







Successful Desensitization with Ferric Carboxymaltose

Özlem ÖZDEDEOĞLU¹ , Kurtuluş AKSU¹ , Buket AKDOĞAN¹ , Hale ATEŞ¹ , Gözde BUHARI¹ ,
İlkay KALKAN¹ , Seçkin ÖZGÜL² , Görkem KAYA² 

¹ Department of Chest Diseases, Division of Allergy, University of Health Sciences, Ankara Atatürk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey

² Department of Internal Medicine, University of Health Sciences, Ankara Atatürk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey

Corresponding Author: Kurtuluş AKSU ✉ kurtulusaksu@yahoo.com

ABSTRACT

Parenteral iron treatment is used especially in patients who need urgent treatment, have intolerance symptoms to oral iron therapy, and/or where therapy with oral iron supplementation is insufficient. Allergic reactions can be observed with intravenous iron containing medicines and they should thus only be administered by trained staff with appropriate resuscitation facilities. The European Medicines Agency does not approve the use of intravenous iron-containing products in patients with previous hypersensitivity reactions to other parenteral iron products in its 2013 recommendations to manage the risk of allergic reactions to intravenous iron-containing medicines. However, it may be an option to administer intravenous iron therapy with desensitization in patients who need urgent treatment, who cannot be treated effectively with oral iron preparations, or display intolerance to these products. Here we present the first case of successful ferric carboxymaltose desensitization in a patient who had suffered a prior reaction with the same medicine.

Keywords: Desensitization, ferric carboxymaltose, hypersensitivity, iron deficiency anemia

INTRODUCTION

Iron deficiency anemia (IDA) is a worldwide disease and may lead to health problems including cardiac problems like tachycardia, arrhythmia, and even heart failure unless it is treated properly. Oral iron supplementation is the traditional approach for treating IDA and intravenous iron is one of the treatment options for the management of IDA when oral iron cannot be administered due to lack of effect or intolerance. In the last decade, three new formulations (ferumoxytol, ferric carboxymaltose [FCM] and iron isomaltoside) that release elemental iron more slowly and allow complete replacement dosing in 15-60 minutes have been approved in the United States and Europe (1). FCM contains a complex carbohydrate shell that tightly binds elemental iron and establishes a stable complex. It has the advantage of having a very low immunogenic potential and low risk of anaphylaxis and also allows administering a large dose of supplemental iron in a short period of time (2). A systematic literature review of published randomised controlled trials in 2014 on the use of FCM in IDA deficiency

has revealed that no cases of anaphylaxis were reported in patients treated with FCM (3). Recent studies have also not reported any anaphylactic reactions with the use of FCM (4, 5). A retrospective pharmacoepidemiological study that evaluated the reporting rate of severe hypersensitivity reactions between 2014 and 2017 has shown that the rate of anaphylaxis per 100.000 daily doses for FCM varied from 0.3 to 0.5 (6). Intravenous iron therapy should be administered by trained staff with appropriate resuscitation facilities. In patients with a history of hypersensitivity reactions to an intravenous iron formulation, other intravenous formulations are also contraindicated. This creates a challenge in the treatment of IDA (7). Here we present the first FCM desensitization in a patient with a history of previous reaction to the substance.

CASE REPORT

A 52-year-old female with a diagnosis of IDA and possible gastrointestinal absorption disorder was referred to the allergy clinic due to a previous systemic hypersensitivity

reaction following administration of intravenous FCM. She had been diagnosed with IDA two years ago and prescribed oral iron treatment. Despite this supplementary treatment, the iron deficiency persisted and she had been placed on intravenous FCM treatment with a total dose of 1500 mg. However, within the first hour of receiving the first dose of intravenous iron treatment (500 mg FCM in 100 ml of 0.9% sodium chloride solution administered as an infusion in 15 minutes), she had experienced generalized itch and hives on her trunk. Due to this hypersensitivity reaction, she had refused using any iron supplementation either orally or intravenously for the following two years. She had been readmitted to the internal medicine clinic due to her severe complaints (intense fatigue, weakness and mild amnesia) two years after the hypersensitivity reaction. Laboratory tests revealed a hemoglobin level of 8 g/dl, hematocrit level of 28.6%, and ferritin level of 4 ng/ml. Regarding her intense complaints and significant iron deficiency and the previous history of anemia that did not resolve with oral iron supplementation, parenteral iron therapy with 1000 mg of FCM was suggested by the internal medicine specialist and she was referred to the allergy clinic. Due to the previous history of hypersensitivity reaction to FCM, we decided to administer FCM by desensitization.

Written informed consent was obtained from the patient. The FCM desensitization protocol of Montandon et al was used with some modifications (8). The patient was premedicated with intravenous 60 mg methylprednisolone, and oral 5 mg levocetirizine and 10 mg montelukast 60 minutes prior to the procedure. We prepared a stock

concentration of 2 mg iron/ml FCM (1 vial of 500 mg Ferinject[®], 250 ml of 0.9% sodium chloride solution) since Ferinject[®] should not be diluted to concentrations less than 2 mg iron/ml for stability reasons (9). The infusion was started at 0.25 mg over 15 minutes at a rate of 0.5 ml/hr. Each dose was infused over 15 minute intervals at an increasing rate until 250 ml/hr was reached. Then, the next 500 mg FCM in 250 ml of 0.9% sodium chloride solution was infused in 1 hour (Table I). With a 4-hour desensitization protocol, the patient received a total dose of 1000 mg of FCM and no allergic reaction was observed.

DISCUSSION

The European Medicines Agency in its 2013 report of recommendations to manage the risk of allergic reactions to intravenous iron-containing medicines does not approve use of intravenous iron-containing products in patients with previous hypersensitivity reactions to other parenteral iron products (7). However the management of IDA with oral iron supplementation can be quite challenging, especially in those who have severe disease, gastrointestinal absorption problems, or intolerance to oral iron preparations. For such patients with a history of hypersensitivity reactions to parenteral iron products, intravenous iron treatment, desensitization may be an option for management of the disease.

There have been seven published intravenous iron desensitization protocols: four to iron dextran in patients with prior reactions to iv dextran, one to iron sucrose in a patient with a prior reaction to oral iron salts; and

Table I. Ferric carboxymaltose desensitization protocol.

Dose number	Infusion Rate (ml/Hour)	Dose (mg)	Cumulative Dose (mg)	Infusion Time (minutes)
1	0.5	0.25	0.25	15
2	1	0.5	0.75	15
3	2	1	1.75	15
4	4	2	3.75	15
5	8	4	7.75	15
6	16	8	15.75	15
7	32	16	31.75	15
8	64	32	63.75	15
9	128	64	127.75	15
10	250	375	502.5	45
11	250	500	1002.5	60

Each 500 mg of FCM was added to 250 ml of 0.9% sodium chloride solution.

two patients to iron sucrose with prior reactions to iron sucrose (10-15). Montandon et al. have published the only intravenous iron desensitization protocol to FCM. The article is a case series of successful intravenous iron desensitization with FCM in two patients with prior anaphylaxis to iron dextran and ferric gluconate, and one patient with prior anaphylaxis to an unknown intravenous iron formulation as well (8).

The present case had a history of a previous mild hypersensitivity reaction to FCM. She was informed about drug provocation tests and desensitization. Since she had severe anemia symptoms and she did not want to lose time, and an additional hospital visit would be needed for a drug provocation test, drug desensitization was suggested. Desensitization to FCM was performed successfully by using the protocol described by Montandon et al. The previous cases in the literature were hypersensitive to iron formulations other than FCM. Herein, we presented the first case of successful FCM desensitization in a patient with a history of a prior reaction to FCM.

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