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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

New Perspectives in Managing HF and HK – The Cardiorenal Angle

Announcer:
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Dr. Kosiborod:
RAASi [renin-angiotensin-aldosterone system inhibitor] therapy is a crucial component of heart failure management. These medications also induce clinical improvement in patients with chronic kidney disease [CKD], diabetes, and ischemic heart disease. However, RAASi therapy is associated with adverse events such as hyperkalemia, and the risk of hyperkalemia is even higher in patients with chronic kidney disease and can lead to increased risk of hospitalization and death. It is this concern of developing hyperkalemia that often leads to clinical delay and suboptimal dosing of RAASi in patients with heart failure with reduced ejection fraction [HFrEF]. So how can we simultaneously maintain optimal RAASi treatment and manage hyperkalemia in our patients with chronic kidney disease in heart failure?

This is CME on ReachMD, and I'm Dr. Mikhail Kosiborod, cardiologist at Saint Luke's Mid America Heart Institute in Kansas City, United States.

Dr. Stack:
And I'm Dr. Austin Stack, a nephrologist from University Hospital in Limerick in Ireland.

Dr. Kosiborod:
So, Austin, let's answer this important question by going over a patient case. Let's say we have a 50-year-old female patient with a history of heart failure with reduced ejection fraction due to ischemic cardiomyopathy, ejection fraction of 37%, and also chronic kidney disease with a EGFR [estimated glomerular filtration rate] of 38. The patient's medications currently include 40 mg of furosemide twice daily, 20 mg of lisinopril, 12.5 mg of carvedilol twice a day, and 10 mg of atorvastatin. Her vitals are stable, but you notice that her recent laboratory evaluation shows a potassium level of about 5 mEq/L.

So, what are the clinical considerations in a patient like this when prescribing RAASi, and what might contribute to the clinical hesitancy and suboptimal dosing we so often see in practice? Because one could certainly argue that this patient is not currently receiving optimal guideline-directed medical therapy [GDMT].

Dr. Stack:
So, Mikhail, this is a common challenge in clinical practice where we see the need to optimize heart failure therapy in a patient with coexisting chronic kidney disease. I think there's 3 important considerations. First is the need to optimize evidence-based and guideline-directed treatment. This patient has heart failure with reduced ejection fraction of 37%, and the current guidelines recommend that this patient should be on multiple medications to improve clinical outcomes: a beta-blocker, an ACE [angiotensin-converting enzyme] inhibitor or an ARNI [angiotensin receptor neprilysin inhibitor], an MRA [mineralocorticoid receptor antagonist], and an SGLT2. That's hugely important.

The second issue which might be causing concern to clinicians is the serum potassium and the level of kidney function at 38%. This patient has CKD stage 3. There is impaired kidney function, reduced excretion of potassium, and that serum potassium of 5 can be pushed up with the addition of an MRA to levels that might be concerning and may lead to worse outcomes like cardiac arrythmia or cardiac arrest.

And the third consideration is one, I believe, of a clinician inertia. And this often leads to hesitancy in prescribing and underdosing and can lead to serious consequences. Under-prescribing and underdosing is common in patients with heart failure in the United States and indeed globally. There is down-titration and discontinuation of therapy, certainly among patients with mild to moderate hyperkalemia, and this most certainly leads to increased mortality. In patients who are on suboptimal treatment, there's a doubling of mortality, and if you stop RAASi therapy, there's almost a tripling of mortality. I think this is what we need to tackle in today's discussion.

Dr. Kosiborod:
So these are great points, Austin, and I guess it's very well documented in a number of registries both sides of the Atlantic, in the US as well as in Europe, that a large proportion of patients with heart failure with reduced ejection fraction are in fact not receiving optimal guideline-directed medical therapy, whether you look at optimal dose of ACE inhibitors, ARB [angiotensin receptor blocker], or ARNI [angiotensin receptor neprilysin inhibitor], whether you look at use of MRAs and optimal doses of MRAs as well other guideline-directed therapies such as SGLT2 inhibitors, as you mentioned. The SGLT2 inhibitors, of course, a relatively recent entrant, but we know those are underused as well.

So, let's just talk for a second about at which point one should be concerned about hyperkalemia. And there is some difference, perhaps, between my specialty, cardiology and how cardiologists perceive the risk of hyperkalemia and what is the thresholds at which they get concerned, and the nephrologist, because you, of course, and folks in your specialty, Austin, see it a lot more frequently than we do and perhaps are a little bit less anxious about certain potassium levels. So, you know, we have kind of this interspecialty discussion here and I think, especially for my cardiology colleagues, it would be important to hear from you about at what threshold should cardiologists or should individuals taking care of these patients become concerned?

So, you know, just to make it real here for this case, let's say we were to initiate this patient on an MRA, spironolactone or eplerenone, for example, for heart failure and reduced ejection fraction, and let's say we get a potassium level in a couple of weeks and, you know, you start at 5 mEq/L and let's say now it's 5.5. Is that the threshold where we now should start getting worried? And if so, what should we do about it?

Dr. Stack:
Mikhail, I think that's a great question, and as you rightly pointed out, I think there's some slight difference between the nephrology camp and the cardiology. And I think we need to meet in the middle and really come to consensus. I do understand that from a heart perspective that cardiologists are concerned when the potassium is above 5.0, above the, really, the upper limit of normal. And, you know, rightly to be concerned because these patients are high-risk cardiac patients, there's ongoing fluctuations, serum potassium, and they've got a great propensity for cardiac dysrhythmias. So, I do think they're right to be concerned with a lower threshold than the nephrologists. Yes, in nephrology we're used to dealing with hyperkalemia. We do know there's an adaptation with worsening kidney function, there's a number of physiological responses that prevents that serum potassium from causing serious arrythmias. However, I'm in favor of, in this particular stage, the cardiology perspective. I believe we need to be concerned when there's persistent potassium values above 5 mEq/L, particularly in the presence of chronic kidney disease and on RAAS inhibitor therapy. So, as kidney function goes down, there is impairment of potassium excretion, there's a risk of acute kidney injury, and any external event, whether it be further blockade of the renin-angiotensin system, a reduction in perfusion can actually push that serum potassium level up to levels that could potentially cause morbidity and even mortality.

So, I would be in agreement that potassium levels above 5 are concerning, certainly where we want to initiate or upregulate or optimize the dose of therapy, particularly treatments that have major impact on survival and in reduction of hospitalization. So, my strategy would be, really, a normalization of potassium in patients with heart failure and chronic kidney disease. I don't think we should dance on the edge because of this propensity for cardiac dysrhythmias and sudden death. And as you may know, Mikhail, in our kidney program, when we start a patient on an ACE inhibitor who's got chronic kidney disease, at the time we start that, we automatically say to put patients on a low-potassium diet. It's immediate. It's kind of unconditional to ensure and to prep them of the risks of ACE inhibitors causing hyperkalemia and the risks of hyperkalemia therein.

Dr. Kosiborod:
For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Mikhail Kosiborod and here with me today is Dr. Austin Stack. We're discussing the impact of suboptimal RASi treatment in response to hyperkalemia and how clinicians can better approach the care of their patients with heart failure and chronic kidney disease.

So, Austin, just to chime in here, I think there is a fair amount of controversy whether the potassium levels, you know, between 5 and 5.5 or even sometimes 5.5 and slightly higher than that, up to 6, are truly a marker or a cause of adverse outcomes. There is no question that those patients have high event rates, things like hospitalizations and death. And we know that despite hyperkalemia, if you look at HFrEF trials, those patients that develop hyperkalemia but they're receiving MRAs still have lower risk of heart failure events, for example, than those that were randomized to placebo, for example, in the EMPHASIS trials, with eplerenone. So, you know, trying to figure out how to keep the patients on optimal GDMT and at the same time reducing the risk of hyperkalemia is really, really important.

Coming back to this question about what do you do, maybe I'll leave the last word to you in terms of what are our treatment options? Do we have an additional way of managing these patients that is not just simply stopping or down-titrating RAASi and MRA specifically? Because we know at least from an epidemiologic standpoint that those patients that have their treatment dose lowered, or medications discontinued, don't tend to do very well.

Dr. Stack:
Absolutely, Mikhail, and I think you hit the nail on the head. I think when we're talking about optimum management, I think we need to bring potassium into the equation at the same time as we're optimizing and dose optimizing RAAS inhibitor therapy, and we've got a number of options. So, I suppose in this particular case where, you know, we would like to add an MRA to the patient like eplerenone and titrate it up, we are concerned that the potassium is 5 and certainly has a propensity for increasing over time. And this is where I would like to introduce a potassium binder that's effective and that has proven efficacy, one, in both lowering serum potassium, number two, keeping it within the normal range, and at the same time, allowing us, the nephrologist or the cardiologist, ensuring our patient is on the optimal dose of RAAS inhibitor therapy.

So, we have new medications like patiromer or sodium zirconium cyclosilicate which have been demonstrated in clinical trials, some led by yourself, that they're effective in lowering serum potassium, they have a predictable effect, and they have a low risk of side effects. So, I think times have changed, in terms of our armamentarium to control this problematic hyperkalemia that we typically see in patients with chronic kidney disease and those patients with low GFR. I think now we have medications that can allow us to expand the therapy to make sure that our patients are on guideline-directed optimal therapy as per the recent ESC [European Society of Cardiology] guidelines in 2021. We talked about the benefits of beta blockade, ACE inhibitor, MRAs, and SGLT2. All these are life-extending therapies. They reduce hospitalization risk, they extend patient survival in patients with heart failure, and I think we have to do the right thing in managing our patients. I think we need to try and avoid this stop-start phenomenon, which is seen for many, many years, and now we have a new addition to the kit with these novel potassium binders.

Dr. Kosiborod:
So, with that, I think this has been a fascinating conversation. Before we wrap up, can you share with the audience kind of what your take-home message is and if there is anything you would like to add to what I just mentioned?

Dr. Stack:
Yes, Mikhail, I think, you know, when we look at the current landscape in 2022 and see that patients with heart failure and chronic kidney disease, they've got huge risk of hospitalization and death. And I think we can do better in enabling them to live longer and healthier lives. There are proven treatments that work: beta-blockers, ACE inhibitors, MRAs, and SGLT2 inhibitors. Hyperkalemia should never be a barrier to optimal care, certainly for these patients.

Dr. Kosiborod:
Right, and I think, with that, I will thank you very much for your time today. As always, a pleasure to be with you and look forward to additional opportunities to discuss this important topic in the future.

Unfortunately, that's all the time we have, so thank you very much for joining me and thank you, Austin, once again for your time and sharing your valuable insights. It was great speaking with you today.

Dr. Stack:
Mikhail, thank you very much indeed and, again, thanks to our audience for joining in.

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