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THE STUDY OF VARIOUS ASPECTS OF THE GAMMA-INTERFERON PRODUCTION IN PATIENTS WITH CHRONIC HEPATITIS B AND C.

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SUMMARY

From the moment of its first discovery in 1957 to the present, interest in the study of interferon in the world has only increased. We conducted a study of spontaneous and induced production of gamma-interferon in patients with chronic viral hepatitis B and C. The purpose of the mini-study was to identify the potential for the production of gamma-interferon, which is an important factor in viral diseases. As a result, it was found that in patients with chronic viral hepatitis B and C, the potential ability of the body to induce interferon gamma is depleted.

KEY WORDS: *Gamma-interferon, induction, immunity, HBV, HCV.*

According to WHO, in 2015, viral hepatitis caused 1.34 million deaths (this figure is much higher than with HIV). The main causes of death were chronic liver disease (720,000 deaths due to cirrhosis) and primary liver cancer (4,700 deaths due to hepatocellular cancer). Worldwide, 257 million people are infected with the hepatitis B virus (HBV) and 71 million with the hepatitis C virus (HCV). The WHO European Region (which includes Uzbekistan) is in second place in the number of people infected with HCV. Such high rates dictate the need to develop new and modify existing methods of immunomodulatory therapy of patients with such diseases, or at least the correct approach to treatment. For the correct approach to therapy, it is necessary to initially identify certain immunological parameters of patients, in particular, the indicators of gamma-interferon (γ-INF). At the same time, not just serum indicators, but also the so-called "spontaneous" and "induced" production of γ-INF.

Interferons (INF) were the first cytokines to be effective in the treatment of viral infections and malignant tumors.[1] Discovered in 1957 as substances produced by virus-infected cells[2], interferons are a family consisting of three types and are pleiotropic cytokines.[3] This individual cytokine family has antiviral, antiproliferative, apoptotic and immunomodulating properties.[3] The classification of a family into three types is based on the fact that genes encoding different types are on different chromosomes, even in the ability to bind to different receptors, etc.

Gamma-interferon (γ-INF), the only member of type II interferons[4], as already mentioned, has a wide range of biological effects that occur when the "inclusion" of a specific element of the immune response against biological pathogens, including HBV and HCV. Produced only by activated T-lymphocytes and natural killers[5], it plays a crucial role in the regulation of immunological processes. More than 200 genes can be activated under the influence of γ-INF.[6] Relatively recently, studies have emerged that prove a strong inhibition of γ-INFV replication of HCV in cell culture models.[6, 7, 8] But since these studies were conducted on models, cell culture of infected HCV, we can not be sure that these studies took into account the natural, internal background for γ-INF.

All these facts indicate the feasibility of studying this cytokine and its evaluation. The level of γ-INF concentration in serum or blood plasma reflects the current state of the immune system, "spontaneous" production indicates how much blood cells have already been activated *in vivo*, and "induced" – allows you to evaluate the potential ability to induce γ-INF.

THE AIM OF THE STUDY

Comparison of the levels of serum, spontaneous and induced indicators of the concentration of γ-INF in patients with chronic viral hepatitis B and C (CHGB; CHGC) with the control group of practically healthy people.

MATERIALS AND METHODS

We studied the sera of 5 patients with HBV (of whom 3 were men and 2 women) and 12 patients with HCV (of whom 2 men and 10 women). The control group included 6 practically healthy people (3 of them are men and 3 women). γ-INF was determined by ELISA, Vector-Best reagents (Novosibirsk) in the laboratory of immunopathology and immunopharmacology. The level of serum γ-INF was determined immediately after the release of serum. Whole blood in each patient was diluted in "Nutrient medium 199" at a ratio of 1: 4 (spontaneous production), 1 ml of diluted sample was taken from the same tube for mitogen induction containing phytohemagglutinin (Cytokine-Stimul-Best kit). Both types of samples were incubated for 24 hours at a temperature of 37 ° C in a thermostat.

The obtained data was statistically processed in Microsoft Excel 2013 by calculating the arithmetic mean value (M), standard deviation (σ), standard error (m), Student's criterion (t) with the calculation of the error probability (P). The results were compared with the corresponding indicators of the control group.

RESULTS AND DISCUSSION

On examination, patients with HBV complained of: fatigue (40%), weakness (60%), loss of appetite (40%), pain in the right hypochondrium (80%), flatulence (60%), nausea (20%), bitter taste in the mouth (40%), headaches (20%); patients with HCV: fatigue (41.6%), weakness (83.3%), loss of appetite (83.3%), pain in the right hypochondrium (66.7%), abdominal pain (33.3%), flatulence (83.3%), nausea (58.3%), bitter taste in the mouth (25%), headaches (8.3%), dizziness (8.3%).

The average statistical indicators of the γ-INF results of patients with HBV: serum - 8.00 ± 0.97 pg / ml, $p < 0.001$ (control - 1.86 ± 0.21 pg / ml); after incubation: spontaneous - 18.8 ± 1.37 pg / ml, $p < 0.001$ (control - 1.9 ± 0.18 pg / ml); induced - 18.77 ± 0.71 pg / ml, $p < 0.001$ (control - 9.5 ± 1.49 pg / ml).

The average statistical results of the γ-INF results of patients with HCV: serum - 7.22 ± 0.5 pg / ml, $p < 0.001$ (control - 1.86 ± 0.21 pg / ml); after incubation: spontaneous - 17.44 ± 0.53 pg / ml, $p < 0.001$ (control - 2.01 ± 0.19 pg / ml); induced - 18.44 ± 1.14 pg / ml, $p < 0.001$ (control - 7.64 ± 1.35 pg / ml) (Table 1.).

Table 1. Comparative table of results (unit of measurement *pg/ml*).

	Patients with HBV	Patients with HCV	Control
Serum	8,00±0,97*	7,22±0,50*	1,86±0,21
Spontaneous	18,8±1,37*	17,44±0,53*	2,01±0,19
Induced	18,77±0,71*	18,44±1,14*	7,64±1,35

It is seen that in the groups of patients all types of indicators are several times higher than the corresponding indicators in the control group. It is noteworthy that patients have no difference between spontaneous and induced production. In the control group, the ratio of indicators of spontaneous and induced γ-INF production is at least 1: 3, which shows the potential for induction. High rates of spontaneous production in patients indicate that the patients' lymphocytes have already been activated *in vivo*, and because of the constant persistence of the virus, the resources in the body have been depleted. Most likely, lymphocytes in patients incubated with mitogen did not react to induction, and therefore the production of γ-INF did not exceed the indices of spontaneous production.

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