

Do We need daily Iron Supplementation? Comments and Controversies

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Introduction

Nutritional anemia has been a subject of considerable interest for many decades. Iron deficiency anemia (IDA) is still a major nutritional and public health problem in developing countries. Several strategies have been developed which include fortification of food with iron, oral medicinal iron and slow release iron preparations. Poor effectiveness of these strategies in developing countries has been attributed to various factors which include inefficient dose, time of supplementation and poor adherence. The paper introduces the concept that medium to long term weekly ingestion of iron supplements has proven efficacious if it is properly supervised.

Nutritional anemia has been a subject of considerable interest for many decades. Iron deficiency anemia (IDA) is still a major nutritional and public health problem in developing countries. The prevalence of IDA among pregnant women and pre-school children in South East Asia is between 50-70%.^{1,2} According to National Health survey of Pakistan report, about 43 to 47% of rural and 35 to 41% of urban women between 15 to 44 years are anemic. Similarly among boys and girls aged 5 to 14 years, 44% of urban girls and 46% of rural boys are anemic.³

Iron, being an integral component of hemoglobin, myo-globin, cytochromes and iron containing enzymes essential for intermediary metabolism, is considered as a main culprit for IDA development. It may be due to higher requirements in children as compared to elderly people, low socioeconomic status, low bioavailability of dietary iron and malabsorptive diseases which contribute to development of IDA. Children are at a higher risk of becoming iron deficient due to rapid growth spurt, worm infestations and in teen age girls due to menstrual loss.⁴ Iron deficiency manifests itself as decreased physical performance⁵, altered cognitive functioning⁶, delayed mental development^{7,8}, poor pregnancy outcomes^{9,10} and slow growth in young children.¹¹

The social, health and economic costs of IDA are not insignificant and in the broad context of public health concerns it should always be considered along with clinical implications. The general measures to control iron deficiency practiced at present include, modification of diet and life style aimed at increasing iron intake bioavailability. These practices include breast feeding, adequate amount and varieties of foods in meals including heme iron, changes in cooking practices to reduce phytates and other polyphenols which inhibit iron absorption.¹⁰ Iron fortification programs to alter the basal consumption of iron and targeted interventions to decrease the intake of known inhibitors of iron absorption are viable alternatives to supplementation programs in some cases and need to be carefully considered. Iron in excess is an active participant in the fenton reaction, which results in the production of free radicals and oxidative damage.^{11,12} Higher doses of iron as fortificant or as dietary supplement may be associated with increased oxidative product formation and initiation of various pathogenic processes such

as cardiovascular diseases, neuropathology and cancer.¹³⁻¹⁵ Thus the implications of adding fortificant iron to food consumed or the provision of very large doses of supplemental oral iron needs to be reconsidered.

Due to high prevalence and serious consequences, several strategies have been suggested to combat the problem. One of these strategies is oral supplementation with medicinal iron. This strategy is especially suggested for the population where fortification programs fail to reach the at risk segments of population. It also has a desirable specificity as it can be targeted at population groups at greatest need for iron or at greatest risk of becoming iron deficient. Supplementation programs do best on pregnant women and children and taken under supervision it prevents the development of anemia.¹⁶

The effectiveness with oral iron supplementation is constrained by several important factors especially in developing countries. Some of these factors are, inadequate coverage of populations in need of services, deficiency in supply and distribution of supplements at health centres, cultural and health beliefs of providers and recipients, colour and other characteristics of supplements and gastrointestinal side effects.¹² The oral administration of iron can cause gastrointestinal side effects in some individuals such as epigastric discomfort, constipation, abdominal cramps, nausea, vomiting and diarrhoea. Individuals taking oral iron develop black stools and may develop staining of teeth which may have no clinical significance and disappear when supplementation is stopped. Another major problem with daily iron supplementation is that the targeted individuals are not motivated to take iron daily for the period of 2-3 months. Much work has been done in the past five years regarding the desirability of intermittent iron supplementation compared with daily iron supplementation. The theory behind intermittent oral iron supplementation is based on concept of mucosal block of iron absorption.¹⁷ The theory argues that mucosal enterocytes down regulate iron absorption in response to daily exposure to high intake of iron. There is an increase in mucosal ferritin synthesis and an increase in the proportion of enterocytes iron to transferrin in the vascular pool.⁴ Recent studies on rats confirm a more efficient uptake of iron with spaced or intermittent administration of iron supplements.^{18,19} The mucosal cells need to be renewed to ensure that iron absorption can begin again. The life span of mucosal cells in rat has been estimated to be three days. A study by Cook and Reddy²⁰, determined efficiency of weekly compared to daily supplementation in adults and showed that with daily administration of iron there is 13% lower absorption compared with weekly supplementation, but the difference was not statistically significant .

A reduction in the frequency of iron supplement administration to once or twice weekly is being widely examined in the developing countries on the assumption that the side effects of oral iron will decrease and there will be lesser inhibition in absorption from iron taken on the previous day. In a study conducted in Indonesia in 1995, Schultink used a randomized, double blind trial of daily supplementation compared with twice weekly ferrous sulphate (30mg) given for two months to 2-5 years old children with iron deficiency anemia. The results of this therapeutic trial showed that daily and twice weekly iron supplements worked equally well, regardless of the severity of anemia.²¹ Another study from China investigated young children aged 3-6 years and primiparous

mothers. They provided either a weekly iron supplement or a daily iron supplement and also included a placebo control group. Protection of maternal iron status as indicated by plasma ferritin level, was equivalent in both the iron supplementations groups.²² An additional intervention trial including a placebo group was done on young children in Bolivia. The study compared dosages of 3 to 4 mg iron per Kg body weight given five times weekly or once weekly to young children for 16 weeks with that of placebo group that received no supplement. There was significant rise in hemoglobin levels in both the groups as compared to group which was on placebo.²³ Hafiz and Ahmed²⁴ carried out a study on anemic children of 1-6 years of age in Lahore (Pakistan). One group of children was given iron daily and other group thrice weekly. All the above studies showed comparable rise in hematological parameters, serum iron, total iron binding capacity and ferritin levels in both daily and weekly supplemental groups. A study was carried out in Berkley, California in which daily vs weekly supplementation therapy trial was done on women of reproductive age group (18-45 years). Group one received daily iron for three months, group two, weekly iron for seven months and group three was control group. Both iron supplemented groups were equally effective in bringing hemoglobin levels above 12.0 to 12.5 g/dl in three months.²⁵ Another weekly supplementation therapy conducted in Indonesian female adolescents (14-18 years). They were divided into three groups. One group received 60 mg elemental iron daily, other the same dose weekly and third group received double dose (120 mg) weekly. After two months, groups that received daily and double dose weekly showed significant improvement in hemoglobin and ferritin levels, while the group that was on single weekly dose showed less increase in ferritin levels.²⁶ Similar studies were carried out in Lima Peru in adolescent girls aged 12-18 years, to assess the efficacy and acceptability of daily and intermittent iron supplementation. Result of this study concluded that daily supplementation led to greater increase in hemoglobin than intermittent iron supplementation but serum ferritin and free erythrocyte protoporphyrin were similar in two groups.²⁷ Supplementation trials in pregnant women that included intermittent dosing schedule were performed in Guatemala. Six to eight times more side effects were reported by women who took iron supplements daily than by those who consumed them weekly.²⁸ Work was carried out at Ziauddin Medical University, Karachi, Pakistan on weekly and daily iron supplementation in children and adults. Comparable rise in hemoglobin, serum iron ferritin and hematological parameters were observed in children after daily and weekly supplementation of iron. But in adults significant rise in hemoglobin, serum iron, hematological parameters and ferritin were observed in daily administered (300mg ferrous sulfate) and double dose weekly group (600 mg ferrous sulfate). However increase in serum ferritin was more in daily group compared with weekly double dose group. Rise was not significant in weekly administered group (300 mg ferrous sulfate).²⁹

Several commentaries question the efficacy of intermittent supplementation stating that if compliance is poor with daily iron supplementation, it would be even worse with an intermittent trial. The answer lies in supervised supplementation therapy, which can easily be possible in children by their school teachers. Controlled situation is necessary for intermittent iron supplementation, which could effectively reduce the prevalence of iron deficiency anemia in several risk groups. As to whether it works well or not, the data regarding responses of iron deficient subjects stratified by severity of anemia strongly

support the contention that anemic and non-anemic iron deficient subjects both benefit. In addition, this therapy may be easily applicable in developing countries due to cost effectiveness. However, compliance and side effects with intermittent supplementation need monitoring.

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