ORIGINAL RESEARCH

Clinical Efficacy and Safety of Liraglutide and Dapagliflozin on Glucose and Lipid Metabolism and Insulin Function in Patients with Type 2 Diabetes Mellitus

Jie Ma, MM; Jingzhi Fu, MD; Ningning Guo, MM; Zhongchao Liu, MM

ABSTRACT

Objective • Observe the changes in clinical indicators of patients with early diabetic nephropathy treated with liraglutide or dapagliflozin, evaluate their clinical efficacy, and provide new ideas for the treatment of diabetic patients.

Methods • In this study, from January 2020 to January 2022, a total of 120 patients with early-stage type 2 diabetic nephropathy who met the inclusion criteria were selected. According to the order of treatment, the patients were randomly divided into traditional group, liraglutide group and dapagliflozin group, with 40 cases in each group. All patients continued their previous conventional hypoglycemic treatment, and the traditional group did not need to adjust the treatment plan; the liraglutide group: added liraglutide (average dose was 1.2 mg daily); the dapagliflozin group: added dapagliflozin (average dose was 10 mg daily). At the same time, all patients received dietary guidance and appropriate exercise intervention for a total of 12 weeks. The changes in blood sugar, blood lipids, pancreatic islet function, liver function, weight, body mass index (BMI) and other indicators before and after treatment were compared, and the adverse reactions that occurred during the medication of the three groups of patients were recorded. Standard doses of liraglutide and dapagliflozin were used in the treatment groups, 0.6 mg daily and 10 mg daily, respectively. These standard doses have been shown to be effective in a wide range of clinical practices and were therefore chosen in this study to ensure consistency and comparability. This helps readers better understand the study methods and results to evaluate these specific dosing options.

Results • Prior to treatment, there were no significant differences in the general data and indicators among the three groups, including FPG, 2hPG, HbA_{1c}, TC, TG, HDL-C, LDL-C, ALT, AST, HOMA-IR, FINS, and HOMA-β (all $P > .05$).

In the conventional group, significant changes were observed in FPG, 2hPG, HbA_{1c}, body weight, BMI, HDL-C, LDL-C, ALT, AST, HOMA-IR, FINS, and HOMA-β compared to the pre-treatment period, and these differences were statistically significant (all $P < .05$).

Both the liraglutide and dagliflozin groups exhibited significant changes in FPG, 2hPG, HbA_{1c}, TC, TG, LDL-C, HOMA-IR, FINS, HOMA-β, body weight, BMI, HDL-C, ALT, and AST when compared to the post-treatment period, and these changes were statistically significant (all $P < .05$).

Post-treatment analysis revealed that in terms of blood glucose, FPG, 2hPG, and HbA_{1c} decreased more significantly in the liraglutide and dagliflozin groups compared to the conventional group (all $P < .05$). Regarding lipids, TC, TG, and LDL-C decreased more significantly in the liraglutide and dagliflozin groups compared to the conventional group (all $P < .05$). For pancreatic islet function, HOMA-IR and HOMA-β decreased more significantly compared to the conventional group (all $P < .05$). Weight and BMI decreased more significantly in the liraglutide and dagliflozin groups compared to the conventional group (all $P < .05$). However, there were no significant differences in hepatic function among the three groups after treatment.

Post-treatment comparisons between the liraglutide and dagliflozin groups revealed significant differences in FPG, HbA_{1c}, body weight, and BMI (all $P < .05$). No adverse events occurred during the treatment period in any of the three groups, and there were no reported deaths.

Conclusion • The addition of liraglutide or dagliflozin to conventional hypoglycaemic drug therapy in early diabetic patients can not only bring blood glucose to a safe and faster standard, but also regulate blood lipids and glucose, and the therapeutic effect of liraglutide is obvious than that of dagliflozin in terms of blood glucose regulation. Study limitations include small sample size, short study duration, unspecified exclusion criteria, unclear randomization method, and the impact of patient compliance. (*Altern Ther Health Med.* [E-pub ahead of print.])

Jie Ma, MM, Attending doctor; **Ningning Guo,** MM**;** Second Department of Endocrinology, Cangzhou Central Hospital, Cangzhou, China. **Jingzhi Fu,** MD, Physical Education Institute, Cangzhou Normal University, Cangzhou, China. **Zhongchao Liu,** MM**;** Medical Engineering Department, Cangzhou Central Hospital, Cangzhou, China.

Corresponding author: Jie Ma, MM
E-mail: Maggie88miao@163.com

INTRODUCTION

Diabetes mellitus is a common chronic disease in clinical practice, which manifests itself as a persistent hyperglycaemic state that affects the ability to release insulin or release levels that are substandard, or both of the above conditions exist simultaneously.[1,2] According to relevant statistics, type 2 diabetes is more than 90% of the total number of people with diabetes, coupled with the trend of population aging in most countries of the world, making

more and more people suffer from type 2 diabetes, which has an impact on physical and mental health and life safety.[3,4] In this regard, it is particularly crucial to choose an active and effective drug treatment in the clinic.

Treatment of type 2 diabetes involves a variety of approaches, including lifestyle interventions, oral medications, and insulin. First-line treatment usually includes improved diet, increased physical activity, and oral medications such as metformin. For some patients, this first-line treatment may not be sufficient to achieve good glycemic control. In this case, the doctor may consider incorporating other oral medications or insulin into the treatment plan. In recent years, antidiabetic drugs such as liraglutide and dapagliflozin have received increasing attention as options for antidiabetic treatment. These drugs act on different biological pathways to improve insulin sensitivity and promote blood sugar control, but they also come with their own potential side effects. Therefore, it is critical to study and compare these novel drugs to help doctors and patients make more informed treatment choices.

Type 2 diabetes is a global chronic disease that has a significant impact on patient's quality of life. Currently, drugs such as liraglutide and dapagliflozin are widely used in the treatment of type 2 diabetes. However, the combined use of these drugs in patients and their efficacy in different situations still require further study. Therefore, this study aimed to evaluate the clinical effects of these two drugs in patients with type 2 diabetes, especially whether they can provide better therapeutic effects when used in combination. The results of this study will provide important guidance for improving the treatment and quality of life of patients with type 2 diabetes.

Dagliflozin is a kind of antihyperglycaemic drug. It inhibits glucose absorption in renal tubules and improves urinary glucose excretion through a non-insulin mechanism, thus effectively controlling blood glucose levels.[5,6] At the same time, it also improves uric acid, blood pressure, and urinary protein levels in the form of glucose non-dependence, thus protecting the kidneys. Sodium-glucose cotransporter-2 inhibitor (SGLT2) not only reduces blood glucose but also improves proteinuria.[7] It also improves renal function in diabetic patients by exerting anti-inflammatory effects, increasing insulin sensitivity, reducing glucose toxicity, decreasing body weight, and lowering blood pressure.[8]

SGLT2 inhibitors are drugs that treat type 2 diabetes and effectively lower blood sugar levels in patients by reducing the reabsorption of glucose by the renal tubules. The drug also improved proteinuria and reduced glomerular hyperfiltration, helping to protect kidney health. Additionally, SGLT2 inhibitors have a positive impact on kidney function by reducing cardiovascular risk factors such as weight, blood pressure, and uric acid levels. Therefore, these drugs may not only improve blood sugar control but also help maintain kidney health in people with type 2 diabetes. Patients should consult their physician before using an SGLT2 inhibitor to ensure an appropriate treatment regimen.

Type 2 diabetes is a metabolic disease that can cause a variety of serious health problems, such as cardiovascular disease, vision problems, neuropathy and kidney disease. To address this global challenge, finding more effective treatments is crucial. Liraglutide is a GLP-1 receptor agonist that works by mimicking naturally occurring GLP-1 to improve blood sugar control, reduce insulin resistance and reduce weight. It also helps control diet and appetite. In contrast, dapagliflozin is an SGLT2 inhibitor that lowers blood glucose levels by reducing renal tubular reabsorption of glucose. The two drugs have different mechanisms of action, giving them both potential in the treatment of type 2 diabetes. But more in-depth research and comparisons are needed to better understand their relative potency and indications.

Glucagon-like peptide 1 (GLP-1) has been widely used in the treatment of diabetes mellitus. GLP-1 reduces the weight of patients while avoiding hypoglycemia. Meanwhile, GLP-1 has a protective effect on the kidney.[9] And the protective mechanism of liraglutide on diabetes may be: (1) Liraglutide can inhibit the activation of endoplasmic reticulum stress and delay the progression of diabetic nephropathy; (2) Liraglutide reduces proteinuria by inhibiting VEGF and VEGF-A, which can play a renoprotective role; (3) ET is abundantly expressed in renal tissues during diabetic nephropathy, and liraglutide may inhibit the progression of diabetic nephropathy by regulating ET; (4) Liraglutide may play a protective role in renal podocytes by regulating oxidative stress and autophagy; (5) Liraglutide can reduce creatinine, urinary microalbumin and blood inflammatory factors TNF-α, IL-1 and IL-6 levels, and delay renal damage by improving the inflammatory state in diabetic nephropathy.[10-13] Now, in order to investigate the clinical effect of applying liraglutide and dagliflozin in patients with type 2 diabetes mellitus, the treatment data of 120 patients with type 2 diabetes mellitus were analyzed, and their treatment effects were summarized as follows. Our study aimed to compare the effects of liraglutide and dapagliflozin alone on clinical indicators in patients with early type 2 diabetes, evaluate their efficacy, and provide new ideas for the treatment of patients with diabetes.

MATERIALS AND METHODS

General information

120 cases of type 2 diabetes mellitus patients treated in our hospital were selected as research subjects and were divided into three groups by random number method, with 40 cases in each group. Randomly divided into the conventional group, liraglutide group, and dagliflozin group, each group of 40 cases. Randomization of patients was performed using a computer-generated random number table. First, all patients meeting inclusion criteria were numbered to assign a unique identification number. The researchers then used the generated table of random numbers to match each patient to a random number in the table, in order of their medical record number. Each patient was

divided into different treatment groups according to their matched random numbers, including the control group, dapagliflozin group, and liraglutide group. This randomization process ensures that the allocation of patients to each group is completely random, reducing potential bias and thereby improving the scientific nature and reliability of the study. This approach helps eliminate confounding factors and ensures a high degree of comparability between groups at the start of the study. In the conventional group, there were 19 men and 21 women; in the liraglutide group, there were 18 men and 22 women; in the dagliflozin group, there were 17 men and 23 women. Comparing the baseline data of the two groups, the differences were not statistically significant ($P > .05$) and were comparable. This study was approved by the Ethics Committee of Cangzhou Central Hospital, and consent was obtained from the participants.

Inclusion criteria

Age 18-75 years old (including the threshold). (2) Body mass index of 25 kg/m^2 ≤ BMI ≤ 40 kg/m^2. (3) Diagnosed with type 2 diabetes mellitus according to the diagnostic and classification criteria of the World Health Organization (WHO, 1999) and in the early stage of diabetic kidney disease (UACR 30-300 mg/g). (4) The patient has no strenuous exercise within 24 hours of monitoring the UACR index, and the HbA_{1c} is > 7%. (5) There is no history of hypertension, or there is a history of underlying hypertension but the blood pressure control is stable and does not exceed 140/90 mmHg. (6) Prior to any trial-related activities (including activities to assess the eligibility of the subjects), the patient voluntarily signs an informed consent form, cooperates with the treatment, and accepts the telephone follow-up visit. (7) No previous use of hypoglycaemic agents or only metformin.

Patients with early diabetic nephropathy are a specific subgroup of diabetic patients whose kidneys have been damaged but have not yet developed advanced diabetic nephropathy. Studying this group can help understand whether early intervention is effective. Patients with early-stage diabetic nephropathy generally have better treatment prospects. Therefore, studying the treatment of early diabetic nephropathy is important to reduce the disease burden.

Exclusion criteria

(1) Received liraglutide and dagliflozin within 3 months before screening. (2) Liver and kidney function impairment. (3) Recurrent urinary tract infection before screening. (4) Pregnant or breastfeeding women, or women or men who plan to have children during the trial period, or who do not use effective contraception. (5) Other conditions considered by the investigator to be unsuitable for participation in the study.

Inclusion and exclusion criteria were set to ensure that the study population was appropriate in the context of investigating early renal disease treatment in type 2 diabetes. These criteria may be based on specific clinical characteristics, disease stage, or other factors.

Methods

Patients who met the requirements for inclusion were randomly divided into the conventional group, liraglutide group, and dagliflozin group. All patients continued the original conventional glucose-lowering treatment (conventional glucose-lowering drugs alone or in combination were not restricted, except for DPP-4 inhibitors), and patients originally taking lipid-lowering drugs continued to take them. Conventional group: patients continued the original conventional glucose-lowering regimen, and the glucose-lowering drugs or doses were adjusted according to the monitored blood glucose; liraglutide group: patients received 1-month dose-adjusted treatment and 3-month maintenance treatment with liraglutide injection on the original glucose-lowering regimen; dagliflozin group: dagliflozin was added to the original glucose-lowering regimen (the average dosage of 10 mg per day). Each group was provided with information and education on diabetic kidney disease and dietary guidance, and the three groups were treated for 3 months. The treatment groups in this study included the conventional group, the liraglutide group, and the dapagliflozin group. In the conventional group, patients continued their previous conventional hypoglycemic treatment and did not need to adjust the treatment plan. Patients in the liraglutide group received additional liraglutide, at an average dose of 1.2 mg per day. Patients in the dapagliflozin group received additional dapagliflozin at an average dose of 10 mg per day. In addition, all patients received dietary guidance and appropriate exercise intervention for 12 weeks.

Observation indicators

(1) Clinical efficiency and safety: the efficacy of the treatment plan is judged by the patient's clinical symptoms and the level of blood glucose indexes; the safety is judged by whether the patients' uncomfortable reactions such as dizziness, nausea, vomiting, and hypoglycemia occur during the treatment.

(2) Blood glucose indicators: HbA_{1c} (glycated hemoglobin), FPG (fasting blood glucose), 2hPG (postprandial blood glucose) indicators were evaluated. Venous blood was drawn from patients in the fasting state at two points of time, before treatment and 3 months after treatment, and the level of HbA_{1c} was detected by ELISA, and FPG and 2hPG indicators were detected by blood glucose analyzer. The data were pooled and statistically analyzed.

(3) Pancreatic islet function indexes: evaluated by HOMA-IR (insulin resistance index), FINS (fasting insulin), and HOMA-β (insulin secretion index) indexes, selecting the two-time points before treatment and after 3 months of treatment, drawing venous blood of patients in fasting state, and FINS indexes by automatic immunoassay analyzer. The data were pooled and statistically analyzed.

The main outcome measures of this study can be divided into the following categories:

Clinical efficacy and safety: Primary outcomes include improvement in glycemic control, improvement in renal

Table 1. General information of the three groups of patients

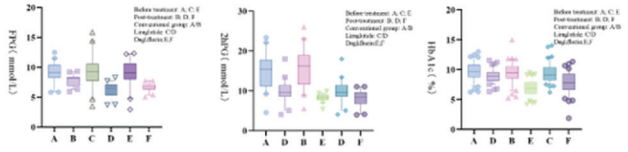
General information	Conventional group (n = 40)	Dagliflozin group (n = 40)	Liraglutide group (n = 40)	F or χ^2	P value
Sex (male/female)	19/21	18/22	17/23	0.20	.904
Age (years)	52.83±9.84	49.83±8.61	50.48±6.51	1.42	.245
BMI/(kg/m^2)	26.55±2.32	27.45±3.54	27.71±2.57	1.81	.1676
Duration of diabetes mellitus (years)	4.3±2.62	4.7±2.26	4.22±2.19	2.095	.1279
Underlying Disease					
Diabetic retinopathy (n)	15	20	18	3.56	.169
Hyperlipidaemia (n)	23	22	25	0.48	.787
Hypertension (n)	22	20	23	0.470	.791
Medication					
Taking lipid-lowering/not taking lipid-lowering	33/7	32/8	31/9	0.322	.856

Table 2. Comparison of blood glucose indicators among the three groups ($\bar{x} \pm s$)

Groups	n	FPG (mmol/L)		2hPG (mmol/L)		HbA_{1c} (%)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Conventional group	40	9.13±1.61	7.72±0.94[a]	14.36±5.20	9.90±2.59[a]	9.69±1.65	8.92±1.21[a]
Liraglutide Group	40	9.20±2.49	6.21±1.16[a,b,c]	14.82±5.55	8.29±0.87[a,b]	9.51±1.88	6.91±1.39[a,b,c]
Dagliflozin group	40	9.10±2.06	6.70±0.65[a,b]	15.01±3.60	8.17±1.91[a,b]	9.53±1.79	7.81±1.97[a,b]
F		0.242	27.231	0.18	0.09	0.11	16.6
P value		.976	<.01	.83	.91	.89	<.01

[a]indicates $P < .05$ compared with pre-treatment in this group
[b]indicates $P < .05$ compared with conventional group
[c]indicates $P < .05$ compared with dapagliflozin

Figure 1. Comparison of various indicators of blood glucose in three groups of patients



function, and incidence of adverse reactions. These indicators will help evaluate the effectiveness of drug treatment and whether there are potential adverse effects.

Blood glucose indicators: These indicators usually include fasting blood glucose concentration (FPG), postprandial blood glucose concentration (PPG), and(HbA_{1c} levels. They are key parameters in assessing the impact of drug therapy on blood glucose levels.

Pancreatic function indicators: These indicators may include insulin resistance index (such as HOMA-IR), C-peptide levels, etc. They can be used to assess improvements in islet function.

Specifically, improvements in glycemic control, such as reductions in FPG and PPG, can indicate that therapeutic agents are having a positive impact on blood sugar levels. The decline in HbA_{1c} reflects long-term glycemic control. Additionally, improvements in kidney function may manifest as increases in glomerular filtration rate (eGFR) and decreases in creatinine levels.

Statistical analysis

In this study, we used three main statistical analysis methods: χ^2 test, analysis of variance (ANOVA), and paired design t-test. The χ^2 test is suitable for comparing categorical data between different groups, and is usually used to analyze significant differences in the incidence of adverse reactions. Analysis of variance (ANOVA) was used to compare the mean differences between different treatment groups on continuous variables (such as blood glucose indicators, pancreatic islet function indicators) to fully understand the differences between the groups. Finally, the paired design t test is suitable for comparing changes in the same group at different time points or conditions, such as blood glucose indicators and pancreatic islet function indicators before and after treatment. The methods were chosen based on the study design and research questions to ensure that the required differences and effects could be detected to support the study conclusions. The difference was considered statistically significant at $P < .05$.

RESULTS

Basic information about patients

120 patients were randomly assigned to three treatment groups, 40 in each group. There was no statistically significant difference between the three groups of patients in terms of male-to-female ratio, age, course of disease, and underlying diseases ($P > .05$); at the same time, there was no statistically significant difference between the number of patients taking lipid-lowering and the number of patients who did not take lipid-lowering in each of the three groups ($P > .05$), which means that the three groups of patients are comparable to each other, see Table 1.

Comparison of blood glucose indicators among the three groups

There was no significant difference in FPG, 2hPG, and HbA_{1c} in each group before treatment ($P = .976, .83, .91, .89$). After treatment, FPG in liraglutide group and dapagliflozin group decreased significantly compared with that before treatment ($P < .05$), and were significantly lower than that in the conventional group ($P < .05$). In terms of 2hPG, the three groups of patients were decreased compared with those before treatment ($P < .05$); and compared with the conventional group, liraglutide group and dapagliflozin group decreased more significantly ($P < .05$). In terms of HbA_{1c}, the three groups of patients were significantly decreased after treatment ($P < .05$), and the liraglutide group and dapagliflozin group were significantly lower than the conventional group ($P < .05$).

There was no significant difference in HbA_{1c} between liraglutide group and dapagliflozin group after treatment ($P > .05$); among the three groups, FPG and 2hPG decreased more significantly in liraglutide patients, and the difference was statistically significant compared with dapagliflozin group ($P < .05$). See Table 2 and Figure 1 for details.

Changes in lipid levels and differences before and after treatment in each group of patients

There were no significant differences in TC, TG, HDL-C, and LDL-C in each group compared with those before

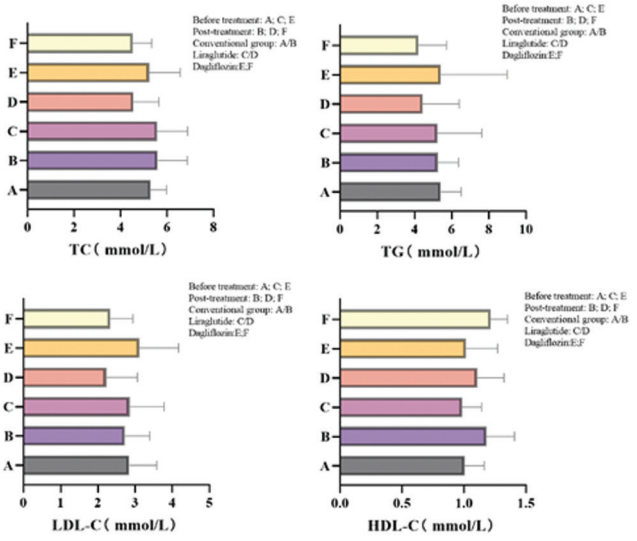
treatment ($P > .05$). In terms of TC, TG, and LDL-C, the liraglutide group and dagliflozin group showed a significant decrease after treatment compared with those before ($P < .05$), and both groups were significantly lower than that of the conventional group ($P < .05$), but the difference between the two groups was not statistically significant ($P > .05$). In terms of increasing HDL-C, the most significant effect was observed in liraglutide group, but the difference was not statistically significant due to a small fluctuation, $P > .05$. The difference between the groups before and after treatment was compared between the groups, and the fluctuation was small, and there was no statistically significant difference, $P > .05$. The details are shown in Table 3 and Figure 2.

Table 3. Blood lipid levels and differences before and after treatment in each group of patients ($\bar{x} \pm s$)

Groups		TC	TG	LDL-C	HDL-C
Conventional	Pre-treatment	5.29±0.69	5.41±1.10	2.84±0.74	1.01±0.16
group	Post-treatment	5.59±1.27	5.25±1.12	2.72±0.67	1.18±0.23[a]
Liraglutide	Pre-treatment	5.57±1.31	5.22±2.39	2.90±0.93	0.98±0.16
Group	Post-treatment	4.60±1.09[a,b]	4.42±1.97[a,b]	2.22±0.83[a,b]	1.11±0.22[a]
Dagliflozin	Pre-treatment	5.23±1.34	5.41±3.57	3.11±1.05	1.01±0. 25
group	Post-treatment	4.52±0.81[a,b]	4.21±1.51[a,b]	2.33±0.62[a,b]	1.21±0.13[a]

[a]indicates $P < .05$ compared with pre-treatment in this group
[b]indicates $P < .05$ compared with conventional group

Figure 2. Statistics of blood lipid levels of three groups of patients before and after treatment



Comparison of islet function indexes among the three groups

In terms of pancreatic islet function, there was no significant difference between the HOMA-IR, FINS, and HOMA-β of the groups compared with the pre-treatment period ($P = .8892$), and in terms of lowering the HOMA-IR and FINS, the liraglutide group and the dagliflozin group were both significantly lower than the pre-treatment period after the treatment ($P < .0022$), and both groups were significantly lower than the conventional group ($P < .05$), but there was no statistical significance in the difference between the two groups ($P = .9602$). In terms of increasing HOMA-β, after treatment, the liraglutide and dagliflozin groups had significant differences compared with the control group ($P < .05$), but the difference between the two groups was not statistically significant ($P = .9931$). The details are shown in Table 4 and Figure 3.

Table 4. Comparison of islet function indexes between the two groups ($\bar{x} \pm s$)

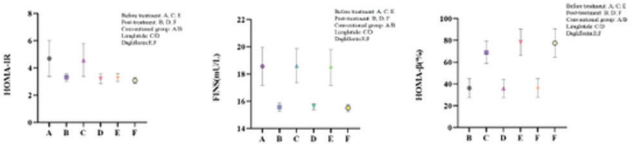
	HOMA-IR		FINS(mU/L)		HOMA-β(%)	
Groups	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Conventional group	4.69±1.32	3.32±0.29[a]	18.56±1.39	15.58±0.30[a]	36.29±8.54	68.98±10.21[a]
Liraglutide Group	4.57±1.21	3.21±0.37[a]	18.61±1.26	15.61±0.22[a]	36.12±8.31	78.26±12.23[a,b]
Dagliflozin group	4.68±1.34	3.08±0.22[a,b]	18.48±1.31	15.51±0.25[a]	36.33±8.49	77.63±13.12[a,b]
F	0.1064	6.4291	0.0986	1.5729	0.007	4.536
P value	.8992	.0022	.9062	.2118	.9931	0

[a]indicates $P < .05$ compared with pre-treatment in this group
[b]indicates $P < .05$ compared with conventional group

Comparison of body weight and BMI among the three groups of patients before and after treatment

In terms of body weight and BMI, patients in the liraglutide group and dagliflozin group showed a significant decrease in body weight and BMI after treatment ($P < .001$), and both groups were significantly lower than the conventional group ($P < .05$); and between the liraglutide group and dagliflozin group, the decrease in body weight and BMI of patients in the liraglutide group was more obvious, and the difference in the dagliflozin group was statistically significant ($P < .001$). See Table 5 for details.

Figure 3. Comparison of islet function indexes between the two groups



Comparison of liver function of the three groups

Before the treatment of the three groups, ALT, AST comparisons are $P = .9895, .4351$, comparable; before and after the treatment of the three groups within the group comparisons, ALT, AST is $P < .05$, the difference between the three groups is obvious; after the treatment of the three groups, ALT, AST comparisons are $P = .4528, .7881$, the difference between the groups is not obvious, see Table 6.

We found significant improvements in LVEF in both the liraglutide group and dapagliflozin group, which may mean these drugs have a positive impact on improving patients' heart function, but we will further explore how this

Table 5. Comparison of weight and BMI of the three groups of patients before and after treatment ($\bar{x} \pm s$)

Groups	Cases	Weight(kg)		BMI(kg/m²)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Conventional group	40	77.87±7.96	76.87±7.26	28.43±1.90	28.07±1.68
Liraglutide Group	40	77.45±9.02	71.53±8.13[a,b,c]	27.72±2.57	25.60±2.30[a,b,c]
Dagliflozin group	40	77.38±5.96	64.10±5.39[a,b]	28.05±1.62	24.07±1.75[a,b]
F		0.0648	7.735	1.1858	43.7441
P value		.9543	.000	.3092	.000

[a]indicates $P < .05$ compared with pre-treatment in this group
[b]indicates $P < .05$ compared with conventional group
[c]indicates $P < .05$ compared with dapagliflozin.

Table 6. Comparison of liver function of three groups before and after treatment ($\bar{x} \pm s$)

Groups	n	ALT(U/L)		AST(U/L)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Conventional group	40	26.37±10.61	24.1±8.34[a]	25.66±4.51	24.73±3.57[a]
Liraglutide Group	40	26.69±9.74	26.33±9.57[a]	25.59±4.36	24.98±4.39[a]
Dagliflozin group	40	26.54±9.12	26.21±8.69[a]	25.76±4.21	25.37±4.3[a]
F		0.0106	0.7977	0.8381	0.2386
P value		.9895	.4528	.4351	.7881

[a]indicates $P < .05$ compared with pre-treatment in this group

improvement correlates with patient survival. or associated with reduced risk of cardiovascular events.

Safety analysis

No adverse events occurred during the treatment of the three groups, and the safety test indicators fluctuated within the normal range.The relatively short period of the study and potential confounders. These limitations will help provide readers with a more comprehensive assessment of the study results.

DISCUSSION

Our findings have clear clinical implications for treatments for type 2 diabetes. First, treatment with liraglutide and dapagliflozin showed significant improvements in patients' glycemic control and pancreatic islet function. This is crucial for people with type 2 diabetes, as good blood sugar control helps reduce the risk of cardiovascular complications and improves their quality of life. Second, our findings suggest that these treatments also had a positive impact on patients' lipid metabolism. Cardiovascular health is closely related to blood lipid levels, so improving blood lipid metabolism can reduce cardiovascular risk, which is particularly important for patients with type 2 diabetes. Additionally, we observed that these treatments contributed to weight loss in patients, which also has important implications for diabetic patients who may be obese. Obesity is a risk factor for type 2 diabetes, so losing weight can help improve your condition.

The prevalence of diabetes mellitus is increasing year by year due to changes in lifestyle and dietary habits in recent years. type 2 diabetes mellitus is an independent risk factor for cardiovascular and cerebrovascular diseases, and disorders of glucose metabolism cause lipid metabolism disorders, which in turn cause damage to the vascular endothelium and increase the risk of atherosclerosis. Epidemiological studies have shown that more than 70% of patients with type 2 diabetes die from complications of cardiovascular and cerebrovascular diseases. Therefore, in the treatment of patients with type 2 diabetes mellitus, in addition to effective control of their blood glucose levels, it is also necessary to regulate their lipid profile to prevent the growth of IMT.

When the patient's insulin β-cell dysfunction and insulin resistance, abnormal glucose-lipid metabolism, and oxidative stress are out of balance, the corresponding indicators can not be normally secreted, resulting in the indicators in the body in a state of disorder. type 2 diabetes mellitus patients with increased levels of TG, TC, LDL-C, and decreased levels of HDL-C.[14]

This study showed that the liraglutide and dagliflozin groups showed significant changes in FPG, 2hPG, HbA_{1c}, TC, TG, LDL-C, HOMA-IR, FINS and HOMA-β, body weight and BMI , HDL-C, ALT, and AST when compared with the post-treatment period, and showed significant differences ($P < .05$). In terms of blood glucose, after treatment, FPG, 2hPG, and HbA_{1c} decreased more significantly in liraglutide and dapagliflozin groups than in the conventional group ($P < .05$); in terms of blood lipids, TC, TG, and LDL-C decreased more significantly in liraglutide and dapagliflozin groups than in the conventional group ($P<0.05$); in terms of islet function, the decrease of HOMA-IR and HOMA-β were more obvious in liraglutide and dapagliflozin groups than those in the conventional group ($P < .05$); compared with the conventional group, the body weight and BMI of liraglutide and dapagliflozin groups decreased more significantly ($P < .05$); in terms of liver function, there was no significant difference between the three groups after treatment. After treatment, FPG, HbA_{1c}, body weight and BMI showed significant differences between liraglutide group and dapagliflozin group ($P < .05$). It can be seen that dapagliflozin or liraglutide treatment is beneficial in improving the clinical treatment rate and glucose and lipid metabolism indicators.

When we compared the two treatments, liraglutide and dapagliflozin, we found that each had some relative advantages and disadvantages. Liraglutide is a GLP-1 receptor agonist that helps lower blood sugar, increase satiety, reduce weight, and improve pancreatic islet function by simulating the effects of glucagon-like polypeptide-1 (GLP-1). This makes liraglutide very effective in dealing with blood sugar control and weight management in people with type 2 diabetes. However, liraglutide usually requires daily injections, which may affect patient compliance with treatment. In contrast, dapagliflozin is an SGLT2 receptor antagonist that reduces blood glucose levels by inhibiting renal tubular glucose reabsorption. It improves blood sugar control by removing excess glucose from the body through urination. In addition, it is also thought to help reduce cardiovascular risk as it reduces blood pressure, weight and improves heart function. Dapagliflozin is usually taken as an oral medication, which is more convenient for patients.

However, dapagliflozin may cause adverse effects such as urinary tract infections and high sodium concentrations. Therefore, when choosing a treatment, doctors and patients need to base their choices on individual needs and tolerance. These relative advantages and disadvantages need to be weighed against the patient's specific circumstances to determine which treatment is best for their diabetes management.

Liraglutide belongs to the GLP-1 receptor agonist commonly used in the clinic, which can improve insulin synthesis and secretion and inhibit glucagon secretion after binding to the GLP-1 receptor of pancreatic B cells, and has a great improvement effect on the lipid level, which confirms that the therapeutic effect of Liraglutide is good, and its efficacy is safe, reliable and has fewer adverse reactions.[11] Dagliflozin belongs to a kind of protein inhibitor, and its dilation should also improve the positive effect of blood vessels, play a better protective effect on blood vessels, and reduce the reabsorption of glucose by the kidneys after injection. The combination of the two drugs, in collaboration with each other, not only improves the blood glucose level, but also has a significant protective effect on renal function, hinders sodium-glucose damage to the kidneys, stimulates the activity of transporter protein 2, accelerates the body's uptake of sodium ions and glucose, and contributes to the gradual lessening of sodium ions and glucose in the incoming renal tubules.[12,15] In this study, the FPG, 2hPG, HbA_{1c} indexes of liraglutide group and dagliflozin group were lower than those of the control group ($P < .05$), which indicated that the choice of dagliflozin or liraglutide helped to improve the blood glucose indexes, and the effect of liraglutide group was more obvious compared with that of the dagliflozin group in regulating blood glucose. Liraglutide has a good hypoglycemic effect, facilitates the control of body mass, and protects β-cells from further damage. In addition, the drug can effectively prolong gastric emptying, making patients feel satiated, so as to control the amount of food eaten by patients, for the prevention of cardiovascular disease, obesity plays a positive role. When the patient's body has elevated blood glucose, liraglutide can inhibit the release of glucagon from pancreatic α-cells, lowering blood glucose and controlling the release of insulin, thus avoiding hypoglycaemia. Dagliflozin is a protein inhibitor, which can improve the urinary glucose excretion rate, and its effect of lowering glucose and controlling blood pressure is good, meanwhile, this drug can regulate the distribution of body fat, and there is no risk of hypoglycaemia after taking it.[16] In addition, the drug can expand and improve vascular endothelial function, protect the cardiovascular system, and control glucose reabsorption in renal tubules, thus enhancing urinary glucose excretion and reducing the burden on the kidneys, so as to achieve the ideal glucose-lowering goal.

In this study, we observed no serious adverse events during treatment in the three groups of patients, indicating that treatment with liraglutide and dapagliflozin is relatively safe. However, to provide a more complete picture, it is worth discussing the known safety profiles of liraglutide and dapagliflozin.

The known safety profile of liraglutide suggests that major adverse events may include nausea, vomiting, pancreatitis, and hypoglycemia. Therefore, the risk of these adverse events needs to be closely monitored when using liraglutide, especially during the initial treatment phase. Liraglutide usually requires daily injections, which may also cause discomfort in some patients.

Dapagliflozin is usually taken as an oral medication and its known safety profile includes the potential for adverse effects such as urinary tract infection, polydipsia, polyuria, and hypotension. These potential risks require close attention when using dapagliflozin.

Although no serious adverse events were observed in this study, individual differences and tolerability of patients still need to be carefully considered in actual treatment. Treatment selection should be determined based on the patient's specific condition and medical recommendations. In summary, by understanding the known safety profiles of liraglutide and dapagliflozin, patients and physicians can better weigh the risks versus benefits of treatment for optimal diabetes management.

The limitations of this study require special consideration. First, the study's generalizability is limited due to the relatively small sample size. Future research could consider expanding the sample size to increase the credibility of the conclusions. Second, the study used a retrospective design rather than a randomized controlled trial, which may have introduced potential selection bias. Additionally, the data relied primarily on self-reports, including quality of life and symptom assessments, which may be affected by subjective factors. We have tried our best to maintain the objectivity of the data, but subjective factors still need to be considered. Furthermore, the time span of the study was relatively short, and long-term effects have not yet been fully considered. Finally, the results of this study apply only to a specific medical setting and diabetic patients, thus their external applicability is somewhat limited. Future research needs to pay more attention to these limitations and validate them in a broader context. These limitations provide directions for further improvement and expansion of research in this area.

Potential avenues for future research are critical. This includes longer-term studies to gain insight into the sustained effects of treatment with liraglutide and dapagliflozin, as well as larger and more comprehensive randomized controlled trials to reduce potential bias and provide more convincing evidence . Additionally, economic studies are critical to explore the cost-effectiveness of these treatments to help policymakers better allocate health care resources. Future studies can also further study which type of patients are most suitable for liraglutide or dapagliflozin treatment to achieve individualized treatment plans. Finally, it is also beneficial to evaluate the impact of these treatments on patients' quality of life to understand whether the treatment has a positive impact on the patient's overall well-being. Through these

future studies, we can more fully understand the role of these treatments in diabetes management, providing more scientific evidence to better meet patient needs.

In conclusion, this study provides an in-depth study of the effects of liraglutide and dapagliflozin in the treatment of early-stage type 2 diabetes. The results showed that these two treatment options showed good efficacy in terms of blood sugar control, pancreatic islet function, blood lipid metabolism and weight management, and are of great significance to patients with early type 2 diabetes. This provides patients with more effective treatment options that improve quality of life and reduce the risk of diabetes-related complications. However, the study had some limitations, including a short study period and a limited sample size. Future studies are needed to further explore the long-term effects of these treatments to provide more reliable evidence. This research has positive clinical significance for improving the treatment and management of patients with early-stage type 2 diabetes.

ETHICAL COMPLIANCE

Ethical approval for this study was obtained from the Ethics Committee of Cangzhou Central Hospital. This committee is responsible for evaluating and approving all medical research involving human patients. The name and contact information of the ethics committee can be provided to the relevant authorities to verify the legality of the approval process.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

JM and JF designed the study and performed the experiments, JF and NG collected the data, NG and ZL analyzed the data, JM prepared the manuscript. All authors read and approved the final manuscript.

FUNDING

This work was supported by the Cangzhou key research and development plan self-funded project

REFERENCE

1. Faselis C, Katsimardou A, Imprialos K, Deligkaris P, Kallistratos M, Dimitriadis K. Microvascular Complications of Type 2 Diabetes Mellitus. *Curr Vasc Pharmacol*. 2020;18(2):117-124. doi:10.2174/1570161117666190502103733
2. Htay T, Soe K, Lopez-Perez A, Doan AH, Romagosa MA, Aung K. Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes. *Curr Cardiol Rep*. 2019;21(6):45. doi:10.1007/s11886-019-1133-9
3. Agashe S, Petak S. Cardiac Autonomic Neuropathy in Diabetes Mellitus. *Methodist DeBakey Cardiovasc J*. 2018;14(4):251-256. doi:10.14797/mdcj-14-4-251
4. Stier-Jarmer M, Frisch D, Neuy S, Schuh A; A 3-Week Naturopathic Intervention Improves HbA(1c), Weight, and Quality of Life Among Overweight and Obese Adults With Type 2 Diabetes: 6-Month Results From a Randomized Trial. *Altern Ther Health M*. 2021;27(61-71.
5. Ou T, Wang W, Yong H, et al. Liraglutide Plus Dapagliflozin for High Uric Acid and Microalbuminuria in Diabetes Mellitus Complicated With Metabolic Syndrome. *Altern Ther Health Med*. 2022;28(6):14-21.
6. Wiviott SD, Raz I, Bonaca MP, et al; DECLARE–TIMI 58 Investigators. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. *N Engl J Med*. 2019;380(4):347-357. doi:10.1056/NEJMoa1812389
7. Heerspink HJL, Jongs N, Chertow GM, et al; DAPA-CKD Trial Committees and Investigators. Effect of dapagliflozin on the rate of decline in kidney function in patients with chronic kidney disease with and without type 2 diabetes: a prespecified analysis from the DAPA-CKD trial. *Lancet Diabetes Endocrinol*. 2021;9(11):743-754. doi:10.1016/S2213-8587(21)00242-4
8. Jongs N, Greene T, Chertow GM, et al; DAPA-CKD Trial Committees and Investigators. Effect of dapagliflozin on urinary albumin excretion in patients with chronic kidney disease with and without type 2 diabetes: a prespecified analysis from the DAPA-CKD trial. *Lancet Diabetes Endocrinol*. 2021;9(11):755-766. doi:10.1016/S2213-8587(21)00243-6
9. Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes - state-of-the-art. *Mol Metab*. 2021;46:101102. doi:10.1016/j.molmet.2020.101102
10. Tamborlane WV, Barrientos-Pérez M, Fainberg U, et al; Ellipse Trial Investigators. Liraglutide in Children and Adolescents with Type 2 Diabetes. *N Engl J Med*. 2019;381(7):637-646. doi:10.1056/NEJMoa1903822
11. Ding HX, Dong NX, Zhou CX, et al. Liraglutide Attenuates Restenosis After Vascular Injury in Rabbits With Diabetes Via the TGF-β/Smad3 Signaling Pathway. *Altern Ther Health Med*. 2022;28(6):22-28.
12. Capehorn MS, Catarig AM, Furberg JK, et al. Efficacy and safety of once-weekly semaglutide 1.0mg vs once-daily liraglutide 1.2mg as add-on to 1-3 oral antidiabetic drugs in subjects with type 2 diabetes (SUSTAIN 10). *Diabetes Metab*. 2020;46(2):100-109. doi:10.1016/j.diabet.2019.101117
13. Shaman AM, Bain SC, Bakris GL, et al. Effect of the Glucagon-Like Peptide-1 Receptor Agonists Semaglutide and Liraglutide on Kidney Outcomes in Patients With Type 2 Diabetes: pooled Analysis of SUSTAIN 6 and LEADER. *Circulation*. 2022;145(8):575-585. doi:10.1161/CIRCULATIONAHA.121.055459
14. Feng WH, Bi Y, Li P, et al. Effects of liraglutide, metformin and gliclazide on body composition in patients with both type 2 diabetes and non-alcoholic fatty liver disease: A randomized trial. *J Diabetes Investig*. 2019;10(2):399-407. doi:10.1111/jdi.12888
15. Petrie MC, Verma S, Docherty KF, et al. Effect of Dapagliflozin on Worsening Heart Failure and Cardiovascular Death in Patients With Heart Failure With and Without Diabetes. *JAMA*. 2020;323(14):1353-1368. doi:10.1001/jama.2020.1906
16. Solomon SD, de Boer RA, DeMets D, et al. Dapagliflozin in heart failure with preserved and mildly reduced ejection fraction: rationale and design of the DELIVER trial. *Eur J Heart Fail*. 2021;23(7):1217-1225. doi:10.1002/ejhf.2249