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The CKD Patient: Thinking Beyond the Numbers and Dialysis

Announcer:
Welcome to ReachMD. This episode is part of the Global Kidney Academy and is brought to you by Medtelligence.

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Dr. Gesualdo:
Chronic kidney disease [CKD] is a global health burden; 850 million people are affected worldwide. All stages of CKD are associated with increased cardiovascular mortality, premature mortality, and/or diminished quality of life. So what can we do to preserve renal function, take the complication head-on, and ultimately enhance the quality of life for those we serve?

This is ReachMD, and I am Dr. Loreto Gesualdo.

Dr. Pollock:
And I'm Dr. Carol Pollock.

Dr. Bakris:
I'm Dr. George Bakris.

Dr. Jayne:
And I'm Dr. David Jayne.

Dr. Gesualdo:
Let's begin by looking at the profound impact of CKD on our patients' daily activities and overall well-being. How can we comprehensively assess this burden in a holistic manner, considering not only the physical aspect, but also the emotional, social, psychological implication, and improve our approach in addressing the unmet needs of our patient with CKD? What are your thoughts, Carol?

Dr. Pollock:
We've been remiss in not focusing on the aspects that are important to patients, such as quality of life, their ability to work, their ability to maintain social interactions, and we've ignored things, such as itch, that really impact on people's quality of life, for instance, their ability to sleep.

We now have tools to be able to measure the impact of these issues that play on people's quality of life, and we have tools to be able to positively impact on them. So we should measure them, we should treat them, and we should really assess the benefit of the treatment.

George, there are other aspects in biochemistry that impact on patient's quality of life – hyperkalemia and also potentially iron deficiency – how we might actually address those?

Dr. Bakris:
We have to educate the patient as to what stage of kidney disease they have and what it means. That's not happening, at least not on the people that I know.

And iron deficiency now is recognized by the cardiologists as a major contributing factor to the development of heart failure, which is the most common problem seen in people with kidney disease. So there really needs to be an integrated kind of cardiorenal approach on the background of the fact that diabetes is the most common cause of kidney failure.

We have very good agents now that can bind potassium. And iron deficiency is something that is not routinely looked for unless the patient has profound anemia and late stages of nephropathy and really should be looked for in earlier stages. And if we put this together and educate the patient to help us with this by telling us how they feel and the better way to tailor therapy, I think that's really an approach that we should be able to change the natural history.

David, what about ANCA [antineutrophil cytoplasmic antibody]-associated vasculitis?

Dr. Jayne:
ANCA vasculitis affects the kidney in 70% of patients and accounts for about 4% of all causes of end-stage kidney disease. But the important point about ANCA-associated vasculitis is that these outcomes are avoidable because we do have effective therapies, but they're critically dependent on the level of kidney function at the time of diagnosis. And delayed diagnosis is the major modifiable factor in the management of these patients.

The majority of patients with renal involvement and ANCA vasculitis already have a reduced glomerular filtration rate [GFR]. And of these patients, 25% will reach end-stage kidney disease within 5 years, and virtually all will develop chronic kidney disease.

This clearly has implications for their general health, their requirement for medications, and of course their quality of life. Vasculitis itself increases cardiovascular risk and chronic kidney disease.

We treat patients, still, with quite high doses of glucocorticoids and also with immunosuppressive drugs. And unfortunately, the adverse effects of therapy are as serious as the disease itself, with serious adverse event rates in the first year of 30% or greater, and the effect of consequences of medication contributes significantly to mortality in the first year.

In terms of assessing our patients with ANCA-associated vasculitis, we really look at 3 different dimensions: assessing the activity with a multiorgan tool, such as the Birmingham Vasculitis Activity Score; we assess all-cause damage from the start of the disease – that's damage caused by the vasculitis or damage caused by the treatment – using a tool such as the Vasculitis Damage Index; and we assess quality of life, at least in clinical trials, previously with a generic tool such as Short Form 36, but we have developed a disease-specific tool, the AAV-PRO, which is slightly more sensitive to changes in quality of life.

The key message for ANCA vasculitis is the importance of early diagnosis, particularly the importance of ANCA testing, testing urine in rheumatology clinics, and of course referring patients to biopsy which confirms the diagnosis.

Loreto, can you tell us more about the impact of IgA [immunoglobulin A] nephropathy and FSGS?

Dr. Gesualdo:
For those just tuning in, you are listening to ReachMD. I am Loreto Gesualdo. Here with me today are Dr. Carol Pollock, David Jayne, and George Bakris. We are discussing the holistic evaluation of patients with chronic kidney disease and how novel therapies can improve the lives of our patients.

IgA nephropathy and focal segmental glomerulosclerosis are the most, you know, frequent form of primary AGN [acute glomerulonephritis] and normally affected younger people than vasculitis patients. In the interim, unfortunately, both develop end-stage kidney disease in at least 40%-45% of patients. The importance of early diagnosis and the importance of the early biopsy to classify following the misclassification, the renal lesions, particularly in the AGN patient.

We have now new drugs that are able to reduce the amount of proteinuria, and we know very well that reducing the amount of proteinuria and inflammation may ameliorate the outcome of our patients.

David, I will turn to you. How can nephrologists and other healthcare providers stay up to date with the latest advances?

Dr. Jayne:
There are really 2 aspects for staying up to date. The first depends on where you work and what ongoing education you have with your colleagues. And the second is an individual's access to formal training and update in chronic kidney disease.

Please let me introduce the mission of the Global Kidney Academy. The Global Kidney Academy is a global nephrology curriculum focused on the current challenges and opportunities to address the unmet needs of the patients with CKD. The Academy aims to improve learner confidence and patient outcomes in the management of CKD and progression to end-stage renal disease through a holistic approach based on current guidelines, evidence-based medicine, and real-world data.

Dr. Pollock:
The Global Kidney Academy focuses on the patient as well as the educational needs of the clinician. So I would like to advocate its use for clinicians, because I think it actually is a site that is dedicated to improve patient outcomes more holistically than what we might get

from just looking at clinical trial results.

Dr. Gesualdo:
I think the Global Kidney Academy is a tool that we can use in our daily life. It's providing us with the moralistic approach.

Dr. Pollock:
I couldn't agree more, Loreto.

Dr. Bakris:
It's important that what this academy serves is it takes into account what the results of the trials are; however, it puts it in the context of how you can improve quality of life of the patients based not just on what we think, but what the patients are telling us in terms of what they want in terms of quality of life.

Dr. Gesualdo:
What are some of the emerging and novel therapies that show promise in alleviating the symptom burden and changing the story of our patients with CKD?

Dr. Pollock:
The emergence of difelikefalin as a selective kappa-opioid receptor agonist for the treatment of itch has been a really standout development where the development of a drug has really come from a patient perspective, saying we need a drug to stop us from itching. It has now had very sort of strong clinical data in the KALM-1 and KALM-2 studies. It has looked at patient-derived endpoints, you know, did they receive benefit from it? And it was done very scientifically with an appropriate assessment of their symptoms before and after the drug.

This really highlights listening to patients, designing a drug, developing a benefit, and now implementing it into clinical practice for patient's symptom relief and benefit, which is really what they want: a better quality of life. And a drug such as difelikefalin to reduce itch has really delivered on that.

Dr. Jayne:
Well, we now have available a new therapy, avacopan, which is a specific oral inhibitor of the complement C5a receptor. And this pathway has shown to be critical for inflammation.

ADVOCATE, which has now led to the approval of avacopan for the treatment of patients with ANCA-associated vasculitis, showed several important potential benefits of avacopan. The first was there was improved disease control over a 12-month time span. The second was there was much faster recovery of quality of life than in the steroid comparator treatment group.

ADVOCATE also demonstrated a better recovery of glomerular filtration rate to the tune of between 3 and 5 mL/minute in patients treated with avacopan, as opposed to those treated with steroids.

So the drug is now approved and is available in several countries around the world. And the most recent guidelines have suggested that avacopan is an alternative to glucocorticoids for the treatment of active ANCA-associated vasculitis. Particular patient groups that are likely to benefit from avacopan are those at high risk of glucocorticoid toxicities, such as in diabetes; those presenting with low GFR in which the additional GFR recovery is likely to have long-term health benefits; and then those patients with refractory disease who typically are exposed to ongoing high doses of glucocorticoids.

Dr. Gesualdo:
After, you know, 25 years where we were only using corticosteroids and RAS [renin-angiotensin system] inhibitors, we have now, in the pipeline, new drugs able to change the natural history of IgAN. Among these drugs, there is sparsentan, a dual endothelin angiotensin receptor antagonist that has been demonstrated in a phase 3 trial that is able to protect renal function because an interim analysis that was recently published demonstrated that sparsentan is able to reduce the amount of proteinuria. As well, on 2 years' follow-up, it was demonstrating a renal protection reducing proteinuria and ameliorating the eGFR slope.

Dr. Bakris:
The therapies to manage hyperkalemia in the scope of things are a bit old and really have not been taken up the way they should. Patiromer, which is one of the first agents to be developed, was approved in 2016 in the US, and subsequent SZC [sodium zirconium cyclosilicate], which is the second compound which is different than patiromer, was approved about 18 months later. Both of these compounds have been looked at in large studies going out with daily use for 1 year, showing good tolerability and the ability to take people that clearly had hyperkalemia and needed therapies that would generate hyperkalemia and maintain potassium levels in the high 4s.

The old potassium binder really has black box warning labels in the US now because of colonic ischemia and other things.

So these are not only safe alternatives, they're better alternatives, and they're enablers, if you will, to allow therapies that we know will slow progression of kidney disease, but have hyperkalemia as a side effect, to be used to maximize therapies.

Now there are also novel therapies for iron deficiency and management of anemia. Those have been around also for a little while in development, and the so-called HIF [hypoxia-inducible factor] inhibitors.

Dr. Gesualdo:
This has certainly been a fascinating conversation, but before we wrap up, Carol, David, George, do you have any take-home messages?

Dr. Pollock:
Now I have a strong focus on listening to patients and really developing treatments that address their concerns rather than our concerns. So I think that to address their concerns, that really requires a multidisciplinary collaboration, and I think if we look at what is the most troublesome consequences of CKD on the patient and their family, we will develop more holistic treatments that actually address these factors that are so important to a patient's quality of life.

Dr. Jayne:
I would add that we have real opportunities now to improve the health of our patients with chronic kidney disease with newer agents. It's exciting times.

Dr. Gesualdo:
I think that it's time to change our standard of care. We have now in pipeline many different drugs that may personalize the treatment of CKD.

Dr. Bakris:
I think if there's ever a time for an integrated approach involving families, social services, and our knowledge of medicine, it’s now.

Dr. Gesualdo:
Unfortunately, that is all the time we have today. So I want to thank our audience for listening in. And thank you, Dr. Carol Pollock, David Jayne, and George Bakris, for joining me and for sharing all of your valuable insights and expertise. It was great speaking with you today.

Dr. Pollock:
And with you, Loreto, David, and George.

Dr. Bakris:
Thank you very much.

Dr. Jayne:
Yes, I very much enjoyed it. Thank you all and goodbye.

Dr. Bakris:
Right. Goodbye.

Dr. Pollock:
Goodbye.

Announcer:
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