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Clinical features of the non-alcohol fat liver disease in advanced age patients with the diabetes mellitus type 2

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Abstract

In a retrospective study, the history of the disease was studied in 143 patients: I group of young age (25-44 years) - 45, II group of middle age (45-60 years) - 60, and III group of the elderly (61-75 years) - 58, patients on NAFLD in combination with type 2 diabetes. The average age of patients in the I group was (40.33 ± 1.02) years; II - (53.09 ± 0.53) years and III - (64.58 ± 0.66) years. The period of diabetes finding in the 1st group was from 1 to 12 years (on average (6.27 ± 0.93) years, in the second group - (9.38 ± 0.80) years and in the third group - 1 to 53 years, on average (14.61 ± 1.43) years, with age in the dynamics of the NAFLD, the number of cases with fatty infiltration decreases to 60 years, at the same time it increases - with steatohepatitis and dyslipidemia. Arterial pressure tends to increase from the 25th year of life ($p < 0.05$). In patients with middle and advanced age, fluctuations of hyperglycemia became more frequent. The size of the right lobe of the liver (17.0 cm) would be in the largest in case of illness for a period of 1 year in young patients, and the smallest (8.5 cm) in patients in group III. As the age of the number of cases with stage I, fatty hepatosis decreases, and the third stage increases accordingly. In I group of patients, the intensity of the mesenchymal-inflammatory syndrome is minimal. The index of thymol test in patients of middle and advanced age is increasing, besides, women exhibit more pronounced signs of mesenchymal-inflammatory syndrome in groups II and III, as compared with men. Both in young and in patients of middle and advanced age, the liver is enlarged, in the last ones little bit more than in young ones. The level of triglycerides in women with age was significantly lower. In the group of patients over the age of 44 years, there is an increase in the level of very low density lipoprotein, and significant deviations in the lipid profile of the blood, which supports the high risk of atherosclerosis, with a greater tendency in men. The attention of a fairly large number of patients with elevated ESR, which is more often found in women, less frequently - in men.

Keywords: Nonalcoholic fatty liver disease, age characteristics of the course, young age, middle age, elderly age

1. Introduction

The problem of developing, course and treating non-alcoholic fatty liver disease (NAFLD) is becoming increasingly important. NAFLD is a polyethiologic disease with a violation (primary or secondary) of lipid metabolism [2, 6, 13]. The prevalence of this disease is quite high and its growth becomes fast (the frequency of NAFLD is not less than 30% of the entire population) [7]. In the formation of liver steatosis in hepatocytes accumulate lipids, which in the amount of more than 5% of the mass of the liver. In half of patients the disease begins and runs asymptomatic, and diagnosed accidentally [11]. According to V. Golofeevsky [4], fatty hepatosis and its next stage - steatohepatitis - are observed more often than are diagnosed in practice. The main task of this is the prompt diagnosis of people at different age periods of the initial stage of NAFLD - fatty liver disease. Fatty liver dystrophy may subsequently be transformed into steatohepatitis and liver cirrhosis, which are trigger liver fibrogenesis [9, 10]. Disturbance of lipid metabolism in patients with NAFLD is one of the symptoms accompanying the course of various diseases, in particular diabetes mellitus, which causes the problem of comorbidity of these diseases [8] and requires deep and comprehensive treatment to ensure effective treatment of NAFLD [1, 5].

The aim of the study. To study the features of the course of non-alcoholic fatty liver disease associated with type 2 diabetes in patients of different age groups.

2. Material and Methods

In a retrospective study, the history of the diseases was studied in 143 patients: Group I - 45 young patients (25-44 years old), II group - 60 middle-aged (45-60 years) - 60 and III group - 58 elderly patients (61-75 years), patients with NAFLD in combination with type 2 diabetes

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mellitus. The average age of patients in the I group was (40.33 ± 1.02) years; The second group - (53.09 ± 0.53) years and the third group - (64.58 ± 0.66) years. The period of detection of diabetes in the 1st group was from 1 to 12 years (on average (6.27 ± 0.93) years, the second group - (9.38 ± 0.80) years and the third group - 1 to 53 years, on average (14.61 ± 1.43) years.

To identify the diagnosis of NAFLD complex of the data of clinical, laboratory, biochemical and instrumental studies were taken into consideration, according to the standards of examination of patients with pathology of organs of the gastrointestinal tract. By the time of the examination, the patients did not receive treatment of NAFLD under standardized procedures. A compulsory diagnostic method was the implementation of an ultrasound study to determine the size of the liver and the stage of development of fatty liver disease. The biochemical blood test included: determination of protein (total protein content, thymol test), lipid (total cholesterol content, triglycerides, high, low and very low density lipoprotein), pigmentary metabolism (total bilirubin), blood glucose levels in the onset of blood; general blood test. Statistical processing of the results was carried out using Statistica 6.1.

3. Research and Discussion

The patients were of moderate severity at the offset stage (code MKH E 11.7).

With age in the dynamics of the NAFLD, the number of cases with fatty infiltration decreases to 60 years, while it increases - with steatohepatitis and dyslipidemia. Thus, NAFLD in the stage of fatty liver infiltration had 73.3% of patients in group II, steatohepatitis, dyslipidemia were diagnosed in 26.7% of cases; in the 2nd group 50.0% and 50.0% respectively; in the third group 48.28% and 51.72%.

Patients in the clinical picture observed numerous complications of diabetes with varying degrees of severity: dyscirculatory mixed encephalopathy, which was diagnosed in young patients. from the 2nd year of illness and II degree - in middle-aged patients from the 4th year; diabetic nonproliferative retinopathy and maculopathy of the OU from several months of the disease; diabetic sensory neuropathy - already at the time of the disease 1 year; dysmetabolic cardiopathy with cardiac insufficiency of Class I and II (at the 5th year of illness), arterial hypertension and diabetic nephropathy (end of year 1). Diabetic encephalopathy is manifested in women with a 5-year period of disease development. Summing up, we can say that complications from the vascular system develop early in both men and women; and myocardiopathy, encephalopathy, nephropathy - earlier in men.

Typical complaints in these patients were general weakness, urination, fatigue, headaches. From the 25th year of life, the propensity to increase blood pressure ($p < 0.05$) appears. The blood pressure was on average equal to $(134.93 \pm 5.76 / 86.67 \pm 3.61)$ mm Hg. Art. (Group I); $(144.91 \pm 1.99 / 89.84 \pm 1.50)$ mm Hg. Art. (Group II) and $(146.01 \pm 2.94 / 85.71 \pm 1.40)$ mm Hg. Art. (III group).

Complaints in patients of this age differed slightly, depending on the age and duration of the disease. Thus, in the case of illness, 1 year of complaints from the digestive organs in patients of Group I was not detected. At sickness for 1 year from the organs of digestion in patients of groups II and III, sensation of saturation, heaviness in the right hypogastric, and flatulence were revealed. With the duration of the disease for up to 5 years, common complaints were associated with

bitterness in the mouth, abdominal discomfort, periodic pain in the right upper quadrant of the abdomen, associated with an magnification of the liver, which protruded from the edges of the arch at 0, 5 - 2.5 cm in 55,17% of cases, in most cases not painful.

In patients with middle and advanced age, oscillations of hyperglycemia became more frequent, complaints of stomach and freezing of the upper extremities appeared. Moderate hyperkeratosis with peeling of the superficial layers of the skin and trophic changes in the nails were observed in each patient. Complaints became more pronounced and their number increased with age and with an increase of the duration of the disease.

During the ultrasound examination, signs of fatty liver dystrophy were revealed. Based on the distal congestion of the signal, diffuse hyperechogenicity of the liver tissue, in comparison with the kidneys, and fuzzy contour of the vascular pattern, steatohepatosis has been diagnosed. At the same time, it was noted that the right share of the liver in these patients was in the range of 17.0, 14.0 cm (group I), 18.6, 13.0 cm (group II) and 17.3, 10.6 cm (group III); left - within 8.6, 6.2 cm (group I), 10.0 and 5.2 cm (group II) and 8.5; 5.5 cm (group III). It turned out that the size of the right lobe of the liver (17.0 cm) was the largest in terms of the disease 1 year in young patients, and the smallest (8.5 cm) - in patients from the III group.

When refining the ultrasonographic picture of the liver, according to a set of signs (slight increase in echogenicity, visualization of the wall of veins of medium and large caliber in the 1st stage of fatty hepatitis is found in 24.4% of cases in group I, 25.0% in group II and 20.9 % in group I. Moderate elevation of echogenicity of the liver, visualization of only partial and segmental veins, which corresponded to II stage of hepatitis, was found in I group 31.1%, in II group - 40.0% and in III group - 51, 73% of cases. In patients of the I group (44.4%), 35.0% of the second group and 27.58% of the third group, the echogenicity of the liver was increased in a significant degree, the walls of intrahepatic veins not vizualizuvalysya - III stage of fatty liver. As you can see, with age in patients NAFLD combined with type 2 diabetes incidence of fatty liver and decreased stage and third stage respectively increased.

The number of cases with increased diameter of the portal vein with age increases. The diameter of the portal vein in the patients of the I group was less than 13 mm and in only one case it reached 1.45 mm with normal parameters of the right and left portions of the liver with a disease period of 1 year. In group II, the diameter of the portal vein was more than 10 mm in 8 patients (13.3%), in group III - in 16 patients (27.58%).

Palpatinously it was found that one of the symptoms of liver damage in patients of Group I was its increase - the protrusion at (1.81 ± 0.28) cm from the edge of the rib arch (0.5 to 3.0 cm) in 53.3 % of cases in group II - (1.54 ± 0.09) cm (from 1,0 to 3,0 cm) in 63,3%, in group II - at $(1,81 \pm 0,07)$ cm (from 1.0 to 2.5 cm) at 62.63%. That is, the liver is enlarged in both young and middle and old patients. In the last ones a little bit more than the young ones.

A biochemical blood test showed that the functional state of the liver remained satisfactory. Protein metabolism was characterized by indicators in the reference limits of the indicator in healthy individuals: protein content was (75.11 ± 2.27) g / l (group I), (72.46 ± 1.3) g / l (group II) and $(71,20 \pm 1,83)$ g / l (group III), that is, no violations of the protein content of the blood were detected.

Intensity of mesenchymal-inflammatory syndrome in patients of Group I is the minimal - index of thymol test is (1.32 ± 0.08) units. Indicator of thymol test in patients of middle and older age is increasing, besides, women exhibit more pronounced signs of mesenchymal-inflammatory syndrome in II and III groups, compared to men: II group (2.54 ± 0.44) units: in men, on average - (1.70 ± 0.32) units, in women - (3.89 ± 0.64) units, III group and (3.10 ± 0.83) units, in men, on average - (1.92 ± 0.32) , in women - (4.09 ± 0.21) units.

The level of total cholesterol in patients of Group I - (5.81 ± 0.48) mmol / l, that is, the upper limit of the norm, with the highest rates in the disease for 5 years; the second group - (5.46 ± 0.21) mmol / l: in men - (5.33 ± 0.28) units, in women - (5.66 ± 0.19) units; in the third group - (5.63 ± 0.23) mmol / l: in men - (5.24 ± 0.12) units, in women - (5.45 ± 0.28) units, that is, near the upper limit of norm and these indicators differed little among themselves, $p > 0.05$.

The content of triglycerides in patients of Group I was determined by the indicator (3.31 ± 0.24) mmol / l, the second group - (3.70 ± 0.61) mmol / l, which exceeded the upper reference level of norm. At the same time, this figure was (3.68 ± 0.85) , in women - (2.61 ± 0.35) units, $p < 0.05$. In the third group the content of triglycerides was determined on average by the indicator (3.95 ± 0.26) mmol / l, which exceeded the upper reference limit: in men - (4.22 ± 0.17) units, in women, their level was probably lower - (2.83 ± 0.43) units.

Low density cholesterol in patients of Group I reached (2.93 ± 0.91) mmol / l, II group - (3.14 ± 0.23) mmol / l; III groups - (3.12 ± 0.83) mmol / l. In this case, the content of very low density lipoproteins was (1.27 ± 0.25) mmol / l (Group I). In the group of patients over the age of 44 years, there is an increase in the level of very low density lipoprotein (1.29 ± 0.22) mmol / l (II group); (1.47 ± 0.16) mmol / l (group III).

For patients in Group I, the content of high-density lipoproteins was (1.095 ± 0.30) mmol / l, in the second group - (2.86 ± 0.57) mmol / l, in the third group - (1.26 ± 0.18) mmol / l. It is known that high-density lipoprotein from the tissues gets into the liver for processing. That is, their low concentration in young people with NAFLD indicates that patients in this group have a sign that there is a high risk of developing atherosclerosis. The increased level of high-density lipoprotein in middle-aged people (Group II) should be considered as a factor that prevents the atherosclerotic process, and in the elderly patients, when their protective mechanisms are weakened, their content is reduced.

The coefficient of atherogeny in patients of Group I was equal (4.49 ± 0.90) , which is higher than the maximum allowable value. That is, patients in this age group showed significant deviations in the lipid profile of the blood with an increased risk of atherosclerosis. In the second group, the coefficient of atherogeny was on average equal (4.19 ± 0.40) . In men, the rate was (4.43 ± 0.56) units, in women - (2.68 ± 0.46) units, which is higher than the maximum allowable and is significantly higher than in women, $p < 0.05$. That is, patients in this age group showed significant deviations in the lipid spectrum of blood, which characterizes the high risk of atherosclerosis, with a greater tendency for men.

Patients in the group III have significant deviations in the lipid profile of the blood, which maintains a high risk of atherosclerosis, with a higher tendency for men, the coefficient of atherogeny was (4.19 ± 0.40) units. In men, the index increases to (4.56 ± 0.33) units, in women it is (3.68 ± 0.57) units, which is higher than the maximum allowable

value and is significantly higher than in women, $p < 0.05$.

Indicators of cytolysis in patients of group I revealed some deviations. The activity of ALAT on average was determined on average, as (55.21 ± 13.77) $\mu\text{mol} / \text{l}$, AsAT (35.24 ± 7.17) $\mu\text{mol} / \text{l}$. The highest rates of ALAT and AsAT were found in patients with a disease period of 4 and 5 years. In patients from the second group, the ALAT activity was (65.39 ± 4.47) $\mu\text{mol} / \text{l}$, AsAT (49.77 ± 3.69) $\mu\text{mol} / \text{l}$, in patients of the third group - (68.61 ± 2.51) $\mu\text{mol} / \text{l}$, AsAT - (41.26 ± 2.24) $\mu\text{mol} / \text{l}$. Increased ALAT and AsAT rates indicate hepatocyte damage in young patients with different incidence of diabetes mellitus, and the most pronounced changes are detected with a 5-year period of the disease. In patients of middle and advanced age, the ratio in the content of ALT and AsAT varies slightly. This corresponds to the results obtained by other researchers at NAFLD [3, 12].

The content of total bilirubin was within the reference values of the normal index - (17.63 ± 2.27) $\mu\text{mol} / \text{l}$, (Group I); (14.64 ± 1.22) $\mu\text{mol} / \text{l}$ (group II). (13.88 ± 1.83) $\mu\text{mol} / \text{l}$ (group III), indicating no disturbances in pigment exchange.

Regarding the peculiarities of the hemogram parameters, we drew attention to the fact that in the patients of the I age group the ESR index, on average, was (11.87 ± 2.70) mm / h. In group II, the attention is paid to a sufficiently large number of patients with elevated ESR. Thus, the rate to 12 mm / h was observed in 38 patients (63.3%), from 13 to 20 mm / h - in 10 patients (16.7%) from 21 to 30 mm - 6 patients (10.0%) and more than 30 mm - in 6 patients (10.0%). The elevated ESR is more often found in women, and rarely in men. Thus, the normal index of ESR was 45.8% for women and 77.8% for men. ESR in the range of 13-20 mm / h was determined in 25.0% of women and 11.1% in men; 21-30 mm / h - 12.5% for women and 11.1% for men, more than 30 mm / h - 16.6% for women, men have not seen such cases. The increase in ESR often leads to the presence of foci of inflammatory process in various organs and tissues. In the presence of signs of fatty liver damage in the examined patients, one can express an opinion on the progression of the inflammatory process precisely in the liver, because the age limits of ESR in the norm differ little in different age groups. In women, this figure is higher, probably due to changes in the hormonal status, since most women of this age are in the menopausal period. In the 3rd group, the ESR, on average, was (14.28 ± 1.85) mm / h. The attention is paid to a fairly large number of patients with elevated ESR, which is more common in women, and less frequently in men.

The content of erythrocytes, leukocytes in the hemogram did not deviate from the reference limits. In the leukocyte formula no significant deviations from the norm were observed.

4. Conclusion

1. Fatty hepatose, as a stage of NAFLD, associated with type 2 diabetes mellitus in young patients has its own peculiarities. NAFLD clinically runs asymptomatic with complaints of dry mouth, general weakness, vertigo, discomfort in the right upper gut region, manifestations of which are supplemented by bitterness in the mouth, discomfort in the abdomen, increased liver size and its increasing from 1 year to 12-year period of the disease. According to the totality of ultrasonographic signs in 24,4% of patients I stage was established, in 31,1% - stage II, in 44,4% - the third stage of fatty hepatosis. The elevated ALAT and AsAT rates indicate hepatocyte damage in young patients with different incidence of

diabetes, and the most pronounced changes are detected with a 5-year period. Patients in this age group showed significant deviations in the lipid profile of the blood with an increased risk of atherosclerosis.

2. In the 2nd group of patients (middle age), the duration of the disease is in average ($9,38 \pm 0,80$) years with the highest number of sick patients, 2 to 5 (28,3%), from 6 to 10 years -36.7% and from 11 to 20 years - 25.0% of patients. NAFLD in the stage of fatty liver infiltration were 50.0% of patients. Patients in this group in 25.0% of cases identified I stage of fatty hepatosis, 40.0% - stage II, 35.0% - stage III. The lipid profile of the blood revealed high levels of HDL cholesterol, LDL and VLDL cholesterol, and a high level coefficient of atherogeny (higher in males than in women). A sufficiently high content of triglycerides in men has been determined and a high rate of thymol test in women. In this age group, there is a fairly large number of patients with elevated ESR, in men of almost one in five patients, and in women - every third patient.
3. In the 3rd group of the elderly patients with NAFLD, the period of the disease was determined on average ($14,61 \pm 1,43$) years, more than half of patients suffered on diabetes mellitus from 11 to 20 years (55,2%). In men, the development of diabetic complications ran like women. However, in women is smaller percentage of cases of dyscirculatory mixed encephalopathy (I st.). In men more than I-III. the greater is the damage of the retina, the angiopathy of the extremities, dysmetabolic myocardial infarction and nephropathy. NAFLD in the stage of fatty liver infiltration were in 46.7% of patients. In 20.69% of cases, it was diagnosed as stage I of fatty hepatosis, in 51.73% of cases - stage II, in 27.58% of cases - stage III. The enlargement of the liver was prominent by palpation (1.81 ± 0.07) cm from the edge of the rib arch (1.0 to 2.5 cm) in 62.63% of patients.
4. Functional state of the liver in patients of all groups remained satisfactory. Protein and pigmentary metabolism were characterized by indicators in the reference limits of the indicator in healthy individuals; thymol test for women showed the expressed signs of mesenchymal-inflammatory syndrome. Patients experienced significant abnormalities in the lipid profile of the blood, which supports a high risk of atherosclerosis, with a greater tendency in men: high levels of high-density lipoprotein, low-density lipoprotein and very low-density lipoprotein levels, coefficient of atherogeny and triglyceride levels where high (in men, higher, comparable with women).

Thus, with age in the dynamics of the NAFLD, the number of cases with fatty infiltration decreases to 60 years, at the same time it increases - with steatohepatitis and dyslipidemia. Blood pressure shows a tendency to increase from the 25th year of life ($p < 0,05$). In patients with middle and advanced age, fluctuations of hyperglycaemia became more frequent. The size of the right lobe of the liver (17.0 cm) was greatest in case of illness for 1 year in young patients, and the smallest (8.5 cm) in patients from the III group. With age the number of cases with stage I of fatty liver is reduced, and the third stage increases accordingly. In patients of Group I, the intensity of mesenchymal-inflammatory syndrome is minimal. Signs of thymol test in patients of middle and older age is increasing, besides, women exhibit more pronounced signs of

mesenchymal-inflammatory syndrome in II and III groups, comparing with men. Both in young and in patients of middle and advanced age, the liver is enlarged, in the last ones little bit more than in young ones. The level of triglycerides in women with age was significantly lower. In the group of patients over 44 years of age, there is an increased level of very low density lipoprotein, and significant deviations in the lipid profile of the blood, which supports the high risk of atherosclerosis, with a greater tendency in men. The attention of a fairly large number of patients with elevated ESR, which is more often found in women, less frequently - in men.

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