

**DEVELOPMENT OF FATTY HEPATOSIS IN PATIENTS WITH DIABETES
MELLITUS**

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SUMMARY: It was made an organized study of the functional condition of hepato-biliary system beside 200 patients with fatty hepatitis and fatty hepatitis with concomitant sugar diabetes. In verification of the diagnosis were used results of the biochemical blood's study, ultrasonography study, computer and MR tomography. All patients were conducted with duodenal tubing with following biochemical bile study. Breach of the functional condition liver was revealed beside majority sick fatty hepatitis, moreover degree of the breaches becomes above under accompanying sugar diabetes. Unidirectional change in biochemical bile characteristic wasn't noted beside patient fatty hepatitis and fatty hepatitis with accompanying sugar diabetes, corresponding to I stage cholelithiasis.

Keywords: fatty hepatitis; sugar diabetes; hepato-biliary system; cholelithiasis.

Non-alcoholic fatty liver disease (NAFLD) includes steatosis, fatty infiltration with inflammation (steatohepatitis), non-alcoholic steatohepatitis with fibrosis progressing to cirrhosis. For a long time it was believed that NAFLD was benign, but in recent years it has been proven that a quarter (27%) of patients develop fibrosis within 9 years, and every fifth (19%) develops cirrhosis of varying severity [1]. With longer observation, progression of fibrosis is detected in 50% of patients with NAFLD, and this process occurs without clinical manifestations [2; 3].

Recently, there has been an assumption about a direct connection between the development of NAFLD and metabolic syndrome (MS) [4; 5; 6; 7; 8]. In fatty hepatitis, a change in the function of hepatocytes, in turn, leads to the formation of defective bile micelles, in which the level of cholesterol (CH) is increased and the content of phospholipids and bile acids (BA) is reduced, which creates the prerequisites for the formation of lithogenic bile [9; 10; eleven].

The purpose of the work was a comparative study of the features of dysfunction of the functional state of the liver and biliary tract in fatty hepatitis and fatty hepatitis with concomitant diabetes mellitus.

MATERIAL AND METHODS OF RESEARCH

200 patients with fatty hepatitis were examined. There were 84 (42%) men, 116 (58%) women, aged from 26 to 65 years. The duration of the disease ranged from 1 year to 30 years. The comparison group consisted of 150 patients with fatty hepatitis, the observation group included 50 patients with fatty hepatitis with concomitant diabetes mellitus. All patients had increased body weight (Kettle body mass index was 32.5 ± 4.1).

When examining patients, along with general clinical data, a number of modern laboratory, instrumental and biochemical studies were used. To verify the diagnosis of "fatty hepatitis," patients underwent ultrasonographic examination of the hepatobiliary system using an S-DH-500 ultrasound device, computed tomography using a Universal MAX device (USA) and magnetic resonance imaging using a CRT-1010 magnetic resonance tomograph (Kyiv). The protein-forming function of the liver was assessed by the level of total serum protein and albumin using an FP901 (M) analyzer from Labsystems (Finland). Protein fractions of blood serum were determined on a Cormay DS 2 analyzer. The level of prothrombin index (PTI) was determined on a Cormay KG 4 analyzer. Lipid metabolism was assessed by the content of cholesterol, β -lipoproteins, triglycerides, high- and low-density lipoprotein cholesterol in the plasma, as well as the atherogenic index, the level of which was determined on the FP-901 (M) analyzer from Labsystems (Finland). The activity of the following enzymes was determined: alanine aminotransferase - ALT, aspartate aminotransferase - AST, alkaline phosphatase - ALP on a Cormay Livia analyzer. Pigment metabolism was assessed by the content of total bilirubin in the blood serum, determined by the unified Jendrassik-Grof method using Vital kits. Radioimmunological determination of insulin was carried out using a standard test kit from the Minsk Institute of Bioorganic Chemistry.

All patients underwent fractional duodenal intubation according to the generally accepted method, followed by macro- and microscopic, biochemical examination of bile. In portions B and C, the total concentration of bile acids and cholesterol in bile was determined, followed by calculation of the cholate-cholesterol coefficient (CCC) according to the method of V. P. Miroshnichenko et al. (1978) [12]. The results of the study were compared with data from the control group, which consisted of 22 practically healthy people aged 22 to 50 years.

The results obtained were processed using a set of programs for calculating statistical indicators. The Student's test was used in the calculations, confidence limits were determined, and the reliability of the difference between indicators and average values was assessed.

RESEARCH RESULTS AND THEIR DISCUSSION

Judging by the data in Table. 1, in patients in the comparison group and the observation group, a significant increase in the level of total protein was found compared to the control. In patients in the observation group, a significant decrease in albumin levels was noted, while in the comparison group it only had a tendency to decrease. The content of total bilirubin was increased in the comparison group (by 17.5%) and the observation group (by 27.9%) compared to the control group. In patients, a significant increase in the level of serum transaminases was noted relative to the control: in the comparison group, ALT indicators increased by 73.14%, AST - by 21.9% and in the observation group ALT - by 124.0%, AST - by 34.7%. Blood cholesterol levels were increased by 19.4% in the comparison group and by 26.1% in the observation group, β -LP by 15.0 and 30%, respectively, triglycerides by 36.2 and 100%, respectively. Compared with the control, fasting blood glucose levels were increased in the comparison group by 32.6% and in the observation group by 104.7%.

A biochemical study of bile (Table 2) in the comparison group revealed a significant increase in the level of cholesterol in bile (in portion B by 398%, in portion C by 332%) and in the observation group (in portion B by 316%, in portion C C - by 369%); on the contrary, the levels of bile acids were reduced in the comparison group by 46.8 and 30.6%, respectively, and

in the observation group - by 54.8 and 19.5%, respectively. As a consequence of this, patients experience a significant decrease in CHC in both portions of bile.

It is important to note that no significant differences in the biochemical composition of bile were detected between patients in the observation group and the comparison group. Consequently, in patients with fatty hepatosis, including those with concomitant diabetes, there is a change in the physicochemical properties of hepatic and cystic bile, corresponding to the first stage of cholelithiasis [13], which is consistent with previously published works [9, 10, 11]. Naturally, in this case, dysfunction of hepatocytes, which are the only place of formation of bile acids, is important, which invariably affects changes in the biochemical properties of bile [14].

When studying the basal level of insulin in the comparison group, there was a tendency for its level in the blood serum to increase to $15.25 \pm 1.99 \mu\text{U/ml}$ compared to the control - $11.85 \pm 1.25 \mu\text{U/ml}$. In the observation group, the insulin content increased significantly to $29.15 \pm 1.34 \mu\text{U/ml}$ compared to the control. Indeed, as our studies have shown, there is a certain relationship between insulin levels and gallstone formation. A negative relationship was found between the cholesterol content of bile and the level of insulin (in portion B $r = -0.37$, in portion C $r = -0.34$), between bile acids and the level of insulin - a negative relationship (in portion B $r = -0.45$, in portion C $r = -0.36$), CHC and insulin level - a positive relationship (in portion B $r = 0.44$, in portion C $r = 0.34$).

There is evidence in the literature of increased levels of insulin in the blood in patients with cholelithiasis [4]. Against the background of insulin resistance, the liver actively synthesizes triglycerides, which contributes to the development of steatosis and its further progression. On the other hand, the liver is a target organ in the development of metabolic syndrome and plays an important role in the development of insulin resistance. This allows us to consider NAFLD as a component of MS, although there are no direct indications of NAFLD among the official criteria for MS.

CONCLUSIONS

1. With NAFLD, the functional state of the liver is impaired, but the degree of impairment increases in patients with concomitant diabetes mellitus.
2. In patients with NAFLD and patients with NAFLD with concomitant diabetes mellitus, a unidirectional change in the physicochemical properties of hepatic and cystic bile is observed, corresponding to the 1st stage of cholelithiasis.
3. In fatty hepatosis, there is a dependence of the formation of lithogenic bile on hyperinsulinemia.

LITERATURE

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