Iron deficiency anemia and educational achievement

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ABSTRACT The present study investigates the effect of iron supplementation on measures of school performance among 78 iron-deficient anemic and 41 nonanemic children in an economically deprived rural area in Central Java, Indonesia. All the subjects were treated for ancylostomiasis before iron supplementation. They were randomly assigned to either an iron or placebo group. Hematological and behavioral measurements were obtained immediately before (T1) and after (T2) the iron and placebo treatments. Iron treatment for a 3-mo period resulted in substantive increases in mean Hgb, Hct, and transferrin saturation among the iron-deficient anemic children. Furthermore, changes in the iron status of iron-deficient anemic children were associated with significant changes in the school achievement test scores of iron-deficient anemic children. T2 evaluation of achievement test scores indicated that the difference between iron-treated anemic and nonanemic children was still statistically significant. However, when T1 scores were entered as a covariate, iron-deficient anemic subjects treated with iron obtained significantly higher delta achievement scores. Findings from the present study indicate that iron supplementation among iron-deficient anemic children benefits learning processes as measured by the school achievement test scores. Am J Clin Nutr 1985;42:1221-1228.

KEY WORDS Iron-deficiency anemia, school achievement

Introduction

Most research on the behavioral effects of iron deficiency and anemia have focused on the cognitive function of infants and preschoolers, and on the physical work productivity of adults (1, 2). With some exceptions (3-5), little attention has been given to the effects of iron deficiency and anemia on the behavior and achievement of school-age children in formal educational settings.

Webb and Oski (3) studied 12- to 14-yr-old junior high school students living in an economically deprived, Black community in Philadelphia. After a hematologic survey of 1,807 students, 193 were selected to participate in the study. Ninety-two of these students were classified as anemic (10.0 ≤ Hgb ≤ 11.5 g/dL) with the remaining 101 students serving as a normal (14.0 ≤ Hgb ≤ 14.9 g/dL) control group. The Iowa Tests of Basic Skills, Levels A-F/Form 3, routinely given in the Philadelphia school system, was administered to both normal and anemic children. Anemic students obtained significantly lower achievement scores than the nonanemic group. Further, a sex × age × hematologic status analysis showed that anemic girls performed less well than nonanemic girls at all ages. On the other hand, anemic boys showed no deficit at 12 yr of age, but greater deficits in performance with increasing age. The investigators pointed out that the difference in performance might not have resulted from the anemic condition, but from a more generalized nutritional deficit or concomitant social factors.

These same children (4) were tested on a visual afterimage task. The anemic group took significantly longer (4.08 s) than nonanemic children (1.81 s) in reporting a visual afterimage. This finding, and the comparative re-

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SOMANTRI

Results of the Iowa Test, along with teacher evaluations indicating that the index cases displayed more conduct problems than the comparison male adolescents (5) suggested that anemia is associated with disturbances in attention and perception. This, in turn, results in poor academic achievement.

There are some critical methodological problems in these studies which preclude conclusive inferences (6). The details of the afterimage task are not given, and it is not clear what other cognitive processes might have been operating in the task. The authors suggest that cerebral metabolism was likely altered, accounting for the results of the afterimage task. Afterimages, however, depend not only on cerebral function, but peripheral aspects of the visual system as well. Moreover, the static-group research design (7) does not allow for a control of confounding factors (eg socioeconomic status); and the causality of the anemia is not determined. The authors' findings do not contradict their hypothesis, but neither do they provide strong support for it.

A recent study (8) conducted in a semiurban community in Egypt showed a positive association between iron status among school-aged children and efficiency in problem solving. Sixty-eight children, with an average of 9.5 yr of age, represented a subsample from 203 children originally selected. This subsample was chosen to optimize the sensitivity and specificity of the iron depletion and iron repletion diagnosis. A discriminant function was used to set the diagnostic criteria. The referent criterion selected for the original classification was change in Hgb ≥ 1 g/dL among 101 children (from the 203 cases selected) treated with iron. The predictive variables included hemoglobin, transferrin saturation, and serum ferritin. On the basis of the discriminant function iron deficiency anemia was defined by a Hgb ≤ 11.5 g/dL, and either a transferrin saturation ≤ 25%, or a serum ferritin ≤ 20 ng/mL. Iron repletion was defined by a Hgb ≥ 13.0 g/dL and either a transferrin saturation > 25% or a serum ferritin > 20 ng/mL.

Of the 203 children, 28 were defined as iron deficient and 40 as iron replete. For about 4 mo 18 of the iron-depleted and 18 of the iron-replete children received, under direct supervision, 50 mg of iron orally as ferrous sulfate; the remaining subjects received a placebo.

Form F of the Matching Familiar Figure Test (9) was administered before and after treatment. Each child was presented with two cards—one displayed a figure and the other six variants of it. The child had to match the standard and one of the alternatives; the time taken for the first response and the errors made before a perfect match was achieved were noted.

The efficiency (a measure ranging from slow-inaccurate to fast-accurate performance) of the nonanemic children before treatment was significantly greater than that of the iron-deficient anemic children. The nonanemic children tended to be faster in response and more accurate than the anemic children. After treatment the efficiency of the iron-treated anemic children was significantly greater than that of the children treated with placebo. There were no significant differences between the iron- and placebo-treated iron-replete children and the efficiency score of the iron-treated anemic children was similar to that of the controls.

A critical question in regard to this study in Egypt is the ecological significance of the findings. That is, whether the differences observed between iron-deficient anemic and nonanemic children have any implications for the behavioral adaptation and learning performance of the children. The study, however, has no data relevant to this issue.

The present study investigates the effect of 3-mo iron supplementation on measures of school performance among iron-deficient anemic children in an economically deprived rural area in Central Java, Indonesia. The data from this study was collected by the first author for his doctoral (PhD) dissertation (10) at the University of Diponegoro, in Semarang, Central Java. In 1984 the data was further analyzed by the present authors at the School of Public Health, University of Texas, Houston. This second analysis is the basis of this report.

Methods

The site and population

The study was conducted in the subdistrict of Kalibawang, on the northern border of the Yogyakarta province. Kalibawang is about 96 km south of Semarang and 35 km northwest of Yogyakarta. This area encompasses 5,104 km² and is 146 m above sea level. The climate in the study...
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Schools and study sample

A total of 1,549 children from eight primary schools in Kalibawang was the original sampling frame. Subsequently this was limited to three schools because of logistic and budgetary reasons. These three schools had similar health programs, and the teachers were willing to cooperate.

The following criteria were used to select the subjects for the study from 588 children in the three schools: above 80th percentile of weight and height, and above 85th percentile of mid-arm circumference of Indonesian growth standards; negative parasite egg count by stool examination after treatment of ancylostomiasis; no evidence of hemato logical-related diseases (e.g., thalassemia, malaria), other severe illness, nutrition deficiency, physical handicaps, and neurological abnormalities; consent of parent to participate in the study; IQ above 75. Two hundred and thirty-one children met these criteria. The stringent criteria insured that the children selected for the study were free from conditions that could confound the effect of iron supplementation. The study was approved by the committee for the Use of Humans as Experimental Subjects in the authors’ institution.

Research design

For the purposes of the study reported here iron deficiency anemia was defined by a hemoglobin (Hgb) ≤ 11.0 g/dL and a transferrin saturation ≤ 15.0%. Iron repletion was defined by a Hgb ≥ 12.0 g/dL and a transferrin saturation ≥ 20%. Accordingly, all subjects with 11 ≤ Hgb < 12 g/dL, and a 15.0 < transferrin saturation < 20.0% were excluded. As indicated in Table 1, 78 and 41 subjects met the iron-deficient anemic and nonanemic definitions respectively. Forty-three of the anemic and 16 of the nonanemic were placed for a period of 3 mo on oral treatment of ferrous sulfate at a dosage of 10 mg/kg/day, which is equal to 2 mg of elemental iron. The remaining subjects received a placebo tablet which contained only saccharine and tapioca. The iron and placebo tablets were given by school teachers and supervised by paramedical personnel every morning during school days. The research protocol also required that the children attend school to take the tablets during weekends and holidays. Whenever necessary, social workers made home visits to deliver the tablets. The hematological and behavioral measurements described below were obtained immediately before (T1) and after (T2) the iron and placebo treatments. All children included in the study took either the iron or placebo no less than 90% of the time throughout the study period.

To determine the sensitivity and specificity of the diagnostic criteria a cross-tabulation was computed between

Table 1

Comparative statistics (means & SDs) of age, anthropometry, and hematologic determinations of iron-deficient anemic and nonanemic children before treatment

<table>
<thead>
<tr>
<th></th>
<th>Anemic</th>
<th>Nonanemic</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>10.66 (1.31)</td>
<td>11.07 (1.27)</td>
<td>0.099</td>
</tr>
<tr>
<td>Wt (kg)</td>
<td>26.14 (4.04)</td>
<td>27.57 (3.49)</td>
<td>0.048</td>
</tr>
<tr>
<td>Ht (cm)</td>
<td>131.30 (6.91)</td>
<td>133.87 (6.43)</td>
<td>0.047</td>
</tr>
<tr>
<td>Arm circ (cm)</td>
<td>18.57 (1.15)</td>
<td>19.16 (1.15)</td>
<td>0.010</td>
</tr>
<tr>
<td>Hgb (mg%)</td>
<td>9.74 (1.23)</td>
<td>13.24 (0.73)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>26.32 (4.13)</td>
<td>40.29 (1.91)</td>
<td>0.001</td>
</tr>
<tr>
<td>TS (%)</td>
<td>9.10 (2.56)</td>
<td>24.67 (3.91)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
the response to treatment of the 43 anemic and 16 non-anemic subjects who received the iron tablets. A Hgb response ≥ 1.0 g/dL was used as the criterion of true disease. This decision followed the consensus that currently the best epidemiologic assessment of iron deficiency anemia is response to treatment (11-13). A sensitivity of 100% and a specificity of 94% (see Table 2) shows that the stringent diagnostic criteria used discriminated effectively between iron-deficient anemic and nonanemic cases. It should be noted that the research design and, as noted below, the statistical analysis of the data closely match the recommendations of the International Nutritional Anemia Consultative Group (14) for the analysis of iron supplementation trials.

Treatment of ancylostomiasis

Based on stool examination, all parasite-positive children were treated with pyrantel pamoate (combination) at the dosage of 10 mg/kg/day for two days. Follow-up stool examination was indicated after 2 wk, and therapy was repeated on those cases with a positive egg count. Stool examination was again repeated on those children who received treatment. Once the children were considered to be free of parasites they were randomly assigned to the placebo- and the iron-treated group.

Blood specimen and analysis

Blood specimens were collected from study subjects by four physicians and assisted by a laboratory technician. A 12 mL venous blood sample was taken from each child. The specimens were sent to the hematology laboratory in Semarang and analyzed on the same day the blood sample was collected. The analyses included determinations of Hgb, Hct, serum iron, total iron binding capacity, total protein, albumin, and globulin. Serum ferritin data on a selected few number of children were also obtained; these data, however, are not part of the present analysis.

Behavioral tests

Raven progressive matrices. Colored progressive matrices (15) were employed to test general intelligence of the children in the study. This is a nonverbal IQ test which is easy to administer, and the instructions were clearly understood by the children. The original Raven test was adapted for the rural population by the staff of the Psychometric Department, Faculty of Psychology of Gajah Mada University, Yogyakarta. This test was only administered before the treatment.

Educational achievement test. This test included four main subject areas; mathematics, biology, social science, and language. The test, prepared by staff from the Secretary of Education in Semarang, was a revised and short version of the standard achievement test used by the public school system. Selection of items for inclusion in the revised version was based on the prediction and discriminatory power of the test items. Accordingly, the construction of the test was biased towards the maximization of differences between high and low educational achievers. A test (T1)-retest (T2) correlation coefficient of 0.93 indicated a robust stability in this measure.

Concentration. The Bourden-Wisconsin test for concentration was employed both before and after the iron and placebo intervention. The test-retest correlation for this measure was 0.67.

Results

The iron-deficient anemic and nonanemic groups were first compared for potentially confounding variables that may influence the results of the between group comparison of IQ, school achievement, and concentration test. These factors include age, socioeconomic characteristics, and anthropometric measurements (Table 1). There were no statistically significant differences between groups in the mean age of the anemic and the nonanemic children. Likewise there were no differences between groups in the income of the families, in the maternal age, and in the ordinal position of the children. However, at T1 the nonanemic children were significantly heavier than the iron-anemic children. Similarly, the former were significantly taller than the latter children. Subsequent analyses, however, showed that initial anthropometry was not related to hematologic status, or to achievement test scores. Accordingly, this section on results includes only brief references to the anthropometric variables.

All analyses of the effects of the treatment on the hematological and psychological measures include the pre- to posttreatment (T2-T1) changes (delta) in the respective values as the outcome measures. These analyses also include pretreatment (T1) values as covariates. This covariate approach precludes the possibility that between-group differences observed on a particular outcome variable might be due to the respective pretreatment values.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Sensitivity and specificity of diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic test</td>
<td>Iron status*</td>
</tr>
<tr>
<td></td>
<td>Anemic</td>
</tr>
<tr>
<td>Positive</td>
<td>42</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
</tr>
</tbody>
</table>

* Anemia is defined as change in Hgb ≥ 1.0 g/dL after iron treatment.

Test positive = Hgb ≤ 11.0 g/dL and transferrin saturation ≤ 15%; test negative = Hgb ≥ 12.0% and transferrin saturation ≥ 20.0%.

Sensitivity = 42/(42 + 0) = 100%.

 Specificity = 16/(1 + 16) = 94%.
Hematological evaluation

The mean (M) and standard deviations (sd) for Hgb, Hct, and transferrin saturation of the iron-deficient anemic and nonanemic children are presented in Table 1. As expected, on the basis of the selection criteria, there were significant between-group (anemic vs nonanemic) differences at T1 in all three hematological assessments.

Table 3 presents the results of an analysis of variance comparing T2–T1 changes in Hgb when T1 values are controlled for. The differences in Hgb between the iron- (M = 0.71 g/dL) and the placebo- (M = −0.25 g/dL) treated groups were statistically significant. The main effects of Hgb status (anemic vs nonanemic) were not statistically significant; however, there was a statistically significant two-way interaction (treatment × hematological status). Accordingly, paired comparisons were calculated to establish the effects of the treatment on the anemic and nonanemic subjects. The difference between the iron-treated (M = 2.67) and placebo-treated anemic children (M = −1.17) was statistically significant. Conversely, in the case of the nonanemic children the iron treatment did not have a statistically significant effect (M Anemic = 0.76; M Nonanemic = 0.67). The initial differences in Hgb between anemic and nonanemic children disappeared after iron intervention (Fig 1).

In the case of T2–T1 changes in Hct the results were slightly different from those of Hgb. There was a statistically significant effect of hematological status on delta Hct (Anemic = −0.28%; Nonanemic = 5.36%). There was also a significant effect of treatment (Iron = 6.10%; Placebo = −1.02%). A statistically significant two-way interaction explains further the nature of the main effects. Among the anemic children there was a statistically significant difference between the means of those who were treated with iron (M = 6.85%) and those who received the placebo (M = −7.41%). Conversely, among the nonanemic subjects the means of those who received the iron (M = 5.35%) and placebo (M = 5.37%) were almost identical.

The results of the covariance analysis on the transferrin saturation values were similar to those observed in the analysis of Hct. Pre- to posttreatment changes in transferrin saturation were significantly different between children given iron (M = 9.14%) and placebo (M = −0.38%), independent of their initial status. Among anemic children, the differences between iron and placebo group are highly apparent (15.47 vs −2.77%). As in the case of Hct, T2–T1 changes among the nonanemic children were almost identical. The effects of the treatment on transferrin saturation are illustrated in Figure 2.

Behavioral evaluation

There was no significant difference in the Raven Progressive Matrices IQ between anemic and nonanemic children (97.7 vs 98.9) before treatment.

Unexpectedly, due to randomization, the group of children assigned to the iron treatment group (M = 408.5; sd = 125.6) obtained a significantly higher score than that in placebo (M = 358.5; sd = 111.7). However, there were no differences between groups of children ini-
Patients diagnosed as anemic and nonanemic (389.5 vs 372.2). The ANOVA on delta concentration (Table 4) including T1 concentration score as covariate showed that there was a significant treatment effect. Once the influence of T1 scores are removed, iron-treated children, independent of hematological status, had significantly higher increase in test scores as compared to children given placebo. For children given placebo, nonanemic had delta concentration higher than anemic children. Further, the effects of the treatment on the delta concentration score remained significant when the height and weight measures were entered as covariates.

In the school achievement test the nonanemic ($M = 42.3; sd = 10.8$) children performed significantly better than the anemic ($M = 31.8; sd = 10.3$) children at T1. On the other hand, there were no significant differences between the children assigned to the iron ($M = 34.9; sd = 11.4$) and placebo ($M = 36.0; sd = 11.9$) treatment (See Fig 3).

An analysis of variance (Table 5) using treatment and hematologic status as independent variables, and T1 achievement scores as covariate indicated a highly significant treatment effect on the adjusted delta (T2 - T1) scores (Iron = 1.67; Placebo = -0.20). Moreover, the adjusted mean delta of the anemic ($M = 1.49$) was larger and statistically different from that of the nonanemic ($M = -0.01$) children. A significant interaction ($p < 0.01$) between treatment and hematologic status explained further the nature of the main effects. Among the anemic cases the adjusted mean delta of the children exposed to the iron treatment ($M = 3.64$) was significantly different from that of those exposed to the placebo ($M = -0.67$). Conversely, among the nonanemic cases there were no significant differences in T2−T1 changes between iron- ($M = -0.29$) and placebo- ($M = 0.28$) treated children. However, posttreatment (T2) evaluation of achievement test scores indicated that the difference between iron-treated anemic (M

<table>
<thead>
<tr>
<th>Anemic</th>
<th>Nonanemic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron treated</td>
<td>20.57b</td>
<td>18.01</td>
</tr>
<tr>
<td>Placebo</td>
<td>-38.63b</td>
<td>6.86</td>
</tr>
<tr>
<td>Total</td>
<td>-9.03</td>
<td>12.44</td>
</tr>
</tbody>
</table>

* Values with the same superscripts are different at a statistically significant level.

<table>
<thead>
<tr>
<th>Anemic</th>
<th>Nonanemonic</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron treated</td>
<td>3.64b</td>
<td>-0.29</td>
</tr>
<tr>
<td>Placebo</td>
<td>-0.67b</td>
<td>0.28</td>
</tr>
<tr>
<td>Total</td>
<td>1.49bc</td>
<td>-0.01c</td>
</tr>
</tbody>
</table>

* Values with the same superscript are different at a statistically significant level.
IRON DEFICIENCY AND SCHOOL ACHIEVEMENT

Unexpectedly, the nonanemic children scheduled to receive a placebo obtained low scores in the concentration task. Their level of performance at T1 was similar to that of the anemic placebo children, and lower than that of the anemic children scheduled to receive iron. However, this relationship between an iron-replete state and low scores in the concentration test is not associated with evidence, among the nonanemic children, that the experimental administration of iron resulted in a salutory change in performance in the concentration test. Changes from T1 to T2 in the scores of the nonanemic children treated with iron was not statistically significant. On the other hand, the delta in the test values of the iron-deficient anemic treated with iron reached the conventional level of statistical significance.

The concentration test is a measure of attention maintenance, requiring accurate visual discrimination among different graphic stimuli over a given period of time. A relationship of iron status and performance in tests of attention observed in this study is in keeping with what has been suggested in other studies on the effects of iron depletion on specific cognitive processes (3-5, 16, 17). Similar conclusions were reached by reviews of the relevant literature in 1976 (18) and 1985 (19), indicating that attention is likely to be adversely influenced by iron depletion. Moreover, as previously noted, a recent study (8) in Egypt demonstrated that efficiency in performance in a test of attention was related to iron status. Accordingly, evidence from other studies along with the evidence from the concentration test in this study suggest that the deficits observed in school achievement is explained in part by a deficit in the children's reception of information, or attentional processes. However, it is not known which of the attentional processes, such as selective attention, attention span, or vigilance, are specifically involved.

Comparatively low performance in school-type tasks due to deficits in attention is not necessarily an indication of an involvement of purely cognitive processes. Attention is also influenced by motivation and physiological arousal which is associated with autonomic mechanisms such as heart rate, skin conductance, or pupillary dilation (20). For example,
attentional deficit disorders in children, a new label for what was previously identified as hyperkinesis, have been explained by both under- and overarousal in the organism (20, 21). Similarly, the attentional deficits apparently present in iron deficiency and anemia might be related to a disturbance in physiological arousal. An important issue in connection with brain function is whether such a disturbance is secondary to hematological changes due to anemia or to sideropenia.

From a health and educational policy perspective, however, the concern has to be focused on the magnitude of the effects on behavioral adaptation. Poor school performance due to iron deficiency and anemia must be a public health concern independent of whether the underlying mechanisms are known or not. This is particularly the case if the modes of prevention are known.

References