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SGLT2 Inhibition in the Diabetic Kidney — From Mechanisms to Clinical Outcome

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Abstract

Diabetic kidney disease not only has become the leading cause for ESRD worldwide but also, highly contributes to increased cardiovascular morbidity and mortality in type 2 diabetes. Despite increased efforts to optimize renal and cardiovascular risk factors, like hyperglycemia, hypertension, obesity, and dyslipidemia, they are often insufficiently controlled in clinical practice. Although current drug interventions mostly target a single risk factor, more substantial improvements of renal and cardiovascular outcomes can be expected when multiple factors are improved simultaneously. Sodium-glucose cotransporter type 2 in the renal proximal tubule reabsorbs approximately 90% of filtered glucose. In type 2 diabetes, the maladaptive upregulation of sodium-glucose cotransporter type 2 contributes to the maintenance of hyperglycemia. Inhibiting these transporters has been shown to effectively improve glycemic control through inducing glycosuria and is generally well tolerated, although patients experience more genital infections. In addition, sodium-glucose cotransporter type 2 inhibitors favorably affect body weight, BP, serum uric acid, and glomerular hyperfiltration. Interestingly, in the recently reported first cardiovascular safety trial with a sodium-glucose cotransporter type 2 inhibitor, empagliflozin improved both renal and cardiovascular outcomes in patients with type 2 diabetes and established cardiovascular disease. Because the benefits were seen rapidly after initiation of therapy and other glucose-lowering agents, with the exception of liraglutide and semaglutide, have not been able to improve cardiovascular outcome, these observations are most likely explained by effects beyond glucose lowering. In this mini review, we present the drug class of sodium-glucose cotransporter type 2 inhibitors, elaborate on currently available renal and cardiovascular outcome data, and discuss how the effects of these agents on renal physiology may explain the data.

diabetic nephropathy cardiovascular disease diabetes mellitus
Benzhydryl Compounds blood pressure Body Weight
Cardiovascular Diseases Diabetes Mellitus Type 2
Diabetic Nephropathies Dyslipidemias Glucose
Glucose Transporter Type 2 Glucosides Glycosuria Humans
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obesity risk factors Sodium Sodium-Glucose Transporter 2
Up-Regulation Uric Acid

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