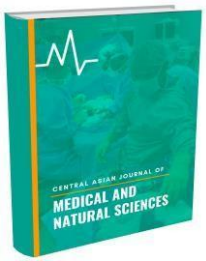

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Article

Clinical and Metabolic Effectiveness of Hypoglycemic Therapy in Patients with Type 2 Diabetes Mellitus Associated with Chronic Hepatitis C Infection

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Abstract: Type 2 diabetes mellitus (T2DM) and chronic hepatitis C virus (HCV) infection remain among the leading global medical and social health challenges due to their increasing prevalence, chronic progressive course, and high risk of disability and mortality. Numerous studies have demonstrated a close pathogenetic relationship between chronic hepatitis C and disturbances in carbohydrate metabolism, particularly insulin resistance and impaired glucose tolerance. In patients with chronic HCV infection, metabolic abnormalities may significantly affect the clinical course of both liver disease and diabetes mellitus. Objective to evaluate the clinical and metabolic effectiveness of various hypoglycemic therapy regimens in patients with type 2 diabetes mellitus associated with chronic hepatitis C infection. The study included 85 patients diagnosed with T2DM and chronic hepatitis C who underwent inpatient treatment at the multidisciplinary clinic of Tashkent State Medical University and the Research Institute of Virology. Patients were divided into four groups according to the administered glucose-lowering therapy: 1. Metformin monotherapy (n=28); 2. Sulfonylurea combined with metformin (n=24); 3. DPP-4 inhibitors combined with metformin (n=18); 4. Insulin therapy (n=15). Clinical examination, anthropometric assessment, fasting plasma glucose, glycated hemoglobin (HbA1c), HOMA-IR index, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels were evaluated before and after 12 weeks of therapy. Statistical analysis was performed using SPSS 18.0 software. Differences were considered statistically significant at $p<0.05$. Patients receiving DPP-4 inhibitors in combination with metformin demonstrated significantly better glycemic control and improved liver biochemical parameters compared with other therapeutic groups. In this cohort, fasting glycemia and HbA1c levels decreased more substantially after 12 weeks of treatment. ALT levels decreased from 54.2±3.1 U/L to 44.2±2.1 U/L, while AST values decreased from 42.6±3.6 U/L to 37.6±1.6 U/L ($p<0.05$). In contrast, patients receiving insulin therapy showed persistently elevated metabolic and hepatic parameters, which may be associated with longer disease duration and more severe metabolic disturbances. Combined therapy with DPP-4 inhibitors and metformin demonstrated the highest therapeutic effectiveness in patients with T2DM associated with chronic hepatitis C infection. This treatment strategy contributed to improved carbohydrate metabolism, reduction of insulin resistance, and normalization of liver enzyme activity.

Keywords: Type 2 diabetes mellitus; chronic hepatitis C; insulin resistance; DPP-4 inhibitors; metformin; HOMA-IR; liver enzymes; hypoglycemic therapy.

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Introduction

Type 2 diabetes mellitus and chronic liver diseases represent major global healthcare problems due to their widespread prevalence, chronic progression, and increasing

contribution to morbidity and mortality worldwide. In recent years, increasing scientific attention has been directed toward the pathogenetic relationship between chronic hepatitis C virus infection and metabolic disorders, particularly insulin resistance and type 2 diabetes mellitus [1].

Chronic hepatitis C is not only a hepatotropic but also a systemic metabolic disease. HCV infection contributes to disturbances in insulin signaling pathways, hepatic glucose metabolism, inflammatory cytokine production, and lipid homeostasis. Several studies have demonstrated that patients with chronic hepatitis C exhibit a significantly higher prevalence of insulin resistance and T2DM compared with the general population [2].

Insulin resistance plays a pivotal role in the progression of hepatic fibrosis, steatosis, and impaired antiviral response in HCV-infected individuals. Furthermore, the coexistence of T2DM and chronic hepatitis C substantially worsens clinical outcomes by accelerating liver injury and increasing the risk of cirrhosis and hepatocellular carcinoma.

Selection of appropriate glucose-lowering therapy in patients with chronic liver disease remains clinically challenging because hepatic dysfunction may alter drug metabolism and increase the risk of adverse effects. Therefore, identification of the safest and most effective hypoglycemic therapy for patients with T2DM and chronic hepatitis C is of considerable clinical importance [3].

The present study aimed to evaluate the metabolic and hepatoprotective effectiveness of different hypoglycemic treatment regimens in patients with T2DM associated with chronic hepatitis C infection [4].

Materials and Methods

This prospective clinical study included 85 patients older than 30 years diagnosed with type 2 diabetes mellitus and chronic hepatitis C infection. Patients were recruited from the Virology Research Institute and the multidisciplinary clinic of Tashkent State Medical University [5].

The diagnosis of T2DM was established according to World Health Organization and ADA diagnostic criteria. Chronic hepatitis C infection was confirmed using serological and biochemical investigations [6].

Inclusion Criteria

- Age above 30 years;
- Confirmed diagnosis of T2DM;
- Chronic hepatitis C infection;
- Signed informed consent.

Exclusion Criteria

- Type 1 diabetes mellitus;
- Duration of T2DM or HCV infection longer than 15 years;
- Age below 30 or above 70 years;
- Liver cirrhosis;
- Acute inflammatory or autoimmune diseases;
- Severe somatic pathology;
- Chronic alcohol abuse;
- Hemoglobinopathies affecting HbA1c interpretation [7].

Study Groups

To evaluate the comparative effectiveness of different hypoglycemic treatment strategies, all enrolled patients were stratified into four therapeutic groups according to the type of glucose-lowering therapy administered at the time of hospitalization and during the observation period. The distribution of patients into groups was performed

based on their routine clinical management and individualized treatment approaches considering disease duration, glycemic control, metabolic status, and concomitant hepatic impairment [8].

Group 1 — Metformin Monotherapy

The first study group consisted of 28 patients receiving metformin as monotherapy since the initial diagnosis of type 2 diabetes mellitus. The average daily dose of metformin ranged from 850 to 2000 mg/day depending on individual metabolic requirements and treatment tolerance. Metformin was selected due to its established role as a first-line antihyperglycemic agent with insulin-sensitizing properties and favorable effects on peripheral glucose utilization. Patients in this group generally demonstrated shorter disease duration and relatively preserved pancreatic β-cell function [9].

Group 2 — Combination Therapy with Sulfonylureas and Metformin

The second group included 24 patients treated with combined oral hypoglycemic therapy consisting of sulfonylurea derivatives and metformin. Sulfonylurea agents were administered at an average daily dose of 2–3 mg/day, while metformin doses ranged from 850 to 1500 mg/day. This therapeutic combination was prescribed to patients who failed to achieve adequate glycemic control with metformin monotherapy alone. Sulfonylureas stimulate pancreatic insulin secretion and are commonly used in progressive stages of type 2 diabetes mellitus; however, their use in patients with chronic liver disease requires careful monitoring due to the potential risk of hypoglycemia and altered hepatic metabolism [10].

Group 3 — Combination Therapy with DPP-4 Inhibitors and Metformin

The third study group consisted of 18 patients receiving combined therapy with dipeptidyl peptidase-4 (DPP-4) inhibitors and metformin. The daily dose of metformin ranged from 500 to 1500 mg/day, while DPP-4 inhibitors were prescribed according to standard therapeutic recommendations. This treatment strategy was selected because of the favorable metabolic profile of incretin-based therapy, including improvement of insulin sensitivity, reduction of postprandial hyperglycemia, low risk of hypoglycemia, and potentially beneficial effects on hepatic metabolic processes. Particular attention was paid to this group due to the increasing scientific interest in the hepatoprotective and anti-inflammatory properties of DPP-4 inhibitors in patients with chronic liver diseases [11].

Group 4 — Insulin Therapy

The fourth group included 15 patients receiving insulin therapy. Patients in this cohort were treated with either basal insulin regimens or combined short- and long-acting insulin preparations depending on the severity and duration of diabetes mellitus. Insulin therapy was predominantly prescribed to patients with long-standing disease, poor glycemic control, marked insulin resistance, or inadequate response to oral hypoglycemic agents. Individuals in this group generally demonstrated more pronounced metabolic disturbances and longer duration of both diabetes mellitus and chronic hepatitis C infection [12].

Comparative analysis among these therapeutic groups allowed assessment of the influence of different hypoglycemic regimens on carbohydrate metabolism, insulin resistance, and liver functional parameters in patients with concomitant chronic hepatitis C infection and type 2 diabetes mellitus.

Clinical and Laboratory Assessment

All patients underwent:

- Anthropometric assessment;
- Body mass index calculation;
- Fasting plasma glucose evaluation;
- Glycated hemoglobin (HbA1c);

- HOMA-IR index assessment;
- Liver function tests including ALT, AST, and bilirubin levels.

All parameters were reassessed after 12 weeks of therapy.

Statistical Analysis

Statistical processing was conducted using SPSS version 18.0. Quantitative variables were expressed as mean ± standard deviation (M±SD). Statistical significance was determined at $p<0.05$ [13].

RESULTS

The study population included 26 men and 59 women. The mean age of participants was 52.7±3.56 years. Obesity of varying degrees was observed in the majority of patients, with mean BMI values corresponding predominantly to grade I obesity.

Patients receiving insulin therapy demonstrated longer duration of both diabetes mellitus and chronic hepatitis C compared with other groups [14].

Carbohydrate Metabolism Parameters

Analysis of carbohydrate metabolism indicators demonstrated significant intergroup differences after 12 weeks of therapy.

Patients treated with DPP-4 inhibitors combined with metformin showed:

- Lower fasting plasma glucose levels;
- Improved HbA1c values;
- Better HOMA-IR indices compared with patients receiving sulfonylureas or insulin therapy.

Metformin monotherapy showed moderate metabolic effectiveness; however, glycemic control remained inferior to DPP-4 inhibitor-based therapy.

Insulin-treated patients demonstrated persistently elevated glycemic indicators, likely associated with prolonged disease duration and severe insulin resistance.

Liver Function Parameters

Bilirubin levels remained relatively stable across all treatment groups. However, significant differences were observed in liver transaminase activity [15].

The most favorable biochemical profile was observed in patients receiving DPP-4 inhibitors combined with metformin:

- ALT decreased from 54.2±3.1 U/L to 44.2±2.1 U/L;
- AST decreased from 42.6±3.6 U/L to 37.6±1.6 U/L ($p<0.05$).

Patients treated with sulfonylureas exhibited comparatively higher transaminase activity, suggesting less favorable hepatic tolerance.

Metformin monotherapy produced only minimal improvements in ALT and AST levels.

Discussion

The present study demonstrated that DPP-4 inhibitor-based therapy combined with metformin provides superior metabolic and hepatic outcomes in patients with T2DM associated with chronic hepatitis C infection.

The pathophysiological association between HCV infection and insulin resistance is mediated through chronic inflammation, oxidative stress, hepatic steatosis, and direct interference with insulin signaling pathways. Consequently, effective glucose-lowering therapy in this patient population should not only improve glycemic control but also minimize hepatic metabolic burden.

DPP-4 inhibitors possess several clinically advantageous properties, including:

- Low risk of hypoglycemia;

- Neutral effect on body weight;
- Favorable hepatic safety profile;
- Improvement of insulin sensitivity.

Our findings are consistent with recent international studies reporting beneficial effects of incretin-based therapies on hepatic inflammation and metabolic regulation in chronic liver disease.

The observed reduction in ALT and AST activity among patients receiving DPP-4 inhibitors may indicate improvement in hepatocellular injury and metabolic inflammation.

The relatively poorer metabolic outcomes in insulin-treated patients may be explained by advanced disease duration, severe insulin resistance, and greater baseline metabolic dysregulation.

Conclusion

Patients with type 2 diabetes mellitus associated with chronic hepatitis C infection demonstrate significant disturbances in carbohydrate metabolism and liver functional activity.

Combination therapy with DPP-4 inhibitors and metformin showed the highest clinical and metabolic effectiveness among all investigated treatment regimens. This therapeutic strategy resulted in:

- Improved glycemic control;
- Reduced insulin resistance;
- Significant reduction in liver transaminase activity;
- Better overall metabolic compensation.

The findings suggest that DPP-4 inhibitor-based therapy may represent an effective and hepatically safe treatment approach for patients with concomitant T2DM and chronic hepatitis C infection.

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