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Effect of IV iron sucrose versus IV carboxymaltose in patients with heart failure

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Abstract

Iron deficiency either absolute or functional, is an independent predictor of all cause and cardiovascular mortality and a major contributor to exercise intolerance, even in absence of anemia. Correcting these comorbidities is attractive and novel therapies targets to improve outcomes. At present, IV iron is preferred route for treatment in such patients. Most studies have used IV iron sucrose (max dose of 200mg/setting) or ferric carboxymaltose (max dose of 1000mg/setting). Our study determines advantage of IV iron carboxymaltose over iron sucrose by being cost effective, requiring fewer injections, lesser duration of hospital stay with minimum adverse effect and equivocal improvement in quality of life and hematological profile in patients with heart failure with either preserved or reduced ejection fraction.

Keywords: IV iron sucrose, IV carboxymaltose, heart failure

Introduction

Background and AIM

Anemia and Iron Deficiency are important and common comorbidities that often coexist in patients with Heart failure. Both conditions, together or independently, are associated with poor clinical status and worse outcome. Recent studies have found that administration of intravenous iron in patients with heart failure and absolute or functional iron deficiency with or without anemia improves symptoms and exercise capacity. At present, 5 IV preparations are available in United States and Europe, of which only two preparations (iron sucrose and ferric carboxymaltose) have been tested prospectively in patients with heart failure. The ESC heart failure guidelines recommends that all patients with heart failure should be tested for anemia and iron deficiency with serum ferritin and transferrin saturations (Class I, Level of Evidence: C recommendations). The ESC guideline recommend treatment with IV FCM in symptomatic heart failure patients with iron deficiency to improve symptoms and quality of life (Class IIa, level of evidence A recommendation). The US guidelines do not recommend any specific formulation, but recommend IV iron in patients with heart failure and iron

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deficiency as class IIb, level of evidence B). No data is currently available for the comparision of these two preparations in Heart Failure patients. In this study we aim at comparing these two IV iron preparations in Heart Failure patients to find a better option for parenteral iron administration.

Material and Method

Randomized Controlled Interventional Non Blinded Prospective Study.
100 Heart Failure with Iron Deficiency Anemia patients were selected over a duration of one year.
50 patients received IV iron Carboxymaltose (Group A) and 50 patients IV Iron sucrose (Group B) respectively.
Eligible subjects included patients who had chronic heart failure of New York Heart Association (NYHA) class I to IV, a hemoglobin level at the screening visit less than 13 g per liter and iron deficiency.
Iron deficiency was diagnosed when the serum ferritin level was less than 100 ug per liter (absolute) or was between 100 and 299 ug per liter when the transferrin saturation was less than 20% (functional).
After a detailed clinical history patients were assigned NYHA groups and baseline Haemoglobin, Mean Corpuscular Volume, Mean Corpuscular Haemoglobin, Iron profile was noted.
50 patients received IV Iron Carboxymaltose at a dose of either 500 mg by slow intravenous bolus injection (patients below 60 kg body weight) or 1 g diluted in 500 mL of normal saline and infused over 30 minutes (patients above 60 kg).
50 patients received IV Iron Sucrose after 25mg of test dose on first infusion only, this was given at a dose of 200mg by intravenous infusion over two hours diluted in 100ml saline, repeated a number of times over following 7-14 days depending upon severity of anemia. (Ganzoni's formula). The median number of injection was 4 and range 3-6.
Four weeks after intravenous iron treatment, patients were reviewed and were categorized into NYHA groups. Repeat samples were taken for full blood count and serum ferritin.

Discussion and Results

The two groups of patients were similar with respect to age, gender, baseline Hemoglobin, red cell indices and serum ferritin.
At four weeks after infusion, patients NYHA classification had improved in both the groups.

Table 1: Comparative change in NYHA between Group A and Group B

NYHA	Group A		Group b	
	Before	After	Before	After
I-II	7 (14%)	41 (82%)	4 (8%)	39 (78%)
III- IV	43 (86%)	6 (12%)	39 (78%)	6 (12%)
DEAD	0 (0%)	3 (6%)	0 (0%)	5 (10%)

Under Group A

41 out of 50 patients improved to NYHA 1/2 6 out of 50 patients remained in NYHA 3/4
3 patients died during the study.

Under Group B

39 out of 50 patients improved to NYHA 1/2 6 out of 50 patients remained in NYHA 3 /4
5 patients died during the study.

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Hematological studies show a mean rise of 1.6g/dl in hemoglobin, 4.75fl/ml in MCV, 1pg/ml in MCH and 38.2microgm/l in serum ferritin with iv carboxymaltose (p value <0.005) compared to mean rise in hemoglobin of 1.09g/dl, 4.4fl/ml in MCV, 0.75pg/ml in MCH and 32.6microgm/dl in serum ferritin with iv iron sucrose (p value <0.005) after 4 weeks of loading dose. There is no statistically significant difference (student t Test p =0.65) between the groups treated with Iron sucrose and Ferric Carboxymaltose. These hematological and clinical outcomes are consistent with the previous studies done in this arena [1-15].

Table 2: Increase from baseline

±SD	FCM	IS
Mean Hb increase (g/dl)	1.6 (0.9-1.9)	1.09 (0.9-1.7)
Mean MCV increase (fl)	4.75 (4.6-7.8)	4.4 (3.6-6.8)
Mean MCH increase (pg/dl)	1 (0.4-1)	0.75 (0.4-0.8)
Mean Ferritin increase (mcg/dL)	38.2 (34-45)	32.6 (30-47)

Our observation during the hospital stay suggests average duration of 5.94 days with iv carboxymaltose compared to 7.44 days with iv iron sucrose. IV FCM requires lesser injections. 90% of hospitalization remained uneventful in carboxymaltose group and 88% remained uneventful in iron sucrose group. 14% patients with FCM showed mild side effects (headache, nausea, tingling) compared to 30% in patients who received IS transfusion. No adverse life threating reactions were observed in either groups.

Table 3: Events during Hospitalization

Events during Hospitalization	Group-A (FCM)		Group B (Iron Sucrose)	
	No.	%	No.	%
Readmission	2	4%	1	2%
Death	3	6%	5	10%
Uneventful	45	90%	44	88%
Total	50	100	50	100%

Table 4: Drug Reaction in Two Groups

Group A	Group B
7/50	15/50

7 out of 50 developed mild itching/headache/reaction in FCM group.
15 out of 50 developed mild itching/fever/dizziness/reaction in ISC group. No severe life threatening reactions observed in any of the groups.
Our study have several limitation, the dose of elemental iron received by the two groups were different, the study is to small to assess differences in adverse effects

Conclusion

The result of our study illustrates that no statistically significant difference in clinical and hematological efficacy is observed in both preparations. None of the preparations could be considered superior over the other. Ferric carboxymaltose however showed lesser duration of hospital stay, cost effectiveness and less number of injections with less adverse reactions

compared to iron sucrose.
Thus, transfusion with Ferric carboxymaltose in patients with Heart Failure and Iron Deficiency Anemia is less cumbersome and has a better patient contentment.

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