Effect of iron supplementation among children living in malaria-endemic area on incidence of malaria

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Children in a malaria-endemic community in Ghana who received a micronutrient powder with iron did not have an increased incidence of malaria, according to a study in the September 4 issue of *JAMA*. Previous research has suggested that iron supplementation for children with iron deficiency in malaria-endemic areas may increase the risk of malaria.

"In sub-Saharan Africa, malaria is a leading cause of childhood morbidity and mortality, and iron deficiency is among the most prevalent preventable nutritional deficiencies. The provision of iron to children with iron deficiency anemia can enhance motor and cognitive development and reduce the prevalence of severe anemia. However, studies have suggested that iron deficiency anemia may offer protection against malaria infection and that the provision of iron may increase malaria morbidity and mortality," according to background information in the article. "In 2006, the World Health Organization and the United Nations Children's Fund released a joint statement that recommended limiting use of iron supplements (tablets or liquids) among children in malaria-endemic areas because of concern about increased malaria risk. As a result, anemia control programs were either not initiated or stopped in these areas."

Stanley Zlotkin, M.D., Ph.D., of the Hospital for Sick Children, Toronto, and colleagues conducted a study to determine the effect of

providing micronutrient powder (MNP) with or without iron on the incidence of malaria among children living in a high malaria-burden area. The randomized trial, which included children 6 to 35 months of age (n = 1,958 living in 1,552 clusters), was conducted over 6 months in 2010 in a rural community setting in central Ghana, West Africa. A cluster was defined as a compound including 1 or more households. Children were excluded if iron supplement use occurred within the past 6 months, they had severe anemia, or severe wasting. Children were randomized by cluster to receive a MNP with or without iron for 5 months followed by 1-month of further monitoring. Insecticide-treated bed nets were provided at enrollment, as well as malaria treatment when indicated.

Throughout the intervention period, adherence to the use of MNP and insecticide-treated bed nets were similar between the iron group and the no iron group. The researchers found that the overall incidence of malaria was lower in the iron group compared with the no iron group, but after adjustment for baseline values for iron deficiency and moderate anemia, these differences were no longer statistically significant. "Similar associations were found during the 5-month intervention period only for both malaria and malaria with parasite counts greater than 5000/μL (severe malaria). A secondary analysis demonstrated that malaria risk was reduced among the subgroup of those in the iron group who had iron deficiency and anemia at baseline."

Overall, hospital admission rates did not differ significantly between groups. However, during the 5-month intervention period, there were more children admitted to the hospital in the iron group vs. the no iron group (156 vs. 128, respectively).

"The findings from the current study not only address a gap in the literature, but also have potentially important policy implications for countries like Ghana that have not implemented iron supplementation or

fortification as part of anemia control programs in part due to the joint recommendation from the WHO and UNICEF. For ethical reasons, we ensured that all participants were not denied existing malaria prevention (insecticide-treated bed nets) or malaria treatment. As such, our results most likely can be applied to other malaria-endemic settings in which similar malaria control measures are in place. Overall, given our findings and the new WHO guidelines recommending iron fortification for the prevention and treatment of anemia among children younger than 2 years (in whom the prevalence of anemia is ?20 percent), there should be renewed interest and consideration for implementing iron fortification in Ghana as part of the national nutrition policy."

In an accompanying editorial, Andrew M. Prentice, Ph.D., of the London School of Hygiene and Tropical Medicine, and colleagues write that the increase seen in this study in hospital admissions among the iron supplementation group, which by definition constitutes a potentially serious adverse event, adds to the concerns about the safety of iron administration in highly malaria-endemic environments.

"Participants in an expert panel convened by the World Health Organization in 2007 speculated that iron given with foods, either by centralized or point-of-use fortification, would be safe. However, the Ghanaian trial reported by Zlotkin et al in this issue of *JAMA* now becomes the fourth trial to question this suggestion, and leaves global health policy makers with an unresolved dilemma. Until a means of safely administering iron in infectious environments has been developed, there remains an imperative to reduce the infectious burden as a prerequisite to moving poor populations from their current state of widespread iron deficiency and anemia."

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