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Intravenous Ferric gluconate-induced Hyperkalemia

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ABSTRACT

Hyperkalemia is a very commonly encountered electrolyte abnormality in the hospital setting. Drugs are a major contributing factor to elevated potassium levels in routine clinical practice. Drug-induced hyperkalemia may be asymptomatic, but it can also occasionally be severe and fatal. We present a case of a 58-year-old male with acute exacerbation of Heart failure along with iron deficiency anemia, who developed acute severe hyperkalemia after he was started on IV Ferric gluconate (FG).

Keywords: Hyperkalemia; Drugs; Heart failure

BACKGROUND

Treatment with intravenous (IV) iron has been shown to have many benefits in patients known to have heart failure with reduced ejection fraction (HFrEF) along with concomitant Iron deficiency anemia (IDA).[1,2] It has been shown to reduce recurrent hospitalizations and decrease mortality in these patients. Various formulations of IV iron like low molecular weight iron dextran, iron sucrose, and ferric gluconate are being used for the treatment of severe IDA.[3] Hyperkalemia can be a rare complication of ferric gluconate (FG), seen in about 1-10% of recipients.[4]

CASE PRESENTATION

A 58-year-old male admitted with a past medical history of HFrEF, with an ejection fraction (EF) of 35%-40% on losartan 100 mg and Carvedilol 6.25 mg, Coronary Artery Disease (CAD) status/post-3-vessel coronary artery bypass graft surgery on dual antiplatelet therapy, Diabetes Mellitus type 2 on an insulin pump, Central Sleep Apnea on Bilevel Positive Airway Pressure (BiPAP) and Hypothyroidism presented to the hospital with worsening dyspnea on exertion, weight gain of 10 pounds (lbs.), and increased swelling in his lower extremities.

Vital signs were remarkable for an elevated blood pressure of 165/85 mm of Hg. On physical exam, the patient had bilateral pitting edema up to his mid-shin and rales at bases. His labs were remarkable for magnesium level of 1.5 mg/dl, pro-BNP 2610 pg/ml, WBC 10.9 k/ul, Hb 10 g/dl, MCV 79.6 fl, iron 41ug/dl, T4 0.2 ng/dl, and TSH 93.7

µIU/mL. Chest x-ray was non-revealing. No pulmonary embolism was detected on computed tomography Angiography and electrocardiography was normal. Transthoracic echocardiography was performed which showed an EF of 35-40%. The patient was started on IV furosemide with an improvement in his symptoms. IV FG therapy was subsequently administered the following day for his newly diagnosed IDA. 24 hours after receiving a dose of IV FG, his metabolic panel showed a potassium of 7.2 mmol/L, which was unchanged on repeat testing. The patient's renal function was at his baseline with a creatinine of 1.2mg/dl and blood urea nitrogen of 29 mg/dl. Serum bicarbonate concentration of 29mg/dl**.** IV FG was discontinued, losartan was held, and the patient was started on calcium gluconate, IV insulin with dextrose, and sodium zirconium cyclosilicate with the resolution of his hyperkalemia. Although Losartan is known to cause hyperkalemia, the patient reported no history of the same in the past and there were no other precipitating factors including kidney injury or use of medications that can worsen hyperkalemia. Based on the Naranjo adverse drug reaction probability score of 4, IV FG is concluded as the most probable culprit. The patient was diagnosed with FG-induced hyperkalemia, and it has been added to his list of allergies.

DISCUSSION

The term "hyperkalemia" refers to a serum potassium level that is more than 5.0 -5.5 mEq/L. Its incidence is found to be 1-10% in hospitalized patients with a mortality rate of up to 1 per 1000.[5] Common causes include pseudohyperkalemia, metabolic acidosis, insulin deficiency, impaired or pharmaceutically inhibited renin-angiotensin system, rhabdomyolysis, burns, and trauma.

IV Ferric Gluconate is the only IV iron formulation that is known to cause hyperkalemia, albeit rarely. It is seen in about 1-10% of patients receiving IV Ferric Gluconate. The exact mechanism by which this happens remains unknown, however, two possible theories were postulated. Intracellular concentrations of sodium and potassium are mainly regulated by the Na-K-ATPase pump. This activity of this pump may be inhibited by a rapid increase in serum levels of iron, due to IV infusion, resulting in higher extracellular potassium.[6] Iv iron can cause acidosis, by impairing the electron transport chain and oxidative phosphorylation pathway, resulting in anaerobic glycolysis and thereby lactic acid accumulation.[7] It can also disrupt the Krebs cycle resulting in a build-up of organic acids, which can lower the pH of blood.[8,9] Acidosis can also worsen hyperkalemia by inhibiting potassium secretion from the distal tubule. In addition, acidosis will result in the intracellular movement of excess hydrogen ions and the extracellular movement of potassium ions through the H+-K+ ATPase pump, thereby causing hyperkalemia.[9] In an animal experiment, it was observed that an increase in serum iron by 20%, will increase serum potassium levels by more than 55% and magnesium levels by 31%.[6] However, no similar studies are available in human beings.

Hyperkalaemia is medically managed, by implementing different strategies simultaneously. This includes stabilization of the myocardium through the administration of calcium, facilitating the intracellular shift of potassium by administration of insulin or beta-agonist inhalation, and removing the excess potassium from the body by potassium binding resins and diuresis.[10,11] In cases where hyperkalemia results in cardiac arrhythmia or

resistance to medical treatment, urgent dialysis is needed. In our case, IV FG therapy was stopped, and the patient was started on calcium gluconate, insulin with dextrose, and sodium polystyrene sulfonate, with a resolution of hyperkalemia.

CONCLUSION

IV FG can very rarely cause hyperkalemia which can be life-threatening and requires prompt discontinuation once hyperkalemia is seen. Hence, clinicians need to be aware of this rare but potentially fatal complication.

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