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IRON DEFICIENCY ANAEMIA AND COGNITION IN SCHOOL AGE GIRLS: A COMPARISON OF IRON AND FOOD SUPPLEMENTATION STRATEGIES

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ABSTRACT

Iron deficiency anaemia (IDA) in school aged girls is an important yet overlooked issue. The present study was undertaken on 8 to 11 year old school girls (n=111) with the objective of studying the correlation between IDA and cognition. The study was also aimed at ascertaining the impact of iron rich food supplementation vis-a-vis iron folic acid syrup supplementation. At baseline, haematological assessment included estimation of haemoglobin (Hb), red cell indices, serum iron, total iron binding capacity (TIBC), serum transferrin saturation and serum ferritin. Psychological assessment was conducted to determine intellectual capacity and scholastic achievement. Anaemic subjects were divided into three groups, *viz*., AE1, which received twice weekly supplementation of iron folic acid syrup (53 mg iron/week); AE2, which received daily supplementation of four niger seed and defatted soy flour biscuits (45 mg iron/week) plus two lemons and AC, which remained unsupplemented to serve as control. Non anaemic group (NAC) was not intervened. Post intervention data was collected after an intervention period of 120 days. The prevalence of anaemia was 77.5% in the study population with 46.0% and 31.5% of the subjects suffering from mild and moderate anaemia respectively. Serum iron, TIBC, transferrin saturation and serum ferritin were significantly lower in anaemic girls when compared with non anaemics. The former had lower intellectual capacity and scholastic performance than those of their non anaemic counterparts. These three parameters had significant correlation with Hb and serum iron. Twice weekly medicinal iron supplementation was effective in raising Hb and building iron stores. Iron rich food plus vitamin C supplementation also improved haematological profile but to a lesser extent. Iron supplementation improved intellectual capacity but did not bring about catch up of anaemics to non anaemics.

KEYWORDS

Anaemic, Haemoglobin, Iron, Iron deficiency anaemia and Supplementation.

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INTRODUCTION

Iron deficiency in school age and early adolescence has been primarily studied for its detrimental effect on haematinic status. However, in iron deficiency, decreased brain iron stores may impair the activity of iron-dependent enzymes necessary for the synthesis, function, and degradation of neurotransmitters[1] and produce scholastic under-achievement or behavioural disturbances in school children[2,3]. Iron thus plays a vital role in cognitive development of growing children and adolescents.

The importance of widespread iron deficiency and anaemia among Indian girls has to be viewed in the context of these functional consequences. Anaemia is at least one nutrient deficiency disease which can be controlled even in the current conditions. Use of appropriate iron supplementation strategies to the vulnerable groups and selection of efficient outlets of distribution of supplements need to be examined and strengthened.

The present investigation was conducted to get an insight into the correlation between IDA and cognition in school age girls. Impact of medicinal iron and iron rich food supplementation were compared with respect to haematological and psychological profile. Standardisation of iron enriched recipes, estimation of total iron and sensory evaluation were also a part of this endeavour.

MATERIALS AND METHODS

Sampling and experimental design

A pre- post- intervention trial along with a control group has been undertaken. The participants of the study were 8 to 11 year old school age girls residing in the hostels of *Banasthali Vidyapith*, a residential educational institution for girls. The study was delimited to the girls studying and residing in a single institution so as to have a group homogeneous with respect to living conditions, eating pattern, intellectual environment and exposure to information and knowledge; factors which can have a confounding effect on the results. After getting the consent from the authorities and the parents of the children, they were screened for haemoglobin (Hb), intelligence quotient (IQ), urinary iodine. Those having severe anaemia or IQ < 75 or having suffered a recent episode of malaria or having attained menarche were dropped. The complete data was thus obtained from 111 girls. On the basis of Hb values anaemic subjects were divided into two experimental and one control groups.

Intervention strategies

Medicinal iron and food based intervention strategies were designed next. After due consultation with medical gastroenterologist specializing in public health nutrition, the subjects in the experimental group 1 were supplemented with iron (1066.66 mg ferrous ammonium citrate /100ml; elemental iron: 213.33 mg/100ml), folic acid (3.33mg/100ml), cyanocobalamin (50 µg/100ml) syrup twice weekly. Supplementation of 25 ml of the syrup provided 53 mg of elemental iron per week. For food based intervention, two iron enriched variants each of biscuit, *handwa, idli* and soy *chat* were prepared. Iron enrichment was done by the addition of ingredients with high iron content like soybean, niger seeds, rice bran, cauliflower greens and acceptability appraisal carried out. Sensory evaluation included selection of semi trained panel using triangle test. Control and iron enriched variants were subjected to 9 point hedonic test, paired comparison test and ranking test by a panel of 17 judges. Defatted soyflour (DSF) and niger seed added biscuits not only had high iron and high acceptability but also the qualities of ease of keeping and distribution. Therefore, these were selected for supplementation. As a sequel to this phase of the research endeavour, the experimental group 2 was to be supplemented with 2 niger seed biscuits and a lemon twice daily, after the 2 major meals. This intervention with 100 percent compliance was to provide approximately 45 mg of iron in a week.

Biochemical and cognitive testing

Baseline data collection included estimation of Hb (cyanmethaemoglobin method), red cell indices namely, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) (using automated haemoanalyser), serum iron and total iron binding capacity (TIBC) (using reagent kits based on Ramsay's method) and serum ferritin in one fourth of the subjects using enzyme linked fluorescent assay (ELFA) technique. Psychological testing included assessment of cognition through determination of IQ (General mental ability test for children), intellectual capacity (Raven's standard progressive matrices) and scholastic performance (based on general classroom ability test). On the basis of Hb at baseline, 86 subjects were found to be anaemic. Randomly, these subjects were divided into three groups, two experimental and one control. The number of subjects were 30, 31 and 25 in the experimental 1 (AE1), experimental 2 (AE2) and control (AC) groups, respectively. The experimental group 1 was supplemented iron syrup (15 ml + 10 ml), twice weekly; experimental group 2 was supplemented four niger seed biscuits and two lemons daily, for 120 days. Control group remained unsupplemented. The initially non anaemic group comprising of 25 subjects was not intervened and served as non anaemic control (NAC). After intervention phase of 120 days, post intervention data was collected which included assessment of haematological and psychological parameters measured at baseline, on all subjects.

Statistical analysis

Minitab® 15.1.0.0 (Minitab Inc.) was used for the statistical analysis of the data. A Pearson correlation coefficient was used to measure the extent to which two continuous variables are linearly related. The student's and paired t test procedure was used to make inferences about the difference between two population means, based on data from two random samples. The null hypothesis for the test was that the two population means are the same. A one-way analysis of variance (ANOVA) was used to test the hypothesis that the means of several populations are equal. The null hypothesis for the test was that all population means (level means) are the same. Significance was defined as $p<0.05$.

RESULTS

Background information

The 8 to 11 year old subjects (mean age 9.9 years) were from varied backgrounds with respect to state of domicile, mother tongue, family composition but they had been staying together in the hostels of the institution at least for a year. They were now exposed to same social and intellectual environment. Their eating pattern (lacto vegetarian) and lifestyles were also similar.

Baseline characteristics

The prevalence of anaemia (Hb< 11.5 g/dl) was 77.5% in the study population; 46.0% subjects had mild anaemia (n=51) and 31.5% had moderate anaemia (n=35). Mean Hb of mildly and moderately anaemics was 10.4 and 9.3 g/dl respectively. Non anaemic subjects' (n=25) mean was 12.1 g/dl. Mean MCV, MCH and MCHC of anaemic subjects were 73.0 fl, 27.6 pg and 31.3% respectively. The means of same indices in non anaemic group were 88.0 fl, 28.8 pg and 32.8% respectively. Serum iron and TIBC mean values were 55.5 and 776.9 µg/dl in moderately anaemic subjects; 86.8 and 663.9 µg/dl in mildly anaemic subjects; 151.5 and 594.2 µg/dl in non anaemic subjects. Per cent transferrin saturation means were 7.2, 13.2 and 26.2 in moderately anaemic, mildly anaemic and non anaemic groups respectively. Mean serum ferritin was 17.1 µg/l in those suffering from moderate anaemia, 18.8 µg/l in mildly anaemics and 50.2 µg/l in those who were not anaemic. There was a significant difference ($p < 0.05$) between anaemic and non anaemic group in all the haematological parameters (Table No.1 and Figure No.1 and 2).

Median IQ of non anaemic subjects was 128.0 followed by that of mildly (115) and moderately anaemic (92) subjects. The highest frequency (42) of anaemic subjects was in average IQ category whereas the highest frequency (8) of non anaemics was in genius category. The median raw scores on RSPM were higher in non anaemic subjects than in anaemics (42.0 vs 38.0). The 10 year old age group had median RSPM score of 40.5 whereas the median of both 8 and 9 year age groups was 37.0. Highest frequency of non anaemic subjects (8) was in II+ (definitely above average intellectual capacity) category and that of anaemics (38) was in III (intellectually average) category. Median scholastic performance scores (maximum possible 30) were 21.0 in nonanaemics, 18.0 in mildly anaemics and 15.0 in moderately anaemics. Majority of non anaemics (19) and mildly anaemics (32) had above average scholastic performance scores whereas the highest frequency (27) of moderately anaemic subjects was in below average category. There was a significant difference between anaemic and non anaemic groups in all the three tests of cognition. The scores on these three tests had significant positive correlation both with Hb and serum iron.

Impact of intervention

While the mean Hb of anaemic intervention groups was approximately 10g/dl at baseline, it was 12.1 g/dl in the non anaemic control group. Twice weekly medicinal iron supplementation to AE1 resulted in a hike in Hb. The mean increment in Hb was of 1.0 g. A mean increment of 0.5 g/dl of Hb was observed in AE2 group wherein iron rich biscuits and lemons were supplemented daily. Although there was an increment in mean Hb of both AE1 and AE2, at post intervention stage there existed a significant difference in their mean Hb values. No significant changes were recorded in Hb levels of anaemic and non anaemic control group. Mean Hb of AE1 and AE2 which were at par with AC at baseline, were significantly different than control at post intervention stage. Significant difference of AE1 and AE2 with NAC persisted at the completion of intervention. MCV of AE1 increased from 73.6 to 77.7 fl and that of AE2 increased from 72.9 to 74.5 fl after supplementation. MCH of AE1 increased from 28.1 to 29.6 pg and that of AE2 increased from 27.6 to 28.2 pg at post intervention stage. MCHC of AE1 increased from 31.5 to 33.1% and that of AE2 increased from 31.5 to 32.5% at post intervention stage. All the changes were significant in the experimental groups but not in non anaemic controls. ANOVA pointed to a significant difference in the mean serum iron and TIBC of the four groups at baseline. Tukey's test revealed that mean of non anaemic group was significantly different than the remaining 3 anaemic groups. In AE1, mean serum iron rose from 74.5 to 83.3 µg/dl, TIBC decreased from 714.1 to 673.2 µg/dl and transferrin saturation increased from 10.6 to 12.9% at post intervention stage. The change in serum iron was from 72.1 to 77. 6 µg/dl, in TIBC from 717.2 to 696.6 µg/dl and in transferrin saturation from 10.4 to 11.6% in AE2 after the completion of supplementation. The changes in AE1 and AE2 were significant and that in AC and NAC were non significant. Medicinal iron supplementation led to a rise in serum ferritin from 18.2 to 24.9 µg/l and the increase was from 15.2 to 19.1 µg/l in iron and vitamin C rich food supplemented group.

RSPM raw scores increased from 36.5 to 41.0 and scholastic performance scores rose from 17 to 23 at post intervention stage. The change in AE2 in RSPM raw scores was from 36.0 to 38.0 and in educational achievement from 16.0 to 22.0 at post intervention stage. RSPM raw scores (median) and scholastic performance test scores also increased in NAC but not in AC. Each of the three anaemic groups had significant difference with non anaemic group in scholastic performance at baseline as determined by ANOVA. There was a significant improvement in RSPM raw scores and scholastic performance scores in AE1, AE2 and NAC at the end of intervention. AC showed significant changes both in RSPM raw scores and scholastic performance scores. Quantitative improvement was higher in AE1 in RSPM raw scores but equal in AE1 and AE2 in scholastic performance scores. Catch up to non anaemics was observed only in scholastic performance (Table No.2 and 3).

Sensory analysis

In hedonic test, control biscuit had a mean of 8.9. The likeability of variant 2, niger seed and DSF containing biscuit was also very high (8.7). The hedonic test scores of control and niger seed biscuits were not significantly different from each other. In paired comparison test all judges marked control as positive for appearance, flavour, taste and after taste when compared with variant 1 of biscuit. The difference was statistically significant. No significant difference existed in either of the attributes between control biscuit and variant 2.

DISCUSSION

The present study was undertaken on 8 to 11 year old school girls of a residential institution in Rajasthan, India. All the girls under study came from all over the country and had been into this boarding since a year or more. The prevalence of anaemia in the study population of this project was 77%. Prevalence of this magnitude has been reported in other surveys from various parts of the country. National Family Health Survey[4] (NFHS 3, 2005-2006) reports prevalence of anaemia to be 70 to 80% in Indian children. At the baseline survey of 3000 school children in Gujarat, 84% had Hb< 12g/dl. No differences were observed in the prevalence of IDA according to sex, but significantly more rural than urban children had IDA (92% versus 78%)[5]. The prevalence observed in this study was similar to that observed by Gopaldas in urban children of Gujarat. Eighty per cent school children were anaemic in a study done by Leela and Shantipriya[6]. The percentage of mildly and moderately anaemics was 46.6 and 33.3 respectively. First- through fourth-grade school children of Zanzibarhad an averageage of 10.5 years, with over 75% of children between 9 and 12 years (range5-19 years). Their iron status was very poor; 63% of themwere anaemic (Hb< 110 g/l), 59% had erythrocyte protoporphyrin values > 80 µmol/molhaeme and 41% had ferritin values <12 µg/L[7].

Early stimulation, socioeconomic status home environment, nutritional status, and interactions between parent and child all influence the mental function of growing children[8]. The present research endeavour was delimited to a residential school setting so as to rule out the effect of many such confounding factors on the results of the study. Longitudinal studies consistently indicate that children who were anaemic in infancy continue to have poorer cognition, school achievement, and more behaviour problems into middle childhood[9]. However, the possible confounding effects of environmental factors, particularly poor socio economic background, prevent causal inferences from being made[10]. The study design in this research project was that of a pre test, post test intervention trial with random allocation of subjects into experimental and control groups. The potential confounding effect of many environmental factors was controlled by undertaking the study on subjects exposed to same living conditions of a residential school.

The 7, 8 and 9 year old primary school girls had mean Hb of 9.0, 9.9 and 9.2 g/dl respectively[11]. Each of the age groups had a mean score of 44.8, 54.0 and 64.75 respectively on Raven's Coloured Progressive Matrices. Hb and iron intake were significantly correlated (p<0.01) with the intelligence level of the children. The results of the present research work are in conformity with the observations of other researchers where they found the IQ and performance on tests of cognition of anaemic children to be lower than that of non anaemics.Hb and serum iron were found to be positively correlated with intellectual capacity of the subjects in this study as has been the observation in aforementioned research endeavour.

From the results of this study as well as from the literature reviewed[12,13], it appears that a long-term supplementation programme, whether once or twice weekly, is likely to be as effective as daily IFA with regard to improvements in Hb levels. In this research work, haematological response to daily iron (6.4 mg iron/day) plus vitamin C (2 lemons providing 30 mg vitamin C approximately) rich food supplementation was also studied. This strategy also brought about a significant improvement in iron status of the subjects but it was quantitatively lower than that brought about by the pharmacologic intervention. Various other researchers have explored the effects of food supplementation on haematinic status of subjects. In a study[14] that evaluated the effectiveness of supplementation with ferrous sulphate and iron bis-glycinate chelate on haemoglobin and serum ferritin levels among school children (7-11 years) one group received 40 mg iron as ferrous sulphate once weekly and the other group received 3.8 mg of iron bis-glycinate chelate-enriched cookies, 3x/week, for 8 weeks. The interventions showed a significant increase in Hb levels (1.1 g/dL) for children who received ferrous sulphate and 0.9 g/dl in those who received iron bis-glycinate chelate.

Literature relating to functional benefits of IFA interventions (such as cognitive abilities) among young adolescents is limited. In a double blind, placebo-controlled clinical trial in Baltimore, post intervention, non-anaemic iron deficient adolescent girls (n=73) (serum ferritin ≤12 µg/l with normal Hb) receiving oral ferrous sulphate performed better on a test of verbal learning and memory than the control group (p<0.02)[15]. Performance on the same educational achievement test is expected to improve with time; in this study supplemented anaemics were better off than their unsupplemented counterparts in educational achievement at post intervention stage which is in conformity with findings of research discussed above. Supplementation with iron could be responsible for better learning and memory as reported by Bruner and coworkers[15] thus enhancing the performance on educational achievement test of supplemented anaemic children. The findings of study by Sen and Kanani[16] indicate that daily and twice weekly iron folate (IFA) supplementation are comparable as regards significant impact on haemoglobin levels as well as cognitive functions of girls in the pubertal phase of development. As a part of this endeavour, the effect of iron rich biscuit plus lemon supplementation on psychological functions of school age girls was also explored. The results were encouraging with respect to the changes observed in the cognitive abilities. Other researchers have investigated the effect of micronutrient fortified recipe supplementation in children. Micronutrient fortified biscuit intervention (containing iron to meet 50% RDA) for 12 months, had a positive effect on cognitive function of rural school children of South Africa[17].

Table No.1: Mean haemoglobin levels of anaemic and non anaemic subjects

S.No	Cut off values	Category	n	Haemoglobin (g/dl) (Mean±SD)
1	Hb< 11.5 g/dl	Total anaemics	86	10.0±0.70
2	Hb 10.0 to < 11.5 g/dl	Mildly anaemic	51	10.4±0.40
3	Hb 7.0 to < 10.0 g/dl	Moderately anaemic	35	9.3±0.55
4	Hb ≥ 11.5 g/dl	Total non anaemics	25	12.1±0.37
5	Total subjects		111	10.4±1.09

Table No.2: Impact of intervention on haemoglobin levels of the four intervention groups

S.No	Groups→		Haemoglobin (g/dl)			
			AE1 (n=30)	AE2 (n=31)	AC (n=25)	NAC (n=25)
			(Mean±SD)			
1	Pre intervention		10.0±0.66	9.9±0.63	9.9±0.85	12.1±0.37
2	Post intervention		11.0±0.54	10.4±0.58	9.9±0.82	12.1±0.37
3	Change	(post-pre)	1.0±0.20	0.5±0.16	0.0±0.21	0.0±0.09

Table No.3: Impact of intervention on performance on different tests of cognition in the four intervention groups

Cognition parameters	Groups → / Intervention stage↓	AE1 (n=30)			AE2 (n=31)			AC (n=25)			NAC (n=25)		
		Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
RSPM raw Scores	Pre	37.3	36.5	8.36	35.0	36.0	9.17	39.5	41.0	6.33	41.0	42.0	7.00
	Post	40.5	41.0	7.43	37.3	38.0	8.79	40.6	41.0	6.16	42.3	44.0	6.80
Scholastic performance scores	Pre	17.3	17.0	1.91	16.4	16.0	2.50	16.5	17.0	2.71	20.9	21.0	2.12
	Post	22.8	23.0	2.10	21.0	22.0	3.14	17.1	17.0	2.69	21.7	22.0	2.09

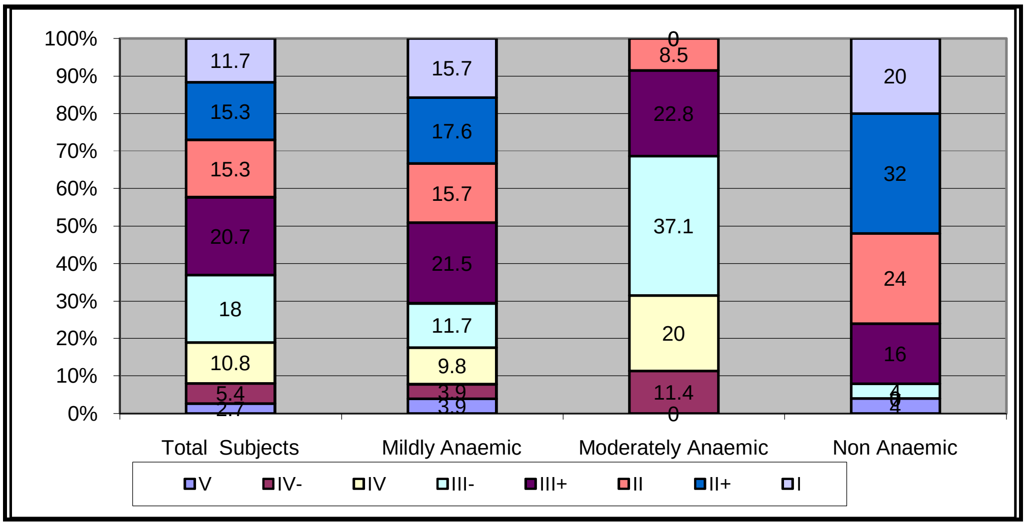

Figure No.1: Percentage of subjects in different categories of intellectual capacity: Baseline evaluation

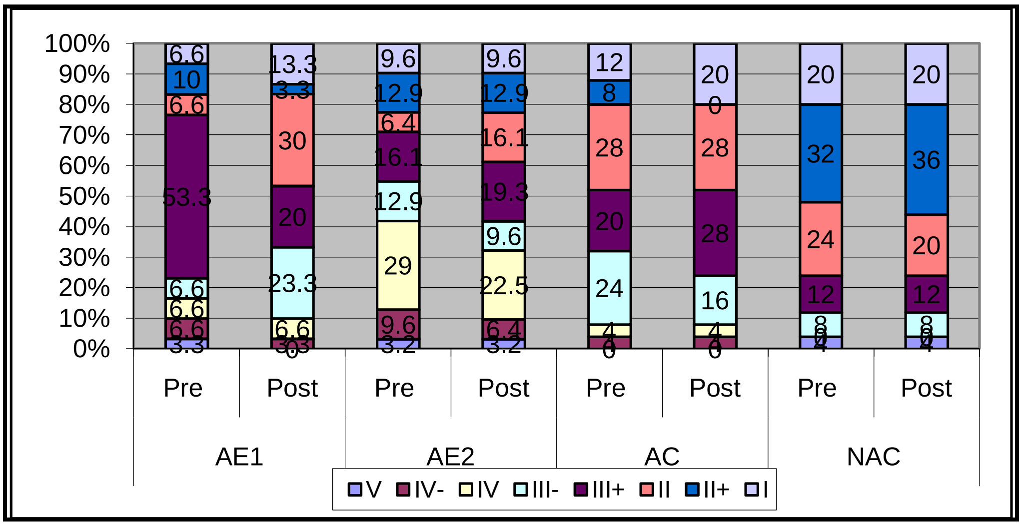

Figure No.2: Percentage of subjects in different categories of intellectual capacity in the four study groups at pre and post intervention stages

CONCLUSION

This study marks the importance of reducing anaemia to improve cognition by showing that higher the magnitude of gain in Hb, higher the gain in cognitive test scores. The results of this study imply that twice weekly iron supplementation could provide an effective means of raising iron stores in school age girls. By protecting them from the cognitive effects of iron deficiency iron supplementation could help girls to get the most out of school. Being members of the population vulnerable to iron deficiency, the school girls included in the study are at an age when adolescent growth spurt would be expected to begin to arise.

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