПОКАЗАТЕЛЬ ДЛЯ ВЫБОРА ЭФФЕКТИВНОЙ И БЕЗОПАСНОЙ ФАРМАКОТЕРАПИИ ХРОНИЧЕСКОГО ГАСТРИТА

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✓ *Резюме,*

В статье приводятся результаты генотипического исследования больных с хроническим гастритом в Бухарском регионе по полиморфизму rs1045642 гена MDR-1 по полиморфному маркеру C3435T. Оказалось, что в настоящем регионе преобладают больные с генотипом CT и по встречаемости преобладает тип B хронического гастрита. При изучении эффективности применяемой классической фармакотерапии в зависимости от генотипа больного с ХГ заболевание заканчивается выздоровлением в основном у пациентов с генотипом CC.

Ключевые слова: ген MDR-1, полиморфизм, хронический гастрит, полиморфный маркер C3435T гена MDR-1, P-гликопротеин.

BEMORNING GENOTIPI - SURUNKALI GASTRITNING SAMARALI VA XAVFSIZ FARMAKOTERAPIYASINI TANLASH UCHUN ASOSIY KO'RSATKICHDIR

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Maqolada MDR-1 genining rs1045642 polimorfizmi C3435T polimorf markeri bo'yicha Buxoro viloyatida surunkali gastrit bilan og'rigan bemorlarda o'tkazilgan genotipik tadqiqotlar natijalari keltirilgan. Ma'lum bo'lishicha, ushbu regionda bemorlar asosan CT genotipli bo'lib, surunkali gastritning B turi ko'proq tarqalgan. Surunkali gastrit bilan og'rigan bemorning genotipiga qarab ishlatiladigan an'anaviy farmakoterapiya samaradorligini o'rganayotganda kasallik asosan CC genotipi bo'lgan bemorlarda sog'ayish bilan tugaydi.

Kalit so'zlar: MDR-1 geni, polimorfizm, surunkali gastrit, MDR-1 genining polimorf markeri C3435T, P-glikoprotein.

Relevance

It was revealed that the MDR-1 gene is one of the main genes that affect the effectiveness of pharmacotherapy [2,4,22]. The MDR-1 gene (multidrug-resistance gene) encodes P-glycoprotein (P-gp), which is located in the cytoplasmic membrane of various cells, performs the function of an ATP-dependent pump and promotes the removal of various xenobiotics outside the cell [7, 21, 26]. Therefore, the expression of the MDR-1 gene contributes to the resistance of the cell to the drug used and plays an important role in the effectiveness of therapeutic measures. Namely, the P-gp protein encoded by the MDR-1 gene, dictates the activity of the drug absorption process, being in the membrane of normal cells of the body. The expression of this protein determines the pharmacokinetics of drugs and, in due course, the effectiveness of pharmacotherapy [1,9,12].

It is known from the literature that the MDR-1 gene has several polymorphisms - T3435C, G2677T, C1236T [3,8,11]. Among them, the C3435T polymorphism is directly related to the expression of the P-gp protein encoded by the MDR-1 gene [6, 10, 25]. The genotypic variants of SS, TT, and CT of this polymorphism have a huge impact on the pharmacokinetic parameters of the drugs used, and, accordingly, on the effectiveness of pharmacotherapy [16,20].

When conducting a subpopulation analysis, it was found that in Europeans, the activity of P-gp was higher in carriers of the SS genotype, and in Japanese-in carriers of the TT genotype [5,15,17].

According to Russian scientists, in patients with rheumatoid arthritis with the TT genotype, the effectiveness of pharmacotherapy is 2.9 times higher than in patients with the SS and CT genotypes [13,24]. The same results were obtained by Japanese researchers. A subpopulation analysis revealed that the SS genotype prevails in Europeans, while the TT genotype prevails in Japanese [14,27]. Therefore,

we think it is necessary to establish the genotypic affiliation of the patient for the prognosis of the effectiveness of pharmacotherapy [18,19].

These circumstances were the reason for choosing the direction and purpose of this study, i.e., to study the genotype of patients with chronic gastritis by the polymorphic marker C3435T of the MDR-1 gene and the association of polymorphism with the effectiveness and safety of therapy for chronic gastritis in people living in the Bukhara region.

Material and method

In accordance with the objectives of the dissertation, a comprehensive examination of 100 unrelated patients with HCG who were on inpatient treatment and follow-up in the 1 – clinic of BuhGMI-in BOMPKB was conducted. These patients made up the main group.

The control group consisted of 50 healthy unrelated and without a history of gastrointestinal pathology persons living in the Bukhara region, corresponding by sex and age to the examined group of patients with chronic gastritis.

The MDR - 1 gene polymorphic marker C3435T was analyzed by standard PCR analysis [23].

A comparative analysis of 50 samples of control DNA revealed a positive correlation between our results and the data obtained by the standardized test system of PF Litech (Moscow). Heterozygous and homozygous genotypes were detected in the same DNA samples, the negative result was confirmed by both methods (high comparability of results). The revealed minor differences were statistically insignificant ($P>0.05$).

Results and discussion

When studying the rs1045642 polymorphism of the MDR-1 gene by the polymorphic marker C3435T in patients with chronic gastritis living in the Bukhara region (fig. 1), the CT genotype prevails (59%).

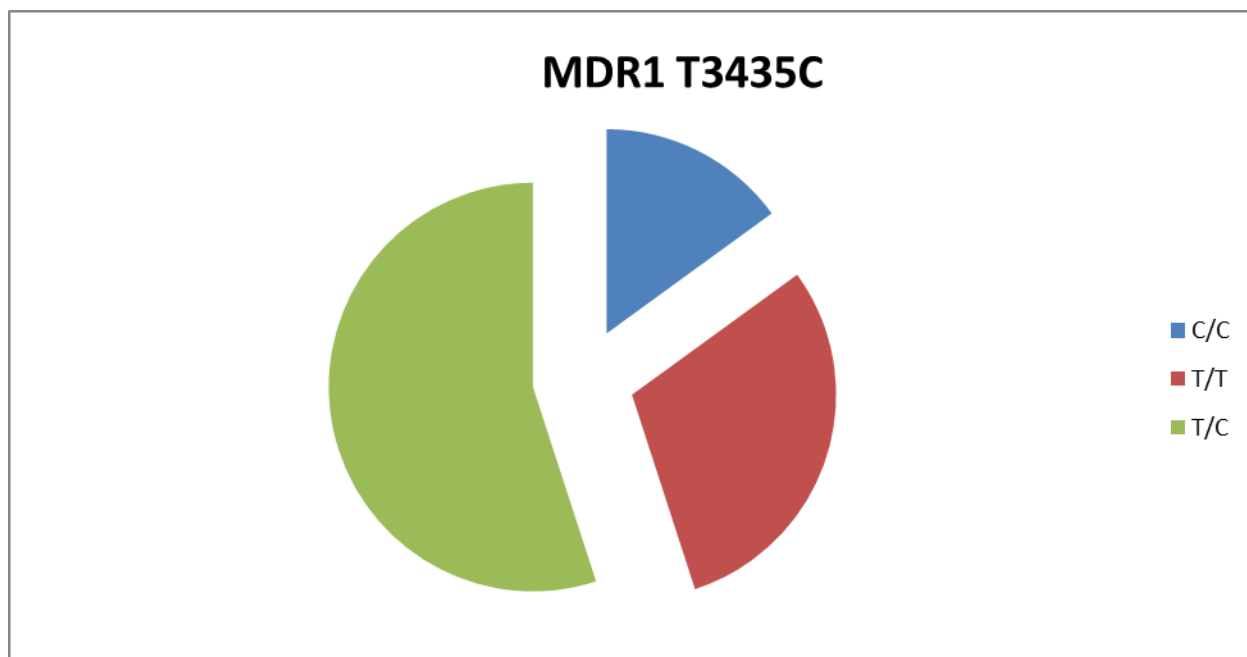


Figure 1. Frequency of distribution of genotypes of the C3435T polymorphism of the MDR-1 gene in patients with chronic gastritis, regardless of the type of gastritis

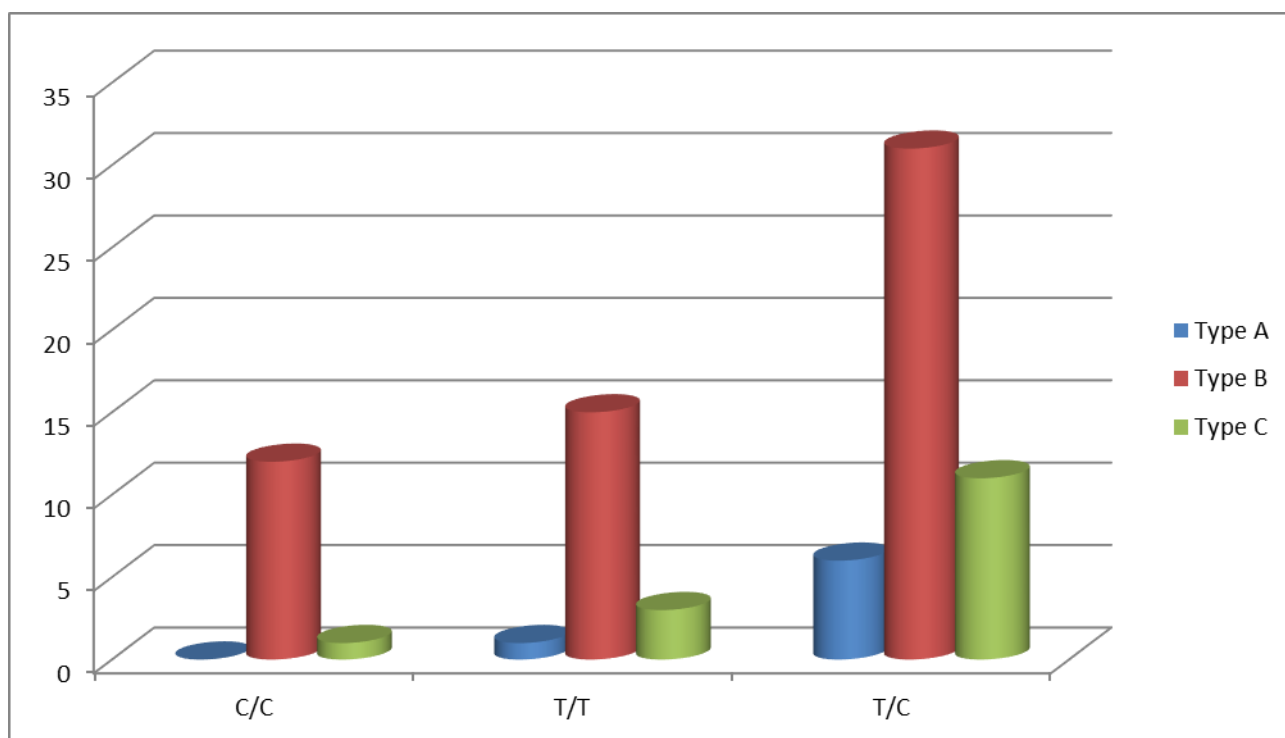


Figure 2. Distribution of types of chronic gastritis depending on the genotypes of the C3435T polymorphism of the MDR-1 gene

When studying the type of HCG, depending on the genotypic affiliation of the patient by the T3435C polymorphism of the MDR1 gene (fig.2), the results showed that in patients with the SS genotype, type B CG prevails (92%), while type C CG was determined in 8% of patients, and there were no patients with the AA

genotype. Also, 79% of patients with the TT genotype had type B CG, and type C CG was 16%, and type A CG was 5%. In patients with the CT genotype, 65% of cases showed type B CG, while in patients with this genotype, type C CG was 13% and type A CG was 12%.

When studying the effectiveness of the classical pharmacotherapy used depending on the genotype of a patient with HCG (fig. 3), we determined that in 46% of patients with the SS genotype, the disease ends with recovery, and in

39% with a similar genotype, there is an improvement, and only in 15% of patients, pharmacotherapy does not give results – without improvement. But there were no aggravations or complications.

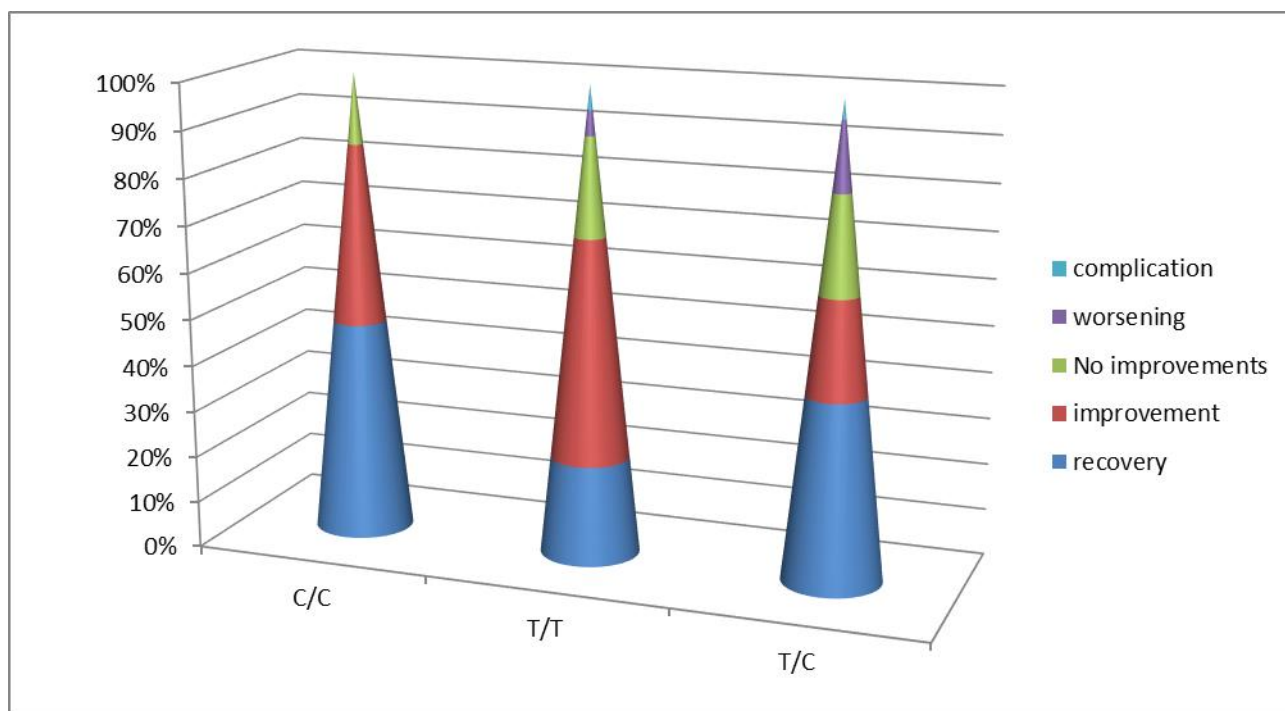


Figure 3. Results of treatment of chronic gastritis and their relationship with the frequency of distribution of genotypes of the C3435T polymorphism of the MDR-1 gene in chronic gastritis

Also, in patients with the TT genotype in 47% of cases there was an improvement, but if in 21% of patients the disease ended in recovery, then in the same percentage of patients there were no improvements from pharmacotherapy, and in 5% of patients there were worsenings, and in 5% of patients there were complications.

In patients with the CT genotype, recovery was 40%, and 20% of cases showed improvement, but in the remaining 20% of patients, no improvement was observed, and 16% had deterioration, and 4% of patients had complications.

Conclusions

Thus, it turned out that patients with the CT genotype predominate in the present region. In terms of occurrence, type B of chronic gastritis prevails. The disease ends with recovery mainly in patients with the SS genotype.

The results of the studies show that in order to choose an effective and safe pharmacotherapy for this pathology, the doctor must have information about the patient's genotype based on the polymorphic marker C3435T of the MDR-1 gene.

We believe that the ineffectiveness of the selected pharmacotherapy in the studied group of patients is dictated by the activity of P-gp encoded by the MDR-1 gene, since P-gp directly affects the pharmacokinetics of the drugs used and the effectiveness of the selected pharmacotherapy depends on the patient's genotype in relation to the polymorphisms of the MDR-1 gene – the gene for multidrug resistance.

Since the human genetic apparatus is individual, unique, we believe that such information about the patient contributes to the individualization of treatment, that is, the personification of pharmacotherapy, which will serve as the basis for safe and highly effective treatment, which in modern medicine is considered relevant and a requirement of the time.

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