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Changes of some clinical-laboratory parameters in patients with chronic hepatitis C, depending on the presence of cardiovascular risks

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Abstract

Hepatitis C in different countries is a serious problem of modern Infectology. Despite the large amount of studies devoted to the study of HCV-infection, the mechanisms of progression of chronic hepatitis C in patients with concomitant pathology today are not quite clear. The aim of this study is to examine the clinical-laboratory peculiarities of chronic hepatitis C, depending on the presence of cardiovascular risks. It was determined that in patients with chronic hepatitis C with concomitant total cardiovascular risk there were significantly higher levels of hyperbilirubinemia and increase of cytolytic syndrome more severe violation of T-cell immune response to antigens of HCV infection that is manifested by the increased levels of IL-4 and TNF- α and the decreased levels of IL-2, and significantly higher levels of viral load.

Keywords: chronic hepatitis C, total cardiovascular risk, biochemical parameters, immunological parameters, the viral load

1. Introduction

Hepatitis C (HC) in different countries is a serious problem of modern Infectology. In Ukraine there is a steady increase in the incidence of hepatitis C, which supersedes in importance hepatitis B. According to the experts of WHO, more than 3% of the world population is infected with the virus HC, and at present there is a pandemic, which in its scope and the number of infected people is 4-5 times higher of the occurrence of HIV-infection. Long-term persistence of the virus in chronic HC (CHC) can be the basis for progressive liver damage and leads to the formation of liver cirrhosis with subsequent high risk of hepatocellular carcinoma [1-3].

In recent years, much attention is paid to study of the peculiarities of CHC against the background of other pathological conditions that can modify the course of the disease. It is extremely important to study peculiarities of CHC course on the background of the most common diseases of the human population- cardiovascular disease, which according to WHO is the leading cause of death worldwide, and according to experts, by 2030, mortality from cardiovascular disease (CVD) will reach 23.3 million persons per year. CVD ranks the first place in the structure of deaths of citizens of Ukraine (66.6%), and this figure is still one of the highest in the structure of mortality in Europe [4]. In the scientific literature there are many reports of a close connection between CVD and liver diseases, which is caused by many factors with different mechanisms, the common effect of which in one direction leads to deterioration of diseases course both of these bodies. Interconnection between the dysfunction of the liver and cardiovascular system should be viewed from two perspectives: on the one hand the changes that occur in the liver, are caused by disorders of central hemodynamics, oxygen starvation and humoral disorders; and on the other - chronic HCV liver pathology can be an important factor for the emergence or strengthening of the existing cardiovascular disorders and can affect prognosis [5]. Many researchers believe that T-cell immunity is the main factor that affects the elimination of the virus, the course and chronization of HCV-infection, but in most cases neither T-link nor B-link of the immunity are unable to stop the abnormal persistence and pathologic impact of HCV. Today there are enough facts confirming the close interaction between the level of cytokines and clinical course of HC [6]. It is proved that pro-inflammatory cytokines are mediators of interaction between cells, they support local inflammation, are capable to perform cardio-depressive effect, enhance myocardial ischemia and thus substantially alter the clinical course of the disease, i.e. they are markers of unfavorable prognosis and high cardiovascular risk [7].

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The Aim of the Research

Study of the clinical and laboratory peculiarities of chronic hepatitis C, depending on the presence of cardiovascular risks.

Materials and Methods

The work is based on examination of 80 patients with chronic hepatitis C in virus replication phase, hospitalized in hepatological center of Ivano-Frankivsk Regional Clinical Infectious Diseases Hospital. Among all of the studied patients there were men 56.25%, women - 43.75%. The age of patients ranged from 18 to 55 years. Of the 80 studied patients there were 63 residents of the city (78.75%). According to epidemiological anamnesis blood transfusion occurred in 21 individuals (26.25%), surgical interventions - in 11 (13.75%), donation - in 6 (7.5%), also all the patients confirmed visiting the dentist. The diagnosis was established on the basis of determining markers of hepatitis C virus (anti-HCV) and RNA HCV. Patients with moderate active hepatitis dominated. All examined patients with chronic HCV-infection were divided into two groups depending on comorbidity. I group (basic) - 40 patients with chronic hepatitis C with increased total cardiovascular risk, II group (comparison) - 40 patients with chronic hepatitis C without increased total cardiovascular risk. The control group: 30 healthy individuals of the same age to establish the limits of normal values of physiometric, biochemical and immunological parameters.

The stratification of cardiovascular risk was performed under unified clinical protocols of primary, emergency and secondary (specialized) medical care "Arterial Hypertension" (Ministry of Health of Ukraine № 384 from 24.05.2012). The major risk factors were determined: blood pressure > 130/85 mm. Hg; abdominal obesity (waist circumference in men > 102

cm, in women > 88 cm); triglycerides (TG) ≥ 1.7 mmol/l; high-density lipoprotein cholesterol (HDL cholesterol) < 1.3 mmol/l; fasting glucose 5.6-6.9 mmol/l.

We have used the following methods: general clinical examination, biochemical tests (bilirubin total and direct, ALT, AST, total protein, creatinine, urea, thymol titer tests, prothrombin index, total cholesterol, triglycerides, HDL cholesterol, blood glucose). For a fuller and deeper understanding of the pathological process in CHC the spontaneous production of several cytokines of tumor necrosis factor- α was studied (TNF- α), interleukin-2 (IL-2), interleukin-4 (IL-4), their levels in blood serum.

Results and Discussion

The highest percentage of patients with chronic hepatitis C with increased total cardiovascular risk is at the age of 20 to 39 years (68.75%), i.e. for the most hard-working and reproductive age. Comparing the incidence of individual symptoms and syndromes it should be noted that there was no significant differences when comparing patients with concomitant cardiovascular risk patients and a comparison group. The only significantly difference ($p < 0.05$) was a symptom of dryness of mucous membranes. The predominant complaints were complaints of general weakness, heaviness in the epigastric, reflection, joint pains and pain in the right hypochondrium.

For a thorough study of cytolytic and cholestatic syndromes, as well as studying the function of lipid metabolism in the liver a detailed study to determine changes in biochemical parameters was performed. It was found that among patients with cardiovascular risk and patients without it, there is significant difference ($p < 0.05$) (Table 1).

Table 1: The levels of biochemical parameters in patients with CHC with increased and without increased total cardiovascular risk (M \pm m)

Indexes	Healthy (n = 30)	I group (n = 40)	II group (n = 40)	P ₁	P ₂	P ₃
Bilirubin total, mmol/l	11.95 \pm 1.05	33.50 \pm 0.25	24.60 \pm 6.34	<0.05	<0.05	<0.05
Bilirubin direct, mmol/l	2.27 \pm 0.21	8.27 \pm 0.50	5.42 \pm 1.79	<0.05	<0.05	<0.05
ALT, mmol/l*h	0.28 \pm 0.01	1.36 \pm 0.21	1.48 \pm 0.14	<0.05	<0.05	>0.05
AST, mmol/l*h	0.39 \pm 0.02	1.62 \pm 0.15	1.35 \pm 0.08	<0.05	<0.05	<0.05
Prothrombin index, %	86.0 \pm 5.3	71.4 \pm 1.9	79.0 \pm 4.7	<0.05	>0.05	<0.05
Thymol test, units	2.8 \pm 0.2	10.2 \pm 1.2	6.1 \pm 0.5	<0.05	<0.05	<0.05
Creatinine, mmol/l*h	77.9 \pm 4.7	86.04 \pm 2.01	78.2 \pm 2.67	<0.05	>0.05	<0.05
Urea, mmol/l	6.3 \pm 0.75	7.02 \pm 0.54	6.25 \pm 0.44	>0.05	>0.05	>0.05

Note: P₁ - significant difference between the patients of the I group and healthy individuals; P₂ - significant difference between the II group patients and healthy individuals; P₃ - significant difference between the patients in groups I and II.

The level of total bilirubin in patients of the main group was 33.50 \pm 0.25 mmol/l, direct- 8.27 \pm 0.50 mmol/l, in patients of comparison group 24.60 \pm 6.34 mmol/l and 5.42 \pm 1.79 mmol/l respectively ($p < 0.05$). The tendency to the increase of aspartate aminotransferase activity index in patients of the main group to the level of 1.62 \pm 0.15 mmol/h*1, compared to the same index in the comparison group (1.35 \pm 0.08 mmol/l*h) ($p < 0.05$). In the main group of patients there was found significantly lower level of prothrombin index - 71.4 \pm 1.9% and rising of thymol test - 10.2 \pm 1.2 un. compared to the comparison group patients (79.0 \pm 4.7% and 6.1 \pm 0.5 un. respectively) ($p < 0.05$). Of the above data we can conclude that a more pronounced cytolytic syndrome and hyperbilirubinemia level were observed in patients with chronic hepatitis C with concomitant total cardiovascular risk.

It should be noted that in the group with increased cardiovascular risk viral load before the treatment was significantly more than 1.8 times than in the group without cardiovascular risk ($p < 0.05$) (4.7*10⁶ \pm 2.5*10⁵ IU vs 2.6*10⁶ \pm 1.2*10⁵ IU, respectively).

Modern proven factors of regulation of the inflammatory responses in the body is an imbalance of inflammatory, pro-inflammatory and growth-stimulating factors. Research in peripheral blood serum of the levels of TNF- α , IL-2, IL-4 allows to determine the depth of involvement of hepatocytes in mitochondrial failure, intracellular activity of inflammatory processes. As a result of studying the cytokine profile there were revealed the following changes in levels of IL-2, IL-4, and TNF- α (Table 2).

Table 2: Levels of IL-2, IL-4, and TNF- α in patients with chronic hepatitis C with increased and without increased total cardiovascular risk (M \pm m)

Indexes	Healthy (n = 30)	I group (n = 40)	II group (n = 40)	P ₁	P ₂	P ₃
IL-2, Pg/ml	10.11 \pm 0.33	3.40 \pm 0.37	4.37 \pm 0.31	<0.05	<0.05	<0.05
IL-4, Pg/ml	2.06 \pm 0.19	7.63 \pm 0.37	6.21 \pm 0.29	<0.05	<0.05	<0.05
TNF- α , Pg/ml	4.85 \pm 1.03	7.66 \pm 1.22	7.06 \pm 1.09	<0.05	<0.05	>0.05

Note: P₁ significant difference between the I group patients and healthy individuals; P₂ - significant difference between the II group patients and healthy individuals; P₃ - significant difference between the patients in groups I and II.

Analyzing the data presented in Table 2, a tendency to the decrease of IL-2 level, the increase of level of IL-4 and tumor necrosis factor- α compared with healthy individuals, was determined. It should be noted that when comparing levels between patients with cardiovascular risk or without it there was revealed a significant difference ($p < 0.05$). Patients of the main group (I group) the level of IL-2 was 1.28 times lower compared to the comparison group (II group). The level of IL-4 in patients of the I group on the contrary has increased 1.22 times compared with patients of the II group. Tumor necrosis factor- α was also higher 1.08 times in patients of the I group compared with those from the II group. The above said indicates that the change of indexes of IL-2, IL-4, and TNF- α in patients with chronic hepatitis C have prognostic criteria of severe complications in the functional state of the liver and suggest tension in the system of pro-inflammatory-regenerative cytokines of hepatocytes.

Conclusions

1. The highest percentage of patients with chronic hepatitis C with increased total cardiovascular risk was in the age of 20 to 39 years, that is the most hard-working and reproductive age.
2. Dim severity of clinical symptoms indicate the difficulty of differentiating between patients with chronic hepatitis C patients with concomitant total cardiovascular risk and without it.
3. In the analysis of biochemical parameters there was revealed that in patients with chronic hepatitis C with concomitant total cardiovascular risk there were significantly higher levels of hyperbilirubinemia and increase of cytolytic syndrome as opposed to the comparison group.
4. In patients with chronic hepatitis C with increased total cardiovascular risk is more pronounced violation of T-cell immune response to antigens of HCV infection is manifested by increased levels of IL-4 and TNF- α and decreased levels of IL-2 as well as significantly higher viral load.

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