Weight Loss, Inflammatory Markers, and Improvements of Iron Status in Overweight and Obese Children

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Objective To assess the effect of a weight-loss program on improving iron status in overweight and obese school-aged children.

Study design The data were analyzed in overweight and obese children (7-11 years of age; 114 girls and 212 boys) with body mass index-for-age z-scores (BAZ) >1 from a weight-loss program. Schools were randomly divided into 2 groups: intervention and control. Children in the intervention group underwent a 1-year, nutrition-based comprehensive intervention weight-loss program. Anthropometric, dietary intake, and physical activity data were collected at baseline and follow-up (1 year). Iron status and inflammatory markers were assessed within a month.

Results In the intervention group, BAZ decreased more than that in the control group (-0.4 ± 0.7 vs -0.1 ± 0.6, $P < .0001$); and iron profiles and inflammation status were improved at follow-up. In multivariable linear regression models, a greater decrease of BAZ and inflammation factors predicted a better improvement of iron status. After adjustment of ΔBAZ, ΔC-reactive protein was significantly associated with Δserum ferritin (β: 1.89; 95% CI, 0.70-3.09; $P = .002$) and Δsoluble transferrin receptor (β: 0.88; 95% CI, 0.16-0.59; $P = .017$); Δinterleukin-6 was significantly associated with Δserum ferritin (β: 1.22; 95% CI, 0.64-1.79; $P < .0001$).

Conclusions Iron status and inflammation were improved by weight reduction. The improvement in inflammatory markers during weight reduction was independently associated with improvements of iron status. *(J Pediatr 2014;164:795-800)*.

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Iron deficiency (ID) is the most common and prevalent micronutrient deficiency in the world.[1] Although the current worldwide prevalence of ID is unavailable in children, it has been estimated that 33% of children between 5 and 15 years of age are iron deficient.[2] It is the only micronutrient deficiency that is prevalent in developing and industrialized countries[3] and has been linked to obesity in both adults and children.[4,5] Recent studies have reported that obese children are more susceptible to ID than normal-weight children.[6,7]

The etiology of ID in overweight and obese children is unclear. However, there are some explanations of the origin of this condition, including insufficient iron intake,[8] increased iron requirement as the result of larger blood volumes,[9] and poor iron absorption.[6] Cross-sectional studies have reported that there are no differences in the iron intake between obese and normal-weight children[7] and between obese and normal-weight adults of poor iron status even when consuming high levels of heme iron.[10] These studies, therefore, suggest that neither the amount nor the type of iron contribute to ID.

In addition, iron supplementation has been less effective in children with high body mass index-for-age z-scores (BAZ),[11] indicating that iron fortification or supplementation may not be an optimal way of improving iron status in obese children. In contrast, weight loss had significant improvements in the iron status of 20 morbidly obese premenopausal female patients who had restrictive bariatric surgery[12] and of 15 obese children and adolescents

BAZ	Body mass index-for-age z-scores	MLRM	Multivariable linear regression model
BF	Body fat	NISCOC	Nutrition-based comprehensive intervention study on childhood obesity
BMI	Body mass index		
China CDC	China Center for Disease Control and Prevention	SF	Serum ferritin
CRP	C-reactive protein	sTfR	Soluble transferrin receptor
Hb	Hemoglobin	TF	Transferrin
ID	Iron deficiency	WHO	World Health Organization
IL-6	Interleukin-6	WHtr	Waist-to-height ratio
MET	Metabolic equivalent task		

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who underwent a 6-month weight loss program.[13] Furthermore, we assessed the relationships between weight-loss, inflammation, and iron status in children.

Methods

The nutrition-based comprehensive intervention study on childhood obesity (NISCOC) program was a multicenter, randomized, parallel control trial for the prevention of obesity among 9750 primary students in China.[14] The NISCOC program consisted of 4 components, which are shown in **Table I**. Children in the control group received no intervention.

There were 1474 children who resided in Harbin and participated in the NISCOC program, provided fasting blood samples, and completed all of the questionnaires. In our study, we analyzed only the data of children with BAZ >1 according to World Health Organization (WHO) criteria[15] (n = 371) in this program. There were 1103 children with normal body weight, 10 children declined to participate, and 35 children with other reasons (acute infections before blood sampling or did not have lunch in school) in the overweight/obese children group were excluded at baseline. Finally, a total of 326 children (intervention group, 58 girls, 102 boys; control group, 56 girls, 110 boys) met inclusion criteria and entered this study; all of them completed the study (**Figure 1**; available at www.jpeds.com). The study was approved by the Ethics Committee of the National Institute for Nutrition and Food Safety of the Chinese Center for Disease Control and Prevention (China CDC) and adhered to Declaration of Helsinki principles. Signed written consent forms were obtained.

The detailed data collection of anthropometric measurements, dietary intake assessment, and physical activity and fitness measurements has been reported elsewhere.[14] The description of how the outcomes (body composition, diet, physical activity, physical fitness, iron status, and inflammation markers) have been assessed and the reasons why they have been selected were presented in **Table II** (available at www.jpeds.com).[16-28] Data were collected from June 2009 (baseline) through June 2010 (follow-up) by trained personnel and supervised by professionals. Investigators who conducted the measurement were blinded. Blood samples were collected following an overnight fast. Serum (5 mL) was obtained by centrifuging the blood samples at 3000 rpm (1000 g) for 10 min (TDL-5-A, Anting Scientific Instrument Factory, Shanghai, China). Serum samples were divided into aliquots and stored at −80°C. All the blood tests were analyzed within a month after blood collection. The indicators of iron status and inflammation markers were selected according to WHO/China CDC expert consultation[24] and WHO report[21] recommendation and previous study.[22,26,27]

Every tenth serum sample was measured twice (correlation coefficient of duplicate measurements was 0.98). The analytical sensitivity was 0.6 ng/mL for serum ferritin (SF), 1.5 ng/ml for transferrin (TF), 0.5 nmol/L for soluble transferrin receptor (sTfR), 0.1 mg/L for C-reactive protein (CRP), and 0.7 pg/mL for interleukin-6 (IL-6), respectively. The coefficients of variation (intra-assay) were <10% for SF, 4.3%-6.2% for sTfR, and 1.7%-4.4% for IL-6, respectively.

Statistical Analyses

Statistical analyses were performed by the use of IBM SPSS Statistics Version 20.0 software (IBM Corporation, Armonk, New York). Independent sample *t*-tests were used to assess differences in anthropometric measurements, dietary intake

Table I. Components of the NISCOC program

Component	Objective	Description
Physical activity	To encourage students to engage in more physical activities	One physical activity training class for teachers
	To increase energy expenditure	Under the guidance of trained teachers, children participated in the "Happy 10" campaign,* which consisted either of 2 times/day with 10 min of physical activity/time or of 1 time/day with 20 min of physical activity/time. This campaign also encouraged after-school physical activities.
Nutrition education	To create a pleasant atmosphere for children to learn about nutrition and physical activities	Four lectures about nutrition and health for teachers.
	To encourage children to learn about nutrition	One class per month (8 times/year) with organized essay competitions on nutrition and nutrition-knowledge contests.
	To promote healthy eating behaviors	Ten classes about the relationship between nutrition, physical activity, and health. These 40-min classes were held on a monthly basis. Children were provided with nutrition handbooks.†
Food service personnel	To teach the concept of balanced meals	Four lectures about nutrition.
	To reduce the consumption of cooking oil by 2-5 g	Cooking oil consumption was reduced by decreasing the preparation of fried foods. Additionally, school meals were frequently monitored by nutritionists.
Parents	To support the children about healthy diet behaviors learned at school	Three lectures about nutrition and health. Parents were provided with nutrition brochures.
	To reduce the consumption of cooking oil	Parents were provided with a limited amount of cooking oil.

Children in the intervention group participated in the intervention for 1 school year; children in the control group received no intervention.
*The "Happy 10" campaign is a classroom-based intervention developed to promote physical activity in school-aged children.
†The nutrition education handbook had a comic style and was developed by China CDC.