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Iron therapy and anthropometry: A case-control study among iron deficient preschool children

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ABSTRACT

Background: Iron deficiency anemia (IDA) causes detrimental effects on physical growth which is attributed to poor appetite, altered endocrinologic profile and neurotransmitter metabolism.
Objective: To investigate the iron status of preschool children with IDA and its association with the degree of growth retardation at presentation, and to detect the effect of iron supplementation on growth velocity (GV) over a period of one year.
Materials and methods: A case-control study conducted in Diabetes Endocrine Metabolism Pediatric Unit in collaboration with the Pediatric Hematology clinic at Children's Hospital, Cairo University included baseline and follow up anthropometric and hematological parameters of 40 IDA patients with mean age 2 ± 0.8 years compared to 40 healthy clinically non-anemic, age and sex-matched controls with mean age 2.7 ± 1.1 years. A daily total dose of 6 mg/kg/day of ferrous sulfate in 2–3 divided doses were given between meals to patients with IDA.
Results: At presentation, patients with IDA had low hemoglobin, hematocrits, serum iron, serum ferritin, height standard deviation score (SDS), weight SDS, and body mass index (BMI) SDS which improved significantly after treatment. The GV of IDA patients correlated significantly with serum ferritin concentration and also their BMI SDS correlated significantly with the serum ferritin concentration.
Conclusion: IDA during the first 6 years of life, when growth is fast, adversely affects both linear growth and weight gain which is reversible with iron therapy, thus adequate iron status is crucial for normal growth (height, weight and GV). The findings of the present study supported the beneficial effects of oral iron supplementation on physical growth parameters of IDA preschool children.

Introduction

Iron deficiency anemia (IDA) is a global public health problem affecting 1.62 billion people, with the highest prevalence in preschool children (47%) especially in third world countries.[1–3]. Increased demands make infants and children at special risk group. Providing additional dietary iron to infants is not easy, as their needs are usually not covered by fortification programs.[4,5]

Iron plays an important role in children's growth and development, such as brain development, cognitive function, motor function, behavior, and immunity. There is enough evidence that showed that decreased appetite, endocrinologic alterations, neurotransmitter metabolism changes, increased metabolic rate, increased catabolism resulting in enhanced morbidity may contribute to the adverse effects of iron deficiency.[6]

The important effects of iron on growth can be explained by its essential role in multiple metabolic processes, including oxygen transport, DNA synthesis and electron transport.[7] In addition, iron deficiency may affect growth through IGF-I dependent mechanism; IGF-I concentration has an important relationship to iron metabolism and protoporphyrin synthesis in children and adolescents.[8] In IDA, plasma norepinephrine, cortisol, parathyroid hormone, urinary excretion of epinephrine and norepinephrine are increased.[9] Elevation of both of the norepinephrine levels in the blood and urine and the metabolic rate of' the IDA subjects lead to slower growth rates and lower body weights of IDA subjects.[10,11] Furthermore, the effects of IDA on growth were shown to be resistant even to the administration of growth hormone.[12] Moreover, thyroid

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gland metabolism is also affected with abnormal thermoregulation and a hyper-adrenergic state seen in hypothyroid individuals suffering from IDA.[13] Appetite is decreased in IDA independently of plasma leptin levels, but it may improve with iron supplementation.[14]

Studies regarding the effect of iron on linear growth have shown heterogeneous results. Some studies indicate that iron supplementation of iron deficient infants leads to slower-length gain and others concluded opposing results. Therefore this study aimed at investigating the iron status in preschool children with IDA and its association with the degree of growth retardation at presentation, and detecting the effect of iron supplementation on growth velocity in preschool children.

Subjects and methods

Subjects

The study was a case-control study conducted from April 2010 to March 2012. The baseline screening included all children attending the Pediatric Hematology Clinic, New Children's Hospital Cairo university fulfilling the following inclusion criteria: 1) age between 6 months and 5 years; 2) IDA was diagnosed based on based on conventional clinical manifestations and the following laboratory results (low hemoglobin (Hb) (<10 gm/dl), low hematocrit (Hct) (<33%), microcytic hypochromic picture in the blood film, low serum ferritin (<10 mg/dl) and low serum iron (<30 μg/dl) [7]; 3) completing the follow up visits till the end of the study. Patients whose lengths (heights) SDS were more than (+2SD) or less than (−2 SDS) according to the percentile curves for the Egyptian children,[15] or with past history of prematurity or were born small for date or with any identified causes of retarded growth or with a chronic systemic illnesses (renal, cardiac, hepatic, endocrine, nutritional) or taking nutritional supplements containing iron prior to the start of the study were also excluded. This study was carried on two groups of children; the patient group was started by 65 infant and children with IDA, 25 patients of them were excluded as 13 patients showed resistance to oral iron therapy, and need further investigations, while another 12 patients couldn't complete their follow up visits till the end of the study for un-known causes. Therefore, only 40 patients (34 males and 6 females), completed this study. The control group included another 40 healthy clinically non-anemic, age and sex-matched recruited from healthy infants and children attending the general pediatric clinics at the New Children's Hospital. The protocol was approved by the local research ethics committee of the pediatric department at Cairo University and all the subjects' guardians gave informed consent.

Methods

The records of all IDA patients and the baseline and data of follow-up visits were reviewed with emphasis on the age at presentation, symptoms of IDA, complete clinical examination; (signs of IDA and to exclude any signs of systemic diseases), and anthropometric assessment. Anthropometric measurements were done according to the recommendations of International Biological Program[16] at the Diabetes Endocrine metabolism Pediatric Unit (DEMPU) outpatient clinic. Anthropometric measurements (including the stature (length for subjects <36 months; height for those ≥36 months) and weight) were taken by the same individual who was duly trained for the task according the adopted protocol at DEMPU at baseline and at follow-up visits. BMI was calculated as weight in kg/height in m2 and BMI (after age 36 months) for all subjects. To calculate BMI for subjects aged <36 months, recumbent lengths were converted to heights by subtracting 0.8 cm[17]. The height (or recumbent length) was measured by using a Harpenden stadiometer (or infantometer) and recorded to the nearest 0.1cm, and the weight was measured by using self-calibrating electronic SECA scale that records to the nearest 0.1 kg. Parental heights were recorded to calculate target height SDS. Measurements were taken and recorded every 3 months for all subjects and the Growth vision computer software provided by Novo Nordisk was employed to assess weight standard deviation score (SDS) and length/height SDS to assess linear growth. Growth velocities (GV) and GV SDS during the period of study were calculated for both groups using the same computer software.

Laboratory investigations

Complete blood count (CBC) was performed for all patients and controls with determination of different indices as Mean Corpuscular Volume (MCV) in fl, Mean Corpuscular Hemoglobin (MCH) in pg, Mean Corpuscular Hemoglobin Concentration (MCHC) in g/dl, red cell distribution width (RDW%), Hemoglobin level (Hb) in g/dl and hematocrite percent (Hct%). Serum iron and ferritin were performed for patients and controls. Reference values for serum iron for children 35–167 μg/dl. Serum iron was assessed by a colorimetric methods. Serum ferritin was done by enzyme-linked immunoassay (ELISA) by using IMX Ferritin assay which is also a (MEIA) for the quantitative determination of ferritin in human serum or plasma[18] with reference values for children (22–293.3 mg/dl). At all ages a serum ferritin value of less than 10–12 pg/l (or ng/ml) indicates a depletion of iron stores.[19,20]

Iron intervention

Oral iron supplementation in the form of ferrous sulfate (20% elemental iron by weight) with daily total dose of 6 mg/kg/day of elemental iron in 2–3 divided doses are given between meals.[21]

Follow up of Laboratory and anthropometric indices

This was performed for all the cases every three months and for one year after starting iron therapy by measuring the blood indices Hb, Hct, MCV, MCH, and MCHC), and iron indices (serum iron, and serum ferritin) for the patient group and assessment of weight and height at each clinical visit by the same devices (at 0, 3, 6, 9, 12 months, not necessarily attending the whole visits; at least 3 visits are required including essentially the first and the last visits). For controls, sampling and anthropometric measurements were only done in the first and last visits.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) software version 12.0 was used for data analysis. All anthropometric data were expressed in standard deviation score (SDS) applying the formula: (variable − mean) divided by 1 SD by using the software Growth Vision version 2 provided by Novo Nordisk Denmark. Data were presented as mean ± SD. For comparison of two groups Student's *t*-test for dependent and independent variables was used. Chi-square test was used to compare qualitative variables. To compare two groups as regards quantitative and qualitative variables unpaired *t*-test and paired *t*-test were used respectively. Mann Whitney Willcoxon U and Willcoxon test were used instead of unpaired *t*-test and paired *t*-test in non-parametric data respectively. Linear Pearson's correlation was also done. P-value is significant if <0.05