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Case Report

Pharmacology Section

Delayed Hypersensitivity with Ferric Carboxymaltose

SURABHI SRIDHARA[1], RAJESH VILAKKATHALA[2], RAVINDRA PRABHU[3], KARAN SARAF[4]

ABSTRACT

Ferric Carboxymaltose (FCM) is widely used in the treatment of anaemia of Chronic Kidney Disease (CKD). The clinicians must be alert of the rare adverse events such as hypersensitivity with subsequent doses of FCM. Here, we report a case of a 59-year-old male a known case of CKD, with anaemia and thrombocytopenia. FCM was the treatment of choice. This case report indicates the onset of adverse reaction with FCM with the second dose even though the first dose was well tolerated.

Keywords: Anaemia, Hypersensitivity, Iron preparations

INTRODUCTION

A 59-year-old male visited the Department of Nephrology with chief complaints of breathlessness and bilateral lower limb swelling since 15 days. He was diagnosed with CKD stage 5 (non dialysis dependent) and type 2 Diabetes Mellitus since eight years, hypertension, hypothyroidism, left cerebrovascular accident and hemiparesis. Diabetes was managed with 12 units of injection Human Mixtard 30/70 in the morning and 6 units at night. This contains 70% of insulin Neutral Protamine Hagedorn (NPH) and 30% of regular insulin. During 2013 he underwent laser treatment for Diabetic retinopathy. In march 2016 he was hospitalized due to volume overload which was diagnosed as CKD-4 and managed with diuretics. On evaluation his biochemical parameters indicated anaemia and thrombocytopenia.

On admission the lab parameters were Reticulocyte percentage (RET%) - 1.12%; Mean reticulocyte volume – 87.5 fl; Red Blood Cells (RBC) - 3.3 x 10^6 cells/µl; Serum creatinine (Scr) – 5.2 mg/dL; Iron (total) –68 µg/dL; Total Iron Binding Capacity (TIBC)- 200 µg/dL; Hct-19.6%; RBC-3.19x106; Mean Corpuscular Volume (MCV)- 61.5 fl; Mean Corpuscular Haemoglobin (MCH)-18.4 pg; Mean Corpuscular Haemoglobin Concentration (MCHC)- 30 gm/dL; Red blood cell Distribution Width (RDW)- 18.5%; Procalcitonin (PCT)- 0.059%; Ferritin- 968.2 ng/mL and Haemoglobin (Hb): 6.5 gm/dL. He was managed with oral diuretics for breathlessness and lower limb swelling. Ferric Carboxymaltose was considered for the management of anaemia and the therapy was initiated on day three of the hospitalization. The weight of the patient was recorded as 74 kg for which 2 gm was the ideal dose based on the standard recommendations but due to financial constraints of the patient, the clinicians decided on administering 1 gm of the drug. The first dose of FCM (Encicarb) 500 mg in 100 ml of normal saline was well tolerated but on the second day with the same dose of FCM, 500 mg in 100 mL of Normal Saline but with a different brand Ferinject, the patient developed chills, breathing difficulty and a temperature spike of 101°F after 15 minutes of administration. The change in brand is attributed to non-availability of the prior one. The vital parameters at the onset of reaction were elevated, BP: 200/120 mmHg, PR: 120 bpm, RR: 26/min. According to the Naranjo's causality assessment a score of five was obtained which categorizes it as a probable ADR [1] and according to WHO it's a probable ADR [2]. The patient was managed with intravenous (IV) administration of a single dose of 45.5 mg Pheniramine maleate and 100 mg of Hydrocortisone to which the symptoms resolved in 30 minutes.

DISCUSSION

Anaemia of CKD is a common complication; the prevalence of anaemia is proportional with increase in the grading of kidney disease. Anaemia is often attributed to various complications such as reduced quality of life, mortality, cognitive impairment and increased hospitalizations [3]. Renal ischaemia and vasoconstriction accounts to one of the major causes of anaemia in this patient population. Anaemia could lead to progression of kidney disease and cardiac complications such as Congestive Heart Failure (CHF) [4]. Management of anaemia in CKD requires optimum balance of the ESA (Erythropoetin stimulating therapy) and iron. Oral or Intravenous (IV) iron supplementation is the choice of therapy in iron-deficient, anaemia in non-dialysis CKD patients, according to the current National Kidney Foundation, Kidney Disease Outcomes Quality Initiative guidelines [5].

Ferric carboxymaltose complex is a non–dextran containing iron agent [6]. This drug was approved in July 2013 by the US-FDA for the treatment of iron deficiency anaemia in adults who are intolerant to or do not respond adequately to oral iron. The product was also approved for anaemia in adults with non-dialysis dependent chronic kidney disease [7]. Large doses of iron can be rapidly injected in a short duration which makes this a unique and novel preparation. FCM can be safely injected as a single dose in the range of 200-1000 mg in a short duration of 15 minutes. This in turn reduces the need for multiple administration of intravenous iron, which makes it a favoured choice for the treatment of anaemia [6]. In comparison with iron gluconate and iron sucrose FCM is less reactive which ensures controlled delivery of iron to the target tissues.

FCM displays better tolerance and efficacy in comparison with oral iron in treatment of non-dialysis dependent CKD patients. Incidents of peripheral oedema, hyperkalemia, urinary tract infection, hypotension, bronchitis, headache and infusion site reaction have been reported with the use of FCM [8]. Serious Adverse Events (SAE) such as dyspnea, hypersensitivity and anaphylactoid reactions have also been reported in clinical trials and post marketing surveillance. The adverse events reported in this case such as fever, chills and dyspnea is seen in uncommon and occurs in more than 1/1000 [9].

Intravenous preperations trigger allergic reactions by immunological IgE response or by Complement Activation Related Psuedoallergy (CARPA). Minimal data is available to contemplate the concept of IgE-mediated hypersensitivity which attributes to current formulations of IV iron. The CARPA can be attributed to infusion related reactions with nano particles. The final common pathway of these processes is likely to include activation of mast cells and basophils, either directly, or via anaphylatoxins (C3a and C5a) that increase in blood as a consequence of complement activation [10]. In this case, the hypersensitivity reaction can be elucidated by the above mechanism. A case report has been reported with (FCM) where the test dose was well tolerated but the patient developed allergic reactions like vomiting and breathlessness on the administration of the first dose of the same [11]. In our case, the patient tolerated the first dose well but developed allergic reaction to the subsequent dose. This case report focuses on the fact that hypersensitivity could occur with subsequent doses of FCM, even though no hypersensitivity was reported on administration of the test dose and the first dose of FCM.

CONCLUSION

This case reports hypersensitivity with subsequent dose of ferric carboxymaltose after the first dose was well tolerated. Hypersensitivity with the use of FCM has been reported but physicians should be alert on this rare manifestation for better management of the disease.

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PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Student, Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal, Karnataka, India.
2. Assistant Professor (Selection grade), Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal, Karnataka, India.
3. Professor and Head, Department of Nephrology, Kasturba Medical College, Manipal, Karnataka, India.
4. Registrar, Department of Nephrology, Kasturba Medical College, Manipal, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Ravindra Prabhu,
Professor and Head, Department of Nephrology, Kasturba Medical College, Manipal University, Manipal-576104, Karnataka, India.
E-mail: aravindraprabhu@gmail.com

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