Association between Diabetes Type 2 and Cardiovascular Diseases and the Role of SGLT2 Inhibitors

Dr. Mohammad Reza Shoghli

Tehran Heart Center Hospital, Iran

Abstract

The number of people who die from kidney disease every year has risen over the past decade and is now estimated at 5 million to 10 million worldwide. The increase in rates of obesity along with associated rates of type 2 diabetes, hypertension, and cardiovascular disease has principally driven the elevated mortality. More than 660,000 Americans have reached the point of requiring intervention for end-stage kidney disease, with 468,000 receiving dialysis and more than 193,000 undergoing kidney transplantation, leading to a major public health and economic burden. Hence, the development of new treatments that may prevent or delay the progression of chronic kidney disease, as well as treat type 2 diabetes, is an important goal. Tight control of glucose levels and blood pressure slows but does not prevent the onset of diabetic nephropathy. The standard approach for retarding the onset of diabetic nephropathy and stabilizing renal function has been blockade of the renin–angiotensin–aldosterone system, particularly with inhibitors of angiotensin-converting enzyme. This approach was first used in the early 1990s in patients with type 1 diabetes; randomized trials subsequently established that such drugs were also effective in type 2 diabetes. Newer classes of agents have also been tried but have not been successful. Inhibitors of sodium–glucose cotransporter-2 (SGLT2) were initially approved as a new class of hypoglycaemic agents that lowered blood glucose levels in patients with type 2 diabetes by enhancing urinary glucose excretion through the inhibition of SGLT2 in the proximal convoluted tubule, where glucose is reabsorbed. SGLT2 inhibitors reduce the renal threshold of glucose from 180 mg per decilitre (10 mmol per litre) to 40 to 120 mg per decilitre (2 to 7 mmol per litre), thereby effectively lowering blood glucose levels.

In 2015, EMPA-REG OUTCOME (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients) changed the landscape in diabetes management by showing a lower risk of cardiovascular death among the 4687 patients who received empagliflozin than among the 2333 controls (172 patients [3.7%] vs. 137 patients [5.9%]) (hazard ratio, 0.62; 95% confidence interval [CI], 0.49 to 0.77). Patients in the empagliflozin group also had a lower risk of death from any cause (269 patients [5.7%] vs. 194 patients [8.3%]) (hazard ratio, 0.68; 95% CI, 0.57 to 0.82) and a lower risk of hospitalization for heart failure (126 patients [2.7%] vs. 95 patients [4.1%]) (hazard ratio, 0.65; 95% CI, 0.50 to 0.85). Recently, the CANVAS Program (Canagliflozin Cardiovascular Assessment Study) showed similar cardiovascular benefits, indicating a class effect of SGLT2 inhibitors. Further support for that finding was noted in the CVD-REAL (Comparative Effectiveness of Cardiovascular Outcomes in New Users of SGLT-2 Inhibitors) and the Health Improvement Network (THIN) trials. As a result, SGLT2 inhibitors are now widely used in patients with type 2 diabetes both to improve glycated haemoglobin levels and to reduce cardiovascular risk. Recent studies have hinted that medications designed to treat diabetes could also confer renoprotection through a mechanism that differs from those affecting glucose homeostasis. Among these drugs, the SGLT2 inhibitors appeared to be the most promising.

Biography

Mohammed Reza Shoghli holds master degree in the field of Biochemistry and has been working in the Tehran Heart Center Hospital for the last 17 years, and has been conducting research about links between diabetes type 2 and cardiovascular complications especially post coronary surgery.

This work was partially presented at
27th International Diabetes and Healthcare Conference on July 18-19, 2019 held in Dubai, UAE