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Use of Sprinkles in high malaria transmission areas – Considerations for distribution programs

Key Message: Consistent with current WHO recommendations, home-fortification using Sprinkles during early childhood should be combined with malaria control strategies in areas where malaria transmission is high.

Iron supplementation in areas of high malaria transmission

The role of iron in the prevention and treatment of anemia in high malaria transmission areas remains a controversial issue. There are concerns that the administration of iron may exacerbate malaria and other illnesses in otherwise healthy, iron sufficient children. A large-scale randomized, double-blind, placebo-controlled trial conducted in Pemba, Zanzibar was recently published in the Lancet ; researchers found that under certain conditions, supplementation may be associated with adverse effects including increased risk of hospitalization and mortality, primarily due to malaria and other infectious diseases.ⁱ These findings raise concerns about the safety of current WHO guidelines for universal iron and folic acid supplementation. As a result, WHO released a statement suggesting that "...caution should be exercised in settings where the prevalence of malaria and other infectious diseases is high"ⁱⁱⁱ when providing iron and folic acid supplementation to young children in malaria endemic regions.ⁱⁱⁱ However "...at the present time WHO policy with regard to prevention and treatment of iron deficiency anaemia remains unchanged". Briefly, the statement advises that, "...until the WHO recommendations are revised it is advised that iron and folic acid supplementation be targeted to those who are anaemia and at risk of iron deficiency." In addition, it recommends that these children "...should receive concurrent protection from malaria and other infectious diseases through prevention and effective case management". Furthermore, the WHO advised that "...these conclusions should not be extrapolated to fortification or food-based interventions for delivering iron, where the patterns of iron absorption and metabolism may be substantially different".



Implications for using Sprinkles

Sprinkles is a food-based intervention since the micronutrient powder is added directly to foods.^{iv} From research in West Africa, it has been determined that the iron from Sprinkles is well absorbed from a maize-based food and that infants have the capacity to regulate the amount that is absorbed according to needs.^v The current INACG/WHO/UNICEF recommendation is to provide daily iron supplementation to all infants 6-24 months where the prevalence of anemia is at least 40%.^{vi} From previous studies to date on the Sprinkles intervention, there is evidence that the administration of 60 Sprinkles sachets is adequate to rapidly improve hemoglobin concentrations and iron stores in a large proportion of young children. After the ingestion of 60 sachets, the hematologic benefits were sustained over a period of at least 6 months. Thus, Sprinkles may not be required for a prolonged period of time thus potentially lowering the risk of adverse effects.

Recommendations

Considering the evidence to date, Sprinkles distribution programs in high malaria transmission areas should be integrated with malaria control programs such as the use of insecticide treated bed-nets or the treatment of detected cases of malaria. When implementing a Sprinkles program and wherever feasible, it is recommended to monitor for safety and adverse effects. Considering the conflicting results to date and the possibility that iron delivery may exacerbate malaria and other infectious diseases, it is crucial to ensure that iron interventions are safe for young children in all regions, especially where malaria is present. From both a biological and practical standpoint and until more data becomes available on the safety of the long-term delivery of iron to young children, we recommend the provision of Sprinkles for a shorter rather than longer period of time. A short-course regimen (e.g. 60 sachets) would ensure higher compliance and acceptability as compared to a longer-course regimen, would be provided at a relatively low cost and would most likely minimize any negative adverse effects on health. Until evidence is available, it would be prudent to withhold giving any iron intervention (including Sprinkles) to a child presenting with fever to minimize the potential that iron could exacerbate the infection. Further research and evaluation of programs should be conducted to develop the most effective strategies for controlling iron deficiency and anemia in regions where malaria transmission is high. The optimal dose, duration and delivery of iron need to be established to ensure that children in these regions gain the benefits of iron during the first years of life without increased risk to malaria or other infectious diseases. The WHO is planning a consultation which will set a research agenda in this area. The Sprinkles Global Health Initiative will continue to seek direction from the WHO on recommendations for iron delivery to children and pursue research to establish the safety of Sprinkles among populations where there is a high prevalence of malaria and infectious diseases.

ⁱ Sazawal S, Black RE, Ramsan M, Chwaya HM, Stoltzfus RJ, Dutta A, Dhingra U, Kabole I, Deb S, Othman MK, Kabole FM. Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial. *Lancet* 2006;367:133-43.

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- ⁱⁱ World Health Organization. Iron supplementation of young children in regions where malaria transmission is intense and infectious disease highly prevalent. WHO Statement, 2006.
- ⁱⁱⁱ de Benoist B, Darnton-Hill I, Lynch S, Allen L, Savioli L. Zinc and iron supplementation trials in Nepal and Tanzania. *Lancet* 2006;367:816.
- ^{iv} Zlotkin SH, Christofides AL, Hyder SMZ, Schauer CS, Tondeur MC, ShariEFF W. Controlling iron deficiency anemia through the use of home-fortified complementary foods. *Indian J Pediatr* 2004;71(11):1015-1019.
- ^v Tondeur MC, Schauer CS, Christofides AL, Asante KP, Newton S, Serfass RE, Zlotkin SH. Determination of iron absorption from intrinsically labeled microencapsulated ferrous fumarate (sprinkles) in infants with different iron and hematologic status by using a dual-stable-isotope method. *Am J Clin Nutr* 2004;80(5):1436-44.
- ^{vi} Stoltzfus RJ, Dreyfuss ML. (1998) Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia. INACG/WHO/UNICEF. International Life Sciences Institute, USA.