VOLUME - 11, ISSUE - 08, AUGUST - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Hematology

IRON DEFICIENCY ANAEMIA PATHOPHYSIOLOGY, ASSESSMENT.

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ABSTRACT

The most common nutritional deficiency in the world, with 30% of the population being affected in iron deficiency anemia (IDA). In women gastrointestinal bleeding and menstruation is the most common causes of IDA, decreased dietary iron and decreased iron absorption are also culpable causes. In the Patients with IDA (Iron deficiny anaemia) should be treated with the aim of replenishing iron stores and returning the hemoglobin to a normal level. This is shown to morbidity ,improve quality of life, , prognosis in the chronic disease and outcomes in pregnancy. Iron deficiency occurs in many chronic inflammatory conditions, including congestive cardiac failure, chronic kidney disease and inflammatory disease. In This article we will provide to you a updated overview and diagnosis and management of IDA in patients with chronic conditions and preoperative in pregnancy.

KEYWORDS :

INTRODUCTION

IDA is the more prevalent in women and children , adult men are also depending on their socioeconomic status (income) and health conditions.(1) The WHO (world health organization) is recognized iron deficiency anemia (IDA) is the most common nutritional deficiency in the world, and 30% of population affected with this condition.(2) The most common causes of IDA (iron deficiency anemia) are gastrointestinal (GI) bleeding and menstruation in women, reduction of iron intake and absorption are also culpable causes Iron and is required for various cellular functions and including but not limited to enzymatic processes, oxygen transport ,DNA synthesis and mitochondrial energy generation.(3 4)

The symptoms of IDA can vary over a wide range. fatigue, palpitations, Shortness of breath, tachycardia and angina can result from reduced blood oxygen levels. This is show the result hypoxemia can subsequently and they cause a compensatory decrease in intestinal blood flow, leading to motility disorder, weight loss and abdominal pain malabsorption, nausea. And Central hypoxia can cause headaches, and lethargy cognitive impairment with several studies and they show improvement in cognitive functions once anaemia is the normalized.(5-6). That is well known as IDA significantly affects quality of life (QoL)(7) and with recent evidence demonstrating that treating IDA improves QoL, regardless of the underlying found anaemia.(8 9)

PATHOPHYSIOLOGY

Iron is the essential element and they are controlled primarily by dietary intake and intestinal absorption, iron recycling.(10) The Dietary iron is found in two forms: haem and non-haem iron. Haem iron is easily absorbed and arises from hemoglobin (Hb) and myoglobin. And myoglobin in the form of animal meat, fish and poultry. Non haem iron is mostly found in plant food but is not as easily absorbable. Compounds such as oxalate, phytate, and tannin, polyphenols which are found in plants, diminish and they uptake of non-haem iron, some drugs, such as proton pump inhibitors.

Ascorbic acid and gastric acid, citrate, conversely, facilitate iron absorption.(11) In healthy diet we include approximately 5–15 mg of elemental iron and 1–5 mg of haem iron are ingested daily only 1–2 mg is ultimately absorbed into the intestine, predominantly in the proximal jejunum duodenum (12) IDA does not develop rapidly in most cases and Three sequential phases evolve until the manifestation of clinical signs and symptoms are apparent.

ASSESSMENT AND DIAGNOSIS, MANAGEMENT

The WHO (world health organization)) defines anemia is blood Hb level below 120g/L in women and 130g/L in men. (17) transferrin saturations (TSAT) and Serum iron will be reduced with TSAT less than 20% and required for the diagnosis of IDA (iron deficiency anemia).(18) for the breakdown of diagnostic criteria for IDA. That is crucial to note that iron deficiency not be excluded in the presence of a normal Hb(hemoglobin) as a significant amount of iron must be lost before the Hb levels begin to decline. Low mean corpuscular Hb with a normal Hb or an increase in red cell distribution width signifies we faund mild iron deficiency without anaemi.(19)

In isolated iron deficiency, serum ferritin (the storage molecule for iron) less than 30ug/L.(20), ferritin is an acute phase protein and they can be increased in the presence of inflammation.(21) there is evidence of concomitant inflammation, such as elevated C reactive protein, ferritin less than 100ug/L is indicative of IDA.(22) And Transferrin, iron transporter, is generally elevated; it is a negative acute phase protein and, they can be normal or decrese in chronic inflammatory states.(23)

The Patients with IDA(iron deficiency anemia) we treated them with the aim of replenishing iron stores and returning of the Hb to the normal level. It has been shown to improve quality of life(QoL), prognosis in chronic disease and morbidity, outcomes in pregnancy.(24) The iron replenishment can occur via three routes: oral iron, parenteral oral and transfusion of packed red cells.

CONVENTIONAL ORAL IRON FORMULATIONS

The systematic review demonstrated that gastrointestinal (GI) side effects and the most problematic with constipation being the most frequent complaint and followed by diarrhoea and nausea.(25) The British Society of Gastroenterology recommends ferrous preparations and specifically ferrous sulphate, as first-line therapy for iron replenishment, Good bioavailability, available in multiple preparations and have been shown to replenish iron stores and correct anemia effectively.(26) there is also many limitations to their use and the most common being the frequency and severity of side effects. This will have a resultant effect on patient, likely leading to cessation and inadequate treatment.

The appropriate dosing of ferrous iron preparations is also a contentious issue between clinicians. To adequately replenish

iron stores and therapeutic treatment of iron deficiency anemia (IDA) is initially felt to require 200 mg of iron sulphate 2–3 times per day and in order to raise Hb by 20g/L over a 4-week period, with treatment continuing for 3 months.(27) The daily doses of elemental iron should not be greater than 100 mg/day.(28) The body can only absorb 10–20 mg of iron per day.(29) And It should be noted that 200 mg of ferrous sulphate is equivalent to 65 mg of elemental iron.(30)

NOVEL ORAL IRON FORMULATIONS

sucrosomial iron is innovative oral ironcontaining carrier and in ferric pyrophosphate is phospholipids belayed membrane forming the 'sucrosome' and creating the gastroresistant complex and they transported to the intestinal mucosa is absorbed without free iron interacting with the gut wall.(31)(32) This unique structure protects iron from acidic environment in the stomach and increases intestinal epithelial absorption and ensures high bioavailability while reducing the risk for potential adverse gastrointestinal (GI) effects.(33) The Despite of lower doses elemental iron and this newer oral iron preparation 30–60mg/day. And they shown greater efficacy in increasing Hemoglobin (Hb) and ferritin concentrations compared with the ferrous sulphate 105–210mg/day and with a mean Hb increase in 2.7g/dL , 1.4g/dL, respectively, over a 12-week course of treatment.

A novel preparation, Ferric maltol, is a non-salt oral iron formulation composed of stable ferric iron complexed with a tri-maltol and sugar derivative. They are licensed in the USA and the European Union and sold under the brand names Accrufer and Feraccru respectively. Absorbed, the maltol ligand remains complexes to iron and which reduces the formation of free iron and facilitates iron transport across the enterocyte.(34) This is the subsequently increases the bioavailability of the iron such that lower doses of elemental iron are required to treat iron deficiency anemia (IDA) compared with the ferrous iron preparations.(35) ferric maltol has been shown to have less of an effect on the gut microbiome.(36) Studies of the use of ferric maltol is limited to patients with inflammatory bowel disease (IBD), and the results demonstrating improvement in Hb levels beyond 12 weeks with sustained normal Hb levels up to 64 weeks and they compared with placebo.(37,38) When compared with the intravenous ferric carboxymaltose, ferric maltol is show to the inferior and did not meet the primary endpoint of increasing hemoglobin (Hb) by 2g/L or Hb normalisation by the 12 weeks (68%vs 85% respectively).(39).

IRON NEEDS IN INFANTS AND CHILDREN

Premature infants they have faster rate growth of postnatal and than infants born at term, so unless the diet is supplemented with iron and they iron depleted more rapidly than full-term in infants. Iron deficiency anemia can develop by 2 to 3 months of age in premature infants (baby). the normal infant iron stores are adequate to maintain of iron sufficiency for approximately 4 months of the postnatal growth. The premature infant and total body iron is lower than in the full-term newborn and although the proportion of iron to body weight is similar.

Mother's Breast milk and cow's milk both contain about 0.5 mg to 1.0 mg of iron / liter and its bioavailability differs significantly. The absorption of iron from breast milk is uniquely high, about 50% of average, and its tends to compensate for low concentration. And In contrast, only about 10% of iron in whole cow's milk absorbed. About 4% of iron is absorbed from the iron-fortified cow's milk formulas that contain 12 mg of iron / liter. Reasons for high bioavailability of iron in breast milk.

The Iron intake must supplement the approximately 75 mg of iron / kgm of body weight that is present at birth time. Iron losses from body are small and relatively constant except during episodes of diarrhea or during the feeding of whole cow's milk and iron loss increased. Approximately two thirds of iron loss in the infancy occur when cells are extruded from the remainder cells and the intestinal mucosa. Remainder cells are shed from the skin and urinary tract. In the normal infant and these losses average approximately 20 mg/kg/day. Infants aged 7 to 12 months need 11 mg of iron in day. Babies younger than 1 year given iron-fortified cereal in addition to breast milk or an infant formula supplemented with iron. (40)

INTRAVENOUS IRON

There are a variety of intravenous iron and preparations with selection of the agent dependent on multiple factors including cost considerations, patient and physician preference, product availability. They are important to note that clinical studies of the various formulations follow different protocols, and there are no large headto-head trials between these formulations comparing efficacy and safety profile.

The Older intravenous iron is preparations such as highmolecular weight dextran iron (Dexferrum) discontinued due to their unfavorable safety profiles with relatively high incidence of anaphylaxis.(41) The lower molecular weight dextran compounds such as Cosmofer and they still in use and shown to be effective with a much lower incidence of anaphylactic reactions.(42) There is not been a study comparing the different preparations and a meta-analysis looking at the overall rate of anaphylaxis with intravenous dextran was 0.61% (43) which is significantly greater than the newer non-dextran intravenous preparations (44)

The alternative oral iron supplementation is parenteral administration. Intravenous iron is preferred route of administration in patients and is increasingly favoured due to its rapid correction of Hemoglobin (Hb), improved safety profile and fewer side effects . The primary advantage of intravenous iron is that it bypasses the gastrointestinal (GI) tract absorption and there avoiding further mucosal aggravation and inflammation and producing less side effects.(45)

Erric derisomaltose (Monofer) is alternative intravenous iron preparation and they often preferred to Cosmofer due to its shorter infusion time, thereby optimizing the use of medical infusion units and nursing time and these drugs are often given a day-case procedures. Monofer is preferred by some can be given as one infusion rather than two infusions. Ferric carboxy maltol (Ferinject) is the preparation widely used in the united kingdom (UK). They can safely administered at single dose of 1000 mg within 15min; And two infusions required in patients, depending on their weight and Hb levels. The iron sucrose (Venofer) is given a slow injection of 100–200 mg 2–3 times a week.(46) they can be shown to effective and although a comparison study show Ferinject to superior. Ferinject was associated with a higher rate of achieving a 2g/dL increase in Hemoglobin (Hb) concentration in comparison to the iron sucrose by relative risk of 1.65.51pationt the major drawback use is the need for multiple infusions and some can not only less acceptable in patients made difficult for overstretched healthcare services.

RED BLOOD CELL TRANSFUSION

The Clinicians are rightly reluctant to transfuse patients unnecessarily and it is associated with not insignificant risks. These include an increased mortality with liberal blood transfusion and the setting of upper gastrointestinal (GI) bleeding.(47) There is increased incidence of transfusion-related reactions and This includes the risk of Transfusion Related Acute Lung Injury and which one of the most serious reactions, the incidence of which is approximately 1 in 5000 transfusions.(48) Furthermore, there remains a small risk for transmitting infections, both viral and bacterial (49-50).

This is the advised that transfusions should be reserved for patients with severe anaemia, haemodynamically unstable or associated comorbid conditions.(51) severe anaemia is defined as hemoglobin(Hb) many of these patients haemodynamically stable and rather have chronic anaemia and remaining asymptomatic. Although a unit of blood contains approximately 200 mg of iron,(52) these patients are very likely to require further iron supplementation to adequately replenish their iron stores and particularly if the cause for their anaemia is chronic and not easily treatable, for example, advanced malignancy or haematological disease.(53)

CONSIDERATIONS IN MANAGEMENT

COMORBIDITIES

Many chronic inflammatory disorders, such as congestive cardiac failure (CCF), chronic kidney disease (CKD), and inflammatory bowel disease (IBD), cause IDA. To make matters more complicated, symptoms like weariness are frequent in many disorders and can be mistaken for IDA symptoms. As a result, IDA management is frequently overlooked. In these situations, untreated IDA might have more serious repercussions, exacerbating the underlying sickness. (54)

CARDIAC CONGESTIVE FAILURE

IDA is one of the most common concomitant conditions in CCF (55), and it can be caused by a variety of causes, including decreased appetite, increased GI blood losses owing to antiplatelet or anticoagulant therapy, and decreased GI absorption due to oedema.(56) The median dose of iron required to adequately replenish iron in patients with CCF and IDA is 1000mg.

59 Patients using ferrous sulphate, the first-line oral preparation, had a bioavailability of only 10% at best 60, requiring a minimum of 50 days at a dose of 200mg/day to cure the iron deficiency. It can take up to 6 months to adequately replenish iron stores, depending on missing doses or non-adherence. (580 As a result, intravenous iron should be regarded first-line therapy for CCF iron insufficiency.(57)

The Ferinject Assessment in Patients with Iron Deficiency and Heart Failure (FAIR-HF) and Ferric Carboxymaltose Evaluation on Performance in Patients with Iron Deficiency in Combination with Chronic Heart Failure (CONFIRM-HF) trials both showed that ferric carboxymaltose improved performance in patients with iron deficiency in combination with chronic heart failure.

In individuals with CCF and IDA, a dosage of 1000mg of iron is required to replenish iron sufficiently.

Kidney disease is a condition that affects the kidneys.

Reduced GI iron absorption, poor diet, and blood loss due to dialysis and frequent blood collection are all factors that contribute to IDA in people with CKD. Intravenous iron is more successful than oral iron in treating IDA in CKD, according to a recent meta-analysis and comprehensive review, regardless of whether dialysis is required.(58 59) Intravenous iron is also recommended as first-line treatment for individuals with stage 5 CKD, according to the Kidney Disease: Improving Global Outcomes clinical practise recommendations.(60) However, a recent trial of 203 individuals given 1 g three times per day found that they needed less hospitalisation.

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