Abstract

Hypochromic Microcytic Anaemias in Children

Hypochromic microcytic anaemias, a heterogeneous group of inherited and acquired diseases, are the most common forms of anaemia in children and adolescents. A variety of factors are involved in the etiology of these disorders, including inadequate intake, malabsorption, defects in heme synthesis or iron acquisition, and blood loss. Nutritional iron deficiency and \( \beta \)-thalassaemia trait are the primary causes of hypochromic microcytic anaemias in children; whereas, bleeding disorders and anaemia of chronic disease are common causes in adulthood. The most common nutritional disorder worldwide is iron deficiency anaemia (IDA), and its prevalence varies amongst different parts of the world. IDA is associated in many publications with psychomotor and cognitive abnormalities and poor school performance in children in the first years of life, although a causal relation has not yet been demonstrated and there are many confounding factors. Children under 5 years of age at risk for IDA are preterm/low birth weight babies, infants older than 6 months who are exclusively breast-fed or who are receiving non-iron fortified formulas and no iron supplementation, those who were introduced to cow’s milk before 1 year of age, children of immigrants with iron-deficient mothers, and children living in developing countries exposed to parasitic infections, particularly hookworm. Risk factors in adolescence include heavy menstrual blood loss and strict fad dieting in females, and vegetarian diet, malnutrition, and parasitic infestation in both sexes. In contrast, decreased iron absorption may be due to conditions such as celiac disease, autoimmune atrophic gastritis, *Helicobacter pylori* gastritis, iron refractory iron deficiency anaemia (associated with a mutation of the serine protease matriptase-2 [TMPRSS6]), or chronic inflammation; whereas, polymenorrhea, peptic ulcer, inflammatory bowel disease, Meckel’s diverticulum, and parasitic infestations are likely causes of blood loss. The proportion of paediatric iron deficiency cases attributable to these factors differs across countries. For example, blood loss and malabsorption are the most common causes in Italy, compared to blood loss and inadequate intake in Taiwan.
Treatment of ID and IDA should not be undertaken until a diagnosis has been made. The two main modalities for treating ID and IDA are dietary measures and iron replacement. Heme-containing dietary sources such as fish, poultry, and meat, provide a higher bioavailability of iron than non-heme sources. The bioavailability of non-heme iron is, however, strongly affected by foods ingested at the same meal.

Iron replacement therapy should be prescribed only if the diagnosis is certain, as additional iron may have negative effects in iron-sufficient children. When indicated, treatment with a cost-effective oral iron preparation with minimal side effects will suffice. The usual dose is 3 to 6 mg/kg/day of elemental iron for infants and children and 60 to 120 mg/day for school-age children and adolescents, with treatment continuing for 3 to 4 months after reversal of anaemia to ensure that body iron stores have been replenished. Failure of response after 2 to 4 weeks of oral iron requires reevaluation for poor compliance with oral iron, other acquired causes associated with GI blood loss, and genetic anaemias. Additional lab tests, such as complete iron studies, HbE or HPLC, or stool exam for occult blood and parasites, should be done. Other tests may be indicated in selected cases. Parenteral iron may be given to patients who have poor tolerance to iron tablets, poor iron absorption, or continued iron loss, or when there is a need to control the anaemia quickly. Parenteral iron is given at a dose of 50 to 100 mg/day IV and should be administered only in a hospital due to the risk of anaphylaxis or bioactive iron reactions. Blood transfusion is rarely necessary, even for patients with severe IDA, and is reserved for those in cardiorespiratory distress, or who are lethargic and/or have very poor nutritional intake. Transfusions should always be given slowly to avoid heart failure. The benefits of correcting ID/IDA in young children include an increase in haemoglobin concentration and, as shown in one publication, the induction of a decrease in upper respiratory tract infections; however, any effects on development are modest. In contrast, iron supplementation in iron-sufficient children may result in adverse growth effects and/or increased risk of severe malaria.

Since early initiation of iron replacement therapy will correct IDA but may not prevent its long-term systemic complications, the key to reducing morbidity is primary prevention—ie, ensuring an adequate intake of iron that meets an infant’s/child’s nutritional
requirements for optimal growth and development. The American Academy of Pediatrics 2005 Recommendations, in conjunction with the ESPGHAN Coordinated International Expert Group 2005 Recommendations for Composition of Infant Formula, provide guidelines for the provision of adequate iron intake for infants, children, and adolescents. Secondary preventive steps include screening for, diagnosing, and treating IDA. The American Academy of Pediatrics recommends screening haemoglobin or haematocrit between 9 and 12 months of age and then 6 months later, and, for patients at high risk, once a year from age 2 to 5 years, as well as annual screening of menstruating girls and screening boys once during the peak growth period. The role of primary healthcare providers in counseling individuals and families about diet and iron, and in screening persons for ID risk and treating affected individuals, is crucial in preventing and controlling ID and IDA.