IRON DEFICIENCY AND IRON DEFICIENCY ANEMIA – A GLOBAL PUBLIC HEALTH PROBLEM

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ABSTRACT

Iron deficiency is defined as a condition in which there is not an adequate iron level necessary to maintain the normal physiologic functions. Having the magnitude of epidemics, anemia is a global public health problem, which affects both the emerging countries and the developed ones, with major consequences for human health and for social and economic development. Nowadays, iron deficiency and especially iron-deficiency anemia, remains one of the most severe and important nutritional deficiencies. Each group of age is vulnerable. Infants, small children, pre-school children and teenagers show a higher risk of iron deficiency. Accordingly, the World Health Organization developed an ample package of public health measures that approaches all the aspects related to iron deficiency and iron-deficiency anemia. Trying to diminish the prevalence of iron deficiency and iron deficiency anemia, the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) has synthesized in 2014 the recommendations used also at present for martial prophylaxis.

Keywords: nutritional deficiency, iron deficiency, iron deficiency anemia

Iron is an important mineral implied in various body functions, including the oxygen transport in the blood. This fact is essential in supplying energy for day-by-day life.

Iron deficiency is defined as a condition in which there is not an adequate iron level necessary to maintain the normal physiologic functions; this results from inadequate iron absorption, such that one cannot supply the iron necessary for the good operation of the organism and for the growth, or from a negative iron balance in the long run. Any of these situations results in the diminution of the iron deposits, measured through serum concentration of ferritine, or the iron amount in bone marrow. The iron deficiency can be accompanied or not by iron deficiency anemia (1).

Having the magnitude of epidemics, anemia is a global public health problem, which affects both the emerging countries and the developed ones, with major consequences for human health and for social and economic development. Data are alarming: two billions of persons, representing 30% of the world population, are anemic, many of them due to iron deficiency, but in areas with poor resources. This fact is frequently exacerbated by a series of other pathological conditions, such as malaria, parasite infections, HIV/SIDA, schistosomiasis, tuberculosis, other nutritional deficiencies and haemoglobinopathies, which constitute very important factors that contribute to the high prevalence of anemia in certain areas (2). At a global level, it has been estimated that about 25% of pre-school children have iron deficiency. In Europe, the prevalence of iron deficiency anemia at infants is usually < 2% before 6 months of age, about 2-3% from 6 to 9 months, and 3% to 9% from one to three years. Similarly, the prevalence of iron deficiency is the highest between 1 and 3 years, since the European figures for prevalence usually varies between 5% and 20% (3).

Nowadays, the iron deficiency, and especially iron deficiency anemia remains one of most severe and important nutritional deficiencies in the world. Each age group is vulnerable. The iron role is exerted from the very first months of life, which imposes the avoidance of iron deficiency from the newborn and infant period, in order to prevent some irreversible consequences.

Infants, pre-school children and teenagers show a higher risk to develop iron deficit, mainly due to the increasing iron necessities during the period of fast growth. Without the intervention at the oppor-

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tune moment, a child whose diet does not offer enough iron will finally develop anemia through iron deficit.

Iron deficit affects children cognitive development until teenage; it affects the myelination, contributes to the diminution of energetic metabolism and is involved in ADHD (Attention Deficit Hyperactivity Disorder) and the syndrome of "tireless feet"; it also has a negative impact on non-specific and specific immune mechanisms, thus being associated with the increase of morbidity (4).

During pregnancy, the iron deficiency is correlated with several negative results for both mother and child, including high risk of bleeding, sepsis, maternal mortality, perinatal mortality, low birth weight (5). One estimates that almost all women have a certain iron deficiency, and more than a half of the pregnant women in the emerging countries suffer of anemia (6). Even in the industrialized countries, the iron deposits are considered as defective for most of the pregnant women. In the end, a 30% depreciation of the capacity of physical work and performance is reported for both women and men with iron deficit. The economical implications of the iron deficiency and of various intervention strategies to fight them, suggest that the approaches based on improved food products and supplements are especially efficient. The highest benefit/cost ratio is reached through food improvement (7).

Iron is essential for all the cells. Iron functions include:

- involvement in the energetic metabolism;
- gene regulation;
- cell growth and differentiation; oxygen bonding and transport;
- utilization of muscle oxygen and its storage;
- neuro-transmitter synthesis;
- protein synthesis.

Iron necessities are bigger at male teenagers, during the peak of puberty, due to a stronger increase of blood volume, muscle mass and myoglobine (8).

After menses installment, the iron necessities keep remaining high at women, due to the loss of menses blood, which is situated at an average of 20 mg iron monthly, and can reach, in particular situations, 58 mg at certain persons. The oral contraceptives diminish the menses losses, while some intrauterine devices can increase these losses. Despite the increased iron necessities, many teenagers, girls especially, can present an iron input of only 10-11 mg total iron/day, which results in about 1 mg absorbed iron. About three quarters of teenager girls do not manage to cover the dietetic iron requirements, as compared to 17% of teenager boys (9).

Conventionally, it is considered that iron deficiency evolves in three stages:

- depletion of iron deposits;
- defective erythropoesis;
- iron deficiency anemia.

During the first stage, the iron deposits are outworn, an aspect quantified through serum ferritine dosage, but this is a reactant of acute phase, being modified in infectious or inflammatory conditions. Transferrine saturation degree (the ration between serum iron and transferrine) is a more reliable marker than serum iron levels and it will decrease in the first or the second stage of iron deficiency. Yet, ferritine is used more often than the saturation degree of transferrine as a marker of iron depletion in the body.

In the second stage, in the iron-deficiency erythropoesis, the serum receivers for transferrine increase in plasma, as markers of increased iron needs in the body tissues. Moreover, erythrocyte zinc protoporphyrine from the red cells in the blood will increase, while haemoglobin concentration (Hb) decreases.

In the third stage, of iron deficiency anemia, the hemoglobin concentration in the blood will be reduced and the erythrocyte indices will be low (10). The combination between Hb and feritine is considered the most sensitive in measuring the efficiency of iron administration, especially in children (11) (Table 1).

TABLE 1. *Iron deficiency anemia – ESPGHAN: Reference values suggested to define anemia, and the values of serum ferritine at various ages*

Marker	Age				
	0-1 weeks	2 months	4 months	6-24 months	2-5 years
Haemoglobin (g/L)	135	90	105	105	110
Serum ferritine (μg/L)	40	40	20	10-12	10-12

The risk factors associated to a high prevalence of iron deficiency include a low birth weight, alimentation with cow milk, reduced amount of iron-rich complementary food or inadequate complementary (diversified) food, vegetarian food, gastro-intestinal affections, lead poisoning, precarious socio-economical status, immigrant status.

The first six months of life, known as the period with the highest growing rhythm, when the iron reserves are depleted, represent the most critical period of life for maintaining the dynamic balance between the nutritional requirements and iron contribution. During the first 4 months of life, iron is provided from milk. Human milk contains 1.0-1.5 mg Fe/liter, 50% of which is absorbed, unlike integral cow milk that contains 1 mg Fe/liter, only 10% of which is absorbed (12).

The interventions proposed to prevent iron deficiency at various ages include iron supplementation at pregnant women, delayed clamping of the umbilical cord, iron supplementation at suckling and underweight new born children (iron drops), milk formulas improved with iron, correct complementary alimentation, avoiding cow milk alimentation. The European Society for Pediatric Gastroenterology, Hepathology and Nutrition (ESPGHAN) developed the recommendations related to iron requirements in infants and children (Table 2).

TABLE 2. *Iron intake in terms of age groups according to ESPGHAN 2014 (3)*

Infants 6 months – 1 year	Children of 1-3 years	Children 4-8 years	Children 9-13 years
0.9-1.3 mg/kg body	0.5-0.8 mg/kg body	0,3-0,5 mg/kg body	0,2-0,3 mg/kg body
7.8-11 mg	5.8-9 mg	6-10 mg	8-11 mg

One does not recommend Iron supplements (ex. iron drops) for long periods for breast-fed infants during the first months of life. ESPGHAN concludes that there is no convincing evidence that iron supplements need to be administrated to infants with normal weight at birth, nourished exclusively with human milk during the first 6 months, among the population with a reduced prevalence of iron deficiency anemia.

Due to a much smaller bioavailability of iron contained in milk formulas, as compared to mother milk, the starting formulas have bigger iron concentration than mother milk; however, there was a long debated controversy regarding the optimum level of fortifying the infant formulas with iron.

At present, most of the standard formulas for infants in Europe include iron in concentrations of 4 to 8 mg/l. Due to the above-mentioned proofs, as well as to the low prevalence of iron deficiency anemia at 6 months babies in Europe, ESPGHAN consider this practice as safe and efficient. Yet, there is clearly a need of controlled randomized studies, to determine accurately the adequate iron level in infant formulas.

Low birth weight (LBW) infants have a smaller total iron amount in their organism and a higher growth rate, as compared to those with normal birth weight, whence an increased iron necessity even before 6 months. The ESPGHAN Guidelines conclude that the administration of 1-2 mg Fe/kg body/day starting with the interval of 2-6 months of life, at low birth weight infants (2,000-2,500 g) up to 6 months age, prevents the installation of iron deficiency anemia without adverse effects and diminishes the risk of subsequent behavior disorders. The LBW infants, weighting less than 2,000 g at birth, need to receive iron supplements at a dose of 2 to 3 mg/kg body, according to ESPGHAN directives for complete nutrition of premature babies.

Starting with the age of 6 months, all the infants should receive iron-rich food in their complementary nutrition and/or iron fortified food.

Integral cow milk should not be administered before 1 year, and after this age the quantity should be limited to 500 ml/day maximum.

Signs and symptoms of iron deficiency at children can include behavior problems, diminution of cognitive performances, repeated infections, loosing the appetite, lethargy, dyspnoea, increased perspiration, strange food preferences (pica), unsatisfactory stature-weight development, decrease of effort resistance, muscle force diminution (13).

Dietetic strategies

Iron sources from food include fish, poultry, lentil, dry bean, cereal products, vegetables, dry fruits and molasses. Those of animal origin are efficiently absorbed by the receptors from intestine, while iron bioavailability from plants is determined by the presence of some food factors that improve or inhibit its absorption (14).

Possible adverse effects of iron

It is worth mentioning that iron is a strong prooxidant and, unlike most of other nutrients, cannot be actively eliminated. In adults, the risk of iron overloading is mainly restricted to people with hereditary haemochromatosis. In children, one must also take into account the iron-overloading risk, even without this genetic predisposition. Excessive iron supplementation at infants can have adverse effects, for instance an increased risk of neuronal affection, diminution of immune defense capacity and an inadequate development (15). Since high iron consumption can have negative effects, it is important to identify the iron needs and the risk groups that should benefit of an increased iron amount. It is also important to keep the iron supplements well closed and far from children reach; those in form of tablets have often been mistaken by children for lollipops.

At present, there are debates concerning anemia multi-deficiency concept. That is why, besides iron deficiency, one must take into account the deficiency of other minor elements (copper, zinc), as well as vitamins (vitamin C, vitamins from the B group – B_2, B_6, B_{12}), with which it associates relatively often and which are known to be involved in iron metabolism and haematopoesis.

WHO has elaborated a comprehensive package of public health measures, which approach all the aspects related to iron deficiency and nourishing deficiencies associated with iron deficiency anemia. This package is implemented in the countries with a high level of iron deficiency and anemia and with a high rate of infections. Among the elaborated measures, one can quote:

- increased iron share: complementary food with iron-rich aliments, including industrial preparations and iron supplements;
- infections control: immunization programs, as well as monitoring infectious diseases (malaria, schistostomiasis);
- improve nourishment status: prevent and monitor other nourishing deficiencies, such as those of copper, zinc and vitamins – C, B_2, B_6, B_9, B_{12} and A (2).

CONCLUSIONS

Iron deficiency and iron deficiency anemia are public health problems of great concern. It is imperiously necessary to monitor age groups of risk, in order to prevent the installation of clinical signs, some having a long-term impact. In addition, one cannot ignore nourishing deficiencies frequently associated with iron deficiency, such that the therapeutic benefit becomes quick and efficient. Recommendations of specialized scientific societies are always revised, but ample studies are still necessary concerning the optimum period to initiate the prophylaxis, the age-group adapted dose, individual peculiarities and nourishment requirements. As it represents a public health problem with major socio-economical implications, the WHO recommendations have been integrated in a package of measures that needs to be implemented in all the areas with increased prevalence of this nourishment deficiency.

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