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Recapping a Narrative Review on the Management of Kidney Disease in T2D

Dr. Buse:
Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and joining us for a discussion on the management of kidney disease in people with type 2 diabetes is Dr. David Cherney. Dr. Cherney is a Professor of Medicine at the University of Toronto and the Director of the Renal Physiology Laboratory at University Health Network in Canada.

Dr. Cherney, thanks so much for speaking with me today.

Dr. Cherney:
It's an absolute pleasure to be here. Thanks for having me, John.

Dr. Buse:
So, David, I loved your narrative review on the management of kidney disease in patients with type 2 diabetes. It's very helpful, has lovely figures, and is certainly timely in that there have been many advances in the field that have outstripped the publication of guidelines both from the kidney societies and from the diabetes societies. So to help frame the discussion, what have been the big advances in chronic kidney disease management and type 2 diabetes over the last five years?

Dr. Cherney:
Yeah. Thanks for the question. So I think in thinking about the major advances over the last five years, the starting point is that the therapies that I'll mention in a moment have really given us important insights into the relevance and ongoing need to screen patients carefully when they have type 2 diabetes because there is an increasing emphasis on albuminuria in addition to GFR, so regular screening is absolutely critical as a starting point for all of the new developments in the treatment of kidney disease in people with type 2 diabetes, especially over the last five years.

And then moving on from screening and the importance of it is the development and identification of therapeutic programs that have identified therapies, including SGLT2 inhibitors on top of RAS inhibitors and ACE or ARB, and then, of course, finerenone or nonsteroidal mineralocorticoid receptor antagonists and their effect in preventing cardiorenal progression in people with type 2 diabetes.

So for SGLT2 inhibitors, these therapies were initially used as glucose-lowering therapies in people with type 2 diabetes, and over time, with the completion of dedicated trials in the CKD space as well as in the heart failure space, in addition to atherosclerosis-related trials and looking at safety, we know that these therapies can be used in people with and without type 2 diabetes to prevent cardiorenal outcomes, including the risk of losing kidney function, ending up on renal replacement therapy, renal death, significant renal function decline, as well as heart failure-related outcomes. And those benefits are clearly similar in people with and without type 2 diabetes, so these therapies are huge advances for patients living with type 2 diabetes, and they prevent major composite outcomes in people with and without type 2 diabetes. So those are the big advances.

Dr. Buse:
And you had a diverse group that put this paper together as you scoped the landscape. What things did you think were important in communicating through the literature about how to move forward in preventing chronic kidney disease progression?

Dr. Cherney:
Yeah. So one of the critical things is the identification of patients who are eligible for these treatments. And we now know starting with SGLT2 inhibitors that we can use them in patients with a GFR of 20 and above. And in the most recent trial, which was EMPA-KIDNEY, we were able to show that there are benefits in people with GFRs of 20–45 essentially regardless of their level of albuminuria, and then

45 and above in people who have albuminuria as their marker of renal risk. And so the implementation is critical in that these therapies can be used across an incredibly broad group of patients who we see in primary care, who we see in cardiovascular practice, renal practice, and endocrine practice, and these patients benefit from SGLT2 inhibitors across this broad range of patients with and without albuminuria depending on their level of GFR.

And the other important thing is that in putting this group of authors together for this narrative review, what we could all agree on is that the use of SGLT2 inhibitors is extremely important but also very easy, so it requires generally very little monitoring. For example, we don't necessarily have to check electrolytes and creatinine after starting SGLT2 inhibitors except if there's a specific reason to in patients who are frail or have volume issues, and so that's different than an ACE or ARB where we typically do still monitor electrolytes and potassium after starting these therapies because of the risk of hyperkalemia with an ACE or ARB, whereas SGLT2 inhibitors don't cause hyperkalemia, and they actually reduce the risk of kidney injury; so there are big differences in the implementation and use of SGLT2 inhibitors.

And then for finerenone and nonsteroidal MRAs, they're also very easy to use, but we typically do measure and check the electrolytes and creatinine after starting finerenone because that's how it was done in the trial, number 1. And number 2, there is a very small risk of hyperkalemia. It's about an absolute increase of somewhere around 1 percent of hyperkalemia leading to stopping the drug; even though this is a low risk of significant hyperkalemia, we do tend to check the electrolytes about two weeks after starting this kind of therapy.

And then the other important thing is going according to our guidelines. In patients with type 2 diabetes, the first-line therapy is typically a RAS inhibitor, an SGLT2 inhibitor, a statin, and specifically a high-intensity statin as well as metformin. And then where we emphasize the role of finerenone is that in patients who have ongoing elevated levels of albuminuria, that's when we would typically start finerenone on top of that standard of care to further reduce cardiorenal risk. And we know from the finerenone trials that there is a significant reduction in the renal composite outcome of by around 23 percent and a reduction in cardiovascular outcomes, especially heart failure, by about 15 percent, so these therapies are clearly beneficial when layered on top of each other.

Dr. Buse:
Just to put a slightly finer point on this for the audience, so I am a diabetologist- endocrinologist. I'm very comfortable with SGLT2 inhibitors, and I have emerging comfort with these newer mineralocorticoid receptor antagonists, but from what I hear from you is that as long as I'm careful about checking the electrolytes and I don't really have much else to fret about with regards to mineralocorticoids and that basically primary care doctors, nephrologists, cardiologists, and endocrinologists all really need to get comfortable with managing patients with these two classes of medications.

Dr. Cherney:
That's a really nice way of putting it. And I think the comparison and the analogy is what we do with an ACE or ARB. And, you know, finerenone based on the FIDELITY trial and the FIDELITY cohort, finerenone is just as easy if not easier to prescribe than an ACE or ARB, and all of the specialist areas and primary care physicians are all used to and very comfortable prescribing an ACE or ARB for patients for hypertension or kidney disease or heart failure or other indications for an ACE or ARB. And so in practice, I would typically wait if the potassium is above that level to get the potassium controlled by starting a diuretic or initiating some dietary modification or other means of controlling potassium in a relatively straightforward way and then starting the finerenone once the potassium is no longer a concern. This therapy can definitely be started in primary care as well as in specialty clinics, and I think it'll just take a couple of prescriptions and a little bit of experience to get our colleagues used to starting this therapy as they're used to starting an ACE or ARB.

Dr. Buse:
For those just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. John Buse, and today I'm speaking with Dr. David Cherney about the management of kidney disease in type 2 diabetes.

Type 1 diabetes has just been understudied with regards to outcomes. Do you have a particular practice pattern that you use in patients with type 1 diabetes and chronic kidney disease?

Dr. Cherney:
Yeah. So it's a really important point, and it's very difficult in clinic when seeing a patient with type 1 diabetes who has, for example, impaired kidney function and albuminuria compared to the approach that we can potentially have in someone with type 2 diabetes. I've mentioned RAS inhibitors, SGLT2 inhibitors, nonsteroidal MRAs, and potential new therapies like GLP-1 receptor agonists. And we really have none of these therapies except for an ACE or ARB that has proven efficacy and safety in people with type 1 diabetes, so our options are extraordinarily limited and almost historical in people with type 1 diabetes. We're limited to lifestyle changes and intensive glycemic control, which we know is of absolute critical importance for reducing cardiorenal risk in people with type 1 diabetes, and also the use of an ACE or ARB in people with albuminuria because we know that primary prevention in the setting of type 1 diabetes has not

been shown to be effective, so we all can only really treat people with type 1 diabetes once they've developed evidence of end-organ injury, which is really not necessarily the way we'd like to practice. We'd like to prevent it from happening in the first place, but we don't have that data. Although there was, of course, a trial that was announced at the American Diabetes Association meeting called FINE-ONE, which will study people with type 1 diabetes in the near future, but we don't have that trial or data yet, so that's an area of ongoing study and investigation.

Dr. Buse:
Well, I would really encourage providers who treat patients with type 2 diabetes and chronic kidney disease to look at this paper and particularly the figures and tables and keep it handy for references needed while they're getting comfortable with using SGLT2 inhibitors and mineralocorticoid receptor antagonists in this population.

Before we close, are there any final thoughts from you, David, for the audience?

Dr. Cherney:
Yeah. So I think I have a couple of messages that I think are useful across different disciplines, and the first is to reinforce this message for screening and for making sure that we have up-to-date information on GFR and albuminuria in patients with diabetes because not only is this of interest for prognosis now, but these are key metrics to determine what new therapies patients are eligible for.

And then beyond that, think about the use of a nonsteroidal mineralocorticoid receptor antagonist in patients with GFRs of 25 and above. And in patients with albuminuria, then there will often be an indication to also add on top of their RAS inhibitor and their SGLT2 inhibitor a nonsteroidal MRA. And then, of course, there are other therapies that we can use such as a GLP-1 receptor agonist either for the metabolic benefits and/or for the cardiovascular benefits that have been shown in various cardiovascular safety studies with those therapies.

So take-home message is there is almost always an indication for newer additional therapies to further reduce residual risk. And again, the emphasis on screening is of paramount importance.

Dr. Buse:
This has been an impactful conversation. Thank you, Dr. David Cherney, for being here and for sharing your insights on the management of kidney disease in type 2 diabetes.

Dr. Cherney:
Thanks for having me. This has been a very enjoyable discussion.

Dr. Buse:
For ReachMD, I'm Dr. John Buse. To access this episode and others from our series, visit ReachMD.com/DiabetesDiscourse, where you can Be Part of The Knowledge. Thanks for listening.