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Research Article

Retrospective Evaluation of Patients With Iron Deficiency Anemia who Need Parenteral Treatment; Iron Carboxymaltose ? or Iron Sucrose?

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Abstract

Objectives: According to World Health Organization, anemia is defined as the value of Hemoglobin (Hb) <13 g/dl in adult males, <12 g/dl in non-pregnant women and <11 g/dl in pregnant women. Iron deficiency anemia (IDA) is the most common cause of anemia. There are limited comparative data in the literature, regarding response to parenteral iron therapy. Data of the patients with parenteral iron therapy for IDA were retrospectively examined in this study to reveal their treatment responses.

Methods: Data of 145 patients underwent parenteral iron therapy for IDA between April 2013-September 2017 at the hematology outpatient clinic of Izmir Bozyaka Training and Research Hospital were reviewed retrospectively. Pre- and post-treatment hemogram and iron parameters were evaluated with a view to examine the efficacy and adverse effects of parenteral Iron Sucrose (IS) and Iron Carboxymaltose (ICM) administrations and compare treatment responses.

Results: 145 patients were included in the study,127(87.5%) female,18(12.5%) male, median age was 43.5(17-87) years. ICM was administered in 65(44.8%), IS in 80(55.2%) patients. Hemoglobin increase was 3.2 g/dl at the end of the 4th week in ICM group while 2.1 g/dl in IS group, which was not statistically significant (p=0.7). Ferritin increase in the first month of treatment displayed a statistically significance in favor of ICM.(48x104, p=0.0001).

Conclusion: Both parenteral treatment options are highly effective and reliable in early response to IDA, and the increase observed in hemoglobin and ferritin levels was more prominent with ICM.

Keywords: Ferric carboxymaltose, iron deficiency anemia, iron sucrose

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World Health Organization defines anemia as hemoglobin (Hb) level below 13 g/dl in adult men, below 12 g/dl in non-pregnant women, and below 11 g/dl in pregnant women. The most common cause of anemia is iron deficiency (IDA).[1] When IDA diagnosis is made, the underlying cause should be investigated, such as insufficient iron intake, decreased iron absorption or conditions causing blood loss should be determined and tried to be corrected. Although the basic treatment of IDA is oral iron therapy (100 -200 mg/day), parenteral iron administration may be required in some cases. Parenteral iron therapy is indicated when patients do not comply with oral iron therapy or de-

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velop drug intolerance, or in cases with deep anemia, ongoing blood loss, re-activation of existing gastrointestinal disease (e.g.inflammatory bowel disease), iron malabsorption, dialysis-dependent chronic kidney diseases, functional iron deficiency (e.g. kidney patient having erythropoietin treatment, cancer patient, autologous blood transfusion candidate).[2] Iron sucrose, Ferric gluconate, Iron dextran and Ferric carboxymaltose (FCM) are parenteral iron therapy options. Comparative studies are limited in the literature concerning patients' responses to these treatments. In the present study, data of our patients who received parenteral therapy with the diagnosis of IDA were reviewed retrospectively and their response to therapy were presented.

Methods

The data of 145 patients who received parenteral iron therapy with the diagnosis of IDA in the period between April 2013 and September 2017 in the hematology outpatient clinic of Izmir Bozyaka Training and Research Hospital were evaluated retrospectively. Diagnosis of anemia was based on WHO criteria. Patients' demographic data, pre-treatment levels of Hb, hematocrit, transferrin saturation and ferritin, and conditions causing IDA were determined. Clinical examination, imaging of the gastro-intestinal system and endoscopic procedures when required were performed for the etiological evaluation. Parenteral iron supplementation and its dosage was determined. Total dose to be administered was calculated by the formula;

Total dose (mg) = Patient's weight (kg) x (Normal Hb.- Patient's Hb.) x 2.4 + 500.

FCM was administered as a daily single dose not exceeding 1000 mg, and iron sucrose was administered as 200 mg every second day. Iron parameters and complete blood count measurements at the 4th week of the treatment as well as post-treatment responses were evaluated, and the side effects during the treatment were examined. Patients' response to the parenterally administered iron sucrose and FCM treatments were examined and compared. All data were saved in SPSS-20 version. $P<0.05$ was considered significant. T-tests were used in comparing the variables for independent samples.

Our study was approved by the Ethics Committee of Izmir Bozyaka Training and Research Hospital on 07/10/2020, with the decision no. 14 and it was carried out in accordance with the Declaration of Helsinki. There is no conflict of interest between the authors.

Results

A total of 145 patients were included in the study, 127 (87.5%) of which were female and 18 (12.5%) were male. The median age at diagnosis was 43.5 (17-87) years. Sixty-five (44.8%) patients received FCM while 80 (55.2%) patients received iron sucrose. IDA was determined in 118 (81.5%) patients while 26 (17%) patients had vitamin B12 deficiency along with IDA, and 1 (0.5%) patient had folic acid deficiency in addition to IDA.

As for the laboratory data of all patients at diagnosis, mean value of hemoglobin was 8.8 g/dl (5.5-11.5 g/dl), mean value of hematocrit was 29% (18-33%), Transferrin Saturation (TS) was 5.8±8.7 (1-80), and diagnostic ferritin level was 5.6±7.6 (1-60) (Table 1).

In the etiological evaluation, clinical examination, imaging of the gastro-intestinal system were performed as well as endoscopic procedures for the required cases. Parenteral iron therapy was indicated due to atrophic gastritis in 61 patients (42%), concomitant malignancy, chronic disease and heart failure in 34 patients (23.5%), malabsorption, ulcerative colitis, and gastrectomy in 22 patients (15.2%), oral iron intolerance in 20 (13.8%) patients, pregnancy in 8 patients (5.5%) (Table 2).

Table 1. Mean laboratory values before and after iron treatment

Initial hemoglobin level (g/dL)	8,8±1,5 (5,5-11,5)
Initial hematocrit (%)	29±4 (18-33)
Initial MCV (fL)	69±9 (52-87)
Initial Transferrin saturation (%)	5,8±8,7 (1-80)
Initial Ferritin (ng/mL)	5,6±7,6 (1-60)
Initial WBC (10^9/L)	7000±1978 (2600-13200)
Initial Platelet (10^9/L)	338,000±115,000 (51,000-760000)
Post-treatment Hemoglobin (g/dL)	11,6±1,6 (7,6-15)
Post-treatment Hematocrit (%)	37±4 (18-47)
Post-treatment Ferritin (ng/mL)	73±68 (10-314)

MCV: Mean Corpuscular Volume; WBC: White Blood Cells.

Table 2. Etiological causes of iron deficiency anemia

Age	**<45 (n=92)**	**>45 (n=53)**
Atrophic Gastritis	33 (35,9%)	28 (53,8%)
Malignancy, Chronic Disease, Heart Failure	24 (26,1%)	10 (18,8%)
Malabsorption, Ulcerative colitis, Gastrectomy	12 (13%)	10 (18,8%)
Oral Intolerance	15 (16,3%)	5 (8,4%)
Pregnancy	8 (8,7%)	

Daily dose of parenteral iron therapy was 500 mg in 38%, 1000 mg in 45%, and 1500 mg in 17% of the patients, and drug-related allergic reaction developed only in 4 patients. One of these cases was on FCM therapy. Allergic reactions were taken under control by administrating antihistaminic and steroid treatments.

Iron test results at diagnosis of IDA and four weeks after initiation of intravenous iron therapy were examined. After the treatment, Hb values were determined as 12.3 g/dl with FCM and 11 g/dl with iron sucrose, thus the increase in Hb was one unit higher with FCM than with iron sucrose, but this difference was not statistically significant (p=0.7). Ferritin values measured in the first month of the treatment displayed a statistically significant increase in favor of FCM (48 vs. 105, p=0.0001) (Table 3).

Given that most of our patients were women and menopausal transition begins around the age of 45, our sample was divided into two groups as the patients under 45 years and those over 45 years of age. Of our 92 patients under the age of 45, 88 (95.7%) were female and 4 (4.3%) were male. Forty-eight of them (52.2%) were administered iron sucrose while 44 (47.8%) had FCM. In patients under the age of 45, post-treatment Hb values were 12.36 g/dl with FCM and 11 g/dl with iron sucrose, which was not statistically significant (p=0.3). Ferritin values measured at the 4th week of the treatment were statistically higher in favor of FCM (38 vs. 102, p=0.0001).

Of our 53 patients over 45 years of age, 39 (73.6%) were female and 14 (26.4) were male. Of these, 32 (60.4%) received iron sucrose while 21 (39.6%) received FCM. After the treatment, Hb values of our patients over the age of 45 were 12.15 g/dl with FCM and 11.2 g/dl with iron sucrose, and there was no statistical significance (p=0.5). Ferritin values measured at the 4th week of the treatment were statistically higher in favor of FCM (62 vs. 108, p=0.014).

Table 3. Parenteral iron treatment results

	Ferric carboxymaltose	Iron sucrose	p
Initial hemoglobin level (g/dL)	8,8 ±1,5	8.9±1,5	
Initial Transferrin saturation (%)	6±11	5,3±5	
Initial Ferritin (ng/mL)	4±3	7±9	
Post-treatment Hemoglobin (g/dL)	12±1,5	11±1,5	0,7
Post-treatment Ferritin (ng/mL)	104±78	48±47	0,0001

Discussion

Iron deficiency is the first cause of anemia in patients that applied to the hematology outpatient clinic, where female patients constitute the majority.[3,4] In our study too, 87.5% of our cases were female patients and 51.2% of them were <40 years of age, in their reproductive years.

The studies evaluating the etiology of iron deficiency anemia in the normal population revealed chronic blood loss from the gastrointestinal tract as the most important cause in adult men and postmenopausal women, and menstruation in premenopausal women.[5]

The aim of this study was to compare the efficacy of iron carboxymaltose and iron sucrose in the treatment of patients with iron deficiency anemia. The studied population was not homogeneous, and the underlying causes of iron deficiency anemia were found to be atrophic gastritis, malignancy, chronic diseases, heart failure, malabsorption, ulcerative colitis, gastrectomy, malnutrition, and pregnancy. Hb, MCV, transferrin saturation, and ferritin level were the parameters used in determining the patient population as well as in calculating iron deficiency and iron replacement dose and evaluating treatment response.

Itching was reported only by one of the 65 patients on iron carboxymaltose treatment, whereas itching, rash, and headache developed in three of the 80 patients using iron sucrose, and all were taken under control in a short period by antihistaminic drugs and dexamethasone. In general, any serious allergic reaction was not induced by any of these drugs, which was also consistent with the literature.[6,7]

In the study by Derman et al. including 491 patients, Hb increased by 2.2 g/dl within 1-5 weeks of the iron sucrose treatment. In our study too, baseline Hb value was 8.9±1.5 g/dl in the patients receiving iron sucrose, and increased by 2.1 g/dl after 4 weeks, and measured as 11±1.5 g/dl.[8]

In the study by Seid et al., an increase of 3 g/dl was detected in Hb value of the patient group receiving iron carboxymaltose. In our study, average Hb value measured at diagnosis was 8.8±1.5 g/dl, which increased up to 12±1.5 g/dl after 4 weeks of treatment, hence an increase of 3.2 g/dl was observed, complying with the literature.[7]

Although the increase in Hb level was higher with iron carboxymaltose treatment, it was not statistically significant (p=0.7). Literature review showed that studies comparing these two drugs were carried out with younger patient groups. The presence of comorbid diseases and accompanying chronic diseases in elderly patients may explain insufficient increase in hemoglobin level.[6,9,10,11]

In our study, 100 ng/dl increase was observed in Ferritin level after 4 weeks of iron carboxymaltose treatment,

indicating a statistical difference with respect to the iron sucrose treatment. In the studies comparing the effects of these two drugs, the increase in ferritin level was reported as 101 ng/dl by Naqash et al., as 125.91 ng/dl by Sharma et al., and as 359 ng/dl by Rathod et al., although all were indicating different levels of increase for both drugs, the differences were significantly higher in favor of iron carboxymaltose.[6,10,11,12]

Conclusion

Both of the parenteral treatment options used in iron deficiency anemia are very effective and reliable in achieving early treatment response, and the increase in Hb and ferritin levels observed were higher with the use of FCM. However, long-term follow-up of the cases, tracing for recurrence and duration of IDA are also important in order to evaluate treatment results. In this respect, broad-spectrum prospective studies are required to determine the conditions at the time of diagnosis and after treatment, supported by laboratory data.

Disclosures

Ethics Committee Approval: Our study was approved by the Ethics Committee of Izmir Bozyaka Training and Research Hospital on 07/10/2020, with the decision no. 14 and it was carried out in accordance with the Declaration of Helsinki.

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