RESEARCH PAPER

Effect of Iron and Zinc Deficiency on Short Term Memory in Children

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Objective: To evaluate the effect of iron and zinc deficiency on short term memory of children in the age group of 6-11 years and to assess the response to supplementation therapy.

Design: Interventional study.

Setting: 100 children in the age group of 6-11 years (subdivided into 6-8 yr and 9-11 yr groups) from an urban corporation school.

Methods: After collection of demographic data, the study children underwent hematological assessment which included serum iron, serum zinc, and hemoglobin estimation. Based on the results, they were divided into Iron deficient, Zinc deficient, and Combined deficiency groups. Verbal and nonverbal memory assessment was done in all the children.

Intervention: Iron (2mg/kg bodyweight in two divided doses) and zinc (5mg once-a-day) supplementation for a period of 3 months for children in the deficient group.

Results: All children with iron and zinc deficiency in both the age groups had memory deficits. Combined deficiency in 9-11 years group showed severe degree of affectation in verbal (P<0.01) and non-verbal memory (P<0.01), and improved after supplementation (P = 0.05 and P<0.01, respectively). In 6-8 years group, only non-verbal form of memory (P =0.02) was affected, which improved after supplementation.

Conclusion: Iron and zinc deficiency is associated with memory deficits in children. There is a marked improvement in memory after supplementation. Post supplementation IQ scores do not show significant improvement in deficient groups in 6-8 year olds.

Key words: *Child, India, Iron, Non-verbal memory, Supplementation, Verbal memory, Zinc.*

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Micronutrient deficiencies are widespread in many developing countries and are common among young persons hailing from low socioeconomic groups [1-3]. Children are particularly at risk for such deficiencies as a result of excessive losses of iron and zinc due to parasitic infections [4,5]. Such deficiencies can have far-reaching health consequences, contributing to impairments in growth, neurobehavioral function, and immune competence, and increases in morbidity and mortality [6,7]. Of the micronutrients, the two micronutrients that have been found to be highly prevalent and linked to cognitive functioning are iron and zinc. Studies have shown that iron-deficient children lag behind controls in terms of anthropometric parameters, cognitive status and various athletic events performed [8-10]. In the case of iron deficiency, whether associated with anemia or not, the results of treatment trials have been conflicting in nature and have been linked to small sample size or lack of placebo group [7], and most of them have concentrated on iron deficient anemia rather than iron deficiency *per se*. Zinc has been causally linked to

various diseases such as diarrhea and pneumonia, but there have been few studies that have studied the impact of zinc deficiency on cognition [11,12]. This study was undertaken with the objective of identifying the role of iron, zinc, and combined iron and zinc deficiency on verbal and nonverbal subsets of memory, and to determine the difference in the affectation of memory between 6-8 and 9-11years age group.

METHODS

This study was conducted during the period from December 2005 to August 2006 at the Government primary school, Porur, Chennai, having students primarily belonging to the upper low socioeconomic background, as assessed by revised Kuppuswamy scale [13]. Permission was obtained from the Dean, Madras Medical College; the Assistant Elementary Education Officer; and Principal, Government Primary School, Porur. This study was approved by the college Ethical Committee. Written informed consent was taken from the parents of children who participated in the study.

One hundred randomly selected children of both sexes in the age group of 6 to 11 years were enrolled for the study and subjected to hematological tests and memory assessment. Children with infection, fever, history of drug intake for any illness, and girls who had attained menarche, were excluded. They were grouped into 6-8 years (Group A; *n*=40) and 9-11 years (Group B; *n*=60). Further sub grouping was done based on hematological results. The tests included hemoglobin estimation by Cyanmethemoglobin method, serum iron and total iron binding capacity (TIBC) by colorimetric method, serum ferritin by Elisa, and serum zinc by atomic absorption spectrophotometry [14,15]. Intelligence was assessed using the Binet-Kamath scale.

Based on serum iron levels, total iron binding capacity (TIBC), serum ferritin and serum zinc values, the children were categorized as Iron deficient (serum iron <60 meq/dL, TIBC ≥360, serum ferritin ≤10 mg/dL and serum zinc >65 mcg/dL) and Zinc deficient (serum iron ≥60 mcg/dL, TIBC <360, serum ferritin ≤10 mg/dL and serum zinc ≤65 mcg/dL). Those with values suggestive of both iron and zinc deficiency, were categorized as Combined deficient, and all others were considered Normal.

Tests for Memory

Six tests were selected, which were generated from different sources [16], including Wechsler memory scale, Mini mental state examination, Mann-Buitar visual memory screen, and Catel's retentivity test, as described below.

Digit forward: The subject is instructed to recite digit sequences of increasing length in the order presented.

Sentence repetition: Five sentences are presented one by one to the subject for immediate reproduction.

Story recall: The logical memory test is used to examine the subject's immediate verbal memory. The examiner reads the story to the child and the child is asked for immediate recall after hearing the story.

Picture recall: Here a row of picture is shown. The examiner then covers the pictures. Then the subject is asked to list the pictures exactly in the same order they saw starting at one end of row each time.

Benton visual retention test: It is a recall of 10 complex and unfamiliar geometrical figures. It has 10 designs on 10 cards. Each design is explored for 10 seconds and the subject is asked to reproduce the design immediately from memory.

Cattell's retentivity test: A card is shown on which 10 geometrical figures are drawn. The subject is allowed to look at them for 30sec and after 2minutes a second card is shown from which the figures that were shown should be identified.

Children who were deficient in iron and zinc were given the following supplements depending on the nutrient(s) they were deficient in: Ferrous sulphate tablets - 2 mg/kg body weight [17], Zinc - 5 mg equivalent once-a-day in the form of syrup: and children deficient in both the minerals were given both tablet and syrup for a period of 3 months. The normal children were advised nutritious food during the study period.

The tests were repeated after supplementation for three months. Due to drop outs, only 81 students

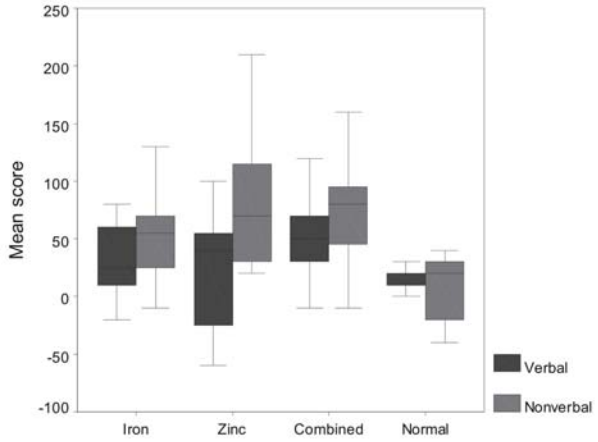

Fig. 1 *Box and whisker plot showing significant memory improvement of 9-11yrs children in the combined deficiency Group and zinc deficiency Group.*

continued in the study. Before supplementation, hematological results indicated an evident correlation between serum iron, total iron-binding capacity and serum ferritin levels. Taking this into consideration and the financial constraints, serum iron was alone performed for estimating iron deficiency. Serum zinc was also estimated.

RESULTS

Sixty-seven of the 100 students in the study were found to be deficient in iron and 43 were deficient in zinc. 35% of 6-8 years and 32% in 9-11 years of age were iron deficient, 10% of 6-8 years and 8.3% in 9-11 years of age were zinc deficient. The incidence of combined deficiency of both iron and zinc were found to be 35% in 6-8 years and 33.3% in 9-11years.

Non verbal memory and IQ assessment showed affectation mainly in the iron deficient and combined deficient groups in the 6-8 years age group. Significant affectation of verbal, nonverbal memory and IQ was seen in 9-11 years age group and the greater mean score difference in the combined deficient group (***Table* I**). Improvement was seen in the verbal, non verbal memory and IQ mainly in the 9-11 years age group, more so in the combined deficient groups as indicated by the difference in the mean scores obtained (***Table* II**).

DISCUSSION

Nutritional anemia is a syndrome and not a disease entity caused by malnutrition in its widest sense. It has been defined by WHO as a condition in which the hemoglobin content of blood is lower than normal as a result of deficiency of one or more essential nutrients [18]. It was also found that estimation of hemoglobin alone could not detect mild forms of iron deficiency which were found out by implementing the criteria involving all tests estimating iron-related indices (serum iron, serum ferritin, iron binding capacity and transferrin saturation). Thus it is vital to differentiate between iron deficiency alone and that associated with anemia, and there have been earlier studies taking this factor into consideration. On supplementation for a period of three months, it was found that all the children in deficient population reached the normal blood values.

Tests of verbal memory assess the immediate verbal memory which does not require any analytical

TABLE I MEMORY SCORES IN DIFFERENT GROUPS BEFORE SUPPLEMENTATION

	Iron Deficiency	Zinc Deficiency	Combined Deficiency	Normal	*P* value
6-8 years					
Verbal memory	161 ± 74.6	175 ± 35.3	130 ± 41.2	250 ± 10.0	0.07
Non-verbal memory	146 ± 64.4	115 ± 21.2	120.9 ± 83.4	245 ± 7.0	0.02
IQ	100 ± 5.5	95 ± 4.2	96.6 ± 4.7	107.5 ± 0.7	0.03
9-11 years					
Verbal memory	171.5 ± 66.3	205.7 ± 49.2	156 ± 57.2	227.1 ± 39.6	<0.01
Non-verbal memory	132 ± 57.5	120 ± 27.6	117.3 ± 24.3	234.2 ± 41.2	<0.01
IQ	98.9 ± 5.5	94.8 ± 4.05	94.7 ± 2.3	107.2 ± 4.2	<0.01

Significance by Mann-Whitney U test; All values are mean ± SD.

WHAT IS ALREADY KNOWN?

- Iron deficiency is known to affect cognition in 6-11 year olds but the role of zinc deficiency in memory is questionable.

WHAT THIS STUDY ADDS?

- Supplementation of iron and zinc was found to improve both verbal and non-verbal memory.

component but only simple immediate repetition. Studies have shown lower values in Wechsler intelligence scale for children of 6-8 years for items on verbal and performance subtests which improved with iron supplementation [7]. Analysis of our scores shows that the verbal memory was affected in both age groups, especially 9-11 years, with more severe affectation in the combined deficiency group. After supplementation for 3 months, 6-8 years age group showed marked improvement, particularly in the combined deficiency group, suggesting a greater tendency to revert to the normal growth.

Picture recall, Benton visual retention test and Cattell retentivity test evaluate immediate memory and visuospatial abilities using visual designs. They also require mental manipulation of figures with physical effort and test the visual nonverbal memory. Otero, *et al*. [19] observed significant impairment of visual memory in anemic children when compared to non-anemic children, whereas with zinc deficiency, there was no change in test scores when 5 year old children were assessed for visual sequential memory [20]. Penland, *et al*. [21] used extensive neuropsychologic battery of tests to asses cognitive and psychomotor functions in 6-9 year old children and observed zinc supplementation improved performance on tasks assessing visual recognition memory. From our results in non verbal tests, it is evident that both age groups are significantly affected in visual memory with more affectation in the combined deficiency subgroup. The results indicate the dependence of non verbal memory on both iron and zinc in both the age groups, in contrast to verbal memory, which showed marked degree of affectation only in the 9-11 years.

Post-supplementation all the groups in the 6-8 years age group showed similar results, the zinc group and combined group of the 9-11 years age group showed better results than the normal indicating a greater tendency of the zinc deficient to revert to normal.

TABLE II IMPROVEMENT IN MEMORY SCORES AFTER SUPPLEMENTATION

	Iron deficiency	Zinc deficiency	Combined deficiency	Normal	*P* value
6-8 years					
Verbal memory	38 ± 35.5	40 ± 28.2	70.9 ± 41.8	20(12.7)	<0.01
Non-verbal memory	33 ± 22.3	50 ± 46.5	56.3 ± 37.7	30(14.14)	0.49
IQ	8.0 ± 2.3	6 ± 1.3	3.8 ± 5.3	8.5(6.3)	0.27
9-11 years					
Verbal memory	30.5 ± 29.2	20 ± 5.9	50.6 ± 37.5	14.2 ± 2.3	0.05
Non-verbal memory	55.5 ± 39.1	84.2 ± 69.7	72 ± 44.7	11.4 ± 6.4	<0.01
IQ	3.97 ± 2.1	12.4 ± 3.3	5.01 ± 3.9	2.5 ± 1.5	0.05

Significance by Mann-Whitney U test; All values represent mean ±(SD).

Children of both the age groups showed IQ affectation before supplement while significant improvement was noticed only in the 9-11 year age group, particularly in the combined deficiency group, after supplementation.

The age for cultivating inspiration and wisdom is from 6-8 years, and 9-11 years is considered to be important in the formative process and reasoning. This is the reason for the focus of our study in this particular age group. Memory is an important tool for a good academic performance and plays an important role in modifying the child's potential for learning, which influences behavior. We conclude that identification of the deficiency at an early age and proper supplementation would prevent severe memory loss in the later age. Deficiency in zinc is not uncommon and has to be looked for on a routine basis as this mineral seems to affect memory more than that caused by iron deficiency alone.

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