鉄の経静脈的補給は心不全症状を改善する（Presentation #885）

CONFIRM HF:鉄欠乏の心不全患者は経静脈的補充により改善する可能性がある

CONFIRM HF: Iron deficient heart failure patients see improvement with intravenous supplementation

鉄欠乏の心不全患者は鉄の静脈内投与をわずか1～2回受けるだけで機能的能力およびQOLの有意かつ持続的な改善を来し、心不全悪化による入院のリスクを軽減することができるとの研究結果が2014年European Society of Cardiology Congressホットラインセッションで発表された。CONFIRM-HFは、鉄欠乏を伴う安定した有症状の心不全患者304人を組み入れた、二重盲検、プラセボコントロールトライアルであった。患者はランダム化され、鉄分（カルボキシマルトース鉄溶液［FCM］）静脈内鉄投与（152人）またはプラセボ（生理食塩水）静脈内投与（152人）を52週間投与される群に割り付けられた。プラセボ群と比較し、FCM群は24週目の6分間歩行テストで33m（p=0.002）、36週目には42m、52週目には36m長く歩行した（36週目および52週目のいずれもp<0.001）。12週以降、FCM治療群患者はプラセボ群と比較し、患者の全般的評価（Patient Global Assessment）において有意な有益性を示し（12週目でp=0.035、24週目でp=0.047および36週目と52週目でp<0.001）、New York Heart Associationクラスの改善においても同様のパターンが認められた（24週目でp=0.004および36週目と52週目でp<0.001）。

Full Text

Heart failure patients with iron deficiency can experience significant and sustainable improvements in functional capacity and quality of life as well as reduced risk of hospital admission for worsening heart failure by receiving just one to two intravenous doses of an iron supplement, according to the results of a study presented at ESC Congress 2014.

Findings from the CONFIRM-HF (Ferric CarboxymaltOse evaluatioN on perFormance in patients with IRon deficiency in coMbination with chronic Heart Failure) trial, presented as an ESC Hot Line and published in the European Heart Journal, point to a simple and safe therapy for a frustratingly common problem, said investigator Piotr Ponikowski, MD, PhD, from Medical University in Wroclaw, Poland.

"Iron deficiency has recently been reported as a frequent co-morbidity in heart failure and has been associated with impaired functional capacity, poor quality of life, and increased mortality, irrespective of the presence of anemia. Therefore, correction of iron deficiency itself should be considered an attractive therapeutic target in this population."

CONFIRM-HF was a double blind, placebo-controlled trial, which enrolled 304 stable, symptomatic heart failure patients from 41 sites across nine European countries.

All patients had iron deficiency, defined as a serum ferritin level of less than 100 ng/mL, or between 100 and 300 ng/mL if transferrin saturation [TSAT] was less than 20%.

Subjects were to receive either intravenous iron (n=152), given as ferric carboxymaltose solution (FCM), or a normal saline placebo (n=152), for 52 weeks. In the FCM arm, the median total dose was 1500 mg of iron during the one-year study period (ranging from 500 to 3500 mg of iron). Over 75% of the patients required a maximum of two injections of FCM to correct and maintain the iron parameters.

Completion of the six-minute walk test (6MWT) was required at baseline, and the primary endpoint of the study was improvement in this test at week 24.

Dosing with FCM compared to placebo resulted in a significant increase in the distance subjects completed during the 6MWT.

Specifically, compared to placebo-treated subjects, those treated with FCM completed 33 extra meters in the 6MWT at week 24 (p=0.002), 42 extra meters at week 36, and 36 extra meters at week 52 (both p<0.001).

"The magnitude of the treatment effect of FCM on the 6MWT distance, is robust and clinically meaningful," noted Professor Ponikowski. "In previous interventional studies, such beneficial effects have only been seen with cardiac resynchronization therapy."

Importantly, improvement in the 6MWT distance was seen across all subgroups, including patients with and without anemia, "which further challenges the traditional view linking adverse consequences of iron depletion with anemia," he added. "Iron depletion impedes oxygen transportation and utilization and so we expected that targeting this depletion would improve patients' exercise tolerance."

The study also showed concomitant improvement in other measures of functional status and quality of life among those treated with FCM compared to placebo.

From week 12 onwards, the FCM-treated subjects showed a significant benefit in Patient Global Assessment compared with placebo (p= 0.035 at week 12, p=0.047 at week 24 and p<0.001 at weeks 36 and 52), and there was a similar pattern seen in improved New York Heart Association class (p= 0.004 at week 24 and p< 0.001 at weeks 36 and 52).

Fatigue scores were also significantly improved in the FCM compared to placebo-treated subjects, as were quality of life scores on both the Kansas City Cardiomyopathy Questionnaire [KCCQ] and European Quality of Life 5D [EQ-5D] questionnaire.

Importantly, compared to placebo, treatment with FCM was also associated with a significant 61% reduction in the risk of hospitalization due to worsening heart failure (hazard ratio [HR] 0.39; p=0.009).

"Hospitalizations due to heart failure are an economic burden for society, resulting in poor outcomes and impaired quality of life for patients. There is evident need for their prevention. In this context the results of CONFIRM-HF are of particular interest. Among recently introduced pharmacological therapies only ivabradine has demonstrated such results," said Professor Ponikowski.

Despite the reduction in hospitalizations among FCM-treated patients, the number of deaths was similar in both groups, suggesting a one-year follow-up may not be long enough to detect differences in mortality, he said.

Adverse events were mild, and occurred at a similar rate in both groups.

"Current ESC guidelines for managing heart failure patients recognize iron deficiency as a common and clinically relevant comorbidity which should always be tested for," concluded Professor Ponikowski. "However at the same time, there is a relatively weak recommendation to manage iron deficiency in such patients, mainly because of a paucity of evidence confirming the benefits of iron repletion. For a stronger recommendation of iron depletion as a valid therapeutic target in heart failure, well-designed and controlled studies with adequate follow-up are needed. CONFIRM-HF was designed and executed with this goal. We believe that the results of this trial will be most important when it comes to defining the role of iron repletion for heart failure iron deficient patients in the next ESC Heart Failure guidelines in 2016."

The study was sponsored by Vifor Pharma Ltd., Glattbrugg, Switzerland.

Professor Ponikowski is a consultant for Vifor Pharma Ltd., and has also received honoraria and research grants from the company. He has also received speaking honoraria from Amgen Inc. Other study authors report receiving either board membership fees, honoraria or research grants from Vifor Pharma Ltd. and Amgen Inc. Three study authors are employees of Vifor Pharma Ltd., with one owning stocks in Galenica.

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