Case Report

Iron Deficiency and Iron Deficiency Anemia due to cows' milk consumption: a case report

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Keywords

Iron deficiency, anemia, iron supplementation, cow milk, case report

Abstract

Iron deficiency is the most frequent micronutrient deficiency among children, affecting two billion people in the world. It can be associated with anemia. Iron deficiency has different etiologies, among them we can find early introduction of cows' milk and late weaning from breastmilk.

We describe a case of severe iron deficiency anemia with early cows' milk introduction as major risk factor for its development.

The aim of this article is to put emphasis on the importance of screening the children at risk of developing iron deficiency and iron deficiency anemia and to make a review of the literature about their diagnosis and treatment.

Introduction

Iron deficiency (ID) is the most frequent micronutrient deficiency among children (1). It can be associated with anemia. ID has different etiologies including early introduction of cows' milk and late weaning.

We describe a case of severe iron deficiency anemia (IDA) in which early cows' milk introduction was one of the risk factors leading to the development of anemia.

Case

We report the case of a 15-month-old Syrian boy presenting with a severe isolated microcytic anemia (hemoglobin (Hb) 6.1g/dl (10.5-13.5g/dl), mean corpuscular volume (MCV) 49.7fL (70-86fL)) discovered during a pre-operative work-up.

After 11 months of exclusive breast feeding, the child started to drink cows' milk mainly due to difficulties in starting the alimentary diversification. He was also suffering from pica, eating first his mother's hair and then cotton fiber, paper and cardboard. There was no failure to thrive with a weight of 11.9 kg (75th percentile) and a height of 80 cm (90th percentile).

The initial biological work-up showed a severe iron deficiency (serum iron (SI) 13µg/dl (50-120µg/dl), transferrin saturation (TSAT) 3% (20-55%), serum ferritin (SF) 3µg/l (30-400µg/l)). There was no sign of lead or zinc intoxication and the hemoglobin electrophoresis was normal.

A first attempt of oral iron supplementation was initiated with a therapeutic dosage of polysaccharide-iron complex (Ferricure®, 4mg/kg/day) without response after one month of treatment (Hb 6g/dl, MCV 50.2fL, SI 21µg/dl, SF 3µg/l). Probably this lack of response was due to poor compliance.

The child was then hospitalized to complete the work-up, excluding parasitic infection, gastrointestinal blood loss, celiac disease and folic acid deficiency. Finally, he received a parenteral therapy with ferric carboxymaltose (Injectafer®, 10mg/kg) with pursuit of the oral supplementation.

One week after the injection, the eating disorder improved with biological improvement of the IDA (Hb 7.5g/dl, Reticulocytes (Rc) 222.500/mm³ (35-100 10³/mm³), SI 46µg/dl, SF 39µg/l). One month later, blood results were still improving (Hb 9.8g/dl, MCV 63.8fL, SI 86µg/dl, SF 27µg/l).

Discussion

Iron deficiency is defined by the World Health Organization's (WHO) as a serum ferritin under 12 µg/l (1). It affects more than two billion people worldwide, its prevalence is evaluated to reach 12% at 12 months of life and up to 15.2% of the toddlers in the United States (1,2). Iron deficiency anemia, where anemia is defined by the WHO as a hemoglobin concentration inferior to 11 g/dl for children aged 12-35 months, has a prevalence of 2-4% in Europe (2).

ID can be due to insufficient iron intake or absorption, excessive iron requirement or abnormal loss (3). Its development can be attributed to economic, dietary and neonatal risk factors (table 1) (2,4). Our case illustrates the importance of investigating the dietary history in the prevention and assessment of ID in infants and young children. Indeed, during the first months of life, the major sources of iron are breastmilk, cows' milk or formula feeds : human and cows' milk containing a similar amount of iron with a lower bioavailability for cows' milk (10% versus 50%) and iron-fortified formula having a better bioavailability than non-fortified ones (2). Vegetarian and vegan diets also increase the risk of iron, zinc, calcium, omega-3 polyunsaturated fatty acids, vitamins B12 and D deficiencies if growing children do not have an adequate meal plan or dietary supplements (5).

Table 1 : Risk factors associated with development of ID and IDA (adapted from Ferrara et al. (2) and Mc Carthy et al. (4))

- Dietary history (2)
  - Low family income
  - Early introduction or excessive consumption of cows' milk
  - Delayed weaning (after 6 months)
  - Low intake of iron-fortified products
  - Overweight
  - Vegan/vegetarian diet (5)
- Antenatal and prenatal history (4)
  - Premature birth (<37 weeks of gestation)
  - Low-birth-weight (LBW) (<2700g)
  - Pregnancy complication (diabetes and fetal growth retardation)
  - Maternal lifestyle factors (obesity, smoking)
- Medications (e.g. proton pump inhibitors) (6)

The prenatal and neonatal history must also be taken into account because some factors may have a negative impact on the infant iron stores as preterm and low birth weight infants are at higher risk of ID because of the higher post-natal iron requirement needed for the rapid growth and the early onset of erythropoiesis (4).

ID and IDA may be associated with non-hematological complications that are important to know because some might not completely recover after supplementation. Indeed, many studies have highlighted the possible causal relation between ID, IDA and delays in cognitive, behavioral and motor development, insisting on the necessity of preventing ID and IDA in young children. The age of onset, severity and duration of the ID as well as the association to anemia may have an impact on the child's development and on the supplementation's efficacy. Although, more evidence is needed to evaluate the efficacy of iron supplementation to correct those symptoms (2,6).

It's also believed that ID increases the infectious risk and can be associated with growth retardation and weight impairment (7).

IDA can also be associated to pica, which is defined as the compulsive ingestion of non-nutritive materials such as plaster, soil, ice, paper, cinder… for more than 1 month. The link between ID and pica needs to be further investigated. Some authors suggest that pica is a consequence of ID and others think that pica is its cause. However, it can be considered as an alert for possible ID and can be resolved after a few days of iron supplementation (8).

Different approaches have been proposed to prevent ID. In a position paper, the European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) recommends delayed umbilical cord clamping, use of iron fortified formulas (iron concentration 4-8mg/l) and of iron supplementation (1-2mg/kg/day between 2000-2500g and 2-3mg/kg/day under 2000g) up to 6 months of life. From the age of six months, they recommend sufficient intake of iron fortified complementary food including meat, iron-fortified follow-on formulas and iron-fortified foods (e.g. cereals), and the eviction of cows' milk as the only milk drink up to 12 months (with maximal intake of 500ml/day for toddlers). In their opinion, there is no benefit in using iron supplementation for pregnant women or in exclusively breast-fed normal birth weight children under six months of life (7).

The Swiss Pediatric Oncology Group proposes to evaluate the iron load for all children presenting signs and symptoms of ID or IDA (6) whereas the American Academy of Pediatrics recommends a systematic screening of anemia at 12 months or a selective screening at any age when risk factors are identified, including risk of inadequate iron intake based on dietary history (1).

Almost all recommendations suggest the use of serum ferritin level for the diagnosis of ID (1), taking into account that inflammation could increase SF (9). Transferrin saturation can be used as a complementary testing with a threshold under 20% (9).

The treatment of IDA should include the treatment of the underlying cause (3). Oral therapy is preferred over intravenously administration. The dosage of elemental iron recommended for children range from 3 to 6mg/kg/day depending on the active iron compounds Fe2+/ Fe3+ (3,6,10). Different formulation of ferrous (Fe2+) and ferric iron (Fe3+) are available. In Belgium, the only formulation commercially available for young children is a solution of polysaccharide-iron complex (Fe3+) which has a lower absorption than ferrous sulfate or gluconate (Fe2+). In table 2, we propose a preparation based on ferrous sulfate tablets that can be used to prepare magistral solution.

The therapy can be considered as effective when there is an elevation of the hemoglobin of 1g/dl after one month of treatment (3). It should be taken sober because its absorption can be reduced by some food components (e.g. phytates, calcium, cows' milk). In addition, medications inhibiting gastric acid secretion (e.g. proton pump inhibitors) will diminish iron absorption. On the other hand, some food components such as vitamin C can enhance iron absorption (2,6). The treatment should be maintained for 3-6 months to restore the iron stores. In case of non-response, poor compliance or absorption of the oral treatment or other causes of iron deficiency should be evaluated. Poor adherence can be increased by the gastro-intestinal side effects (such as diarrhea, constipation, abdominal discomfort, dyspepsia, and vomiting) (3,10). In those cases of poor response or compliance to polysaccharide-iron complex, a change of formulation could be tried.

Table 2 : Oral iron suspension (Fe 18,7 mg/ml / FeSO4 57,7 mg/ml))

Qualitative and quantitative composition

- Tardyferon pills : Fe2+ 80mg /Fe SO4 dehydrated 247,25mg =7 pills
- Citric acid monohydrate ..... 0,2462 g
- Simple syrup ..... 24,410 g
- Raspberry aroma ..... 0,45 ml
- Water for injection ..... ad 30 ml

A parenteral therapy could be considered in case of poor tolerance, inefficacy or poor absorption of oral iron or need for rapid hemoglobin correction (3,10). Its advantages are that it has less gastro-intestinal side-effects, a better adherence, and the possibility of administrating a greater amount of iron in a shorter time (9). The immediate side-effects include headache, vomiting, abdominal pain, flushing, myalgia, pruritus, and hypophosphatemia (10). The major risk of parenteral therapies is anaphylactic reaction whose severity is variable and which is mostly encountered with the high-molecular-weight iron dextran (3,9). It can be reduced by slow injection and close monitoring. The use of antihistaminic premedication is still under debate but antianaphylaxis medication should be available and ready to use without delay during the infusion (6,10).

The increase of the reticulocytes after 5-10 days is an early sign of response to parenteral therapy (6).

Transfusion should be considered according to the hemoglobin level and the clinical state of the patient. There isn't any standard recommendation regarding its indication in case of IDA (3).

There is no universal recommendation about the monitoring after iron supplementation, but some authors recommend to follow the total blood count every three month during one year (3).

Conclusion

Iron deficiency anemia can be associated with complications such as delays in cognitive and behavioral development, growth retardation and pica. Thus, it is of great importance to prevent it and to detect the children at potential risk, more especially by taking the nutritional history into account. Indeed, early introduction or excessive consumption of cows' milk associated with late weaning or delayed food diversification are risk factors for the development of ID and IDA.

The authors have no conflict of interest to declare.

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