ORIGINAL ARTICLE

Sustainability of the effects of medicinal iron and iron rich food supplementation on haemoglobin, intelligence quotient and growth of school aged girls

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Abstract

Anaemia in school aged girls is an important but neglected issue. Since iron supplementation programmes have had little reported success in reducing anaemia, interest is turning to food based approaches that have higher potential for achieving far reaching benefits. The purpose of the study was to observe sustainability of the effect of iron and food supplementation on haemoglobin (Hb), intelligence quotient (IQ) and growth of the subjects. At baseline, estimation of haemoglobin (Hb), red cell indices, serum iron, total iron binding capacity, serum transferrin saturation and serum ferritin was done. IQ, weight and height were measured using standard procedures. Anaemic subjects were divided into three groups, viz., (i) twice weekly supplementation of iron folic acid syrup (53 mg iron/week); (ii) daily supplementation of 4 niger seed and defatted soyaflour biscuits plus 2 lemons (45 mg iron/week) and (iii) control. Non anaemic group (NAC) was not intervened. Endline data was collected after 120 days. Follow up for Hb, IQ, weight and height was done 4 months after cessation of supplementation. The prevalence of anaemia was 77% in the study population; 46% subjects had mild anaemia and 32% had moderate anaemia. Iron status was lower in anaemic subjects (p<0.001). Iron supplementation was more effective in raising Hb and building iron stores than iron rich food supplementation. Iron supplementation improved IQ but did not bring about catch up of anaemics to non anaemics. Iron rich food supplementation was better than medicinal iron in promoting growth in anaemic girls. The impact of iron rich food supplementation on Hb, IQ and growth sustained for 4 months while that of medicinal iron did not. Effects of food supplementation are sustainable for 4 months, therefore, this strategy holds more potential to control anaemia.

Key Words

Anaemia; Haemoglobin; Intelligence quotient; Iron deficiency; Supplementation

Introduction

Anaemia has different reasons, but almost 50 percent of anaemia occurs due to iron deficiency (WHO, 2001). Global Burden of Disease (GBD) 2000 estimates provide a new basis for advocating the control of iron deficiency. Compared with other forms of malnutrition included among the 26 risk factors in GBD 2000, iron deficiency ranks #9 overall in terms of disability adjusted life years lost, falling lower than underweight (#1), and slightly higher than zinc deficiency (#11) and vitamin A deficiency (#13). There is no excuse for the scientific and public health community to be complacent about iron deficiency (Stoltzfus, 2003). Regarding the relationship of iron deficiency to child development, cognition, and work productivity (Walter, 2003), evidence is mounting that early iron deficiency significantly affects children’s neural physiology and behaviour (Beard, 2001). Well controlled observational studies show that iron deficiency anaemia (IDA) is associated with behavioural differences, developmental delays, and lower intelligence quotient (IQ) and poorer school performance (Grantham-McGregor and Ani, 2001). Two published randomized controlled trials of iron supplementation in early childhood have both
shown benefits to children’s development (Idjradinata and Pollitt, 1993; Stoltzfus et al, 2001). There is need for further studies on children who are in the pre-adolescent years, so that the consequences of iron deficits can be described in social, economic, and educational terms in this less studied age group too.

Effective strategies to address iron deficiency (ID) and IDA usually have three main objectives: to increase intake of absorbable iron; to enhance absorption of ingested iron; and to reduce iron losses, particularly those associated with infections and parasites. Iron supplementation and fortification are practical approaches to achieve the first two objectives, while other public health measures are expected to help achieve the third one. Iron supplementation is seen as an effective means of increasing intake of iron and, eventually, other anaemia related nutrients. Iron supplementation is probably the best available option to effectively address ID/IDA in pregnant women and children (Schultink and Gross, 1996). However, some technical and practical barriers have precluded the full realization of the potential impact of iron supplementation on ID/IDA.

One of the issues still to be resolved is sustainability of improved iron status, as a period of negative iron balance tends to occur because absorption is down-regulated, thus, benefits of supplementation are likely to be temporary if diets are low in available iron. Still pending is a clear definition of the role of supplementation as a treatment of existing anaemia or as a preventive measure to reduce the risk of acquiring it. There is, however, some consensus in that daily supplementation would be the fastest way to treat ID/IDA. There is some evidence that intermittent supplementation might also work (Mora, 2002). Despite the high prevalence and large disability burden associated with childhood anaemia, affordable, high-quality, and appealing supplemental forms of iron designed for children are generally not available in less-developed countries.

**Aims & Objectives**

To observe sustainability of the effect of iron and food supplementation on haemoglobin (Hb), intelligence quotient and growth of school aged girls.

**Material and Methods**

A pre- post- intervention trial along with a control group was 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 delimitated 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 obtaining informed consent from the authorities, medical officer of the university and the parents of the children, they were screened for Hb and IQ. 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 group.

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. In order to enhance the bioavailability, processing techniques like fermentation were used in handwa and idli and germination was used in soy chat. Six variants of bajra flour bhakhri were prepared and food grade iron salts, viz., ferrous citrate, ferrous fumarate and ferrous sulphate were added at two concentrations on 1mg and 0.5 mg per g flour. Bhakhri had lowest acceptability and were dropped. 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.
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 TIBC (using reagent kits based on Ramsay’s method) and serum ferritin in one fourth of the subjects using ELFA technique. Determination of IQ was done by using General mental ability test for children (Srivastava and Saksena, 1985). Anthropometric assessment included measurement of weight (using platform weighing balance) and height (using measuring tape fixed on a wall). Body mass index (BMI) was derived from these two measurements and children classified as normal, underweight, overweight and obese using the cut offs recommended by Center for Disease Control. 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 (53 mg iron/week); experimental group 2 was supplemented four niger seed biscuits (45 mg iron per week) 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). Post intervention data was collected after 120 days which included assessment of haematological, psychological and anthropometric parameters measured at baseline, on all subjects. A follow up was conducted 4 months after the completion of supplementation and all the subjects were appraised for Hb, IQ, weight, height and BMI so as to compare the sustainability of supplementation effects of the two strategies.

Statistical analysis was conducted using the statistical software Minitab® 15.1.0.0 (Minitab Inc.). Descriptive statistics included computation of mean, median (only for psychometrics), standard deviation and correlation. Inferential statistics included hypothesis testing through student’s and paired t test and analysis of variance at 95% level of significance.

Results

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 µ g/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.

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 Pearson’s correlation between Hb and IQ was +0.697 which was statistically significant.

The mean age of the non anaemic group was 9.6 years where as that of the anaemic group was 10.0 years; mean weight of former was 31.1 kg and that of latter was 33.0 kg. Height of non anaemic subjects was 135.9 cm in terms of mean whereas it was 140.0 cm in case of anaemic subjects. Mean BMI of anaemics was 16.7 and that of non anaemics was 16.8 kg/m². Amongst the anaemics, 4% subjects were underweight and 13% were overweight. Out of the 25 non anaemic subjects, 1 was overweight and remaining were normal. There was no significant difference (p=0.967) in the BMI of anaemic and non anaemic subjects.

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
Supplemented group. Iron and vitamin C rich food supplementation led to a rise in serum ferritin from 15.2 to 17.3 g/dl. In controls, there was non-significant change. Medicinal iron supplementation increased serum transferrin saturation from 10.4 to 12.0% in AE2 after completion of intervention. The changes in transferrin saturation were the same in AE1 and AE2 with NAC. 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 and non anaemic control group. Mean Hb of AE1 and AE2 which were at par with AC at baseline, were significantly different (p<0.05) 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.

The mean IQ of non anaemic group at baseline was 128 (Figure 2) and that of the anaemic intervention groups ranged from 103 to 111 approximately. F ratio proves a significant difference in the mean IQ of the four study groups at the pre intervention stage. Tukey’s test puts forth the fact that AE1, AE2 and AC did not differ with each other with respect to the mean IQ. These three groups differed significantly from NAC. At the post intervention stage, there was an improvement in the IQ of AE1 by 5 median points. There was a mean increase in IQ by 3 and of 2 median points in AE2. These changes at post intervention stage were significant when compared to the baseline values by paired t test. Non-significant changes in AC and NAC were recorded. The difference between the mean IQ of supplemented anaemics and non anaemics persisted.

The mean weight of both the anaemic experimental groups increased by approximately 1.0 kg (Fig 3), so was the case in NAC. On the other hand, mean weight of anaemic control group increased by 0.5 kg in a span of 120 days. The change in all the 4 groups was statistically significant. Statistically significant change (pre vs post intervention) in height was observed in all 4 groups. The lowest increment in mean height (Figure 4), when measured at post intervention stage, was 0.6 cm in AC. In experimental group supplemented with medicinal iron (AE1), mean height increased by 1 cm. Increment of mean height was 1.2 cm in iron rich food supplemented anaemics and also in NAC. Mean BMI of all four groups increased by approximately 0.3 kg/m² after 120 days of intervention. The changes in mean weight were statistically significant (p<0.05).

**Sustainability of supplementation effects:** The mean change in Hb was of 1.0 g/dl after completion of twice weekly medicinal iron supplementation. Four months hence, the Hb dropped by 0.2 g/dl. Iron and vitamin C rich food supplementation brought about an increase of 0.5 g/dl. When 120 days elapsed without any intervention, a further increase of 0.2 g/dl of Hb was noted in AE2 (Fig 1). The changes were statistically significant. The IQ (Fig 2) of AE1 dropped by one and half median points at the follow up stage after 4 months of completion of supplementation. On the other hand, an enhancement of IQ by 1 median point was observed in the iron and vitamin C rich food supplemented (AE2) anaemic group. The change in both the anaemic experimental groups (post intervention vs four months after intervention) was significant. Weight increased in all the groups when measured at an elapse of four months post supplementation (Figure 3). Quantitative change was highest (0.8 kg) in NAC, followed by AE2 (0.7 kg), AC (0.6 kg) and AE1 (0.5 kg). The changes were statistically significant. In height, NAC showed hike of 1.0 cm at follow up. The difference in mean height at four months after and immediately after intervention was 0.8 in AE2, 0.6 in AC and 0.5 in AE1 (Figure 4). The increase in height in all four groups was significant. The BMI also showed significant
change in the four groups. The changes were on positive side of scale but quantitatively small.

**Discussion**

According to Dreyfuss et al (2000) two billion children are affected with iron deficiency anaemia worldwide. The prevalence of anaemia in the study population of this endeavour was 77%. Prevalence of this magnitude has been reported in other surveys from various parts of the country. National Family Health Survey (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%) (Gopaldas, 2005). Even in the present investigation, 46% subjects had mild anaemia and 31% had moderate anaemia which attunes with the results of other studies. Severely anaemic girls were not made a part of the study.

Early stimulation, socioeconomic status home environment, nutritional status, and interactions between parent and child all influence the mental function of growing children (Engle, 1992; Vazir and Kashinath, 1999). 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. Most observational studies in children have found associations between iron deficiency anaemia and poor cognitive and motor development, and behavioural problems (Lansdown and Wharton, 1995). 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 (Grantham-McGregor and Ani, 2001).

India is struggling with dual burden of malnutrition. Undernutrition attracted the focus of health workers, as childhood obesity was rarely seen. But over the past few years, childhood obesity is being observed with the changing lifestyle. The urban middle to high income group is grappling with problems related to overnutrition and high prevalence of undernutrition is a commonplace in rural population as well as in low income groups. Hidden hunger, i.e., deficiency of micronutrients affects all. This has been an observation in the present research that girls are overtly well nourished but anaemic. In fact, the prevalence of overweight was more than that of underweight in the anaemic subjects of this study. Kapil et al (2002) and Subramanyam et al (2003) reported high prevalence of overweight as well as obesity.

**Impact of supplementation:** Intermittent iron supplementation has yielded encouraging results in bringing about a change in iron status in this study. At the end of 120 days supplementation period Hb, serum iron, TIBC and other haematological parameters showed an improvement in the twice weekly medicinal iron supplement group. No significant changes were noticed in the control group. Several other researchers have reported likewise. The effect of daily vs twice weekly iron supplementation on iron status was studied in preschool children with low iron status. For 8 weeks one group received a daily supplement of 30 mg Fe, while the other group received 30 mg Fe twice per week. It was concluded that in preschool children with low iron status, twice weekly iron supplementation has an effect on iron status similar to that of daily supplementation (Schultink et al, 1995). Eight weeks of oral iron supplementation (135 mg elemental Fe/d) in iron-depleted, non anaemic women resulted in a progressive decrease in mean serum transferrin receptors (sTfR) and a more than twofold increase in mean serum ferritin (from 14.3 to 36.9 µg/l) (Zhu and Haas, 1998).

In this research work, haematological response to daily iron 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. Study by Santos et al (2007) 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, although not significant in the inter-group comparison. The beneficial effect of iron rich food supplementation as discussed above, have been observed in the present research work also. Although only 2 out of 31
anaemic subjects became non anaemic post iron rich biscuit intervention but half of the moderately anaemic subjects progressed to a stage of mild anaemia.

A soup powder fortified with 20 mg elemental iron in the form of ferrous fumarate and 100 mg ascorbic acid per serving was evaluated in 6 to 8 year old primary school children over a period of 6 months. The intervention was associated with positive changes in Hb, MCV and serum ferritin. The effects were greater in children with low iron status at baseline (Kruger et al 1996). Similar observations were made in this study too. Daily supplementation of DSF and niger seed incorporated biscuits (4 in number; 6.4 mg% iron) was carried out on one of the anaemic experimental groups in this study. Such food products have been tried and tested in other research endeavours also. Six soy malt biscuits containing 5.14 mg% of iron were supplemented daily for 90 days to 20 moderately anaemic girls, 16 to 18 years old. Significant improvements were observed in Hb, serum iron, TIBC and SF. Non-supplemented control group did not show any change (Anuradha and Sangeetha, 2001).

Iron syrup and iron rich food supplementation improved cognition and school competence of the children in this study. Other researchers have reached to similar conclusions. Reviewers (Grantham-McGregor and Ani, 2001) concluded that, in general, poorer test performance of children with IDA tended to improve with iron treatment in children >2 years of age.

To begin with, non anaemic children of the present study were lighter and shorter than anaemic children in this study. The probable reason could be the fact that many 8 year olds composed the non anaemic group, thus making it the youngest group of the study in terms of mean age. The increment in weight and height was higher in supplemented anaemic subjects than in controls. Treatment with 10 mg ferrous sulfate.kg-1.d-1 for 12 week, in rural Indonesian school children resulted in a significant improvement in anaemic subjects' growth velocity, and level of morbidity (Chwong et al, 1988). The weight gain observed in this study was of the level reported by Kanani and Poojara (2000). In their study, a significant weight gain of 0.83 kg was seen in adolescent girls in the experimental group supplemented with iron folic acid capsule, whereas the controls showed a little weight gain.

Sustainability of supplementation effects: It is pertinent to explore the sustainability of the effect of supplementation. In this study, food supplementation strategy yielded better sustainability results than the pharmacological intervention. The Australian Iron Status Advisory Panel advocates dietary intervention as the first treatment option for mild iron deficiency (SF = 10 to15 µg/l). Iron deficient women of child bearing age having high iron diet produced smaller increase in SF than the medicinal iron supplementation group but the former continued to show improvement in Hb and SF during a 6 months follow up period (Patterson et al, 2001). The long term effectiveness of micronutrient fortified biscuit supplementation programme to primary school children was evaluated over a period of 45 months. Iron status
returned to pre-intervention levels after the school holiday break (van Stuijvenberg, 2005). In this study, the Hb and IQ in the medicinal iron supplemented group decreased at a 4 month follow up post supplementation. On the other hand, Hb and IQ continued to rise at a small pace in iron rich food supplemented group. The rate of growth was found to be better in food supplemented initially anaemic children at this stage. This suggests that the effects of food supplementation, although quantitatively low, are able to sustain themselves even after cessation of supplementation which is not the case for medicinal iron supplementation. This observation puts food supplementation over and above medicinal iron supplementation.

**Conclusion**

This study marks the importance of reducing anaemia to improve IQ by showing that higher the magnitude of gain in Hb, higher the gain in IQ scores. It further indicates that to improve cognition, twice weekly iron supplementation is effective. Iron and vitamin C rich food supplementation is better in improving growth in school age girls. Medicinal or food iron supplementation brings an improvement in IQ of anaemic girls but catch up to non anaemics does not take place. A longer intervention may bring about the catch up. Sustainability of the positive increments in Hb, IQ is possible with food based supplementation.

**Recommendation**

Iron deficiency in young girls is a problem of public health concern. Schools can serve as effective channels for providing the desired intervention for its control. It can be recommended that school feeding programme should be envisaged in a manner that it can also play a role in providing a sustainable solution to combat iron deficiency and its physical and cognitive manifestations in girls.

**Limitation of the study**

Intervention period is of four months and serum ferritin estimation has not been done for all subjects.

**Relevance of the study**

The study provides an insight into the association of cognition and iron deficiency anaemia in an age group which has been scantily studied. It brings to fore that iron supplementation in this age group increases haemoglobin but food based supplementation is better not only for promoting growth but it also yields positive effects which are more sustainable.

**Authors Contribution**

The study has been planned and conducted by the author.

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**References**

16. Santosh MMD, Nogueira NN, Diniz AS. Effectiveness of different iron supplementation strategies on hemoglobin and ferritin
levels among schoolchildren in Teresina, Piauí State, Brazil. Cadernos de Saúde Pública 2007;23(7):1547-1552.
