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Original research article

Effects of intravenous iron therapy in patients with heart failure with iron deficiency

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Abstract:

Objective: This study aimed to determine whether treatment with intravenous iron (ferric carboxymaltose) in patient who had heart failure, and iron deficiency, either with or without anemia, would improve hematological and biochemical response, clinical determinants of the patients and functional status and capacity of the patients.

Background: Recently it has been recognized that patients with heart failure (HF) may be prone to the development of iron deficiency (ID). Iron deficiency with or without anaemia diminishes aerobic performance, precipitates fatigue and exercise intolerance and consequently worsens the clinical symptoms of patients with HF. A recent randomized, double-blind study (Anker et al. 2009) showed that intravenous iron supplementation in ID patients with or without anemia and chronic heart failure (CHF) exerts favorable effects on functional status and quality of life. Therefore ID lately acquired a unique role in the field of HF and is the subject of novel studies.

Methods: This prospective pre test and post test design study has been conducted in SRN hospital, M.L.N medical college, Prayagraj over 50 clinically stable patient of heart failure of NYHA class II or III, a left ventricular ejection fraction 45% or less with iron deficiency (ferritin level <100 micro gm per litre or between 100 and 299 micro gm per liter, if the transferrin saturation was <20%). Exercise capacity has been quantified using six minute walk test. Then patient has been received bolus of ferric carboxymaltose over 30 minute. Reassessment of symptoms of patients was made according to NYHA functional classification and exercise capacity using 6 minute walk test on day 90.

Results: On day 90 it was observed that treatment with FCM significantly prolonged 6 MWT distance (pre-treatment 254.3±45.3 m vs. post-treatment 353.6±45.6 m, p value - <0.05), an improvement in NYHA was detected with statistical significance (p value <0.05), statistically

significant reduction in value of BNP (pre-treatment 1174.6±560.6 pg/mL vs post-treatment 898.3±451.5 pg/mL, P value- <0.05) observed.

Conclusion: Treatment with intra venous iron in patients with chronic heart failure and iron deficiency anemia, improves symptoms of heart failure, functional capacity and quality of life.

Key words: Iron, Heart failure, NYHA, BNP (Brain natriuretic peptide), Ejection fraction, 6MWT (6 Minute walk test).

Introduction:

The European Society of Cardiology Heart Failure Survey indicate that 74% of chronic heart failure patients have at least one co morbidity, the most common of which are diabetes, renal dysfunction and anemia. The pathogenesis of anemia in heart failure patients is considered to be complex and multi factorial, consisting of elements such as renal dysfunction, decreased erythropoietin production and resistance, hemdilution, chronic inflammation, and in particular iron deficiency [1]. Recently it has been recognized that patients with heart failure (HF) may be prone to the development of iron deficiency (ID) as a result of depletion of iron stores, or due to mechanisms present in anemia of chronic disease [2, 3]. ID with or without anaemia diminishes aerobic performance, precipitates fatigue and exercise in tolerance and consequently worsens the clinical symptoms of patients with HF [4]. A recent randomized double-blind study showed that intravenous iron supplementation in ID patients with or without anaemia and chronic heart failure (CHF) exerts favourable effects on functional status and quality of life. Therefore ID lately acquired a unique role in the field of HF and is the subject of novel studies [5,6].

Method:

Patient population: We conduct prospective uncontrolled open label study. The study was conducted in Swaroop Rani Nehru hospital, Moti Lal Nehru Medical College, Prayagraj, from September 2018 to August 2019. In patients of chronic heart failure diagnosed by history of appropriate symptoms for more than six month, and confirmed by physical examination, ECG and 2D echo-cardiography, and a left ventricular ejection fraction less than or equal to 45% with iron deficiency (ferritin level < 100 µgm /L or between 100 and 299 µgm /L, if the transferrin saturation was <20%). Selected randomly from cardiology OPD/IPD. Patient having heart failure with duration of symptoms <6 month, patient requiring blood transfusion, renal dysfunction

(serum creatinine > 1.2 mg/dl), Known case of any other chronic disease excluded from the study.

Study protocol: After obtaining written informed consent from the subjects and local ethics and research committees, Patient receive infusions of 10 ml of iron (which is the amount of Ferric carboxymaltose that is equivalent to 500 mg of iron) were administered diluted in 100 ml of sterile 0.9% sodium chloride solution and given in more than or equal to15 minute into a peripheral vein on day 1.

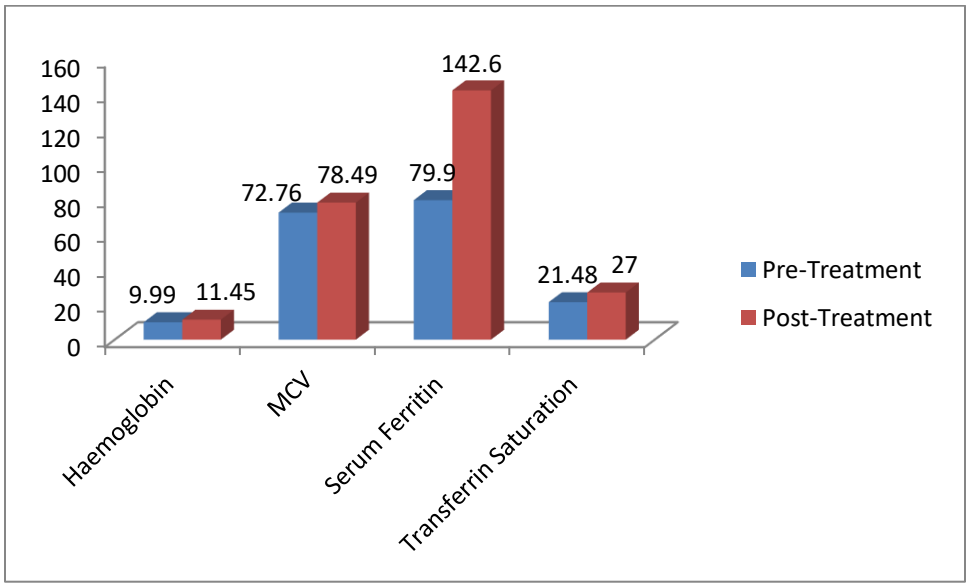
Evaluation: Patient has been assessed as for hematological indices, NYHA classification of symptoms, LVEF by 2D echocardiography and exercise capacity has been quantified using six minute walk test. After receiving IV iron infusion on day 90 assessment was done again of the markers of clinical determinants, hematological indices and functional capacity.

Statistical analysis: Quantitative variables with a normal distribution were expressed as mean ± SD; those without normal distribution were expressed as median and interquartile range. Qualitative variables were expressed as relative frequencies. SPSS version 23 was used to analyze the data. Comparison of means between same group before and after intervention performed depending on the variable's distribution with paired t test. A p value < 0.05 was considered to be statistically significant.

Result:

In our study 26 (52%) were male and remaining 24 (48%) were female. At the time of patient selection mean hemoglobin was 9.97 mg/dl. After intravenous iron therapy to same group of patient analysed again after 90 days, the mean haemoglobin was found to be 11.49 gm/dl. There was significant difference in mean values of haemoglobin before and after treatment with intravenous iron therapy. Significant increase was also found in mean values of MCV, serum ferritin level and serum transferrin saturation percentage before and after intravenous iron therapy.

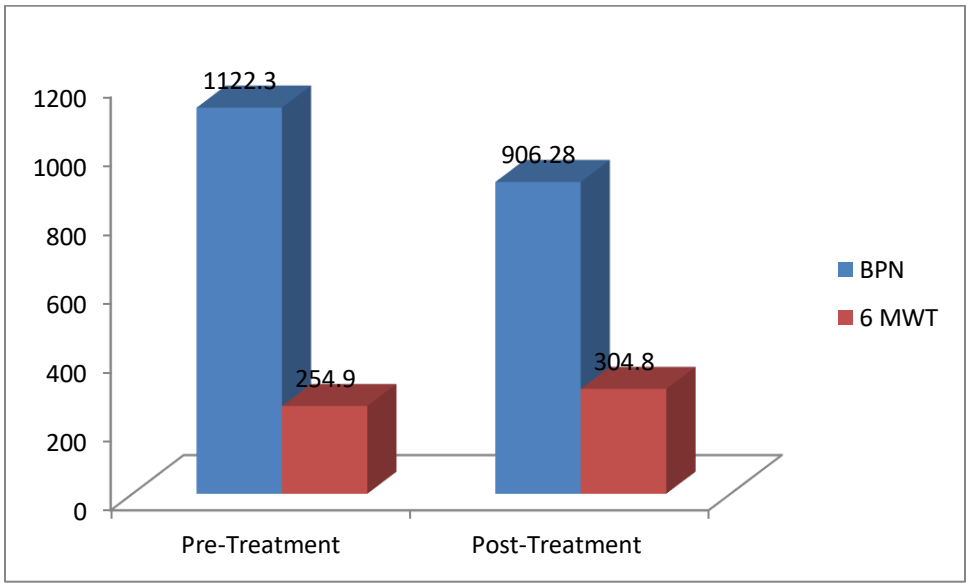
Comparative analysis of mean of patient's haemoglobin, MCV, serum ferritin and transferring saturation before and after IV iron therapy-



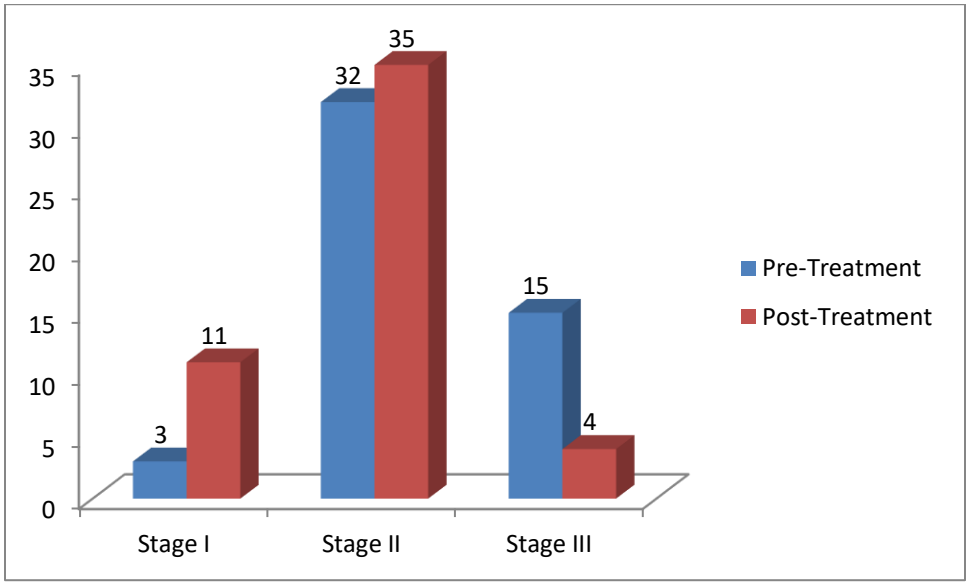
2D-echocardiography was done of the entire 50 patient before and after intravenous iron therapy, Left ventricular ejection fraction has been calculated and analyzed. Significant difference found in mean of ejection fraction of same group of patient before and after IV iron therapy.

Brain natriuretic peptide of the entire 50 patient before and after treatment investigated and analyzed, mean and standard deviation has been calculated and compared. Significant difference has been found between mean values of BNP before and after treatment of the patients.

Every patient selected for the study examines for 6 minute walk test before and after iv iron therapy, distance covered were analyzed, mean and standard deviation calculated and compared. Significant difference was found between mean of 6 minute walk test before and after iv iron therapy.



The entire patient included in study has been examined for NYHA (New York Heart Association) grading before and after IV iron therapy. Number of patient in each class calculated before and after treatment. There was a significant difference in number of patient in each grade before and after treatment.



Discussion:

This study demonstrate that intravenous administration of iron (Ferric carboxymaltose) to patient with CHF and iron deficiency with or without anemia results in significant increase in haemoglobin values of the patients, and improvement in other blood and biochemical

parameters. At the time of patient selection mean of haemoglobin of fifty patients was 9.97gm/dl. After intravenous iron therapy, 500 mg of ferric carboxymaltose (FCM), to same group of patient was again analyzed after 90 days; the mean of haemoglobin of 50 patient was 11.49gm/dl. Mean corpuscular volume (MCV) analyzed before and 90 days after administration of iron therapy, mean value calculated with standard deviation and compared after intravenous therapy, statisticaly significant increase was found in MCV. Mean value of serum ferritin level calculated with standard deviation and compared; significant increase was found from 79.9 µ gm /L to 142.6 µ gm /L in serum ferritin level. Mean value of transferrin saturation level calculated with standard deviation. Significant increase in serum transferrin percentage was found in patient after intravenous iron therapy. A similar study conducted by Aidan P Bolger et.al showed increase in haemoglobin from 11.2 ± 0.7 to 12.6 ± 1.2 g/dl [7]. Beck-de-silva et al also reported that there was an incensement in haemoglobin level in heart failure patients after introduction of oral or IV iron therapy [8]. Reed and Blair et al assessed hematological parameters at 1-4 weeks after accelerated therapy,iv iron increased haemoglobin level by 1.2 gm/dl [9].

2D-echocardiography was done in all 50 patients before and after intravenous iron therapy. In this study improvement was found in ejection fraction of same group of patient after IV iron therapy, but the difference was statistically not significant. Significant decrease in mean BNP level was found after treatment with intravenous iron, denoting improvement in cardiac function.

Functional capacity of the patients improved. Every patient selected for the study was examine for 6 minute walk test before and after IV iron therapy, distance covered were analyzed, mean and standard deviation calculated and compared ,improvement was found in mean 6 minute walk test after iv iron therapy. Intravenous iron therapy alleviates symptoms. There was a significant decrease in number of patient in NYHA class III, and increase in number of patient in NYHA class II, and I after treatment with IV iron therapy. Most of the results are consistent with previous studies.

Toblli JE and Lombrana A et al. carried a studied on 40 patient, 20 patient in group (b) received IV iron sucrose and reported that the left ventricular ejection fraction percentage were improved in this group (35.7 +/- 4.7 vs. 28.8 +/- 2.4). They also found decrease in BNP level after intravenous iron therapy [10]. Pioter Ponikowaski et al also reported that there was improvement in functional capacity (6MWT) after receiving IV iron therapy [11].

In 2016,Van Veldhuisen et al studied on 172 patients with heart failure and received Ferric Carboxymaltose showed significantly increased serum ferritin and transferrin saturation and patients' global assessment and functional class as assessed by the New York Heart Association improved on FCM versus standard of care [12]. Aidan P Bolger et al. enrolled 17 patient,16 completed the study. At the study entry 9 participants had NYHA class II symptoms, and remainder class III. After administration of IV iron sucrose at fallow up, all patient were in class II [7].

Conclusion:

On the basis of our finding we concluded that treatment with intravenous iron in patient of chronic heart failure with iron deficiency with or without anemia, improve hematological and biochemical response, symptoms, functional capacity of the patients. The side-effect profile is acceptable. The limitations of study are small sample size, and it is non randomized.

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