LITERATURE REVIEW MOLECULAR-GENETIC RESERCH IN NON-ALCOHOLIC FATTY LIVER DISEASE.

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ABSTRACT

The article relates to the study of literature on the subject of genetic polymorphism genes of xenobiotic detoxification in liver cirrhosis, one of the important issues in the area of internal diseases.

Liver cirrhosis (LC) in terms of its socio-economic and medical significance occupies one of the leading places in pathology human beings, characterized by a global distribution, a steady upward trend morbidity, transition to hepatocellular carcinoma, high level in structure of mortality in the world. CP is a polyetiological disease, a universal ending to many inflammatory liver diseases. According to most experts, the most common causes of the disease are alcohol abuse and hepatitis viruses

In various countries, non-alcoholic fatty liver disease (NAFLD) affects from 3 to 30% of the population. Among overweight people, the frequency of detection of various forms of fatty liver disease is 67%, and for obesity – 94% [6]. The development of NAFLD involves cytokines, adipokines, free radical oxidation products that contribute to the development of the inflammatory reaction, necrosis of hepatocytes and ultimately leading to fibrosis up to the stage of liver cirrhosis, but to date there is no consensus on the role of oxidative stress and the antioxidant system in the development of hepatosteatosis in NAFLD [5, 7].

Non-alcoholic fatty liver disease (NAFLD) is the most common diffuse liver disease worldwide. In recent years, the relationship between disorders of lipid metabolism in the liver, changes in antioxidant status and polymorphism of genes affecting fatty acid metabolism in NAFLD has been emphasized.

Most often, NAFLD is benign, but fatty liver is associated with inflammatory processes in hepatocytes with the development of non-alcoholic steatohepatitis (20–30%) and subsequent fibrosis [2, 3]. The rate of onset of irreversible fibrotic transformations in NAFLD is less compared to other chronic liver diseases, such as toxic (alcoholic) or viral, but due to the high prevalence of this pathology, decompensated cirrhosis of the liver as a result of this problem is the third among the reasons for liver transplantation in a number of countries [4–6]. In addition, patients with NAFLD have a high risk of early cardiovascular morbidity and mortality [7]. It is alarming that up to 50% of NAFLD-associated hepatocellular carcinomas may occur in the absence of cirrhosis, thereby worsening prognosis [8].

Most of the work on genetic markers for liver diseases are devoted to alcoholic liver damage. It is known that only a small some long-term alcoholics develop CP.

The risk is associated with both hereditary and other factors. In the work of Miranda-Mendez A. et al., 2010 showed that alcohol-induced organ damage may be associated with hereditary variability in both enzymes involved in alcohol metabolism and enzymes related to free radicals and lipid metabolism (glutathione S-transferases and apolipoprotein E).

Identified genetic disorders concern not only diseases associated with exposure to toxic agents, but also infectious pathogens. Hereditary susceptibility to infectious agents associated with two factors: relatively rare genetic defects leading to immunodeficiencies, as well as (more common) a combination in an individual “normal” gene alleles, separately having a weak effect, but the totality which leads to the formation of immune characteristics that predispose to development of an infectious disease [30, 36].

To date, numerous works have been published on the elements of the multifactorial pathogenesis of NAFLD: changes in lipid metabolism, mitochondrial dysfunction, parenchymal inflammation, oxidative stress, the role of intestinal microbiota in the pathological process. Much attention is paid to the molecular mechanisms of transformation of steatosis into steatohepatitis, the role of oxidative stress as one of the important links in the pathogenesis of chronic liver diseases and the search for candidate genes potentially associated with the development of liver steatosis [9–12].

The role of polymorphisms of some antioxidant defense genes in NAFLD

Antioxidant defense mechanisms in the liver include chemicals such as glutathione (GSH), vitamins C and E, and the enzymes superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), glutathione S-transferase (GST), glutathione reductase (GRx) , peroxiredoxins and thioredoxins [30]. The GST gene system plays an important role in the processes of ensuring and maintaining the normal functioning of all living organisms. This is primarily due to the fact that the genes that make up this system encode enzymes that catalyze various types of chemical transformations in the cell. It is this gene system that plays a primary role, taking part in the second phase of detoxification (neutralization) of xenobiotics and in protecting cells against oxidative stress [31].

Scientists' opinions on the processes of transformation of the antioxidant defense system in the liver in NAFLD are currently contradictory. It has been shown that hepatic GSH content and SOD activity are reduced in patients with hepatic steatosis and are further reduced in patients with steatohepatitis [33]. An animal study (fa/fa mice fed a high-fat diet) confirmed a decrease in hepatic GSH levels as well as a decrease in GRx, GPX, SOD, and CAT activity [34].

Better knowledge of the molecular signaling pathways involved in the pathogenesis of NAFLD and contributing to the progression of hepatic steatosis may open the way to scientific strategies for prevention and therapy, such as pharmaceuticals directly targeting the antioxidant system or acting through nuclear receptors or genes, including . uncoupling proteins, as well as on FA metabolism. Nevertheless, continued scientific research in this direction is justified, since understanding the impact of gene polymorphism on the pathogenesis of NAFLD will help determine the risks of the disease and determine effective treatment strategies

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