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MOLECULAR GENETIC FEATURES CLINICAL COURSE OF CHRONIC PANCREATITIS WITH EXTERNAL SECURITY INSUFFICIENCY

Abstract: Mutation of the N34S gene of the pancreatic secretory inhibitor of trypsin is detected significantly more often in patients with chronic pancreatitis than in healthy individuals, which is 9.2% and 2.8% respectively, while the homozygous for patients with HP also was greater – 5.4% and 0, 9%, respectively ($p < 0.05$), which suggests a significant role of these genetic changes in the development of chronic pancreatitis.

Keywords. Chronic pancreatitis, molecular genetic studies.

Chronic pancreatitis (CP) is an inflammatory disease of the pancreas (PZ) characterized by a prolonged progressive course with the development of irreversible morphological changes in the parenchyma and the duct system [1, 2]. Currently, CP is a relatively frequent disease leading to temporary disability, and in the future – and disability, which makes CP is an important social and economic tion problem of modern medicine [3].

A significant contribution to the modern understanding of the pathogenesis of pancreatitis has been the discovery of genes that directly lead or contribute to the risk of developing the disease.

The data of clinical studies show the features of the clinical course and diagnostic signs of various subtypes of NP, differing in genetic defects and the type of inheritance [4, 5].

Mutations in the genes of SPINK1, PRSS1, CFTR are detected with a relatively high frequency in NP patients, for example, in the CFTR gene, 13.4–37.0%, in the SPINK1 gene, 20.0–23.0%, which is 2.7–7.4 times the frequency of the carriage of mutations in these genes in a healthy population [4]. These genetic changes can independently determine the development of HP or be a risk factor. Thus, the probability of developing alcoholic CP in a patient with a mutation of R122H in the PRSS1 gene exceeds 40% [5].

The purpose of this work is to study the clinical and genetic peculiarities of the flow of various forms of chronic pancreatitis in adult patients and determine the value of mutations in the genes of SPINK1, PRSS1, CFTR in the development and progression of chronic pancreatitis.

Material and methods: During the research, we used linguistic, genetic.

Results and its discussion. As part of a one-stage study with monitoring, genetic screening of patients with chronic pancreatitis was performed. For the first time, the frequency of carriage of mutations in the genes CFTR, SPINK1, PRSS1 was determined for various chronic forms of pancreatitis in adult patients in the Russian population. For the first time, the most common mutations in the CFTR and SPINK1 genes were detected in Uzbekistan with different forms of pancreatitis. For the first time the features of the course of CP, the effectiveness of therapy, the prognosis, possible combined risk factors in patients with the presence of N34S mutation in the SPINK1 gene were studied.

The data of the clinical studies carried out demonstrate the features of the clinical course and diagnostic signs of various subtypes of HP, differing in genetic defects and the type of inheritance.

Mutations in the genes SPINK1, PRSS1, CFTR are detected with a relatively high frequency in patients with CP, for example, in the CFTR gene, 13.4–37.0%, in the SPINK1 gene, 20.0–23.0%, which is 2.7–7.4 times the frequency of the carriage of mutations in these genes in a healthy population. These genetic changes can independently determine the development of HP or be a risk factor. Thus, the probability of developing alcoholic CP in a patient with a mutation of R122H in the PRSS1 gene exceeds 40%.

In patients with HP of different etiologies, a mutation of the SPINK1 N34S gene is found reliably in relation to healthy individuals, determining a higher risk of structural changes in the pancreas, determining a higher risk of complications of chronic pan-creatitis, and being an unfavorable prognostic response factor to the ongoing cure -th. Mutation N34S is often found in persons without pancreatitis, which presupposes its action as a modifier of the disease, determining an increased risk of chronic pancreatitis and its more severe course in patients with other risk factors-biliary pathology, smoking,

alcoholism, etc. The wide occurrence of N34S mutation with increasing accessibility of genetic methods of investigation will allow to isolate patients in HP, homozygous carriers of this mutation, characterized by a more favorable prognosis and increased risk of complications.

Patients with chronic pancreatitis had a rare occurrence of mutations in the gene of the transmembrane regulator of cystic fibrosis, the absence of homo-zygotic carriers in this mutation, and the absence of mutations in the cationic trypsinogen gene, which indicates that these mutations do not contribute to the pathogenesis of chronic pancreatitis in mixed the Russian population.

The frequency of homo- and heterozygous mutations of the N34S gene of the pancreatic secretory inhibitor of trypsin is significantly more frequent in patients with chronic pancreatitis (9.2% and 5.4%) than in healthy individuals (2.8% and 0.9%), which assumes a significant role of these genetic changes in the development of chronic pancreatitis.

Conclusions. The presence of mutation N34S deter mines the acceleration of the progression of chronic pancreatitis, determines the earlier development of the disease, the greater likelihood of pronounced structural changes in the parenchyma and duct system of the pancreas and the development of complications, increases the risk of severe leakage and the worst response to a conservative treatment.

The presence of mutation N34S determines the low risk of developing chronic pancreatitis without taking into account the etiology – 1.55, moderate risk of toxic chronic pancreatitis – 2.19), high risk of idiopathic chronic pancreatitis 4.62.

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