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CHANGES IN BIOCHEMICAL PARAMETERS AND FIBROSIS PROCESS BEFORE AND AFTER ANTIVIRAL THERAPY WITH EXTRAHEPATIC MANIFESTATIONS OF CHRONIC VIRAL HEPATITIS C

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Abstract
Global morbidity and mortality fromhepatitis C virus (HCV) infection continue to increase. Its complications, which include cirrhosis of the liver, hepatocellular carcinoma (HCC), and livercfailure, cause approximately 700,000 deaths each year. Antiviral therapy can completely cure patients with HCV infection. However, since the disease is initially asymptomatic, many infected people are unaware of their condition, and those who are correctly diagnosed often do not have access to treatment.

Introduction

Purpose of the study

Study of biochemical parameters and assessment of fibrogenesis in patients with chronic viral hepatitis C with extrahepatic manifestations before and after antiviral therapy

Object and subject of research

150 patients with chronic viral hepatitis C with extrahepatic manifestations (main group) aged 30 to 69 years and 40 healthy individuals (control group 2) will be examined.

Research methods

The following research methods will be used:
1. Clinical Features
2. Blood test:
- General blood test
- Biochemical analysis of blood (Bilirubin, ALT, AsAT, ALP, GGTP, total protein, albumin, urea, creatinine, amylase);
- the method of molecular biology (PCR diagnostics);
- serological tests (ELISA diagnostics).
- Fibrotest (determination of the level of collagen III and collagen IV)
3. Instrumental (ultrasound and liver fibroscanning);
4. Statistical (use of special computer programs for medical and biological research).

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Topicality of the topic

Global morbidity and mortality from hepatitis C virus (HCV) infection continue to increase. Its complications, which include cirrhosis of the liver, hepatocellular carcinoma (HCC), and liver failure, cause approximately 700,000 deaths annually [1,2]. Antiviral therapy can completely cure patients with HCV infection. However, since the disease is initially asymptomatic, many infected people are unaware of their condition, and those who are correctly diagnosed often do not have access to medical care [3,4].

The significance of this pathology is due to a high level of morbidity, an increase in the number of virus carriers, a change in the age structure of infected people with a predominance of young people, and an increase in the percentage of extrahepatic manifestations. It was found that after 10 years from the moment of infection, 5-10% of patients with chronic hepatitis C develop a complication of hepatitis cirrhosis, and after 20-30 years, 20% -25% of patients (Rakhimova V. Sh. etal., 2020) have this complication.

Chronic HCV infection is a disease that occurs not only with liver damage, but also with extrahepatic manifestations, the most common of which are mixed cryoglobulinemia and vasculitis [4]. Patients who have developed cryoglobulinemic syndrome are a complex population, whose effective treatment requires, first of all, elimination of the etiological factor (appointment of antiviral therapy), pathogenetic drugs, and consolidation of efforts of specialists of various profiles [5-7]. The clinical course of hepatitis C virus (HCV) infection is sluggish and can affect several organ systems. A variety of extrahepatic manifestations (EP) of chronic HCV infection have been reported, including mixed cryoglobulinemia (SC), thrombocytopenia, aplastic anemia, autoimmune thyroiditis, arthropathy, membranoproliferative glomerulonephritis (MG), peripheral neuropathy, pulmonary fibrosis, and skin diseases such as lichen planus. late skin rash syndrome, type 2 diabetes, and moray eel ulcer [8,9,10].

It has been established that the pathogenesis of extrahepatic manifestations in chronic hepatitis C is based on various mechanisms: the possibility of hepatitis C virus replication in the extrahepatic region, the manifestation of immunocompetent cells, the connection of HCV infection with B-lymphocyte using CD 81; genotype heterogeneity and frequent mutations of the virus genome due to prolonged presence of the virus in the body; induction of a cascade of immunopathological reactions which will lead to activation of lipid peroxidation processes in the hepatic parenchyma. [11,12]. It is well known that HCV leads to cirrhosis, end-stage liver disease, and hepatocellular carcinoma [13-16]

HCV disease is a serious, mostly hidden public health problem that requires large direct and indirect costs. The possibility that HCV infection can now be eradicated with new antiviral treatments is important from a therapeutic and preventive point of view in relation to the hepatic and other consequences of the disease [17,18]

The possible role of such predictors as insulin resistance and type 2 diabetes mellitus, pathology of the kidneys, thyroid gland, eyes, stomach, cardiovascular system, and inducing the development of rheumatological, neurological, and dermatological diseases in the pathogenesis is considered [19]. In addition, in chronic hepatitis C, clinical manifestations of extrahepatic complications can be detected even before the appearance of liver disorders.

The mechanisms of extrahepatic lesions are not fully understood. Cytokine release and oxidative stress are mentioned among the causes that lead to them [20-22]. The disease is more common among the elderly, mainly women with a long history of HCV, and also occurs in 40% of patients

at the stage of established cirrhosis of the liver [17]. The development of neurological complications is mainly associated with immune disorders and demyelination [23]. At the same time, the severity of neurological disorders, including peripheral nerve damage, does not depend on the severity of the underlying disease [24].

However, as it was found out, the direct pathological influence of the hepatitis C virus is also important. Most often, HCV is associated with mixed infection.

cryoglobulinemia (type II or III) and its complications (cutaneous, neurological, renal, rheumatological), the frequency of which, according to some data, is 20-80% [19].

In the pathogenesis of mixed cryoglobulinemiacaused by HCV infection, the key point is the deposition of cryoprecipitate on the endothelium of small vessels with subsequent development of vasculitis with signs of lymphocytic infiltration around the vessels without necrosis sites [22]. In patients with HCV and cryoglobulinemia нередко поражается , the peripheral nervous system is often affectedwith manifestations of polyneuropathy [20]

A common characteristic of all chronic liver diseases is the appearance of fibrosis and its progression to cirrhosis [23]. Assessment of the severity of liver fibrosis is of great importance for determining risk factors for its progression, prognosis of the disease, and prescribing antiviral and antifibrotic treatment. In clinical practice, there are several ways to determine the stage of liver fibrosis [24].

It has been established that extrahepatic manifestations in any form appear in 74% of patients with chronic HCV infection, long before manifest liver disease, manifested by various non-specific health disorders, including malaise, fatigue, nausea, weight loss, and musculoskeletal pain [16] Studies have shown that extrahepatic manifestations include arthralgia, myalgia, glomerulonephritis, Raynaud's phenomenon, Sjogren's syndrome, Hashimoto's thyroiditis, Graves ' disease, ulcerative keratitis, peripheral neuropathy, and cryoglobulinemic vasculitis [17,18].

Nevertheless, the currently used antiviral therapy is effective in eliminating CHC with a stable negative virological response [19].

Persistent HCV infection is the leading cause of chronic liver disease.

It is noteworthy that extrahepatic manifestations occur in three-quarters of patients with chronic HCV infection, and cryoglobulinemia is the most common manifestation, in 40-60% of infected patients [20].

The pathophysiological mechanism that leads to these outcomes is persistent inflammation, followed by progressive fibrosis and, ultimately, vascular and architectural changes in cirrhosis. Timely diagnosis and treatment of advanced fibrosis can prevent complications and death; however, optimal risk stratification is necessary to avoid unnecessary and potentially wasteful resource allocation [21].

Despite the above, all the details of the diagnosis of extrahepatic manifestations of CHC have not yet been definitively revealed, there is little information on the clinical and diagnostic characteristics of fibrosis in these patients, and materials on the relationship between the level of serum cytokines and the stages of liver fibrosis in these patients are rare and scattered [22].

Conclusion

Determination of the level of collagens of the third (Col3) and fourth types (Col4) in CHC of various etiologies is used by researchers in different countries both to recognize the stage of fibrosis and to monitor the effectiveness of the therapy used, but further accumulation of

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information on the clinical significance of fibrogenesis and fibrolysis products in these diseases is required.

Thus, many questions concerning the mechanisms of the damaging effect of hepatotropic viruses on the liver, in the progression of pathology, and the development of extrahepatic manifestations remain open.

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