A Review on Iron Deficiency Anemia

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Abstract

The quarter of the people in the world have anemic in spite of scientific development and worldwide economic, half of them due to iron deficiency anemia. Here clinical and laboratory features discussed for this type of anemia such as hemoglobin, hematocrit, serum iron, serum ferritin, total iron binding capacity, soluble transferrin receptor and other types of test. Also many Strategies mention in order to control iron deficiency anemia include iron supplementation by oral or parenteral iron therapy and fortification dietary diversity.
Key words: Iron deficiency, iron-deficiency anemia, diagnostic, treatment

مقال حول فقر دم نقص الحديد

عبير جياد يوسف الفتلاوي

الخلاصة

يعاني ربع سكان العلم من مرض فقر الدم بالرغم من من التطور العلمي والاقتصادي حول العالم, ويصاب نصف هذا العدد بفقر دم نقص الحديد. هنالك العديد من الاختبارات السريرية والمختبرية تستخدم لغرض تشخيص هذا النوع من الانيميا بعد عملية سحب الدم منها: كمية الهيموغلوبين، حجم الخلايا المرصوصة كمية الحديد المخزون، نسبة الفرتين,نسبة الحديد الكلي المرتبط ومستقبلات الترانسفرين. ذكرت العديد من الاستراتيجيات للسيطرة على نقص الحديد من خلال تناول مكملات الحديد في هذا النوع من الانيميا منها اعطاء الحديد كعلاج بواسطة الفم، بالحقن واعطاء تنوع غذائي غني بهذا العنصر.

Introduction

Anemia is a common problem in all population and ages occur when the concentration of hemoglobin (Hb) decrease than normal level of healthy peoples at the same ages and sex [1]. More (1.6) billion peoples are anemic, even numerous scientific and economic progress over the last decades[2], the global incidence of anemia has, at best, been slightly reduced [3]. The World Health Organization (WHO) reports that 42% of pregnant women, 30% of non-pregnant women (15-50 years of age), 47% of pre-school children (0-5 years of age), and 12.7% of men over (15 years) of age have anemic [4].

Iron deficiency anemia (IDA)

Iron forms 5 percent of the earth's crust, the redox state makes it useful for biological processes in evolution, four general protein types include iron element [5]: (1) Mononuclear iron protein “e.g: superoxide dismutase” (2) protein diiron-carboxylate “e.g. Ribo-nucleotide reductase and ferritin” (3) iron sulfur “e.g. Aconitase” (4) heme “e.g., hemoglobin proteins”, the first three classes of proteins are identified at low level but essentially functional while human's hemoglobin is the most protein that containing iron [6]. Iron deficiency anemia among the most prevalent diseases in the world the involvement of hypochromic microcytic anemia and biochemical evidence for the loss of body iron stores make the diagnosis relatively straightforward in most cases [7]. Diagnosed

typically with laboratory tests, such as serum ferritin and transferrin saturation, however these tests markedly affected by inflammation making difficult to recognize between "IDA" and "ACD" related with infection or malignancy [8].

Requirement and metabolism of Iron

Iron consider the most microelement that needed by different microorganisms especially by humans, because of play fundamental position in the different biological processes [9]. Dietary iron is composed of about (5-15) mg of iron and (1-5 mg) of heme , while only (1-2 mg) taken by intestine, Kids, men and women at postmenopausal needed (10 mg) daily from iron element, the requirement rises by two to threefold in premenopausal and pregnant women [10].

Iron absorption regulated primarily by intestine once iron has been absorbed, stored iron as ferritin non-reactive state in cells or in transferrin which also holds iron in non-reactive state, inside cell ferritin stored in the cytoplasm, nucleus or mitochondria and transport through cell membranes by "assistance divalent metal transporter 1 (DMT-1)" and exporting protein called ferroportin [11]. protein hepcidin can bounded with Ferroportin then prevent it from export this led to decrease of serum iron levels, while serum or within cells, increase level of ferritin [12]. It is possible to absorb inorganic iron by protein "DMT-1", that carries a variety of metals in divalent form, such as ferrous iron "Fe^{+2}". The dietary iron in duodenum is likely to be ferric iron, particularly from plant sources "Fe^{+3}". For this reason ferrireductase found in a cytochrome membrane that reduced "Fe^{+3}" to "Fe^{+2}" [10] [13].

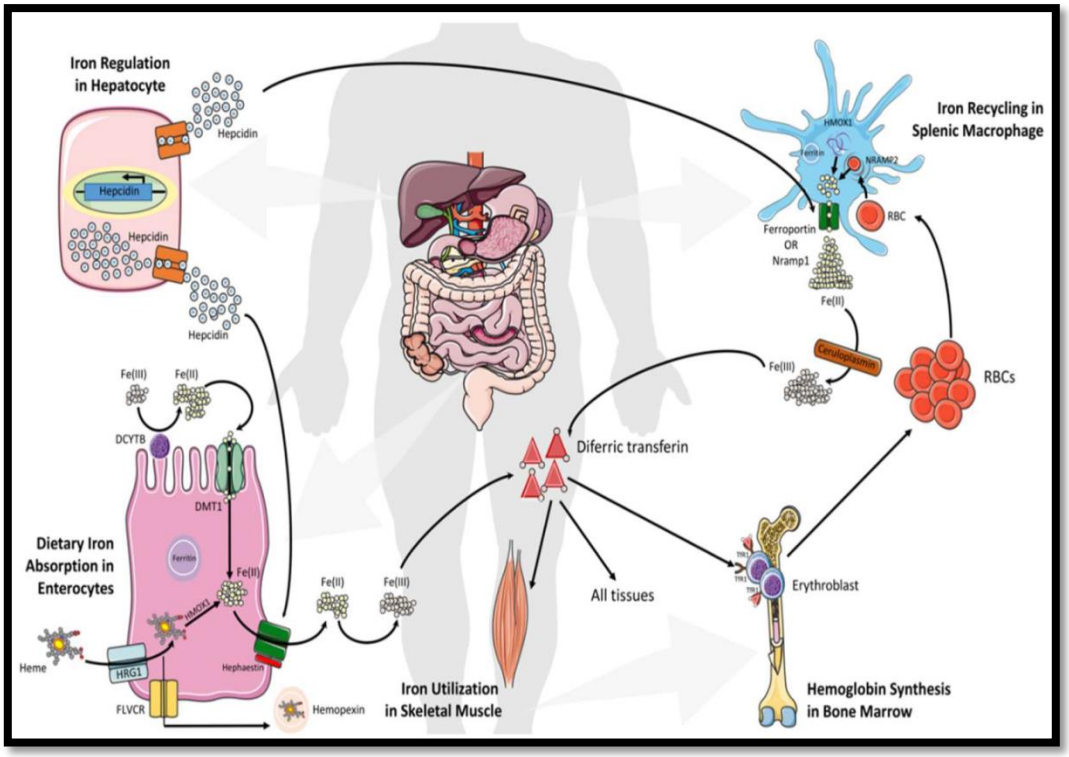

Fig.1: Mechanism iron absorption [14].

Table (1) : daily iron requirement according to the ages [15]

Infants from 5 to 12 months and children need 1 mg
Infant up to 4 months need 0.5 mg
Pregnancy women need 3-4 mg
Menstruating women need 3 mg
postmenopausal women and Adult men need 1 mg

Causes of Iron deficiency anemia

This type of anemia may resulted from four major causes, one of these "**inadequate iron intake** or **malnutrition"** from food, "**defect in absorption (malabsorption)",** "**increased requirements from iron"** during growth, and finally "**excessive iron losses"** [15] all these causes can classified in details as follow:

1. **Physiologic factors:**
- **Increase demand:** Childhood, rapid development (adolescence), pregnancy (second and third trimesters), blood loss menstrual, blood donation.
2. **Environmental factors:** due to poverty, malnutrition, diet such as vegetarian, vegan.
3. **Pathologic factors:**
- **Decreased absorption:** *H. pylori* infection, gastritis with atrophy, inflammatory bowel diseases and Gastrostomy.
- **Chronic blood loss:** hookworm, erosive gastritis, peptic ulcer, intestinal cancer, intravascular hemolysis, autoimmune hemolytic anemia and march hemoglobinuria.
4. **Drug related factor:** IDA related with used drugs such as proton-pump inhibitors, Glucocorticoids, Glucocorticoids and NSAIDs.
5. **Genetic factors:** Iron-refractory iron-deficiency anemia.
6. **Iron restricted erythropoietin:** such as "**ACD" ,** "**CKD**" and Treatment with erythropoiesis-stimulating agents [3][6] [16].

Risk factors of iron deficiency anemia

1. **Pregnant and Lactating Women:** Typically, iron deficiency in the reproductive age of females is the outcome from pregnancy and menstrual cycle disorders [15]. prevalent iron deficiency in Pregnant women, not only for required a lot of amount from iron for growth both embryo and placental, but also because so many enter pregnancy, especially in developing countries, without adequate iron stores[17][18].
2. **Women of reproductive age:** usually resulted from menstrual disorders and pregnancy [19].
3. **Infants less than 5 years:** In this ages ADI can related to poor dietary intake, infant iron status can be affected by factors that arise before birth [20].
4. **Obesity:** even dietary deficiency associated with IDA, increased blood flow and subclinical inflammation as suggested mechanisms [21].
5. **Race**: black human have lower mean hemoglobin compared to white humans, even after the iron level was changed. Among Mexican women that living in the United States, there

is a high rate of IDA not accounted for by dietary intake or parity, indicating that there may be an unexplained, probably ethnic factor predisposing these women to iron deficiency [22] [23].

6. **Elderly:** in older people iron deficiency resulted from GIT bleeding.
7. **Vegetarian diet**
8. **blood donors**
9. **Adolescents** [24]

For many vitamins and minerals, including iron, the United States Food and Nutrition Board publishes Dietary Reference Intakes (DRI), 18 mg daily for women with menstruating; and (16 mg) daily for vegetarians peoples [25].

Clinical Feature

- **Clinical Feature of Anemia in general**
  Anemic Patients may have unspecific signs of anemia include fatigue, simple tiredness, exertion breathlessness, tachycardia, and heart murmur [15][26].
- **Clinical symptoms related to Iron Deficiency anemia (IDA)**

IDA was asymptomatic and chronic disease can therefore frequently undiagnosed. Weak, pallor, tiredness that due to decrease oxygen supply to different body organs and reduced iron containing enzyme activity. Pregnancy with sever IDA causes increased risk of mortality of newborns and mothers, decrease weight of neonatal and premature labor , also Precipitate hearts failure, and trigger leg syndrome of restlessness. Some common signs, including koilonychias or (spoon nails), glossitis or dysphagia this called Plummer Vinson or (Patterson-Kelly) syndrome, these changes resulted from loss of iron-containing enzymes [16] [24].

Diagnostic of Iron Deficiency anemia (IDA)

1. **Low hemoglobin (HB) and packed cell volume (PCV).**
2. **Peripheral Blood Examination:** when preparation of blood smear RBCs appear microcytosis and Hypochromia, variation in shapes and size found elongated cell called pencil cells, total count of WBC is normal or decrease mildly, increase Platelets especially when found blood loss[15].
3. **Indices of red blood cells:** MCV, MCH and MCHC reduced, with the degree of reduction being proportional to the anemia severity, "RDW" increased with "ADI".
4. **Bone Marrow Examination:** micro-normoblasts decrease in size and number than normal state cytoplasm of these cells appears as vacuolated with ragged boundaries, defective in Haemoglobinisation cytoplasm with normal. Line of granulocytic and megakaryocytic.
5. **Serum Ferritin (SF):** it have direct correlation between serum ferritin and storage iron, therefore this test used for diagnosis iron overload and iron deficiency, normal value of serum ferritin varies from 15 to 1300 µg/dl , when level below 12 µg/dl that indicators for strongly lack of storage iron.
6. **Serum iron (SI):** normal level of serum iron about 50-150 µg/dl this value slightly lower in women also this value decrease malignancies and chronic inflammation, in IDA serum iron become <50 µg/dl.
7. **Total iron binding capacity (TIBC): it mean** transferrin found in circulation normal level from 300-400 µg/dl, which increased during IDA to about > 400 µg/dl, while decrease during chronic infections.
8. **Transferrin saturation (TSAT):** define as the ratio between serum iron to the TIBC, normal level about 20-55%, while during IDA transferrin **saturation decrease than 15%.**

9. **Soluble Transferrin Receptor (TfR):** value of serum (TfR) associated with number of transferrin Receptors, during IDA increased receptors of transferrin on erythroid cells for this reason serum level also increased, this increased follow by decrease iron storage. Therefor this test beneficial for differentiating IDA from ACD, also diagnostic IDA from other with chronic inflammation in patients.
10. **Free Erythrocytes Protoporphyrin "FEP":** in normal state this types of protein combination with iron to form haem within erythroid mitochondria, IDA not occur this combination then increase level of **FEP**, also this increase can observed in ACD that lead to poisoning.
11. **Fecal Occult Blood Test (FOBT):** in patients with IDA highly positive with locus bleeding from "GIT" when loss of blood 10 ml per day then FOBT test require, (30) ml/day associated with (93%) patients positive.
12. **Erythrocytes Zinc Protoporphyrin "ZnPP":** another laboratory test used for measure status of iron, DMT-1 is up-regulated with IDA in which increase transport zinc through membrane of intestinal in order to replace iron loss that protoporphyrin ring formation, "ZnPP" is important but not very specific test because of it is also increase in lead poisoning, inflammation and ACD[27].
13. **Reticulocytes Hemoglobin Content "CHr":** bone marrow contain iron used for RBCs synthesis when ages of reticulocyte cells only (1-2) day, CHr decrease with IDA patients. However CHr in many disorder when reduced availability of iron for hemoglobin synthesis such as erythropoietic stimulating agents and inflammation.
14. **Percentage Hypochromic RBC "PHRC":** another biomarker for hemoglobin concentration within RBCs dependent on RBCs size, it used for diagnostic IDA in the presence of ACD and inflammation[24] [28] [29] [30].

Treatment of Iron Deficiency anemia (IDA)

Iron deficiency anemia (IDA) treatment must begin with diet replacement such as (red meat, breads and fortified cereals, beans and green vegetable, but if food alone is insufficient to iron stores and Hb to the normal value, treatment with iron supplementation in severe case must be carried out. If serum Hb decrease than (8 g/dl) with symptomatic of shortness breath, extreme fatigue, or signs of heart ischemia, blood transfusion then is essential. However, if the patient is asymptomatic and the level of Hb within an acceptable range, care should start with oral iron [31].There are many strategies for treating such as:

1**.Delayed Clamping of the Umbilical Cord:** a delay for five minutes of umbilical cord clamping allows additional blood volume 166 mL added for a 3.5 kg of infant, the goal of preventing iron deficiency during the first (6 months) of life has been understood clearly[32] [6].

2**.Term for Breastfed Infants:** when infants born have iron stores until 4 to 6 months old, these facts led to the supposition that very little iron is required for breastfed infants. The small amount of iron in human milk is believed to be adequate for the exclusively breastfed baby [33][17].

3**.Oral Iron Therapy:** Oral iron is easy, inexpensive to administer, the dose recommended daily for adults about 100-200 mg\kg of body weight, while for children about 3-6 mg\kg of body weight as liquid preparation and the drug should be given in different doses, without food, for both groups. vitamin C improve iron absorption, also low level of hepcidin increase iron absorption and rapid hemoglobin recovery, ; however, the replenishment of iron stores and the normalization of serum ferritin levels require 3 to 6 months of treatment. Long-term therapy use of oral iron is restricted by side effects, including diarrhea, nausea, constipation and metallic taste [16].

4**.Parenteral Iron Therapy:** iron administration by Intravenous can used when we need rapid elevated level of Hb in some case like chronic blood loss, malabsorption and genetic IRIDA and

inflammatory bowel disease that iron cannot be control by used oral iron therapy. The cost of this therapy is high but the number of patients or clinical visits needed is greatly reduced, also circumvents the iron absorption problem, it is more efficient and raises the levels of hemoglobin faster than oral iron[34][16].

5**.Recombinant Erythropoietin:** EPO hormone may be indicate in several situations such as GIT disorder, IDA is common with GI cancer, then give intravenous iron with EPO to the cancer patients that reduces for blood transfusions needed [35].

Conclusion

Iron deficiency anemia is a major public health problem in the word that can have deteriorating clinical implications across genders, age, geographies and clinical conditions**.**We have reviewed of iron metabolism and it important role and requirements for each ages. Also method for diagnostic and types of treatments. Future study must be investigation markers of tissue IDA based on iron physiology and metabolism and evaluation outcome of treatments.

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