Transcript Details
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Exploring Metabolic Biomarkers for Earlier Detection and Treatment of DKD

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD. On this episode, Dr. Kumar Sharma will explain how metabolic biomarkers could enable earlier detection and treatment of diabetic kidney disease. He's the Chief of the Division of Nephrology and Vice Chair for Research in the Department of Medicine at UT Health San Antonio. Let's hear from Dr. Sharma now.

Dr. Sharma:
Patients with diabetes don't get kidney damage and overt kidney disease for five to 10 years at a minimum. So there's a long latent phase where there's a lot of metabolic dysfunction going on in the glomerulus and in the tubules before we see damage and see an elevation in the creatinine levels in the blood, which indicates a problem with the glomerulus not filtering all of the waste products. and they start building up in the blood and damage in the urine, where protein gets from the blood side to the urine side and there's too much in the urine, so we get proteinuria or albuminuria.

So those are the markers that we have clinically. But what we want to understand is what happens subclinically, because these are just markers. They're just telling us there's injury. But what is driving the process of causing reduced GFR, reduced filtration rate, and leakage of proteins and tubular dysfunction? So we need to start staging DKD into these different stages and characterizing it at a metabolic level. So one of the really cool ways that we're able to do that now is by linking the metabolites that we see are dysfunctional or produced in excess or too much or too little and measure that in the blood and the urine. So by linking what's happening at a metabolic level in the proximal tubule, for example, and seeing what the consequence of that is in blood metabolites or urine metabolites, we can say that "this pathway is activated" or "this glycolytic effect is going on," and it's too much or too little and put into context of progression.

So we've really gone, I think, in the last few years toward translating the molecular changes from the kidney to blood and urine measurements. I think what we're able to do in the very near future is characterize the metabolic phenotype of the kidney with blood and urine measurements without a kidney biopsy. We could do a kidney biopsy if we need to, but by and large, that's not going to be feasible for many people. But we can get a lot of liquid biopsy information by measuring it in the blood and the urine and characterizing it.

So then the next question is: how do we intervene? And now that we can characterize the metabolic image of the kidney in the space and time, what is the best way to change its metabolic rewiring back toward the normal kidney, a healthy kidney? And we have some great therapeutics right now, such as the SGLT2 inhibitors, which block the excess glucose from going into the proximal tubule in the first place. So it's been a game changer how we can protect the kidney with these SGLT2 inhibitors.

Now, what we want to do on top of the SGLT2 inhibitors is look at other ways of metabolic rewiring by looking at the specific pathways and enzymes involved in enhancing glycolysis and shifting it back to using its mitochondria properly and growing and regrowing the mitochondria to a healthy state. And so that's what the challenge is: how do we find those therapeutics that tweak the metabolic rewiring to a direction where the mitochondria are healthy again, and we are producing less of these toxic metabolites?

Announcer:
You just heard Dr. Kumar Sharma discussing how metabolic biomarkers could support earlier detection and treatment of diabetic kidney disease. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

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