Is It Time to Change Guidelines for Iron Supplementation in Malarial Areas?1,2

Dear Editor,

In 2006, the recommendations of the WHO for routine iron supplementation of infants and young children were radically changed. Following publication of the results of a large clinical trial of iron and folic acid supplementation in Zanzibar (1), a WHO consultative group issued recommendations that no children under 2 years of age living in malaria-endemic areas should be provided iron supplementation without appropriate screening for iron deficiency (2). In response to this policy, iron supplementation programs have come to a halt around the world, potentially putting millions of children at risk for the adverse impacts of iron-deficiency anemia.

There is now an urgent need for experts in nutrition worldwide to forthrightly discuss the safety of iron interventions and to reexamine the current WHO guidelines for iron supplementation in malaria-endemic areas. In this commentary, we raise 4 questions that policy makers should address when deciding the future of iron supplementation programs.

How strong is the evidence?

A recent review by the Cochrane Collaboration (3) challenged the body of evidence used by WHO to make its recommendations. This meta-analysis found that iron supplementation of children does not increase the risk of clinical malaria in the presence of regular surveillance of malaria and appropriate treatment. In addition, the authors concluded that screening for iron deficiency prior to iron supplementation is not needed. The high rates of malaria transmission and poor malaria control in Zanzibar, which may have contributed to the findings of harm (4), no longer exist in many countries due to scaled-up malaria control programs. Therefore, the targeted iron supplementation policy may no longer apply when improved and integrated malaria treatment is part of iron programs.

Is screening feasible?

Results from a substudy of the Zanzibar trial suggested that the detrimental effects of iron were confined to children who were iron replete (1,4), which led to the WHO recommendation for screening. However, widespread screening for iron deficiency is unlikely to be practical or affordable in the developing world (3). More accurate measures of iron status require blood collection and laboratory testing and are therefore more expensive, are risky because they involve the handling of blood, and are potentially not feasible because of logistics and cultural taboos (5). Thus, noninvasive screening methods for iron deficiency are urgently needed.

Are there alternative ways to deliver iron?

Because the absorption and metabolism of iron depends in part on the form of supplementation, the effect of supplemental iron on susceptibility to infection can be expected to vary by delivery method. Home-fortificants, such as micronutrient powders (e.g. Sprinkles), may be less likely to increase the risk of infection because they are mixed with food and thus are absorbed differently, yielding lower peak concentrations of iron (6). Preliminary data from our work in Kenya suggests that use of Sprinkles is not associated with measurable increases in hospitalizations or clinic visits due to malaria (7).

How should risks and benefits be weighed?

While it is possible that withholding universal iron supplementation of young children would prevent some hospitalizations and deaths due to malaria, this policy would also increase the number of negative health outcomes related to iron deficiency anemia, in particular adverse effects on child development, such as impairments in cognitive function and motor development, growth, and immune function (8).

Determining how to weigh the effects of one policy against the other is a challenging assignment, especially given the difference in measures. The Zanzibar trial suggests that ceasing universal iron supplementation would reduce malaria-related hospitalizations and deaths in high-malaria areas; that study found that those receiving supplementation (iron plus folic acid) were 12% more likely to die or need hospital treatment for an adverse event than those receiving placebo (1). In contrast, Ojukwu et al. (3) estimated that the lack of iron supplementation in many areas of the world has contributed to a 49% increase in preventable iron deficiency anemia.

The great difference between the 2 policies in terms of the time course to negative consequences also makes this decision difficult. The impact of a malaria-related hospitalization or death is immediately noticeable, while the insidious consequences of a case of childhood iron deficiency anemia may last for decades. The effects of the latter outcome, while not experienced acutely, must be weighed in full, and a misstep on this policy decision could lead to a generation of chronically disabled individuals.

Medical and public health practitioners have been trained for centuries to abide by the ethical imperative of non-maleficence, primum non nocere. This disposition may have influenced policy makers to avoid a potentially harmful intervention like universal iron supplementation. But such a demand must be balanced with its equally important corollary of beneficence. Public health policy must be as willing to intervene as it is to refrain from intervening when the most complete analysis of evidence suggests otherwise.

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Literature Cited

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