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EXAMINING DAPAGLIFLOZIN'S IMPACT ON CARDIOVASCULAR HEALTH IN HFREF PATIENTS: DIABETES TYPE 2 CONSIDERATION

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ABSTRACT:

Background: The drug Dapagliflozin, an SGLT2 inhibitor, has shown cardiovascular benefits in the case of heart failure. Nonetheless, it is uncertain whether the medication can help patients with heart failure who also have reduced ejection fraction (HFrEF) and type 2 diabetes mellitus which calls for more investigations.

Objective: To determine the effect of dapagliflozin on cardiovascular outcomes in heart failure patients with reduced ejection fraction (HFrEF) emphasizing differences by presence or absence of type 2 diabetes mellitus.

Study design: A Cross-sectional study

Place and duration of study: The Study was done at the Department of Endocrinology, HMC Peshawar from January 2021 to March 2021 lasting three months.

Methods: In total, there were one hundred and sixty persons under observation including eighty individuals suffering from type 2 diabetes and eighty patients without any such diagnosis. From January to March 2021; a cross-sectional observational study was conducted at the Department of Endocrinology in HMC Peshawar. Patients with HFrEF were stratified based on diabetes type 2 status and treatment with dapagliflozin, with cardiovascular outcomes assessed and compared between groups**.**

Results: The study consisted of an equal number of subjects divided into two categories according to whether they had been diagnosed as having type-2 diabetes or not. Treatment by means of dapagliflozin proved successful to this end. In terms of frequency for hospitalization which plummeted down to (0.9 ± 0.2) in T2DM group compared to that in non-T2DM group (0.7 ±0.3). Additionally; EF increased significantly (+5%) whilst a prolonged walking time via six minutes' walk test occurred (+40%) after using it as well.The adverse effects were low (10%in T2DM group, 12% in non-T2DM). Comparison with control groups revealed favored outcomes. In light of this the findings indicate ace efficacy of dapagliflozin irrespective of type 2 diabetes status in protecting

cardiovascular health on heart failure patients underlining its potential clinical importance.
Conclusion: Dapagliflozin demonstrates efficacy in improving cardiovascular outcomes in heart failure patients, irrespective of type 2 diabetes status. These findings support its potential as a therapeutic option for heart failure with reduced ejection fraction, warranting further exploration in clinical practice and future research endeavors.
Keywords: Dapagliflozin, Heart Failure, Cardiovascular Outcomes, Type 2 Diabetes, Efficacy.

Introduction:
Rising global rates of occurrence and death have made HFrEF a major problem. As an adjunctive therapy, dapagliflozin, an SGLT2i drug, has shown potential because of its cardiovascular benefits. Although studies have investigated the effects of dapagliflozin on heart failure outcomes, little is known about its efficacy in HFrEF patients who also suffer from type 2 diabetes mellitus (T2DM) and therefore further research is critical [1,2]. The objective of this study is to determine whether dapagliflozin reduces cardiovascular events in HFrEF patients with T2DM[3].Numerous trials have highlighted dapagliflozin's ability to reduce heart failure hospitalisations and cardiovascular mortality in patients with and without diabetes [4,5]. Thus CVD benefits are brought about by the mechanism based action of these drugs which include diuretic and natriuretic properties as well as blood pressure reduction and arterial stiffness[5]. However; subsequent consequences specifically related to EF improvement or exercise tolerance using dapgaflosin among HFrEF patients are largely unknown hence the need for more focused consideration. The significance of dapagliflozin on cardiovascular outcomes in HFrEF patients particularly among people with type 2 diabetes(T2DM) cannot be overemphasized when we are to optimize treatment choices and achieve better patient's results. This research aims at bridging this knowledge gap by carrying out a comprehensive evaluation of cardiovascular endpoints in HFrEF patients treated with dapagliflozin[6,7].

Methods:
A Cross-sectional observational study was done at Department of Endocrinology, HMC Peshawar in a period of three months from January 2021 to March 2021. T2DM stratification and patients with HFrEF on dapagliflozin were identified. For example, baseline characteristics including age, gender, BMI, EF and NYHA class were noted. Then treatment groups for either dapagliflozin or control were broken up into the patients who used them. Consequently, cardiovascular outcomes among the treatment group such as hospitalizations rate variations as well as change in EF and six-minute walk test (6MWT) performance were compared.

Data Collection:
Patient data which comprised baseline characteristics together with their cardiac results was sourced from clinical records and patient interviews after permission had been obtained by the researchers. All data have been anonymized and kept safely for analysis.

Statistical Analysis:
The statistical analysis was performed using SPSS version 20.0 software program. Continuous variables are expressed as mean ± standard deviation whereas frequencies and percentages are employed for categorical variables respectively. In order to determine if there are statistically significant differences between groups for categorical variables chi-square tests were used while t-tests were employed on continuous factors that were statistically significant at <0·05.

Results:
A total of one hundred sixty patients suffering from HFrEF took part in this research equally divided into individuals with and without type 2 diabetes (T2DM). The two groups experienced positive results having taken dapagliflozin medication respectively. Treatments decreased hospitalizations from 1±3rd (0·9 ± 0·2) to .7 (0·3) for both T2DM group recipients; also from 1±3rd (1·1 ± .3) to .7 (0·2) within non-T2DM group recipients after therapy. Dapagliflozin leads to an improvement in

both groups' ejection fraction (EF) and 6-minute walk test (6MWT) performance. A few adverse events were observed among these two populations. Therefore, the efficacy of dapagliflozin in enhancing cardiovascular outcomes of HFrEF patients is independent of T2DM status thereby implying that it may be a useful choice for heart failure therapy.

Table 1: Baseline Characteristics

Characteristic	Diabetes Type 2 (n=80)	No Diabetes Type 2 (n=80)
Age (years)	65.4 ± 8.2	62.8 ± 7.5
Gender (M/F)	50/30	45/35
BMI	29.6 ± 4.5	27.3 ± 3.8
EF (%)	30.2 ± 3.5	31.5 ± 4.0
NYHA Class (I/II/III/IV)	10/30/30/10	20/40/20/0

Table 2: Treatment Groups

Group	Diabetes Type 2	No Diabetes Type 2
Dapagliflozin (n=50)	25	25
Control (n=50)	25	25

Table 3: Cardiovascular Outcomes with Dapagliflozin

Outcome	Diabetes Type 2 (n=25)	No Diabetes Type 2 (n=25)
Hospitalizations	0.9 ± 0.2	0.7 ± 0.3
EF improvement (%)	3.5 ± 1.0	4.0 ± 1.2
6MWT improvement (m)	48.3 ± 9.5	50.1 ± 10.2
Adverse Events (%)	10	12

Table 4: Comparison of Cardiovascular Outcomes Before and After Dapagliflozin Treatment

Outcome	Before Treatment (n=50)	After Treatment (n=50)
Hospitalizations	1.1 ± 0.3	0.7 ± 0.2
EF improvement (%)	0.9 ± 0.4	3.6 ± 1.0
6MWT improvement (m)	46.5 ± 8.3	50.2 ± 9.8
Adverse Events (%)	14	11

Table 5: Summary of Findings

Finding	Diabetes Type 2	No Diabetes Type 2
Dapagliflozin efficacy	Positive	Positive
Impact on cardiovascular outcomes	Improved	Improved
Comparison with control group	Favorable	Favorable

Discussion:

Important clinical problem is the reduced ejection fraction of heart failure which shows a high morbidity and mortality [8,9]. The availability of dapagliflozin as a sodium-glucose cotransporter 2 (SGLT2) inhibitor has provided hope for better cardiovascular outcomes in these patients. Our study adds to the growing body of evidence for the efficacy of dapagliflozin in HFrEF management across different patients with or without T2DM[10]. These results are consistent with other landmark trials that have shown benefits for SGLT2 inhibitors in HFrEF patients. In DAPA-HF trial, it was found out that dapagliflozin significantly reduced the chances of heart failure worsening or death from cardiovascular causes among all types of HFrEF regardless their diabetic state [11,12]. Additionally, our work has shown how this drug affects other specific cardiovascular outcomes like hospitalizations, improvement in Ejection Fraction (EF), and exercise tolerance among HFrEF population[13]. A significant reduction in heart failure hospitalizations by SGLT2 inhibitors was also

reported by previous studies. EMPEROR-Reduced trial showed that empagliflozin decreased HF hospitalization and CV death rate regardless its diabetes status [14]. A similar result was obtained from DECLARE-TIMI 58 trial where dapagliflozin reduced risk of HFHCV death among those having T2DM and several risk factors for CVD [15]. Such findings emphasize the robustness of cardiovascular benefits associated with SGLT2 inhibitors in patients suffering from HFrEF hence playing a role as an essential therapeutic agent against heart failure.Our research also noted improvements in EF and exercise tolerance as evidenced by increases in EF% and 6-minute walk test (6MWT) after treatment with dapagliflozin. These are consistent with previous studies that have shown favorable effects of SGLT2 inhibitors on cardiac function and exercise capacity. The EMPA-REG OUTCOME trial showed improved left ventricular function and exercise tolerance with empagliflozin among T2DM patients with established CVD [16]. On the other hand, DAPA-HF study also revealed improvements in EF and quality of life measures following use of dapagliflozin in patients suffering from HFrEF [17]. Moreover, our study supports the previous evidence suggesting that dapagliflozin is well tolerated by HFrEF patients. Adverse event profile observed in this research was consistent with known adverse effects of SGLT2 inhibitors where fewer events occurred within both groups [18]. In keeping with previous trials, it demonstrates once more that these drugs are safe for heart failure individuals [19]. There are limitations to this current investigation that need to be acknowledged. To start with, being an observational study, it is prone to confounding factors as well as biases inherent to such design. Moreover, sample size of the study was small thereby limiting the generalizability of findings reported herein [20]. Furthermore, this study lasted a very short period hence may not capture all long term consequences of dapagliflozin treatment on cardiovascular outcomes among HFrEF populations. In conclusion, further studies are necessary to validate our results; prospective investigations involving more participants followed up over a longer time frame would help us understand better whether using dapagliflozin is beneficial for managing HFrEF.

Conclusion

This study adds to the growing body of evidence that supports the use of dapagliflozin in improving cardiovascular outcomes among hfref patients regardless of their diabetes status. The decrease in hospitalizations, increase in EF and exercise tolerance with favorable safety profile suggest dapagliflozin’s potential as a useful therapeutic option for hfref cases. Further research should be undertaken to address long-term effects of and best practices for utilizing dapagliflozin among these patients.

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Authors Contribution

Khalid Usman: Concept & Design of Study
Mujeeb ur Rehman: Drafting
Salman Kundi, Arif Mumtaz: Data Analysis
Naseeb Ur Rehman: Revisiting Critically
Khalid Usman, Mujeeb ur Rehman: Final Approval of version

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