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Evaluation of the Efficiency of Treatment of Type 2 Diabetes Mellitus in Patients Infected with Chronic Viral Hepatitis with Drugs to Lower Blood Sugar

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Annotation: Currently, a number of scientific studies are being conducted and there is a lot of data on the high prevalence of chronic viral hepatitis C in type 2 diabetes mellitus. Markers of seroconversion of HCV infection in type 2 diabetes mellitus are detected in more cases than in type 1 diabetes mellitus. Identification of biochemical and instrumental changes in patients with a comorbid course of chronic viral hepatitis C with type 2 diabetes mellitus, as well as the study of pathogenetic factors in the development of insulin resistance in patients with hepatitis C, the influence of chronic viral hepatitis C on the course and manifestations of type 2 diabetes mellitus, as well as the study of a specific approach to Treatment with hypoglycemic agents in these patients is of particular importance.

Keywords: chronic viral hepatitis C, diabetes mellitus, insulin resistance.

Successful registration of new hypoglycemic drugs or justification of the efficacy and safety of drugs used in clinical practice at a meeting of the Endocrinological and Metabolic Diseases Drugs Advisory Committee of the UK Food and Drug Administration (FDA). Confirmed by many scientists that long-term clinical trial data are needed to prove their safety and efficacy in patients with type 2 diabetes in relation to cardiovascular and metabolic complications, including serious changes in the liver. Regarding the treatment principles, when type 2 diabetes is observed together with liver disease, appropriate recommendations for physical exercise for these patients can reduce IR, but vigorous physical exercise and strict diet may not be suitable for all patients, that is, malnutrition in patients with liver disease can Interfere with this process can lead to deepening [4]. Therefore, it is recommended to treat patients with drugs even in low doses. Patients with type 2 diabetes mellitus and SVGC need to take hypoglycemic agents to control glycemia. However, these drugs are metabolized in the liver. Therefore, it is necessary to strengthen control of laboratory tests in patients. Metformin reduces IR, increases insulin sensitivity, and is involved in lipid metabolism. Metformin cannot be recommended for patients with liver cirrhosis due to the risk of lactic acidosis, but some scientists believe that it reduces the risk of liver complications [9]. Sulfonylurea derivatives have the property of stimulating insulin production by affecting beta cells. It is dangerous only for elderly patients due to hypoglycemia, and the glycoside should not be used in liver diseases if possible, since it is metabolized in the liver. Meglitinides, drugs of this group, are rarely used in liver diseases caused by hypoglycemia; their effectiveness has not been studied. Alpha-glucosidase inhibitors reduce the absorption of carbohydrates in the intestine. In a study of patients with liver diseases, it was found that it significantly reduces postprandial glycemia [5]. Thiazolidinediones increase insulin sensitivity in the target group. However, they are not recommended for liver disease due to a sharp increase in ALT levels. However, according to the conclusion of some studies, on the contrary, patients receiving rosiglitazone had improved liver function and normal enzymes. GPP 1 receptor agonists act on incretins and increase glucose-dependent insulin secretion, reduce glucose-dependent glucagon secretion, and increase the sensitivity of β-cells to glucose; Gliflozins (sodium-glucose cotransporter-2 inhibitors). This is a new group of drugs that lower blood sugar levels. An increase in blood sugar also leads to an increase in glucose levels in primary urine. Paradoxically, in diabetes, glucose reabsorption increases and the renal threshold rises. Although basal and bolus insulin therapy is considered liver-friendly, in many cases, especially in patients with cirrhosis, enhanced monitoring is necessary due to the high risk of hypoglycemia. Objective: to study the clinical efficacy of treatment with hypoglycemic

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drugs in the treatment of patients with type 2 DM and VGC. Material and methods of the study: The study was conducted in the endohematology department of the multidisciplinary clinic of the Research Institute of Virology and the Tashkent Medical Academy during 2018-2021. The main group included 104 patients with both type 2 diabetes mellitus and type 2 diabetes mellitus, these patients were examined and divided into groups depending on the hypoglycemic agents used in the treatment of type 2 diabetes. In the study, patients were divided into groups according to the level of activity of SVGC, the anamnesis included patients who took antidiabetic drugs for more than six months. 23 patients were treated with metformin (1000-2500 mg metformin per day), 21 patients were treated with SM and metformin (2-3 mg SM and metformin 850-1500 mg per day), 25 patients were treated with a combination of DPP4 inhibitors and metformin (sitagliptin or vildagliptin 100 mg and metformin 1000 mg once daily), 4 were recipients of SM and basal insulin, and 30 were patients with insulin (short-, intermediate-, or long-acting). GPP-1 (glucagon-like peptide-1) receptor agonists and SGLT2 (sodium glucose cotransporter-2) inhibitors were not detected in patients.

In the selected groups, the average age of patients in group 1 was 50.8±1.7 years, 66.7% were women and 33.3% were men. The duration of SVGS in these patients was 3.1±0.20; It was found that the duration of type 2 DM was 3.8±0.29. The average age of patients receiving SM and metformin in group 2 was 53.5±1.1 years, 52.2% were women and 47.8% were men (Fig. 1). In these patients, the duration of SVGC was 3.8±0.25, and the duration of type 2 CT was 4.0±0.28. Recipients of group 3 of DPP4 and metformin had an average age of 50.3±0.91, women - 55.6%, men - 44.4%. The duration of the SVGC was 2.9±0.27; The duration of type 2 CT was determined at the level of 2.9±0.23. The average age of our last 4th group, i.e. insulin recipients, was 57.4±0.83 years, women accounted for 59.3%, men - 40.7%. Among the patients, in addition to them, those receiving basal insulin and hypoglycemic drugs were observed in a very small percentage, i.e. 3.8% of patients, therefore, it was not possible to statistically analyze these patients among the patients. Type 2 DM was 7.3±0.32. When examining patients with type 2 DM and chronic viral hepatitis C, the ALT level was minimal and low activity, and carbohydrate indicators were determined depending on the hypoglycemic drugs they took. In patients taking metformin who had an increase in ALT (<1↑) during the period of minimal activity, the level of postprandial blood glucose was 8.3±0.13, postprandial glycemia was 12.2±0.29, HbA1c was 8.0±0.16 (Table 1). In patients taking sulfonylurea drugs and metformin, the postprandial blood sugar level was 7.2±0.12, postprandial glycemia was 11.8±0.19, HbA1c was 7.5±0.15. In those receiving a combination of DPP-4i and metformin, the blood glucose level was 6.2±0.18, postprandial glycemia 10.8±0.12, HbA1s 6.8±0.11, which is a reliable difference compared to groups 1 and 2.

Table 1. Carbohydrate indices according to the data of taking hypoglycemic drugs in patients with increased ALT with minimal activity (<1↑)

ALT at minimum activity (<1↑)	Metformin=15	SM and Metformin=8	DPP-4i and Metformin n=8
Dietary sugar	8,3±0,13	7,2±0,12*	6,2±0,18*^
Postprandial glycemia	12,2±0,29	11,8±0,19	10,8±0,12*^
HbA1c	8,0±0,16	7,5±0,15	6,8±0,11*^

Note: * - the difference compared to the indicators of group 1 is reliable (*-P<0.05); ^ - the difference compared to the indicators of group 2 is reliable (^-P<0.05);

In patients taking metformin, with an increase in ALT (3-5 times), observed at low activity, the level of postprandial blood glucose was 8.6 ± 0.23, postprandial glycemia 12.7 ± 0.39, HbA1c 8.2 ± 0.26 (Table 2). In patients taking sulfonylurea drugs and metformin, the postprandial blood sugar level was 7.7 ± 0.32, postprandial glycemia 12.5 ± 0.29, HbA1c 7.8 ± 0.15. In those receiving a combination of DPP-4i and metformin, the blood glucose level was 6.8±0.28, postprandial glycemia 11.7±0.22, HbA1c 7.0±0.10, which is a reliable difference compared to groups 1 and 2.

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Table 2. Carbohydrate indices increase against the background of taking hypoglycemic drugs in patients with low ALT activity (↑ 1-3 times)

Increased ALT at low activity (1-3 times ↑)	**Metformin=6**	**SM and Metformin=11**	**DPP-4i va metformin n=14**
Food sugar	8,6±0,23	7,7±0,32*	6,8±0,28*^
Postprandial glycemia	12,7±0,39	12,5±0,29	11,7±0,22*
HbA1c	8,2±0,26	7,8±0,15	7,0±0,10*^

Note: * - the difference compared to the indicators of group 1 is reliable (*-P<0.05); ^ - the difference compared to the indicators of group 2 is reliable (^-P<0.05);

In patients taking insulin with moderate and high ALT activity, postprandial blood sugar levels were 7.2±0.13 and 7.6±0.22, postprandial glycemia was 12.4±0.18 and 13.5±0.35, HbA1s was 7.8±0.15 and 8.0±0.25 (Table 3). Although the results included patients with elevated ALT levels, timely and adequate insulin therapy makes it possible to achieve target glycemia values.

Table 3. Carbohydrate indices depending on insulin intake in patients with elevated ALT levels with moderate and high activity

	Insulin recipients n=25	**Insulin recipients n=6**
	Increased ALT with moderate activity (up to 3-5 times ↑)	**Increased ALT with high activity (5-10 or more ↑)**
Dietary sugar	7,2±0,13	7,6±0,22
Postprandial glycemia	12,4±0,18	13,5±0,35
HbA1c	7,8±0,15	8,0±0,25

In patients with type 2 diabetes mellitus, a high-calorie diet and a sedentary lifestyle cause postprandial hyperlipidemia, as well as activation of lipolysis and, as a consequence, excessive production of free fatty acids (FFA), which have a direct lipotoxic effect on β-cells. pancreas and stimulate glycogenolysis in the liver. Excessive concentrations of FFA and postprandial hyperlipidemia are additional predictors of insulin resistance, hyperinsulinemia and the development of atherosclerosis. The study analyzed lipid metabolism parameters among groups of patients with chronic hepatitis C and DM type 2, which were divided according to the use of hypoglycemic agents. The amount of total cholesterol in patients of the 1st group was 6.5±0.14, in the 2nd group - 6.7±0.19, in the 3rd group - 5.6±0.19, compared with the 1st and 2nd groups. A reliable difference was found in the group (P <0.01). The amount of cholesterol in patients of the 4th group receiving insulin therapy was 6.0±0.18, while between them and the 3rd group there was a reliable difference (P <0.05). Hypertriglyceridemia was observed in all groups of patients, and in the 3rd group in individuals taking DPP-4i and metformin, it was 3.0±0.20 compared with the 1st group (4.2±0.08) and the 2nd group (3.7±0.09), which is a relatively reliable indicator. no difference was observed (r<0.01). The atherogenicity index was recorded in high results in patients of all groups; in patients of the 3rd group (3.7±0.30) compared to patients of the 1st group (4.4±0.20) and the 2nd group (4.7±0.29) it was determined at a low level. no reliable difference (r<0.05).

During the study, the percentage of liver fibrosis indicators was analyzed among groups of patients with type 2 chronic hepatitis C and CT receiving hypoglycemic agents. According to these results, among patients of our group 3 receiving DPP-4i and biguanide, patients with stage F 0-1 were observed and amounted to 4.1%. Among the other group of patients, this stage was not observed. Changes characteristic of stage F1 fibrosis were not observed among recipients of only biguanide in group 1, among recipients of SM and biguanide - group 2 - 4.7%, among recipients of DPP4 inhibitors and biguanides - 52.1%, among recipients of insulin - 3.3%, observed in % of patients. Fibroscan F stage 2, i.e. moderate liver fibrosis, was 91.4% in group 1, 90.6% in group 2, 43.8% in group 3 and 54.8% in group 4. Fibrosis F stage 3 was detected in 8.6% of patients in group 1, 4.7% in group 2,

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32.2% of patients receiving insulin, and severe liver fibrosis was not detected among patients receiving a combination of DPP-4 inhibitors and biguanide. Changes specific to stage F4 were detected in 9.6% of patients in group 4, in the remaining patients no changes specific to this stage were detected.

Summary

Hypoglycemic treatment of patients with chronic hepatitis C and type 2 diabetes mellitus showed that the best indicators of carbohydrate, lipid spectrum and fibroscanning stages were in the group receiving a combination of dipeptidyl peptidase-4 inhibitors and metformin ($r<0.05$). In patients with more than a fivefold increase in transaminases, switching to insulin therapy when stages F3 and F4 were detected allowed achieving compensation in this group ($r<0.05$).

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