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Expert Insights: Managing Patients with CKD, Hyperkalemia, and Continued RAASi Therapy Through a Case Study Approach

Announcer:
Welcome to CME on ReachMD. This activity is part of a series entitled “Expert Insights: Managing Patients with CKD, Hyperkalemia, and Continued RAASi Therapy Through a Case Study Approach” and is provided by Medtelligence.

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Dr. Weir:
Welcome to our discussion entitled “Expert Insights: Managing Patients with CKD, Hyperkalemia, and Continued Renin Angiotensin-Aldosterone System Inhibition Therapy Through a Case Study Approach.” I’m Dr. Matthew Weir, and I’m pleased to be joined today by two good friends, Drs. Robert Toto and Gates Colbert. Welcome to our program, gentleman.

Dr. Toto:
Thank you, Matt, this is Bob. It’s a pleasure to be here with you today.

Dr. Colbert:
Yes, this is Dr. Colbert. It’s great to be with you both, as well.

Dr. Weir:
In this first chapter, we’re going to look at who is at risk for hyperkalemia, and I’d like to start our program by sharing a case with you. We have a 54-year-old White male with stage 3 CKD [chronic kidney disease] and an estimated GFR of 48 mL/min. He has type 2 diabetes and resistant hypertension, and he’s on a large number of medications, including: amlodipine 5 mg, candesartan 32 mg, doxazosin 4 mg, 50 mg of hydrochlorothiazide, and for his diabetes, metformin 500 mg twice daily, glipizide 5 mg, and glargine insulin 36 units per day, along with a sliding scale. His A1c is at 7.4, and his 24-hour urine showed about 880 mg of protein. Plus, his serum potassium was about 4.8 mEq/L, his blood pressure is 154/90, heart rate 76, and he has had intermittent ankle swelling since going on the amlodipine, despite the undercurrent use of both the hydrochlorothiazide and the candesartan. As you can see, even with several medications, his blood pressure is still quite elevated at 154/90, and his potassium is on the high side, at about 4.8 mEq/L. We know that if we consider introducing other medications for better blood pressure control, such as an MRA [mineralocorticoid receptor antagonist], his hyperkalemia may become an important concern.

So, Gates, which patients, typically in your practice are most at risk for hyperkalemia, and what are its clinical effects?

Dr. Colbert:
We eliminate about 90% of our potassium through the kidney and 10% in the gut. And so if you don’t have a perfectly working kidney, or if you have a disease state or a medication that’s hindering the kidney’s ability to do everything that it’s supposed to, you’re going to start accumulating potassium in the body and in the serum. Additionally, disease states such as diabetes mellitus or congestive heart failure also result in some potassium retention. And then these medicines, such as RAAS inhibitors, which frequently our patients are taking, also prevent maximal secretion of potassium. And so the clinical effects are highly variable. The most common effect is

asymptomatic. Some clinical effects that we have to watch out for are arrythmias, muscle weakness, palpitations, and our most feared side effect is a sudden cardiac arrest. And we know that mortality increases with hyperkalemia. And unfortunately, this is compounded as a patient has multiple disease states, such as chronic kidney disease, diabetes, and heart failure, which frequently run together for a lot of our patients.

Dr. Weir:
Older age is also another issue which comes into play. So the real question is how do we best use these types of medications appropriately, yet also get the patient's blood pressure better controlled?

Bob, what do you think should be done next to get this patient better controlled from a blood pressure standpoint?

Dr. Toto:
I agree with you, Matt, that he needs better blood pressure control. I think a couple of options are here. One could consider increasing his amlodipine. That might worsen the edema that he already has, but it ought to bring his blood pressure down some, although I don't think it'll get it to the goal we'd like to see him at. Another option would be to switch him to a loop diuretic from the hydrochlorothiazide to try to control his blood pressure better since he is edematous, and that may also lower his potassium a little bit. And then using a mineralocorticoid receptor antagonist such as spironolactone would be another option.

Dr. Weir:
I agree Bob. You know, more often than not, adding an MRA to somebody already on an ACE or and ARB can increase their serum potassium by about 0.5 mEq/L, and that would put him at around 5.3 or so, and you never know, with some dietary indiscretion, it might even go a little bit higher, so there might be some concern in that regard.

In this particular case, spironolactone was started at a low dose, 12.5 mg daily, with instructions to return in 10 days So, please join us in chapter 2 to find out what happened once the spironolactone was added to his medication regimen.

In Chapter 1, we discussed a patient with stage 3 CKD, diabetes, and resistant hypertension. He is on multiple medications for his blood pressure management. In Chapter 1, he presented with a potassium of 4.8 and a BP of 154/90. The decision was made to start spironolactone 12.5 mg daily. Ten days have passed, and our patient has returned to clinic for his follow-up blood pressure and clinical care. Of note, blood pressure 148/84, his potassium is 5.3, and a 24-hour urine revealed a potassium of 80 and a sodium of 340. Both are on the high side. Other labs are stable. So what should we do next?

Gates, many clinicians are tempted to stop the RAAS blockers at this particular juncture, since the potassium is over 5. Why should they be concerned?

Dr. Colbert:
So we definitely want to be thinking about the potassium, but we also want to be thinking about the clinical benefits that you get from RAAS inhibitors. And specifically, at their maximal tolerated doses. And so RAAS inhibitors have a long track record of lowering proteinuria, preserving the GFR decline over time, improving our cardiovascular outcomes, and actually improving mortality. And we have historical trials that back this up. The RENAAL trial and the IDNT trial, both showed in patients who have diabetes and chronic kidney disease that RAAS inhibitors showed great clinical benefits and outcomes.

And this has been reflected in our contemporary guidelines that we use for these patients to try and control their chronic kidney disease, maintain their GFR, and control their blood pressure.

Dr. Weir:
Good points. So, Bob, if we continue the RAAS inhibitor therapy, including the spironolactone, the potassium will likely continue to rise or remain elevated. Should we consider potassium binders, and if so, what are our options in this regard?

Dr. Toto:
Based on what you and Gates have both pointed out, we want to keep this patient on RAAS blockade for all the reasons given. And we can use potassium binders to facilitate that. So there's clear benefit of the potassium binders. And there's data now with 2 relatively new potassium binders, patiromer and [sodium] zirconium cyclosilicate, that indicate that the short-term as well as long-term use of these agents can effectively control the potassium in patients who remain on RAAS blockade. And so your trial, published in the *New England Journal* in 2015, with patiromer clearly showed the benefit of patiromer to lower potassium in patients who are on RAAS inhibitors.

And then the trial, AMETHYST-DN, using patiromer over a year period of time showed that you could have a sustained control of the potassium. And similarly, we've seen with sodium zirconium cyclosilicate, another relatively new potassium binder, both short-term benefit in terms of getting the potassium down promptly and then the use of it over a longer period of time to control the potassium. So

we have both of these available to us now in the clinic on top of our old standby of Kayexalate or sodium polystyrene sulfonate, which itself is not a great option compared to patiromer or zirconium, in my opinion, because of the side effects that have been observed with Kayexalate.

Dr. Weir:
Yeah, I would agree, Bob. I mean, there's certainly good data with both of these therapies demonstrating very important benefits in terms of controlling serum potassium and in fact reducing it by an average of about 1 mEq/L. The fact that they are well tolerated with very few discontinuations.

So the decision for this patient was to start patiromer at a dose of 8.4 g per day. Bob, what would you do about the persistent elevation of blood pressure next given the fact that we can now use the patiromer to control the potassium?

Dr. Toto:
I think my first maneuver would be to try to increase the amlodipine to see how he does on that, and then I'd certainly be willing to go up on the spironolactone once I had his potassium under control.

We could also switch him, as I mentioned earlier, to a loop diuretic. That may be just as effective or more effective than hydrochlorothiazide and it will help lower his potassium level, as well.

Dr. Weir:
So, in fact, his amlodipine dose was increased to 10 mg per day, and he was asked to return in another 10 days. So stay tuned to Chapter 3 to see what happens next.

This is CME on ReachMD. I'm Dr. Matthew Weir, and I'm joined today by Drs. Gates Colbert and Robert Toto, and we are discussing strategies to manage hyperkalemia while maintaining renin-angiotensin system inhibition therapy in a patient with CKD and resistant hypertension.

So in Chapter 1, we met our patient who had a history of stage 3 CKD, diabetes, and resistant hypertension on 4 medications for his blood pressure. We added spironolactone in the presence of a serum potassium of 4.8. In Chapter 2, the blood pressure came down slightly, but certainly was not yet at goal. His potassium rose to 5.3, patiromer, a potassium binder, was started, and the amlodipine was increased to 10 mg daily. Now, in Chapter 3, 10 days have passed, and the patient has returned for follow-up. Today, his blood pressure was 142/83, and his serum potassium is 4.9.

Gates, what do you think about our progress, and what would you do next?

Dr. Colbert:
So I'm glad to see our blood pressure continues to move down as we're moving towards a goal therapy. And our potassium has also come down, as well, with the addition of patiromer. And so with a potassium of 4.9, I think we would feel comfortable increasing that spironolactone up to a full dose of 25 mg per day so we can achieve our long-term outcomes, as well as lowering that blood pressure.

Dr. Weir:
Bob, do you think you'd do the same thing?

Dr. Toto:
Yeah, Matt, I do agree. I think it's very reasonable to up-titrate his spironolactone. That may raise his potassium some, so there are things we can do to help keep that down beyond the patiromer, which, by the way, we could up-titrate the dose if his potassium goes up. We can educate the patient to lower his potassium intake, because as you pointed out, his 24-hour urine indicates that he's on a relatively high-potassium as well as high-sodium diet. So lowering the sodium in his diet would help control his blood pressure for us and for him, and lowering the potassium diet would reduce the risk that he's going to get more hyperkalemic with a higher dose of spironolactone.

I think it's also important to remind patients to avoid things that can aggravate hyperkalemia, such as non-steroidal anti-inflammatory drug use or use of over-the-counter supplements or other things they can purchase off the internet that are high in potassium. One other thing to consider would be to measure his serum bicarbonate. And if he has a metabolic acidosis, adding sodium bicarbonate to his diet could also help to lower the serum potassium. So there are lots of adjunct things in our armamentarium to help control potassium and continue the RAAS blockade.

Dr. Weir:
Well, thanks, Bob. I'll be honest with you. I'm not a big fan of the belief that long-term dietary modifications really are going to play a role both in terms of controlling his blood pressure or, for that matter, reducing his dietary potassium intake. I'm more of a fan of altering

medications as a strategy to deal with it just because I think people would rather take pills than they would to cut back on the foods that they enjoy eating.

Dr. Toto:
Matt, you're absolutely right about that. On the other hand, you know, nonpharmacologic therapy is part of the cornerstone of our treatment, so I try that, but like you, I usually end up adding medications to my patients' regimen.

Dr. Weir:
Well, Gates, we have this gentleman on a potassium binder. Is this going to be a long-term management strategy for him? What are your thoughts?

Dr. Colbert:
Yes, I think it definitely can be part of his medical regimen to combat his hypertension and chronic kidney disease. From the data perspective, I feel like we can be comfortable using these medications long term. From a physician experience and prescriber experience, patiromer's been out for about 5 years, and SZC's been out for about 3 years.

Dr. Weir:
Well, that's good news. I don't think this serum potassium problem's going to go away in this gentleman. And if anything, since renal disease tends to be progressive, it may start to get worse.

But in this particular case, the spironolactone was increased to 25 mg daily. The patiromer had to be increased to 16.8 g per day given the fact that they were going up on this spironolactone and wanted to maintain the serum potassium. And basically, all of the other medications were continued as ordered. The patient returned in another 10 days, blood pressure was now improved and into the 130s at 137/78, potassium was 4.6, and he was seen in follow-up after another 10 days to make sure his blood pressure, potassium, and other labs were in order. At this point, he was instructed to see me again in 1 month.

Well done, gentleman. I'd like to call this case a success.

Now, I'd like to end our program by asking each of you for one key take-home message. Gates, we'll start with you first, followed by Bob.

Dr. Colbert:
So my main message that I would like for our viewers is that we need to maintain the highest tolerated dose of RAAS inhibitors for our patients like this patient today, who has chronic kidney disease and diabetes. Try not to lower or eliminate the RAAS inhibitors if you have mild or moderate hyperkalemia because we now have good management options.

Dr. Weir:
Bob, thoughts?

Dr. Toto:
Yes, so my take-home message is that we now have potassium binders that enable all of us to maintain our patients on RAAS blockade, and we can do it long term and we can do it safely.

Dr. Weir:
Well, thanks, Bob. And my take-home clearly is we have, now, options which are better than dietary avoidance or pushing up the diuretic doses. This is going to be a lot more palatable for most of our patients because potassium binders, the newer ones, are odorless, they're tasteless, they're easy to take. You do have to separate them from other medications by 2 to 3 hours. But aside from that, they do provide the opportunity for using guideline-based medical therapy for both heart disease and kidney disease.

So, that's it. We're out of time. I'd like to thank our audience for listening and offer a special thank you to my colleagues and friends, Gates Colbert and Bob Toto, for sharing their thoughts with us today. It was great having this discussion with both of you.

Dr. Toto:
Great, thanks very much Matt. I enjoyed it. Great case.

Dr. Colbert:
Yes, thank you both, gentleman.

Announcer:
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