A Study on Enhancing Pancreatic Islet Function in Type 2 Diabetes and Coronary Heart Disease Patients with Liraglutide and Metformin Combination Therapy

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Abstract: *Objective:* To investigate the impact of combining liraglutide with metformin on the enhancement of pancreatic islet function in patients with type 2 diabetes and coronary heart disease. *Methods:* 60 patients with type 2 diabetes and coronary heart disease admitted from February 2022 to August 2023 were selected as research subjects. They were randomly assigned to either control or treatment groups, with 30 patients in each. The control group received metformin alone, while the treatment group received liraglutide in combination with metformin. Various indicators, including blood sugar levels, pancreatic islet function, and cardiac function between the two groups were compared. *Results:* The results of FPG, 2hPG, HbA1c, HOMA-IR, NT-proBNP, and LVEDD in the treatment group were lower than those in the control group, whereas the values of FINS, HOMA-β, E/A, and LVEF in the treatment group were higher than those in the control group ($P < 0.05$). *Conclusion:* The use of liraglutide in combination with metformin significantly benefits patients with type 2 diabetes and coronary heart disease. It leads to improved pancreatic islet function, better blood sugar control, and enhanced cardiac function. This combination therapy is recommended for clinical adoption.

Keywords: Liraglutide; Metformin; Type 2 diabetes; Coronary heart disease; Pancreatic islet function

1. Introduction

Type 2 diabetes affects approximately 95% of diabetic patients. Prolonged high blood sugar levels can lead to chronic damage to the cardiovascular system and further complicate coronary heart disease [1,2]. The combination of type 2 diabetes and coronary heart disease is prevalent in clinical practice, hastening the progression of the patient's condition and posing a serious threat to their health. Therefore, timely and effective clinical treatment is crucial to delay the disease's advancement.

Metformin is currently the primary clinical treatment for type 2 diabetes, mainly working by regulating glucose processing in various systems [3-5]. However, its effectiveness as a standalone treatment is often

unsatisfactory, necessitating combination therapy with other drugs. Liraglutide, a human glucagon-like peptide-1 (GLP-1) analog, can enhance the glucose concentration-dependent secretion of insulin from pancreatic β cells, thereby improving pancreatic islet function [6]. This study aims to analyze the impact of liraglutide in combination with metformin on islet function in patients with type 2 diabetes and coronary heart disease. To achieve this, 80 patients were observed as part of the study.

2. Materials and methods

2.1. General information

A total of 60 patients with type 2 diabetes and coronary heart disease admitted from February 2022 to August 2023 were included as the research subjects of this study. The random number table method was employed to divide the patients into control and treatment groups, with 30 cases in each. In the control group, there were 18 males and 12 females, aged 46–75 (mean age 58.13 ± 3.09) years, with disease duration of 2–11 (mean duration 6.32 ± 0.60) years; in the treatment group, there were 17 males and 13 females, aged 47–76 (mean age 58.20 ± 3.11) years, with disease duration 2–10 (mean duration 6.29 ± 0.58) years. A comparison of the baseline data between the two groups showed no significant differences ($P > 0.05$), indicating comparability.

Inclusion criteria included patients meeting the diagnostic criteria for type 2 diabetes and coronary heart disease [7,8], confirmed by various auxiliary examinations, aged 40–80 years, with complete clinical data. Exclusion criteria included patients with type 1 diabetes, complications such as ketoacidosis, secondary hyperlipidemia, and others, patients with the presence of organic heart disease, severe liver, or kidney insufficiency, patients who are unable to communicate effectively with medical staff, pregnant or lactating women, patients who have taken drugs or hormones that affect weight during menstruation, and patients who are allergic to the drugs used in the study.

2.2. Method

All patients received standard treatment for coronary heart disease, including anti-thrombotic, antihypertensive, and lipid-lowering treatments, as well as a low-salt, low-fat diet, and refrained from smoking or alcohol consumption while engaging in appropriate exercise.

The control group received metformin alone, in the form of metformin hydrochloride tablets (Sino-American Shanghai Bristol-Myers Squibb Pharmaceutical Co., Ltd., national drug approval number H20023370, 0.5 g × 20 tablets). This was taken orally three times a day, before breakfast, lunch, and dinner, at a dosage of 0.5 g per time.

The treatment group received liraglutide in combination with metformin, with the same manufacturer, usage, and dosage of metformin as in the control group. Liraglutide injection (Novo Nordisk, Denmark, national drug approval number J20160037, 3 mL:18 mg) was administered subcutaneously once a day, starting at 0.6 mg and adjusted according to the patient's tolerance, not exceeding 1.8 mg. Both groups continued their treatment for three months, with close monitoring of clinical symptoms and immediate medical attention in case of discomfort.

2.3. Observation indicators

The following indicators between the two groups were compared:
  (1) Blood glucose indicators: Fasting blood glucose (FPG), two hours postprandial blood glucose (2hPG), and glycated hemoglobin (HbA1c). FPG and 2hPG were measured using the glucose oxidase method, while HbA1c was analyzed with a glycosylated hemoglobin analyzer using high-performance liquid

chromatography (HPLC).

(2) Pancreatic islet function indicators: Fasting insulin (FINS), insulin resistance index (HOMA-IR), and pancreatic islet β-cell function index (HOMA-β). These were determined using an immunoenzyme-linked adsorption method. HOMA-IR was calculated using the formula FPG × FINS ÷ 22.5, and HOMA-β was calculated as 20 × FINS ÷ (FPG - 3.5).

(3) Cardiac function indicators: Plasma N-terminal pro-brain natriuretic peptide (NT-proBNP), left ventricular early/late diastolic peak velocity ratio (E/A ratio), left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD). NT-proBNP was measured using a fully automatic chemiluminescence immunoassay analyzer with the chemiluminescence method. Other indicators were assessed using echocardiography.

2.4. Statistical processing

SPSS 20.0 was used for data analysis. All results followed a normal distribution. Measurement results were expressed as mean ± standard deviation (SD), and a t-test was conducted. Counting results were described as %, and a χ^2 test was applied. When the result was $P < 0.05$, it indicated a statistically significant difference.

3. Results

3.1. Comparison of blood glucose indicators between the two groups

Before treatment, there was no significant difference in the levels of FPG, 2hPG, and HbA1c between the two groups ($P > 0.05$); after treatment, the levels of the above indicators in the treatment group were at a lower level than those in the control group ($P < 0.05$). See **Table 1** for details.

Table 1. Comparison of blood glucose indicators between the two groups before and after treatment (mean ± SD)

Group	n	FPG (mmol/L)		2hPG (mmol/L)		HbA1c (%)	
		Before	After	Before	After	Before	After
Treatment group	30	8.41 ± 0.82	5.28 ± 0.49	12.59 ± 1.02	7.76 ± 0.74	9.21 ± 0.89	7.39 ± 0.70
Control group	30	8.37 ± 0.79	6.06 ± 0.57	12.52 ± 1.00	8.58 ± 0.82	9.18 ± 0.87	8.04 ± 0.77
t	-	0.192	5.684	0.268	4.066	0.132	3.421
P	-	0.848	0.000	0.789	0.000	0.895	0.001

3.2. Comparison of pancreatic islet function indicators between the two groups

Before treatment, there was no significant difference in the levels of FINS, HOMA-IR, and HOMA-β between the two groups ($P > 0.05$); after treatment, the FINS and HOMA-β values in the treatment group were higher than those in the control group, and the levels of HOMA-IR were lower than those of the control group ($P < 0.05$). See **Table 2** for details.

3.3. Comparison of cardiac function indicators between the two groups

Table 3 shows that the NT-proBNP level, E/A reaction, LVEF, and LVEDD for both the treatment group and the control group had no significant differences before treatment. However, NT-proBNP and LVEDD of the treatment group were lower than the control group, whereas E/A and LVEF were higher than the control group ($P < 0.05$).

Table 2. Comparison of pancreatic islet function indicators between the two groups before and after treatment (mean ± SD)

Group	n	FINS (pmol/L)		HOMA-IR		HOMA-β	
		Before	After	Before	After	Before	After
Treatment Group	30	4.61 ± 0.43	9.58 ± 0.92	4.16 ± 0.38	2.82 ± 0.25	16.48 ± 1.31	38.57 ± 3.52
Control group	30	4.66 ± 0.45	6.94 ± 0.66	4.21 ± 0.40	3.47 ± 0.31	16.52 ± 1.33	32.16 ± 2.98
t	-	0.440	12.771	0.496	8.940	0.117	7.612
P	-	0.662	0.000	0.622	0.000	0.907	0.000

Table 3.

Group	n	NT-proBNP (mmol/L)		E/A ratio		LVEF (%)		LVEDD (mm)	
		Before	After	Before	After	Before	After	Before	After
Treatment Group	30	583.15 ± 52.02	404.67 ± 35.13	1.42 ± 0.11	0.98 ± 0.09	47.62 ± 4.43	68.05 ± 6.47	62.04 ± 5.97	51.83 ± 4.85
Control group	30	584.07 ± 52.26	441.50 ± 35.82	1.40 ± 0.10	0.83 ± 0.07	47.70 ± 4.45	60.49 ± 5.71	62.10 ± 5.99	56.34 ± 5.30
t	-	0.068	4.021	0.737	7.206	0.070	4.799	0.039	3.438
P	-	0.946	0.000	0.464	0.000	0.945	0.000	0.969	0.001

4. Discussions

Diabetes is a chronic disease characterized by hyperglycemia, with the majority of cases being type 2 diabetes. The incidence of the disease is increasing annually, and the age of onset is progressively advancing. It not only affects the health of patients but also places a substantial burden on society [9]. One of the main pathogenic mechanisms of type 2 diabetes is pancreatic β-cell dysfunction, leading to inadequate insulin secretion. The continuous elevation of blood sugar levels results in metabolic dysfunction, affecting vascular permeability and, in turn, contributing to the development of coronary heart disease [10]. Maintaining blood sugar within a reasonable range can reduce damage to the vascular endothelium and support the overall function of the heart [11]. Therefore, clinical treatment should prioritize blood sugar control.

Metformin is a widely used hypoglycemic drug in clinical practice. Its primary mode of action involves increasing the glucose utilization rate by tissue cells and inhibiting hepatic glycogen generation production and intestinal wall cell glucose uptake [12]. While it has a specific effect, it may not be as effective for some patients, necessitating a combination with other medications.

This study demonstrated that the treatment group had lower values for FPG, 2hPG, HbA1c, HOMA-IR, NT-proBNP, and LVEDD compared to the control group, while the treatment group exhibited higher levels of FINS, HOMA-β, E/A ratio, and LVEF ($P < 0.05$). This suggests that the combination of liraglutide and metformin is effective in controlling blood sugar levels and improving pancreatic islet function. Liraglutide, an endogenous incretin hormone, increases the number and function of pancreatic beta cells, promoting insulin release and enhancing blood sugar control. It also prolongs gastric emptying time, contributing to blood sugar stability [13]. Studies have indicated that liraglutide can enhance cardiac function in patients [14]. Liraglutide, when combined with metformin, exhibits a synergistic effect in patients with type 2 diabetes and coronary heart disease. This combination helps regulate blood sugar levels and protects vascular endothelial function, ultimately reducing damage to myocardial cells and improving metabolism and cardiac function in patients [15].

In summary, the use of liraglutide in combination with metformin for treating patients with type 2 diabetes and coronary heart disease has a significant and positive effect. It effectively enhances pancreatic islet function, leading to better control of blood sugar levels and improved cardiac function. Thus, it is recommended for clinical adoption.

Disclosure statement

The author declares no conflict of interest.

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