Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/optimizing-raasi-therapy-patients-hyperkalemia-role-potassium-binders/12767/

Released: 08/26/2021
Valid until: 08/26/2022
Time needed to complete: 15 minutes

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

Optimizing RAASi Therapy in Patients with Hyperkalemia: The Role of Potassium Binders

Announcer:
Welcome to CME on ReachMD. This episode is part of the Global Heart Failure Academy and is brought to you 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. Butler:
It is well understood that in the management of patients with heart failure, RAASi therapy is critical. We also know that hyperkalemia is quite common in these patients and that its presence often leads to suboptimal RAASi dosing, which results in poorer patient outcomes. So how, then, do we maintain optimal RAASi therapy and manage hyperkalemia in our patients with heart failure? This is CME on ReachMD and I'm Dr. Javed Butler.

Dr. Rosano:
And I am Dr. Giuseppe Rosano.

Dr. Butler:
Great. So let's get on with it, Giuseppe. Let's answer that important question by starting with a case presentation. So let's think about a patient that you and I see very frequently, a middle-aged patient with history of heart failure with reduced ejection fraction who's been hospitalized for decompensated, worsening heart failure. The patient has history of hypertension, diabetes, and chronic kidney disease. They were on optimal RAASi therapy, but they developed hyperkalemia in the past and, as per the guideline recommendations, their ACE inhibitor dose was reduced and their MRA dose was stopped. But now they come into the hospital with decompensated failure.

So my question to you is, how does suboptimal RAASi therapy impact outcomes for patients like this with heart failure?

Dr. Rosano:
This is very important question, Javed. First of all, we have to say that we may have patients where we see an acute, episodic hyperkalemia. So that is not a major issue. But then we have patients like the one you just described that has repetitive episodes of hyperkalemia that are chronic recurrent hyperkalemia, so more than 2 episodes per year. And this is frequent in heart failure because the ACE inhibitors, the MRAs, and the ARBs together with the comorbidities like diabetes and renal failure have an effect on potassium levels. And we know that from different studies like the EMPHASIS-HF that patients were receiving MRAs of significantly more frequent episodes of hyperkalemia. And in the EMPHASIS-HF, roughly 11% of patients had potassium greater than 5.5 whilst on an MRA. And if we look at patients with hyperkalemia on RAASi therapy, we see that from the different registries 30% to 35% of patients have more than one episode of hyperkalemia per year. Roughly 30% have an episode of mild hyperkalemia per year. And whenever these episodes occur, there is always a reduction in the dose of the medications. And we see that in the vast majority of cases, drugs are either reduced or discontinued. And in those patients where the drugs are discontinued, we can observe an increased mortality or rehospitalizations for heart failure, and this is more frequent in patients with heart failure and comorbidities.

Now, we have a lot of registry studies that have demonstrated that there are some predictors of discontinuation of MRAs. One of these is an episode of hyperkalemia. The other one is the low EGFR IH [immunohistochemistry] and the fact that patients are not seen into the

cardiology care. And we also have evidence from the CHAMP registry that included nearly 4,000 patients from primary care and cardiology, that in 30% to 35% of patients, ACE inhibitors, beta-blockers, ARNi are underdosed. And the European registry, the ESC-HFA long-term registry, has shown that patients with suboptimal doses of either MRAs or ACE inhibitors are at increased risk of mortality, morbidity, and rehospitalization.

So, this case is very pertinent as a reduction in ACE inhibitors and MRAs or the discontinuation of either of the two will lead to an increased risk of mortality and an increased risk of rehospitalizations.

Dr. Butler:
Well, thank you for those insights, Dr. Rosano. So hyperkalemia is a real problem in these patients because it can lead to a reduction of necessary therapies. What is the clinical evidence for the use of potassium binders in the management of hyperkalemia in these patients with heart failure?

Dr. Rosano:
So the potassium binders have been used and, up until now, mostly for the acute treatment of hyperkalemia. The most common drug that is used is the SPS that is used in patients with impaired renal function and hyperkalemia but can be used just for a few days. Now we have evidence that the two new drugs, patiromer and sodium zirconium cyclosilicate ZS-9, are effective in reducing potassium levels acutely and chronic. They have been used in patients with mostly with CKD. The patiromer in the PEARL and AMETHYST study demonstrated a very significant effect in reducing potassium levels within the first 24 hours, and the AMETHYST study demonstrated a very good long-term effect keeping the potassium levels within the normal range for 52 weeks.

Then patiromer has been also tested in patients with heart failure that were randomized to receive either placebo or patiromer and they were on a big round of spironolactone. And patients with heart failure receiving patiromer had less frequent episodes of hyperkalemia – actually, they never experienced hyperkalemia and had significantly lower levels of potassium compared to patients who were randomized to placebo.

As for the ZS-9 that was tested in the HARMONIZE study, that demonstrated a fast effect on reduction of hyperkalemia in the acute phase and was followed by a sustained effect of the 52 weeks with potassium levels that remained within the normal range. So basically now, we have 2 new drugs that can be used acutely but also that are very effective chronically, and therefore they can be used in order to optimize the RAASi therapy in patients with heart failure, heart failure and comorbidities, like patients with heart failure/CKD, heart failure/CKD and diabetes.

Dr. Butler:
For those just tuning in, you're listening to CME on ReachMD, and I am Dr. Javed Butler. And here with me today is Dr. Giuseppe Rosano. We are discussing the impact of suboptimal RAASi therapy in response to hyperkalemia and the role of potassium binders in acute and long-term therapy.

Yeah, so, you know, you really have highlighted some very important points. There are some advantages that we have with patiromer and sodium zirconium cyclosilicate, the new novel potassium binders, or SPS, you know, one is the issue of palatability. So, again, in the short term, if you are going to give somebody a therapy for one or two days, perhaps palatability is not that big an issue. But in the long run, that becomes an issue. GI tolerance is another big advantage; these drugs are much better tolerated.

But let me ask you a question about long-term management with these potassium binders. You gave some really good data about the short-term management of hyperkalemia, but then you also sort of mentioned about some one-year studies. So a couple of questions for you. One is, are there any subgroups of patients where this therapy doesn't work? Like, you know, maybe it works in patients without CKD but not CKD; without heart failure but not those with heart failure; or pretty much everybody that can develop hyperkalemia, these therapies can work? What are some of the considerations in the long-term management, and can you enable RAASi therapy with these?

Dr. Rosano:
I mean, basically since drugs are working into the guts, there are no different comorbidities that may reduce the effect of these drugs. All the long-term studies have clearly shown that they are very safe. There were some issues with the higher dose of ZS-9 that has been suggested to induce some sodium retention. But that occurred for doses that I used for the acute and not for chronic. There's no drug-to-drug interaction. So they can be safely used and used continuously. And as you as you've mentioned, palatability is very important, especially if you use it chronically. And if you use it chronically, I mean, these basically taste like water. They have no significant aftertaste.

What is important is that we have to look at these drugs as we do for drugs that are used as enablers. Like the enablers that we use for cancer. I mean, if we have a patient with cancer that has nausea, then of course we use an antiemetic. And we don't ask ourselves

whether they have an effect on long-term mortality or morbidity. We know that if we use low dose of RAASi, there is an increased risk of mortality, an increased risk of morbidity. Therefore, the way we should look at these drugs is like the enablers, and the enablers will basically favor the use of a higher dose of RAASi therapy and most likely [have] an effect on mortality and morbidity. I wouldn't be interested too much into having data on mortality and morbidity because we do know that lower doses of RAASi's are associated with an increased mortality and morbidity.

Dr. Butler:
Yeah. So we're very thankful for those words of wisdom. And as you mentioned, we actually have data on drug-drug interaction, not a big problem with many of the drugs. But rather than remembering which certain drugs may interact, actually the guidelines are actually pretty simple. And that is with sodium zirconium cyclosilicate, which used to be called ZS-9, and patiromer, it's about a 2-hour window before and after for sodium zirconium cyclosilicate and a 3-hour window before and after patiromer that you're asked not to take any other medications. But that really facilitates that you can easily take twice-a-day medications. You sort of take one in the morning, take your binder in the afternoon, and then take other medications in the evening. So it's very easy to use these medications in the long run as well.

Well, this has certainly been a fascinating conversation, but before we wrap up, Dr. Rosano, can you share your one take-home message with our audiences?

Dr. Rosano:
It is very important to maximize RAASi therapy as much as possible. We know that suboptimal RAASi therapy is associated with an increased mortality and morbidity, and now we have drugs that can enable the use of RAASi therapy, can enable the up-titration of these drugs, and therefore we should be using them whenever is needed in patients with chronic hyperkalemia in order to avoid episodes of hyperkalemia. But also in those patients where we need to up-titrate the RAASi therapy and the potassium level is borderline high.

Dr. Butler:
Very well stated. And I would add to that that clinicians are very used to thinking about acute hyperkalemia when the potassium levels are high. We don't think about chronic hyperkalemia and its consequences as much as we should because what ends up happening is that, very much like the patient we discussed, we stop RAASi therapy, potassium levels come down, but potassium levels led to compromising RAASi therapy, further worsening the disease. And that actually is a complication of hyperkalemia, but we don't necessarily tend to link these two things and think about hyperkalemia as a chronic disease with chronic consequences.

Well, unfortunately, that's all the time we have today, so I want to thank our audience for listening and thank you, Dr. Giuseppe Rosano, for joining me and for sharing all your valuable insights. It was great speaking with you, today.

Dr. Rosano:
Thank you for having me.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Medtelligence.

To receive your free CME credit, or to download this activity, go to ReachMD.com/HeartFailure. Thank you for listening.