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CHANGES IN THE STRUCTURE OF THE LIVER DURING OBESITY (LITERATURE REVIEW)

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The article analyses scientific literature on the actual problem of medical science of the present concerning study and analysis of structural and functional changes in the liver during obesity. One of the most common chronic liver diseases in the modern world is non-alcoholic fatty liver disease which becomes a pandemic on the background of obesity. Data of researches of domestic and foreign scientists about non-alcoholic fatty liver disease represent important evidence of significant structural changes in the liver at different levels of organ organization (organ, tissue, cell, and molecule). The results of scientists` researches point at the fact that 75% of patients with obesity have non-alcoholic fatty liver disease. Almost all the patients have non-alcoholic fatty liver disease during the morbid obesity which is one of the most common liver diseases all over the world and gets the status of the pandemic one nowadays. Pathogenetic mechanisms of non-alcoholic fatty liver disease development are complicate enough and still are the question for scientists to be discussed. Non-alcoholic fatty liver disease is the main hepatic demonstration of the metabolic syndrome and has close connection to the obesity and to the insulin resistance. Obesity leads to changes in the structural organization of the liver which affect on its functional state and metabolic processes. Non-alcoholic fatty liver disease combines several pathological statuses, fatty steatosis or fatty liver dystrophy which has mostly benign character, non-alcoholic steatohepatitis, which is characterized with the progress to the liver fibrosis, and then to the liver cirrhosis, moreover cirrhosis passes into the hepatocellular carcinoma. Many researchers are trying to find the pathological, genetic and morphological features of non-alcoholic liver steatosis and non-alcoholic steatohepatitis during obesity. They are two morphological features or stages of disease: steatosis and steatohepatitis are mentioned in the International Statistical Classification of Diseases and Related Health Problems. Morphologists are still using such terms as "fatty liver dystrophy", "fatty liver", "fatty liver degeneration" and other ones in order to determine two possible forms as stages of disease: steatosis and steatohepatitis. Fatty liver disease is characterized with the fatty scurf in the liver, which leads to the failure of the normal development of hepatocytes. Healthy cells are replaced by the products of the fat exchange (metabolism) and the liver stops its biological functioning. This stage is called liver steatosis and is characterized by the fatty dystrophy of the liver cells. Liver steatosis is the histological indication of non-alcoholic fatty liver disease, development of which one is characterized with the insulin resistance, hyperinsulinism and increased quantity of the liberal fatty acids. The high concentrations of the liberal fatty acids in conditions of the insulin resistance are the main mechanism of forming the steatosis among people with non-alcoholic fatty liver disease. This regularity is confirmed by the results of the clinic and laboratory researches. Accumulation of the certain percent of lipids in the liver cells leads to the appearance of the second stage of the fatty disease – steatohepatitis, which is characterized with the inflammatory processes in the liver and with the necrosis or hepatocytes. The professional literature mentions that investigating the liver biopsy in the conditions of experimental model of non-alcoholic fatty liver disease we can indicate the apoptosis of hepatocytes and expressive changes of the structure and form of hepatocytes (phenomenon of polymorphism). The following factors can cause appearance of the steatohepatitis and non-alcoholic fatty liver disease: obesity, endogenous disorders of the lipid and carbohydrate metabolism, metabolic failures, the syndrome of malabsorption, medication use etc.

The third (the last) stage is characterized with the replacing of the liver cells by cells of the connective tissue. Respectively, we can watch the development of fibrosis and later – cirrhosis, so the liver loses its main functions.

In the professional editions researchers point at the fact that non-alcoholic fatty liver disease appeared due to the bacterial growth in the small intestine. Oxidative liver stress could depend not only on the high concentration of circulating liberal fatty acids during obesity, but also on the high concentration of endotoxins on the background of disbiotic violations being characteristic features of the syndrome of enormous

bacterial growth. Increasing the amount of circulating endotoxins in the portal blood activates the liver Kupfer's cells which lead to the appearance of anti-inflammatory cytokines and chemokines which are the substrate of the inflammatory component of steatosis transformation during non-alcoholic steatohepatitis and induction of fibrogenesis. The study of pathogenetic mechanisms for the development of non-alcoholic fatty liver disease, the classification of risk facts, criteria of diagnosis, estimation of the prognosis of the course of the disease are important for the search and substantiation of effective methods of prevention and treatment.

Keywords: obesity, non-alcoholic fatty liver disease, steatosis, metabolic syndrome, fatty dystrophy.

Introduction. Obesity is one of the most important factors, which is connected to the non-alcoholic fatty liver disease (hereinafter – NAFLD). Metabolic syndrome belongs to those diseases which occur due to obesity, and the main hepatic demonstration of this syndrome is NAFLD. The results of scientific researches point at the fact that 75% of patients with obesity have NAFLD. Almost all the patients during the morbid obesity also have NAFLD which nowadays is one of the most common liver diseases all over the world and gets the status of the pandemic one [9, 12, 13, 24]. Pathogenetic mechanisms of NAFLD development are complicated even nowadays and they are still incomprehensible and discussed by scientists. NAFLD is the main hepatic demonstration of the metabolic syndrome and has close connection to the obesity and to the insulin resistance. Obesity is mostly connected to the illnesses of hepatobilliar tract. Those maladies are quiet spread and are associated with the signs of atherogenic dyslipidemia and morphological and functional changes of liver which ones are characteristics of the steatohepatitis [7]. Scientists set up the higher prevalence the cardiovascular diseases among those patients who has NAFLD, so quantitative indicators of mentioned patients among patients with steatosis and non-alcoholic steatohepatitis increase in 4 and more times. Wherein the level of mortality from cardiovascular diseases in the group of non-alcoholic steatohepatitis is above the level of mortality from liver diseases and is respectively 36% against 6.8% [14, 27, 39]. Epidemiologic researches data pointed at the tendency of raising the amount of patients at the age of 50 and more in two times [5, 6]. The main risk factors among those patients are: the metabolic syndrome, the abdominal obesity, hypertriglyceridemia (up to 46% when the norm is 5%), and arterial hypertension. NAFLD combines several pathological statuses, fatty steatosis or fatty liver dystrophy which has mostly benign character, non-alcoholic steatohepatitis (hereinafter – NASH), which is characterized with the progress to the liver fibrosis, and then to the liver cirrhosis, moreover cirrhosis passes into the hepatocellular carcinoma [13, 26, 32, 33, 34, 35, 36]. A number of authors pointed at the fact that NASH increases the risk of forming the liver cirrhosis and the liver failure. We are often to differ the NAFLD from the alcoholic fatty liver disease (hereinafter – AFLD), which has the same stages but other causes and quick development of pathological process [8, 9, 31, 40].

NAFLD has a tendency to grow its prevalence all over the world and one of the acute questions is its rather diagnostics and effective methods of treatment [8, 9].

There is lack of information on the topic of pathogenetic mechanisms of development of steatohepatosis during obesity.

Analytical literature review. Histological changes of liver were described for the first time by J. Ludwiq in 1980. Learning of pathological and genetic mechanisms of NAFLD development during obesity is an actual problem of the nowadays. Many researchers are trying to find the pathological, genetic and morphological features of non-alcoholic liver steatosis (hereinafter – NALS) and NASH during obesity. They are two morphological features or stages of disease: steatosis and steatohepatitis are mentioned in the International Statistical Classification of Diseases and Related Health Problems [22]. Morphologists are still using such terms as "fatty liver dystrophy", "fatty liver", "fatty liver degeneration" and other ones in order to determine two possible forms as stages of disease: steatosis and steatohepatitis [2, 3, 18, 25, 26]. The number of researches pointed at the fact that NAFLD at the stage of NASH can progress to the cirrhotic stage (cirrhosis and hepatocellular carcinoma) [2, 3, 37, 38].

Fatty liver disease is characterized with the fatty scurfs in the liver, which leads to the failure of the normal development of hepatocytes. Healthy cells are replaced by the products of the fat exchange (metabolism) and the liver stops its biological functioning. This stage is called liver steatosis and is characterized by the fatty dystrophy of the liver cells. Liver steatosis is the histological indication of NAFLD, development of which one is characterized with the insulin resistance, hyperinsulinism and increased quantity of the LFA. The high concentrations of the LFA in conditions of the insulin resistance are the main mechanism of forming the steatosis among people with NAFLD. This regularity is confirmed by the results of the clinic and laboratory researches [10, 20, 21, 28, 32].

Accumulation of the certain percent of lipids in the liver cells leads to the appearance of the second

stage of the fatty disease – steatohepatitis, which is characterized with the inflammatory processes in the liver and with the necrosis or hepatocytes. Professional literature writes that we can indicate the apoptosis of hepatocytes and expressive changes of the structure and form of hepatocytes (phenomenon of polymorphism) by investigating the liver biopsy in the conditions of experimental model of NASH. The causes of appearance of the steatohepatitis and NASH can be found in different factors: obesity, endogenous disorders of the lipid and carbohydrate metabolism, metabolic failures, the syndrome of malabsorption, medication use etc.

The third (the last) stage is characterized with the replacing of the lever cells by cells of the connective tissue. Respectively, we can watch the development of fibrosis and later cirrhosis, so the liver loses its main functions [2, 16].

In the pathogenesis of NAFLD the main hypothesis is the theory of "two kicks" [10, 16]. It was proposed by Day and his co-authors in 1988. First of, certain amount of lipids accumulates in hepatocytes and admission of LFA increases. The high concentration of LFA oppresses the density of hepatocytes to insulin and leads to insulin resistance which is the cause of failure of lipid and carbohydrate metabolism [4, 11, 29] and to the liver steatosis (the first kick). The second 'kick' is characterized with the fatty dystrophy and oxidation of LFA with formation of products of lipid peroxidation and reactive forms of oxygen, which leads to damage of liver cells and formation of steatohepatitis and then – liver fibrosis. The main role in the second stage is performed by inflammation which damages the hepatocytes and leads to their apoptosis and necrosis and provokes the activation of fibrogenesis and then liver cirrhosis [10, 16, 19]. The professional editions point at the fact that NALFD appeared due to the bacterial growth in the small intestine. Oxidative liver stress could depend not only on the high concentration of circulating LFA during obesity, but also on the high concentration of endotoxins on the background of disbiotic violations being characteristic features of the SEBG. Increasing the amount of circulating endotoxins in the portal blood activates the liver Kupfer's cells which lead to the appearance of anti-inflammatory cytokines and chemokines which are the substrate of the inflammatory component of steatosis transformation during NASH and induction of fibrogenesis [1, 8, 10, 15, 17, 23, 30, 31, 32].

Conclusions. In this way NALFD is clearly described by many researchers today and consists of the range of the liver damages: fatty liver dystrophy (steatosis), fatty dystrophy with inflammation and damage of hepatocytes (non-alcoholic or metabolic steatohepatitis) and fibrosis which can lead to the cirrhosis. Researches of dynamics of the structural liver changes (during obesity) and possible methods of their correction and treatment stays nowadays an actual medical problem, important for theoretical and practical medicine

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ЗМІНИ СТРУКТУРНОЇ ОРГАНІЗАЦІЇ ПЕЧІНКИ ПРИ ОЖИРІННІ (ОГЛЯД ЛІТЕРАТУРИ)

Примаченко В. І.

Резюме. У статті проаналізовано сучасну наукову літературу щодо актуальної проблеми медичної науки сьогодення – вивчення і аналіз структурно-функціональних змін в печінці при ожирінні. Однією з найбільш розповсюджених хронічних хвороб печінки в сучасному світі є неалкогольна жирова хвороба печінки на тлі ожиріння, яка набуває характер пандемії. Дані проведених досліджень вітчизняних та іноземних науковців про неалкогольну жирову хворобу печінки відображають важливі свідчення про значні структурні зміни в печінці на різних рівнях організації органу (органному, тканинному, клітинному, молекулярному).

Результати досліджень вчених вказують на те, що 75% пацієнтів з ожирінням мають неалкогольну жирову хворобу печінки. Патогенетичні механізми розвитку безалкогольної жирової хвороби печінки ускладнюються і залишаються питанням для науковців. Неалкогольна жирова хвороба печінки є головною печінковою демонстрацією метаболічного синдрому, і має тісний зв'язок з ожирінням і резистентністю до інсуліну. Ожиріння призводить до змін структурної організації печінки, що відображається на її функціональному стані та процесах обміну.

У фахових виданнях дослідники вказують на те, що неалкогольна жирова хвороба печінки з'явилася через зростання бактерій в тонкій кишці. Окиснювальний стрес в печінці може залежати не тільки від високої концентрації циркулюючих вільних жирних кислот при ожирінні, але й від високої концентрації ендотоксинів на тлі дисбіотичних порушень, які є характерними ознаками синдрому величезного зростання бактерій. Збільшення кількості циркулюючих ендотоксинів в портальної крові активує клітини печінки Купфера, що призводить до появи протизапальних цитокінів та хемокінів, які є субстратом запального компонента трансформації стеатозу під час неалкогольного стеатогепатиту та індукції фіброгенеза.

Вивчення патогенетичних механізмів розвитку неалкогольної жирової хвороби печінки, класифікації, факторів ризику, критеріїв діагностики, оцінки прогнозу перебігу хвороби має важливе значення для пошуку і обґрунтування ефективних способів профілактики та лікування.

Ключові слова: ожиріння, неалкогольна жирова хвороба печінки, стеатоз, метаболічний синдром, жирова дистрофія.

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ИЗМЕНЕНИЯ СТРУКТУРНОЙ ОРГАНИЗАЦИИ ПЕЧЕНИ ПРИ ОЖИРЕНИИ (ОБЗОР ЛИТЕРАТУРЫ)

Примаченко В. И.

Резюме. В статье проанализировано современную научную литературу относительно проблемы медицинской науки современности – изучение и анализ структурно-функциональных изменений в печени при ожирении. Одной из наиболее распространенных хронических болезней печени в современном мире есть неалкогольная жировая болезнь печени при ожирении, которая приобретает характер пандемии. Данные проведенных исследований отечественных и зарубежных ученых о неалкогольной жировой болезни печени отображают важные сведения о значительных структурных изменениях в печени на разных уровнях организации органа (органном, тканевом, клеточном, молекулярном).

Результаты исследований ученых показывают, что у 75% пациентов с ожирением диагностируется неалкогольная жировая болезнь печени. Патогенетические механизмы развития безалкогольной жировой болезни печени осложняются и остаются вопросом для ученых. Неалкогольная жировая болезнь печени является главной печеночной демонстрацией метаболического синдрома, и имеет тесную связь с

ожирением и резистентностью к инсулину. Ожирение приводит к изменениям структурной организации печени, что отражается на ее функциональном состоянии и процессах обмена.

В профессиональных изданиях исследователи указывают на то, что неалкогольная жировая болезнь печени развивается из-за роста бактерий в тонкой кишке. Окислительный стресс в печени может зависеть не только от высокой концентрации циркулирующих свободных жирных кислот при ожирении, но и от высокой концентрации эндотоксинов на фоне дисбиотических нарушений, которые являются характерными признаками синдрома огромного роста бактерий. Увеличение количества циркулирующих эндотоксинов в портальной крови активирует клетки печени Купфера, что приводит к появлению противовоспалительных цитокинов и хемокинов, которые являются субстратом воспалительного компонента трансформации стеатоза во время неалкогольного стеатогепатита и индукции фиброгенеза.

Изучение патогенетических механизмов развития неалкогольной жировой болезни печени, классификации, факторов риска, критериев диагностики, оценки прогноза течения болезни имеет большое значение для поиска и обоснования эффективных способов профилактики и лечения.

Ключевые слова: ожирение, неалкогольная жировая болезнь печени, стеатоз, метаболический синдром, жировая дистрофия.

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