

The Impact of Sodium-Glucose Cotransporter 2 Inhibitors on Individuals with Diabetes Mellitus Type two and Heart Failure: Review Article

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ABSTRACT

SGLT2 Inhibitors are a new family proven by FDA to treat diabetes mellitus type two and because of their cardioprotective effect now used widely in diabetic patients suffering from heart failure. **Objective:** This study's goal is to determine the effect of cardioprotective SGLT2 Inhibitors on patients with diabetes mellitus and heart failure.

Methods: We collected and analyzed fourteen articles, which were published from the period 2015 to 2023, all looking for an influence of SGLT2 inhibitors on diabetics with heart failure.

Results: all SGLT2 inhibitors caused a significant decrease in symptoms and hospitalization, morbidity, and mortality and expand the life pattern in patients with heart failure due to the cardiac inflammation reduction, hypertrophy reduction and fibrosis reduction by which they reduce cardiac remodeling.

Conclusion: All SGLT2 inhibitors are equally effective in mortality and morbidity reduction in diabetic patients suffering from HF.

KEYWORDS: SGLT₂ Inhibitors; Diabetes mellitus; Heart failure.

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INTRODUCTION

SGLT2 Inhibitors are a group of medicines approved by the FDA to manage patients with type two diabetes mellitus⁽¹⁾. This group includes empagliflozin, dapagliflozin, sotagliflozin, and canagliflozin. They act as an anti-hyperglycemic agent by inhibiting SGLT-2 protein which re-absorbs glucose in renal proximal convoluted tubules. In addition to lowering the blood glucose in DM patients there are many indications for SGLT2 inhibitors such as use in patients with heart failure due to decrease hospitalization and cardiovascular death also use in a patient with chronic renal failure by reduce the deterioration in glomerular filtration rate also decrease the risk of stroke and myocardial infarction and one of the most important use was FDA approval of dapagliflozin to manage heart failure with low ejection fraction⁽²⁾⁽³⁾.

All SGLT2 inhibitors are well absorbed after oral intake and not effect by food and they are metabolized by uridine 5'-diphosphate-glucuronosyltransferases (UGT) and then excreted by renal⁽⁴⁾. Sodium-Glucose Co-transporter 2 Inhibitors take one morning dose due to their long half-life. All SGLT2 inhibitors do not need to dose adjustment for

hepatic impairment and renal impairment and consider contraindicated in pregnant women⁽⁵⁾.

The common side effect related to SGLT2 inhibitors is a genital mycotic infection which is more common in females, pyelonephritis and urinary tract infection in addition to other uncommon side effect like lower limb amputation, diabetic ketoacidosis, acute kidney injury, bladder cancer⁽⁶⁾.

In this article, we will focus on diabetics with heart failure who use the medication SGLT 2 inhibitors and their impact on the heart in addition to its effect on the level of sugar in the blood.

METHOD

This literature review examines the impact of SGLT2 inhibitors on individuals diagnosed with diabetes and concurrent heart failure.

We collected and analyzed fourteen articles, which were published from the period 2015 to 2023, all looking for the influence of SGLT2 inhibitors on diabetics with HF, in order to know what is the mechanism of these drugs and how they protect the heart and reduce the rate of admission to the hospital in addition to reducing the deterioration of the disease and which one is better than this family.

RESULT AND DISCUSSION

Diabetes mellitus is one of the world's public diseases that affects all ages and is divided into two types, the first type, which affects children and is caused by the failure of beta cells to secrete insulin, and the second type, which affects adults, and is a result of several causes, including lack of insulin secretion, resistance to insulin action, or an increase in SGLT2 receptors, which targeted treatment SGLT2 inhibitors. Diabetics also have many complications, including heart failure, stroke, kidney failure, neuropathy, and others. SGLT 2 inhibitors decrease blood sugar by preventing its re-absorption in nephrons in addition many studies showed other benefits such as protecting the heart, reducing cardiovascular injury, reducing hospital stay, and reducing hospitalization. Here are several studies that have been done looking for the influence of SGLT 2 inhibitors on heart failure. The Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure study conducted on more than 4,000 patients with heart failure to assess dapagliflozin vs placebo found that dapagliflozin there was a great reduction in symptoms and hospitalization, morbidity, mortality and improve life pattern in patients with heart failure ⁽⁷⁾.

In yet another study, Empagliflozin was administered to patients with heart failure and a reduced ejection fraction.. A trial conducted on more than 3,000 patients with heart failure to assess empagliflozin also showed a higher reduction in symptoms and hospitalization, morbidity, mortality and improve life patterns in heart failure patients ⁽⁸⁾.

The impact of sotagliflozin on the frequency of hospitalizations among individuals diagnosed with diabetes mellitus type two and worsening heart failure.: a randomised trial conducted on more than 1,000 patients with heart failure found that it reduces death rate and reduces hospital stay ⁽⁹⁾.

The study conducted on over 10,000 individuals with diabetes mellitus type two and heart failure, known as CANVAS program, demonstrated that Canagliflozin resulted in significant reductions in hospital stay, hospitalization rate, and mortality rate. ⁽¹⁰⁾.

Also, there were many studies that were conducted on a smaller number of patients around the world, all of which proved the same results that confirm the benefit for patients with heart failure SGLT2 inhibitors ^{(11) (12) (13) (14)}.

The method by which SGLT 2 inhibitors provide cardiovascular protection is multifactorial which includes reduction of blood pressure due to the diuretic effect because they promote an osmotic effect due to increase glucose level in urine which acts as osmotic material also will increase sodium excretion ^{(15) (16)}.

On the other hand, SGLT2 inhibitors improve glucose levels which had an impact on cardiovascular risk and weight reduction through increased glucagon levels which lead to increased lipid metabolism ^{(17) (18)}.

All SGLT2 inhibitors reduce cardiac inflammation, hypertrophy and fibrosis by which they reduce cardiac remodeling ^{(19) (20)}.

CONCLUSION

We conclude from this study that all SGLT2 inhibitors have the same effect on protecting the heart in the same way, and there is no one better to be preferred for the treatment of type Two diabetics with heart failure.

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