

EPISODE 24: TREATMENT OF DIABETIC KIDNEY DISEASE

Rita Kalyani, MD: Welcome to *Diabetes Deconstructed*, a podcast for people interested in learning more about diabetes. I'm your host, Dr. Rita Kalyani at Johns Hopkins. We developed this podcast as a companion to our Patient Guide to Diabetes website. If you want a trusted and easy to understand resource for diabetes or to listen to previous podcasts, please visit hopkinsdiabetesinfo.org.

Today we are so glad to have Dr. Knicely back again to talk about treatments available for diabetic kidney disease. Dr. Knicely is an associate professor of medicine at the University of Virginia School of Medicine and an expert in diabetic kidney disease. Dr. Knicely is also the physician leader for home therapies at UVA Dialysis. Thanks for being here again, Dr. Knicely.

Daphne Knicely, MD, MEHP: Thank you again. It's always a pleasure.

RK: What are some of the drug treatments, that as a kidney specialist or nephrologist, you would prescribe for your patients and at what stage would usually prescribe them?

DK: And actually endocrinologists usually start the steps before I do. I would just say, "Well, I like that. Maybe go up on this." So the big thing is, especially when they start having changes within the kidney, is a blood pressure medicine that actually is protective for the kidney. One of those is called an ACE inhibitor or an ARB. Common ACE inhibitors end in "-pril," so Lisinopril, Enalapril, Benazepril, just to give you examples. Or the ARBs, or angiotensin receptor blockers, are the ones that end in "-sartan," so Losartan, Valsartan, Olmesartan to give you ideas. And these are blood pressure medicines. Sometimes we'll start them on folks just because of the protein in the urine and try and increase the dose without lowering their blood pressure too much for those people that have normal blood pressure. The way those work is if we go back to the changes that happen in these filtering units, and they're actually ending up filtering a whole lot, the firehose. What this does is it takes the fire hose down to a regular spigot. It allows there to still be cleaning that goes on, but it's not adding so much pressure in these filtering units that it's causing damage.

Now, with adding any of those medicines on, you're going to see a little increase in your creatinine or a little decrease in your GFR just by the mechanism of how they work. Because you were filtering a whole lot with all that pressure, and then I just gave you something that slows down the filtering a little bit/to take down the pressure. So I'm not filtering a lot of that creatinine into my urine. So it's going to be up a little bit in the blood. And so that's why it's really important whenever those medicines are initiated to get labs in two to four weeks afterward just to make sure that you're tolerating it well. And anytime the dose is increased, they should check again in two to four weeks just to make sure you're okay and the kidneys are handling it okay. And over the long term, what I tend to do if you have a lot of protein in the urine is, I try to maximize those to the max dose as much as I can to help decrease the amount of protein in your urine because that's going to have a good prognosis over time on your kidneys: the less protein you lose in the urine, the better the kidneys do over time. They've even done studies on this. People that have tons of protein in their urine and they're able to decrease it to have it regressed back to no protein in the urine or the normal amount, they actually do just as well as somebody who've never had protein in their urine; compared to somebody who has tons in it and it never regresses, they're going to go on to like worse kidney function over time. The less protein in the urine, the better. Those medicines are great for it. Now you never do both of them at the same time; it's usually one or the other. Whenever you do the ACE inhibitors, sometimes people will have side effects: the biggest one that says cough that they'll get because there's a buildup of enzyme. Most people don't have that problem, but some will. They'll just have this kind of dry cough that doesn't go away with rosuvastatin, and they don't really have a cold. But they'll stop it, and a month later, it usually goes away. If they develop that side effect with the ACE inhibitors, we'll put them on an ARB. Those medicines that end in "-sartan," and they don't get that cough with those. There's also, with that enzyme that builds up, a small percentage of 1 to 2%, that will actually get a bad allergic reaction to a swelling of their face and lip. It's more common in African Americans, but I've seen it in Caucasians as well, in that you can never have one of those medicines again. It's bad, and if that happens, you go to the hospital right then because it could affect your breathing. But the likelihood of it happening with one of those ARBs that end in "-sartan" is less likely. I think it doesn't build up that enzyme. It's less than 5% that ever have that chance. Some people will still try to avoid those. I tend to see the benefits of them on your blood pressure and the protein in the urine. I still try to do one of those other medicines.

Now there's newer diabetic medicines, which this is your realm; I don't usually start them. But there's newer diabetic medicines that actually have been shown to have some renal benefits and cardiovascular benefits, and these are the SGLT-2 inhibitors. So the way they work is—when you have all these filtering units, they're all connected to the tube; sugar and salt get filtered in those little filter units, and then they usually get reabsorbed in the tubules. This medicine actually stops you from absorbing salt and sugar in those tubes, and you just pee it out. So your urine has a ton of sugar and salt in it. And this actually does the same thing that these other medicines I just talked about

for blood pressure. It actually will slow down that filtering as well. So it just kind of feeds back on it. And so you'll actually take it down from the fire hose to the spigot by use of these diabetic medicines. And they've actually been shown to be helpful for slowing the progression of kidney disease and diabetic kidney disease. They've actually seen some improvement in kidney function with using them as well. There are some side effects, though; because you have a lot of sugar in your urine, bacteria love it, and so do fungi. So, you can get urinary tract infections, or you can get genital funguses that will happen. Because you're peeing out so much sugar and water, there's a chance you could get really dehydrated. I've actually seen people we started on it and they lose so much water weight. They lose weight, and they can get really dehydrated. And if they're on other medicines that they take just to lose extra water, it can be worse. So a lot of times when these medicines are stopped, if you're on any other kind of diuretics (we call them), we hold those and we decrease the dose to prevent that. And I also check the labs at least a month after starting it to make sure that you're tolerating it okay and you're able to keep up with your fluids and everything. The one downside: these are great medicines, but they're new. And so they're actually kind of expensive. And I've had a lot of people that we try to get them for them, but they just can't afford it; they're on a limited budget. But if the folks can afford it, then I try to give it to them. There's also these GLP-1 inhibitors for diabetes as well. And they, you can correct me if I'm wrong, just increase your insulin sensitivity, essentially, and through other mechanisms, they actually make you pee out a lot of salt. And it causes again that slowing down the filtering and little filtering units in the kidneys. It's kind of that similar mechanism for most of these drugs. If we take off that harsh filtering that happens in kidney disease, or diabetic kidney disease, then it actually improves the kidney function over time. And so these GLP-1 inhibitors are Liraglutide, and some of those. I see Liraglutide most of the time, but they're good glycemic medicines as well.

RK: It is so exciting that the newer classes of medicines for diabetes as mentioned SGLT-2 inhibitors in particular such as Canagliflozin and Dapagliflozin and Empagliflozin can have effects on the kidney to be beneficial in addition to their effects and lowering blood glucose. And as you mentioned, the injectable medications, too such as Liraglutide or Dulaglutide and Semaglutide. They also have benefits on protein in the urine, [specifically] reducing protein in the urine. So it is very exciting for us as diabetes specialist to be working with you as the kidney specialist and really using these medications not only to treat the diabetes, but also to protect the kidneys.

You've mentioned dialysis. I wonder if you could talk a little bit more about when that is needed. You'd mentioned that it's when the glomerular filtration rate or the GFR is usually less than 10 and what that means. This is something that sometimes patients who've had family members who have been on dialysis, they might be a little bit fearful of happening to them. What proportion of patients does this happen to and what are the steps that usually then move towards eventually a kidney transplant?

DK: Whenever somebody starts dialysis, this is what we call end-stage renal disease or end-stage kidney disease. And probably I think it's about 40 to 45% of them have diabetes as their primary cause for their kidney failure. And so the important thing of seeing a nephrologist is we kind of help planning for this. If you're seeing the nephrologist, we're kind of watching your labs. And when your GFR starts to get to 20 and persistently stay below that, then that's when I start talking to you about - "Dialysis might be in the future. That doesn't mean I want to start. I just want you to get information on it. Because there's a lot of different types of dialysis out there and I want the one that's going to kind of work best with your lifestyle."

When it's about that 20%, we start talking about transplant, hemodialysis, peritoneal dialysis, and home hemodialysis. And we even talked about what if you choose not to do dialysis. Once your GFR is less than 20, I can go ahead and send you for a transplant evaluation. And that's really important because if you go for transplant evaluation, then you can go ahead and get active on the list before you ever need dialysis. So you're building up time before you need dialysis on the transplant list. And usual wait times or any on the East Coast is for about three to five years. And so getting that time in now is important versus somebody who doesn't who waits to do a transplant evaluation. They do it once they start dialysis. Well then the first day they're active on the list is the first day they started dialysis. So they could have started months or years before that and built up extra time on it and limited their time on dialysis. And then I talked to them about the hemodialysis which can be done at home or in a center and we talk about which would fit their lifestyle. And then we talk about peritoneal dialysis, which is kind of a different type of dialysis where you kind of do your cleaning of your blood through a catheter that's kind of in your belly and figure out which they prefer to do. But we don't really start any of the planning for that until we really look like you're on that trajectory you need to start. If your GFR still going down then you want to do a blood type of dialysis like hemodialysis in the center or at home, then I actually will go ahead and get access in your arm terms for that. You need a big blood vessel to do that type of dialysis. And so what they do is typically sew an artery and a vein together or connect it with the synthetic material. Now, the surgery is just an outpatient procedure, but it takes up to three months sometimes for that access to work. And sometimes they need more than one procedure to make it work. And so that's why we plan. You can always do the blood type of dialysis with a catheter in the neck, but it's a catheter in the neck; it could get infected, there could be problems. We don't want to do that. We prefer to have something more permanent in your arm to be able to do it. That doesn't mean that when it's ready, we start dialysis. It means we have it. And what I find is with my diabetic patients, sometimes they have bad circulation and these accesses that are put their arm between where they sew together the artery

and vein or they put in one of the grafts, they don't always work initially, or they might need more than one procedure to get it to work. That's why it's important for figuring that out early so they never have to start with a catheter in their neck in a big vein in their neck because that risk of infection and that catheter ends right at the heart. And if they get a bad infection, they get a heart infection too. And that could be really bad with needing surgery or something like that.

Now the peritoneal dialysis is a little different, you don't really have to get access with that. We wait till you get some symptoms of kidney failure which is around that 10 mark. Everybody's a little different. Most of the time, 40% of the patients, when we look at the data, they start dialysis about that kind of 10 mark — 5 to 10. But there's a good portion that start before that and there's some that start after. It just kind of depends on what symptoms people have and what symptoms they're okay with. Some of those symptoms can be just really bad fatigue, metal taste in their mouth, nausea, vomiting, decreased appetite and that's probably about when you have to start. We don't want them to be up there around where they have tremors or are forgetful or actually have coma; that's too late. We'd like to start before then. With peritoneal dialysis, you start getting some of those minor symptoms and that's when we say "Hey, we need to get a catheter in your belly, we need to go ahead and start that peritoneal dialysis within a month or two." Even when we say that it's about time, you have to get into the surgeon's office and put in the catheter. We have to let it rest for a month so still about three or four months before we can use it. This planning again all starts whenever you hit 20. We look at your trend. Are you 20 and stable? Are you 20 and getting worse? And that 20 and getting worse is when I start really talking about these things and planning for the future. The question that always comes up to me is, 'Is any of these dials is better for me versus one or the other?' They're all the same. It's not like you do one, it's going to make you live longer. Obviously, transplant is the best. That's the one we want for everyone. Some people benefit from either a pancreas transplant as well. And they work that up whenever we send them for transplant, which will help their diabetes too. Choosing these types of dialysis depends on what they can stick with. And if they pick one and they do hurt for peritoneal dialysis, and if they're like, "I don't like it" then they can switch to one of the others. They can't switch every week. But we can switch between and find the one that works best for them. Along that way, we just kind of take care of them. The one thing with peritoneal dialysis, I'll mention this, the fluid that we put in the belly to help with that dialysis is sugar-based. So we actually work with their endocrinologist closely to let them know, "Hey, they're going on peritoneal dialysis." So you can adjust their medicines and take that into account to cover the sugar that they might absorb from it and that sort of thing. But it still works fine for diabetics.

RK: And dialysis is basically an artificial kidney, if you will, right? A machine that's attached through this catheter and your arm or sometimes your neck like you mentioned, which kind of filters out all the toxins, filters out the water, and does the job of the kidney until you can eventually get a kidney transplant. And usually I know for my patients, it's usually two or three sessions a week for the hemodialysis, correct?

DK: It's usually three sessions a week. Very rarely do people ever do less than that. And it's those are really special cases. It's usually three times a week for in-center hemodialysis. For home hemodialysis, it's either every other day or four days a week or up to seven. It just depends on how much they need. The more times you do it during the week, the less each amount of time is. That's probably the benefit of home hemodialysis. You're doing it more frequently. So, to think your kidneys work 24/7, and if I'm doing in-center, three days a week, I'm only getting about 12 hours each week of cleaning. That's 12 hours of kidney function, I guess artificial kidney function. Versus if you do home hemodialysis you can get at least 12 hours but sometimes we get a little bit more and people tend to feel better with it with more cleaning. And with peritoneal dialysis, it's usually daily. Every day you do it, it's more kind of continuous cleaning compared to the other two. And so, people tend to feel a little bit better with that as well. But it just depends on the patient which they are comfortable doing.

RK: I wonder if you have parting words for patients who are interested in preventing the risk of kidney disease. What would you say to them? What would you recommend?

DK: I recommend for people that are newly diagnosed with diabetes to really get on the bandwagon to control their high sugars and to control their blood pressure. The sooner you get it controlled, the better your prognosis is over time. It's kind of [like] you create this metabolic memory. The quicker you get your sugars under control, the better the kidneys are going to do and the less likely they're going to be affected by the diabetes. If you do get kidney disease, it's not the end of the world. Not everyone needs dialysis. 37 million have kidney disease in the US. 35 million are stable. It's not the end of the world if you do get a kidney disease and not everyone's going to go to dialysis. Think of it whenever you get diabetes, get it under control. If you get a little protein in the urine, that's a big warning sign that you got the kidneys affected. Really try hard to start controlling things and start controlling your diet and working towards preventing any further progression.

RK: Thank you so much for being here today. We truly appreciate all your expert input and advice.

DK: Thank you so much for having me. It was a pleasure.

RK: I'm Dr. Rita Kalyani, and you've been listening to *Diabetes Deconstructed*, a companion podcast to the Johns Hopkins Patient Guide to Diabetes website, which also has useful information about diabetes, including videos and animations, a lifestyle and nutrition blog, and a comprehensive diabetes glossary among many other things.

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