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Beyond Anemia: Understanding the Significance and Treatment of Iron Deficiency

Announcer:

Welcome to CME on ReachMD. This activity, entitled "Beyond Anemia: Understanding the Significance and Treatment of Iron Deficiency" is provided by Medtelligence and is supported by an independent educational grant from Vifor Pharma.

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Dr. Jankowska:

It has been already in 2016 when the European Society of Cardiology Heart Failure Association guidelines implemented for the first time recommendation to screen every patient with heart failure for iron deficiency. And, most importantly, the significance for screening for iron deficiency was positioned on the same level of significance like screening for diabetes or thyroid dysfunction, so we should definitely re-pose the question now: Why now iron deficiency is so important and how it relates to heart failure.

Welcome to CME on ReachMD. I am Ewa Jankowska, and joining me today to discuss iron deficiency in the context of heart failure is Dr. Stefan Anker. Welcome to the program.

Dr. Anker:

Thank you.

Dr. Jankowska:

Dr. Stefan Anker, what do you think why iron deficiency is so important for heart failure? Is it common? Is it important for outcomes? What do you think?

Dr. Anker:

Yes, it's all of the above. Iron deficiency is common. Iron deficiency is related to poor quality of life, to symptoms, to bad prognosis. Iron deficiency is something that you really should be aware of and consider in your patients whenever these patients are symptomatic and whenever you feel that their prognosis is going downwards. So assessing it is for the good of the patient and for the care of the patient, something that should be an integral part, exactly as you said, like assessing also diabetes, because we can do something about it, and this is making all the difference. A diagnostic test that has a therapeutic consequence, that's what we are looking for, and it's possible with iron deficiency.

Dr. Jankowska:

What is more common in patients with heart failure, iron deficiency or anemia?

Dr. Anker:

Well, the answer is actually very straightforward. Iron deficiency is much more common than anemia. Anemia in patients with heart failure, depending on the exact clinical circumstances, occurs in maybe 3 to 5% in ambulatory stable patients and maybe at most in 10 to 20% of patients when they are hospitalized. And basically, in patients with heart failure, we see iron deficiency much more frequently, more like in the order of 30 to 40% in patients that are not anemic and about 50 to 60% of patients who are anemic. In total,

I would say iron deficiency is about 5 to 10 times more frequent in heart failure than is anemia.

Dr. Jankowska:

We should screen iron deficiency also in patients who have normal hemoglobin level. Is that right?

Dr. Anker:

Absolutely. We should screen for iron deficiency independently of the hemoglobin level, but we should really—if you want to restrict it to something, we should restrict it to symptomatic patients. The evidence that we can make a positive difference for our patients is in the symptomatic patients, and if we are keeping up the rule that you should do a diagnostic test, particularly when it has a therapeutic consequence, you should stick to the symptomatic patients. But there, we may consider it in almost anybody and definitely independently of high or low hemoglobin.

Dr. Jankowska:

Indeed, it's very important that in current times we link iron deficiency with abnormal energy metabolism rather with only low hemoglobin level. So let's look now at the short animation which demonstrates the mechanisms which lead to consequences of iron deficiency.

Announcer:

Iron deficiency is a common complication of chronic heart failure associated with impaired exercise capacity, reduce quality of life, and poor prognosis. Iron is crucial to the transport of oxygen by hemoglobin. Iron is also essential for mitochondrial energy production and cellular oxygen storage. With iron deficiency, hemoglobin levels can be normal or diminish causing anemia and loss of oxygen delivery. It is hypothesized that iron deficiency also causes declines in energy production in cells with high energy demands, such as cardiac and skeletal myocytes. Both iron deficiency and iron deficiency anemia can contribute to reductions in heart function and exercise capacity. In patients with chronic heart failure with reduced ejection fraction repletion with intravenous iron can help improve symptoms, activity levels, and quality of life.

Dr. Jankowska:

For those just tuning in, you're listening to CME on ReachMD. I'm Ewa Jankowska, and I'm speaking with Stefan Anker on iron deficiency in patients with heart failure.

Dr. Anker, another important question: We base our decisions on the evidence that we have from clinical trials. Could you comment? What evidence at the moment is the most important, which on the one hand led to the formulation of the guidelines in 2016 and what else we know now in 2020?

Dr. Anker:

Well, the most important part of the evidence is, of course, our clinical trials where, in randomized settings, we tested intravenous iron, particularly ferric carboxymaltose, compared to giving no therapy or to give, like, a saline infusion acting as a placebo.

Now, these trials were, first of all, small trials that—basically, they were done to get a feeling for how responsive patients are. And when these trials basically showed that patients are on average very responsive, both with and without anemia, the first designed FAIR-HF trial that was published in 2009 and only had a total of 450 patients, and second, to confirm the results of the FAIR-HF trial, we designed the CONFIRM-HF trial which had 300 patients. The first trial was half a year in duration, the second trial 1 year in duration, and both trials in a very similar way showed that symptoms are improved, exercise capacity, particularly 6-minute walk test, is improved, and then also several different aspects of quality of life assessed by questionnaires are also improved in these patients. This means we have now robust and, from repeat studies, evidence that symptoms, quality of life, and exercise capacity are improved, and these trials were the foundation for then giving the good recommendation in the guidelines about this.

Dr. Jankowska:

The trials that you have mentioned tested intravenous iron supplementation in patients with heart failure. Some people think that maybe oral iron would also work in patients with heart failure. Do we have any evidence supporting this?

Dr. Anker:

Interestingly, for oral iron, we have such a trial, which is the IRONOUT study. And the IRONOUT study investigated oral iron versus placebo in heart failure patients and whether or not symptoms, quality of life, exercise capacity can be improved. And the clear answer is, with oral iron you cannot achieve any of this, and most likely this is because the oral iron is simply not absorbed.

Dr. Jankowska:

Yes, we need to emphasize that European guidelines recommend only intravenous iron supplementation for iron-deficient patients with heart failure. But going to the identification of patients with heart failure who may benefit from intravenous iron supplementation, what would be your advice how we should screen patients for iron deficiency in everyday clinical practice?

Dr. Anker:

A ferritin level less than 100 already is sufficient to diagnose iron deficiency in heart failure—in my opinion, actually in any chronically ill person—but there is an alternative. If the ferritin is a little bit higher, up to 300, however is accompanied by a percent transferrin saturation of less than 20%, that also is a sufficient degree of evidence for iron deficiency being present. So ferritin less than 100 or ferritin 100 to 300 plus TSAT less than 20%.

Dr. Jankowska:

As we know how to screen and diagnose iron deficiency using very simple parameters, what would be your recommendation how to dose iron that needs to be supplemented intravenously to patients with heart failure?

Dr. Anker:

Well, thank you so much for the question. Dosing is, of course, an important issue, but it is rather straightforward for these patients. The base amount that we should give heart failure patients with iron deficiency is 1,000 mg. We add another 500 mg if hemoglobin of the patient is less than 10.0, and if the body weight is above 70 kg, we add another 500 mg. We basically then give in total during the correction phase 1,000, 1,500, or 2,000 mg. When you are doing this with 2 infusions, the 2 infusions should be at least a week apart, and the application should be done in such a way that the patient then in the end gets the full correction. You are reassessing the patient for iron deficiency only after 3, 4, or even 6 months. In the first 8 weeks for sure, ferritin and transferrin saturation will be high and will be establishing a full correction.

Dr. Jankowska:

Some people are very afraid of side effects of intravenous iron. Do we need to do any allergy tests before giving intravenous iron?

Dr. Anker:

With the modern intravenous iron, you don't need to do a starting dose or test dose. It is enough, basically, to really give a slow infusion of 15 to 30 minutes in the first 500 or 1,000 mg that you want to give to the patient, and that is enough also to observe.

Dr. Jankowska:

Yes, and I think it's also important to emphasize that this treatment is allowed to be administered both in inpatients but also in outpatients just because very high safety profile of this treatment.

Dr. Anker:

I agree.

Dr. Jankowska:

There is no doubt that there is overwhelming evidence that intravenous iron improves quality of life, lessens heart failure symptoms, but there are obviously many questions which need to be answered. Do we have any evidence whether intravenous iron can improve clinical outcomes?

Dr. Anker:

Well, I would say we have such evidence already because there are several meta-analyses published that indeed, in the more than 800 patients that were part of the double-blind randomized trials we did in the past, that we had seen such reductions in cardiovascular or heart failure hospitalizations combined with cardiovascular mortality. And indeed, these reductions are very strong and were almost, like, 40% or more. However, of course these trials were not primarily designed for event reductions, and the duration of these trials was only half a year to 1 year, so we are now doing several bigger, event-focused clinical trials. And these trials should answer the question that you are just posing in a much more detailed and powerful way, starting at the end of this year with the AFFIRM-HF trial and then leading to the FAIR-HF II trial to the IRONMAN trial and maybe even the heart FIT trial in the next 2 to 3 years. There will be a number of studies investigating this, but as of today, yes, we do have already some evidence, but it's limited, and we need more.

Dr. Jankowska:

We know that in the current era, many patients have heart failure with preserved ejection fraction. What is your opinion about using intravenous iron in this population?

Dr. Anker:

We know that more than 50% of heart failure patients with preserved ejection fraction are iron deficient, and also, in these patients, the degree of iron deficiency relates to the poor performance and poor symptom status of patients. We haven't done intervention trials yet. One such trial is ongoing. I'm very optimistic that it also works for these patients, but we do not yet have the proper evidence for this. But there is every reason to believe it will also work in these patients.

Dr. Jankowska:

It looks like there are a lot of activities ongoing in the area of iron metabolism in patients with heart failure, but this is all that we have for you for today. Dr. Anker, do you have any final thoughts or comments you would like to share with our audience?

Dr. Anker:

Well, the most important thing in this context is to think about iron deficiency and do the screening. If you don't have a diagnosis of iron deficiency, you shouldn't treat a patient for it, and you can only make a difference by treating. So step No. 1 is the key step for everything. Think of iron deficiency and diagnose it in your symptomatic patients. And once you give the intravenous iron, I believe you will be surprised how fast the patients are positively responding, feeling better. This is something that really makes also the relationship between patient and physician stronger by doing something and having an almost immediate impact for the patient in a positive way.

Dr. Jankowska:

I couldn't agree more. Dr. Anker, thank you very much for joining me today.

Dr. Anker:

Thank you so much.

Announcer:

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