Iron Deficiency And Child Health: A Permanent Challenge

Luiz Antonio Del Ciampo and Ieda Regina Lopes Del Ciampo

Abstract—Iron deficiency (ID) is the most common widespread nutritional disorder in the world in both developing and developed countries and remains a leading cause of anemia mainly affecting children between the ages of 6 to 59 months. ID can be understood as a state in which there is insufficient total body iron to maintain normal physiologic functions and which can vary in intensity from mild forms to the most severe condition which is anemia. The prevalence of ID among children under the age of three years old is high, varying according to the regions of the world, between about 10% in the USA to 33% in African countries, South-East Asia and Eastern Mediterranean. In view of the importance of ID for human health, with its physical, emotional, social and economic repercussions, it is important to know all aspects related to this nutritional deficiency so that actions for prevention, identification and early treatment of those affected can be developed. This article briefly reviews the importance of iron for children's health, highlighting metabolism, clinical changes, diagnosis and measures that can solve or minimize this serious public health problem.

Index Terms— Iron deficiency, iron anemia, child health, nutrition.

I. INTRODUCTION

Iron deficiency (ID) is the most common widespread nutritional disorder in the world in both developing and developed countries and remains a leading cause of anemia mainly affecting children between the ages of 6 to 59 months [1,2,3] ID can be understood as a state in which there is insufficient total body iron to maintain normal physiologic functions and which can vary in intensity from mild forms to the most severe condition which is anemia [4]

Although this condition can affect individuals in any age group children are part of one of the most affected groups due to a great amount of iron needed to synthesize new tissues, expanding blood volume and to maintain correct hemoglobin concentration [5,6].

The prevalence of ID among children under the age of three years old is high, varying according to the regions of the world, between about 10% in the USA to 33% in African countries, South-East Asia and Eastern Mediterranean, affecting more than 300 million children worldwide [4,7,8].

In view of the importance of ID for human health, with its physical, emotional, social and economic repercussions, it is important to know all aspects related to this nutritional deficiency so that actions for prevention, identification and

early treatment of those affected can be developed. This article briefly reviews the importance of iron for children's health, highlighting metabolism, clinical changes, diagnosis and measures that can solve or minimize this serious public health problem.

Iron

Iron is a metal highly abundant in the earth's crust, biologically classified as a micronutrient, essential for human life and that can be found, with exception of some species of lactobacillus, in all living being cells [2,9]. It is fundamental for the transportation of oxygen, is an integral part of some proteins (hemoglobin, myoglobin, flavoprotein, lactoferrin) and participates in more than 200 enzymatic systems that are essential for cellular functions such as adenosine triphosphate generation, cytochromes, catalases, and peroxidases [2,5,10,11].

The distribution of iron in the body shows that 65% is linked to hemoglobin, 4% as myoglobin, 1% hemic compounds, 0.1% combined with transferrin. Between 15% and 30% are stored in the liver, spleen and bone marrow in the form of ferritin or hemosiderin [2,5]. At birth healthy term children have high to normal hemoglobin concentrations (15 – 17 g/dL) and iron stores which remain iron replete until 6 months of life. After birth, iron can be obtained by means of three dietetic forms: breast milk (iron bound to lactoferrin with high bioavailability), heme iron and nonheme iron forms [11].

Heme iron is found in the structure of the protoporphyrin ring of hemoproteins, being soluble in the alkaline medium of intestinal light and easily absorbed [9,12], while nonheme iron complex (from plant sources and bound to organic molecules in the form of ferric iron) is degraded during digestion in the gastrointestinal tract owing to the action of pepsin and hydrochloric acid. In addition to dietary sources, humans have complex mechanisms for conserving recycled iron from the release of deposits from the body and the breakdown of red blood cells [2,13].

Iron absorption occurs by the mature enterocytes in the villus of duodenum and the upper part of the jejunum (where it is oxidized) and initially linked to specific sites on the mucous membrane. From there it is transported to the basolateral membrane where it binds to transferrin [9,12,14]. Iron status is regulated by intestinal absorption and transport. Absorption is regulated by the peptide hormone hepcidin [7] - a negative iron regulator, synthesized in the liver and secreted into the circulation – which acts primarily on a basolateral surface of enterocytes and facilitates the iron uptake into the plasma from the intestine [3,15,16].

In order to be better absorbed iron must be presented with high bioavailability (which is the fraction effectively absorbed and used). The more soluble the iron compound,

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the greater is the potential absorption. Ferrous iron form has generally been assumed to be better absorbed than ferric iron [2,5,12]. Compounds such as ascorbic acid, fructose, citric, malic, lactic, succinic and tartaric acids, that reduce iron from ferric to ferrous generally increase bioavailability [2]. On the other hand, plant compounds (polyphenols, tea, coffee, chocolate, spices, seeds), oxalic and phytic acids, interactions with metallic or mineral ions (calcium, zinc, cobalt, manganese, copper) and synthetic additives and chelators (such as sodium alginate), tetracyclines and ethylenediaminetetraacetic acid (EDTA) form insoluble precipitates and inhibit absorption [2,16]. Only small amounts of iron are excreted by the body through bile, feces, bleeding and epithelial peeling.

II. ID CAUSES

There are several causes for ID and can be classified as [4,5,15,17-20]:

A. Prenatal and Perinatal

Maternal iron deficiency, fetal-maternal hemorrhage, twin-twin transfusion syndrome, prematurity.

B. Postnatal

Poor supply dietary deficiency, poor absorption (duodenal disorders, giardiasis), imperfect metabolism, high loss (gastrointestinal blood loss due to hookworm infestation, inflammatory bowel disease, cow milk protein proctocolitis).

III. ID EFFECTS

ID effects are particularly important on cells with high metabolic rates [21]. Even before the anemia is installed, the reduction of iron in the body can cause several changes in all systems due to the reduced effectiveness of and cytokine production by lymphocytes [7,11], changes in the phagocytic activity of macrophages, oxidative burst in neutrophils, and slow neural transmission [22,23].

Although ID is associated with multiple health problems, including anemia and defective organ functions, children with ID can be seemingly normal because this condition is frequently asymptomatic and thus may often go underdiagnosed. Most mild symptomatic patients may experience fatigue, pallor, reduced interest in physical activities, loss of appetite, pica (craving for nonfood items), irritability and increased absorption of heavy metals intoxication. In more intense cases can be observed sensitivity to cold, angular cheilitis, koilonychia, spoon nails, hair loss, dry and rough skin, and glossitis [2-4,15,20,24-26]. Some authors have described other problems related to ID such as restless leg syndrome [15,26,27], attention deficit hyperactivity disorder ADHD [4], sleep disorders [4,22,27], recurrent acute respiratory tract infections and gastroenteritis [28,29], thrombosis [4,30,31].

IV. IRON AND THE DEVELOPMENT OF CENTRAL NERVOUS SYSTEM

The blood-brain barrier controls the iron concentration in the cerebral structures and brain's iron status is compromised before the iron status of the red blood cells

[21,32]. Brain iron is vital to multiple functions including adenosine triphosphate (ATP) synthesis, neurotransmitter (dopamine, serotonin) synthesis and myelination [25,33]. Tissue iron is more concentrate in basal ganglia structures such as globus pallidus, caudate, putamen and nucleus accumbens [34, 35].

Until the age of three the central nervous system (CNS) is in rapid anatomical and functional development and suffers great physical and emotional influences from the external environment. ID has been associated with impaired brain development and long-term damage of behavioral and cognitive performance that may irreversible [35-38]. The most important changes that can be observed in the CNS due to ID are [2,11,17,22,25,39-46]: reduced myelination, slower neural conduction velocity, high prevalence of abnormal neurologic reflexes, decreased psychomotor and mental developments, impaired hippocampal function, decrease in verbal abilities, low discrimination memory, poor mathematical and writing abilities, deficits in visual and auditory systems, anxiety and depression symptoms, altered child-mother interaction [48,49].

V. ID DIAGNOSIS

A presumptive diagnosis of ID is made by the combination of risk assessment and laboratory findings [50]. Every child should have a careful prenatal information (gestational age, weight birth, twinning, blood loss), dietary history and review of risk factors for ID (infection, intestinal parasitic infestation, chronic diseases) and undergo a complete physical examination [51]. The World Health Organization recommends the use of low concentrations of ferritin ($<12 \mu\text{g/L}$ in children <5 years or $<15 \mu\text{g/L}$ in children ≥ 5 years) as ferritin reflects iron stores in the body [52]. The American Academy of Pediatrics suggests a routine screening for ID/ID anemia for all children at the age of 12 months (33).

VI. TREATMENT

To correct the ID it is necessary to identify and treat the basic causes (human hookworm is one of the most important and neglected of all human parasitic infection which afflicts more than 470 million people) and establish a plan of actions aimed at [15,33,53,54]:

1. dietary modifications to address the underlying etiology of the iron deficiency,
2. ensure adequate consumption of iron complementary foods rich in vitamin C
3. appropriate dose and scheduling of iron therapy,
4. follow-up assessment for response and control.

Oral iron treatment is preferred primarily because is economical and has few side effects. The most used dose is 3 – 6 mg/Kg/day of sulfate, gluconate, fumarate, succinate, carbonyl or polysaccharide complex iron salts, for 3 consecutive months [26].

VII. THE IMPORTANCE OF DIET

Children must obtain about 30% of their daily iron from diet to provide the necessary for new tissues, growth spurt and red blood cells [5,15]. The adequate intake of iron for 0

– 6 months old infant has been estimated as 0,27 mg/day and the recommended daily allowance for 7 – 12 months of age is 11 mg/day [12]. Therefore, in addition to breastfeeding, it is necessary to eat foods from animal sources (heme iron) such as beef, chicken, fish, seafood, eggs, and from vegetal sources (cereals, dried fruits, dark green vegetables) in quantities that can also supply all the daily energy needs. The combination of foods of plant origin with sources of heme iron (animal origin) favors the absorption of ingested iron.

VIII. IRON SUPPLEMENTATION

Iron supplementation for children at risk for ID has been widely discussed. Several authors agree that the critical period for providing supplementation to ensure iron deficiency to protect neurodevelopment is earlier in life and late fetal period [21,55,56]. World Health Organization recommends iron supplementation to prevent ID in instances where the prevalence of anemia is 40% or higher [4]. This supplementation can be done with some types of iron salts like sulfate, fumarate, succinate or gluconate [15] and close monitoring of iron status and iron homeostasis is very important [21] in order to detect possible adverse effects such as staining of the teeth, dyspepsia, nausea, vomiting, abdominal pain, constipation, diarrhea, and alterations in the composition of the gut microbiome [15]. Supplementation programs need to be monitored and motivated by the target population to ensure that iron is administered over time, avoiding abandonment for unjustified reasons [57]. In addition, it is necessary to know the individual and collective health conditions in order to prevent the indiscriminate administration of iron from causing harm, as in the case of malaria-endemic regions [58]. In malaria-endemic areas, the provision of iron supplementation in infants and children should be done in conjunction with public health measures to prevent, diagnose and treat malaria [59-60].

IX. FOOD FORTIFICATION

Fortification of foods with iron has also been a strategy adopted in several countries. Several challenges need to be overcome so that the iron incorporated as a fortification is well tolerated, easily absorbed, does not alter the taste or appearance of the food or cause adverse effects. The most important results have been achieved with powder infant milk formulas [61], cereal foods for the weaning [62], maize flour [63], iron-fortified juice [64], bouillons [65], and water [66].

X. ACTIONS AGAINST ID

Given the magnitude of this serious public health problem, many actions have been developed worldwide [3,16,20,67]:

- a) increase and improve prenatal care,
- b) encourage exclusive breastfeeding,
- c) consume of iron fortified formula after weaning,
- d) educating the family with nutritional recommendations,
- e) increase access to and consumption of iron-rich foods,
- e) enrichment of foods (rice, maize, flour, cornmeal) with iron.

XI. CONCLUSION

ID is one of the main public health problems in the world and reducing its prevalence is a priority because long-term negative effects on physical and mental health, educational attainment, and job potential impact in the future of people and nations lowering intelligence quotients [3,7,15,35]. All efforts should be made at individual and collective levels, mobilizing people from the health, education, food security and the whole of society to improve the living conditions of populations most vulnerable to nutritional deficiencies and their undesirable consequences.

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