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Current Treatment Options for AMKD and Critical Updates on Clinical Trials: What Tools Do We Have?

Announcer:
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Dr. Kovesdy:
Hi. My name is Csaba Kovesdy. I am the Fred Hatch Professor of Medicine at the University of Tennessee Health Science Center in Memphis, Tennessee. I'm also a practicing nephrologist, and I will speak to you about current treatment options for AMKD and critical updates on clinical trials: what tools do we have?

To get started, I will give you a case presentation. So, our patient is a 55-year-old African American male who was referred to us by his primary care provider. The reason for the referral was an evaluation of an elevated serum creatinine, which was detected during a routine healthcare assessment. The patient had no complaints on presentation aside from chronic knee pain from a sports injury about 10 years ago. He is also unaware of having kidney disease.

His comorbidities include hypertension, which was first detected when undergoing an employment physical about 20 years ago. He also suffers from hypercholesterolemia, obesity, chronic arthritis, and gastroesophageal reflux disease. His family and social history includes prior exposure to smoking. He quit about 10 years ago but has a 20-pack-year history. He consumes alcohol socially, and he does not consume illicit drugs. He works as a store manager. And as far as his family history goes, his mother and maternal uncle were both on dialysis before passing away.

He also has a niece who has a kidney transplant. His current medications include lisinopril 20 milligrams daily, carvedilol 25 milligrams twice daily, chlorthalidone 25 milligrams daily, atorvastatin 80 milligrams daily, and he uses ibuprofen 400 milligrams twice a day, but only as needed. On exam, his blood pressure is 134/82 millimeter mercury with a heart rate of 65 per minute. His BMI is 32 kilograms per square meter. He's euvolemic, and his exam is largely negative for any abnormalities. In terms of diagnostic findings, he has an eGFR of 35, a UACR of 1,940 milligrams per gram. The UA is unremarkable. And the major electrolyte findings include a sodium of 141, potassium of 4.1, and a serum bicarbonate of 26. We performed a kidney ultrasound, which showed kidney sizes that were within normal limits, but had increased cortical echogenicity, suggestive of chronic kidney disease.

After much deliberation, due to the elevated proteinuria, we performed a kidney biopsy, which indicated the presence of focal segmental glomerulosclerosis with moderately increased interstitial fibrosis and tubular atrophy. At this point, the diagnosis of FSGS is made with a clinical suspicion of APOL1-mediated kidney disease or AMKD.

So how about treatments? At this point, due to the elevated proteinuria level, we increased the dose of the patient's lisinopril to 40 milligrams daily, and we also added that dapagliflozin 10 milligrams daily for additional renal protection. We also advised the patient to abstain from NSAID use in the future as much as possible.

During follow-up a month later, the patient remains asymptomatic, and he reported no adverse reactions after starting the dapagliflozin and the increased dose of lisinopril. He also uses now acetaminophen for his knee pain, and his blood pressure is down to 118/75 millimeter of mercury with a heart rate of 62 per minute. His pertinent labs at this point are an eGFR of 29 mL per minute, and a UACR of 950 milligrams per gram.

At this point, our patient has reached several therapeutic milestones. His blood pressure is well controlled at the level of 118/75. It is less than 120, which is recommended by KDIGO based on the SPRINT trial as it is considered ideal. His lab work indicates that his albuminuria decreased by about 50%, which is a therapeutic success likely in response to the enhance those of the ACE inhibitor, which is the maximum tolerated dose at this point, and the addition of the SGLT2 inhibitor, dapagliflozin. We noticed that his eGFR has declined somewhat by about 10 to 15%. This is likely a result of the enhanced ACE inhibitor dose and the addition of the SGLT2 inhibitor, and it is expected based on their hemodynamic effects. It is very important that we do not decrease the doses of these medications in response
to the eGFR value.

His serum potassium has remained normal despite the enhanced dose of the ACE inhibitor. The addition of dapagliflozin is probably helpful in this respect, as it can temper the effects of RAAS inhibition on hyperkalemia development. Despite all of these therapeutic successes, we have to note that the patient still has substantial albuminuria, and is now CKD stage 4, hence, his risk for end-stage kidney disease remain high. Currently, there are no approved therapeutic interventions that we could offer him to decrease the residual risk of end-stage kidney disease.

So in summary, our patient has FSGS likely mediated by APOL1 mutations. We implemented strict blood pressure control and state of the art RAAS inhibition combined with SGLT2 inhibition to lower his risk of end-stage kidney disease. But despite of this, the residual risk of end-stage kidney disease and adverse consequences remains substantial. It is therefore imperative that, for this particular disease state, new medications and new therapeutic interventions be developed. I thank you for your attention and have a good day.

Announcer:
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