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Review Article

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SGLT2 Inhibitors: A Promising New Tool in Cardiology

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Abstract

Sodium-glucose cotransporter 2 (SGLT2) inhibitors have emerged as a promising class of medications in the field of cardiology. Originally developed for the treatment of type 2 diabetes, these agents have shown significant cardiovascular benefits beyond their hypoglycemic effects. This review article aims to provide an overview of the mechanisms of action, clinical evidence, and potential applications of SGLT2 inhibitors in the management of cardiovascular diseases.

1. Introduction

Cardiovascular diseases remain a leading cause of morbidity and mortality worldwide. Despite advancements in treatment, there is a need for novel therapeutic approaches to improve outcomes in patients with cardiovascular conditions. In recent years, SGLT2 inhibitors have garnered attention for their potential cardioprotective effects, making them a topic of interest in the field of cardiology.

2. Mechanisms of Action

SGLT2 inhibitors act by inhibiting the sodium-glucose cotransporter 2 in the proximal renal tubules, resulting in increased urinary glucose excretion. This leads to improved glycemic control in patients with diabetes. However, emerging evidence suggests that the benefits of SGLT2 inhibitors extend beyond glucose lowering. These medications have been shown to exert favorable effects on various cardiovascular parameters, such as blood pressure, body weight, endothelial function, and cardiac remodeling [1,2].

3. Clinical Evidence:

Several landmark clinical trials have investigated the cardiovascular outcomes of SGLT2 inhibitors in patients with type 2 diabetes and established cardiovascular disease. These trials have consistently demonstrated significant reductions in major adverse cardiovascular events, including myocardial infarction, stroke, and cardiovascular death.

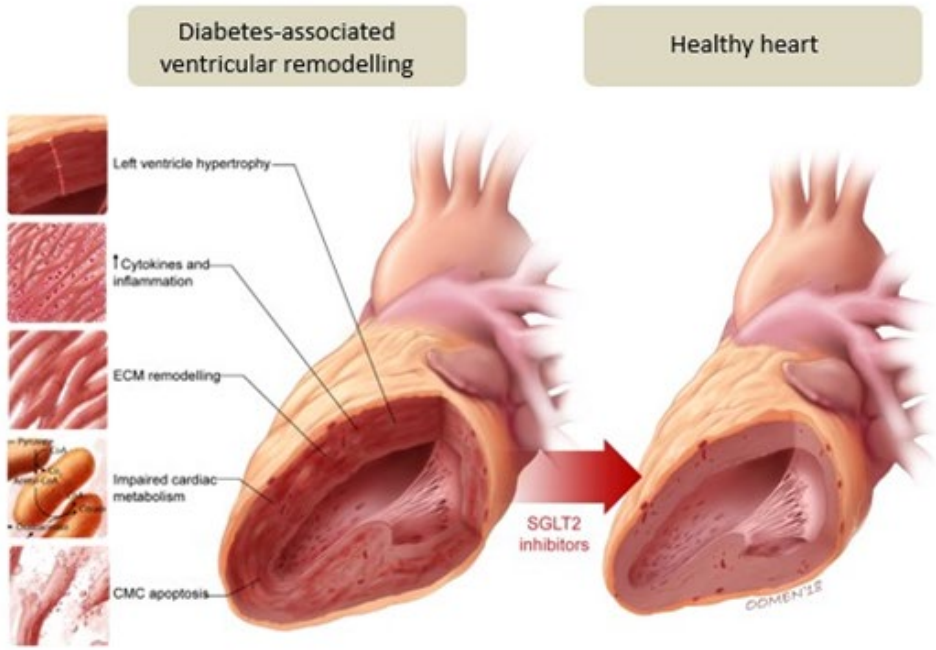
The EMPA-REG OUTCOME trial, a landmark study with empagliflozin, showed a 14% reduction in the risk of major adverse cardiovascular events compared to placebo in patients with type 2 diabetes and high cardiovascular risk [3]. Another trial, the CANVAS Program, evaluated the cardiovascular outcomes of canagliflozin and reported a 14% reduction in the risk of major adverse cardiovascular events in patients with type 2 diabetes and a history of cardiovascular disease [4]. The DECLARE-TIMI 58 trial investigated dapagliflozin and demonstrated a reduction in the composite outcome of cardiovascular death or hospitalization for heart failure in patients with type 2 diabetes and multiple cardiovascular risk factors [5]. The VERTIS CV trial evaluated ertugliflozin and showed no significant difference in the risk of major adverse cardiovascular events compared to placebo in patients with type 2 diabetes and atherosclerotic cardiovascular disease [6].

Furthermore, SGLT2 inhibitors have demonstrated remarkable benefits in heart failure management. The DAPA-HF trial investigated the efficacy of dapagliflozin in patients with heart failure and reduced ejection fraction, irrespective of their diabetic status. The trial showed a significant reduction in the risk of cardiovascular death or heart failure hospitalization with dapagliflozin compared to placebo [7]. The EMPEROR-Reduced trial evaluated empagliflozin in patients with heart failure and reduced ejection fraction, regardless of diabetes status, and demonstrated a reduction in the risk of cardiovascular death or hospitalization for heart failure [8]. The EMPEROR-Preserved trial is currently investigating the effects of empagliflozin in patients with heart failure and preserved ejection fraction [9].

4. Potential Mechanisms

The exact mechanisms underlying the cardiovascular benefits of SGLT2 inhibitors are not fully understood. However, several hypotheses have been proposed. It is believed that the diuretic effect

and natriuretic properties of SGLT2 inhibitors lead to reductions in intravascular volume and blood pressure, which may contribute to their cardiovascular protective effects. Additionally, these medications have been shown to improve endothelial function, reduce oxidative stress, and modulate cardiac metabolism, leading to improved myocardial function and reduced cardiac remodeling [2].



Diabetes-associated ventricular remodelling (a) is characterised by left ventricular hypertrophy, inflammation, increased extracellular matrix (ECM) production, impaired cardiac metabolism and cardiomyocyte (CMC) apoptosis. SGLT2 inhibitors may offer salutary effects on several of the fundamental molecular and cellular pathways involved in the development and natural history of cardiac failure in diabetes (as illustrated by a healthy heart in (b)

5. Safety and Adverse Events

SGLT2 inhibitors are generally well-tolerated; however, there are some important considerations regarding safety. Adverse events such as urinary tract infections and genital mycotic infections have been reported at a slightly higher frequency in patients treated with SGLT2 inhibitors compared to placebo. Additionally, there have been rare cases of euglycemic diabetic ketoacidosis, particularly in patients with type 1 diabetes or in those with risk factors for ketoacidosis. Therefore, careful patient selection and monitoring are essential when prescribing SGLT2 inhibitors [1,4].

6. Future Directions and Conclusion

The cardiovascular benefits of SGLT2 inhibitors have opened up new avenues for research and clinical practice. Ongoing trials are exploring the potential benefits of SGLT2 inhibitors in patients without diabetes, such as those with heart failure with preserved ejection fraction and chronic kidney disease. Additionally, the role of combination therapy with SGLT2 inhibitors and other cardiovascular medications is being investigated.

In conclusion, SGLT2 inhibitors have emerged as a promising class of medications in cardiology. Their cardiovascular benefits, beyond glucose lowering, have been demonstrated in clinical trials. Further research is needed to elucidate the underlying mechanisms and determine the optimal use of these agents in the management of cardiovascular diseases.

References

1. Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., Hantel, S., ... & Inzucchi, S. E. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine, 373(22), 2117-2128.
2. Verma, S., & McMurray, J. J. (2018). SGLT2 inhibitors and mechanisms of cardiovascular benefit: a state-of-the-art review. Diabetologia, 61, 2108-2117.
3. Fitchett, D., Zinman, B., Wanner, C., Lachin, J. M., Hantel, S., Salsali, A., ... & Inzucchi, S. E. (2016). Heart failure outcomes with empagliflozin in patients with type 2 diabetes at high cardiovascular risk: results of the EMPA-REG OUTCOME® trial. European heart journal, 37(19), 1526-1534.
4. Neal, B., Perkovic, V., Mahaffey, K. W., De Zeeuw, D., Fulcher, G., Erondu, N., ... & Matthews, D. R. (2017). Canagliflozin and cardiovascular and renal events in type 2 diabetes. New England Journal of Medicine, 377(7), 644-657.
5. Wiviott, S. D., Raz, I., Bonaca, M. P., Mosenzon, O., Kato, E. T., Cahn, A., ... & Sabatine, M. S. (2019). Dapagliflozin and cardiovascular outcomes in type 2 diabetes. New England

Journal of Medicine, 380(4), 347-357.
6. Bhatt, D. L., Szarek, M., Steg, P. G., Cannon, C. P., Leiter, L. A., McGuire, D. K., ... & Pitt, B. (2021). Sotagliflozin in patients with diabetes and recent worsening heart failure. New England Journal of Medicine, 384(2), 117-128.
7. McMurray, J. J., Solomon, S. D., Inzucchi, S. E., Køber, L., Kosiborod, M. N., Martinez, F. A., ... & Langkilde, A. M. (2019). Dapagliflozin in patients with heart failure and reduced ejection fraction. New England Journal of Medicine, 381(21), 1995-2008.
8. Packer, M., Anker, S. D., Butler, J., Filippatos, G., Pocock, S. J., Carson, P., ... & Zannad, F. (2020). Cardiovascular and renal outcomes with empagliflozin in heart failure. New England Journal of Medicine, 383(15), 1413-1424.
9. ClinicalTrials.gov. Empagliflozin Outcome Trial in Patients with Chronic Heart Failure With Preserved Ejection Fraction (EMPEROR-Preserved). Updated April 2021. Accessed May 5, 2021.