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CASE REPORT

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Acute hypersensitivity reaction following intravenous ferric carboxymaltose injection for iron deficiency anaemia: a case report.

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ABSTRACT

Ferric carboxymaltose (FCM) is a non-dextran iron preparation used for intravenous treatment of iron deficiency anaemia (IDA) in adult patients with intolerance or poor response to oral iron therapy. Acute hypersensitivity reactions (HSRs) during iron infusions are very rare but can be life-threatening even after receiving a prior test dose. Here, we report a case of 42 years old female patient who underwent total laparoscopic hysterectomy with bilateral salpingo-oophorectomy. On the next postoperative day she received an injection of ferric carboxy maltose. She was diagnosed with IDA. She presented with the picture of an adverse drug reaction due to injection FCM. She was managed with oxygen, vasopressors, antihistaminics, intravenous fluids and, corticosteroids. She recovered well within 24 hours of intensive care unit admission following this adverse drug reaction. So, careful and precise observation is required in management of adverse reaction following ferric carboxymaltose and prompt recognition and treatment based on severity is warranted.

KEY WORDS: Ferric carboxy maltose, hypersensitivity reaction, intensive care unit.

INTRODUCTION

Iron deficiency anaemia (IDA) is common in pregnancy. Oral iron therapy and blood transfusion are frequently used for the management of IDA but they have significant adverse events and drawbacks. A high dose of oral iron causes significant side effects and they are mainly non-compliant. Intravenous (IV) iron is increasingly used for the treatment of IDA in cases of poorly tolerated oral iron therapy or inappropriate blood transfusion. Intravenous iron produces a better haematological response than oral iron, including a faster increase in haemoglobin and rapid replenishment of body iron stores and may provide an alternative to transfusion in profound IDA [1]. All available iron preparations for parenteral use can cause short-term side effects, including anaphylactic reactions. We report an acute anaphylactic reaction following intravenous infusion of ferric carboxy maltose (FCM) in a 42 years old woman after total laparoscopy hysterectomy. Informed consent was obtained from the patient for the publication of all information and images.

CASE REPORT

PATIENT INFORMATION: A 42 years old female patient underwent total laparoscopic hysterectomy with bilateral salpingo-oophorectomy (TLH+BSO) surgery. On the first post-operative day she received an injection of ferric carboxy maltose (FCM) 1 gram diluted in 100 mL normal saline infused over 20 minutes. But nearly 25 minutes after the infusion, the patient developed sudden shortness of breath, severe itching and three episodes of vomiting.

CLINICAL FINDINGS: Apart from a history of oral iron intake she has a history of co-existing hypertension, diabetes mellitus, hypothyroidism, IgA nephropathy and Iron deficiency anaemia on initial workup. She underwent TAH+ BSO after completing his child bearing age. At presentation Pallor: ++, Temp: 39 ℃, Glasgow coma score (GCS): 15/15, heart rate (HR): 144 bpm, non-invasive blood pressure (NIBP): 75/60 mm Hg, respiratory rate (RR): 34/min, SpO2: 88% on room air and swelling over the lips and face with hoarseness of voice. On Auscultation chest was clear with no crepts and wheezing, and heart sounds were normal. The patient was anxious but oriented to time, place and person. She was having angioedema of lips and eyelids with urticaria on her upper limbs (figure 1). She was not on any routine medications. Abdominal examination was normal. She doesn't give any history of allergy to different iron oral formulations. She did not have any previous history of drug or food allergies. She was given an FCM test dose before administering the drug intravenously and she did not develop any reaction.

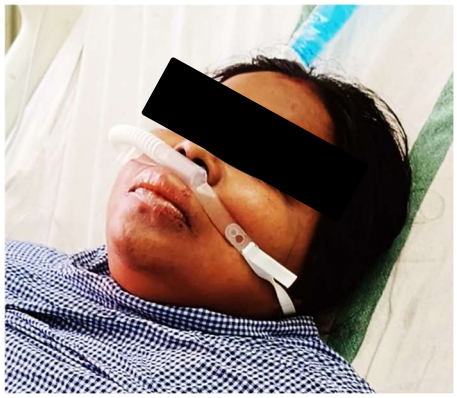

Figure 1. Shows angioedema of lips as acute hypersensitivity reaction following infusion of ferric carboxy maltose with high flow nasal cannula support.

DIAGNOSTIC ASSESSMENT: Initial Arterial blood gas (ABG) obtained showed features of acute respiratory alkalosis PH 7.33, PCO_2 12.9, PO_2 145, HCO_3 19.8, Lactate 4.2, Hb 7.3 g/dl, PO_2 and FiO_2 ratio was 203. Random blood sugar was 266 mg/dl

THERAPEUTIC INTERVENTION: The patient was further investigated and managed in the intensive care unit (ICU). She was managed with oxygen administration through a non-rebreathing face mask (NRM) at the rate of 15 L/min, intravenous epinephrine 1 mg (1:1000), dexamethasone 8 mg and Pheniramine 45 mg. One litre bolus crystalloid fluid was administered from the peripheral line, meanwhile, right internal jugular vein cannulation was secured and injection noradrenaline infusion at the rate of 5-10 microgram/min was initiated. Thereafter maintenance fluid was continued at the rate of 100 ml/hr. The patient was shifted to a high-flow nasal cannula (HFNC) providing oxygenation at FiO2 of 50% and flow rate of 60L/min as her respiratory rate was more than 30/min on NRM. A repeat dose of intravenous dexamethasone 8 mg was given to decrease the progressive swelling. However, nebulisation of 1 ml epinehrine (1:1000) in 5 ml of normal saline (0.9%) was added to reduce severe laryngeal oedema. An urgent chest x-ray was done which showed normal clear lung fields with normal cardiac shadow.

The patient gradually improved symptomatically and her cardiorespiratory parameters became stable and she was maintaining a urine output of more than 1 ml/kg/hour. The patient was hemodynamically stable and no new deterioration was seen on next day. Gradually the noradrenaline infusion was tapered she was maintatining a mean arterial pressure (MAP) of > 75 mm Hg. Oxygen requirements gradually decreased, but overnight HFNC was continued with FiO2 of 50 per cent and flow of 30 L/min. On 3rd day of ICU admission she was given a NRM trial and she was comfortable with respiratory rate of 20/min and oxygen saturation of > 94%.

Table 1. Hourly progress of the patient after ICU admission.

Time in ICU (Hours)	Inj.Noradrenaline (microgram/min)	Oxygen support	Heart rate (per minute)	Mean blood pressure (mm Hg)	SpO_2 (%)	Urine output (ml/hr.)
6	10	HFNC at 60 lit/min and FiO_2 of 50%	142	40	98	0.5
12	4	HFNC at 30 lit/min and FiO_2 of 50%	118	74	94	1.0
24	1	NRFM at 10 lit/min and FiO2 of 50%	98	90	96	1.0
48	0	Nasal cannula at 4 lit/min and FiO2 of 40%	85	82	94	1.0

ICU: intensive care unit, HFNC: high flow nasal cannula, NRFM: non rebreathing face Mask, SPO_2: oxygen saturation

DISCUSSION

There are five formulations like iron dextran, Iron-sorbitol-citric acid, iron sucrose, ferric carboxymaltose, and iron isomaltoside are currently commercially available for intravenous iron therapy. Short-term side effects like the metallic taste, nausea, vomiting, diarrhoea, abdominal pain, hypotension, and allergic or even anaphylactic reactions are reported. In our case, she presented symptoms of acute anaphylaxis like shortness of breath dyspnoea, angioedema, and urticaria with hypotension following the first dose of parenteral iron (FCM). The systemic reaction observed in response to the first dose of intravenous iron preparations has not been always found to be IgE mediated and is therefore described as an anaphylactic or anaphylactoid reaction [2]. Any history of drug sensitivity, a history of immune/inflammatory/allergic disease, mastocytosis, and a high infusion rate are some of the risk factors responsible for hypersensitivity reactions related to IV-iron administration [3]. FCM is a non-dextran third-generation IV-iron preparation that has the advantage of normalizing haemoglobin and replenishing iron stores over a short period because it can be administered fast and in high doses [4].

In our case, an adverse drug reaction occurring a few minutes after infusion of the first dose of FCM suggests a hypersensitivity reaction rather than immediate dose-related toxicity. WHO causality assessment scale indicated a probable relationship between the hypersensitivity reaction and FCM as the causal drug [5]. We have not analysed the serum IgE or tryptase levels due to the non-availability of biochemical kits, we were not able to establish whether this reaction was an anaphylaxis or an anaphylactoid reaction.

CONCLUSIONS

The tolerability and efficacy of newer parenteral iron preparation ferric carboxymaltose have been safely used in treating anaemia in pregnant and non-pregnant patients. However, Ferric carboxymaltose usually doesn't required a test dose before its administration. However, acute hypersensitivity reactions may develop when newer iron preparations are used, even after tolerating the prior test dose. So, careful and precise observation is required in management of adverse reaction following ferric carboxy-maltose and prompt recognition and treatment based on severity is warranted.

SUPPLEMENTARY INFORMATION

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Institutional Review Statement: *The study was conducted according to the guidelines of the Declaration of Helsinki.*
Informed Consent Statement: *Informed consent was obtained from all subjects involved in the study.*
Data Availability Statement: *The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.*
Conflicts of Interest: *The authors declare no conflicts of interest.*

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