Drug class provides cardiovascular benefit for all patients with type 2 diabetes

January 31 2020

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All type 2 diabetes patient subgroups are likely to achieve cardiovascular protection from the use of SGLT2 inhibitors, according to a large multi-study review published in the *Journal of the American Heart Association*.

Lead author and Senior Research Fellow at the George Institute for Global Health Dr. Clare Arnott said that while previous studies of SGLT2 inhibition in type 2 diabetes (T2DM) have shown cardiovascular benefits, it was primarily in those with established cardiovascular disease (CVD) or renal disease.

"In this meta-analysis of large event-driven SGLT2 inhibitor outcome trials we found SGLT2 inhibitors protected against cardiovascular disease and death in diverse subsets of patients with type 2 diabetes regardless of their cardiovascular disease history," she said.

"While the extent of this protective effect may vary across patient types, the consistency of the findings suggests significant and broad cardiovascular protection can be achieved from use of this drug class."

Sodium-glucose cotransporter 2 or SGLT2 inhibitors were developed to lower glucose levels for people with diabetes. Early studies showed they reduced levels of protein in the urine leading to great hopes they would protect against kidney failure. Since then, several large studies have been designed to examine whether SGLT2 inhibitors also prevented heart attack, stroke and kidney disease. These studies showed a clear reduction in CVD events in established atherosclerotic CVD, but whether that translated to those without CVD was still uncertain.

George Institute for Global Health researchers conducted a review and meta-analysis, pooling data from four major randomised controlled trials to define the cardiovascular benefits and the effects on key safety outcomes of SGLT2 inhibition, overall and separately among participants with and without established CVD, reduced kidney function, or heart failure.

Four studies involving 38,723 patients with T2DM which assessed three SGLT2 inhibitors—canagliflozin, empagliflozin, and

dapagliflozin—were included in the meta-analyses. Overall there were 3,828 major adverse cardiac event (MACE) outcomes, 1,192 hospitalizations for heart failure, 1,506 cardiovascular deaths, and 2,612 deaths from any cause. The results showed that those treated with an SGLT2 inhibitor compared with placebo achieved:

- an overall 12% proportional reduction in MACE
- an overall 17% relative reduction in cardiovascular death
- a 32% relative reduction in hospitalisation for heart failure
- consistent cardiovascular benefits regardless of baseline history of cardiovascular disease, heart failure or reduced kidney function
- a possible reduction in stroke events in those with reduced kidney function.

Type 2 diabetes mellitus is a global pandemic, with an estimated 370 million people currently affected. It is a major risk factor for both cardiovascular disease and chronic kidney disease, with CVD the leading cause of death in people with T2DM.

"Our study has shown that we have a class of drug in our treatment arsenal that could potentially have a significant impact on the cardiovascular complications of type 2 diabetes," said Dr. Arnott.

More information: Clare Arnott et al, Sodium-Glucose Cotransporter 2 Inhibition for the Prevention of Cardiovascular Events in Patients With Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis, *Journal of the American Heart Association* (2020). DOI: 10.1161/JAHA.119.014908

Provided by George Institute for Global Health