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REVIEW

Systematic review of sodium-glucose cotransporter 2 inhibitors: a hopeful prospect in tackling heart failure-related events

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Abstract

In modern cardiology, sodium-glucose cotransporter 2 (SGLT2) inhibitors are critical components of heart failure (HF) treatment algorithms and exert their effects primarily by preventing glucose reabsorption and facilitating its urinary excretion. The objective was to systematically review randomized controlled trials (RCTs) assessing the effects of SGLT2 inhibitors, particularly canagliflozin, empagliflozin, dapagliflozin, ertugliflozin, sotagliflozin (dual SGLT inhibitor), and their use in HF. Systematic searches of PubMed/Medline, The Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov databases were performed. There were no restrictions imposed on the date and status of publication; however, there were restrictions on language for the searched studies. A total of 1139 records were identified in the bibliographic searches from both databases and the register of choice for this systematic review. Following duplicate removal, screening for titles and abstracts, and thorough assessment of full-text articles, 12 RCTs met the inclusion criteria. Altogether, 83 878 patients were included in this review. Among the included studies, two RCTs, with six respective reports, investigated canagliflozin, four RCTs with 13 derived reports investigated dapagliflozin, three RCTs with 12 separate reports studied the effects of empagliflozin, one RCT and its three respective reports assessed ertugliflozin's effects, and two RCTs with one added report investigated the dual inhibitor sotagliflozin. Pooled meta-analytic effects of SGLT2 inhibitors were as follows: on atrial fibrillation odds ratio (OR) = 0.83, 95% confidence interval (CI): 0.68–1.01, prediction interval (PI): 0.57–1.19; on HF hospitalization OR = 0.69, 95% CI: 0.60–0.78, PI: 0.60–0.78; on cardiovascular death OR = 0.82, 95% CI: 0.58–1.15, PI: 0.42–1.60; and on major adverse cardiovascular events OR = 0.90, 95% CI: 0.77–1.06, PI: 0.71–1.15. SGLT2 inhibitors significantly improve the quality of life in HF patients. Their beneficial effects on HF, especially in left ventricular dysfunction, have made their use possible irrespective of diabetes mellitus or atrial fibrillation status.

Keywords Heart failure; Sodium-glucose transporter 2 inhibitors; Diabetes mellitus; Hypoglycaemic agents

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Introduction

The emergence of novel therapeutic strategies for diabetes mellitus has been fuelled by the growing interest in the role of the sodium-glucose cotransporter 2 (SGLT2), the principal protein in the proximal renal tubule responsible for reabsorbing filtered glucose. SGLT2 inhibitors are a new class of drugs that were originally designed to target glycaemic regulation in diabetes mellitus, but their scope of application is now widely acknowledged, particularly in cardiovascular disease.[1,2]

The story of the discovery of SGLT2 inhibitors is one of serendipity, and it begins in 1835, with the isolation a naturally occurring, non-selective SGLT inhibitor from the apple