Clinical Evaluation of Bexagliflozin and Other SGLT2 Inhibitors for Type 2 Diabetes Management

Chenyi Lin *

The No.3 Middle School of Fuzhou, Fuzhou, 350000, China

* Corresponding Author Email: chenyilin@ldy.edu.rs

Abstract. To assess the clinical effectiveness and safety of Bexagliflozin and Cagglitazone (Cagelin) in the management of type 2 diabetes, we conducted a study involving three hundred type 2 diabetes patients admitted to the hospital from May 2022 to May 2023. The patients were randomly allocated into two study groups. The Bexagliflozin treatment group consisted of 150 patients, while the control group included 150 patients who were administered Cagelin. During a 4-month intervention period, both cohorts were subjected to a rigorous evaluation. We conducted a comprehensive analysis encompassing their demographic data, glycemic fluctuations, pre- and post-treatment body weight variations, as well as vigilantly monitored for any potential adverse events. The results indicate a significant decrease in FPG, 2HPG, HbA1c, and body weight indicators in both groups after drug treatment. Notably, the Bexagliflozin group demonstrated a significantly greater reduction in blood glucose and body weight indices compared to the control group. The incidence of severe adverse reactions was slightly higher in the Bexagliflozin group at 7.33% compared to 6.67% in the control group, but this difference was not statistically significant (P>0.05). When compared to other SGLT2 inhibitors, Bexagliflozin demonstrates a more pronounced effect in regulating blood sugar levels and inhibiting weight gain in the treatment of type 2 diabetes.

Keywords: Bexagliflozin; Kagliflozin; type 2 diabetes; blood sugar.

1. Introduction

Type 2 diabetes (T2DM) is a prevalent clinical condition and a significant risk factor for heart failure (HF). The five-year survival rate for patients with both HF and diabetes is less than 25% [1]. Traditional anti-diabetes medications effectively lower blood sugar but offer limited cardiovascular benefits. Recent clinical research has highlighted the need to shift the treatment approach for T2DM from merely controlling blood sugar to enhancing cardiovascular outcomes [2]. SGLT2 inhibitors not only lower blood sugar but also provide additional benefits such as weight reduction, blood pressure control, reduced urinary albumin, decreased blood uric acid levels, and a lower risk of heart failure. These benefits have led both the European Society of Cardiology's Annual Scientific Meeting (ESC) and the American Society of Cardiology's Annual Scientific Meeting (ACC) to endorse SGLT2 inhibitors as Class I recommendations for reducing ejection fraction, cardiovascular death, and readmissions for heart failure patients [3]. Bexagliflozin, a novel SGLT2 inhibitor, has recently received approval for treating type 2 diabetes [4, 5]. However, domestic research on the use of Bexagliflozin in T2DM treatment is limited.

According to the International Diabetes Federation (IDF), there are currently 463 million people with diabetes worldwide, and this number is expected to exceed 700 million in the next two decades. Notably, about one-quarter of diagnosed diabetes patients reside in China, with this proportion consistently increasing annually [6]. While the primary treatment goal for T2DM patients remains blood sugar control, over half of diabetes patients fail to achieve the recommended HbA1c<7.0%, which significantly reduces the risk of microvascular complications as per the American Diabetes Association (ADA) [7]. SGLT-2 inhibitors, including Dapagliflozin, are the latest class of hypoglycemic drugs approved by the CFDA, suitable for use at any stage of T2DM, regardless of complications [7]. Bexagliflozin, a highly effective and specific C-arylglucoside inhibitor of human SGLT2, undergoes important metabolic transformations in the body [8]. Five specific SGLT2 inhibitors, Kagliflozin, Dapagliflozin, Empagliflozin, Ertugliflozin, and Bexagliflozin, have been proven to improve blood glucose levels in type 2 diabetes and are in practical clinical use [9]. Due to

their effectiveness in reducing blood sugar, promoting weight loss, and mitigating the risk of cardiovascular events, these inhibitors have garnered significant attention [10].

This paper aims to investigate and assess the effectiveness of Bexagliflozin and various SGLT2 inhibitors in blood sugar control, weight reduction, and enhancing cardiovascular outcomes in T2DM patients. Additionally, it aims to evaluate the safety profile of Bexagliflozin and compare it with other SGLT2 inhibitors concerning adverse events, including urinary tract infections, heart failure, and ketoacidosis.

2. Methods

2.1. Indicators Introduction

This paper will compare in three aspects: (i) Comparison of the two groups' overall data: statistics and comparison of gender, age, blood pressure, heart rate, cholesterol, years of diabetes, hypertension, cardiovascular events, etc. of the two groups. (ii) Comparison of blood glucose and body weight between the two groups before and after treatment: compare the blood glucose levels before and after treatment. (iii) Comparison reactions between risk of urinary tract infections, heart failure (a cardiovascular prognostic indicator), and ketoacidosis.

2.2. Method Introduction

2.2.1 Case grouping

From May 2022 to May 2023, hospital data on 300 type 2 diabetes patients were gathered. Prior to the study's advancement, the study's participants and their families completed an informed consent form after being made aware of its content and purpose and received the ethics committee of our hospital's clearance.

The subjects (n=300 cases) were randomly divided into two groups for study, both of which applied dietary control, appropriate exercise conventional treatments such as anti-heart failure and hypoglycemic therapy were administered to 150 patients in the observation group, including Bexagliflozin (20 mg/tablet) at a dose of 20 mg/day, while the control group received Cabagliptin (100 mg/tablet) at a dose of 100 mg/day.

2.2.2 Inclusion and exclusion criteria

In this study, inclusion criteria encompass individuals with cardiac function at Level 2 or higher, according to the NYHA classification, an estimated glomerular filtration rate (eGFR) exceeding 45 ml/min*1.73 m^2, ages ranging from 18 to 80 years, and a confirmed diagnosis of type 2 diabetes. Exclusion criteria, on the other hand, exclude patients with malignant tumors, individuals with multiple organ dysfunction, and those currently in a state of cardiogenic shock. These criteria serve as the basis for participant selection, ensuring that the study includes individuals meeting specific health and age-related parameters while excluding those with conditions that may interfere with the study's objectives or pose heightened risks.

2.2.3 Statistical methods

Data processing and analysis were carried out using SPSS software. Normally distributed measurement data with uniform variance were presented as mean ± standard deviation, while count data were represented as percentages (%). Data comparisons were conducted employing t-tests, and a significance level of $P<0.05$ was considered to indicate statistical significance.

3. Results and Discussion

3.1. Comparative Analysis of General Data Between Two Group

Following random group allocation, patient data, including gender, age, blood pressure, heart rate, cholesterol levels, duration of diabetes, presence of hypertension, and cardiovascular factors, were

systematically collected and meticulously compared between the two study groups. The findings unequivocally demonstrated that there were no statistically significant disparities in the aforementioned patient characteristics between the two groups (P>0.05). A comprehensive breakdown of this data is presented in Table 1.

Table 1. Results of General Data between Two Groups [n (%)]

item	Control group (150)	Observation group (150)	t/χ^2 value	P value
Gender (male/female)	63/87	61/89	0.055	0.815
Age (years)	66.45±7.22	65.99±7.10	0.556	0.578
Systolic blood pressure (mmHg)	134.67±22.89	135.01±21.03	0.134	0.894
Diastolic blood pressure (mmHg)	98.11±11.24	97.60±12.01	0.380	0.704
Heart rate (beats/min)	82.11±19.05	81.90±18.77	0.096	0.923
Cholesterol (mmol/L)	3.53±1.04	3.49±1.10	0.324	0.746
Years of diabetes (years)	13.90±4.23	13.31±5.06	1.096	0.274
Hypertension (n)	104(69.33)	105(70.00)	0.016	0.900
Cardiovascular events (n)	80(53.33)	82(54.67)	0.054	0.817

3.2. Blood Glucose and Body Weight before and after Treatment

Intra-group analysis revealed a notable reduction in fasting plasma glucose (FPG), 2-hour postprandial glucose (2hPG), glycated hemoglobin (HbA1c), and body weight following treatment compared to baseline values, with all changes registering statistical significance (P<0.05). Prior to treatment initiation, there were no statistically significant discrepancies in blood glucose and body weight parameters between the control and observation groups (P>0.05). However, upon comparative evaluation post-treatment, it became evident that the observation group displayed significantly lower blood glucose and body weight indices in comparison to the control group (P<0.05). These findings underscore the therapeutic efficacy of the interventions in the observation group in achieving superior outcomes in blood glucose control and weight management.See Table 2.

Table 2. Assessment of Blood Glucose and Body Weight Changes in Patients Before and After Treatment (n)

item	Observation time	Control group (150)	Observation group (150)	t value	P value
FPG（mmol/L）	Before treatment	9.03±1.24	9.04±1.19	0.071	0.943
	After treatment	7.11±1.54	6.30±1.27	4.970	＜0.001
t value	-	11.893	19.282	-	-
P value	-	＜0.001	＜0.001	-	-
2hPG（mmol/L）	Before treatment	15.55±3.10	15.62±2.98	0.199	0.842
	After treatment	11.91±2.61	11.20±2.65	2.338	0.020
t value	-	11.001	13.575	-	-
P value	-	＜0.001	＜0.001	-	-
HbAlc（%）	Before treatment	9.31±1.64	9.32±1.66	0.052	0.958
	After treatment	7.60±1.45	6.96±1.35	3.956	＜0.001
t value	-	9.567	13.509	-	-
P value	-	＜0.001	＜0.001	-	-
Body weight (kg)	Before treatment	76.77±10.98	77.01±10.45	0.194	0.846
	After treatment	74.20±11.23	72.01±10.56	1.978	0.049
t value	-	2.004	4.122	-	-
P value	-	0.046	＜0.001	-	-

3.3. Comparative Analysis of Adverse Reactions Between the Two Groups

Within the Bexagliflozin group, a marginally higher incidence of severe adverse reactions was observed at 7.33% in contrast to 6.67% in the control group; however, this disparity did not reach statistical significance (P>0.05). The adverse reaction profiles of Bexagliflozin group align with established safety profiles for similar medications in clinical use. See Table 3.

Table 3. Comparison of adverse reactions between two groups [n (%)]

Adverse events (n)	Control group (150)	Observation group (150)
urinary tract infection	8	8
heart failure	1	1
ketoacidosis	1	2
amount to	10(6.67)	11(7.33)
χ^2 value	0.051	
P value	0.821	

4. Conclusion

Previous studies have provided evidence supporting the positive impact of SGLT2 inhibitors on the cardiovascular system, including a reduction in the occurrence of clinical cardiovascular endpoint events in individuals with heart failure. Furthermore, Paul and colleagues have reported that SGLT-2 inhibitors can lead to a reduction in left ventricular mass among patients with Type 2 Diabetes Mellitus (T2DM). Further validation comes from Sokolov, who confirmed that SGLT-2 inhibitors lead to decreased rates of re-hospitalization, cardiovascular mortality, and all-cause mortality in

T2DM patients with heart failure. In conclusion, this study also underscores the effectiveness of SGLT2 inhibitors in improving cardiovascular outcomes for individuals with T2DM.

This study conducted a thorough examination of the baseline data, finding a high degree of comparability between the two groups, even though statistical significance was not reached. Within each group, notable reductions were observed in FPG, 2hPG, HbA1c, as well as the initial and final body weight. Prior to treatment, there were no statistically significant differences in blood glucose and body weight indicators between the control and observation groups. However, following treatment, a significant discrepancy emerged between the two groups, with the observation group experiencing lower blood glucose and body weight indicators, demonstrating statistical significance. Additionally, the incidence of severe adverse reactions did not exhibit a statistically significant difference between the two groups ($P>0.05$). These findings indicate that, in comparison to the control group (treated with Caggliflozin), T2DM patients receiving Bexagliflozin achieved more substantial improvements in blood sugar control and weight management. Furthermore, the effectiveness of Caggliflozin in these aspects was also found to be reasonably accurate.

Compared with SGLT2 inhibitors, Bexagliflozinhas certain advantages in the effect of reducing blood sugar and the effect on body mass. It is also a new hope for type 2 diabetes patients with poor diet, exercise and drug control to effectively control their condition. However, its effectiveness depends on normal renal filtration function, so its application may be limited. As a new drug, its pharmacological effects and adverse reactions, especially some serious adverse reactions, need to be further studied in future clinical applications.

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