Method of treatment of type 2 diabetes mellitus comorbid with chronic toxic hepatitis with dpp-4 ingibitors and alpha-lipoic acid

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Type 2 diabetes mellitus (DM-2) is one of the most topical health and social problems of modern mankind. Liver disease comorbid with DM-2 is quite a common clinical situation. Liver injury is considered as one of the major complications of diabetes, so the severity of diabetes depends on the functional state of the liver. Chronic toxic hepatitis (CTH) had become a significant problem over past decades due to the growing industrialization and increasing prevalence of this disease. However, many issues concerning CTH remain understudied, including its diagnostic, therapeutic and preventive aspects.

Objective: to determine the dynamics of metabolic parameters in patients with type 2 diabetes mellitus (DM-2) and CTH who had been treated with dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors) and alpha - lipoic acid (ALA).

Materials and Methods: 30 patients (17 men and 13 women) with subcompensated DM-2 and CTH of moderate activity were examined. The age of patients ranged from 28 to 60 years. The average age was 45,6 ± 4,7 years. The mean duration of DM-2 was 10,1 ± 1,1 years. All patients with DM-2 comorbid with CTH were divided into groups according to prescribed treatment: the first group (n = 15) included patients who followed the diet, took hypoglycemic drugs or insulin, and hepatoprotectors from silymaringroup (the dose was 90 mg three times daily). The second group (n = 15) included patients who followed the diet, took hypoglycemic drugs or insulin, DPP-4 inhibitors (vildagliptin) - the dose was 50 mg twice daily, and ALA preparations- the dose was 600 mg daily for 10 days intravenously, followed by oral intake of 600 mg per day.

Evaluation of clinical efficacy of the proposed treatment included the following complex of clinical, laboratory, and instrumental studies before and after treatment: an assessment of patient's major clinical syndromes, clinical and biochemical blood parameters (fasting blood glucose (FBG), glycosylated hemoglobin (HbAlc), total

bilirubin and its fractions, alanine aminotransferase(ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), triglycerides (TG), total cholesterol (CH), high-density lipoprotein (HDL), low-density lipoprotein (LDL). Liver ultrasound was performed to evaluate the morphological and functional state of the liver.

The results: the examination of patients showed that the most common clinical syndromes in case of DM-2 comorbid with CTH were asthenic, dyspeptic, abdominal pain, and hepatomegaly that had different manifestations. It was found that after the initiation of treatment, patients reported clinical improvement: in the first group - after 5-8 days, in the second group - after 3-6 days. All patients had subcompensated state of carbohydrate metabolism. Comparative analysis of biochemical parameters after 12 weeks treatment showed that in the first group FPG changed from 8.6± 0.11 to 7.2± 0.12 mmol / l, HbA1c – from 8,5 +0,16 to 7.3 + 0.13% ($p < 0.05$), ALT - from 0,87 ± 0,02 to 0,68 ± 0,02 mmol / hr * l ($p < 0.05$), AST from 0,71 ± 0, 2 to 0,65 ± 0,2 mmol / hr*l ($p<0.05$), ALP - from 5,2 ± 0,17 to 4,2 ± 0,13 ($p < 0.05$). TGlevel decreased from 2,8 ± 0,16 to 1,94 ± 0,16 mmol / l, CH -from 7,1 ± 0,1 mmol / l to 6.16 ± 0.11 mmol / l ($p < 0.05$), LDL - from 2,72 ± 0,05 mmol / l to 2,27 ± 0,05 mmol / l ($p < 0.05$), HDL increased from 0,9 ± 0,05 to 1,11 ± 0,05 mmol / l ($p < 0.05$). The second group also showed a positive dynamics of data: FPG dropped to 6.5±0.11 mmol / l, HbA1c decreased to 6,5 ± 0,12 mmol / L, ALT reached 0.57 ± 0,02 mmol / hr * l, AST - 0,65 ± 0,02 mmol / hr* l, ALP - 3,1 ± 0,11 ($p < 0.05$), TG - 1,42 ± 0,23 mmol / l, CH - 5,3 ± 0,13 mmol / l, LDL - 1,83 ± 0,08 mmol / l ($p < 0.05$), HDL - 1,1 ± 0,04 mmol / l. Patients treated with DPP-4 inhibitors and ALA also had more significant decrease in liver size and restoration of its echostructure according to liver ultrasound.

Conclusions: The inclusion of DPP-4 inhibitors and ALApreparations into therapeutic regimens has led to more efficient clinical and laboratory changes, improvement of carbohydrate and lipid metabolism and enhancement of the functional state of the liver in patients with DM type-2 accompanied with CTH.