SHORT REPORT

Association between blood lead concentrations and body iron status in children

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Blood lead concentrations and body iron status were investigated in 279 children. Blood lead concentrations showed no increase during iron depletion phase (stage I) but markedly increased from the phase of iron deficient erythropoiesis (stage II). Increased blood lead concentrations in anaemic subjects significantly decreased after iron supplementation.

Iron deficiency develops in sequential changes over a period of negative iron balance. These stages include the iron depletion phase (stage I), iron deficient erythropoiesis (stage II), and iron deficiency anaemia (stage III).¹ During the iron depletion phase, iron stores are exhausted; however, anaemia or decrease of serum iron are not present. In iron deficient erythropoiesis, serum iron and serum ferritin concentrations are decreased; however, anaemia and hypochromia are still not detectable. Lead poisoning is the common environmental paediatric health problem. Some investigators have reported that blood lead concentrations were high in iron deficient children,² and that higher dietary iron intake was associated with lower blood lead concentrations.³ However, other investigators showed that iron depletion does not affect blood lead concentrations.⁴

The aims of this study were to investigate the changes in blood lead concentrations during three stages of iron deficiency, and to evaluate the alteration of blood lead concentrations in anaemic subjects after iron supplementation.

METHODS

We measured haemoglobin, serum iron, serum ferritin, and blood lead concentrations in 279 children (age range 10-15 years) residing near an industrial area with contaminated environments. The subjects were divided into four groups: iron depletion phase (stage I, $n = 51$), iron deficient erythropoiesis (stage II, $n = 22$), iron deficiency anaemia (stage III, $n = 39$), and healthy controls ($n = 167$). This survey was explained to both parents and directors at each education centre. The study was approved by the Ethics Committee of Inha University, and informed consent was obtained from all subjects.

Non-anaemic subjects with a normal serum iron concentration ($>50 \mu\text{g/dl}$), but with a decreased ferritin concentration ($<12 \mu\text{g/l}$), were classified as being in the iron depletion phase. Iron deficient erythropoiesis was defined as serum ferritin concentration $<12 \mu\text{g/l}$ and serum iron concentration $<50 \mu\text{g/dl}$ without overt anaemia. When the subjects who showed a decreased serum ferritin concentration and a decreased serum iron concentration also had a decreased haemoglobin concentration ($<12 \text{ g/dl}$), we considered them to have iron deficiency anaemia.

Complete blood cell count was measured with EDTA anticoagulated blood using an electronic counter. Serum iron was assayed with an automatic chemical analyser, and serum ferritin was measured by the chemiluminescence method. Blood lead concentration was determined by atomic absorption spectrophotometry. The 39 anaemic subjects were supplemented with ferrous sulphate (3-6 mg/kg of elemental iron per day for one month). The compliance for iron supplementation was checked by interview throughout the period of treatment; blood samples were obtained from 34 of these subjects for assays of iron parameters and blood lead concentrations. Data analysis was performed using the Mann-Whitney U test and Wilcoxon signed ranked test; p values ≤ 0.01 were considered statistically significant.

RESULTS AND DISCUSSION

There were no significant differences in blood lead concentrations between ferritin alone depleted group (stage I; $4.5 (1.3) \mu\text{g/dl}$) and non-anaemic healthy controls ($4.3 (1.1) \mu\text{g/dl}$). However, blood lead concentrations increased abruptly from the time that both the serum iron and serum ferritin were depleted (stage II; $6.7 (1.4) \mu\text{g/dl}$). The subjects in stage III exhibited no significant differences in blood lead concentrations compared to the individuals in stage II, although mean haemoglobin concentrations showed large differences between the two groups (table 1). These results suggest that ferritin alone depletion has no influence on blood lead values; however, once serum iron as well as serum ferritin declines, it may have a significant effect on lead absorption irrespective of haemoglobin concentrations.

Our results are in line with a previous report, in which the mean blood lead concentrations were significantly higher in

Table 1 Blood lead concentrations according to body iron status in 279 children

	Healthy control group ($n = 167$)	Iron depletion group (stage I, $n = 51$)	Iron deficient erythropoiesis (stage II, $n = 22$)	Iron deficiency anaemia (stage III, $n = 39$)	p value (stage I v stage II)
Haemoglobin (g/dl)	13.4 (0.6)	13.2 (0.8)	12.8 (1.1)	9.4 (0.9)	NS
Iron markers					
Serum iron ($\mu\text{g/dl}$)	74.5 (17.6)	72.3 (16.2)	38.1 (5.4)	21.2 (9.7)	<0.01
TIBC ($\mu\text{g/dl}$)	305.9 (37.8)	338.2 (46.3)	399.0 (42.5)	424.5 (50.4)	NS
TS (%)	24.6 (10.7)	21.5 (8.5)	9.5 (4.2)	5.1 (3.6)	<0.01
Serum ferritin ($\mu\text{g/l}$)	41.9 (12.5)	10.7 (4.9)	9.6 (3.7)	8.1 (2.3)	NS
Blood lead ($\mu\text{g/dl}$)	4.3 (1.1)	4.5 (1.3)	6.7 (1.4)	6.9 (1.5)	<0.01

Data are expressed as mean (SD).

TIBC, total iron binding capacity; TS, transferrin saturation; NS, not significant.

Table 2 Changes in blood lead concentrations and iron parameters after iron supplementation

	Serum iron ($\mu\text{g/dl}$)	Serum ferritin ($\mu\text{g/l}$)	Blood lead ($\mu\text{g/dl}$)
Stage III children (n=34)*			
Before supplementation	20.6 (10.5)	8.2 (3.4)	6.8 (1.7)
After supplementation for one month	64.8 (16.2)‡§	33.6 (15.8)‡§	2.7 (1.2)‡§
Mean changes	44.1 (13.6)	25.4 (12.7)	-4.1 (1.5)
Stage II children (n=12)†			
Initial values	31.3 (6.8)	8.7 (3.6)	6.3 (1.2)
Without supplementation for one month	32.7 (7.1)¶	9.1 (3.2)¶	6.5 (1.4)¶
Mean changes	1.4 (3.2)**	0.4 (1.7)**	0.2 (1.3)**

Data were expressed as mean (SD).

*Anaemic subjects were supplemented with ferrous sulphate for one month.

†Stage II children with no iron treatment were checked one month after initiation of this study.

‡p<0.01 versus stage III children before supplementation, computed by Wilcoxon signed rank test.

§p<0.01 versus stage II children without supplementation for one month, computed by Mann-Whitney U test.

¶Not significant versus initial values of stage II children, computed by Wilcoxon signed rank test.

**p<0.01 versus mean changes of stage III children, computed by Mann-Whitney U test.

Table 3 Mean values of haemoglobin and iron parameters based on blood lead concentrations

	Haemoglobin (g/dl)	Serum iron ($\mu\text{g/dl}$)	Serum ferritin ($\mu\text{g/l}$)	Blood lead ($\mu\text{g/dl}$)
Blood lead concentrations				
<10 $\mu\text{g/dl}$ (n=258)	12.7 (1.2)	67.8 (20.8)*	30.3 (7.5)*	4.2 (1.3)*
$\geq 10 \mu\text{g/dl}$ (n=21)	11.4 (0.8)	25.4 (12.6)	16.3 (9.2)	12.4 (1.9)
Correlation coefficients (versus blood lead concentrations)				
Boys (n=145)	-0.11	-0.25†	-0.23†	NA
Girls (n=134)	-0.08	-0.22†	-0.19†	NA

*p<0.01 versus $\geq 10 \mu\text{g/dl}$, computed by Mann-Whitney U test.

†p<0.01, assessed by Spearman correlations.

NA, not applicable.

iron deficient children compared to normal subjects.⁵ However, some researchers showed that there were no differences in iron status between children with low and moderate lead exposure.⁶ Furthermore, it has been reported that the percentage of abnormal blood lead values in subjects with normal serum ferritin was similar to that in subjects with one or two abnormal iron parameters.⁴ In contrast, in our study, blood lead concentrations increased gradually as body iron status falls, and the mean blood lead concentrations averaged 1.6-fold higher than non-anaemic healthy subjects when the children attained a state of frank iron deficiency anaemia.

Interestingly, in our paired group study, increased blood lead concentrations in stage III children (n = 34) had significantly declined after one month of iron supplementation. Similar findings were also observed in the unpaired group: stage II children (n = 12), who had no iron supplementation, had persistently increased mean values of blood lead concentrations even after one or more months (table 2). On the other hand, serum iron and serum ferritin concentrations in the subjects with blood lead concentrations of $\geq 10 \mu\text{g/dl}$ were 25.4 (12.6) $\mu\text{g/dl}$ and 16.3 (9.2) $\mu\text{g/l}$, significantly lower than those for the subjects with blood lead concentrations of <10 $\mu\text{g/dl}$ (67.8 (20.8) $\mu\text{g/dl}$ and 30.3 (7.5) $\mu\text{g/l}$, respectively; p < 0.01).

Blood lead concentrations correlated weakly but significantly with serum iron concentrations in both boys (r = -0.25) and girls (r = -0.22) (table 3). Similarly, previous work showed that a significant negative correlation existed between blood lead and dietary iron intake in preschool children.³ These results suggest that an evident association exists between blood lead concentrations and iron parameters, and that increased lead values can efficiently decline with iron administration.

In conclusion, the iron deficient state may constitute a predisposing factor for lead poisoning in childhood. The decrease in blood lead concentrations in the stage III children following iron supplementation suggests that improving iron status may help decrease blood lead concentrations, but further study in an experimental setting would be needed to verify this finding.

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