Transcript Details

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Translating the Latest KDIGO Guidelines Into Practice: IV Iron Therapy in Patients With Non–Dialysis-Dependent CKD

Announcer:
Welcome to CE on ReachMD. This activity, titled “Optimizing Iron Deficiency Management in CKD: IV Iron Replacement Therapy Amid the Latest KDIGO Guidelines” is provided by Medtelligence.

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Dr. Núñez:
This is a continuing education on ReachMD. And I am Dr. Julio Núñez, a heart failure and cardiorenal specialist. With me today is my friend and colleague, Dr. Patrick Rossignol. Hello, Patrick.

Dr. Rossignol:
Hello, Julio.

Dr. Núñez:
In the next minutes, we will discuss about iron deficiency assessment and treatment in patients with CKD. Very interesting topic. Let me start with a clinical case.

This is a 78-year-old man with a history of hypertension, type 2 diabetes, and the patient presents stable chronic kidney disease classified as CKD G3bA2. The patient is receiving a stable GDMT, including a statin therapy, ACE inhibitor, thiazide-like diuretic therapy, dapagliflozin 10 mg daily, semaglutide up to 1 mg weekly, and also finerenone 20 mg daily. On the visit, the evaluation was blood pressure 132/82 mmHg. Electrocardiogram shows sinus rhythm 70 beats per minute, non-anemia, normal glycated hemoglobin 6.5%, normal, no dyskalemia, and GFR stable, GFR about 38, and UACR about 32 mg, great.

Patrick, I have a question for you. Do you miss iron deficiency evaluation in this patient?

Dr. Rossignol:
Yes, indeed. According to the latest KDIGO guidelines, the proper evaluation should include a complete blood count, reticulocytes, ferritin, and a transferrin saturation, TSAT. Such screening should be performed at referral and regularly during the follow-up and when symptoms suggest anemia. Minimum testing frequency increases with CKD progression and other CKD severity: annually in CKD grade 3, twice yearly in grade 4, and every 3 months in grade 5 or dialysis.

And why should we proceed so? There are indeed many observational studies which showed an association between iron deficiency and adverse outcomes, overall mortality, adverse cardiovascular outcomes, but also impaired quality of life. And in several of these

studies, the association of iron deficiency with adverse outcomes was found independent of the presence of anemia.

And finally, I should mention that the strongest evidence supporting a causal effect of iron deficiency on outcomes stems from the PIVOTAL trial we will talk later on, but which show that IV iron used proactively compared to a more conservative approach led to better cardiovascular outcomes, and these data provide a rationale for diagnosis and treating iron deficiency in people with CKD.

Dr. Núñez:
Thanks, Patrick, for your clear response. You convinced me. Here we have the hemoglobin and also iron deficiency assessment in this patient. The patient had a ferritin level of 80 pg/L, and also TSAT, transferrin saturation index, was 18. And also, remember that the patient has no anemia, hemoglobin 13.5 g/dL.

Dr. Rossignol:
Julio, can you tell us a little more about this? What about the differences and potential causes?

Dr. Núñez:
First, this patient displayed non-anemic iron deficiency. Specifically and according KDIGO guidelines, the patient has systemic iron deficiency characterized by low ferritin or low TSAT.

In CKD, we may also classify a patient as iron-restricted erythropoiesis when the patient has low TSAT but also higher values of ferritin in values above 100 ng/mL. So we need to distinguish this type of both classifications.

In heart failure, we have the similar, but with different names. But regardless the type of iron deficiency, when we look for recent a registry in order to know what the prevalence of iron deficiency in CKD patients, we uniformly see that in most registries, most patients, up to 50% to 70% of patients with CKD exhibit some degree of iron deficiency.

But most importantly, in most cases, Patrick, iron deficiency is not assessed; it's not measured. The main problem is that we, in many cases, physicians, are not recognizing iron deficiency because it is not measured.

And what are the potential causes of iron deficiency in CKD patients? Multifactorial. Bleeding, most often gastrointestinal, also urogenital. Chronic inflammation may also play a crucial role. Remember also iatrogenic use of drugs like anticoagulants, multiple blood testing, patients on hemodialysis, and also increased iron consumption due to erythropoiesis stimulant agents, use of these drugs.

So you also state that iron deficiency is associated with increased risk of adverse events beyond the presence of anemia. This is true in heart failure, and this is true in CKD, but also increased risk of major adverse events, but also importantly decreased quality of life, more fatigue, worse concentration, lower well-being, more anxiety, more depressive symptoms, and also worsening of neurocognitive results, especially decreased memory status, mental speed, and attention.

We have pointed out the importance and the prevalence and the clinical associated effects of iron deficiency in CKD patients, but what do the recent KDIGO guidelines say about iron deficiency treatment in CKD patients?

Dr. Rossignol:
Yes, thanks, Julio. As a matter of fact, there are 2 major statements in the latest KDIGO guidelines. One statement concerns patients on dialysis. It is now recommended to implement a proactive iron management strategy. In other words, initiating iron therapy is suggested if ferritin is below or equal to 500 ng/mL and TSAT below or equal to 30%.

And the proactive approach, in other words regular maintenance doses, is preferred over reactive approach to ensure stable iron status and potentially improved cardiovascular outcomes. And as I stated earlier, this statement essentially stems from the PIVOTAL trial results, which randomized more than 2,100 participants with CKD stage 5 on dialysis to receive either high-dose iron sucrose administered intravenously in a proactive fashion compared to a more conservative, less reactive fashion with a lower target from TSAT and ferritin.

And importantly, the rate of the composite outcome of fatal or nonfatal myocardial infarction, fatal or nonfatal stroke, or hospitalization for heart failure after a median of 2.1 years was significantly lower in the group receiving proactive versus reactive treatment, with a

hazard ratio of 20%.

What about patients not on dialysis? For patients not receiving dialysis or also not receiving peritoneal dialysis, initiation of iron is suggested at less stringent ferritin/TSAT thresholds, reflecting different iron losses and inflammation burdens, with ferritin below 100 ng/mL and TSAT below 40% or ferritin between 100 and 300 ng/mL and TSAT below 25%.

Regarding the preferred route of administration, IV iron is preferred in hemodialysis patients because of its efficacy, efficiency, and reduced pill burden with the proactive approach depicted. And for those patients not receiving hemodialysis, of course either oral or IV iron is suggested, but this is based on the individual patient's values, preferences, tolerability, and costs. Acknowledging the fact that IV iron may lead to faster correction of anemia with fewer side effects, and in any case, if oral iron has an inefficient effect after 1 to 3 months or is poorly tolerated, patients should be switched to IV iron.

Dr. Núñez:
Excellent summary, Patrick. It is absolutely evident that KDIGO guidelines recommend to move for a more proactive not just assessment but also treatment of iron deficiency in CKD.

Dr. Rossignol:
Julio, as a cardiologist, what guidance can you give nephrologists regarding the use of the IV iron therapies?

Dr. Núñez:
So in heart failure, we have a lot of experience and trials assessing the effect of iron deficiency treatment in patients with chronic but also in acute heart failure. So as a summary of the evidence endorsing the use of iron treatment in iron-deficiency patients, first, iron deficiency is highly prevalent in heart failure, similar as we see in CKD. In several registries, iron deficiency is about 50% to even 80% in an acute heart failure setting. So iron deficiency is highly prevalent, similarly as occurs in CKD.

Second point, oral iron treatment seems not the best choice in heart failure patients. There is one randomized clinical trial that evaluated the use of oral iron treatment in patients with iron deficiency, heart failure patients. And at 16 weeks, we were not able to find any differences in terms of functional capacity assessed by peak VO_2, no difference also in 6-minute walk test, and no differences in another endpoint. So with the evidence we have right now, we cannot suggest in heart failure patients a regular or proactive treatment with oral iron.

Third, the clinical benefit in heart failure patients is independent of the presence of anemia. So I think it's very crucial point. We just need to separate what anemia and what iron deficiency is. And in heart failure patients, the benefit is similar. Most patients benefit regardless of the presence of anemia.

And finally, I would like to say that looking at the most important trials in heart failure, iron supplementation appears to have the greatest benefits in those patients with lower values of TSAT. In this setting, there are some others that suggest that we should simplify the iron deficiency definition and treatment just based on TSAT. in heart failure, there are some others suggesting we need to simplify and treat patient just based on TSAT lower than 20%.

Dr. Rossignol:
Thank you very much, Julio. These were great points, and that convinced me as a nephrologist.

Dr. Núñez:
Thank you, Patrick. And before we close this session, we want to give the audience some take-home messages. Let’s start with Dr. Rossignol.

Dr. Rossignol:
Thanks, Julio. I will call our colleagues to action, highlighting the importance of screening anemia, iron deficiency on the one hand, but also the role of IV iron replacement therapy in iron-deficient CKD patients, both on dialysis and in non–dialysis-dependent CKD patients.

Dr. Núñez:
Thanks, Patrick. I just want to just repeat the similar message than provided by Patrick. I would like all colleagues that assess patients

with CKD, that you need to proactively assess and treat iron deficiency in CKD patients. And just treat and assess and treat these patients beyond the presence of anemia.

Thanks for being here, and that's all the time we have today. So we thank our audience for joining us, and thank you, Patrick, for joining this interesting session.

Dr. Rossignol:
It was a pleasure, Julio. Goodbye.

Dr. Núñez:
Goodbye.

Announcer:
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