Iron deficiency anemia in children

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Abstract

Objective: to present the aspects involved in iron deficiency anemia in children and several measures for its control.

Method: the authors performed an extensive review of national and international literature and associated findings to their own personal experience in this area. The study included general aspects of iron metabolism, iron deficiency, and the mechanisms that trigger iron deficiency anemia (IDA). In addition, the authors focused on the current situation of IDA in Brazil, its prevention and treatment.

Results: iron deficiency is still one of the most serious public health issues in Brazil despite all the available knowledge about intervention measures. The studies found in the literature show excellent results through the fortification of foods and/or iron supplementation, in association with nutritional education.

Conclusion: the authors concluded that Brazil detains sufficient knowledge regarding IDA, and that the proposed intervention measures have proved to be efficient. There is, however, a lack of political will and focus at all governmental levels (Federal, State and Municipal), and a greater commitment on the part of health professionals that allow the alarming prevalence rates of iron deficiency anemia in our population at higher risk (i.e. children) to be reversed.


Definition

Anemia is defined as a pathological process in which hemoglobin (Hb) concentration in red cells is abnormally low, considering variations as to age, gender, sea-level altitude, as a result of several situations such as chronic infections, hereditary blood conditions, deficiency of one or more essential nutrients that are necessary for the formation of hemoglobin e.g.: folic acid, B12, B6 and C vitamins, and proteins.¹ Therefore, there is no doubt that iron deficiency is the cause of most anemias. It is called iron deficiency anemia.

Some aspects about iron metabolism

There are two forms of iron: ferrous iron (Fe++) and ferric iron (Fe+++). The iron content in the human body is equivalent to 3 to 5g; part of it is used for metabolic and oxidative functions (70% a 80%), and the rest is stored as ferritin and hemosiderin in the liver, spleen and bone marrow (20% a 30%).

Over 65% of the iron content is found in hemoglobin, whose major function is to transport oxygen and carbon...
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Iron is an essential nutrient for the human body. It is a key component of hemoglobin, myoglobin, and a variety of enzymes involved in the body's metabolism. A daily intake of iron is necessary to maintain adequate levels of this essential nutrient. The table below summarizes the daily iron requirements for different age groups:

<table>
<thead>
<tr>
<th>Age</th>
<th>Daily Iron Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>10 mg</td>
</tr>
<tr>
<td>Men</td>
<td>8 mg</td>
</tr>
<tr>
<td>Women</td>
<td>18 mg</td>
</tr>
<tr>
<td>Adolescents</td>
<td>15 mg</td>
</tr>
<tr>
<td>Infants</td>
<td>10 mg (6-36 months)</td>
</tr>
<tr>
<td>Children</td>
<td>12 mg</td>
</tr>
<tr>
<td>Pregnant</td>
<td>20 mg</td>
</tr>
</tbody>
</table>

Requirements and recommendations

Since iron is an important micronutrient, the body has a very efficient mechanism to avoid its loss. This way, the iron content is maintained within certain limits with the aim of adequately using it. Even the iron that originates from red cells, taken from the circulatory system, whose half life is 120 days, is reused. Daily iron losses are about 1 mg, mainly due to cell desquamation. In addition, small quantities are lost through urine, sweat, and feces. Other situations such as menstruation, lactation, and parasitosis may cause additional iron loss.

The intestinal tract plays a very important role in the recycling mechanism of body iron, since absorption may change according to body needs, that is, when reserves are low, there is a significant increase in absorption, and when they are high, absorption is inhibited.

As body iron requirements are associated with different stages of life, the rate of iron absorption by the intestinal tract is also related to age group. For instance, a 12-month infant presents an absorption rate four times higher than others in different age groups.

By considering these aspects, we may conclude that daily iron requirements are low and vary according to the stage of life. Therefore, considering an absorption rate of 10%, RDA (Recommended Dietary Allowances) preconizes a daily 10 mg intake of elemental iron for infants aged between 6 months and 3 years; 12 to 15 mg for male and female adolescents, respectively; 10 mg for male and female adults after they stop menstruating, and 15 mg for women at reproductive age and nuruters. Pregnant women need a daily intake of 30 mg of iron.

Food sources

Iron is found in several foods of animal origin (all kinds of meat, milk, and eggs) and of vegetable origin (dark green vegetables, beans, soy beans, among others). However, it is necessary to clarify the capacity of the body of absorbing the available iron so that it can accomplish several functions, which determines its bioavailability.

Absorption and transport

Duodenal iron absorption depends on the nature of the iron complex that is present in the intestinal lumen, as well as on the presence of facilitating and inhibitory factors in the diet, in addition to organic reserves.

Iron absorption can be classified as heme and nonheme absorption. The iron linked to the heme comes from foods of animal origin (hemoglobin, myoglobin, and other heme proteins), which is well absorbed due to its high bioavailability and, in addition to improving the absorption of nonheme iron pool.

Nonheme iron is found in foods of vegetable origin under the form of ferric complex, which is partially reduced to the ferrous form during digestion, thus facilitating absorption, by the action of hydrochloric acid, bile, and pancreatic juice.

After digestion, most of the iron forms an intraluminal deposit; therefore, its absorption is determined by facilitating factors (ascorbic acid, all kinds of meat, amino acids such as lysine, cysteine, and histidine, citric and succinic acids, and sugars such as fructose) or inhibitors (phytates, found in cereals; phenolic compounds such as flavonoids, phenolic acids, polyphenols, and tannins, found in black tea and maté, coffee and some soft drinks; calcium and phosphate salts, found in milk protein sources; egg fibers and protein).

Therefore, we should take into consideration that there are iron-rich foods such as beans, which present low bioavailability due to the presence of phytates and fibers. On the other hand, meats have much lower iron contents, with high bioavailability. Milk is another interesting example of bioavailability because mother’s milk and cow’s milk have basically the same amount of iron; mother’s milk, however, presents high absorption rate while cow’s milk presents low bioavailability due to its calcium and phosphate salt contents.

The absorbed iron may be stored in the enterocyte cytoplasm in different ways: as ferritin conjugate, protein linkers (mobilferrin) or nonprotein linkers (AMP, ADP, amino acids), also in charge of transporting iron from the enterocyte into the basolateral membrane. Part of the iron that is stored this way may return to the intestinal lumen through desquamation.

Transferrin transports iron through the bloodstream. Each transferrin molecule joins two Fe+++ ions. This way,
the measurement of serum transferrin saturation (\% of serum iron ratio and the total capacity of iron linking) is considered an important indicator of body iron content.

It is necessary to have specific receptors, which exist in great quantities in the tissues that need iron more urgently (bone marrow, liver, placenta), so that the body can use iron appropriately. Usually, about 70 to 90\% of the iron is absorbed by the bone marrow for the production of hemoglobin.

In the liver, spleen and bone marrow, iron may be deposited, bound to ferritin and hemosiderine up to twenty times beyond its normal amount.\(^9\)

Iron reserves formed during pregnancy are extremely important for new-borns as these reserves will form an important source of endogenous iron, which, together with the exogenous iron from breastmilk, will meet iron requirements up to 4-6 months of life.

This way, the dosage of serum ferritin is an important indicator of body iron stores as it is directly proportional to the amount of body iron levels.

Clinical signs and lab exams for the detection of iron deficiency and anemia

Iron deficiency occurs at three stages. The first stage - iron depletion - occurs when iron content is not enough to meet body requirements. At the beginning, there is a reduction in iron deposition, characterized by serum ferritin below 12 \(\mu\)g/l, without functional changes.

If the negative balance persists, the second stage begins - iron-deficient erythropoiesis - characterized by a reduction in serum iron, transferrin saturation below 16\% and an increase in the free erythrocyte protoporphyrin level. At this stage, work capacity may be reduced.

At the third stage - iron deficiency anemia - hemoglobin is below the standards for age and gender. This stage is characterized by the development of microcytosis and hypochromia.

Iron depletion at the initial stages is substantially higher than anemia itself. The Panamerican Health Organization / World Health Organization estimates that for each person with anemia there is at least another one with iron deficiency. Thus, a population in which 50\% of children suffer from anemia - as is the case of Brazil, 100\% actually have iron deficiency.\(^10\)

The operational definition of anemia, in terms of hemoglobin levels, was established by the World Health Organization, adopting the level of 11.0 g/dl for children under the age of six and pregnant women. For children aged between 6 and 14 years and nonpregnant adult women, the level was 12 g/dl, and 13 g/dl for adult men.\(^1\)

The clinical signs of anemia are not easily recognizable, and many times go unnoticed. These signs include paleness, anorexia, apathy, irritability, reduced attention and psychomotor deficiencies.\(^11\)

Etiology of iron deficiency anemia

Usually, anemia originates from blood loss and/or prolonged iron deficient diet, especially in periods in which requirements are high, as in the case of children and adolescents who have accelerated growth rate. In addition, pregnancy and lactation are periods in which there is a lot of iron requirement.

The causes of iron deficiency anemia and iron deficiency may have their onset in the intrauterine life. Physiological reserves of iron (0.5g/kg in full-term new-borns) are formed during the last three months of pregnancy, and together with the iron found in breastmilk, meet the demands of breast-fed infants until their sixth month of life. Therefore, we may conclude that prematurity, due to lack of time, and low weight at birth, due to reduced reserve, associated with early interruption of exclusive breast-feeding, are the most common causes that contribute to iron depletion in breast-fed infants. During the first childhood, the problem is aggravated by incorrect feeding, especially at weaning, when breastmilk is usually replaced with iron-deficient foods. Cow’s milk is a good example, because, although it has the same iron content as breastmilk, its bioavailability is too low, and more often than not, mothers replace a meal with bottle feeding.

Other aspects that aggravate and most times determine insufficient iron deposition have to be considered. These aspects include low socioeconomic and cultural level, poor sanitation conditions and difficult access to health services, and poor mother/child relationship.\(^12,14\)

Acute or chronic blood loss depletes body iron reserves and may cause pathologies such as gastroesophageal reflux, intolerance to cow’s milk protein and intestinal parasites.\(^12\) Parasites such as Ancylostoma duodenale or Necator americanus may cause considerable iron loss, either through the blood sucked by the parasite or through the bleeding caused by the lesion to the intestinal mucosa, also caused by the parasite. Other parasites like Ascaris lumbricoides and Giardia lamblia cause bleeding as they compete for food. In general, the incidence of these parasites occurs in children who are older than 5 years.

Prevalence of iron deficiency anemia

Iron deficiency and iron deficiency anemia are considered the major public health problems and the most common nutritional deficiency around the world\(^13\) due to their high prevalence, effects on development and growth, resistance to infections and association with the mortality of infants younger than 2 years.
Iron deficiency anemia is universally distributed. There is an estimate that 25% of the world population are affected by iron deficiency; the population groups which are most affected are infants aged between 4 and 24 months, school-age children, female adolescents, pregnant women and nurturing mothers.  

Iron deficiency anemia affects 43% of preschool children all over the world, especially in developing countries, which present prevalence rates four times higher than those found in industrialized countries. This high prevalence is associated with poor sanitation conditions, low socioeconomic conditions and high morbidity among infants.  

In Americas, approximately 94 million people are believed to suffer from iron deficiency or iron deficiency anemia, especially in the Caribbean and in the Andes, having affected around 60% of pregnant women in 1997.  

A meeting held in Buenos Aires in 1992 presented the results of different studies carried out in several Latin American countries (Argentina, Bolivia, Brazil, Chile, Paraguay, Peru, Uruguay, Costa Rica, Cuba, El Salvador, Venezuela, Haiti and countries in the Caribbean). The prevalence of anemia for pregnant women ranged between 13 and 61%; and 18 and 45% in preschool children. According to a national study carried out in Ecuador, iron deficiency anemia affected 70% of infants between 6 and 12 months and 45% of infants between 12 and 24 months.  

In Brazil, there are no national data on the prevalence of iron deficiency anemia. However, punctual studies carried out in the last few decades in several regions of the country have shown a significant increase in the prevalence and severity of iron deficiency in risk groups, regardless of their economic level. In the age group comprising infants younger than 2 years, the prevalence of iron deficiency anemia is between 50% and 83%.  

In the city of São Paulo, the prevalence of iron deficiency anemia has been increasing. In 1974, anemia was present in 23% of infants aged between 6 and 60 months, in a representative sample of the city’s population. In 1984, another study registered a rate of 36%, in which the highest prevalence rates were found among infants aged 6 to 11 months (54%) and 12 and 24 months (58%).  

The Public Sector Basic Units attends to people with low socioeconomic level, which are at greater risk for nutritional problems. In Recife, 85% of infants aged between 6 and 11 months, and 82% of infants aged 12 and 23 months were found to suffer from anemia.  

In a sample of 2992 infants aged between 6 and 23 months, who were attended on spontaneous demand at 160 Basic Health Units, in 63 municipalities of the state of São Paulo, 59% presented hemoglobin rates below 11.0 g/dl. and, 25%, rates below 9.5 g/dl.  

### Prevention

Iron deficiency anemia prevention should be established through the following four approaches: nutritional education and improvement of diet quality, including breast-feeding incentive, medicine supplementation, food fortification and control of infections.  

When recommending a diet for infants, some aspects should be dealt with carefully, guaranteeing better body iron content; this includes maintenance of exclusive breast-feeding up to the 4th - 6th month of life and initiation of complementary feeding with iron-rich foods, which facilitate iron absorption (all kinds of meat, citrus fruits). On the other hand, inhibitory agents such as black tea, maté, coffee and soft drinks should be avoided during meals. Ideally, meat should be cooked instead of fried; the broth should be used too.  

Therefore, the adequate choice of complementary foods is of paramount importance, since children’s diet should be diversified, balanced and rich in high-bioavailability iron.  

Medicine supplementation is very efficient in preventing and controlling anemia. However, some studies have already shown that this kind of intervention presents a drawback that significantly reduces the impact over the hematological conditions of the infants who were followed up, namely lack of mother/child relationship, regardless of nutritional status. Thus, as the mother does not interact satisfactorily with her child, she does not realize how severe the disease is and, consequently, she does not give her child the medication. Therefore, only the preconization of medicine supplementation with ferrous sulphate is not enough to assure health professionals that the child is really receiving the supplementation.  

The Brazilian Society of Pediatrics preconizes the profilactic iron supplementation as follows:  

1) **Full-term new-borns, with adequate weight for gestational age:** during breast-feeding period, after the 6th month, or when weaning is initiated (weaning is when the infant is fed any other kind of food besides breastfeeding), up to the 24th month of life, should be given 1 mg of elementary iron / kg of weight/day, or a weekly dose of 45 mg, except for infants who are receiving iron-fortified formulas.  

2) **Low-weight preterm and new-born infants:** after the 30th day of life, 2 mg/kg of weight/day, during 2 months. After that, use the same recommendation for full-term new-borns with adequate weight for their gestational age.  

In public health services such as day care centers and schools, the weekly proposal has shown better results than the daily regimen since its administration is facilitated. The use of fortified foods has been an alternative that is preferred by industrialized countries for over 50 years, presenting excellent results.
The great advantage of fortified foods is that mothers do not have to agree to the proposal; this way, when the food is ingested, we know for sure that the iron was ingested too. When choosing the foods to be fortified, it is important to remember that foods should be easily accessible, have a low cost and belong to the usual eating habits of the region, without changing their taste or aspect; compounds with good bioavailability should be used.

The Group for International Counseling on Nutrition-based Anemias suggests the following recommendations for the control and prevention of nutrition-based anemias:

a) Nutritional education that motivates the consumption of iron-rich foods, respecting the population’s eating habits, associated with breast-feeding incentive programs;
b) Improvement of basic sanitation systems and medical assistance to all, with control over intestinal parasitosis;
c) Design of iron supplementation programs in prophylactic doses for risk groups, with supervision and follow-up;
d) Design and incentive to food fortification programs, currently regarded as the best preventive measure on the long run, with lower costs.

The use of milk-based formulas and milk fortified with ferrous sulphate, chelate iron, and elementary iron presents rewarding results for infants younger than 2 years.28,29

In Ribeirão Preto, in the interior of the state of São Paulo, 21 low-income families and a total of 88 infants between 1 and 6 years were analyzed. These infants were fed water fortified with ferrous sulphate at a concentration of 10mg of elementary iron per liter of solution. The fortified water had good acceptance and improved Hb levels.30

Milk powder fortified with ferrous sulphate and vitamin C was used as an experiment against iron deficiency anemia that assessed 107 infants/children at 13 day care centers in the metropolitan area of São Paulo and 228 infants/children who received medical care at a Health Basic Unit. The milk powder contained 9 mg of iron and 65 mg of vitamin C per 100g of powder, and was fed to the children during 6 months. In this research, the initial levels of anemia were respectively 66% and 73%; whereas at the day care centers and basic health units, the prevalence rates dropped respectively to 21% and 18% after fortified milk was used; in addition, nutritional status was improved.29,31

In an innovative experiment using chelate amino acid iron in a town in the interior of the state of São Paulo, 9 mg of iron and 2000 IU of vitamin A per liter of milk were fed to the children who participated in the antianemia program. With an initial prevalence of 76%, this town presents, today, rates that are compatible with those of industrialized countries, that is, a prevalence of 4% for assisted children.32

These results confirm that the anemia status can be easily reversed provided that health professionals are properly aware of and involved in their tasks. At the same time, political decisions should be taken.

Treatment

The objective of the iron deficiency anemia treatment is to correct the rate of circulating hemoglobin and restore iron deposition into the tissues where it is stored.

It is recommended that iron salts be used, preferably by means of oral administration. Iron salts (sulphate, fumarate, gluconate, succinate, citrate, etc) are inexpensive and quickly absorbed; however, they produce more side effects - nausea, vomiting, epigastric pain, diarrhea, intestinal obstipation, dark feces and, on the long run, the development of dark spots on teeth. Absorption is higher when iron salts are ingested one hour before meals.

Salts contain different iron content. The suggested posology is 3 to 5 mg of elementary iron per kilo of weight per day, divided into 2 to 3 doses.33

The medication should be ingested together with fruit juice rich in vitamin C, if possible, since this facilitates iron absorption.

Another recommendation is that medication cannot be administered together with polyvitamin and mineral supplements. There are interactions of iron with calcium, phosphate, zinc and other elements, thus reducing iron bioavailability. Other factors that inhibit iron absorption such as black or maté tea, coffee and antacids should be avoided during or after the ingestion of medication.

It is essential that the diet followed during treatment be balanced so that erythropoiesis can be restored, assuring enough nutrients, especially proteins in order to guarantee the supply of amino acids that are essential to the production of hemoglobin; calories, to prevent these amino acids from being used as source of energy; and foods rich in vitamin C, to increase iron bioavailability in the diet.

Treatment response is fast and duration of treatment depends on the severity of the disease. Absorption of iron ions is higher during the first weeks of treatment. There is an estimated iron absorption of 14% during the first week of treatment, 7% after 3 weeks and 2% after 4 months. The first month of therapy is crucial for a successful treatment. A positive response may be measured by the daily increment of 0.1 g/dl in the concentration of hemoglobin after the fourth day of treatment. A maximum increase in reticulocyte is observed between the 5th and 10th day of treatment, and a substantial increase in the concentration of hemoglobin is observed around the third week.

Medication should be continued for about 6 weeks after hemoglobin reaches normal concentration so that iron organic reserves can be restored.

Blood transfusion is only recommended for infants whose hemoglobin concentration is less than 5 g/dl or who present signs of heart discompensation. In these cases, it is advisable to use 10 ml/kg of concentrated red blood cells, in slow venoclise and monitoring of vital signs.

Therefore, it is necessary that the problem with the treatment of iron deficiency anemia be approached globally.
This way, measures that go beyond the isolated view of iron deficiency anemia treatment can be adopted.

Final considerations

The reviewed literature has clearly shown that there are a great number of alternatives for controlling iron deficiency anemia. It is also clear that whatever measure is adopted (medication supplements, food fortification and/or nutritional education), the response is always positive, although presenting variations as to response time, in lower or higher proportions. In Brazil, however, iron deficiency anemia is a public health issue that is, unfortunately, a far cry from a definite solution despite all the knowledge that has been available on the subject and, consequently, on the measures that could be used for its control. Nevertheless, what is not well established yet, and is decisive in making any changes in the critical status of the disease in our country is an effective and clearly defined public health policy adopted by federal, state and municipal governments. Obviously, the responsibility of health professionals cannot be overlooked since the lack of commitment, which is easily noticeable throughout the years, can aggravate the situation of our people. This easygoing behavior must be changed. There is much to be done in the health sector for the well-being of children, who should not wait longer for their right: life at full potential.

References


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