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Personalising glucose-lowering therapy in Type 2 Diabetes and CVD patients

Type 2 diabetes mellitus (T2DM) is a complex disease with a pathogenesis that is multidimensional. Recently, several specific glucose-lowering agents have been demonstrated to improve cardiovascular outcomes and may be favoured in T2DM patients with coexisting cardiovascular disease (CVD), according to a review paper in the journal Endocrinology and Metabolism Clinics of North America.

Owing to its low cost, absence of significant long-term adverse consequences, and possible inherent cardiovascular (CV) benefit, metformin is endorsed as the best initial therapy by most prevailing treatment guidelines. Beyond metformin monotherapy, however, there remains substantial debate regarding the optimal drug (or even drug class) to use for individuals needing additional reduction in haemoglobin A1c (HbA1c).

"Since 2015, however, the results from several major CV outcome trials involving diabetes medications have been released. These data are now allowing for a more refined approach to the management of T2DM, incorporating evidence-based strategies in antihyperglycaemic therapy, particularly in patients with heart disease," writes the report author, Silvio E. Inzucchi, MD, Yale Endocrinology, New Haven, CT.

According to the author, personalised therapy in T2DM patients with established cardiovascular disease (CVD) involves the control of hyperglycaemia and the management of other frequently coexisting atherosclerosis risk factors. "The treating clinician should first determine the optimal haemoglobin A1c target for the individual, based on a variety of patient and disease characteristics," Dr. Inzucchi explains.

Over the past two decades, there has been a six-fold increase in the available categories of glucose-lowering drugs for T2DM patients. Clearly, the management of this disease has become a complicated enterprise, the author notes. "The artful navigation through this expanding pharmacopeia is particularly important for clinicians treating T2DM patients who have CVD, given that some agents may present unique risks, whereas others possess key benefits in this population," he adds.

In the setting of overt CVD, the author says, the intensiveness of glycaemic control may need to be tempered "particularly when there is a need to use agents associated with hypoglycaemia." The specific glucose-lowering strategy should then be considered, typically beginning with lifestyle changes and metformin. When this no longer controls glucose levels adequately, Dr. Inzucchi says additional therapies are warranted, with many treatment options now available, each with a specific mechanism of action, and certain advantages and disadvantages.

"In the context of CVD, evidence-based glucose-lowering therapies should be favoured. These now include specific drugs from the following classes: SGLT-2 inhibitors, GLP-1 RAs, and TZDs," the author says. In the patient with primarily peripheral arterial disease, either a GLP-1 RA or an SGLT-2 inhibitor is indicated. However, canagliflozin should be avoided, given the amputation signal from CANVAS (Canagliflozin Cardiovascular Assessment Study), the author cautions.

The coexistence of chronic kidney disease (CKD) in the CVD patient might also favour an SGLT-2 inhibitor, given the benefits on renal functional outcomes in this class. Ongoing studies with SGLT-2 inhibitors focused on patients with heart failure and CKD, including both diabetic and nondiabetic individuals, should further elucidate the overall effectiveness of these drugs on long-term outcomes, according to Dr. Inzucchi.

Treatment guidelines will likely soon be updated in favour of these new therapies to improve CV outcomes in high-risk patients, the author adds.

Source: Endocrinology and Metabolism Clinics of North America
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