

Original Research Article

Effect of dapagliflozin on blood glucose control, cardiac function, and myocardial injury markers in patients with type 2 diabetes and heart failure

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Abstract

Purpose: To investigate the impact of dapagliflozin treatment on blood glucose control, cardiac function, and myocardial injury markers in patients with type 2 diabetes and heart failure.

Methods: In a retrospective analysis of clinical data for 132 patients with type 2 diabetes and heart failure admitted to Beijing Tongren Hospital, China from January 2020 to June 2021, these patients were stratified into two groups (66 patients each). Control group received conventional pharmacotherapy and study group received additional treatment with dapagliflozin. Both treatment courses lasted for 6 months. The levels of blood glucose control, cardiac function, and myocardial injury markers before and after 6 months of treatment were compared between the two groups, as well as safety during treatment.

Results: After 6 months of treatment, both groups exhibited significant reductions in fasting plasma glucose (FPG), 2-h postprandial glucose (2 h PG), glycated hemoglobin (HbA1c), N-terminal pro-brain natriuretic peptide (NT-proBNP), cardiac troponin I (cTnI), creatine kinase-MB isoenzyme activity (CK-MB), aspartate aminotransferase (AST) levels, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and Minnesota Living with Heart Failure Questionnaire (MLHFQ) score, with study group showing a greater improvement ($p < 0.05$).

Conclusion: Dapagliflozin enhances blood glucose control and cardiac function, improving quality of life in patients with type 2 diabetes and heart failure. Furthermore, Dapagliflozin demonstrates a safe and well-tolerated profile. Future studies will require establishing the mechanism of dapagliflozin action in a larger and more diverse population.

Keywords: Type 2 diabetes, Heart failure, Dapagliflozin, Blood glucose control, Cardiac function, Cardiac injury biomarkers, Safety

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INTRODUCTION

Type 2 diabetes is a common metabolic disease that induces various cardiovascular diseases.

Chronic heart failure is the end stage of various heart diseases. Patients with type 2 diabetes and heart failure have complex conditions,

characterized by poor treatment outcomes and severe symptoms of heart failure [1,2].

Choosing antidiabetic drugs for patients with type 2 diabetes and heart failure is more complicated than for patients with general diabetes. Not only is there a need to consider blood glucose control, but there is also the need to observe whether the drug improves the symptoms of heart failure and ultimately improves prognosis. At present, clinical treatment predominantly centers around metformin for managing hypoglycemia. However, for certain patients, the use of metformin alone may not yield satisfactory results in addressing relative insulin deficiency [3,4].

Dapagliflozin is a sodium-glucose cotransporter 2 (SGLT2) inhibitor that improves blood glucose without increasing insulin secretion. However, the application effect and mechanism of dapagliflozin in type 2 diabetes and heart failure have not been fully clarified. Building upon this premise, a retrospective study involving 132 patients diagnosed with both type 2 diabetes and heart failure was conducted. The study aimed to investigate the impact of dapagliflozin on blood glucose regulation, cardiac function, and myocardial injury markers in this specific patient population.

METHODS

General information

The clinical data of 132 patients with type 2 diabetes and heart failure admitted to Beijing Tongren Hospital, China from January 2020 to June 2021 were retrospectively analyzed. These patients were divided into control group and study group according to their treatment plan, with 66 cases in each group. The study was conducted following the Declaration of Helsinki [5] and was approved by the ethics committee of Beijing Tongren Hospital, (approval no. 2020-05-012). All the patients were informed about this study and signed the informed consent form.

Control group consisted of 35 males and 31 females, with an age range of 43 to 79 years and an average age of 65.86 ± 5.56 years. The New York Heart Association (NYHA) functional classification was grade II in 42 cases and grade III in 24 cases. The body mass index (BMI) ranged from 18 to 30 kg/m², with an average of 22.02 ± 1.20 kg/m². Study group consisted of 33 males and 33 females, with an age range of 41 to 73 years and an average age of 66.12 ± 6.28 years. The NYHA functional classification was grade II in 39 cases and grade III in 27 cases. The BMI ranged from 18 to 29 kg/m², with an

average of 21.95 ± 1.13 kg/m². There was no significant difference in the general information between the two groups ($p > 0.05$).

Inclusion criteria

The following patients were admitted into this study: Patients who meet the diagnostic criteria for type 2 diabetes as outlined in the "Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (2017 edition)" [6], exhibit symptoms such as polyuria, polydipsia, polyphagia, and weight loss; Patients with FPG levels exceeding 7.0 mmol/L or random blood glucose levels exceeding 11.1 mmol/L; patients who fulfill the diagnostic criteria for heart failure, as described in "Internal Medicine" [7], showing evidence of organic heart disease, reduced exercise tolerance, and fluid retention, and confirmed by imaging and laboratory tests; patients without contraindications for the study drug, are conscious and free from mental illness.

Exclusion criteria

Patients with malignant tumors or severe infections; patients who have undergone heart transplantation or left ventricular assist device implantation; pregnant women with gestational diabetes; patients with severe gastrointestinal diseases that may affect drug absorption; patients with liver and kidney dysfunction; individuals with a history of drug abuse or alcoholism, and so on were all excluded from the study.

Drug administration

Control group of 66 patients received conventional drugs for the treatment of heart failure, including diuretics, statins, antiplatelet drugs, and nitrate drugs. Study group of 66 patients received dapagliflozin in addition to conventional treatment given to control group. Both groups were treated for 6 months. The hypoglycemic regimen for control group was oral metformin hydrochloride tablets (0.25 g, Guoyao Zhunzi H22021184, Changchun Boao Biochemical Pharmaceutical Co. Ltd.), 0.5 g per dose, twice daily. In addition to this, study group received dapagliflozin tablets (10 mg, Guoyao Zhunzi H20213836, Beijing Fuyuan Pharmaceutical Co. Ltd.) once daily in the morning, after breakfast. Both groups were treated for 6 months.

Evaluation of parameters/indices

Blood glucose control

Before and 6 months after treatment, 2 mL of fasting venous blood samples and 2 mL of venous blood samples 2 h after meals were collected from both groups. Serum was obtained after centrifugation at 3,000 rpm for 10 min and FPG and 2 h PG were measured using hexokinase method. The reagent kit was provided by Shanghai Gaotrace Medical Equipment Technology Co. Ltd. Serum HbA1c levels were assessed via immunofluorescence chromatography using serum prepared from fasting venous blood samples. The kit was provided by Jiangxi Dayou Medical Technology Co., Ltd.

Cardiac function and quality of life

Before and 6 months after treatment, the LVEDD, LVESD, and left ventricular ejection fraction (LVEF) were measured using a color Doppler ultrasound diagnostic instrument (Vivid iq) provided by General Electric Medical Systems (China) Co. Ltd. The MLHFQ [8] was used to evaluate the quality of life of the two groups. The MLHFQ covered physical, emotional, and other domains, with scores ranging from 0 to 105 points. The higher the score, the worse the patient's quality of life.

Cardiac injury markers

Blood samples were collected before and 6 months after treatment, and serum was prepared as detailed in section 1.3.1. Serum levels of NT-proBNP, cTnI, CK-MB, and AST were quantified using enzyme-linked immunosorbent assay. The reagent kit was provided by Roche Diagnostics GmbH, Germany.

Safety

Detailed scrutiny was conducted during the treatment period to evaluate the frequency of hypoglycemic events, occurrences of hypotension, gastrointestinal reactions, and any

indications of liver function impairment in both groups.

Statistical analysis

The SPSS 21.0 statistical software was used for data analysis. Continuous variables are presented as means \pm standard deviation (SD) and were compared between groups using independent samples t-tests, while paired samples t-tests were employed for within-group comparisons. Categorical variables are presented as n (%) and were compared using the chi-square test. Statistical significance was established at $p < 0.05$.

RESULTS

Blood glucose control status

Compared with before treatment, FPG, 2 h PG, and serum HbA1c levels in both groups decreased after 6 months of treatment, and the reduction was more significant in study group ($p < 0.05$; Table 1).

Cardiac function and quality of life

Compared with before treatment, the LVEDD, LVESD and MLHFQ levels were decreased in both groups after 6 months of treatment, and the reductions were greater in study group ($p < 0.05$). The LVEF levels increased in both groups after treatment, and the increase was greater in study group ($p < 0.05$; Table 2).

Cardiac injury marker

Compared with before treatment, the serum NT-proBNP, cTnI, CK-MB, and AST levels in both groups were decreased after 6 months of treatment, and the reduction was more significant in study group ($P < 0.05$; Table 3).

Table 1: Comparison of blood glucose control between the two groups before and after treatment for 6 months (n=66)

Time	Group	FPG (mmol/L)	2h PG (mmol/L)	HbA1c (%)
Before treatment	Study	9.03 \pm 2.17	12.85 \pm 2.08	9.82 \pm 2.01
	Control	8.92 \pm 2.03	13.12 \pm 2.16	10.11 \pm 2.97
	<i>t</i>	0.301	0.731	0.657
	<i>P</i> -value	0.764	0.466	0.512
6 months after treatment	Study	6.21 \pm 0.74*	7.54 \pm 1.22*	5.22 \pm 1.58*
	Control	7.78 \pm 0.67*	9.29 \pm 1.08*	6.95 \pm 1.67*
	<i>T</i>	12.777	8.726	6.113
	<i>P</i> -value	0.000	0.000	0.033

* $P < 0.05$ vs. before treatment

Table 2: Comparison of cardiac function and quality of life between the two groups before and after treatment (n = 66)

Time	Group	LVEDD (mm)	LVESD (mm)	LVEF	MLHFQ (points)
Before treatment	Study	57.96±1.74	52.06±2.72	40.94±4.79	70.26±4.31
	Control	58.10±1.78	51.94±2.85	41.13±4.72	69.06±5.40
	<i>t</i>	0.457	0.247	0.230	1.411
6 months after treatment	<i>P</i> -value	0.648	0.805	0.819	0.161
	Study	50.25±1.34*	46.96±1.36*	47.47±1.42*	42.03±3.34*
	Control	54.89±1.41*	49.12±1.74*	45.02±1.48*	51.62±4.33*
<i>t</i>	19.379	7.946	9.704	14.247	
<i>t</i>	<i>P</i> -value	0.000	0.000	0.000	0.000

P* < 0.05 vs. before treatmentTable 3:** Comparison of cardiac injury markers between the two groups before and after treatment (n=66)

Time	Group	NT-proBNP (ng/L)	cTnl (ng/mL)	CK-MB (U/L)	AST (U/L)
Before treatment	Study	3417.51±296.47	3.02±0.73	37.08±5.51	66.97±4.64
	Control	3434.63±315.53	2.94±0.72	35.92±5.36	67.12±3.68
	<i>T</i>	0.321	0.634	1.226	0.206
6 months after treatment	<i>P</i> -value	0.749	0.527	0.222	0.837
	Study	1252.04±137.37*	0.78±0.14*	15.20±3.31*	29.35±2.34*
	Control	2561.53±157.35*	1.64±0.23*	20.67±2.36*	36.79±2.41*
<i>T</i>	50.931	25.948	10.931	17.994	
<i>P</i> -value	0.000	0.000	0.000	0.000	

P* < 0.05 vs. before treatmentTable 4:** Comparison of safety between the two groups during treatment (n=66)

Group	Hypoglycemia	Low blood pressure	Gastrointestinal reaction	Impaired liver function	Occurrence of adverse reactions
Study	2(3.03)	2(3.03)	1(1.52)	1(1.52)	6(9.09)
Control	1(1.52)	1(1.52)	0(0.00)	2(3.03)	4(6.06)
χ^2					0.433
<i>P</i> -value					0.511

Safety during treatment

The incidence of adverse reactions was compared between the two groups during treatment, and the analysis revealed no statistically significant difference ($p > 0.05$; Table 4).

DISCUSSION

Based on prior research [9,10], it is evident that type 2 diabetes has evolved into a significant public health concern. Persistent hyperglycemia induces myocardial inflammation, exacerbates oxidative stress, and leads to microvascular dysfunction and coronary artery disease, ultimately resulting in heart failure. Both type 2 diabetes and heart failure are chronic and incurable diseases, that seriously threaten patients' life and health, as well as consume a large number of medical resources. Consequently, there is a pressing need for

effective treatment strategies in clinical practice. Currently, metformin is the cornerstone of blood glucose control for type 2 diabetes. However, as the disease progresses, monotherapy may not be effective and its role in improving heart failure is insufficient. This study introduced dapagliflozin as a treatment for type 2 diabetes with heart failure and achieved certain results. The kidney is an important organ for regulating blood glucose. SGLT2, which is mainly expressed in the kidney, is located on the luminal side of the S1 segment of the proximal tubule and promotes glucose reabsorption. Dapagliflozin is the world's first approved non-insulin-dependent hypoglycemic agent. It mainly reduces glucose reabsorption in the proximal tubule and lowers blood glucose levels by lowering the pathological threshold for renal glucose reabsorption and promoting urinary glucose excretion [11,12]. Taylor *et al* [13] showed that dapagliflozin is effective in treating type 2 diabetes, and effectively regulates sugar and lipid metabolism,

thus continuously controlling blood glucose levels. Shin *et al* [14] also reported that dapagliflozin exhibits a robust targeting effect with a reduced likelihood of causing gastrointestinal reactions or liver damage. It primarily adjusts to elevated blood glucose levels, thereby reducing the risk of hypoglycemic or hypotensive symptoms. In this study, after 6 months of treatment, the FPG, 2h PG, and serum HbA1c levels of study group were lower than those of control group. The incidence of adverse reactions during treatment did not show statistically significant differences between the two groups. This implies that dapagliflozin treatment for type 2 diabetes and heart failure effectively enhances blood glucose control in patients while maintaining a favorable safety profile. Mitigating myocardial damage, enhancing cardiac function, and effectively managing disease progression are pivotal objectives in the clinical treatment of individuals with both type 2 diabetes and heart failure. In this study, after 6 months of treatment, the LVEDD, LVESD, MLHFQ scores, and serum levels of NT-proBNP, cTnl, CK-MB, and AST were lower in the treatment group, while LVEF was higher. These findings indicate that dapagliflozin treatment for individuals with type 2 diabetes and heart failure effectively enhances cardiac function and quality of life. This improvement may be attributed to dapagliflozin's capacity to mitigate myocardial damage markers. The mechanism behind this lies in dapagliflozin's ability to reduce chronic systemic inflammation resulting from the accumulation of visceral and subcutaneous fat, consequently managing myocardial damage and preventing the release of cTnl, CK-MB, and AST from myocardial components into the bloodstream [15].

Dapagliflozin's osmotic diuretic properties contribute to the reduction of both blood pressure and blood volume. This effect helps maintain a proper balance of body water and sodium, subsequently alleviating both pre- and post-load stress on the heart. In doing so, it inhibits the release of NT-proBNP under increased cardiac load, effectively managing myocardial fibrosis, reducing ventricular remodeling, and lowering both LVEDD and LVESD [16,17]. Dapagliflozin additionally promotes the conversion of fatty acids to ketones, elevating ketone levels within myocardial cells. This effect leads to an enhancement of myocardial energy metabolism, a reduction in the activity of membrane ion exchange proteins at the membrane's active center, an increase in mitochondrial calcium levels in the heart, and ultimately an augmentation of myocardial contractility. Giugliano *et al* [18] have also demonstrated the

efficacy of dapagliflozin in the treatment of diabetes with concurrent heart failure. Furthermore, dapagliflozin is shown to contribute to improvements in endothelial function, a reduction in inflammatory factors within the body, and subsequently, a decrease in myocardial cell damage, aligning with the findings of this study.

Study limitations

The sample size was small and only a single study center was used. Therefore, this result cannot be applied on a global scale. The mechanism of dapagliflozin enhancement therapy for type 2 diabetes and heart failure has also not been established in this study.

CONCLUSION

Dapagliflozin treatment for individuals with type 2 diabetes and heart failure results in significant enhancements in blood glucose control, cardiac function, and overall quality of life. These improvements are closely associated with its capacity to reduce myocardial injury markers. Furthermore, it exhibits a reasonable safety profile. Future studies will require establishing the mechanism of dapagliflozin on blood glucose regulation, cardiac function, and myocardial injury markers in a larger and more diverse population.

DECLARATIONS

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Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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