Study reveals insights into diabetic kidney disease and how anti-obesity drugs work

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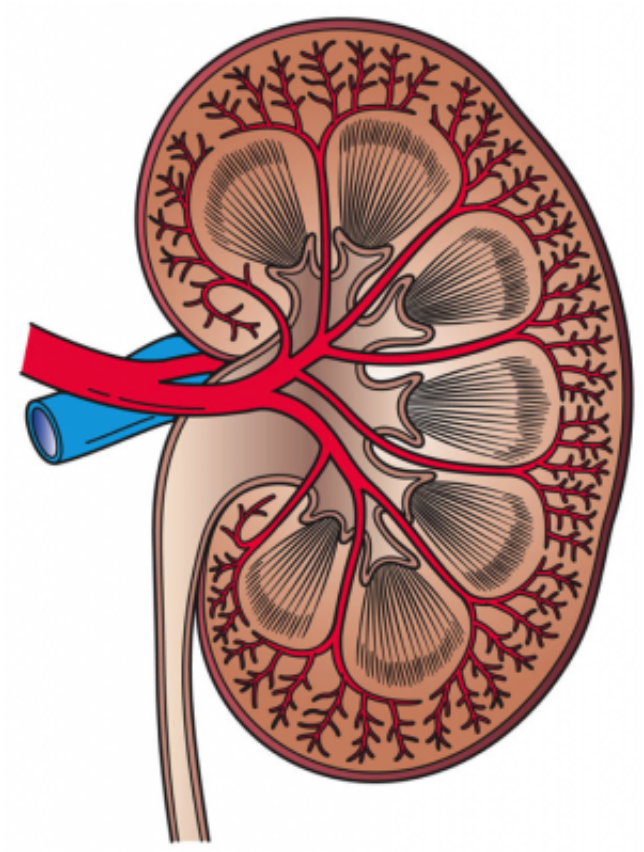

This image shows a cross section of a kidney. Credit: Holly Fischer/Wikipedia

Data from Australian researchers could partly explain why a trial of a new drug for diabetes, was recently halted because it was found to be so effective. Importantly, the data also reveals how anti-obesity drugs like Ozempic, actually work, which to date has been a mystery.

In early November the FLOW trial of the drug semaglutide on the progression of renal impairment in people with type 2 diabetes and chronic kidney disease was halted ahead of schedule because of the drug's efficacy.

Part of the rationale for the cessation of the trial could be explained by research led by Monash University's Associate Professor Melinda Coughlan, and published in the journal, *Kidney International*, showing that a drug that targets a particular hormone GLP1, also interacts with a receptor called RAGE, to control the kidney damage that is the hallmark of type 2 diabetes.

The discovery of the importance of RAGE opens up new therapeutic drug targets for the prevention of kidney disease in people with diabetes. Diabetic kidney disease (DKD) occurs in up to 40% of individuals with diabetes.

According to Associate Professor Coughlan, the outlook for DKD has improved over recent decades as a result of improved blood glucose control and blood pressure management through new therapies, "however, a significant proportion of individuals with diabetes will still progress to end stage kidney disease or die prematurely from a cardiovascular event," she said.

"Our study opens up a way to potentially prevent kidney disease in those people who are, so far, treatment-resistant."

According to another co-author of the study, Professor Mark Cooper, also from Monash University's Central Clinical School, the discovery of how the RAGE receptor works in diabetes, could also explain how the obesity drug, Ozempic, and similar drugs targeting obesity, work.

"To date, we know these drugs, which were developed to tackle diabetes,

help with weight loss; however, their mode of action has not been understood, particularly in reducing diabetic complications including kidney disease," he said.

"We know that the RAGE receptor promotes kidney injury but by blocking interactions between drugs such as Ozempic and this RAGE receptor we now have new information to expand and develop new drugs to protect the kidney."

More information: Glucagon-like peptide-1 receptor signaling modifies the extent of diabetic kidney disease through dampening the receptor for advanced glycation end products -induced inflammation, *Kidney International* (2023). DOI: 10.1016/j.kint.2023.09.029

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