No difference in iron status between children with low and moderate lead exposure

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We compared the iron status between children 11 to 33 months old with confirmed blood lead levels of 20 to 44 μg/dL and demographically similar children with blood lead levels of <10 μg/dL. There were no differences. Laboratory investigation or empirical treatment for iron deficiency is not justified on the basis of moderately elevated blood lead levels alone. (J Pediatr 1999;135:108-10)

For children with elevated lead levels, guidelines from the Centers for Disease Control and Prevention state that iron status should be evaluated and iron intake encouraged.[1] It is not clear whether there is a physiologic association between lead exposure or absorption and iron depletion[2,3] or whether some other common factor, perhaps poverty, leads to both.[1] It is important to identify and treat iron deficiency anemia in lead-exposed toddlers because both conditions are thought to contribute to abnormal cognition and development.[4] In this study we explore whether moderately elevated lead levels are associated with measures of iron status, adjusting for other relevant social variables.

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METHODS

We compared iron status between 2 groups of children. The children with moderate lead exposure came from among those recruited for a clinical trial, the Treatment of Lead-Exposed Children Trial, which used oral chelation to attempt to prevent lead-associated developmental delay.[5] These children had blood lead levels of 20 to 44 μg/dL. We compared them with children selected from the third National Health and Nutrition Evaluation Survey who were demographically similar but had low lead levels (<10 μg/dL).

Recruitment for TLC is described elsewhere.[5] Briefly, children were recruited from lead referral and primary care sites in 4 urban centers between August 1994 and October 1996. Eligible children were between 11 and 33 months old and had lead levels of 20 to 44 μg/dL confirmed by the CDC laboratory. At their first visit to a TLC clinic, children had venipuncture for complete blood count and determination of ferritin and blood lead levels. Although TLC excluded children with hemoglobin concentrations of <9 g/dL from further participation, we included those children in this analysis. Because of over 70% of subjects in the TLC were African American and because hemoglobin concentration is lower in black children, we confined the analysis to them.[6]

CDC	Centers for Disease Control and Prevention
FER	Serum ferritin
MCV	Mean corpuscular volume
NHANES III	Third National Health and Nutrition Evaluation Survey
RDW	Red cell distribution width
TLC	Treatment of Lead-Exposed Children Trial

NHANES III was conducted from 1988 to 1994.[7] This survey collected nationally representative data from household interviews, direct standardized physical examinations, and phlebotomy. A total of 24,894 persons aged 1 year and older were examined, of whom 12% were (self-reported) African American and 15% (of the total) were 5 years old or younger. Laboratory data included complete blood count and ferritin and blood lead levels. We selected all African Ameri-

can children aged 11 to 33 months who resided in an urban area with lead levels <10 μg/dL.

Definition of Iron Status

Iron depletion was defined as (1) serum ferritin <10 μg/L or (2) FER <10 μg/L and red cell distribution width >14.5%.[8,9] Iron deficiency was defined as FER <10 μg/L and mean corpuscular volume <70 fL.[8,9] Iron deficiency anemia was defined as (1) hemoglobin <11 g/dL and FER <10 μg/L; (2) hemoglobin <11 g/dL, FER <10 μg/L, and RDW >14.5%; or (3) hemoglobin <11 g/dL, FER <10 μg/L, and MCV <70 fL.[8,9] Note that although ferritin is an acute-phase reactant, there is no reason for variation in ferritin not caused by iron status to be different in these groups of children.[9]

Laboratory Analysis

Serum ferritin and blood lead levels were analyzed at the CDC. Serum ferritin was measured by using the Quantimmune Ferritin IRMA kit, which is a single-incubation 2-site ^{125}I-immunoradiometric assay (Bio-Rad Laboratories, Hercules, Calif).[10] Blood lead levels were measured with a Perkin-Elmer model 4100-ZL graphite furnace atomic absorption spectrophotometer (Perkin-Elmer, Norwalk, Conn) with Zeeman-effect background correction. Complete blood counts were done at the clinical sites for subjects in the TLC and at the CDC for those in NHANES III with Coulter counters (Coulter Inc, Hialeah, Fla).[10]

Statistical Analysis

SAS (SAS Institute, Cary, NC)[11] and S-PLUS (Statistical Sciences, Inc, Seattle, Wash) were used to calculate means, frequencies, and Pearson's correlation coefficient; Student t test was used for continuous variables, and χ^2 test was used for dichotomous variables. The association between FER and blood lead levels was explored by using a nonparametric local regression smoothing method.

Table I. Characteristics of TLC and NHANES III patients

		TLC	NHANES III	*P* value for group comparison
Sample size		787	222	
Age (mo)				
	Mean	22.9	23.1	.585
	SD	5.6	6.2	
	N	787	222	
Female				
	%	43.4	49.1	.131
	N	786	222	
Either parent finished high school	%	60.2	77.2	.000
	N	777	219	
Either parent employed	%	36.0	61.2	.000
	N	774	214	
Medicaid assistance received by family	%	85.5	67.2	.000
	N	761	186	
Blood lead level (μg/dL)				
	Mean	26.8	5.0	.000
	SD	5.6	2.1	
	N	787	222	
Ferritin level (μg/L)				
	Mean	27.2	27.0	.904
	SD	18.4	20.4	
	N	756	211	
Hemoglobin (g/dL)				
	Mean	11.6	11.8	.002
	SD	0.9	0.8	
	N	784	212	
RDW (%)				
	Mean	14.3	13.5	.000
	SD	1.8	1.5	
	N	778	212	
MCV (fL)				
	Mean	75.4	78.0	.000
	SD	5.9	5.4	
	N	761	212	

RESULTS

In the data from the TLC, of the 1201 children with eligible blood lead levels of 20 to 44 μg/dL, 1194 were aged 11 to 33 months. Of those, the 787 who were African American constitute the children with moderate lead exposure for this analysis. In the NHANES III data there were 2596 children between 11 to 33 months of age. Of these, 1511 had lead levels <10 μg/dL. Of those, 789 were living in an urban area, defined as an area where 1 million or more persons reside; and of those, the 222 children who were African American constitute the children with low lead levels. Age, sex, and

Table II. Prevalence (sample size) of iron depletion, iron deficiency, and iron deficiency anemia in the TLC and NHANES III patients

	TLC	NHANES III	*P* value
Iron depletion			
FER <10 mg/L	11% (756)	13% (212)	.46
Iron deficiency			
FER <10 µg/L and RDW >14.5%	7% (748)	5% (204)	.27
FER <10 µg/L and MCV <70 fL	4% (730)	3% (204)	.99
Iron deficiency anemia			
FER <10 µg/L and hemoglobin <11 g/dL	3% (753)	4% (204)	.52
FER <10 µg/L, RDW >14.5%, and hemoglobin <11 g/dL	3% (748)	3% (204)	.65
FER <10 µg/L, MCV <70 fL, and hemoglobin <11 g/dL	2% (727)	2% (204)	.99

ferritin levels were not significantly different between the moderate and low lead exposure groups (Table I).

The prevalence of iron depletion, iron deficiency, and iron deficiency anemia were similar in the 2 groups (Table II). The correlation coefficient between blood lead and FER levels for the children with low lead exposure was –0.04, (CI –.173, 0.96; $P = .57$) and –0.04, (CI –.112,.030; $P = .26$) for the children with moderate lead exposure. We found no significant differences when we divided the groups by lead levels (not shown).

DISCUSSION

Our data demonstrate no difference in the prevalence rates of iron depletion, iron deficiency, and iron deficiency anemia in children with moderate lead exposure compared with those with low exposure. Because fewer parents in the TLC group had completed high school, fewer were employed, and more received medical assistance, one might expect that they would have higher levels of iron deficiency based on these issues alone. This is not what the data demonstrated. This study had a power of 80% to detect a 10.3% difference in iron deficiency or iron deficiency anemia between the 2 groups. Venipuncture is painful, laboratory work is expensive,[12] and iron may be toxic and is a common pediatric ingestion. Thus laboratory workup or empirical treatment with iron should be reserved for children whose risk derives from factors other than a moderately increased blood lead level.

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