Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

SHORT COMMUNICATION

DAPAGLIFLOZIN: A NEW TREATMENT OPTION FOR CHRONIC HEART FAILURE

MUSAVVIR SAMIN[1], HAM NAZMUL AHASAN[2]

Received: 16.5.2021 *Accepted: 28.5.2021*
DOI: https://doi.org/10.3329/bjm.v32i2.53806

Citation: *Samin M, Ahasan HAMN. Dapagliflozin: A new treatment option for Chronic Heart Failure. Bangladesh J Medicine 2021; 32: 175-176.*

Introduction:

Heart failure is a global escalating public health issue. Its prevalence increases with age and with other comorbidities like Hypertension, Diabetes mellitus, Obesity, Chronic lung diseases etc. MI, stroke, limb ischaemia have traditionally been considered as long-term complications of DM, but now-a-days heart failure has been recognized as one of the earliest, most common, and most serious cardiovascular disorders in patients with DM. Following its onset, diabetic patients experience marked deterioration, frequent hospitalization and ultimately, death.[1] In the recent past, the therapeutic agents which were used to treat DM, were either ineffective (e.g. DPP-4 inhibitors) or harmful (e.g. Thiazolidinediones) in treating heart failure, and therefore, there was a dire need for an effective and safe therapeutic option for diabetic patients with heart failure.[2]

SGLT-2 inhibitor is one of the novel therapeutic strategy used to treat T2DM. To maintain glucose homeostasis in human body, Kidneys regulate gluconeogenesis, glucose uptake from circulation, and glucose reabsorption from urine filtered in the renal glomeruli. There are two types of SGLT: SGLT2 which is responsible for more than 90% of glucose absorption and SGLT1 which is responsible for the rest. In T2DM, SGLT2 inhibitor reduces the renal threshold of glucose excretion by almost 55% and thus lowers HbA1c by up to 1.0 in addition to lowering body weight. The mechanism is quite unique in this sense that it does not involve with insulin or incretin pathways. Currently, Empagliflozin, Canagliflozin and Dapagliflozin are approved to treat T2DM.[3]

In 2015, Zinman et al. tried to evaluate the effect of Emplagliflozin, on cardiovascular mortality and morbidity in patients with T2DM. A total of 7020 patients were treated randomly with 10 or 25mg of Emplagliflozin or Placebo once daily. Those who had emplagliflozin showed significantly lower death from cardiovascular disease, hospitalization from heart failure and death from any cause; although there were higher incidence of genital infection. This trial supported long term use of this drug for patients with T2DM and heart failure.[4]

The CANVAS Program in 2017 incorporated data from two trials involving a total of 10,142 participants with T2DM and high CVD risk. Participants were randomly designated to receive canagliflozin or placebo and were followed for a mean of 188.2 weeks. The primary outcome was death from CVD, nonfatal MI, or nonfatal stroke. In those two trials patients receiving Canagliflozin had lower risk of CVD in addition to possible benefit of progression of albuminuria and reduction in eGFR but with a greater risk of amputation.[5]

Declare: TIMI58 trial was a randomized, double-blind, multinational, placebo-controlled, phase 3 trial of dapagliflozin in patients with type 2 diabetes and established atherosclerotic cardiovascular disease or multiple risk factors for atherosclerotic cardiovascular disease. Patients with T2DM who had or were at risk for atherosclerotic CVD were randomly allocated to receive either dapagliflozin or placebo. The primary efficacy outcomes were Major Adverse Cardiovascular Events (MACE), defined as cardiovascular death, MI or ischaemic stroke and death or hospitalization for heart failure.At the end of evaluating 17,160 patients who were followed for a median of 4.2 years, the trial showed: in patients with T2DM who had or were at risk for atherosclerotic CVD, treating with dapagliflozin did not result in a higher or lower rate of MACE than

1. Trust Grade Doctor, Department of Diabetes and Endocrinology, Bassetlaw District General Hospital, UK
2. Professor, Department of Medicine, Popular Medical College and Hospital, Dhaka, Bangladesh.
Address of Correspondence: Dr. Musavvir Samin, Trust Grade Doctor, Department of Diabetes and Endocrinology, Bassetlaw District General Hospital, UK. E-mail: musavvirsamin@yahoo.com

placebo but did result in a lower rate of cardiovascular death or hospitalization for heart failure.[6]

All these clinical trials involving patients with T2DM showed reduced risk of hospitalization, but most participants did not have a heart failure at baseline. Therefore, SGLT-2 inhibitors role in reducing the risk of heart failure was reflected and more data were needed to see the effects of SGLT-2 inhibitors in patients with established heart failure and reduced EF. DAPA-HF trial (funded by AstraZeneca) was designed contemplating this need and randomly assigned 4744 patients with NYHA class II, III, or IV heart failure and an EF of 40% or less to receive either dapagliflozin (10 mg once daily) or placebo, in addition to recommended therapy. A composite of worsening heart failure (hospitalization or an urgent visit resulting in intravenous therapy for heart failure) or cardiovascular death was the primary outcome.Among patients with heart failure and a reduced ejection fraction, the risk of worsening heart failure or death from cardiovascular causes was lower among those who received dapagliflozin than among those who received placebo, regardless of the presence or absence of diabetes. Dapagliflozin was as effective in the 55% of patients without type 2 diabetes as in those with diabetes. This provides support for earlier suggestions that treatment with SGLT-2 inhibitors has beneficial actions other than glucose lowering. Thus, these findings potentially extend the therapeutic role of dapagliflozin beyond patients with diabetes.[7]

Considering all these trials, NICE (National Institute for Health and Care Excellence) recommends Dapagliflozin as a treatment option for symptomatic chronic heart failure and reduced EF in adults, only if is used as add on to optimized standard care with ACE inhibitors or ARB, with beta blocker and if tolerated MRA (Mineralocorticoid Receptor Antagonist) or Sacubitril- Valsartan with beta blocker and if tolerated MRA. NICE also recommends for it to be started by a heart failure specialist and monitored by appropriate healthcare professionals.[8]

SGLT-2 inhibitor isa promising new drug to treat heart failure, at the very least. Its mechanism to help patients with heart failure are still poorly understood and when it will be understood, it will open doors for inventing new medications for heart failure. For resource poor countries like Bangladesh where nonpharmacological interventions for heart failure are often not feasible, this medication can overall reduce the hospitalization and overall cardiovascular morbidity and mortality in patients with heart failure.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

No specific funding was received for this study.

References:

1. Packer M. Heart Failure/ : The most important, preventable, and treatable cardiovascular complication of type 2 diabetes [Internet]. Vol. 41, Diabetes Care. American Diabetes Association Inc.; 2018 [cited 2021 Apr 15]. p. 11-3. Available from: https://0-doi-org.libus.csd.mu.edu/10.2337/dci17-0052. https://0-doi-org.libus.csd.mu.edu/10.2337/dci17-0052. PMid:29263193

2. Joshi SS, Singh T, Newby DE, Singh J. Sodium-glucose co-transporter 2 inhibitor therapy: Mechanisms of action in heart failure [Internet]. Vol. 0, Heart. BMJ Publishing Group; 2021 [cited 2021 Apr 15]. p. 1-7. Available from: http://0-heart.bmj.com.libus.csd.mu.edu/ https://0-doi-org.libus.csd.mu.edu/10.1136/heartjnl-2020-318060. PMid:33637556

3. Sodium Glucose Cotransporter 2 - an overview | ScienceDirect Topics [Internet]. [cited 2021 Apr 15]. Available from: https://0-www-sciencedirect-com.libus.csd.mu.edu/topics/medicine-and-dentistry/sodium-glucose-cotransporter-2

4. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med [Internet]. 2015 Nov 26 [cited 2021 Apr 15];373(22):2117-28. Available from: http://0-www.nejm.org.libus.csd.mu.edu/doi/10.1056/NEJMoa1504720. https://0-doi-org.libus.csd.mu.edu/10.1056/NEJMoa1504720. PMid:26378978

5. Neal B, Perkovic V, Mahaffey KW, de Zeeuw D, Fulcher G, Erondu N, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med [Internet]. 2017 Aug 17 [cited 2021 Apr 15];377(7):644-57. Available from: http://0-www.nejm.org.libus.csd.mu.edu/doi/10.1056/NEJMoa1611925. https://0-doi-org.libus.csd.mu.edu/10.1056/NEJMoa1611925 PMid:28605608

6. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med [Internet]. 2019 Jan 24 [cited 2021 Apr 15];380(4):347-57. Available from: http://0-www.nejm.org.libus.csd.mu.edu/doi/10.1056/NEJMoa1812389. https://0-doi-org.libus.csd.mu.edu/10.1056/NEJMoa1812389 PMid:30415602

7. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med [Internet]. 2019 Nov 21 [cited 2021 Apr 15];381(21):1995-2008. Available from: http://0-www.nejm.org.libus.csd.mu.edu/doi/10.1056/NEJMoa1911303

8. Recommendations | Dapagliflozin for treating chronic heart failure with reduced ejection fraction | Guidance | NICE.