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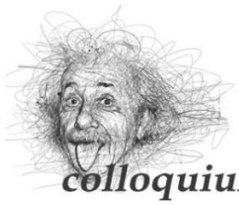

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THE INTENSITY OF FIBROUS FORMATION IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS AND CHRONIC KIDNEY DISEASE.

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ІНТЕНСИВНІСТЬ ФОРМУВАННЯ ФІБРОЗУ У ХВОРИХ НА НЕАЛКОГОЛЬНИЙ СТЕАТОГЕПАТИТ ТА ХРОНІЧНУ ХВОРОБУ НИРОК

Summary.

The article summarizes the clinical study, which showed that in non-alcoholic steatohepatitis that develops on the background of obesity and chronic kidney disease I-III stage, the presence of fibrotic changes in the liver tissue was found, which according to the biochemical index of fibrosis, exceeds those in patients with non-alcoholic steatohepatitis without comorbidity with kidney pathology. In patients with non-alcoholic steatohepatitis, which was accompanied by obesity, a significant increase in the synthesis of collagen and glycosaminoglycans which was accompanied with an ineffective resorption of newly formed collagen due to inhibition of the collagenolytic activity of blood plasma, due to significant activation of proteinase inhibitors (α2-MG) was observed with a significant imbalance in the system of connective tissue metabolism. Under the conditions of the comorbidity of non-alcoholic steatohepatitis with chronic kidney disease I-III stage, collagen synthesis and resorption are activated, but the anabolism processes predominate, in spite of the compensatory activation of collagenolysis, a substantial hyperproduction of actinic-phase proteins, fibronectin, glycosaminoglycans, fibroblast growth factor and lead to progressive fibrosis of the liver and disturbance of its functions.

Резюме.

В статье обобщается клиническое исследование, в котором показано, что при неалкогольном стеатогепатите, который развивается на фоне ожирения и хронической болезни почек I-III стадии, было обнаружено наличие фиброзных изменений в ткани печени, что согласно биохимическому показателю фиброз, превышает показатели у пациентов с неалкогольным стеатогепатитом без сопутствующей патологии почек. У пациентов с неалкогольным стеатогепатитом, который сопровождался ожирением, значительное увеличение синтеза коллагена и гликозаминогликанов, которое сопровождалось неэффективной резорбцией новообразованного коллагена из-за ингибирования коллагенолитической активности плазмы крови из-за значительной активации ингибиторов протеиназы (α2-MG) наблюдался со значительным дисбалансом в системе метаболизма соединительной ткани. В условиях сопутствующей патологии неалкогольного стеатогепатита с хронической почечной недостаточностью I-III стадии активизируются синтез и резорбция коллагена, но преобладают процессы анаболизма, несмотря на компенсаторную активацию коллагенолиза, существенную гиперпродукцию белков актинической фазы , фибронектин, гликозаминогликаны, фактор роста фибробластов и приводят к прогрессирующему фиброзу печени и нарушению ее функций.

Ключевые слова: *безалкогольный стеатогепатит, хроническое заболевание почек, фиброз печени.*
Key words*: non-alcoholic steatohepatitis, chronic kidney disease, liver fibrosis.*

Introduction. An important role in the pathogenesis of the progression of liver and kidney diseases is played by the components of the connective tissue system of the extracellular matrix [3, 7]. According to the literature, non-alcoholic fatty liver disease (NAFLD) in progress leads to the development of both liver cirrhosis and hepatocellular carcinoma, the incidence of which on the background of NAFLD substantially exceeds the indicators in the population. There are numerous attempts by scientists to find new probable biochemical markers of the intensity of fibrosis formation [9, 10], increasing the diagnostic value, sensitivity and specificity of existing methods, and developing methods of influence to inhibit these processes.

The objective of the article: to find out the features of biochemical markers of liver fibrosis with non-alcoholic steatohepatitis in patients with I-II degree obesity and chronic kidney disease I-III stage

Material and methods of research: 98 patients with non-alcoholic steatohepatitis on the background of I-II degree obesity were examined: 52 patients with non-alcoholic steatohepatitis (1st group) (without accompanying chronic kidney disease), 46 patients with non-alcoholic steatohepatitis with a comorbid chronic kidney disease I-III stage (2nd group). The control

group consisted of 20 practically healthy persons (PHPs) with the corresponding age and sex. Biopsy of the liver was performed on 32 patients with non-alcoholic steatohepatitis with the accompanying of chronic kidney disease I-III stage, 28 patients with non-alcoholic steatohepatitis without chronic kidney disease. Patients on both groups of non-alcoholic steatohepatitis received heparhizine treatment (glycyrrhizin 40 mg, glycine 400 mg, L-cysteine hydrochloride 20 mg) by intravenous administration of 20 ml of the drug for 10 days followed by enteral administration of 2 tablets of heparhizine (1 tablet: glycyrrhizin 25 mg, glycine - 25 mg, methionine - 25 mg) 3 times a day for 80 days. Patients with non-alcoholic steatohepatitis with a comorbid flow of non-alcoholic steatohepatitis, obesity and chronic kidney disease of the I-III stage, except heparisin, they received baseline therapy of chronic kidney disease I-III stage: chronic pyelonephritis (course of antibacterial drugs, uroseptics, cainfron). The examinations were carried out prior to treatment and on the 90th day of treatment. The statistical analysis was performed using parametric and non-parametric criteria (Student, Pearson) on PC AMD Athlon 64 using Statistica 5.1 software (StatSoft, Inc., USA) and SPSS 10.0.5. Standart Version.

Results of the research: Based on the obtained results, among the examined patients with NASH in 1st group, the zero stage of fibrosis (F0) occurred in 28.6% of patients, while 42.8% of patients registered probable fibrotic changes (F1) in the liver tissue. In patients with NASH 1st group F2 stage was registered in 17.9% of patients, F3 - in 10.7%. Thus, fibrotic changes in the F1 stage were most often recorded. In the group of patients with NASH 2nd group, F0 stage of fibrosis was observed in 9,4% of patients. F1 stage was recorded in the ratio of 28.1%, F2 - 37.5%, F3 stage was registered in 25.0% of patients in 2nd group. F4 stages in this contingent were not detected. The obtained results indicate the involvement of chronic kidney disease in the induction of liver tissue fibrous with the background of NASH and obesity.

In order to identify possible risk factors in the progression of liver fibrosis and additional biochemical markers of the intensity of fibrous reactions, we carried out a correlation analysis between the biochemical index of fibrosis and markers of basic biochemical syndromes of NASH, which established the existence of a potential direct correlation between the biochemical index of fibrosis and ALT activity ($r = 0.67$, $p < 0.05$), alkaline phosphatase activity ($r = 0.53$, $p < 0.05$), blood bile acid content ($r = 0.51$, $p < 0.05$). The given data indicate that the intensity of the fibrous reactions in patients with NASH, developed on the background of obesity, depends on the activity of the cytolytic syndrome and cholestasis. With the progression of the stage of fibrosis, the detoxification function of the liver decreases (with the activity of arginase ($r = -0,62$, $p < 0,05$)).

The analysis of the intensity of the fibrous reactions in patients with NASH, depending on the presence of a comorbid chronic kidney disease, indicates a probable increase in the content of protein-bound oxyproline in the blood of patients in the 1st group - 1.6 times compared with practically healthy person ($p < 0.05$), patients in 2nd group - 2.0 times ($p < 0.05$), which indicates the high activity of collagen anabolism in this contingent of patients. At the same time, the index of free oxyproline in blood, which is the biochemical marker of collagen catabolism, in patients with NASH in the 1st group was 1.2 times lower than that in a practically healthy person ($p < 0.05$). That is, in patients with NASH an intensification of collagen formation processes is observed with the background of resorption processes reduction of newly formed collagen. At the same time, in patients in the 2nd group, the free oxyproline content in the blood exceeded the content in a practically healthy person by 1.4 times ($p < 0.05$), indicating an increase in collagen degradation in the background of its high synthesis. The interdependence of the above-mentioned changes confirms the presence of a correlation between the content of free oxyproline and α2-MG ($r = 0.51$, $p < 0.05$), the content of protein-bound oxyproline and collagen anabolism ($r = 0.43$, $p < 0.05$); the content of free oxyproline and collagen anabolism ($r = 0.53$, $p < 0.05$) in the 2nd group.

The obtained data testify that in patients with NASH, which arose on the background of obesity, a significant increase in the synthesis of collagen and glycosaminoglycans was observed, which was accompanied by an ineffective resorption of newly formed collagen due to inhibition of collagenolytic activity of blood plasma at NASH, which arose as a result of activation of proteinase inhibitors (α2- MG), a significant imbalance in the metabolism of connective tissue, which leads to progressive liver fibrosis and violation of its functions. Under conditions of the comorbidity of NASH with CKH of the I-III stages, synthesis and resorption of collagen are activated, but the processes of anabolism prevail, despite the compensatory activation of collagenolysis, with a significant hyperproduction of acute-phase proteins, fibronectin, fibroblasts growth factor and increased degradation of fucoglycoproteins.

The use of the drug heparizin showed the presence of its effect on the substantial correction of the revealed disturbances of homeostasis components extracellular matrix. Thus, the average index of fibro test in patients with NASH in 1st group after treatment was decreased by 1.5 times ($p < 0,05$), in 2nd group - 2,0 times ($p < 0,05$). We found a significant effect of heparizin on the content of fibroblasts growth factor in the blood-reduction in both groups after treatment in 1.7 times ($p < 0.05$). Thus, we have established a significant corrective effect of heparizin on the metabolic rate of the extracellular matrix connective tissue system of the liver, both in terms of comorbidity with and without chronic kidney disease.

Conclusion. In non-alcoholic steatohepatitis that develops on the background of obesity and chronic kidney disease I-III stage, the presence of fibrotic changes in the liver tissue, which according to the biochemical index of fibrosis exceeds those in patients with NASH without comorbidity with kidney pathology, has been established. Heparizin therapy for 3 months contributed to the achievement of a collagen ana- and catabolism balance by activating collagen lysis, inhibiting the ac-

tivity of proteolytic inhibitors and collagenolysis, inhibition of fibroblast growth factor secretion, acute phase inflammation indicators, degradation of liver extracellular matrix fucoglycoproteins, and in general, reducing the activation of connective tissue components, by evidence of a decrease in the index of liver fibrosis according to the fibro test in the range of 1.5-2.0 times.

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ANALYSIS OF THE PATHOLOGICAL CONDITIONS OF THE FEMALE BODY.

Abstract:
The pathology associated with the female organism remains an actual problem in medicine and therefore in our work the aspects of tumor processes based on literature are reflected.

Ключевые слова : *организм ,аспекты,анализ,патология ,кисты,процессы.*

In modern medicine, an important aspect of the study remains the cystic formations in the ovaries. Benign neoplasm of ovary, which refers to tumor-like processes, which is a cavity that is filled with liquid contents, i.e. cysts - the most common pathology of the female body.

Statistics showed that the ovarian cyst is very often observed in young women, it is much less common in women after 50 years.

Specialists noted that the cyst of the yellow body is a tumor with thickened walls, filled with a liquid of yellow color, it can be supplemented with blood. Usually such a growth occurs only on one side. The reason for the appearance is that after ovulation the follicle does not fill with cells of the yellow body, instead the follicle grows and becomes filled with liquid. Luteal cysts were more often identified as two-sided and single entities. The inner surface of the wall is lined with a layer of tekalutein cells, under which there is granulosis without luteinization.

The follicular cyst and the cyst of the yellow body refer to the functional formations that form in the ovary itself. The walls of benign neoplasms are formed from a highly stretched follicle or yellow body. The reason for their formation is a hormonal imbalance. Typically, such formations do not come in large sizes and grow toward the abdominal cavity. Follicular cysts were more often represented as a one-sided and one-chamber thin-walled formation with a smooth inner wall. According to statistical data, the frequency of this pathology has increased over the past 10 years from 6-11% to 19-25% among other tumors of the female genital organs. About 75-87% of all true ovarian tumors account for the proportion of benign tumors. According to the WHO classification, there are two groups of cystic for-

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