Iron Supplementation in Children with Malaria: Timing the Treatment1–3

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Iron is essential for brain development, and poor iron status early in life is associated with lasting disruptions in cognitive and behavioral development (1–3). In a study assessing the global and national burden of diseases in children, iron deficiency anemia was identified as a leading cause of years lived with disability in children and adolescents, affecting >600 million children in 2013 (4). Similarly, malaria is a global public health problem with devastating effects on children, particularly in Africa. For example, malaria is a leading cause of school absenteeism (5), and it causes 50% of deaths in school-aged children in sub-Saharan Africa (6).

Research studies have identified a potential link between iron status and the frequency of malarial infections and associated morbidities. In a large randomized, placebo-controlled trial (n = ~8000/group), Sazawal et al. (7) found that routine supplementation with iron and folic acid in children aged 1–35 mo with high rates of malaria was associated with an increased risk of illness and death. Others found that poor iron status was associated with a reduced risk of parasitemia, severe malaria, all-cause mortality, and malaria-associated mortality (8, 9). It has been hypothesized that poor iron status and/or the sequestration of iron because of the physiologic actions of hepcidin in response to inflammation may protect against malaria and its associated morbidities by restricting the availability of iron to the parasitic infection (10). Importantly, a recent Cochrane review (11) sought to evaluate the safety and efficacy of iron supplementation in children living in malaria-endemic areas. This study included 35 trials (31,955 children) and concluded that iron did not cause an excess of clinical malaria in populations in which anemia was identified as a leading cause of years lived with disability in children and adolescents, affecting >600 million children in 2013 (4). Similarly, malaria is a global public health problem with devastating effects on children, particularly in Africa. For example, malaria is a leading cause of school absenteeism (5), and it causes 50% of deaths in school-aged children in sub-Saharan Africa (6).

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iron incorporation into red blood cells in the group that received delayed iron supplementation, in contrast to earlier studies suggesting that hepcidin may be the most consistent predictor of iron incorporation in children with anemia (14). Further research is necessary to better understand the balance of factors (i.e., iron status, inflammation, and use of fortified foods or micronutrient powders) affecting the temporal response to iron supplementation. Most importantly, morbidity was not significantly different between study groups, although there was a trend toward increased return visits to the health clinic in the group that received immediate concomitant iron supplementation and antimalarial treatment. As such, future trials must be statistically powered to assess morbidity after immediate or delayed onset of iron supplementation. Similarly, if delaying iron supplementation were to prevent morbidity, ethical questions would remain regarding the acceptability of transiently poor iron status during early childhood, especially given the critical role of iron in brain development and the lasting effects of poor iron status early in life (1–3).

The importance of identifying methods to optimize iron status for brain development in young children while protecting against malaria and its associated morbidities cannot be understated. Data from the study by Cusick et al. (13) bring the field one step closer to understanding the potential benefits of concomitant iron and antimalarial therapy, although important research and ethical questions remain with regard to the balance between iron needs for early childhood development and the prevention of malaria and its associated morbidity.

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