

Iron Supplementation in Infancy: Which Preparation and at What age to Begin?

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Iron deficiency anemia (IDA) is a major public health concern worldwide affecting almost one-third of the population especially those between 4-23 months of age [1]. Supplementation of iron is a key strategy for anemia reduction [2]. In a new born delivered at term gestation, eighty percent of the body iron is received from mother during the third trimester of pregnancy. Various maternal conditions like anemia, hypertension with intrauterine growth restriction, or diabetes can result in reduced fetal iron accrual. Term healthy infants usually have sufficient iron stores until 4 to 6 months of age [3]. WHO recommends iron supplementation for infants aged 6-23 months in populations where the prevalence of anemia exceeds 40% [2]. However, some countries have now adopted iron supplementation starting at 4 months [3,4].

In the current issue of *Indian Pediatrics*, Kilic et al [5] report results of a retrospective study from Turkey, which evaluated the comparative efficacy of various iron preparations (ferrous, ferric or liposomal iron) for iron prophylaxis in healthy term infants. 371 infants aged 6-12 months were initiated on different iron formulations (1 mg/kg/day of elemental iron) at 4 months of age; the hemoglobin and serum ferritin levels were assessed after a mean duration of 5 months. 143 infants (38.5%) had iron deficiency (ID) and 35 (9.5%) developed IDA. Iron deficiency was noted in 46%, 44.5% and 5% of infants receiving liposomal iron, ferric iron and ferrous iron formulations, respectively. None of the infants receiving ferrous iron developed IDA. The study demonstrated superior efficacy of ferrous iron in preventing ID and IDA in infants. However, adverse effects leading to non-adherence to therapy due to different iron preparations were not studied [5].

There are various oral iron preparations available for prophylaxis and treatment of IDA. The most commonly used oral iron preparations are ferrous salts with ferrous sulphate being the current standard treatment for IDA [6]. Due to its large size, the diffusion of iron polymaltose complex (IPC) across the intestinal mucosa is 40 times

slower than ferrous iron [7]. Consequently, the bioavailability of ferric preparations is 3 to 4 times lower than those of ferrous salts [8]. Liposomal iron is a new generation oral iron preparation in which ferric pyrophosphate is carried within a phospholipid and lecithin membrane and the iron gets directly absorbed across the intestine without coming in contact with intestinal mucosa [9]. The gastrointestinal adverse effects are present in a third of patients receiving ferrous iron leading to poor tolerability and non-adherence to therapy [10]. Ferric iron and liposomal iron are generally better tolerated [11].

The comparative efficacy of various iron preparations for the prevention and treatment of ID /IDA has been studied. A prospective, multicenter study evaluated response to different oral iron preparations in children with IDA. At the end of therapy, those receiving ferrous preparations achieved a higher increase in hemoglobin, compared to those receiving bis-glycinate iron, ferric and liposomal iron [12]. Rosli et al conducted a meta-analysis in which iron polymaltose complex (ferric) was found to be less effective than ferrous sulphate in increasing hemoglobin and serum ferritin levels in children with IDA [13]. This study by Kilic et al has reported ID and IDA in a significant proportion of infants receiving iron prophylaxis as seen in other studies as well [4,14]. Therefore, there is a urgent need to evaluate the efficacy and appropriate dosing of various infant iron preparations.

Another important question with regard to iron prophylaxis is at what age to begin preventive iron supplementation in infancy? The WHO and the Anemia Mukht Bharat Program in our country recommend initiating iron prophylaxis at 6 months age [2,17]. The American Academy of Pediatrics recommends iron supplementation of 1 mg/kg/day starting from 4 months of age to all exclusively or primarily breastfed term infants [3]. 'Iron Like Turkey' Program also recommends iron supplementation starting at 4 months age [4]. Such recommendations are based on the prevalence of ID and IDA in exclusively breastfed infants in this age group. Hay et al

reported the prevalence of ID in a cohort of 11,284 term Norwegian infants as 4% at 6 months and 12% at 12 months of age [18]. Some Indian studies also have reported an increasing prevalence of ID/ IDA in this age group. Hemachitra et al observed that 65% of infants aged 3-6 months were anemic [19]. In a prospective study from North India, the prevalence of ID was found to be 12.09%, 25.81% and 34.04% at ages 4, 5, and 6 months, respectively [20]. However, another study from North India reported that only 6.2% of infants born at term were anemic at 14 weeks and only one out of 102 had anemia at 6 months [21]. The varied results are due to the different hemoglobin cut-offs to define anemia [19,21].

Early iron supplementation has been shown to result in better hemoglobin after a few months of supplementation. In a meta-analysis Pasricha et al have shown that daily iron supplementation improves hemoglobin and iron indices in children aged 4-23 months and thereby substantially reduces the risk of ID and IDA [16]. Similar results were reported by Friel et al in exclusively breastfed infants aged 1-6 months after iron supplementation [15].

Early iron supplementation results in improved Bayley Psycho-motor Developmental Index (PDI) and visual acuity at 13 months of age as demonstrated by Friel et al. However, there are variable results on effect of early supplementation on growth of infants. Friel et al observed no effect on weight, length and head circumference after early iron supplementation but the meta-analysis by Pasricha et al concluded impaired gain in weight and length with daily iron supplementation in infants [15,16]. Such adverse effects of early iron supplementation on growth, development and increased risks of certain infections have been widely reviewed [22]. Therefore, before deciding on a change in the age at which to start iron prophylaxis, the pros and cons of early age iron supplementation should be carefully viewed.

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