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Pearls of Wisdom: Optimizing Hyperkalemia Management in Patients with CKD

### Announcer:

Welcome to CME on ReachMD. This activity, titled “Pearls of Wisdom: Optimizing Hyperkalemia Management in Patients with CKD” is provided by Medtelligence. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

### Dr. Weir:

Patients with CKD are at risk for hyperkalemia, yet healthcare providers may be challenged in treatment and management. Today, we will explore the evidence for using potassium binders in patients with CKD and how to design patient-oriented hyperkalemia management plans.

This is CME on ReachMD, and I'm Dr. Matthew Weir.

### Dr. Kelepouris:

I'm Dr. Ellie Kelepouris.

### Dr. Desai:

And I'm Dr. Nihar Desai.

### Dr. Weir:

So, Ellie, let's begin with you. Can you review how providers should optimize guideline-directed medical therapy to manage hyperkalemia in patients with CKD?

### Dr. Kelepouris:

The prevalence of hyperkalemia in CKD is high. Prevalence rates have been reported from 17% to 30% or 40%, and the severity of chronic kidney disease is the most important risk factor for hyperkalemia. And the lower the GFR, the higher the hyperkalemia rate, and it increases exponentially above a GFR of less than 20 ml per minute.

And there is an unmet clinical need for guidelines that are best practices that address this issue, given the fact that RAS blockade and MRAs are now cornerstone management and have cardiovascular and renal protective effects but do have the side effect of hyperkalemia.

So, the unmet need is there. And the guidelines really have not been updated to incorporate ways to control the potassium elevation while continuing guideline-directed medical therapy like RASi blockade and MRA use.

In a recent large population database presented at the ASN from Sweden, almost greater than 2,000 patients, they demonstrated that

MRAs were down-titrated almost 20% to 50% of the time by 1 year because of the incidence of hyperkalemia in spite of the availability of second-generation potassium binders. That really could mitigate the hyperkalemia effect and continue use of agents that truly are cardio and renal protective.

So, the need for improved implementation of guideline-directed medical therapy exists. I think best practice guidelines need to be updated to include second-generation potassium binders. And the benefits of early intervention, adequate control of hyperkalemia in CKD, are huge because hyperkalemia is associated with very poor clinical outcomes, increasing hospitalization rates. And the lowest risk is observed in patients who are normokalemic. So, that really is our goal.

**Dr. Kelepouris:**

Nihar, do you have any comments to make about this?

**Dr. Desai:**

From our perspective on the cardiovascular medicine side, I think you rightfully noted that maybe even our guidelines previously kind of advocated for down-titration or discontinuation of RASi blockers and MRAs in the setting of hyperkalemia.

And I think we're in the mixed of a very important paradigm shift that we should no longer do that, just given how important those therapies are for many of the patients that we serve. And instead, we should be thinking about implementing potassium binders as a way to facilitate and enable the use of evidence-based therapies.

**Dr. Weir:**

And I would add as well, it's not unusual for serum potassium levels to go up 0.4, 0.5 mEq/L with renin-angiotensin-system blockade. And so, obviously, the higher the serum potassium at the time of initiation of RAS blockade, the greater the proclivity for people to have higher serum potassium levels. And certainly, in the 5 range.

But I think we need to have much more focus on mitigating hyperkalemia rather than stopping renin-angiotensin-system blockade because patients who have either reduced or stopped renin-angiotensin-system blockade have greater morbidity and mortality. And we have certainly also have safety data showing that one can successfully mitigate hyperkalemia in these kinds of patients.

**Dr. Kelepouris:**

Thank you, Matt. Thinking more about treatment, what is the evidence for early intervention and using potassium binders in patients with chronic kidney disease?

**Dr. Weir:**

Well, there is now more than sufficient safety and efficacy information available with the use of potassium binders in people with chronic kidney disease, and also in people with heart failure and reduced ejection fraction.

We completed a study a couple a years ago entitled the DIAMOND study, which illustrated that even in people with estimated GFR below 45 that the use of patiromer as a potassium binder could provide greater opportunity for maintaining the use of mineralocorticoid receptor antagonism on top of renin-angiotensin-system blockade in people with heart failure and reduced ejection fraction.

Not only was there greater opportunity to use MRA and RAS blockade together, but there was also evidence of safety, and no evidence of attenuation of the benefit of maintaining serum potassium levels in a desirable range, even in people with a reduced GFR. And this was, again, most apparent in people the lower the GFR. So, it is quite clear now that we have opportunities to mitigate hyperkalemia quite effectively.

So, I think this is an exciting time. And, Dr. Desai, you were mentioning earlier about cardiovascular medicine. I mean, quite clearly, heart failure and a reduced ejection fraction is such a serious illness that any opportunity we have to get patients on proper therapy earlier in the course of disease is much, much preferred.

**Dr. Desai:**

I think that's such an important point, and more and more of our patients that have heart failure and reduced ejection fraction also have other comorbidities like diabetes, and chronic kidney disease, and other cardiovascular diagnoses. And so, the profile of the patients

that we're seeing really is one where there is a heightened or increased risk for developing hyperkalemia. To your point, the evidence to support guideline-directed medical therapy for our heart failure patients is now overwhelming.

And I think it's really on us, as sort of the clinical community now, to think about the important role of potassium binders to enable and facilitate the use of these highly effective therapies. And so, I think the DIAMOND data, amongst others, are so helpful to kind of guide clinical practice and decision-making.

**Dr. Weir:**

Ellie, do you have anything to add to what we just heard from Nihar?

**Dr. Kelepouris:**

I think that interprofessional care models are really very important in achieving these goals. There's cardiorenal clinics that are becoming more and more important in bringing both cardiologists and nephrologists together in the same space with the patients so that we can both plan an approach for not only heart failure and CKD but other comorbidities associated with hyperkalemia.

And what we shouldn't forget is the patient's voice. The patients want current state-of-the-art treatments for heart failure and chronic kidney disease, and our ability to provide those really, in a collaborative space, I think, is very important.

**Dr. Weir:**

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Matthew Weir, and I'm here today with Dr. Ellie Kelepouris and Dr. Nihar Desai. We're discussing hyperkalemia management plans for patients with CKD while incorporating evidence-based potassium binder strategies.

**Dr. Weir:**

So, Nihar, you specialize in cardiovascular medicine. Obviously, patients with heart failure and reduced ejection fraction have a very serious, in a sense, timeline for their progression of disease. They're on multiple medications. Discuss with us a little bit about the safety of utilizing various potassium binders in these types of patients. And obviously, the opportunity to enhance earlier use of guideline-based medical therapy in these types of patients.

**Dr. Desai:**

When we think about the two different potassium binders, SZC and patiromer, it is important to note that there are some differences in terms of the mechanism of action. Specifically, the exchange cation, obviously being sodium for SZC and being calcium for patiromer.

And, thinking about the care of heart failure specifically, I think there was always some concern on the safety side for exchanging the potassium for sodium. And what that might mean for patients that have heart failure or other related clinical syndromes.

So, what we saw, in some of the earlier experience with SZC, was an increase in the risk of edema events. And that is, obviously, something that's included in the label for that therapy, not there in patiromer, because there you've got calcium being exchanged for the potassium.

But even more recently, we've seen in some clinical trials and also in some complementary real-world studies, now an increase in heart failure events and urgent heart failure care with SZC relative to patiromer. And so, think what that means for us: I mean, there haven't been any head-to-head trials, so we don't have that level of evidence to kind of guide care.

But I think we are seeing some signals now, both in randomized data and in non-randomized real-world data, that do show a potential difference between the two potassium binders that are out there. And when we think about our patient with heart failure, we do think that that's an important consideration for all of us to take into account as we think about how to optimize their regimen.

Hyperkalemia is commonly something that comes up for us. And so, as we think about options that we have available across the two different potassium binders, I think these safety data and other data I think can be integrated into our decision-making as well.

**Dr. Weir:**

Well, thanks, Nihar. I think that's very helpful. Any other thoughts, Ellie, on this topic?

**Dr. Kelepouris:**

I agree with Nihar. The guidelines state that we have to be very careful about, in the case of edema, optimizing diuretic use because the use of diuretics at high doses really can precipitate, particularly when RASi optimization is being introduced into the patient care; you may precipitate renal insufficiency, further hyperkalemia, and an acute rise in the serum creatinine. That would lead to discontinuation of the RASi or the MRA. So, it's really a vicious cycle.

And the other important thing to remember is that regular potassium monitoring is really important and that the potassium treatment should be individualized based on patient's profile.

And also, diabetes because patients with preserved renal function or GFR that is above 45 ml per minute, like aldosterone in some cases, and have a tendency to hyperkalemia. So, every patient is different, and treatment paradigms really need to be put in place for individualized patient care.

**Dr. Weir:**

Well, thanks, Ellie. And I want to emphasize that these newer potassium binders are very well-tolerated, they're safe, can be utilized once a day. There are recommendations to separate it from other medication by a few hours, just for safety, to make sure there's no risk for interfering with absorption. But I think these are all very important opportunities to move forward: to use guideline-based medical therapy.

Well, this certainly has been a productive and fascinating conversation. But before we wrap up, I'd like both of you to provide a final, kind of single overriding communication take-home message for clinicians so that they'll better be able to really optimize managing hyperkalemia in clinical practice.

Ellie, why don't you go first?

**Dr. Kelepouris:**

I think the time is right, Matt, for clinicians to come together as a group. And address a new iteration of the guidelines maximizing best practices to incorporate the new second-generation potassium binders so that lifesaving therapy, cardiovascular and renal saving therapy, in the form of MRAs and RASi blockade really can be continued in the treatment course of patients and not discontinued. I think these are really important issues.

**Dr. Weir:**

Nihar? Thoughts?

**Dr. Desai:**

Yeah, Matt. I think Ellie certainly said it really well. I think maybe, to add, I would just say we have to resist the temptation to down-titrate or discontinue highly effective therapies. But if hyperkalemia becomes an issue for a patient, that we have highly effective, safe therapies available as potassium binders to facilitate and enable the use of these other really effective, really important therapies.

And so, working together, I think we know what's in the best interest of our patients, and now it's really on all of us to now implement what the evidence would suggest is.

**Dr. Weir:**

Yeah, and I agree, Nihar. I think we have to avoid clinical inertia. I think we have to be proactive about mitigating hyperkalemia. I think we have to realize and develop some clinical experience so we can do the right things for our patients.

I think doing the right thing earlier on, preferably with guideline-based medical therapy, will make a difference in terms of cardiorenal disease progression and, ultimately, survival.

So, unfortunately, that's all the time we have today. I want to thank our audience for listening in. And thank you, Ellie and Nihar, for joining me today and sharing with us all of your valuable clinical experience and insights. It was great working with you today. And I just wish you a very best and safe experience moving forward and appreciate very much your opportunity to work together today.

**Dr. Kelepouris:**

Thank you, Matt.

**Dr. Desai:**

Yeah. Thanks again, Matt.

**Announcer:**

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