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Iron Deficiency Anemia in Patients Presenting with Abnormal Uterine Bleeding: The Role of Oral Iron Supplementation

Announcer:

Welcome to CME on ReachMD. This activity, entitled "Iron Deficiency Anemia in Patients Presenting with Abnormal Uterine Bleeding: The Role of Oral Iron Supplementation" is provided by Omnia Education.

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Dr. Shulman:

In my office this week, I saw a woman who came for a variety of problems, the most important one being chronic fatigue and heavy menstrual bleeding. My examination showed that she had a large fibroid uterus, and when I took the routine bloodwork, it showed that she had iron deficiency anemia. The best way for me to describe this particular common situation in a gynecologic practice is that in a sense, this fibroid uterus represents a hole in the bucket. We as women's healthcare providers are excellent in detecting why there's a hole in the bucket and, in most cases, being able to fix the hole in the bucket. Where we have been somewhat left behind, though, is being able to refill that bucket, and today we're going to talk about the approaches, both from an oral and intravenous therapeutic option, to actually refill that bucket once we have repaired the hole.

This is CME on ReachMD, and I'm Dr. Lee Shulman. I'm joined today by my distinguished colleague, Dr. Stephanie Martin.

Iron deficiency anemia, or IDA, is undermanaged for a number of reasons in general, and especially when it results from abnormal uterine bleeding, or AUB. IDA also frequently present for patients with comorbidities beyond AUB, including inflammatory bowel disease, chronic kidney disease, and cancer. However, this activity will focus mainly on patients with abnormal uterine bleeding. So let's get started.

Dr. Martin:

Lee, maybe we should start with reviewing some of the basics. So maybe you could take us through, you know, the definition, the epidemiology, and the kind of patient disparities you see with AUB and IDA.

Dr. Shulman:

Stephanie, abnormal uterine bleeding is an incredibly common occurrence in a general gynecology practice. AUB is thought to lead to about one-third of all outpatient visits in a reproductive population. This makes up about 2.5 million visits to gynecologists for the evaluation of AUB, in both reproductive and even early postmenopausal women. The impact of abnormal uterine bleeding on a patient's quality of life can range from mild to profoundly severe. Most women with AUB experience some impairment, and some actually may experience substantial impairment in their ability to function in work or in school environments and have reductions in their psychological well-being. Abnormal uterine bleeding also contributes to maternal morbidity and mortality in pregnant women, especially those with preexisting AUB-related anemia.

Because of the critical concern about iron deficiency anemia in women with abnormal uterine bleeding, it is incredibly important to assure that all women who present with abnormal uterine bleeding are, in fact, evaluated for iron deficiency anemia, and that includes

both a CBC [complete blood count] as well as an assessment of the iron status. It's important to also recognize that there are great disparities in how women are managed for their fibroid uterus. Research has shown that the management of AUB differs significantly by age and race and ethnicity, but interestingly enough, not by BMI [body mass index] or insurance status.

Dr. Martin:

I mean, that's really striking to hear, you know, this difference, and I think our audience is probably familiar with this role and this relationship of iron and anemia. But what people may not understand, it's also really key with the processes involved in energy generation, cell proliferation, neurotransmission, and even immune function. So let's delve in a little bit further. Lee, maybe you could talk about IDA and quality of life issues in general in women who have AUB or iron deficiency anemia or both.

Dr. Shulman:

Well, Stephanie, IDA has been identified by the World Health Organization as a global health issue in the top 20 causes of disability. It's associated with a wide array of morbidity and even mortality in both a gynecologic and obstetrical population. In the OB population, which, Stephanie, you're incredibly well aware of, it's associated with preterm delivery and low birth weight. It's implicated in the development of postpartum depression. But I think when we look outside of the OB population, that impact is perhaps even more profound. There was a study performed a few years ago, that found that women with iron deficiency anemia, regardless of the etiology, had a comparable adverse impact on their sense of well-being, on their quality of life similar to individuals who were undergoing hemodialysis for chronic renal disease, who were dealing with cancer, and a variety of other problems.

Fatigue is associated with significant physical, emotional, psychological, and social consequences impacting virtually every aspect of a woman's daily life.

Dr. Martin:

I think that's really true, and I think our patients tend to downplay their symptoms and their issues or maybe describe them due to something else, or maybe, even if they do take them seriously and bring them up with a provider, they may not be heard and get the necessary treatment. So I think it's really important that we all understand how important it is to diagnose and treat IDA. In pregnant patients, it can be so easy to discount the association, you know, because preterm delivery and low birth weight are not rare outcomes. So when you have an anemic patient that has one of these outcomes, it's very easy to dismiss the association and assume that it's related to something else. But it's so important to recognize that IDA is associated with outcomes during the pregnancy, and correcting it improves those outcomes. But also about the mom's physical and mental well-being.

So, you know, preterm birth and low birth weight are not rare outcomes, so it becomes real easy to say, "Oh, it's due to something else," and not really recognize the association that's been described. But the good news is, this is very manageable. This is very easy to take care of if you recognize the importance of addressing it, and that goes both for patients and for providers.

Dr. Shulman:

For those just tuning in, you're listening to CME on ReachMD. I'm Dr. Lee Shulman, and I'm here with Dr. Stephanie Martin. We're just about to tackle broader issues using iron supplementation to address health-related quality of life in patients with iron deficiency anemia, or IDA.

Based on your clinical experience, can you discuss iron supplementation's role in addressing health-related quality of life in women?

Dr. Martin:

I see a lot where physicians or nurse practitioners or whoever are very comfortable ordering and interpreting CBCs, and they may recognize the anemia, but they perhaps don't understand how to interpret the iron studies, and they may just start a patient on an oral iron over the counter and then hope for the best, without much follow-up to make sure that the patient's actually responding to that oral therapy, because I think we all recognize it's not necessarily easy to tolerate some of these oral therapies, and compliance may not be very good.

Dr. Shulman:

You know, leaving it to the patient to get some sort of over-the-counter iron supplement and then only when that patient failed that and had other symptoms and problems – instead of us looking to take care of it, referring the patient out. So, in one very real sense, this is something that all of us understand, and yet many of us don't take it to the next step so that we can be able to, again, fix the bucket, take care of the problem of the chronic, even acute bleeding, and at the same time, refill the bucket so that the patient can go on with her life.

Dr. Martin:

Absolutely. I mean, ob-gyns and women's health practitioners are more than able to diagnose and manage iron deficiency anemia in

pregnant and nonpregnant patients. That's certainly within their wheelhouse. So along those lines, Lee, what are the most recent, pertinent guidelines that we should be using when we're treating these patients?

Dr. Shulman:

Well, Stephanie, the good news – it's sort of a good news/bad news situation. The good news is that there are some very recent guidelines from ACOG. They've been revised so that they do represent the new interventions that are available, and they've been revised in an evidence-based fashion. The reality is, sort of the bad news, is that these guidelines have not been widely implemented in routine clinical practice. ACOG published a practice bulletin that's entitled "Management of Acute Abnormal Uterine Bleeding in Nonpregnant Reproductive-Aged Women." You could not ask for a more specific and focused guideline with regard to the diagnosis, treatment, and management of patients with anemia related to abnormal uterine bleeding. The 3 steps that were described in the ACOG guideline was rapidly assessing the clinical picture to determine patient acuity, determine the most likely etiology of the bleeding, and choose the most appropriate treatment for the patient. I will underline that treatment is not just stopping the bleeding, which is obviously critical. Treatment also has to include getting that patient back to a hemodynamic status that's going to allow her to continue on with her life.

Dr. Martin:

In practical terms, how will those patients benefit from this evolving landscape of the oral irons that are available now?

Dr. Shulman:

It's been a fascinating trip in watching the evolution of iron therapies. The iron therapies, in particular IV and oral iron therapies, actually date back to the 19th century and the early 20th century. This is not new. And yet, some of the issues with those early iron salts and supplements either have been removed, taken care of, but some of them still persist. In a very real sense, the usual approach, especially when there's not a need for rapid repair of the anemia, is to start with an oral iron. And oral iron supplements are readily available, both prescriptive and over the counter. They're available either as a ferrous salt, such as ferrous fumarate, or a ferric salt, such as ferric iron polymaltose complex. These iron supplements do the trick if the patient can continue to use it. And what I mean by that is many of these iron supplements incur a considerable adverse event profile, mostly GI. You then put on top of that the issues with absorption. So we mentioned earlier that for some women, the issue isn't, say, a fibroid uterus or abnormal uterine bleeding; it may be inflammatory bowel disease. And so if you're unable to absorb the orally dosed iron, it's not going to work. So for many of these women and men, we have the ability to provide an intravenous iron supplement. This is where the older IV iron supplements have continued to sort of muddy the water because many of them were not well tolerated. Not going into great and specific detail, the newer IV iron supplements are far better tolerated but are costly and require, usually, more than 1 infusion.

So because of the adverse reactions to many of the oral iron therapies, we have increasingly witnessed the use of IV iron. Now it's IV iron, especially in the early therapies that were available starting at the turn of the 20th century, that were associated with a wide variety of anaphylactic reactions and toxic reactions and even with death. Clearly though, the newer IV irons that have been developed in the last decade are considerably more – not just effective but are considerably safer. Yet, there are still issues with intravenous iron therapies. One can still get adverse reactions and thus not achieve the adequate gains in hemoglobin. IV iron cannot be done at home. It requires patients to be treated in a setting that is prepared to treat for the uncommon, but not totally unheard of, anaphylactic reactions with any of the newer IV irons. Most IV irons require more than 1 transfusion, and that means it requires at least 3-5 days between treatments, and for some, even 7 days. And because of that, as well as the cost of IV iron, I think many people who are involved in evaluating and treating women and men with anemia have looked to potentially find an oral regimen that would be better tolerated.

What I'm somewhat happy to say is that there has been advances, an oral iron supplement that is better tolerated, that is better absorbed, and is more likely to be used to correct the iron deficiency anemia. And I'm speaking specifically about, ferric maltol. Studies of ferric maltol used in its approval by the FDA showed that the mean increase in hemoglobin levels per patient in the active ferric maltol arm was clinically significant at 2.45 g/dL for the intent-to-treat population, and 2.57 in the per-protocol population. And that was compared with 3 g and 3.05 g for IV-treated patients.

It's something that we've never observed with previous oral supplements. In fact, in this study, by week 24, 65% of those ferric maltol patients still being monitored had achieved normal levels of hemoglobin, and therefore were nonanemic, compared with 68% of IV patients. This is an incredible advancement in the ability of oral iron to provide a comparable benefit to IV iron therapies.

Dr. Martin:

Yeah and, you know, in our pregnant patients, if we're talking about giving them IV iron, which I frequently do, they have to go to an infusion center, and you can imagine how happy that infusion center is to see a hugely pregnant patient walking through their doors. I mean, pregnant women tend to terrify all non-obstetric providers. I think that's another huge benefit, other than the obvious benefits, of having an oral therapy as an alternative to an IV therapy.

Dr. Shulman:

You know, I think the development and use of a far-better-tolerated oral regimen has been, in a sense, on the wish list not just of women's healthcare providers but of all providers. Clearly, the development and approval of ferric maltol is an important first step. We're able to, in the modern age of telemedicine, be able to follow them and be able to get their blood with mobile phlebotomy. Again, improving patient convenience is ultimately going to improve patient outcomes.

Dr. Martin:

Yeah, and compliance. The easier it is for a patient to comply with our therapy, then the better results we can expect overall.

Dr. Shulman:

Stephanie, I want to thank you so much for joining me here. It was great speaking with you today.

Dr. Martin:

Thanks, Lee. It's always a pleasure talking with somebody who shares my passion for preventing and treating IDA.

Announcer:

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