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Efficacy of ferric carboxymaltose therapy in celiac patients

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ABSTRACT

Aims: Iron deficiency anemia (IDA) is the most common cause of anemia worldwide. IDA can be caused by reduced iron intake, impaired iron absorption or losses. Celiac disease can cause iron malabsorption by decreasing the surface absorption area in the duodenum and consequently can cause IDA. Oral or intravenous iron preparations are used in the treatment of IDA. In this study, we wanted to investigate the efficacy of ferric carboxymaltose (FCM) in celiac patients with RIA.

Methods: Twenty-three patients who were followed up in the gastroenterology outpatient clinic of İnönü University Medical Faculty Hospital Turgut Özal Medical Center with the diagnosis of celiac disease and who received FCM were included in the study. The hemogram, ferritin, iron and iron binding levels of the patients were retrospectively screened through the hospital medical record system.

Results: Of the 23 patients included in the study, 3 (13.05%) were male and 20 (86.95%) were female. Hemoglobin concentration, iron and iron binding capacity before and after treatment showed a significant increase in all parameters after treatment. Ferritin value increased, although not significantly.

Conclusion: In our study, we found that FCM is an effective and safe treatment modality in the treatment of IDA in celiac patients

Keywords: Anemia, celiac disease, ferric carboxymaltose

INTRODUCTION

Iron deficiency anemia (IDA) is the most common cause of anemia worldwide, affecting about one third of the population. IDA leads to a hypochromic microcytic anemia. Causes of IDA can include reduced iron intake or impaired absorption in the gastrointestinal (GI) tract, losses (such as chronic GI and menstrual bleeding), or increased need, such as during puberty and pregnancy.[1,2] Celiac disease (CD) is one of the unexplained causes of IDA. CD is an immune-mediated disease in which iron malabsorption and consequently ADEs develop due to a decrease in the surface absorption area in the duodenum due to an inflammatory process in the intestine.[1]

Oral iron therapy (OIT) is usually the first line treatment for anemia due to definite iron deficiency. However, a significant proportion of patients do not respond to OIT. This is because some patients do not comply with the treatment due to GI side effects. In addition, OIT may not be appropriate in cases of poor absorption of iron due to GI disorders and in cases of severe IDA where rapid response with OIT is not achieved.[3] In such cases, IV iron administration has been found to be more effective in correcting IDA without significant safety concerns.[1]

In this study, we aimed to present data on the efficacy and safety of ferric carboxymaltose (FCM) treatment in patients with CD presenting with IDA.

METHODS

Between January 2009 and December 2023, 23 patients who were followed up in the Gastroenterology Outpatient Clinic of İnönü University Medical Faculty Hospital Turgut Özal Medical Center with the diagnosis of CD and who received FCM were included in the study. Ethical approval was obtained from İnönü University Scientific Researches and Publication Ethics Committee for the study (Date: 02.04.2024 Decision No: 2024/5716). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The hemogram values, iron, iron binding and ferritin levels of the patients were retrospectively screened through the hospital medical record system. None of the patients received oral iron therapy in the last 6 months before FMC treatment.

The diagnosis of CD was accepted as positive if the titer of tissue transglutaminase IgA antibody in serum samples was >18 AU/ml. Upper gastrointestinal endoscopy was performed in patients with positive serologic tests and duodenal biopsy was performed. Marsh-Oberhuber criteria were used for histopathologic staging.

Pre-treatment values of the patients and control values after FCM intake were obtained. Patients were administered 500

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mg / 10 ml of FCM in 100 cc isotonic water by infusion over 15 minutes, 2 times with an interval of 1 week. Statistical evaluation was performed using SPSS 22 (Statistical Package for the Social Scinces) version. Student t test was used and p<0.05 was considered significant.

RESULTS

Of the 23 patients included in the study, 3 (13.05%) were male and 20 (86.95%) were female. The median age of the patients was 33.7 years (21-50 years). When the distribution of median hemoglobin concentration, iron and iron binding capacity before and after treatment was analyzed, a significant increase was observed in all parameters after treatment (p<0.005). Ferritin level increased, although not significantly. The distribution of hemoglobin concentration, ferritin level, iron and iron binding capacity before and after treatment is shown in Table. No serious side effects were observed in any patient receiving intravenous FCM treatment.

Table. Intra venous ferric carboxymaltose therapy

	Pre-treatment (mean)	Post-treatment (mean)	p*
Hemoglobin	10	12.3	<0.001
Ferritin	15.4	29.2	0.22
İron	29.5	89.8	<0.05
IBC	387.6	298.3	<0.05

IBC; iron binding capacity

DISCUSSION

Anemia as defined by the World Health Organization (WHO), hemoglobin (Hb) below 13 g/dl in men over 15 years of age, below 12 g/dL in women over 15 years of age and not pregnant, and below 11 g/dL in pregnant women. The degree of IDA can be determined by serum ferritin and transferrin saturation. In patients without evidence of inflammation, a ferritin level of less than 30 µg/liter or a transferrin saturation of less than 16% is required for the diagnosis of IDA.[4,5]

FCM is a novel iron complex consisting of a ferric hydroxide core and a carbohydrate shell that stabilizes it. FCM allows controlled delivery of iron to the cells of the reticuloendothelial system and the release of large amounts of ionic iron in serum minimizes the risk. The incidence of adverse events in patients receiving intravenous FCM was similar to that in patients receiving oral ferrous sulfate, with a lower rate of adverse events compared to iron sucrose recipients.[6]

FCM has been approved for use in patients with iron deficiency who do not respond well to oral iron therapy, have intolerance to oral iron preparations, or are on dialysis due to end-stage renal failure, rather than as first-line treatment.[5] In a study by Raquel Ballester-Clau et al.[8] involving 34 patients with liver cirrhosis and GI bleeding, it was observed that early FCM treatment achieved optimal serum Hb levels in patients. It was thought that FCM could be included in first-line treatment.[7] FCM was found to be effective in randomized controlled trials with diseases such as inflammatory bowel disease, chronic kidney disease with or without hemodialysis, chronic heart failure, uterine bleeding, and postpartum anemia.

IDA is the only abnormality observed in approximately 40% of CD. The cause is inflammation of the duodenal mucosa leading to villous atrophy. However, some CD continue to have IDA despite a gluten-free diet and normalization of villous atrophy and are resistant to oral iron supplementation. These patients require periodic intravenous iron administration.[9]

In a study involving 184 individuals, 47 of whom were in the control group and 137 of whom were iron deficiency patients. It was observed that 45 of 137 patients did not respond to iron treatment. Serology was positive for CD in 19 (10.3%) of 184 patients. Of these patients, 13 were treatment-resistant patients, 5 were patients who recovered with treatment and 1 was a control group. Celiac serology positivity was significantly higher in the treatment-resistant group compared to the other two groups.[10] Since the incidence of CD is higher in IDA patients compared to the normal population, serum screening tests for CD should be performed in these patients.

The main treatment for CD is a gluten-free diet. The CD diet may improve mild forms of IDA. Differences of opinion persist regarding oral or intravenous treatment for iron supplementation. Ferrous sulfate is the most widely used treatment because it is inexpensive, easy to administer and has no risk of life-threatening adverse events. Gastrointestinal side effects in 50% of these patients limit its use. With a gluten-free diet in CD, healing of intestinal lesions is delayed and therefore iron stores are replenished later than in normal individuals. In recent years, IV iron agents such as Fe-sucrose and Fe-carboxymaltose have been developed and are under investigation.[11] In our clinic, we observed that anemia improved significantly in patients who received FCM.

Nausea, headache, abdominal pain, diarrhea, hypophosphatemia and rarely hypersensitivity reactions may occur after FCM intake.[12] No serious side effects were observed in any of our patients.

The limitations of this study were that it was retrospective and was conducted in a small group of patients.

CONCLUSION

In this study, we examined hemoglobin, iron, iron binding and ferritin values to evaluate the effectiveness of FCM treatment in CD with iron deficiency. We found that FCM treatment is effective and safe in correcting these parameters. However, we think that prospective studies in larger patient populations are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval was obtained from İnönü University Scientific Researches and Publication Ethics Committee for the study (Date: 02.04.2024 Decision No: 2024/5716).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Elstrott B, Khan L, Olson S, Raghunathan V, DeLoughery T, Shatzel JJ. The role of iron repletion in adult iron deficiency anemia and other diseases. *Eur J Haematol.* 2020;104(3):153-161.
2. Kumari R, Bharti RK, Singh K, et al. Prevalence of iron deficiency and iron deficiency anaemia in adolescent girls in a tertiary care hospital. *J Clin Diagn Res*. 2017;11(8):BC04-BC06.
3. Bregman DB, Goodnough LT. Experience with intravenous ferric carboxymaltose in patients with iron deficiency anemia. *Ther Adv Hematol*. 2014;5(2):48-60.
4. World Health Organization. Iron deficiency anemia. assessment, prevention, and control. A guide for programme managers. 2001;47-62.
5. Koduru P, Abraham BP. The role of ferric carboxymaltose in the treatment of iron deficiency anemia in patients with gastrointestinal disease. *Therap Adv Gastroenterol*. 2016;9(1):76-85.
6. Lyseng-Williamson KA, Keating GM. Ferric carboxymaltose: a review of its use in iron-deficiency anaemia. *Drugs*. 2009;69(6):739-56.
7. Ballester-Clau R, Torres Vicente G, Cucala Ramos M, et al. Efficacy and safety of treatment with ferric carboxymaltose in patients with cirrhosis and gastrointestinal bleeding. *Front Med (Lausanne)*. 2020;17(7):128.
8. Bailie GR. Efficacy and safety of ferric carboxymaltose in correcting iron-deficiency anemia: a review of randomized controlled trials across different indications. *Arzneimittelforschung*. 2010;60(6a):386-98.
9. Stefanelli G, Viscido A, Longo S, Magistroni M, Latella G. Persistent iron deficiency anemia in patients with celiac disease despite a gluten-free diet. *Nutrients*. 2020;12(8):2176.
10. Shahriari M, Honar N, Yousefi A, Javaherizadeh H. Association of potential celiac disease and refractory iron deficiency anemia in children and adolescents. *Arq Gastroenterol*. 2018;55(1):78-81.
11. Talarico V, Giancotti L, Mazza GA, Miniero R, Bertini M. Iron deficiency anemia in celiac disease. *Nutrients*. 2021;13(5):1695.
12. Hussain I, Bhoyroo J, Butcher A, Koch TA, He A, Bregman DB. Direct comparison of the safety and efficacy of ferric carboxymaltose versus iron dextran in patients with iron deficiency anemia. *Anemia*. 2013; 69107.