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ORIGINAL RESEARCH

Dapagliflozin and Empagliflozin in Heart Failure with Reduced Ejection Fraction: A Retrospective Study

Zhengyang Hao, Yanzhou Zhang

Department of Cardiology, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, 450052, People's Republic of China

Correspondence: Yanzhou Zhang, Department of Cardiology, the First Affiliated Hospital of Zhengzhou University, Zhengzhou, 450052, People's Republic of China, Email zhangyanzhou666@outlook.com

Objective: Dapagliflozin 10 mg and empagliflozin 10 mg have been recommended to treat heart failure with reduced ejection fraction (HFrEF), and the purpose of this study was to compare the efficacy and safety of them in HFrEF.

Methods: Two hundred and thirty-three patients with HFrEF admitted to a tertiary hospital of Zhengzhou and commenced to take dapagliflozin 10 mg/d or empagliflozin 10 mg/d were retrospectively included and separated into the dapagliflozin group (n=105) and the empagliflozin group (n=128). Their cardiac function indices before and after therapy were compared, together with the ratios of adverse events during therapy.

Results: After 6 months of therapy, left ventricular ejection fraction was higher, and the ratio of New York Heart Association functional class III or IV, left ventricular end-diastolic diameter, and N-terminal pro-B-type natriuretic peptide were lower in the empagliflozin group than the dapagliflozin group (P<0.05). During 6 months of therapy, there were no statistically significant differences for the ratios of hypotension, deteriorating kidney function, and genitourinary infections between the dapagliflozin and empagliflozin groups (P>0.05).

Conclusion: Despite its many limitations, this study suggested that different SGLT2 inhibitors might have differences regarding efficacy in HFrEF. We look forward to future studies to verify our conjectures.

Keywords: dapagliflozin, empagliflozin, heart failure with reduced ejection fraction

Introduction

Sodium-glucose cotransporter-2 (SGLT2) inhibitors, including dapagliflozin and empagliflozin, are a new type of oral glucose-lowering drugs that can control blood glucose by inhibiting SGLT2 in the kidney. The DAPA-HF trial[1] and the EMPEROR-Reduced trial[2] suggested that dapagliflozin and empagliflozin, respectively, could lower the incidences of cardiovascular adverse events in patients suffering from heart failure with reduced ejection fraction (HFrEF).

Dapagliflozin 10 mg and empagliflozin 10 mg are recommended to treat HFrEF, but it is undetermined whether or not they are different in terms of efficacy and safety in HFrEF. This study was performed to compare the efficacy and safety of dapagliflozin 10 mg and empagliflozin 10 mg in HFrEF.

Methods

Study Patients

A total of 233 patients with HFrEF admitted to a tertiary hospital of Zhengzhou and commenced to take dapagliflozin 10 mg/d or empagliflozin 10 mg/d were included in this single-center retrospective study. Patients in this study were in New York Heart Association (NYHA) functional class II or III, had a left ventricular ejection fraction (LVEF) of less than 40% measured by transthoracic echocardiography, and had been treated with dapagliflozin 10 mg/d or empagliflozin 10 mg/d for more than 6 months.

The study was approved by the ethics committee of the hospital, and all included patients were informed and consented.

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Study Design

Data of these patients were acquired by the electronic medical record system. Basic data contained demographic characteristics, vital signs, laboratory indicators, diseases, and medications.

Cardiac function indices, containing NYHA functional class, transthoracic echocardiographic indicators [containing LVEF and left ventricular end-diastolic diameter (LVEDD)], and N-terminal pro-B-type natriuretic peptide (NT-proBNP), before and after 6 months of therapy were recorded.

Adverse events, containing hypotension, deteriorating kidney function, and genitourinary infections, during 6 months of therapy were also recorded. Patients would be diagnosed with hypotension if their systolic blood pressure was below 90 mmHg, and when their serum creatinine increased by more than 25% or 0.3 mg/dL compared to before therapy, they would be diagnosed with deteriorating kidney function.

Statistical Analysis

Continuous variables and categorical variables were reported as means ± standard deviations and frequencies (percentages), respectively. Comparisons of the variables between the dapagliflozin and empagliflozin groups were made using independent sample t-test, Pearson's chi-square test, or Fisher's exact test. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Basic Data

Among the 233 patients, 105 were on dapagliflozin and 128 were on empagliflozin. The age of the dapagliflozin group was 68.6±12.9 years, 62 were males and 43 were females, and the age of the empagliflozin group was 67.5±13.1 years, 71 were males and 57 were females. There were no statistically significant differences regarding demographic characteristics, vital signs, laboratory indicators, diseases, and medications between the dapagliflozin and empagliflozin groups ($P>0.05$). Table 1.

Cardiac Function Indices

After 6 months of therapy, LVEF was higher, and the ratio of NYHA functional class III or IV, LVEDD, and NT-proBNP were lower in the empagliflozin group when compared with the dapagliflozin group ($P<0.05$). Table 2.

Adverse Events

During 6 months of therapy, there were no statistically significant differences for the ratios of hypotension, deteriorating kidney function, and genitourinary infections between the dapagliflozin and empagliflozin groups ($P>0.05$). Table 3.

Discussion

This study showed that after 6 months of therapy, LVEF was higher, and the ratio of NYHA functional class III or IV, LVEDD, and NT-proBNP were lower in the empagliflozin group compared with the dapagliflozin group. Meanwhile, during 6 months of therapy, the differences in the ratios of hypotension, deteriorating kidney function, and genitourinary infections between the dapagliflozin and empagliflozin groups were not statistically significant. These results suggested that different SGLT2 inhibitors might have differences in efficacy when treating HFrEF.

SGLT2 inhibitors can bring multiple benefits to patients suffering from HFrEF. The literatures[3,4] suggested that they could not only reduce the volumes of left atrium and left ventricle, but also benefit life quality. A study[5] suggested that SGLT2 inhibitors could shift utilization of myocardial fuel away from glucose to branched-chain amino acid, free fatty acid, and ketone bodies, and this is perhaps one of the mechanisms by which LVEF increases among some patients. In addition to these, SGLT2 inhibitors may ameliorate interstitial myocardial fibrosis, inflammatory markers, as well as aortic stiffness.[6]

The glucose-lowering effects of different SGLT2 inhibitors may be different.[7] In this study, after 6 months of therapy, LVEF was higher, and the ratio of NYHA functional class III or IV, LVEDD, and NT-proBNP were lower in the

Table 1 Basic Data

Variables	Dapagliflozin Group (*n*=105)	Empagliflozin Group (*n*=128)	*P* value
Demographic characteristics			
Age, years	68.6±12.9	67.5±13.1	0.526
Female, *n* (%)	43 (41.0)	57 (44.5)	0.583
Body mass index, kg/m^2	26.4±3.0	26.0±2.9	0.316
Vital signs			
Systolic blood pressure, mmHg	120.3±10.4	119.6±9.8	0.588
Diastolic blood pressure, mmHg	75.3±6.9	74.5±6.5	0.378
Heart rate, beats/min	79.5±9.7	80.9±10.5	0.293
Laboratory indicators			
Serum creatinine, μmol/L	91.6±10.3	92.5±11.0	0.533
Serum potassium, mmol/L	4.3±0.3	4.3±0.3	0.804
Hemoglobin, g/L	135.7±9.4	134.7±10.3	0.441
Diseases, *n* (%)			
Ischemic cardiomyopathy	55 (52.4)	59 (46.1)	0.339
Hypertension	34 (32.4)	48 (37.5)	0.416
Atrial fibrillation	28 (26.7)	26 (20.3)	0.253
Diabetes	103 (98.1)	128 (100.0)	0.202
Medications, *n* (%)			
ARNI/ACEI/ARB	88 (83.8)	105 (82.0)	0.720
Beta blocker	97 (92.4)	116 (90.6)	0.634
ARA	68 (64.8)	89 (69.5)	0.440

Abbreviations: ARNI, angiotensin receptor neprilysin inhibitor; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin-receptor blocker; ARA, aldosterone receptor antagonist.

Table 2 Cardiac Function Indices

Variables		Dapagliflozin Group (*n*=105)	Empagliflozin Group (*n*=128)	*P* value
NYHA functional class III or IV, *n* (%)	Before therapy	52 (49.5)	66 (51.6)	0.757
	After therapy	34 (32.4)	26 (20.3)	0.036
LVEF, %	Before therapy	30.1±3.2	30.6±3.4	0.246
	After therapy	34.5±3.9	38.6±4.3	<0.01
LVEDD, mm	Before therapy	66.2±3.8	65.7±3.6	0.298
	After therapy	62.6±3.5	59.7±3.1	<0.01
NT-proBNP, pg/mL	Before therapy	4268.2±2175.8	4574.4±2347.0	0.307
	After therapy	3508.6±1845.7	2891.2±1120.4	<0.01

Abbreviations: NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; NT-proBNP, N-terminal pro-B-type natriuretic peptide.

Table 3 Adverse Events

Variables	Dapagliflozin Group (*n*=105)	Empagliflozin Group (*n*=128)	*P* value
Hypotension, *n* (%)	3 (2.9)	6 (4.7)	0.519
Deteriorating kidney function, *n* (%)	1 (1.0)	0 (0.0)	0.451
Genitourinary infections, *n* (%)	2 (1.9)	1 (0.8)	0.590

empagliflozin group than the dapagliflozin group, suggesting that empagliflozin 10 mg might ameliorate heart function more significantly among HFrEF patients compared with dapagliflozin 10 mg. On the other hand, this study also found that the ratios of hypotension, deteriorating kidney function, and genitourinary infections during 6 months of therapy between the two groups were statistically insignificant, suggesting that dapagliflozin 10 mg and empagliflozin 10 mg might have similar safety profiles when treating HFrEF.

Limitations

This study has many limitations, for instance: 1. Echocardiography examinations were performed by different sonographers, which might have influenced the results. 2. The doses of other drugs, including sacubitril/valsartan, metoprolol, and spironolactone, were not recorded, which might not be conducive to the comparison of these two SGLT2 inhibitors. 3. The effects of dapagliflozin and empagliflozin on the prognosis of HFrEF patients were not compared.

Conclusion

Because of the limitations of this study, we could not conclude that 10 mg of empagliflozin is superior to 10 mg of dapagliflozin when treating HFrEF. After 6 months of therapy, the differences in several cardiac function indices between the two groups were statistically significant, therefore, we speculated that the efficacies of different SGLT2 inhibitors in HFrEF might be different. We look forward to future studies to verify our conjectures.

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Disclosure

The authors report no conflicts of interest in this work.

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