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Assessment Of The Process Of Acetylation And Lipid Composition Of Blood In Patients With Chronic Periodontitis Against The Background Of Viral Hepatitis C

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Annotation. The purpose of this study was to study the relationship between alel variants of acetylation and the lipid composition of blood in patients with chronic periodontitis against the background of viral hepatitis C. Biochemical studies were carried out in 42 people aged 18-45 years (24 men and 18 women) diagnosed with chronic periodontitis against the background of chronic hepatitis C. The phenotype of acetylation in saliva and the lipid spectrum of blood were studied. The prevalence of the disease among patients with slow type of acetylation in saliva was noted at an average of 17% in the examined patients of the study group. In patients with slow type of acetylation, a high level of triglycerides was noted, which was accompanied by a low concentration of cholesterol, high and low density lipoproteins in the blood.

Key words: chronic generalized periodontitis, viral hepatitis C, acetylation phenotype, blood lipid spectrum.

Introduction

Numerous studies have shown that population-based studies of phenotyping significantly increase the effectiveness of pharmacotherapy and reduce the number of side effects during its implementation [4,5,9,27]. In this regard, the study of acetylatory phenotypes of the population has recently become increasingly interesting, since it has been established that acetylation processes occupy a central place in interstitial metabolism. In addition, as recent studies have shown, an individual's belonging to a particular group of acetylators may be one of the factors that determine different resistance to liver disease [11,13,18,21].

Acetylation processes occupy a central place in intercellular metabolism. For example, oxidative decarboxylation of pyruvic acid, synthesis and breakdown of fats, synthesis of acetylcholine, steroids, etc. are carried out by acetylation [14,15,31,37].

Acetylation is considered as the genetically determined ability of an organism to metabolize compounds containing amino groups in its molecule. Depending on the rate of acetylation in the human population, two groups are distinguished. One of them includes individuals metabolizing test drugs at a high rate (rapid acetylation), the other includes individuals who metabolize test drugs at a low rate of process (slow acetylation) [17,19,20,52].

It is known that the level of cholesterol in the blood depends on genetic factors and partly on the content of cholesterol in food. Cholesterol synthesis is carried out in the cells of almost all organs and tissues, in significant quantities — in the liver (80%), the wall of the small intestine (10%) and the skin (5%) [23,24,39]. It should be noted that in the works of Shevchenko O.V. and co. (2012), proven. that "slow" allelic variants of the NAT2 gene contribute to a decrease in the level of the enzyme N-acetyltransferase by slowing down the conversion reaction of acetyl CoA to acetoacetyl-COA and disrupting the multistep chain of cholesterol synthesis. It should be noted that lipid metabolism is deeply involved in the molecular mechanisms of the viral hepatitis infection cycle [42,43,49]. Based on the above, the unique interaction between the hepatitis virus and lipid metabolism makes it possible to deeply study the role of lipids at all stages of the viral infection cycle, especially in the manifestations of periodontal diseases chronic periodontitis secondary to viral hepatitis C, which could potentially help to better understand the role of certain lipids in cellular metabolism [33,34,36,44,51].

The purpose of this study was to study the relationship between alel variants of acetylation and the lipid composition of blood in patients with chronic periodontitis against the background of viral hepatitis C.

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Material and methods of research

To achieve this goal, we conducted a biochemical study in 42 people aged 18-45 years (men - 24 and women - 18),
who are on inpatient treatment in the Scientific and Practical Medical Center for Epidemiology, Microbiology, Infectious and Parasitic Diseases, in the II Department of Chronic Viral Hepatitis with a diagnosis of chronic hepatitis C. The studies were conducted in strict accordance with the requirements of biomedical ethics in accordance with the Geneva Convention on Human Rights (1997) and the Declaration of Helsinki of the World Medical Association (2000) on the basis of the permission of the local ethics committee. All patients received written voluntary informed consent to participate in the study.

Inclusion criteria: verified diagnosis of chronic viral hepatitis C detected by PCR using the test system, patients who have not used drugs in the last six months and have not received antiviral therapy. Patients under 18 years of age with concomitant viral hepatitis B, D or other diseases causing liver damage, HIV infection, history of pulmonary tuberculosis, autoimmune, oncological diseases, as well as pregnant women were excluded from the study. In order to determine the control values of the studied parameters of the hemostasis system, 16 healthy individuals aged 25 to 45 years who gave informed consent to the examination were examined. who did not differ from patients by sex and age, who did not have the results of biochemical and serological studies of viral hepatitis, as well as other liver diseases according to the anamnesis, the results of biochemical and serological studies. All patients underwent a standard clinical and laboratory examination according to the liver pathology program. Diagnosis of chronic hepatitis was carried out on the basis of clinical (liver pain, dyspeptic syndrome, astheno-vegetative syndrome, hepatomegaly, jaundice) and laboratory (cytolysis syndrome, cholestasis, inflammation, minor liver failure) syndromes. Indication of HCV-PHK, determination of the genotype of the virus, viral load level by polymerase chain reaction (PCR). Glycemia, lipid spectrum (total cholesterol (CS), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, very low-density lipoproteins (VLDL), triglycerides (TG)), apolipoproteins A (ApoA1) and B (ApoB) were determined.

Patients and individuals in the control group took 0.5 g of sulfodimezin on an empty stomach. The level of free and total sulfodimezin (DM) was determined by spectrophotometry at a wavelength of 400 nm. The level of acetylated DM was determined by the formula: ACS = OBS - SHS, where ACS - acetylated DM, OBS - total DM, SHS - free DM. When assessing the type of acetylation, the phenotyping criterion was the value of the fraction of the dose of the free drug substance excreted by saliva. For this purpose, the content of the freely excreted test drug was found in hourly saliva samples within 7 hours after drug administration.

Determination of sulfadimezin in saliva when using the BPO reagent. 1 ml of saliva was taken, 1 ml of water was added, then 1 ml of 10% zinc sulfate solution and 1 ml of 0.75 M sodium hydroxide. Centrifuged for 10 minutes at 9000 rpm. Next, 3 ml of supernatant liquid was taken, 1 ml of phosphate buffer (pH 6.86), 0.5 ml of BPO was added. Optical density was measured at a wavelength of 500 nm. The acetylation phenotype (fast and slow acetylators) was determined by the method of B. Evans (1969) in the modification of L.N. Bulovskaya (1982) by the percentage of acetylated sulfademyzine in the blood of patients 5 hours after taking the drug. At the same time, fast acetylators were considered to be persons in whom 50% of sulfadimezine or more was acetylated in 5 hours, and slow - less than 50%.

Statistical processing of the results was carried out using the applied analysis package of the spreadsheet editor Microsoft Excel 2002. The mean sample and the error of the mean *(M ± m) were calculated*. The significance of the differences for dependent and independent samples between the two means was evaluated by the Student's f-test. Differences in the compared indicators were taken as reliable results at $p < 0.05$.

Research results and discussion

As can be seen from the presented results of the studies presented in Table 1, from the main composition of the examined patients with chronic periodontitis against the background of viral hepatitis C, the fast type of acetylation (acetylation rate >50%) was observed in 36 patients from the total number of examined, while slow acetylation (acetylation intensity <50%) was observed in 6 patients from the total number of examined.

Table 1

61,42+5,26

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Показатель	Быстрое ацетилирование n=36	Медленное ацетилирование n=6
Интенсивность ацетилирования ,%	38,58+3,24	61,42+5,26

Analysis of the results of serological diagnostics and the type of acetylation revealed that in patients with a very high level of acetylation, chronic inflammation of the periodontium against the background of viral hepatitis C was more often found in saliva liver damage and signs of hypersensitivity to drugs. Consequently, patients with slow acetylation have a significantly higher risk of developing extrahepatic diseases and many complaints of hypersensitivity to drugs induced by viral hepatitis C, while patients with high acetylation have a lower response to the dental drugs used. This condition can also be one of the causes of insufficient delivery of lipids by the liver and an imbalance of their content in the blood. As a result of impaired synthesis and delivery of lipids to various organs and tissues, the pathogenetic mechanisms of the permeability of membrane structures are disrupted, manifested as inflammation and contact sensitization due to low antimicrobial protection of the oral mucosa.

The study of the state of lipid metabolism indices in 42 patients with chronic periodontitis against the background of viral hepatitis C showed the following dynamics presented in Table 2. As evidenced by the data of Table 2, dyslipidemia is observed in the blood serum of patients with rapid acetylators, which is expressed in a significant increase in the content of total cholesterol, low-density lipoproteins and triglycerides in comparison with the control group. In contrast, this group of patients showed a decrease in HDL levels.

Table 2

2.52±0.24*

Показатели	Здоровые лица n=16	Больные с вирусным гепатитом n=42	
		Быстрые ацетиляторы n=36	Медленные ацетиляторы n=6
Холестерин ммоль/л	4,68±0,27	4,71±0,31	3,39±0,27*
ЛПВП. ммоль/л	1,23±0,12	1,19±0,12	1,01±0,11
ЛПНП. ммоль/л	2,19±0,14	2,31±0,24*	2,08±0,16
Index	Rapid Acetylation	Slow acetylation	Acetylation intensity, %
38,58+3,24	61,42+5,26	1,42±0,15*	2,52±0,24*

Note: * - the significance of the differences P< 0.05 relative to the indicators of the comparison group

A different dynamics was observed in patients with a slow acetylator. Thus, a significant decrease in blood cholesterol by 27.6%, HDL - by 18%, LDL - by 5.1% was noted. On the contrary, in this group of patients, the VLDL content increased by 66% and the concentration of triglycerides in the blood by 2.25 times. In our opinion, mutations in the NAT2 gene leading to slow acetylation disrupt the process of cholesterol synthesis N-acetyltransferase, slowing down the conversion reaction of acetyl-CoA to acetoacetyl-CoA and disrupting the multistep chain of cholesterol synthesis [7]. At the same time, gene polymorphisms of cholesterol metabolism can be an important factor in changing the level of cholesterol and VLDL, which can also affect the immunoregulatory effect of cholesterol in the skin.

Findings

1. Patients with chronic periodontitis against the background of viral hepatitis C are statistically heterogeneous in the activity of acetylation processes, where the prevalence of the disease among patients with a slow type of acetylation in saliva is on average 17%.
2. In the peripheral blood of patients with chronic periodontitis against the background of viral hepatitis C in the group with a slow type of acetylation, a high level of triglycerides was noted, which was accompanied by a low concentration of cholesterol, high-density and low-density lipoproteins in the blood.

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