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Original Article

Clinical effect of using a sodium-glucose cotransporter 2 inhibitor in type 2 diabetes mellitus

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Abstract: Objective: To study the clinical efficacy of inhibition of sodium-glucose cotransporter 2 (SGLT2) in the treatment of type 2 diabetics. Methods: A total of 92 type 2 diabetics were selected. They were equally divided into two groups according to a random number table method: control group (conventional hypoglycemic treatment) and observation group (dapagliflozin). Glycated hemoglobin (HbA1c), Urine glucose/Urine creatinine level, waist circumference, weight, HDL-C, LDL-C, TC, TG, drug-related adverse events, FPG and 2 h postprandial blood glucose were analyzed and compared. Results: After treatment, the HbA1c of both groups was decreased, and the HbA1c level of the observation group was lower; the Urine glucose/Urine creatinine levels of both groups was increased, and the Urine glucose/Urine creatinine levels of the observation group was higher ($P < 0.05$). The waist circumference and body weight of both groups were lower, and the waist circumference and body weight of the observation group was lowest ($P < 0.05$). The LDL-C, TC, and TG in both groups were decreased, and the observation group was lower; HDL-C in both groups was higher, and the observation group was highest ($P < 0.05$). The incidence of drug-related adverse events in the control group (23.91%) was significantly higher than observation group (6.52%) ($P < 0.05$). Compared with the control group, the FPG of the observation group was lower ($P < 0.001$), and the FPG level of both groups has a tendency to decrease with time ($P < 0.001$). Compared with the control group, the 2 h postprandial blood glucose of the observation group was lower ($P < 0.001$), and the 2 h postprandial blood glucose of the two groups 2 h after a meal had a tendency to decrease with time ($P < 0.001$). Conclusions: SGLT2 inhibitors have a significant clinical effect on type 2 diabetes patients.

Keywords: Sodium-glucose cotransporter 2, type 2 diabetes, clinical effect

Introduction

Diabetes is a common disease caused by abnormalities in the endocrine system. The pathogenesis is a deficiency of the pancreatic islet β-cell function and insulin resistance [1, 2]. At present, the clinical purpose of treatment is to improve the role of pancreatic islet β cells and regulate endocrine disorders. A variety of drugs are used to regulate blood lipids, anti-inflammation, and control blood sugar [3]. However, during the course of disease, diabetics suffer from pancreatic β-cell function that is extremely weak in the later stages of the disease, obese patients generally increase their obesity due to excessive insulin dosage, and poor blood glucose control. Metformin and dipeptidyl peptidase IV inhibitors and other drugs have a certain relief effect, but the overall treatment effect is not good, so clinical treatment needs to be more effective, and reliable with effective drugs to help diabetics [4, 5]. Dapagliflozin as a sodium-glucose cotransporter 2 (SGLT2) inhibitor, is a new oral hypoglycemic drug, and its mechanism of action is to inhibit the reabsorption of proximal renal tubular sodium-glucose. The goal of lowering blood sugar is achieved by promoting the excretion of urine sugar [6]. Related research also shows that SGLT2 inhibitors have a marked effect on preventing hospitalization for heart failure and progression of kidney disease [7], and in a cardiovascular event trial, patients with type 2 diabetes and cardiovascular disease treated with SGLT2 inhibitors had significantly reduced mortality and hospitalization risks [8]. Therefore,

this study explores the clinical effect of SGLT2 inhibitors in type 2 diabetics and provides a reference for the clinical use.

Materials and methods

General information

This study selected 92 type 2 diabetics who were treated in our hospital's Endocrinology Department from November 2018 to October 2019 as the research subjects. Inclusion criteria: ① Diagnosed with type 2 diabetes [9]. ② The initial diagnosis and the blood sugar could not be controlled by diet and exercise, need oral hypoglycemic drugs or oral hypoglycemic drugs combined with basal insulin therapy. ③ Age > 18 years old, and 7.5% ≤ HbA1c ≤ 10.5%. ④ No allergic reaction to the drugs used in this research. ⑤ Sign the informed consent. Exclusion criteria: ① Type 1 diabetes, pregnant and lactating women. ② Combined with severe diseases such as in the liver, kidney and heart. ③ There are malignant tumors and autoimmune diseases. ④ Complicated with diabetic ketosis or hyperosmolar nonketotic coma. ⑤ Have a history of secondary fractures and severe osteoporosis. ⑥ At the same time receive treatment outside this study. Finally, 92 patients were included and equally divided into two groups according to a random number table method: control group (n = 46) and observation group (n = 46). This study has been approved by the ethics committee of our hospital.

Treatment of control group patients

Give routine hypoglycemic therapy [10]. Provide patients with diet control, health education and exercise guidance related to diabetes. Oral insulin (Sihuan Pharmaceutical Co., Ltd., approval number: National Pharmaceutical Standard H11020548, specification: 10 ml: 400 units), according to the patient's body weight, according to the daily insulin dosage required. When the patient has a marked hypoglycemic response or hypoglycemia, reduce the insulin dose. Take for 12 consecutive weeks.

Treatment of observation group patients

In addition to treatment in the control group, Dagegliflozin (manufacturer: AstraZeneca Pharmaceutical Co., Ltd.; import drug registration certificate number: JX20140204; approval number: H20170119; specification: 10 mg/tablet) was given orally. One piece/time/d. It could be taken before or after meals, with a starting dose of 5 mg/d. If the patient needs strengthen blood glucose control and can tolerate a dose of 5 mg/d, the dose can be adjusted to 10 mg/d. Take for 12 consecutive weeks.

Observation index

(1) HbA1c and Urine glucose/Urine creatinine levels: tested before and after treatment, the normal value of HbA1c is 4% to 6% (currently, the control standard for HbA1c in diabetic patients is set at 6.5% or less) [11]. (2) Waist circumference and body mass: measured before and after treatment. (3) Blood lipid level: indicators include HDL-C, LDL-C, TC, and TG, which were detected before and after treatment using a blood lipid detector from 4 ml of venous blood collected in the morning in the fasting state of the patient, and serum was collected after centrifugation at 3000 rpm for 10 min and stored at -20°C [12]. (4) Drug-related adverse events: Statistics of hypoglycemia, hypotension, urogenital system infection, liver dysfunction, abnormal renal function, malignant tumors, etc. during the statistical treatment [13]. (5) FPG, 2 h postprandial blood glucose: before treatment, on the 2nd day of hospitalization, on the 5th day of hospitalization, and on the 10th day of hospitalization. Value: 3.9-6.0 mmol/L, normal blood glucose 2 h after meal: < 7.8 mmol/L [14, 15].

Statistical analysis

This study used SPSS 20.0 statistical software for data analysis. Quantitative data was represented by "mean ± SD". t-test was used for the comparison between the two groups. The t-test uses t-distribution theory to infer the probability of the difference, so as to compare whether the two averages are significantly different. Comparison of data at different time points between groups was performed by repeated measurement analysis of variance. Qualitative data was represented by n (%) and chi-square tests were performed. When 1 ≤ theoretical frequency < 5, using the exact chi-square. The chi-square test is usually used in the statistical inference of categorical data, including the chi-square test for comparing two rates or two constituent ratios, multiple rates or chi-square

Table 1. Comparison of gender, age, course of disease and BMI between the two groups

Group	Gender		Age	Course of disease	BMI
	male	female			
Control group (n = 46)	29 (63.04%)	17 (36.96%)	47.46±8.61	8.41±4.52	28.79±3.28
Observation group (n = 46)	25 (54.35%)	21 (45.65%)	48.21±8.32	8.16±4.24	29.02±3.51
χ^2/t	0.717		0.425	0.274	0.325
P	0.397		0.672	0.785	0.746

Table 2. HbA1c and Urine glucose/Urine creatinine (mean ± SD)

Group	HbA_1c (%)		Urine glucose/Urine creatinine	
	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Control group (n = 46)	8.71±0.93	8.02±1.01[A]	1.18±0.21	18.06±0.04[A]
Observation group (n = 46)	8.85±0.72	7.15±0.89[A]	1.12±0.17	25.58±5.66[A]
t	0.807	4.383	1.506	9.011
P	0.422	< 0.001	0.136	< 0.001

Remarks: compared to before treatment, [A]*P* < 0.05.

Table 3. Waist circumference and body mass (mean ± SD)

Group	Waist circumference (cm)		body weight (kg)	
	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Control group (n = 46)	92.86±10.75	88.24±10.36[B]	68.56±12.67	63.04±12.38[B]
Observation group (n = 46)	93.06±10.66	84.12±8.03[B]	67.73±12.52	58.19±7.26[B]
t	0.090	2.132	0.316	2.292
P	0.929	0.036	0.753	0.024

Remarks: compared to before treatment, [B]*P* < 0.05.

test of multiple composition ratio comparison. Repeated measures ANOVA was used to perform statistical analysis of comparison among multiple time points in the two groups. When P < 0.05, the difference was statistically significant.

Results

General information

In the control group (n = 46), there were 29 males and 17 females. Age was (47.46±8.61) years old. Course of disease was (8.41±4.52) years. BMI was (28.79±3.28) kg/m^2. In the observation group (n = 46), there were 25 smale and 21 females. Age was (48.21±8.32) years old. Course of disease was (8.16±4.24) years. BMI was (29.02±3.51) kg/m^2. General data such as gender, age, course of disease, Body Mass Index (BMI), etc. between the two groups were not significantly different, and were comparable (P > 0.05) (**Table 1**).

HbA1c and urine glucose/urine creatinine

Before treatment, the HbA1c and Urine glucose/Urine creatinine between the two groups were not much different (P > 0.05). After treatment, the HbA1c in both groups was lower, and the observation group was lowest. The Urine glucose/Urine creatinine in both groups was higher, and the observation group was highest (P < 0.05) (**Table 2**).

Waist circumference and body mass

Before treatment, the waist circumference and body weight between the two groups were not much different (P > 0.05). After treatment, the waist circumference and body weight in both groups were lower, and the observation group was lowest (P < 0.05) (**Table 3**).

Blood lipid levels

Before treatment, the HDL-C, LDL-C, TC, TG between the two groups were not much differ-

Table 4. Blood lipid levels (mmol/L, mean ± SD)

Group	HDL-C		LDL-C		TC		TG	
	Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Control group (n = 46)	1.23±0.19	1.59±0.36[c]	3.63±1.05	3.03±1.04[c]	5.92±1.09	4.02±1·03[c]	2.82±0.92	2.05±0.26[c]
Observation group (n = 46)	1.25±0.21	2.01±0.38[c]	3.61±1.02	2.47±0·51[c]	5.83±1.12	2.91±0·08[c]	2.79±0.87	1.75±0.35[c]
t	0.479	5.442	0.093	3.279	0.391	7.287	0.161	4.667
P	0.633	< 0.001	0.926	0.001	0.697	< 0.001	0.873	< 0.001

Remarks: compared to before treatment, [c]*P* < 0.05.

Table 5. The occurrence of drug-related adverse events [n (%)]

Group	Hypoglycemia	Hypotension	Malignant tumor	Abnormal kidney function	Hepatic insufficiency	Genitourinary system infection	Total adverse events
Control group (n = 46)	3 (6.52)	2 (4.35)	0 (0)	2 (4.35)	3 (6.52)	1 (2.17)	11 (23.91)
Observation group (n = 46)	0 (0)	1 (2.17)	0 (0)	1 (2.17)	1 (2.17)	0 (0)	3 (6.52)
χ^2							4.128
P							0.042

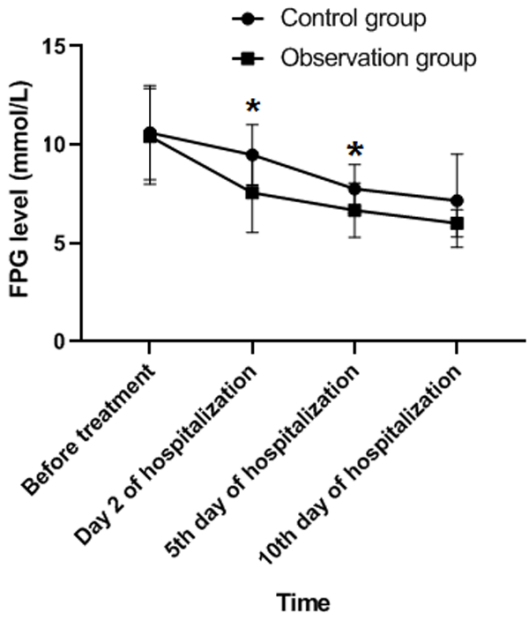

Figure 1. FPG levels between the two groups, *P < 0.05.

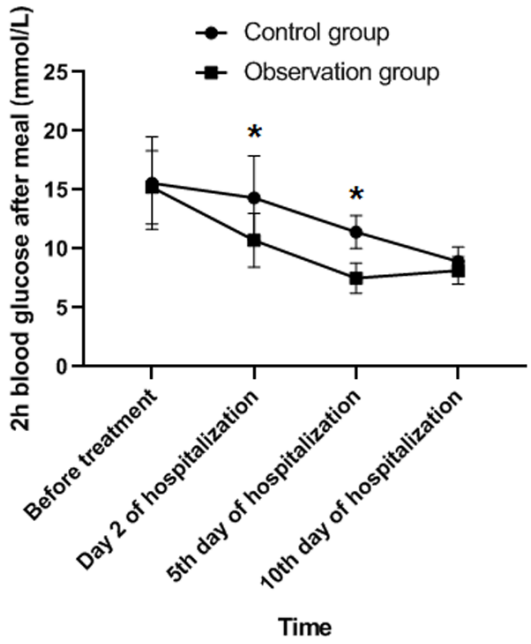

Figure 2. Blood glucose level 2 h after meal between the two groups, *P < 0.05.

ent (P > 0.05). After treatment, the LDL-C, TC, and TG in both groups were lower, and the observation group was lowest. HDL-C in both groups was higher than before treatment, and the observation group was highest (P < 0.05) (**Table 4**).

Occurrence of drug-related adverse events

Compared with the control group, the incidence of adverse drug reaction events was lower in the observation group (P < 0.05) (**Table 5**).

FPG levels between the two groups

Compared with the control group, the FPG of the observation group was lower (inter-group effect: F = 80.840, P < 0.001), and the FPG level of both groups had a tendency to decrease with time (time effect: F = 31.530, P < 0.001). Time has interactive effects (interactive effects: F = 3.350, P = 0.019) (**Figure 1**).

Blood glucose level 2 h after meal

Compared with the control group, the blood glucose level 2 h after a meal in the observation group was lower (intergroup effect: F = 144.700, P < 0.001), and the 2 h postprandial blood glucose of both groups had a tendency to decrease with time (time effect: F = 69.390, P < 0.001). There is an interactive effect between grouping and time (interactive effect: F = 12.840, P < 0.001) (**Figure 2**).

Discussion

Currently, the incidence of diabetes in China is increasing annually, and the physical and mental health of patients has been greatly threatened. Therefore, it is of great clinical significance to find a drug that can effectively help patients control blood sugar. Under normal physiological conditions, the glucose filtered through the glomeruli can be completely reabsorbed by the renal tubules. However, when the blood glucose concentration is too high, and even exceeds the renal glucose threshold (10 mmol/L), due to the limited ability of renal tubular reabsorption, excessive glucose reabsorption fails and is excreted with urine, eventually resulting in diabetes [16]. When the kidneys of the body are affected by a high glucose environment for a long time, the renal glucose threshold rises, and the ability of the renal tubules to reabsorb glucose is enhanced, which in turn causes the increase of blood glucose in the body [17]. The SGLT2 inhibitor drugs currently approved for clinical treatment of type 2 diabetes include dapagliflozin, cagliflozin and igliflozin.

Our results showed that; (1) after treatment, the HbA1c, Urine glucose/Urine creatinine, waist circumference, body mass, FPG, and 2 h postprandial blood glucose were improved, and the improvement in the observation group was significant compared to that in the control group ($P < 0.05$). This shows that compared with conventional hypoglycemic therapy, treatment of type 2 diabetics with SGLT2 dapagliflozin can evidently reduce the levels of HbA1c, waist circumference, body mass, and 2 h postprandial blood glucose, while increasing Urine glucose/Urine creatinine levels. The reason for this may be that dapagliflozin can block SGLT-2, reduce the reabsorption of glucose by the proximal tubules of the kidney, and thereby promote the excretion of urine glucose, and the level of blood sugar drops. Increase, effectively reduce the patient's waist circumference and body mass [18]; SGLT2 inhibitors have a novel mechanism of action, providing new ideas for the treatment of diabetics. (2) The improvement of HDL-C, LDL-C, TC and TG in the observation group was higher, indicating that dapagliflozin can effectively improve blood lipid levels. According to the data, high blood lipids can promote abnormal glucose metabolism, increase blood viscosity and promote blood cell aggregation, thereby further promoting the formation of microthrombi, which can eventually lead to vascular disease, which is not conducive to the patient's prognosis; so dapagliflozin can be effective in helping patients reduce blood lipids, with more systematic management of the treatment of type 2 diabetes, and is more conducive to improving treatment effects [19]. (3) The incidence of adverse drug reaction events was lower in the observation group. This shows that the use of SGLT2 inhibitor dapagliflozin can significantly reduce the occurrence of drug-related adverse events, the treatment is safer and more reliable, and it is more conducive to improving the prognosis of patients. Due to the continuous excretion of urinary glucose in diabetic patients, the urinary and reproductive system is highly prone to infections, with an incidence rate as high as 4.8% to 5.7%. The main infections in female patients include vulvovaginitis, vaginal candidiasis and vulvovaginal fungal infections. The infections in male patients are mainly candidal penile foreskinitis and balanitis, which cause a great burden on patients' psychology and physiology [20]. The use of dapagliflozin can reduce the occurrence of adverse drug events such as urogenital infection, hypoglycemia, hypotension, liver dysfunction, abnormal renal function, and malignant tumors. It may be because dapagliflozin effectively reduces blood sugar and blood lipids, etc. The effect further reduces the burden on the body, the function of the body is also less affected, and the risk of hypoglycemia, hypotension, and infection is also reduced. Related research results show that SGLT2 inhibitors can not only increase HDL-C and reduce TG, but also play a role in weight control and lipid-lowering, which is similar with the results of this study [21, 22]. This study may be due to insufficient sample size, which results in a certain bias in the result data, we need to expand the sample size for further confirmation.

In summary, the clinical efficacy of SGLT2 inhibitors in type 2 diabetics is remarkable. It can effectively reduce body weight, lower blood sugar and blood lipids. The treatment is safe and reliable, which is worthy of clinical promotion.

Disclosure of conflict of interest

None.

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