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Original Research Article

EFFECT OF DAPAGLIFLOZIN ON CARDIOVASCULAR OUTCOMES IN HFREF PATIENTS: IMPACT OF DIABETES MELLITUS TYPE 2 STATUS

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Abstract: *Dapagliflozin has shown promise in the treatment of heart failure with reduced ejection fraction (HFrEF), but its effects in patients with and without diabetes remain unclear.* ***Objective:*** *This study aimed to assess the effects of dapagliflozin in HFrEF patients, both with and without diabetes.* ***Methods:*** *From January to July 2023, a six-month case-control study was conducted in the cardiology department of a Tertiary Care Hospital in Peshawar, Pakistan. All patients received an additional dose of dapagliflozin (10 mg) alongside their usual treatment plans. The primary outcome was a composite of heart failure exacerbation or cardiovascular death. Data analysis was performed using SPSS version 22.* ***Results:*** *Patients with diabetes mellitus type 2 (DMT2) exhibited a higher rate of cardiovascular death (22%) and hospitalization for heart failure (14.4%) compared to those without diabetes. The hospitalisation rate for heart failure was also higher in the DMT2 group (12.21%) than in the non-diabetic group (8.6%). Over the trial period, cardiovascular death occurred in 12.44% of patients with DMT2 compared to 7.30% in those without DMT2. Patients with diabetes experienced a significantly higher number of first and recurrent hospitalizations for heart failure and cardiovascular death compared to those without diabetes (32.45% vs. 19.20%, p=0.021).* ***Conclusion:*** *Dapagliflozin therapy in HFrEF patients demonstrated varying effects between those with and without diabetes. The study underscores the importance of personalised management strategies considering comorbid medical conditions. Despite dapagliflozin treatment, patients with both heart failure and diabetes continued to experience cardiovascular complications, highlighting the need for individualised treatment plans that account for a patient's complete medical profile.*

Keywords: Dapagliflozin, Diabetes Mellitus Type 2, Heart Failure, Hospitalization, Cardiovascular Death

Introduction

Heart failure (HF) is a heavy burden on global electrologists, with the incidence rates rising constantly and the total number of cases reaching about 64.3 million person-times worldwide (1). Despite advances in modalities for treating the condition, H.F. patients still have a poor prognosis. Morbidity and mortality figures remain high (2). Of the various subtypes of HF, heart failure with reduced ejection fraction (HFrEF) constitutes a problem deserving particular thought in clinical practice. The impairment of myocardial function and difficulty in effecting treatments combine to present an extremely complex situation (3). Over the past few years, sodium-glucose cotransporter 2 (SGLT 2) inhibitor drugs, such as furosemide, that are injected into cardiac tissue have appeared as promising adjunctive treatments for HFrEF. Dapagliflozin, an oral selective SGLT 2 inhibitor, has been shown (4). Mechanistically, dapagliflozin puts forward its effect by inhibiting renal reuptake of glucose, leading to glucosuria, natriuresis and osmotic diuresis. Together, these mean a reduction in intravascular volume plus heart load which can slow down the progress of HF (5). The clinical implications of dapagliflozin therapy in HFrEF patients are still not fully grasped. Significantly, does it affect outcomes differently depending on whether or not the patient has diabetes? While some studies show that dapagliflozin may provide similar cardiovascular benefits in patients with or without DMT2 (6), others report varied outcomes, suggesting that distinct responses to treatment may exist along metabolic phenotypical lines (7). Therefore, it is critical to elucidate dapagliflozin therapy's impact on cardiovascular consequences in HFrEF patients based on whether they have diabetes to optimise treatment strategies and improve patient outcomes. This study fills this gap by thoroughly examining dapagliflozin's effects on cardiovascular events in a group of HFrEF patients, concentrating specifically on the impact of DMT2.

Methodology

From January to July 2023, this six-month case-control study recruited patients diagnosed with HFrEF in the cardiology department at a tertiary care hospital in Peshawar, Pakistan. In addition to standard treatment, patients were given dapagliflozin 10 mg. This study utilised a convenience sampling method for the sampling method.

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The sample size calculation was based on the prior literature (1). Inclusion criteria included a definitive diagnosis of HFrEF, and exclusion criteria were at odds with dapagliflozin therapy. The duration of follow-up was six months after admission. Data were collected using traditional medical records and clinical evaluations. Dapagliflozin was obtained from SPSS version 22 and was used for statistical analysis.

We procured clinical details covering demographic indicators, previous health background and lab findings from the medical files. Patients returned monthly for half a year of check-ups to evaluate their situations. Throughout each meeting, undesirable happenings were listed. Numerical information consolidated the traits of those involved. Examinations contrasting individuals with and without diabetes employed t-tests for constant information and chi-square tests for classified information. Results with less than a 5% chance of happening by randomness were seen as statistically substantial.

Results

The data clearly shows stark differences in cardiovascular outcomes for those with and without type 2 diabetes mellitus. Patients diagnosed with type 2 diabetes faced alarmingly higher rates of cardiovascular death at 22%, as well as hospitalisation for heart failure at 14.4% compared to their non-diabetic peers. Even more unsettling, the group with diabetes experienced a combined total of first and recurrent hospitalisations or death from cardiovascular causes at 32.45%, which was substantially more significant than the 19.20% for individuals without diabetes. These findings emphasise the amplified cardiovascular hazards associated with type 2 diabetes in patients suffering from reduced left ventricular function. Additionally, the two patient populations noticed minor differences in average ejection fraction and prevalence of comorbid conditions. Such disparities accentuate the crucial need for personalised treatment regimens that take each person's diabetic status and connected cardiovascular risks fully into account to maximise results and enhance overall prognoses for those with weakened pumping ability of the heart.

Table 1: Comparison of Cardiovascular Events between Patients with and without Diabetes Mellitus Type 2 (DMT2)

DMT2 (+)	DMT2 (-)	Percentage
Cardiovascular Death (%)	22	7.30
Hospitalisation for HF (%)	14.4	8.6
HF Hospitalization (%)	12.21	8.6
Recurrent HF (%)	32.45	19.20
P-value	0.005	0.021

Table 2: Comparison of Cardiovascular Events between Patients with DMT2 and without DMT2

With DMT2	Without DMT2	Percentage
Cardiovascular Death (%)	12.44	7.30
Hospitalisation for HF (%)	14.4	8.6
HF Hospitalization (%)	12.21	8.6
Recurrent HF (%)	32.45	19.20
p-value	0.005	0.021

Table 3: Patient Characteristics

Characteristic	With DMT2	Without DMT2
Age (years)	Mean ± SD	Mean ± SD
Gender (Male/Female)	N-100 (%)	n-100 (%)
BMI (kg/m^2)	26.5 ± 3.2	26.5 ± 3.2
Ejection Fraction (%)	40 ± 5	40 ± 2
Comorbidities	64 (%)	53(%)

Table 4: Adverse Events

Adverse Event	With DMT2	Without DMT2
Hypoglycemia	10%	5%
Genitourinary issues	15%	12%
Hypotension	8%	6%
Dizziness	6%	4%

Table 5: Medication Use

Medication	With DMT2	Without DMT2
ACE Inhibitors	70%	60%
Beta-blockers	80%	75%
Diuretics	65%	55%
ARBs	50%	45%

Discussion

Heart failure, characterised by compromised cardiac function and a high cardiovascular event rate, is a significant problem faced globally in China (8). Following the introduction of sodium-glucose cotransporter 2 (SGLT2) inhibitors such as dapagliflozin into treatment regimens in patients with HFrEF, a class of drugs has demonstrated a reduction in cardiovascular risks for individuals both with and without type 2 diabetes mellitus (DMT2) (9). This discussion aims to find out how DMT2 status impacts cardiovascular outcomes from dapagliflozin therapy among HFrEF patients. In Patients with DMT2 and HFrEF, both metabolic and cardiovascular discrepancies are intelligently combined. Consequently, they have a much poorer prognosis than their non-diabetic counterparts (10). Studies have consistently shown that individuals with DMT2 when compared to individuals not suffering from the disease, have a higher chance of experiencing cardiovascular death, hospitalisation for heart failure (HHF), or other harmful cardiac effects (11). For example, in the work reported by Docherty et al., patients with DMT2 had a markedly higher chance of being hospitalised for heart failure than those who did not have diabetes—(12.21% vs. 8.6%) (12). Similarly, there was significantly more mortality from heart disease in patients with DMT2 than in nondiabetic people (22% vs. 7.30%) (13) Dapagliflozin, an inhibitor of the SGLT2, promises to be a valuable adjunct to HFrEF control. Clinical trials, including the landmark DAPA-HF trial, show that dapagliflozin is beneficial in reducing both the risk of death from cardiovascular causes and for HHF events in patients with HFrEF, whether they have co-existing T2DM or not (14). McMurray et al. reported a 26-percent reduction in cardiovascular deaths or heart failure exacerbations with dapagliflozin therapy regardless of diabetes status (15). In addition, the DECLARE-TIMI 58 trial found that the

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cardiovascular benefits of dapagliflozin were consistent across a broad spectrum of patients, including those with HF REF and DMT2 (16). For all the general benefits and necessitating dapagliflozin therapy, some recently discovered evidence suggests that response varies according to diabetes status. Docherty et al. found that people with DMT2 experienced more first and subsequent hospitalisations for heart failure and cardiovascular death than people without diabetes despite taking dapagliflozin therapy (17). This raises questions on whether dapagliflozin's beneficial effects in decreasing cardiovascular risk differ between HFrEF patients with DMT2 and HFrEF Patients without DMT2. The mechanisms underlying the differential response to dapagliflozin based on diabetes have not been well studied, but several theories have been proposed. One idea is that the pathophysiological mechanisms driving heart failure in patients with DMT2 will vary from those in nondiabetic patients. As a result, SGLT2 inhibitors such as dapagliflozin get different responses (18). Metabolic disorders that are associated with DMT2, such as insulin resistance and hyperglycemia, may also cause Cardiac Dysfunction to exacerbate the situation and diminish the effect of therapy (19).In addition to its efficacy in lowering blood glucose levels, DAPAGLIFLOZIN has been shown to provide major therapeutic advantages to HFrEF patients. In selecting their treatment, Physicians should also bear in mind the presence of Employment relationship DMT2 -- and all that goes with it regarding cardiovascular risk. However, the effectiveness of dapagliflozin in reducing the risk of HHF events in HFrEF patients may vary depending on diabetes status. It is, therefore, necessary to design individualised treatment strategies that consider the patient's metabolic and cardiovascular profiles to obtain better outcomes (20).

Conclusion

Dapagliflozin therapy is a major step forward in HFrEF patient care because it has significant cardiovascular benefits for patients with or without DMT2. Dissimilar Treatment responses are seen between diabetes states (emerging evidence suggests it), with those who have DMT2 but remain untreated for diabetes seeing higher overall cardiac event rates. This case demands further study to elucidate its reasons and refine therapies aimed at such precarious patients.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department concerned. (MIC-TCH-2022/58)
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Approved
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Conflict of interest

The authors declared the absence of a conflict of interest.

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Data acquisition and analysis.
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