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A TWO-WAY PROBLEM: INSULIN RESISTANCE AND NON-ALCOHOLIC FATTY LIVER DISEASE

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Annotation: We live in an era when infectious diseases as the main causes of death in economically developed countries have been replaced by chronic non-infectious diseases, among which a significant placeassigned to cardiometabolic pathology. Massive urbanization and the rapidly changing way of life could not but affect the health indicators of the population. The heavy burden of metabolic disorders and their consequences forces doctors of all specialties to increasingly raise this topic [1]. In 1922, G. F. Lang concluded that between. There is a clear connection between arterial hypertension and obesity, carbohydrate metabolism disorders and gout, which was later confirmed by numerous studies [2, 3].

Keywords: cardiometabolic pathology, metabolic syndrome X, hyperinsulinemia, insulin resistance, NAFLD, MAFLD.

Relevance. We live in an era when infectious diseases as the main causes of death in economically developed countries have been replaced by chronic non-infectious diseases, among which a significant placeassigned to cardiometabolic pathology. Massive urbanization and the rapidly changing way of life could not but affect the health indicators of the population. The heavy burden of metabolic disorders and their consequences forces doctors of all specialties to increasingly raise this topic [1]. In 1922, G. F. Lang concluded that between. There is a clear connection between arterial hypertension and obesity, carbohydrate metabolism disorders and gout, which was later confirmed by numerous studies [2, 3]. Later, in 1988, GM Reaven introduced the concept of “metabolic syndrome X”, which included insulin resistance, hyperinsulinemia, impaired glucose tolerance, dyslipoproteinemia, hypertriglyceridemia and hypertension [4]. Today, the accumulated knowledge allows us to take a much broader look at the problem of metabolic syndrome (MS), to specifically consider certain risk factors and choose more personalized approaches to diagnosis and treatment. As part of this review, an analysis of current theories of the pathogenesis of non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes mellitus (T2DM), in which the main place is given to insulin resistance and obesity, is carried out. The literature search was carried out using the keywords “non-alcoholic fatty liver disease”,“type 2 diabetes mellitus”, “insulin resistance” and “obesity” in the Pubmed and Elibrary.ru databases for the period from 1998 to 2021 Current prevalence of NAFLD is 25%, and there is a steady trend towards a steady increase in this indicator [8].It is alarming that NAFLD is already the leading etiology of chronic liver diseases around the world. However, it often tends to progress to liver cirrhosis and hepatocellular carcinoma (HCC), and also increase the risk of both general andand liver disease-associated mortality. Moreover, NAFLD and its consequences most often lead to the need for liver transplantation [9]. So, as mentioned above, NAFLD is associated with metabolic disorders, and, according to some data, it itself represents MS, beingits hepatic component [10, 11]. Thus, in 2020, an international expert consensus statement was published offering doctors of all specialties a new definition - MAFLD: Metabolic (dysfunction) associated fatty liver disease

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[12]. Given the definition fully reflects both the connection between fatty hepatosis and metabolic disorders, and the very versatility of this disease, which affects influence on other organ systems and have consequences far beyond the liver. One of the tips of the iceberg of metabolic disorders, actively discussed today in the medical community, is NAFLD, or, as we now have the right to call it, MAFLD. Another equally serious problem associated with MS is T2DM. Thus, in 2019, the number of patients with diabetes aged 20 to 79 years was 463 million [13]. At the same time, according to forecasts of the International Diabetes Federation, by 2030 every
One in ten adults will have T2DM. [14]. Linking diabetes with liver diseases, it is worth noting that the incidence of NAFLD among patients with T2DM is two times higher than in the general population, which in figures is 55.5% [15]. It is worth noting that in routine endocrinological practice, liver pathology in patients with diabetes often remains in the shadows [16]. Lack of proper
alertness on the part of the primary care physician has its consequences. The combination of these two pathologies not only increases the risk of developing a more severe form of NAFLD and associated with this conditionhospitalizations, but also makes it difficult to achieve glycemic control in people with diabetes and contributes to the development of atherogenic dyslipidemia [17]. Thus, T2DM and NAFLD often coexist, synergistically increasing the risk of adverse outcomes among affected individuals [18–22]. At the same time, the core of such a multifaceted problem as MS is the liver. Being the main body regulating carbohydrate and fat metabolism, the liver combines NAFLD and T2DM. Insulin resistance and obesity are two pathological conditions that choose the liver as one of the main target organs. However, the question of the sequence and mechanisms of development of the significant disorders in NAFLD and T2DM: do these two
diseases in parallel, aggravating the course of MS and increasing thus reducing the risk of cardiovascular mortality ties (CCS), or they represent a chain of sequences body stages of one metabolic continuum. The number of patients with chronic metabolic disorders such as obesity, type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease (NAFLD) is increasing at an alarming rate worldwide in both developed and developing countries. The worldwide prevalence of NAFLD is approaching 25%. Among patients with T2DM, 70–80% are diagnosed with NAFLD[17,18]. Insulin resistance (IR) is recognized as one of the main pathogenetic factors in the development of the most common chronic liver disease - NAFLD. Recently, the problem of non-alcoholic fatty liver disease (NAFLD) has attracted the attention of many clinicians, due to the increasing prevalence and diagnosis of this pathology in the population. Clinically, NAFLD is asymptomatic, and patients seek medical help at the stage of already pronounced changes in the liver[19,20]. Unfortunately, the clinical picture, instrumental and laboratory research methods do not always allow verification of this nosology in the early stages. The only standard for determining the degree of tissue damage remains a morphological examination. In this regard, the problem of early diagnosis and identification of signs of NAFLD is extremely relevant. For many years, changes in the liver due to impaired carbohydrate metabolism were considered a relatively benign condition. In 1980, when Ludwig first introduced the new concept of “non-alcoholic steatohepatitis”, a definition was first formulated [21,22]. Non-alcoholic steatohepatitis (NASH) was regarded as an independent nosological entity, which is characterized by increased activity of liver enzymes in the blood and morphological changes in liver biopsies, similar to changes in alcoholic hepatitis; however, patients with NASH do not drink alcohol in amounts that can cause liver damage [23,24]. In the last few years, researchers have paid close attention to studying both fatty liver disease in general and its variant, non-alcoholic fatty liver disease (NAFLD). The concept of “NAFLD” is clearly defined and covers a spectrum of liver damage, including fatty degeneration (FA), fatty

degeneration with inflammation and damage to hepatocytes - non-alcoholic (metabolic) steatohepatitis (NASH) and fibrosis (with the possibility of progression to cirrhosis) [25,26].

Purpose of the study. This exploratory work aims to determine the contribution of the degree of IR to the progression of NAFLD; comparison of the gold standard for determining IR (clamp test) and using a mathematical model (HOMA-IR).

Research methods. An observational, cross-sectional, open comparative study was conducted on the "case-control" principle. The subjects of the study were patients with overweight and obesity who had not previously been diagnosed with carbohydrate metabolism disorders, without secondary causes of fat accumulation in the liver. During the examination, clinical and laboratory studies were carried out, IR indices were obtained (M-index, HOMA-IR index), a diagnosis of carbohydrate metabolism disorders (or lack thereof) was made, a liver biopsy was performed, and morphological and clinical diagnoses were verified.

Research results. The analysis included information on 60 patients, they were divided into 3 groups: without NAFLD (7 people), with steatosis (18 people), with non-alcoholic steatohepatitis (NASH) (35 people). The groups were comparable in age, gender, body mass index (BMI), and glycated hemoglobin. When assessing the degree of IR using the hyperinsulinemic euglycemic clamp test, a severe degree of IR was detected in 19 people, a moderate degree in 28 people, a mild degree in 8 people, and no IR was detected in 5 people. In the three study groups, the median IR corresponded to the average degree and did not differ significantly. When comparing the gold standard for determining IR and using a mathematical model (HOMA-IR), an inverse significant correlation was revealed (p=0.0001).

Conclusion. The study did not reveal a correlation between the degree of IR and the severity of NAFLD. This result indicates the presence of other pathogenetic factors influencing the progression of NAFLD.

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