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KDIGO Conversations in Nephrology: Management of Dyskalemias

Announcer:
Welcome to KDIGO Conversations in Nephrology. This episode is titled: Management of Dyskalemias. 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, I'm a Nephrologist and a Senior Research Scientist at Arbor Research Collaborative for Health, and a Professor of Medicine at the Pontifical Catholic University of Paraná. Joining me to talk about the management of dyskalemia is Dr. Chuck Herzog, Professor of Medicine at the University of Minnesota and a Cardiologist at Hennepin Healthcare. Chuck, welcome to the program.

Dr. Herzog:
Thanks very much, Roberto. I'm very delighted to be here with you virtually.

Dr. Pecoits-Filho:
So Chuck, let's dive right in. Let me ask you a basic question. What is the definition you use for dyskalemia?

Dr. Herzog:
So it's a bit arbitrary and it's partially based on population sampling, but acute hyperkalemia is defined, and by the KDIGO group, to be greater than 5.0 millimoles per liter or above the reference range of the laboratory, if there is a reference range available, which to me is not terribly helpful as a standalone threshold. And I'd like to just review the KDIGO classification scheme related to hyperkalemia, which I think is a bit better. Hypokalemia has attracted a little less attention and it's arbitrarily defined as less than 3.5 millimoles per liter. In the KDIGO Miami Consensus Conference, which you and I both participated in, the group came up with a classification scheme that both reflects plasma levels and the presence or absence of electrocardiographic changes. So mild hypokalemia was defined to be 5 to 5.9, but at the same levels with ECG changes suggestive of hyperkalemia, would be defined to be moderate. And consistent with this, a 6 to 6.4 was defined to be moderate without ECG changes and severe in the presence of changes attributed to hyperkalemia, and any patient with a value of 6.5 or higher acutely would be considered to be severe acute hyperkalemia.

Dr. Pecoits-Filho:
You're an experienced and seasoned clinician and see patients with hypo- and hyperkalemia all the time, right, Chuck? And I wonder, what is the thing that you see as a biggest challenge in clinical practice, in the management of dyskalemias?

Dr. Herzog:
Roberto, I think the biggest challenge is being able to monitor and respond appropriately in real-time, both to hyper- and hypokalemia. When it's available, management algorithms, which are embedded in electronic medical records, can be helpful and they should be evaluated by each institution for the safety and efficacy for the platform being used on your own campus. Of course, many countries do not have electronic medical records, but you can do the same thing without an EMR using paper orders or even verbal orders. It just takes a little longer to implement and to carry them out, but the same algorithmic approach for treatment can be applied across the board no matter where you are. It's just the question of what the platform is.

Dr. Pecoits-Filho:

And what is the most important consequence of these episodes of hypo- and hyperkalemia that you see?

Dr. Herzog:
Well, ignore the non-cardiac ones, the most important ones are arrhythmia, both hyper- and hypokalemia can lead to lethal arrhythmic events, such as torsades de pointes degenerating into ventricular fibrillation in hypokalemia patients and also asystole in severe hyperkalemia. People with severe hyperkalemia, besides having asystole, can also develop ventricular fibrillation. In my personal experience, I would say, in the setting of hypokalemia, particularly in the intensive care unit or in acute illness, I think that it also contributes to other arrhythmic events, which are magnified by the comorbid conditions of whatever's going on with the patient, particularly, one of those arrhythmias is atrial fibrillation. So sometimes we see patients who come in with acute illness, the question comes up is, is the arrhythmia, in this case, atrial fibrillation, related to the low potassium levels or is it just a coincidence?

So in this type of setting, the normal range, which is defined as 3.5 or higher, 3.5 actually might be too low because from an electrophysiologic standpoint, the ideal serum potassium actually might be closer to 4.5 to 5.0, but this can be very hard to implement safely because if you think about clinical setting, there has to be a margin of safety on the upper end too, [inaudible] acute hyperkalemia. Practice, we sort of aim for a sweet spot and our own EMR driven algorithms, the sweet spot is probably in the range of 4.0 to 4.3. Totally arbitrary, but that seems to be a reasonable place to be because it gives safety on the high end, and I think it is associated with better results than just shooting for 3.5.

My own experience is that not unusual to replace people's potassium levels who come in with acute atrial fibrillation in the setting of an acute illness, you correct the potassium, and then they go into sinus rhythm. Now, whether that's causal or coincidental, it's very hard to determine that, but I have to say, that's just an observation that if I had a choice on where a potassium level's going to be in a hospitalized patient, it's probably going to be aiming a goal somewhere in the 4.0 to 4.2 or 4.3 range. Arbitrary, but pretty much experience-based.

Dr. Pecoits-Filho:
Well, thanks so much, Chuck. I really think that those tips are pretty useful in the daily management of these patients we see all the time. Chuck, you mentioned that being able to monitor and respond quickly to dyskalemias in real time is a special challenge for us clinicians, it sounds like you had something in mind.

Dr. Herzog:
Yes. I think you can divide it into two parts. First is appropriate treatment, which is probably actually the easier one because there are good treatment algorithms for acute hyperkalemia, and I would just refer the audience back to the KDIGO Controversies Conference document, which has a very nice flow diagram, which summarize evidence-based therapies. So hypokalemia has actually attracted less attention in the literature, and in my own institution, we have an EMR-based treatment algorithm, which actually predates the electronic medical record and we started with old-fashioned paper charts. This was literally a five-year project that I spent time working with one of our cardiology inpatient pharmacists, and the algorithm takes into account both the dose of potassium and the timing and frequency of monitoring related to real-time serum potassium, EGFR, concomitant medications affecting potassium levels, and type of IV access or ability to receive oral potassium replacement.

I've also encouraged clinicians dealing with patients, who are, particularly those treating patients with acute decompensated heart failure, where there's a fairly large diuresis and a concomitant kaliuresis, to use the urine output and spot urine potassium as a way of anticipating ongoing potassium replacement requirements. So two spot urine potassiums 12 hours apart, take the average and multiply times the 24-hour urine output, and you have a reasonable idea of what the patient lost in that 24 hour period of time and what they might perhaps would need in the next 24 hours. I do encourage clinicians to think about this process because I think it's inherently safer to be doing this in an algorithmic approach rather than to just to do ad hoc or potassium orders, where somebody has a low potassium and they in the middle of the night get a call and they say, "Okay, we'll just do the potassium, X amount of potassium." And that's not likely to be as safe or accurate in that procedure. So each hospital needs to have its own approach and hopefully, it's been tested too to make sure it works in the individual institution.

Dr. Pecoits-Filho:
Yeah, and I fully agree with you that the hypokalemia has not received enough attention despite being a big, big clinical problem. Now, remember, this generated interesting discussions in the Miami meeting during our KDIGO Controversies meeting on the management of hypokalemia. And by the way, just reminding our audience that the report of that meeting is available in a publication that came out on Kidney International and is free for access at the KDIGO website.

So for those tuning in just now, you're listening to the KDIGO Conversations in Nephrology. Today's episode is on management of dyskalemias. I am Dr. Roberto Pecoits-Filho and here with me is Dr. Chuck Herzog.

Okay, so let's shift to the other side of the spectrum of dyskalemias and talk about hyperkalemia. What are your thoughts about big challenges in patients presenting with high potassium levels?

Dr. Herzog:
Thank you, that's a good question. It's also a little more complicated. I think the most challenging issue is what I would refer to as the unexpected trajectory of acute hyperkalemia in hospitalized patients. James Wetmore and I recently published a paper in the American Heart Journal on hypokalemia and hyperkalemia in hospitalized patients at our own institution, using our electronic medical record. The paper covered five years of hospitalizations, 2012 through 2016, and we actually had at our disposal nearly a hundred thousand admissions where a serum potassium was done. Then to make this method a little more rigorous, we randomly picked one unique hospitalization at a patient-level so that we were not affected by survivor bias by having people with multiple potassium levels over different hospitalizations. So we had a sample of 47,000 unique hospitalizations over five years where a potassium value was available, randomly selected from all hospitalizations.

And in this study, 1.3% of those 47,000 patients had a potassium value of at least 6 or higher and a little over 4% had a potassium value of below 3.5. So it's not something that's frequent, but it's enough to be of concern. One of the things about the analysis which struck me as being quite important was that in some of the patients with hyperkalemia, there was an unusually rapid trajectory. And I would use the analogy of commercial aviation to think about this, where if a pilot does not realize how fast a plane might be descending and responds too late with dire consequences, the plane crashes because they actually didn't know how fast they were falling. The same thing sort of strikes me as being similar with the acute hyperkalemia example, where if the clinicians don't realize how fast the potassium value is rising, they will be caught unaware with very potentially dire consequences to the patient because they didn't have enough time to respond to the rapidly changing value and to start treatment.

I would refer the audience to the paper to take a look because it's fairly dense, but I think it's an interesting study because it's very difficult to construct these types of temporally driven studies without a good EMR. So please take a look if you have a chance. So the take-home message is potassium levels can rise faster than you might think.

Dr. Pecoits-Filho:
Is acute hypokalemia really only a problem for hospitalized patients, Chuck?

Dr. Herzog:
Well, no, not really. Of course not, but it is [inaudible] question. If we actually don't monitor outpatients closely, then acute or chronic hyperkalemia can cause out-of-hospital sudden cardiac death and how would we know that was the reason if we weren't actually monitoring them? So it may be more of a monitoring issue. There's also a widely held perception that I think is really unique to the nephrology world, that chronic hyperkalemia is well-tolerated, including the belief — and I say it's a belief, it's not really based on any publications — that a hyperkalemic patient with no ECG changes related to hyperkalemia is not a pressing clinical issue. I tried to actually look this up one time before the conference and I went back actually 50 years and I couldn't find a paper that actually verified this, so I would say it's a perception that really is not evidence-based.

So a couple of practical issues, we may not actually have ready access to the patient's baseline electrocardiogram anyway and left ventricular hypertrophy and other causes of repolarization abnormality, they confuse the issue of what is actually a normal electrocardiogram for the individual patient. Also, a single electrocardiogram is a snapshot in time, and what happens hours or even minutes might look different. So when we see a patient with a single ECG and a single lab value, we don't have the ability to see the trajectory of hyperkalemia prospectively. We don't know what's going to happen four hours in the future. So another issue unique to the nephrology world is conventional hemodialysis patients, who are hyperkalemic only at certain times, particularly after the long interdialytic interval on say Monday morning, if they dialyze Monday, Wednesday, or Friday, or Tuesday morning, if they dialyze Tuesday, Thursday, or Saturday. It's really a type of cyclic hyperkalemia with a rapid drop occurring during hemodialysis run and the large delta K, which occurs during the dialysis run, is also likely an incubator for certain type of arrhythmias, particularly paroxysmal atrial fibrillation.

So when the patient develops hyperkalemia, they may be at risk for other types of arrhythmias too, not just ventricular fibrillation, but there's also the issue of they have a high potassium and then they suddenly have a low potassium. This topic, by the way, is now the subject of a placebo-controlled randomized double-blind perspective trial in hemodialysis patients with chronic hyperkalemia. The trial is called DIALIZE-Outcomes. It has just started and I would, again, if anyone's interested, you can go to trials.gov to check it out, but it's testing the efficacy of a potassium binder versus placebo for reducing cardiovascular events in hyperkalemic hemodialysis patients.

Dr. Pecoits-Filho:
Chuck, as a cardiology, you probably do a lot of echoes in the evaluation of transplant candidates. Do you see particular challenges in that group of patients?

Dr. Herzog:
Great question, Roberto, because this is something that I like to rail about with my colleagues. They don't like to hear it because it's like certain things just go away. My biggest personal headache with outpatient hyperkalemia, because of my unusual practice, is in the setting of cardiac stress testing in kidney transplant candidates. So in the US, either are on dialysis or have an EGFR less than 20 to be transplant-eligible. Some of our patients may come from as far as 300 kilometers away, and we may not have recent lab testing for either electrolytes, including potassium, or even a baseline electrocardiogram.

And I might add that when it actually comes to the practice of doing stress testing, in the US at least, there are no societal guidelines related to what a potassium value should be for a stress test nor are there ones for hemoglobin or serum glucose, it's more don't ask, don't tell. So a not infrequent occurrence for me is when an outpatient shows up with ECG changes that are sort of nondescript, can't really tell if they might be new or old, and we don't have a recent potassium. So as you can imagine, trying to figure out if somebody has a potassium value in the mid 6 range, and this has happened to me on multiple occasions, it is not good for our workflow to have to deal with a patient with severe hyperkalemia and then try to manage them in the echo lab, because that's not what they're there for.

I did actually present one of these cases at ASN Kidney Week in 2019, so the topic is not totally unknown, but I would say it's something that's just another thing that people don't want to hear about because it just it complicates life and people don't want their lives to be complicated anymore than it has to be. So don't ask, don't tell has sort of been the informal recommendations for this particular issue, but as you can imagine, Roberto, I'm never comfortable with not asking questions and not answering questions.

Dr. Pecoits-Filho:
Now, do you have an opinion about the use of oral potassium binders in hospitalized patients and also in those in transition to outpatient care?

Dr. Herzog:
That's a real interesting and somewhat controversial question. If you look at the KDIGO diagram in the manuscript about the treatment of acute hyperkalemia, there is a suggestion of consider oral potassium binders. And I think it's a niche therapy in hospitalized patients, but we definitely have used it in our own institution and I'll give an example of where it might help. An episode occurs at three in the morning and you're doing everything else that works, including redistributive therapies. You still may have a problem where the trajectory of hyperkalemia puts you into very dangerous territory and you would like something to slow it down just a little bit, if possible. So why not just put the patient on acute dialysis? The answer is, well, three in the morning sometimes ... That's not a five minute procedure in a lot of institutions. In Minnesota, we have big snowstorms so sometimes the ability even to do acute dialysis might be affected by the weather and things like that in terms of availability of emergency technical staff. So the oral potassium binder might buy you a little time.

It's not going to prevent dialysis, it's not going to make the person necessarily normal kalemic, but it might buy a little extra time before you get into the lethal hyperkalemia range. There isn't much downside. So I think it's sort of a niche therapy by the clinicians and it's usually something you would do really in an acute setting. It's not instead of dialysis. Dialysis is still the main therapy for removing potassium from the body and it's going to be the mainstay of therapy for nephrology practice, but it might help be a little bit of a buffer to give the patient a little more time to get to the point where they can safely initiate acute dialysis.

Then sometimes the patient who develops acute hyperkalemia might transition to chronic therapy when they leave the hospital. So if the thought is that they're likely to be at risk for the episode again, then it makes sense to continue the therapy. But I think the bottom line is that these decisions have to be individualized at an individual patient level. I would say it's not routine practice to be giving patients in hospital oral potassium binders, it's kind of a niche therapy.

Dr. Pecoits-Filho:
Well, that's all we have for today. Thank you for listening and I hope you enjoyed the program. And thank you, Chuck, for joining me and sharing all those very valuable insights. It was a true pleasure speaking with you today.

Dr. Herzog:
Thanks, Roberto. It's been a pleasure being on this podcast with you and always good to be working with KDIGO.

Dr. Pecoits-Filho:
I'm Dr. Roberto Pecoits-Filho, and to access this and other episodes of the series, visit kdigo.org/podcast. Thanks, for listening.

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