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COMPARATIVE ANALYSIS OF THE SPECTRUM OF BILE ACIDS WITH NON-ALCOHOLIC FATTY DISEASES OF THE LIVER AND BILE

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ABSTRACT: This article provides a comparative analysis of the spectrum of bile acids in non-alcoholic fatty liver disease and gallstones with specific examples. Conclusions on the topic are made.

KEY WORDS: Non-alcoholic fatty liver disease, cholelithiasis, spectrum of bile acids, oncological diseases, gamma-glutamyltranspeptidase.

Non-alcoholic fatty liver disease (NAFLD) takes a leading position among chronic liver diseases, forwarding the damage of viral and alcoholic etiology. According to the literature data and the results of our observations, NAFLD is commonly common to cholelithiasis. So, in case of non-alcoholic steatosis and steatohepatitis, gallstones are diagnosed in 18.2 and 31.1% of patients, respectively. In turn, at the pre-stone stage of that, NAFLD is diagnosed in 24.6% of cases, and at the stage of formed stones - in 39.1% of cases. In connection with this, the question arises: do NAFLD and cholelithiasis have different pathogenesis, or is cholelithiasis a manifestation of NAFLD?

One of the most sensitive indicators in the assessment of the functional state of the liver and biliary tract is the state of exchange of gilic acids (GA). In last year the important value of cholelithiasis in gall stone formation has been shown. However, the nature of changes in the cholelithiasis spectrum, both in the case of NAFLD and in the case of cholelithiasis, remains insufficiently studied.

The purpose of our work was a comparative study of the features of changes in the spectrum of GA in bile in patients with NAFLD and gald.

Inclusion criteria were age 18-60 years, NAFLD under hepatic steatosis stage, the patient a signed informed consent for screening, exclusion criteria - under 18 and over 60 years, fibrosis and cirrhosis, acute hepatitis, alcoholic and viral liver damages, oncological diseases, chronic diseases in the stage of decompensation.

In the examination of patients, addition to routine clinical data used biochemical blood analysis involves assessing total cholesterol (CHS) and triglyceride, alanine aminotransferase (ALT), aspartate - aminotransferazy (AST), alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT), bilirubin with the help of analyzer company labsystems (finland).

The verification of NAFLD was used the results of ultrasonic studies (increased liver size, increased echogenicity, lower sound conductivity and liver density). The determination of elasticity and degree of liver fibrosis was carried out using the method of sonoelastography on the apparatus aixplorer (france).

Biopsy of the liver was conducted using a fast gun biopsy pistol (sterylab, italy) with the following study of ultrafine sections in a JEM 1200 EXII transmission microscope. In the diagnosis of the pre-stone stage of cholelithiasis, used data of ultrasonic studies of the gall bladder (dense inhomogeneous gall, smear-like gall or viscous gallbladder)and vesiculate gallbladder. In bile obtained by multifractional duodenal intubation, determine the concentration of the total pool of cholelithiasis (landmark-paid-in cholic acid) and ch by spectrophotometry-metric method then calculates holatoholesterinovy factor for the portion of "b" and "c" bile.

GA fractions in bild was determined on an amazonx mass spectrometer (bruker daltonik gmbh, bremen, germany).

The measurements were conducted in the registration mode of positive and negative ions in the range m / z from 100 to 2000. Voltage on the capillary - 4500 v. as a dryer gas nitrogen with a temperature of 1 to 8 literature was used as a dryer gas. Bile was dissolved in distilled water at a 1: 1 concentration. then 1 mcl of the solution was added to 1 ml with water. Data processed using the dataanalysis 4.0 program (bruker daltonik gmbh, bremen, germany).

The study used ich's good clinical practice guidelines. the examination of the patients was conducted on the basis of their signing of the informed voluntary consent of the patient according to order no. 390n of the ministry of health and social development of the RF of 23 april 2012 (registered by the ministry of justice of the russian federation on may 540 2012).

The calculation of the required number of observations based on the calculation of the sample volume with the statistical power level of the research $p = 0.80$ and performed with the use of statistical software packages usa statistica 6.1. The distribution of patients into groups was conducted by the method of a typological sampling. Used parametric (calculation of relative values, average and average error, student criterion) statistical methods. Intergroup differences were considered statistically significant at the probability of the zero hypothesis about the absence of difference between groups $p < 0.05$.

The control group considered 30 persons in the age of 18-60 years old without complaints from the hepatobiliary system.

Our surveillance was 140 patients, among them 50 - with NAFLD and 90 - with cholelithiasis. Among NAFLD patients women were 36, men - 14, the medium age was 50.2 ± 1.1 years. In the group of patients with gallstone disease, there were 68 women, 22 men, and the average age was 40.3 ± 2.6 years. By the results of a biochemical study of blood, the most of the examined patients discovered an increase in the level of total CHS and triglycerides, as well as markers of cholestasis with taps. In addition, in NAFLD, a significant increase of cytolysis markers (ALT, AST) is observed with regard to the control group and the group of patients with GI.

During biochemical study of bild, a decrease in the total quantity of GA in portion "b" of bild (28.49 ± 1.1 mmol / l, p <0.05 in patients with NAFLD and 22.8 ± 2.2 mmol / l, p <0 05 in patients with cholelithiasis), in portion "c" bild (13.29 ± 0.54 mmol / l, p> 0.05 in patients with NAFLD and 7.0 ± 1.4 mmol / l, p <0.05 in patients with gallstones) compared to the control group (54.6 ± 5.4 and 17.4 ± 2.9 mmol / l, respectively). The content of CHS in bild had a tendency to increase in patients in both groups compared to the control group. in the determination of cholatocholesterol coefficient, its reliable decrease in portion "b" of bild (0.9 ± 0.07 mmol / l, p <0.05 in patients with NAFLD and 4.6 ± 0.1 mmol / l, p <0 05 in patients with gallstones), in portion "c" of bile (0.89 ± 0.13 mmol / l, p <0.05 in patients with NAFLD and 2.2 ± 0.8 mmol / l, p <0.05 u of patients with gallstones) in comparison with the control group (12.1 ± 3.3 and 6.1 ± 0.8 mmol / l, respectively). Results mass spectrometry in general, most of the surveyed us patients showed a decrease the level of free cholelithiasis (mainly cholic) and elevated conjugated cholelithiasis (glycocholic, glycodeoxycholic, taurocholic, taurodezoksiholevoy) in a portion of the "b" and "c" pitta compared with the control group (table 2). At the same time, the decrease in the content of cholic acid in the vesicular and hepatic bile of patients with NAFLD was significant and reliably reduced in relation not only to the control group, but also to patients with gallstones.

Chenodeoxycholic acid had a tendency to decrease in portions "b" of bild in patients of both patients, and in portions of "c" bild change of its concentration has been differently directed: in the patients without best contents and glycodeoxycholicglycocholic acids in patients with NAFLD in both portions of bile substantially exceeds that of the control group and patients with gallstone disease, and the concentration of taurocholic acids tended to increase in patients with NAFLD in both portions of bile relative to the control group and patients with cholelithiasis. Thus, NAFLD patients have a more significant decrease in the content of free fas and a more significant increase in the concentration of conjugated fas in comparison with the control group and patients with gas. The content of ursodeoxycholic acid in portions "b" and "c" of bild in patients with NAFLD and close has a tendency to increase in comparison with the control group. The concentration of deoxycholic acid in bladder blood is considerably lower

in patients with NAFLD and close in comparison with the control group, but this reduction is more noticeable in patients with NAFLD in hepatic bile, the content of deoxycholic acid had a tendency to increase in patients with NAFLD and gallstones compared to the control group.

It is known that free fas are synthesized exclusively in the liver, corresponded a reduction of their concentration indicates hepatocytes damage. In the present work, increased increase in patients with NAFLD of cholestasis and cytolysis markers. In case of cholestasis, cholelithiasiss are capable of destroying the apical membranes of hepatocytes and damaging the epithelium of the gall ducts, and, as a consequence, increasing the content of GGT in the blood.

Synthesis of fas from cholelithiasis occurs in the hepatocyte and includes 17 different enzymes, which are located in cytozol, endoplasmic reticulum, mitochondria, and peroxisomes. In fatty hepatosis, regardless of etiological factors, hepatocytes damage by free fatty acids, which are a substrate of peroxide nose, lipvidous musculosis. This leads to a sharp reduction of synthesis and excretion of cholelithiasis in the background of increased secretion of CHS.

But it is necessary to consider that the synthesis of the cholelithiasis affects not only state of the liver and cholelithiasis, which are on an negative feedback contributed to the increase or decrease in their content and cholesterol, thyroid hormones, glucocorticoids, insulin, circadian rhythms. In the maintenance of homeostasis, the small intestine is actively involved through the synthesis of fibroblast growth factor-15 by enterocytes, which regulates a number of enzymes, which are responsible for the synthesis of GA.

There we studied patients showed increase in the content of conjugated cholelithiasis, more pronounced in patients with NAFLD, but to comply with the right relationships glycine conjugate (glycocholic and glycodeoxycholic lcd) to taurine (taurocholic and taurodezoksiholevoy lcd) 3: 1. The degree of GA conjugation to determine is depending on the diet and the intestinal microflora.

CONCLUSION

Determination of cholatocholesterol coefficient, indicator of litogenicity of bild, is based only on the data of studies of CHS and cholic acid. More complete information about cholelithiasis exchange in NAFLD and cholelithiasis gives the determination of cholelithiasis composition in bitch. Thus, when mass spectrometry to identify decrease in the total number of free cholelithiasis (cholewa, henodezoksi- cholic, deoxycholic) and elevated conjugated cholelithiasis (glycocholic, taurocholic, ursodeoxycholic), most pronounced in patients with NAFLD. One-directional changes in the cholelithiasis spectrum in NAFLD and cholelithiasis give the basis to believe that the liver is the starting mechanism in disorders of cholelithiasis exchange. Reduction of primary GA, imbalance of phospholipids and CHS disrupt the stabilization of bild, leading under unfavorable conditions in the child tract, hypotonia and anomalies of the development of the pump.

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