Long-term effect of intravenous iron supplementation on iron status in HFrEF

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Objective

Iron deficiency (ID), both absolute and functional, is prevalent in chronic diseases, particularly in patients with heart failure with reduced ejection fraction (HFrEF). Intravenous iron (i.v.) administration results in beneficial effects on physical status, NYHA class, quality of life, NT-proBNP and reduces risk of heart failure hospitalizations and currently holds a IIa recommendation in the ESC guidelines.2-7 Concomitant amelioration of irons status has been documented up to 52 weeks after i.v. iron supplementation, however long-term data are lacking. The aim of this study was to follow the iron status of patients with HFrEF after intravenous iron application up to 36 months.

Patients and Methods

Patients with HFrEF who received i.v. iron infusion (Ferriccarboxymaltose) were included from a prospective registry of the Heart Failure Unit of the Medical University of Vienna between 01.01.2015 and 15.03.2021. Demographic and laboratory data including iron parameters (i.e. plasma ferritin, transferrin concentration, transferrin saturation (TSAT), red cell distribution width (RCDW), mean corpuscular volume (MCV), NTproBNP and hemoglobin (Hb)) as well as clinical follow-up was documented. Baseline was defined as the last laboratory test before i.v. iron supplementation and follow-up timepoints were defined at 6+-3, 12+-3, 18+-3 and 24-36 months, respectively. Parameters of iron status were compared between timepoints by non-parametrical tests. The association between irons status and outcome was investigated in an exploratory manner.

Results

54 Patients with at least one-time i.v. iron were included into the analysis. 30% of patients were female, median age 68,5 (IQR: 56-78) and patients were well-treated by HF therapy. 89% of patients have a baseline ferritin <100ug/ml, the iron need calculated by Ganzoni's formula was 984mg (IQR: 797-1188) and most patients (94%) received 1000mg iron.
7 patients received 1000mg iron instead of 1500mg the first time. Interestingly 9 patients underwent a second i.v. infusion during FUP, whereas only 2 of them received 1000mg instead of 1500mg as an optimum iron dose. Heart failure severity reflected by NT-proBNP was not correlated to ferritin but to TSAT values. Hemoglobin was comparable at long-term FUP to baseline values (Figure 1). Iron status improved after i.v. iron supplementation as expected, whereas improvement in ferritin, transferrin and TSAT levels were significantly increased even after 18 months and longer (p-values shown in Figure 1).
Over time, however, a trend to re-worsening towards values compatible with iron deficiency was observable in the TSAT parameter.

Patient characteristics , n=54	
Age, years (IQR)	68,5 (56-78,25)
Female gender, n(%)	16 (29,6%)
BMI, kg/m², (IQR)	25,8 (23,8-29,4)
Systolic BP, mmHg (IQR)	115 (101,5-132)
Diastolic BP, mmHg (IQR)	75 (70-80)
HR, bpm (IQR)	70 (61-82,5)
NYHA class II/III, n(%)	23/23 (42,6/42,6)
Comorbidities	
Known ischemic CAD, n(%)	25 (46,3)
Arterial Hypertension, n(%)	22 (40,7%)
T2DM, n(%)	18 (33,3%)
Atrial fibrillation, n(%)	16 (29,6%)
PM/ICD/CRT, n(%)	2/2/3 (3.7% /3,7%/5,6%)
Medication	
BB, n(%)	45 (83,3%)
≥50 % of target dose achieved	95,2%
RAS-inhibitors, ACE-I / ARB /ARNi, n(%)	25/56/14 (46,3%/11,1%/25,9)
≥50 % of target dose achieved (ACE-I. ARB)	88,9/ 100%
MRA, n(%)	36 (66,7%)
≥50 % of target dose achieved	100%
Ivabradine, n(%)	7 (13%)
Diurectics, n(%)	19 (35,2)

Table 1: Baseline patients' characteristics, n=54
BMI= body mass index, BP= blood pressure, HR= heart rate, CAD= coronary artery disease, T2DM= type 2 diabetes mellitus, PM= pace maker, ICD= implantable cardioverter defibrillator, CRT= cardiac resynchronization therapy, BB=beta-blocker, ACE-I=ACE-Inhibtor, ARB=angiotensin-II-receptor-blocker, ARNi= angiotensin receptor-neprilysin inhibitor, MRA= Mineralcorticoid-receptorantagonist

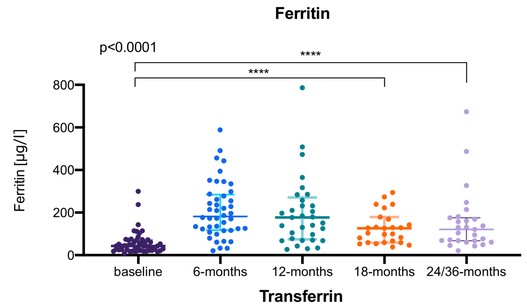

Figure 1: Distribution of Iron-parameters (Ferritin, Transferrin ,TSAT) and Hemoglobin at BL, 6 months FUP, 12 months FUP, 18 months FUP and 24 months to 36 months FUP
*= p<0,005, ns=not significant, p>0,005

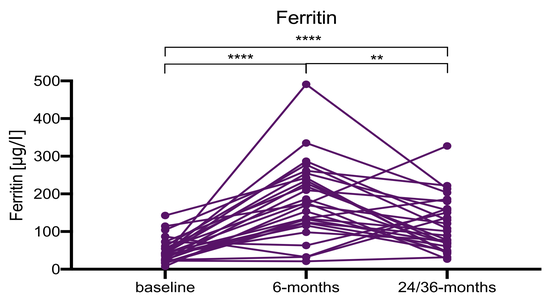

Figure 2: Developement Iron-parameters Ferritin, Transferrin and TSAT at BL, 6 months FUP and 24 months FUP paired in all 54 patients.
*= p<0,005, ns=not significant, p>0,005

Conclusion

The results demonstrate that patients with HFrEF and iron deficiency receiving intravenous iron supplementation show a subsequent marked improvement in iron status, however a re-worsening is observable after a follow-up as short as 2-3 years with most patients again fulfilling the indication for i.v. iron. The mechanisms of iron redistribution as well as the significance or multiple iron supplementation needs to be elucidated in further studies.

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