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SPECIFICITIES OF GENOTYPIC VARIATIONS OF CYP2C19 GENE WHILE PEPTIC ULCER TREATMENT

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✓ ***Resume***

This article presents the results of researches of patients with peptic ulcer disease living in the Bukhara region by genotypic accessories for the CYP2C19 gene. It was found that in all genotypic variations of the gene, the main symptoms of peptic ulcer disease and related diseases do not differ much from each other.

Key words: CYP2C19 gene, variations of CYP2C19, peptic ulcer disease, symptoms of peptic ulcer disease.

ОСОБЕННОСТИ ГЕНОТИПИЧЕСКИХ ВАРИАНТОВ ГЕНА CYP2C19 ПРИ ЯЗВЕННОЙ БОЛЕЗНИ

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✓ ***Резюме***

В данной статье приводятся результаты исследований пациентов с язвенной болезнью проживающих в Бухарском регионе по генотипическим принадлежностям по гену CYP2C19. Оказалось, что во всех генотипических вариантах гена основные симптомы язвенной болезни и сопутствующие заболевания мало чем отличаются друг от друга.

Ключевые слова: ген CYP2C19, генотипы гена CYP2C19, язвенная болезнь, симптомы язвенной болезни.

YARA KASALLIGIDA CYP2C19 GENI GENOTIPIK VARIANTLARINING XUSUSSIYATLARI

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✓ ***Rezyume***

Maqolada Buxoro viloyatida yara kasalligi bilan og'rigan bemorlarda CYP2C19 genining polimorfizmi genotipik variantlarini o'rganish bo'yicha olib borilgan izlanishlar natijalari keltirilgan. Ma'lum bo'lishicha, ushbu regionda CYP2C19 genining barcha genotipik variantlarida kasallik simptomlari va unga yondosh kasalliklar bir-biridan juda kam farq qilar ekan.

Kalit so'zlar: CYP2C19 geni, CYP2C19 geni genotipi, yara kasaligi, yara kasaligi simptomlari

Relevance

Cytochrome P450 was discovered in 1954-1956 by M. Klingenberg and D. Garfinkel in microsomes of liver in rats [5, 8, 11, 12, 17, 18, 25].

For the first time, in 1994, De Marais et al. was examined and studied cytochrome P450 polymorphism that encode the structure of the enzyme CYP2C19.During of researching of metabolism and clinical efficacy of the anticonvulsant drug S-mephenytoin, it was found that these performances directly depend on the polymorphism of the CYP2C19 gene, which is

expressed in that, due to mutation and replacement of only one nucleotide in the 5th exon of the CYP2C19 gene during the synthesis of CYP2C19 hydroxylase, it becomes shorter by 20 amino acids and consequently, functionally inactive [2, 6, 15, 21, 26].

The CYP2C19 gene is a member of the IIC subfamily of cytochrome P-450 genes, which is involved in the metabolism of a number of drugs: proton pump inhibitors (omeprazole, pantoprazole, lansoprazole, rabeprazole and esomeprazole), antidepressants (tricyclic antidepressants – amitriptyline, clomipramine, imipramine, selective serotonin reuptake inhibitors – citalopram, MAO – moclobemide inhibitor), antiepileptic drugs (diazepam, phenytoin, phenobarbital, clonazepam), nonsteroidal anti-inflammatory drugs (diclofenac, indomethacin), anticoagulants (warfarin), antiplatelet agents (thienopyridines, including clopidogrel), antifungal drugs (voriconazole), b-blockers (propranolol), antitumor drugs (cyclophosphamide), certain hormones (e.g. progesterone), and other medications [3, 9, 20, 24].

The metabolism of proton pump inhibitors mainly occurs in the liver with the involvement of CYP2C9, CYP2C19, CYP2D6 and CYP3A4, which are isoenzymes of cytochrome P450. The polymorphism of the genes of the cytochrome CYP2C19 system is the determining factor that the rate of occurrence and duration of the antisecretory effect of PPIs in patients differ significantly [1, 4, 14, 22].

It was found that in the Russian population, the CYP2C19 gene encoding the metabolism of the proton pump inhibitor is widespread and it turns out that from 8.3 to 20.5% of patients are resistant to a single dose of PPIs [7, 10, 13].

However, there are no studies on the effect of allelic variants of the CYP2C19 gene on the effectiveness of treatment for peptic ulcer disease, which was the basis for this research [16, 27].

Based on the above, the **purpose** of this research is to study the effect of allelic variants of the CYP2C19 gene on the pharmacotherapy of ulcer disease in order to develop a method of differentiated use of PPIs for the treatment of this pathology.

Material and methods

In accordance with the objectives of the article, researched a comprehensive examination of 100 unrelated patients with chronic gastritis who were on treatment and follow-up in the State clinic №1 of the Bukhara State Medical Institute These patients made up the main group.

The control group consisted of 50 healthy unrelated and non-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 polymorphic marker C3435T of the MDR1 gene was analyzed using 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 ($P>0.05$).

Result and discussion

We studied the relationship of the genotype for the allelic variant G681A of the researched gene to the symptoms of Chronic gastritis (Fig. 1). It turned out that in patients with genotype A/A, the main clinical manifestations of the disease are fasting pain, belching, feeling of overeating and flatulence – each symptom in 25% of cases, other symptoms were not rare. These symptoms in patients with the G/A genotype were determined from 5% to 18% of patients, while in patients with the G/G genotype, these clinical manifestations occurred on average up to 10% of cases. The predominant clinical manifestations in patients with the G/G genotype were aching pains in the epigastric region (22%) and heartburn (15%), while these symptoms in patients with the G/A genotype were determined in 10% of cases. Other clinical manifestations in patients with genotype G / G and G/A were observed in the range from 2% to 11% of cases.

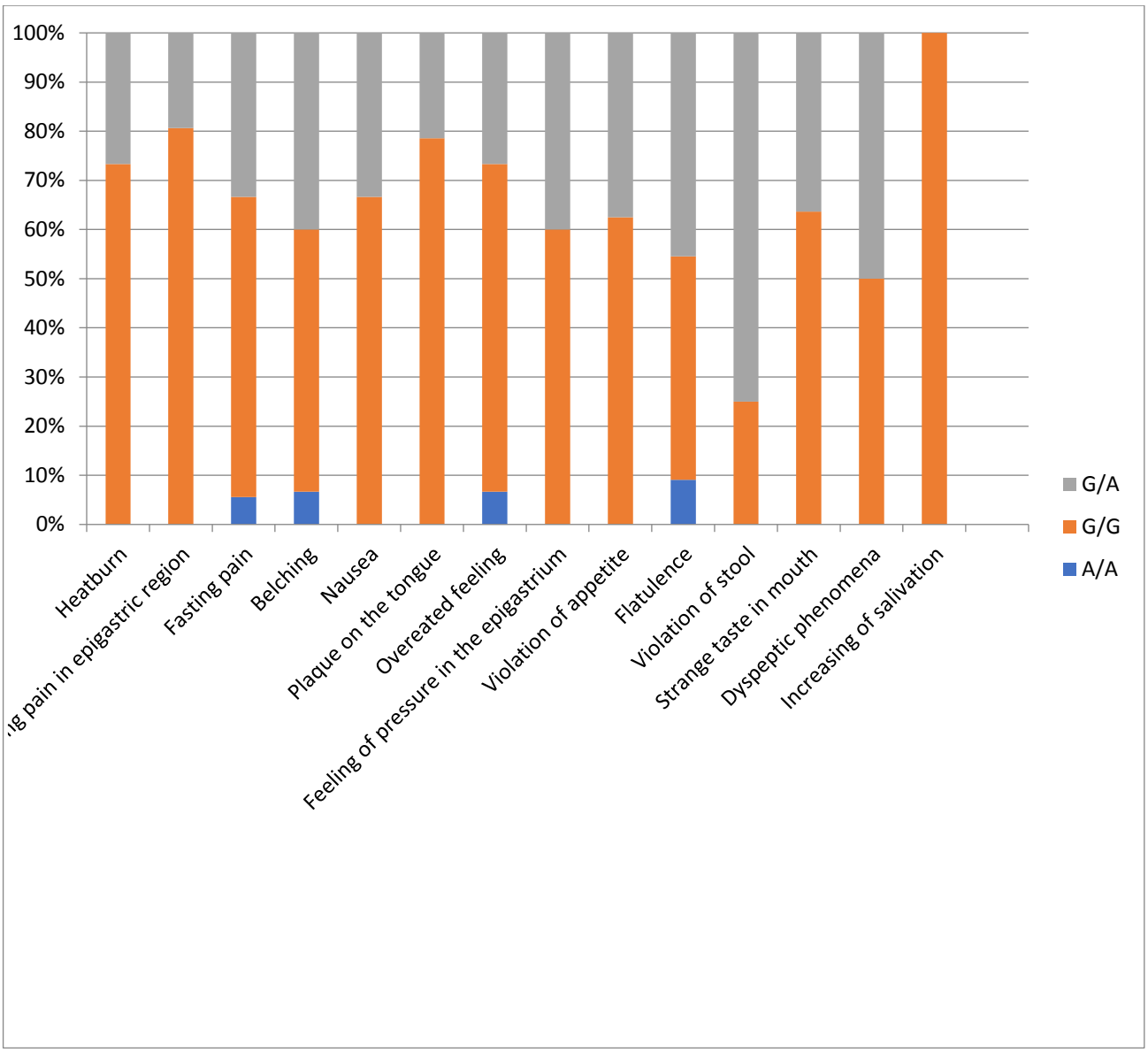

Figure 1. Characteristics of the clinical manifestations of peptic ulcer disease and its relationship with the genotypes of the SUR2C19 gene for the allelic variant G681A.

An interesting fact was the frequency of occurrence of concomitant diseases depending on the genotype of the gene CYP2C19 for the allelic variant G 681 A (Fig. 2). In patients with genotype A/A, the frequency of occurrence of opportunistic diseases was low, and in isolated cases of chronic gastritis were associated with chronic cholecystitis and chronic gastritis, anemia, hepatitis, etc.

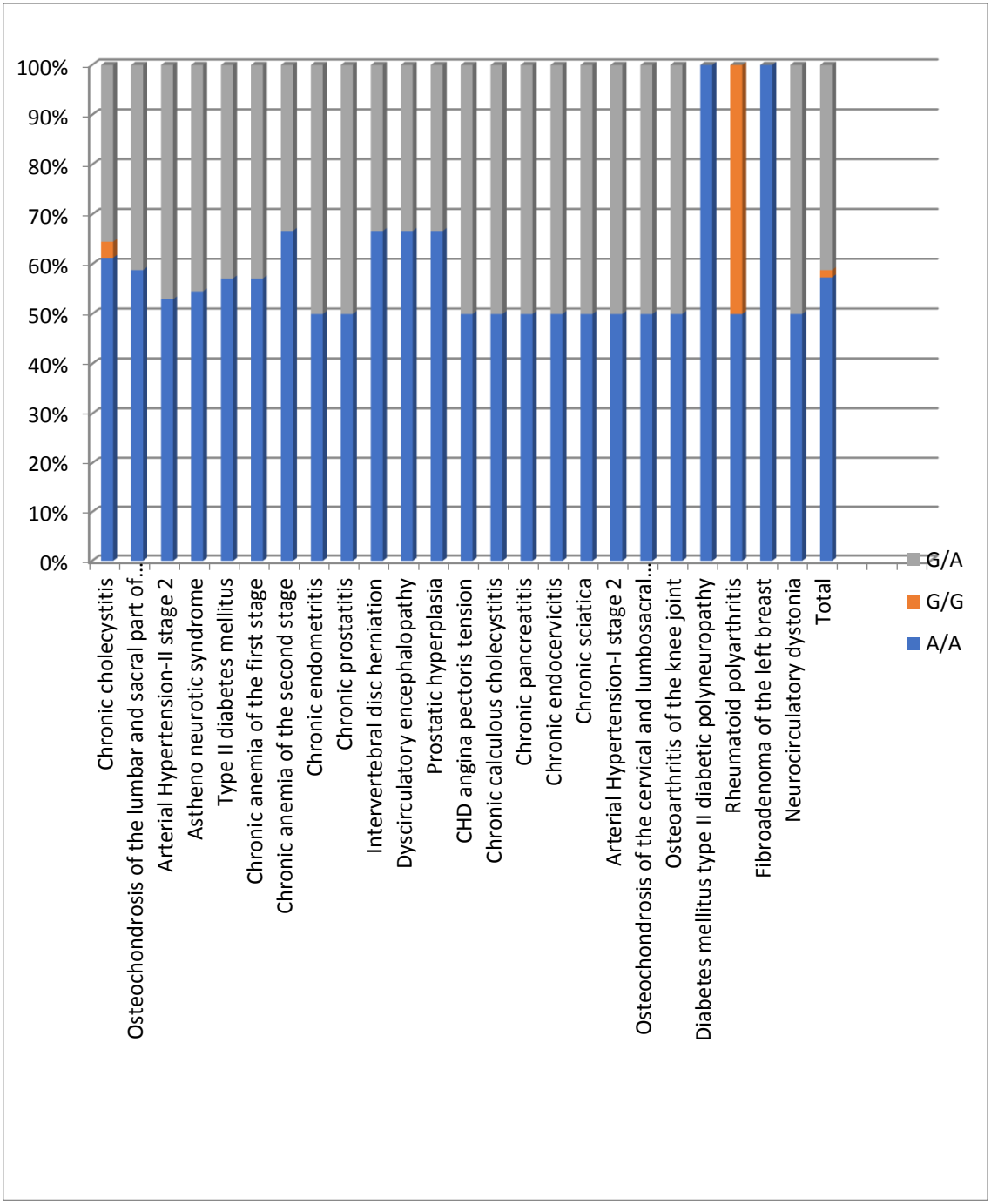

Figure 2. The frequency of concomitant diseases with peptic ulcer diseases, depending on the genotypes of the gene CYP2C19 for the allelic variant G681A

The main concomitant diseases of Peptic ulcer disease in patients with the G/G genotype were chronic cholecystitis (about 22% of cases), hypertension (12%), spinal osteochondrosis (12.5%), asthenoneurotic syndrome (about 9% of cases), diabetes mellitus (7%) and anemia (8%), and other diseases occurred in isolated cases. In patients with genotype G/A, the most common diseases were about 34% of cases of chronic gastritis and about 15% of cases of chronic cholecystitis, other diseases were registered in isolated cases.

Conclusions

It should be noted that in patients with chronic gastritis living in the Bukhara region in all genotypic groups, the main symptoms of chronic gastritis were fasting pain, heartburn, belching, feeling of overeating and flatulence. Also, in all genotypic manifestations of the SUR2C19 gene, the main concomitant diseases were chronic cholecystitis, hypertension, anemia, and diabetes mellitus.

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