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KDIGO Conversations in Nephrology: Approaches to RASi Optimization

Announcer:
Welcome to KDIGO Conversations in Nephrology. This episode is titled "Approaches To RASi Optimization." For disclosure information, please go to kdigo.org/podcasts. Here's your host, Dr. Roberto Pecoits-Filho.

Dr. Pecoits-Filho:
Hello and welcome to the KDIGO Conversations in Nephrology. I am Dr. Roberto Pecoits-Filho, Senior Research Scientist at the Arbor Research Collaborative For Health and Professor of Medicine at the Pontifical Catholic University of Paraná. On the program with me today to discuss approaches to the optimization of Renin-Angiotensin-Aldosterone System inhibition is Dr. Patrick Rossignol. Dr. Rossignol is a Nephrologist and Vascular Medicine Specialist. So certainly the perfect guest for our topic today. Patrick, welcome to the program.

Dr. Rossignol:
Thank you very much Roberto, delighted to be here.

Dr. Pecoits-Filho:
Patrick, it looks like as years go by, therapies that inhibit the Renin-Angiotensin System, or RASi as I'll refer to this from now on, they continue to be important tools in the management of patients with CKD. Still in the real world, clinicians struggle to align with recommendation. What is your approach to RAASi optimization?

Dr. Rossignol:
RAASi titration is indeed desirable roads of cardiorenal continuum as universally emphasized by international guidelines. This is true in Chronic Kidney Disease patients with or without hypertension as emphasized again by the latest 2021 KDIGO Guidelines on Blood Pressure Management in CKD. For instance, stating that RAASi S inhibitors or ARB should be administered using the highest approved dose that is tolerated to achieve the benefits described because the proven benefits were achieved in trials using these doses. This is also true in patients with heart failure on reduced ejection fraction as confirmed by the latest European Therapy Guidelines published August 2021.

Importantly, CKD mostly defined as GFR below 60 ml per minute per 1.73 square meters is a highly prevalent condition in patients with acute and chronic heart failure. Approximately one third, according to a meta analysis published some years ago, by Kevin Daman in the European Arginine into a certain of 57 studies comprising more than 1 million patients. In both settings, especially in elderly patients and in patients with diabetes, hyperkalemia was formed earlier toward RAASi optimization.

In the other setting we and others, we brought it that hyperkalemia is one of the main triggers of RAASi non-use, underdosing on discontinuation, thereby leading to decrease our patients for these [inaudible 00:03:16] agents on partly mediating, the observed association between hyperkalemia on poor outcomes in cardiorenal patients.

Dr. Pecoits-Filho:
Looking at the conversations in the nephrology and cardiology, it seems like the community has finally decided to approach the problem of hyperkalemia in a more of a proactive approach. Don't you think so?

Dr. Rossignol:
Yes, indeed. So let us do a 2021 KDIGO guidelines and Blood Pressure Management in CKD stated that hyperkalemia associated with use of RAASi can often be managed by measures to reduce the sodium potassium levels rather than decreasing the dose of stopping RAASi on that potassium restriction, discontinuation of potassium supplements, certain salt substitutes, hyperkalemic drugs. Adding potassium wasting diuretics and or potassium binders.

In CKD patients receiving RAASi we develop hypokalemia. The latter can be controlled with newer or potassium binders in many patients with the effects that RAASi can be continued as a recommended dose. Furthermore, the latest 2021 ESC guidelines stated that administration of the catering agents, patiromer or sodium zirconium cyclosilicate may allow Renin Angiotensin Aldosterone system inhibitor initiation or uptitration in the larger proportion of patients.

Dr. Pecoits-Filho:
That's really interesting, Patrick. So you were an experienced clinician and you probably treat patients with these therapies a lot in a daily basis. Can you provide our audience with your approach to monitoring measures in patient starting in long-term RAASi therapies?

Dr. Rossignol:
Well, it is universally acknowledged that creatinine and potassium must be adequately monitored in CKD on all of your patients. Why? The proper monitoring was unfortunately reported to be poor after Mineralocorticoid receptor antagonists initiation in heart failure patients both in the U.S. and in Europe. The latest 2021 clinical guidelines on blood pressure management in CKD stated that changes in blood pressure, some creatinine and certain potassium should be checked within two to four weeks of initiation or increasing the dose of a RAASi, depending on the current [inaudible 00:05:37] and serum potassium.

Furthermore, in patients at risk for hyperkalemia measuring serum potassium before at one to two weeks after initiation of RAASi is recommended. Patients should also be monitored for symptomatic hypotension, hyperkalemia and serum creatinine within two to four weeks after initiating or changing the dose of the drug with the time interval, depending on baseline blood pressure serum creatine and serum potassium.

Finally, the shorter time interval is indicated is a baseline serum creatinine is I, or some potassium is already I know more, or is there is a history of hyperkalemia, or an extra rise in serum creatinine with a blood pressure lowering or RAASi. As far as ESC guidelines are concerned, so [inaudible 00:06:44] ESC guidelines repeatedly stated that in heart failure on reduced ejection fraction. Firstly, after S individuals, ARB initiation were check blood chemistry. In other words, urea, BUN, creatinine, potassium one to two weeks after initiation and one to two weeks after final dose titration. Monitor blood chemistry, four months these are after. Serum Potassium monitoring is warranted in patients within reason, mineralocorticoid receptor antagonist, check blood chemistry to one onto four weeks after starting increasing dose on that eight on 12 weeks, six, nine on 12 months, four months these are after. [00:07:28] The close potassium monitoring is warranted under potassium lowering agent.

Dr. Pecoits-Filho:
For those just joining us. This is KDIGO Conversations in Nephrology. I'm Dr. Roberto Pecoits-Filho and I'm speaking with Dr. Patrick Rossignol on approaches to RAASi optimization. Patrick, the guidelines are providing a clear message in terms of the importance of keeping patients on this life-saving therapies. However, it's not really an easy task to optimize patients. And this requires a diversity of strategies, different phases of treatment, acute or chronic in the hospital or ambulatory. Can you provide some tips on how to optimize the therapies?

Dr. Rossignol:
Well, Roberto, it should be emphasized that as yet, no monitoring regimen has been prospectively evaluated in patients initiating potassium bromide agent for the treatment of hyperkalemia, the [inaudible 00:08:24], but from Peter Knight published a couple of years ago in pharmacological research, two or 17, we however suggested the following regimen based upon the experience in initiating these agents in the pivotal clinical trials on our own experience on RAASi, on diuretic management as a basis for discussion on frozen prospective evaluation. First serum potassium should be measured before initiation of a potassium-lowering agent, on should be above five minimal per liter on a non embolized blood sample. In patients without life-threatening hyperkalemia, it will be prudent to repeat the measurement on to confirm that serum potassium is truly above five minute per liter before initiating a potassium-lowering agent. One should also measure some magnesium, bicarbonate on assess when malfunction is the EGFR

Second, after initiating your potassium lowering agent, serum potassium should be measured within 48 to 72 hours on repeated at one week. If at one registrar potassium remains above five millimoles per liter, considerations should be given to increasing the dose of the potassium lowering agent on towards check some potassium, no liters, at one week later. Once the serum potassium is below five millimole per liter, it would appear reasonable to based upon the experience in the pivotal trials of procurement on SDC to measure some potassium at one months and then, every three to six months at regular follow-up visits. Importantly, anytime that the change in

electrolyzed stages is suspected, such as during an episode of diarrhea or vomiting or after each RAASi or diuretic change, serum potassium and creatinine should be remeasured on some monitoring sequence repeated.

Dr. Pecoits-Filho:
I'm sure that there are different regional realities and- but really the fragmentation of care and the problems with the communication between specialties that they care of the patients is really difficult. Don't you think? Why do you think this lack of communication exists, especially between cardiology and nephrology emergency medicine?

Dr. Rossignol:
Well, Roberto, in my view of the workload is certainly a measure of [inaudible 00:10:57], along with some inconsistencies between nephrology and cardiology guidelines, for instance, regarding [inaudible 00:11:05] to discontinue [inaudible 00:11:08] in the presence of reasoning and malfunction, or Atrial Anemia.

Dr. Pecoits-Filho:
And I fully agree with that Patrick. Well, any final advice to clinicians?

Dr. Rossignol:
Sure. Please don't hesitate to titrate RAASi as much as you can with monitoring creatinine and potassium closely and be ready to introduce a new potassium binder to enable RAASi as repeatedly demonstrated with [inaudible 00:11:35]. For instance on that trial, I was involved in the steering committee in patients with advanced chronic kidney disease on a resistant hypertension, but compared to placebo enables a more persistent choose as a [inaudible 00:11:50]. Spironolactone is the primary end point of this phase two trial.

Dr. Pecoits-Filho:
Well that takeaway in mind, I want to thank my guest Dr. Patrick Rossignol for joining me in discuss the different approaches to RAASi optimization, Patrick, it was great having you in the program.

Dr. Rossignol:
My pleasure Dr. Roberto.

Dr. Pecoits-Filho:
I am Dr. Roberto Pecoits-Filho. To access this and other episodes in these series, please visit kdigo.org/podcasts. Thanks for listening.

Announcer:
This episode was provided by KDIGO and supported by Vifor Pharma.