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Navigating Iron Deficiency Anemia: A Practical Guide for Gastroenterologists

Dr. Buch:
This is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm joined by Dr. Thomas DeLoughery to discuss what gastroenterologists need to know about iron deficiency anemia. Dr. DeLoughery is a Professor of Medicine in the Division of Hematology and Oncology at Oregon Health and Science University in Portland.

Dr. DeLoughery, welcome to the program.

Dr. DeLoughery:
Thank you. I'm very excited to be here because I love talking about iron.

Dr. Buch:
Thank you, sir. So, Dr. DeLoughery, let's start out with fundamentals. How frequently should we administer oral iron, and what role does vitamin C play in enhancing absorption?

Dr. DeLoughery:
Well, those are both great questions. I'm always amazed that since medical school, we have been arguing about this. And so my general advice, and I'll expand on this, is iron at most should be given once a day. And it's very interesting. What happens when we take an iron pill—I took an iron pill this morning. My body absorbed the iron, and then my body made a protein called hepcidin. Hepcidin rises, blocks further iron absorption, and amazingly, that can take up to 48 hours to get better. And so there was a classic study done years ago of comparing people taking iron. It was 15 versus 50 versus 50 TID. And what was interesting is there's absolutely no difference in the rise in ferritin with the 15 versus the higher doses, and people had lower GI tolerance, so I think most of us accept iron once a day.

Now, interestingly, there have been studies to show that absorption of iron is actually better if you take iron every other day, and so this led to the big, "Should it be every day? Should it be every other day?" controversy. And what it's really come down to is that if you take iron every day, your ferritin levels will go up faster because you get better total absorption, but if you take it every other day, the GI tolerance is much improved. So I think it's really dealer's choice. I tend to start with every day just because I'm human, people are human, and I can never remember to take things every other day. In people who have tolerance issues, I go to every other day. Colleagues of mine will start with every other day, but I tend to go with everyday iron.

Now, the other thing that's interesting and what's still controversial is vitamin C. And I think vitamin C really helps in several situations. One, there is a good study that if you take iron with food, such like milk or fiber, taking a vitamin C along with it will help the iron be absorbed. It neutralizes the bad effects of the calcium and the fiber, so I actually recommend a lot of my patients take iron with food because it improves tolerance. And I think the vitamin C helps there. There are good studies to show that if you just take iron alone on empty stomach and vitamin C, the absorption of iron improves. Now, curiously, in some studies, that's not translated to a ferritin rise, but it does look like vitamin C improves iron absorption, so I fall on the side of a vitamin C pill.

One other trick I use is there's good studies to show that if you take iron and any type of meat or fish—poultry included—it actually doubles the absorption of iron. So I joke my ideal meal is a hamburger with vitamin C and iron pill for better absorption.

So that's been my approach to oral iron. I don't push it. I use one once a day. I do like to give vitamin C with it. And often, if patients are willing to do it, have them take it with a little bit of meat.

Dr. Buch:

Thank you very much. So let's now move on to IV iron. Are there any notable differences among the available formulations, and how common is anaphylaxis with these therapies?

Dr. DeLoughery:
So there's about six forms of IV iron on the market—two formulations like iron sucrose that they use in renal disease tend to need multiple dosings, so I tend not to use those. What we like to focus on is the once or twice dosing iron, so low-molecular-weight iron dextran and ferumoxytol can be dosed in one or two dosings. And those are preferable because you can load the patient up fast and get it used easier.

Now, interestingly, as far as safety, all the irons are actually pretty safe. We did a study, and this has been validated in other studies. We over six years gave 35,000 doses of IV iron, and our rate of severe reactions like anaphylaxis sending people to the ER was very low—like one in 15,000—and that's been seen in other studies. What's interesting is that minor reactions are pretty common, and these are like what we call infusion reactions like you see with rituximab and a lot of the biologics, where the iron nonspecifically activates complement. And we can talk a little bit more about that later. But true anaphylaxis is very rare.

So when I approach what iron I give, I tend to use low-molecular-weight iron dextran just because for our center, giving it once is the most cost-effective way of doing it. The one interesting difference is there's one iron product called iron ferric carboxymaltose, and with this product, the carbohydrate moiety actually can lead to hypophosphatemia. It raises a protein called FGF23 that leads to renal phosphorus wasting. It actually turns out it's more than lab abnormality. There's a wonderful paper in people with inflammatory bowel disease where even though their ferritin went up, if they got the hypophosphatemia, they still felt fatigue. And half of people who get this iron product have some degree of hypophosphatemia.

So as far as short-term reactions, all the irons are basically equal, and our challenge and what we decide is basically just on what's best for our clinic—a once or twice-a-day iron—and for us, our iron of choice is low-molecular-weight iron dextran. And I think many of us are concerned about ferric carboxymaltose and the hypophosphatemia, and we've been shying away from that.

Dr. Buch:
Thank you for that. So let's talk about this. How long does it take to fully replenish tissue iron stores?

Dr. DeLoughery:
We are big fans of using the ferritin, and if you look at oral iron, the majority of people should replenish in about three months with oral iron and get the ferritin above 50. IV iron in theory should be pretty instantaneous. You give, let's say, 1,000 mg of IV iron at once, but it's actually a little bit more subtle because it goes into storage, and then it's released from storage to the tissues.

So people within a month should see their hematocrit get back to normal and their iron stores replenished. Again, if somebody's in a very big iron deficit, they need an extra dose of IV iron, but IV iron should be pretty quick. With PO iron, it should be within a few months. And one trick we do is if somebody's anemic and their hemoglobin doesn't go up by a point in two weeks of oral iron, they're not going to respond, and so we'll switch them over to IV iron.

Dr. Buch:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Thomas DeLoughery about clinical approaches to iron deficiency anemia in gastroenterology.

So, Dr. DeLoughery, I'd like to ask you about nuances among certain patient populations. If we focus on bariatric surgery patients, what are some key considerations when managing iron deficiency?

Dr. DeLoughery:
Well, there's some interesting things about obesity. Curiously, obesity can predispose to iron deficiency. People who, especially if they're very obese, they actually have a mild inflammatory state. So again, hepcidin goes up; you get decreased iron absorption. So one thing we've worked with our bariatric surgeons about is to actually screened for iron deficiency even before a bariatric procedure and to make sure they're tanked up before then.

I always tell my patients, when you get a bypass, one of the things you bypass is iron absorption. And what's interesting is even in surgeries that are relatively noninvasive or minor, we still see a high incidence of iron deficiency, and some people reported up to 80 percent in five years. And so the problem is, with the bypass, even with relatively less invasive stomach procedures, with decreased food intake and alterations of absorption, most people will become deficient, so we tend not to use oral iron. And in those patients, we're pretty aggressive about screening for iron deficiency and then using intravenous iron in those patients.

One thing we're seeing and wrestling with is with the rise of the GLP-1 inhibitors—will they lead to iron deficiency? And certainly, I and many of my colleagues have seen iron-deficient patients, and is it just something to do with the GLP-1 drugs? Is it just because they're

eating less? We don't know. I think that's an unanswered question, but that may be another population we'll have to think about a nuance for bariatric patients.

Dr. Buch:
When we're talking about inflammatory bowel disease, when should we consider IV iron over oral iron?

Dr. DeLoughery:
I tend to be a little bit on the aggressive side with that compared to some of my colleagues. And inflammatory bowel disease can lead to iron deficiency in multiple different ways. There's bleeding, the bowel inflammation can do it, but again, inflammation, hepcidin, and decreased absorption. Iron pills can be a little bit inflammatory. There are some theoretical considerations that even in well-controlled people with inflammatory bowel disease, oral iron may set off inflammation or make an adverse microbiome, so I tend to be pretty aggressive with IV iron in patients with inflammatory bowel disease.

I know some my GI colleagues will try oral iron in very well-controlled patients, and that could be another reasonable approach, but if people don't respond, I'm pretty aggressive. And one thing I've been struck by is some people with very severe disease may need pretty frequent dosing every few months to keep their iron stores up. And as long as you're following the ferritin, you can't overdose somebody on iron because you're following the ferritin. And so I think one approach I do is to not only give the iron but try to be pretty scrupulous in follow-up. We check ferritin four to six weeks later, and in people we think are at risk, we're pretty frequently checking the ferritin. And we pull the trigger on IV iron if the ferritin number is under 50 because that seems to be where the body responds to becoming iron deficient.

Dr. Buch:
What's the recommended approach for patients with portal hypertensive gastropathy?

Dr. DeLoughery:
In patients where my GI colleagues have no other means to control that, I've been very impressed at the rate of iron loss. And we need to absorb a milligram or two of iron a day to keep up with our body stores, and as I tell patients, even if you're not having overbleeding, if you're losing 10 milliliters of blood day in and day out, 24/7, you're going to get an iron deficit. And many of these patients are losing a lot more blood to their lesions with that.

So I've had some patients with this where we've been giving IV iron once a month to a 1,000 milligrams just to keep up. And again, we're pretty aggressive with these patients because if you keep up with the iron loss, you can really cut down the transfusions in these patients. These are patients in our clinics that we set up on an aggressive program. Basically, some patients I've had, they'll come in, and we actually schedule for monthly iron, check a ferritin beforehand, and they're almost always low, and keep up with that. But I think with aggressive iron replacement, we keep these people on the transfusion suite.

Dr. Buch:
As we wrap up, Dr. DeLoughery, what additional thoughts might you have that you'd like to share with our audience?

Dr. DeLoughery:
Well, I think one other group of patients I share often with our GI colleagues is HHT, or hereditary hemorrhagic telangiectasia. And we very frequently give IV iron for that, and that's been very useful; but interestingly, we've also been called in more with some of the off-label therapies for that. So I think there's a great need for very aggressive iron replacement in these patients, because especially as these patients get older, I view iron as an adjunct to lasering their lesions and fixing their lesions. But for patients who have refractory disease and a lot of trouble, we're coming up with interesting new therapies. So we're always glad to help out.

Dr. Buch:
As those insights bring us to the end of the program, I want to thank my guest, Dr. Thomas DeLoughery, for joining me today to share his thoughts on how gastroenterologists can help manage iron deficiency anemia.

Dr. DeLoughery, thanks so very much for this practical and informative update.

Dr. DeLoughery:
Great. Well, thank you very much. It was an absolute delight to be on this show.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you again very soon.