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Optimizing RAASi Therapy: The Role of Personalized Medicine

Announcer
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Dr. Bakris:
Electrolyte disturbances can occur frequently in patients with heart failure. Of particular concern is hyperkalemia, which is associated with an increased risk of hospitalization and death. The incidence of hyperkalemia is further elevated in patients with chronic heart failure, and especially in those with chronic kidney disease. It is this concern of developing hyperkalemia that can often lead to clinical delay and suboptimal dosing of RAAS inhibitors in these patients. So what can we do for our patients who have heart failure and chronic kidney disease to ensure they receive optimal RAAS inhibitor therapy?

This is CME on ReachMD. I'm Dr. George Bakris, and I'd like to introduce Dr. Giuseppe Rosano.

Dr. Rosano:
Hi, George. Thank you, it's a pleasure to be here.

Dr. Bakris:
So, Giuseppe, let's approach this topic by first discussing a patient case. Let's say we have a 48-year-old male patient with a history of heart failure with reduced ejection fraction of 38% and chronic kidney disease with a GFR of 40 mL/min. Medications include 50 mg of furosemide twice daily, 20 mg of lisinopril, 10 mg of atorvastatin, and 81 mg of aspirin. Vitals are stable, but his potassium level is around 5 milliequivalents/liter. So our mission is to pursue guideline-recommended dosing of foundational heart failure therapy in this patient.

So, Giuseppe, can you give us an overview of your approach for this patient? And how can we manage his potassium levels and protect him from further development of hyperkalemia?

Dr. Rosano:
Yes, thank you, George. My approach today, in a patient with that, after SGLT2 inhibitors, recheck his potassium levels and try to introduce an MRA like eplerenone or spironolactone and recheck his potassium levels and then take it from there.

Dr. Bakris:
Okay. Very good. You know, it's important – one of the things that we didn't talk about is appropriate diuretic dosing for level of kidney function. And it's very clear, with the exception of chlorthalidone, which we now know is very effective in people with stage 4 CKD, going down to GFRs in the 20s, that loop diuretics are needed.

And so what is your opinion of torsemide, which is longer acting, versus furosemide, which is shorter acting, even though you're giving it BID? I mean, clearly there's a role there. So what do you think?

Dr. Rosano:

Yeah, I think that the data's out there. I mean, of course, when we discuss about differences, there are statistically different, and we need to test individual patients. That is an option. Start on also torsemide and change to furosemide for torsemide, as you suggested, and then recheck his potassium after having restarted also the MRA.

Dr. Bakris:
So this is an important point, because you can't just put people on RAASi therapy. You have to have them at a maximal tolerated dose because that's what's used in the trials. And so one of the things that I think a lot of people are not aware of is, what are the risk factors for developing hyperkalemia? And there's basically 2. One is a GFR below 45 and a potassium greater than 4.5 when you're already on an appropriate diuretic for therapy. If those 2 things are present, it's not that you shouldn't give RAASi therapy, it's that you should monitor the patient a little more closely and titrate the dose up effectively.

So, Giuseppe, what do you think about that?

Dr. Rosano:
I think that is appropriate. I mean, we have a sort of a different approach, like if you have patients with, say, potassium levels which are just around 5, and then you need to up-titrate the RAASi therapy, which European Society of Cardiology suggests, to give a potassium binder and up-titrate the RAASi therapy, whether that is just the introduction of an MRA, whether is the up-titration of the dose of the MRA and the ACE inhibitors. So that is the guidance we have given. Of course, we are still in a phase where we don't have clear, scientific evidence, but at least with the potassium binders, that will facilitate our work in increasing the RAASi therapy and get to a target dose of RAASi.

Dr. Bakris:
Well, Giuseppe, we do have some data, and that is that both the new potassium binders that are available do have 1-year daily dosing data that they're safe and well tolerated and maintain a reduced potassium. So the days of the SPS are over, and we do have better agents that are there, and there is a study going on now in heart failure and HFrEF looking at mortality outcomes with the use of a potassium binder facilitating spironolactone therapy. So that data, hopefully, will be available within the year. So we'll have some outcome data in the context of that, too. So this is, I think, important to keep in mind.

I think the big thing that people get scared of is they give a RAAS blocker, and it's not just that the potassium is going to go up, but along with that, the creatinine is going to go up, and people get scared of that. Let's be clear on one thing: acute kidney injury – and I'm saying this as a nephrologist – acute kidney injury needs a 50% increase in serum creatinine, and if you don't have that, you haven't caused acute kidney injury. You've reset the kidney to work at a lower level; it is going to be more volume sensitive. So those are important factors to keep in mind. But you didn't cause any kidney injury, so there's no need to be stopping these agents for the – at least in the US, they're stopping at the drop of a hat. And it's a real problem, and I don't know if it's fear of lawyers or lack of understanding of physiology or both, but there is really a lot of suboptimal heart failure therapy that's going on. I mean, I don't know. How is it in Europe?

Dr. Rosano:
Yeah, you're absolutely right. This is something that we put in writing, into the latest guidelines on the management of heart failure. The European Society of Cardiology and the Heart Failure Association. So basically, if we don't see more than 50% of an increase in a creatinine or it doubling or a significant reduction in eGFR, then there's no need to stop any medications and no need to stop the RAASi therapy. So absolutely, in line with what you just said.

Dr. Bakris:
Let me ask you another related question. If somebody comes into the ED with an acute hyperkalemic episode – obviously, they're coming in; they didn't know they had hyperkalemia. It's measured, and let's say it's 6. Is there a role for potassium binders in that setting, or is it just in the chronic acute management?

Dr. Rosano:
No, we use it in the acute setting together with all the other interventions, and the reason being that you have a faster normalization of potassium, and then it's an easier transition into the chronic therapy, especially that is efficient with recurrent episodes of hyperkalemia. A patient that has already had a previous episode of hyperkalemia where you foresee that you have to keep them on a chronic therapy with the potassium binder, that it would be the best way to start the medication, have an immediate effect, and bridge towards the chronic.

Dr. Bakris:
So that's an important point. So if they're started in the acute setting, it's maintained in the chronic setting, and then the patient goes home on the potassium binder. Correct?

Dr. Rosano:

Yes, absolutely.

Dr. Bakris:
That's important.

Dr. Rosano:
Yeah, and from my point of view, I understand we have different thresholds to get worried about renal function, potassium, and for yourself maybe regarding other cardiac parameters, but when should the clinicians be concerned about hyperkalemia, and how should we manage this in patients with heart failure and reduced ejection fraction?

Dr. Bakris:
Well, I think, to be honest with you, if you look at – there's one very large study, in over 900,000 patients, and it looked at people with heart failure and kidney disease; heart failure, kidney disease, and diabetes; diabetes alone; et cetera. All the combinations. It turns out that if you have diabetes, heart failure, and chronic kidney disease, with GFRs below 45, that the potassium level should not be quite as liberal. It should be probably the cutoff is around 5, 5.2. And the reason for that is that they had a higher all-cause mortality. Now, maybe that's just because of disease burden and a number of other things. It's an epidemiology study, but nevertheless, those were the findings from a couple of years ago. However, if you had any other disease – if you had heart failure alone, if you had kidney disease alone – the traditional cutoff point of 5.5 for potassium is really, you know, there was no major difference there.

So I would say that there's a very nice metanalysis that was just published in one of the heart failure journals, and it was a well-done metanalysis. It basically showed that in heart failure, you're far more at risk of dying from hypokalemia than hyperkalemia. And having seen patients come into the emergency room with potassiums in the mid-7s that did just fine, I tend to believe that. So, I mean, those are my thoughts. What about you?

Dr. Rosano:
Yeah, I think it depends how rapid is the change in potassium. Say you have a patient that goes from 4.5 to 6. Probably I would be very worried. If you have a patient that is always around 5.6, 5.8, and comes in with a 6, 6.2, then probably I will worry much less. This is why I think we have to be wary of the importance of the fluctuations in potassium. And the new potassium binders are good, in a way, that they will avoid all this fluctuation, because we have to be pragmatic.

Dr. Bakris:
So I want to super, super, super-emphasize that point. It is the change in potassium, not the potassium level. That's a very important point. And so thank you for saying that.

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. George Bakris, and here with me today is Dr. Giuseppe Rosano. We're discussing a personalized approach to the management of heart failure and the implications of renal status and hyperkalemia.

Before we go on, one last issue. There have been now 3 reports in the literature with SGLT2s showing that SGLT2s, when used concomitantly with mineralocorticoid receptor antagonists, actually blunt the risk of hyperkalemia. I think it's important to know that while SGLT2s are part of the pillars of therapy for heart failure, they're partially enabling, as are the potassium binders, for use of MRAs and reduce your worry for hyperkalemia.

Well, this has certainly been an excellent conversation, but before we wrap up, Dr. Rosano, can you share a take-home message with our audience?

Dr. Rosano:
Before concluding also, what is important is the cardio-nephrology collaboration. And, I have to say, I'm very, very fortunate in my institute, where the cardio-nephrology clinic that is run together, and basically, we run this clinic, seated next door, and with us seeing nephrology patients with cardiac issues and our nephrologist colleague seeing our cardiac patients with renal problems and hyperkalemia. This has led to a reduction in the need for hospitalizations, and I think this is something that should be replicated wherever there's a good cardiology and nephrology collaboration.

Dr. Bakris:
I couldn't agree more. Let me just say that there's a couple of programs in the US. I have been actively involved in collaborating with the heart failure cardiologists for the last 10 years; in fact, we've published a number of things, and I've edited a book on this. So there's no question that the heart and the kidney are married, and just like any spousal relationship, if one is having a trouble, the other one's going to have trouble. So they try to help each other out, but it's an issue. So please try and set these up, because where they have been set up, people are getting better therapy. We haven't looked at outcomes yet, at least not in a major way, but clearly it's the way to go.

Well, unfortunately, that's all the time we have today, so I want to thank our audience for listening, and I want to thank Dr. Giuseppe

Rosano for joining me and sharing all of the valuable insights that he has. It was great speaking with you today, Giuseppe.

Dr. Rosano:
Thank you, it's been my pleasure, and I have enjoyed very much our conversation. I look forward to seeing you in person soon.

Dr. Bakris:
Yeah, absolutely. Thank you very much.

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