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Potassium Binders: Safety Comes First!

Announcer:
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Dr. Kelepouris:
This is CME on ReachMD, and I'm Dr. Ellie Kelepouris. Here with me today is Dr. Javed Butler. Welcome, Javed.

Dr. Butler:
Glad to be here.

Dr. Kelepouris:
Javed, when clinicians think of using potassium binders, what's the clinical evidence in terms of safety, efficacy, and administration requirements that they should be evaluating?

Dr. Butler:
Yeah, I mean, there is a plethora of evidence. I mean, if you look at number of clinical trials and then real-world registry data that have come out over the years, we've been at it for almost a decade now. So let me see if I can summarize some of the lessons learned from that.

So one, if you look at the classic potassium binders like SPS, the problem here is that we don't have large outcomes trials. We don't have trials following the patient in long term. These are relatively very few patients. But the biggest issue with things like SPS is just their tolerability. GI intolerance, but not only sort of nausea, vomiting, constipation, diarrhea sort of things, but also some serious side effects like colonic necrosis have been reported.

They're really not options—SPS, CPS—for like long-term management. And what we are really concerned about, long-term enablement and continuation of RAAS inhibitors—ACE, ARBs, ARNIs, MRAs—in patient population in which these drugs are indicated. These are high-risk patients, but these are the very same patients that are at risk of hyperkalemia, and we either down-titrate the doses or restart the therapies, right? So we are now looking at it from a chronic management lens.

We have two really good options now. We have patiromer, and we have sodium zirconium cyclosilicate. So these are two therapies. We have trials with both of these agents in patients with hyperkalemia of all varying ranges, in trying to control hyperkalemia and bring the people back to normokalemia.

Then we have trials that have managed these patients for longer term, for maintenance of normokalemia. And then in real-world patients living their lives, doctors are doing whatever the doctors are doing, medications are being changed, the patients are in the real-world setting, eating and whatever their behaviors are, in long term, all the way up to a year, showing that you are very beautifully able to manage hyperkalemia, keep the patient in the normokalemic range while they are taking their RAAS inhibitors as well.

Moreover, a few other things that we have learned. So all of the patient phenotypes where you are concerned about hyperkalemia—so patients with heart failure, patients with diabetes, older patients, patients with CKD, patients at higher doses of RAAS inhibitor—all of those were represented in these long-term studies showing that potassium can be managed very stable in the long run in these patients.

There is a dose-dependent effect. The higher the dose that we use, especially in people with acute hyperkalemia, the more is the potassium lowering. But overshooting it and getting into hypokalemia is very rare. Usually you come to about the middle 4, and then you kind of maintain the levels there.

There are detailed drug–drug interaction studies that were done. And on the basis of that, there is a little bit of a window—2 hours with sodium zirconium cyclosilicate and 3 hours with patiromer—that when you take these binders, 2 or 3 hours window around that dose, not to take the other medications. But there are no contraindications.

Now, can you really differentiate between the two drugs? Yeah, there are subtle differences. So for instance, patiromer, it exchanges potassium for calcium and works primarily in the colon. So it may take a few extra minutes before it starts binding potassium because it has to go all the way down to the colon. But it is not absorbed.

Sodium zirconium cyclosilicate, that is also not absorbed but tends to work across the GI system, so maybe acts a little bit faster. But on the other hand, though, it exchanges sodium for potassium. And sodium load does become a little bit of a concern, especially in people who are sicker with heart failure or those patients needing higher doses of sodium zirconium cyclosilicate. So there are some data in terms of fluctuations in natriuretic peptide or lower extremity edema. So those are some of the concerns that we have.

But overall, I would summarize by saying that we have data in patients who are hyperkalemic, data for maintenance of normokalemia, data with all sorts of combinations of comorbidities and doses.

I will end by saying one more thing, and that is one beautiful message that we have seen from these longer-term studies that have lasted all the way up to a year—that just because you have controlled potassium levels for a year, that does not mean that the patient phenotype has changed. And what we see is that when the study ends and you stop the potassium binder, potassium levels start going up after that. So these are long-term treatments. And if you're going to stop potassium binder and we have enabled RAAS inhibitor on the basis of potassium binder, be careful in monitoring their potassium levels, and perhaps it's just best to use these therapies long term.

Dr. Kelepouris:
Thank you. I mean, those are excellent comments and a great summary of the findings so far. I would reiterate that it's very, very important to recognize that although low potassium diets are really prescribed for patients with hyperkalemia, in the absence of potassium binders, they really don't work effectively. So if you are going to stop the potassium binders, counting on a low potassium diet alone is really not going to keep patients in potassium balance where, if you're looking for a potassium level of close to 4 or mid 4s, as you said.

Dr. Butler:
Ellie, you make such an important point about the low potassium diet, and I think that's a real problem. Look, low potassium diet is really, really important as an adjunct to the other medical therapy that you're giving. But the two places where we are really concerned right now. One is the potassium levels are high, to bring them down, and obviously that's not the role of low potassium diet; it's for maintenance. But also, it is one thing that somebody does not have hyperkalemia, you're not changing the medication, and you're trying to ask the patient to take a low potassium diet. It's a completely different thing when you're actually enabling RAAS inhibitor therapy and expecting the patient to take a low potassium diet 24/7, 365, and avoid the risk of hyperkalemia. That is just not going to happen.

So low potassium diet and recommendations are really important as an adjunct to medical therapy, but not as sort of the only thing.

Dr. Kelepouris:
And this has been a great discussion, Javed, but our time is up. Thanks, everybody, for listening.

Announcer:
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