



Iron Deficiency Anemia An Updated Review

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Abstract

Anemia influences one-fourth of the world's population, and iron deficiency is one of the predominant causes. Anemia is associated with persistent fatigue, impaired cognitive function, and diminished well-being. Proper administration improves satisfactory of life, alleviates the signs of iron deficiency, and reduces the want for blood transfusions. Treatment choices encompass oral and intravenous iron therapy; however, the efficacy of oral iron is restrained in certain gastrointestinal conditions, such as inflammatory bowel disease, celiac disease, and autoimmune gastritis. This review article presents a critical precis of the analysis and therapy of iron deficiency anemia. In addition, it consists of an administration algorithm that can help the clinician decide which sufferers are in want of further gastrointestinal evaluation. This allows the identification and treatment of the underlying circumstance and avoids the unnecessary use of invasive techniques and their related risks.

Keywords: Iron deficiency, Hemostasis, Nutritional, Iron loss

Introduction:

Iron stability is imperative for all cell life. Iron homeostatic mechanisms developed to keep away from iron extra and the era of damaging reactive oxygen species through reutilizing physique iron and limiting its uptake from the environment. The inevitable different aspect of the coin is the convenient improvement of iron deficiency.

Iron deficiency is the depletion of total-body iron, particularly of macrophage and hepatocyte iron stores. Because the biggest quantity of iron is bump off for hemoglobin (Hb) synthesis to produce 200 billion erythrocytes daily, anemia is the extra evident signal of iron deficiency, and iron deficiency anemia is regularly viewed synonymous with iron deficiency. However, iron deficiency is a broader situation that regularly precedes the onset of anemia or shows deficiency in organs/tissues different than these concerned in erythropoiesis, such as skeletal

muscular tissues and the heart, the latter incredibly iron based for myoglobin and electricity manufacturing to preserve mechanical contraction. This article insights in to the mechanisms of adaptation to iron deficiency anemia, and discuss about treatment and lab diagnosis of iron deficiency anemia.

Etiology:

Iron deficiency may also manifest as a end result of persistent blood loss, diversion of iron to fetal and child erythropoiesis for the duration of being pregnant and lactation, inadequate dietary iron intake, malabsorption of iron, intravascular hemolysis with hemoglobinuria, diversion of iron to nonhematopoietic tissues like the lung, genetic factors, or a mixture of these factors. Of these, gastrointestinal or menstrual blood loss is the most common. Iron-deficiency anemia is the most frequent anemia worldwide, and is particularly common in

female and teens in areas the place meat intake is low, meals is no longer fortified with iron, and malaria, intestinal infections, and parasitic worms are common. ⁽¹⁻³⁾ Women with frequent pregnancies might also be specifically susceptible. In the United States, iron deficiency is most frequent in young people ⁽¹⁾ to four years historic and in adolescent, reproductive age, or pregnant women. ⁽³⁻⁶⁾ According to the Global Burden of Disease Study 2016, iron deficiency anemia is 1 of the 5 main motives of years lived with incapacity burden and is the first purpose in women. ⁽¹⁾ Adopting the World Health Organization–recommended cutoff for anemia (Hb <13 g/dL in males, <12 g/dL in females, <11g/dL all through pregnancy), an international survey confirmed that in 2010, anemia nevertheless affected one 0.33 of the population, with about half of the instances ensuing from iron deficiency. The estimate is that ~1.24 billion persons journey iron deficiency anemia, even though with big editions from low- to high-income countries. ⁽²⁾ The international occurrence of iron deficiency besides anemia stays elusive, even though the cautioned parent is at least double that of iron deficiency anemia. The trouble will become even greater applicable if we take into account purposeful iron deficiency, which takes place when iron is rarely mobilized from stores, as in continual inflammations/infections or when the energetic erythropoietic enlargement by way of exogenous or endogenous erythropoietin (EPO) reasons an acute disproportion between iron demand and supply.

Globally, iron deficiency anemia has applicable scientific and social impacts, accounting for impairment of cognitive overall performance in younger children, ⁽³⁾ detrimental consequences of being pregnant for each mother and newborns, ⁽⁴⁾ reduced bodily and working capacities in adults, and cognitive decline in the elderly. ^(5,6) From on hand data, the relative contribution of iron deficiency to these terrible results is tough to disassociate from that of anemia.

Blood loss

Blood loss can happen from the gastrointestinal tract or different chronic diseases such as tuberculosis, ulcers or intestinal disorders, heavy, lengthy or accepted menstruation, baby birth, normal blood donations, accidents, hemorrhage, surgery, positive

medicines and intravascular hemolysis (a situation in which pink blood cells destroy down in the blood stream, releasing iron that is then misplaced in the urine. This now and again happens in human beings who interact in lively exercise, specifically jogging).

Impaired Absorption

Impaired Absorption Dietary iron is on hand in two chemical forms: heme iron, which is discovered in meat; and non-heme iron, which is determined in plant and dairy foods. The absorption of heme iron is, minimally affected via the composition of ingredients and gastrointestinal secretions. The absorption of non-heme iron from a vegetarian eating regimen (1-5%) is terrible as in contrast to hem iron (8-10%). Therefore, vegetarian girls, particularly after menarche are at greater hazard of growing anemia ^[7].

Chronic blood loss from esophageal or gastric varices can lead to iron-deficiency anemia. Hemorrhoidal bleeding may additionally lead to severe iron-deficiency anemia. Chronic blood loss may additionally end result from diffuse gastric mucosal hypertrophy (Ménétrier disease). Peptic ulcers of the stomach or duodenum are frequent motives of iron deficiency, and an

association between contamination with *Helicobacter pylori* and iron-deficiency anemia has been documented in severe studies. Some of these iron-deficient sufferers who are contaminated with *H. pylori* do now not respond to oral iron alone, however do reply to eradication of *H. pylori*. ⁽⁸⁾

Pathophysiology of iron deficiency

Anemia ensuing from iron-restricted erythropoiesis is occurs thru quite a few mechanisms. In iron deficiency, depleted iron stores are due to an asymmetry between iron uptake and usage. Anemia may also no longer be present at first due to the fact of iron recycling from erythrocyte turnover. he quantity of iron getting into the circulation. Iron deficiency deeply influences iron homeostasis, inducing adaptive mechanisms on the hepcidin-ferroprotein (FPN) axis, the iron regulatory protein (IRP)/iron responsive factor (IRE) machinery, and different regulators. The goal is to optimize iron utilization through erythropoiesis and to counteract the physiological inhibition of iron absorption.

Iron-Containing Proteins

As the physique turns into depleted of iron, modifications manifest in many tissues. Hemosiderin and ferritin definitely disappear from marrow and other storage sites. Hemoglobin synthesis in the marrow decreases, first as an end result of fewer erythroblasts,⁽⁹⁾ however sooner or later additionally per erythroblast if iron deficiency will become extra severe, ensuing in hemoglobin-deficient erythrocytes. The concentration of many different iron-containing proteins is affected, frequently in an organ-specific manner.⁽¹⁰⁾

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Neurologic Changes

Iron deficiency is related with each developmental abnormalities in children and with stressed leg syndrome in adults, however in neither case has iron deficiency been set up as the predominant cause. The substantia nigra is a in particular iron-rich place of the brain and contains dopaminergic neurons that are suspected of involvement in stressed leg syndrome. In mouse fashions of iron deficiency, iron depletion of the substantia nigra is particularly strain-dependent, suggesting that iron deficiency and as but incompletely characterized genetic variants may additionally cooperate in the pathogenesis of stressed leg syndrome by using permitting the depletion of iron from prone brain areas concerned in dopaminergic signaling.⁽¹²⁾

Growth and Metabolism

Iron-deficient youngsters have been suggested to go through from increase retardation but it is hard to isolate the impact of iron deficiency from other nutritional and environmental reasons of stunting. Two comprehensive analyses of randomized managed trials did no longer observe an impact on growth of iron supplementation alone. Decreased

thermoregulation in response to bloodless publicity is considered in each people and laboratory models. It has been attributed to the conflicting consequences on blood flow of lowered oxygen content material of blood and wants to decrease warmth loss, as well as the impact of iron deficiency on thyroid function.⁽¹²⁾

Mechanisms Of Adaptation:

Systemic regulation

Liver hepcidin is the grasp hormone that physiologically limits iron entry into plasma. Binding to its receptor FPN, hepcidin blocks iron export each with the aid of occluding the exporter central cavity⁽⁷⁾ and by using inducing its degradation.⁽⁸⁾ Because of the excessive FPN expression on expert iron exporter cells, such as enterocytes and macrophages, hepcidin suppression in iron deficiency enhances each iron absorption and its launch from macrophages to plasma. Multiple elements down regulate hepcidin transcription. The BMP-SMAD signaling pathway is repressed, due to the fact in iron deficiency, expression of BMP6 legend is low,⁽⁹⁾ the BMP co receptor HJV is cleaved through Tmprss5^(6,10) and TFR2 is eliminated from the cell surface.⁽¹¹⁾ In addition, the histone deacetylase HDAC3 erases activation markers from the hepcidin locus,⁽¹²⁾ presenting an epigenetic contribution to hormone suppression. The feature of ERFE, launched by means of erythroid cells inspired via erythropoietin,⁽¹³⁾ is much less applicable in iron deficiency besides anemia, due to the fact hepcidin is downregulated when iron deficiency is prompted in ERFE^{-/-} mice.⁽¹²⁾ However, ERFE performs a function in the presence of anemia and hypoxia.⁽¹³⁾ Local mechanisms amplify intestinal iron absorption. Hypoxia-inducible component 2 α (HIF2 α) upregulates the expression of each the brush border equipment (DMT1 and DCYTB) that uptakes iron from the lumen and the iron exporter FPN at the basolateral membrane by way of binding hypoxia-responsive factors of these gene promoters.⁽¹⁴⁾ Macrophages swiftly recycle iron derived from the phagocytosis of senescent pink cells. However, the absolute quantity of iron recycled from hypochromic erythrocytes by way of heme-oxygenase⁽¹⁾ decreases in parallel with the severity of iron deficiency, due to the fact Hb content material per phone (mean corpuscular Hb [MCH]) is reduced. A novel mechanism associated to erythrocyte FPN, which is

fairly expressed in iron deficiency, may also make a contribution to preserving circulating iron levels. ⁽¹⁵⁾

Laboratory Diagnosis:

The World Health Organization defines anemia as blood hemoglobin values of much less than 7.7 mmol/l (13 g/dl) in male and 7.4 mmol/l (12 g/dl) in female. Typically, the comparison of the reason of anemia consists of a entire blood cell count, peripheral smear, reticulocyte count, and serum iron indices. The severity of anemia is based totally on the patient's hemoglobin/ hematocrit level. Iron deficiency anemia is characterized by way of microcytic, hypochromic erythrocytes and low iron stores. The suggest corpuscular quantity is the measure of the common purple blood telephone quantity and imply corpuscular hemoglobin attention is the measure of the attention of hemoglobin in a given quantity of packed crimson blood cells. The regular reference degree for imply corpuscular quantity is 80–100 fL and suggest corpuscular hemoglobin awareness is 320–360 g/l. The patient's cells are stated to be microcytic and hypochromic, respectively, when these values are much less than the ordinary reference range. Of note, up to 40% of sufferers with actual iron deficiency anemia will have normocytic erythrocytes (i.e., a everyday suggest corpuscular quantity does no longer rule out iron deficiency anemia) [Bermejo and Garcia-Lopez, 2009]. The red cell distribution width is a measure of the version of red blood cell width and is used in aggregate with the suggest corpuscular extent to distinguish an anemia of combined reason from that of a single cause. The ordinary reference vary is 11–14%; an increased red cell distribution width fee signifies a variant in red cell size, which is acknowledged as anisocytosis. The purple cell distribution width may also be improved in the early levels of iron deficiency anemia or when a affected person has each iron deficiency anemia and folate with or except nutrition B12 deficiencies, which each produce macrocytic anemia. It is now not distinguished for the platelet count number to be larger than 450,000/ μ l in the presence of iron deficiency anemia. Upon examination of a patient's peripheral smear with persistent iron deficiency anemia one will usually see hypochromic, microcytic erythrocytes; thrombocytosis may also additionally be apparent. It is essential to observe that microcytosis seen on the peripheral smear may also

be considered prior to abnormalities on the entire blood cell count. If the affected person has coexistent folate or diet B12 deficiency, the peripheral smear will be a combination of macrocytic and microcytic hypochromic erythrocytes, alongside with normalization of the imply corpuscular volume. Chronic gastrointestinal bleeding is related with a range of lesions and can manifest at any vicinity inside the gastrointestinal tract. Iron deficiency anemia is specially inclined to appear in these taking aspirin or nonsteroidal anti-inflammatory tablets chronically. For these with angiodysplasia or different structural lesions, the website can regularly be visualized by means of endoscopic contrast (e.g., video pill endoscopy) of the gastrointestinal tract. However, in 10–40% of sufferers with occult gastrointestinal bleeding the reason stays difficult to understand Although, the records and bodily examination can lead to recognition of the situation and assist set up etiology, IDA is specifically a laboratory prognosis that may want to be performed thru 4 tests: – Serum iron (SI), Serum transferrin saturation (TS) or complete iron binding capability (TIBC), Serum ferritin (SF) and Hemoglobin degree (Hb). Among these tests, Serum ferritin is the most touchy and desired preliminary diagnostic test. Total iron binding capability (TIBC) is often measured at the equal time as serum iron. This size shows the practicable ability of transferrin molecules to bind with serum iron. Individuals with danger elements for diabetes, cardiovascular diseases, stroke, liver ailments and most cancers face amplified dangers proportional to the quantity of stored physique iron over and above the most beneficial range. A diagnostic criterion for IDA is given under ^[13-15].

Iron-Binding Capacity and Transferrin Saturation

The iron-binding ability is a measure of the quantity of transferrin in circulating blood. Normally, there is sufficient transferrin current in 100 mL serum to bind 4.4 to eight μ mol (250 to 450 mcg) of iron; because the ordinary serum iron concentration is about 1.8 μ mol/dL (100 mcg/dL), transferrin may also be determined to be about one-third saturated with iron. The unsaturated or latent iron-binding capacity (UIBC) is without difficulty measured with radioactive iron or via spectrophotometric techniques. The sum of the UIBC and the plasma iron represents total iron-binding capability (TIBC). TIBC

can additionally be measured directly. In iron-deficiency anemia, UIBC and TIBC are frequently improved and serum iron concentrations are reduced so that transferrin saturation of 15 percentage or much less is commonly found. Because transferrin

concentration and TIBC are reduced in the course of inflammation, a ordinary value for transferrin saturation frequently accompanies a low serum iron concentration in the anemia of persistent inflammation. ⁽¹⁴⁾

Table 1: Diagnostic criteria for IDA

Tests	Normal Range	IDA
TIBC	240-450 µg/dL (male & female)	High
SI	55-160 µg/dL (male) 40-155 µg/dL (female)	Low
TS	20%-50% (Adults) >16% (Children)	<12 - 16%
SF	15-200 ng/ml (women) 20-300 ng/ml (men) 25 - 75 ng/ml (Optimal for male and female)	<15ng/ml) (in a healthy person) or <50ng/ml (in a person with an underlying source of chronic inflammation
Hb	130 g/L (male) 120 g/L (female) 110 g/L (pregnant female and preschool children)	Low

Management:

Prevention Efforts to amplify get entry to and consumption of iron-rich ingredients need to usually be in place. Iron absorption enhancers (ascorbic acid) or inhibitors (calcium, phytates [cereals], tannins [tea and coffee]) ought to additionally be regarded when supplying iron-rich meals. Enrichment of meals (rice, maize flour, cornmeal) with iron is additionally practiced in some countries, such as in Asia, Africa and Latin America, and advocated by way of the WHO ^[11-14].

Conclusion:

Iron deficiency anemia is an extensive public health challenge that can reason debilitating clinical consequences throughout age groups, genders, geographies and medical conditions. Early prognosis and effective administration are for that reason wanted to avoid associated sequelae. This can solely be achieved with accelerated recognition of the incidence and causes of IDA, as properly as the advantages of treatment, amongst healthcare professionals. Although effective means for iron supplementation exist, making the proper and well-timed desire between oral and intravenous iron formulations is integral to avoid unnecessary delays in iron repletion and correction of anemia

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