World Health Organisation

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Joint Statement

Iron supplementation of young children in regions where malaria transmission is intense and infectious disease highly prevalent

INTRODUCTION

Iron deficiency with its attendant anaemia is the most prevalent micronutrient disorder on a worldwide basis. In 2001, the UN General Assembly at the Special Session on Children recommended that the prevalence of iron deficiency and anaemia be reduced by one third in children by the year 2010. If achieved, this would contribute greatly to the realization of the Millenium Development Goals. In most countries, national policies have been implemented to provide iron supplements to pregnant women, and to a lesser extent to young children, as the primary strategy for preventing iron deficiency and anaemia.

Although the benefits of iron supplementation have generally been considered to outweigh the putative risks, there is some evidence to suggest that supplementation at levels recommended for otherwise healthy children carries the risk of increased severity of infectious disease in the presence of malaria and/or undernutrition (1).

RESULTS OF TWO IRON AND ZINC SUPPLEMENTATION TRIALS IN ZANZIBAR AND NEPAL

Two large community-based randomized controlled trials designed to evaluate the impact of zinc and iron plus folic acid supplementation on morbidity and mortality in young children were recently conducted in Zanzibar, where malarial transmission is intense and occurs year round, and Nepal, where exposure to malaria is low (2,3). On advice from the trial Data Safety Monitoring Board, the iron-folic acid and iron-folic acid plus zinc arms were discontinued after approximately 20 months. Data on children randomized to zinc alone have not been included in the published analysis. While confirming that iron supplementation is effective for reduction of iron deficiency and anaemia in iron deficient children, the trial in Zanzibar showed that under certain conditions supplementation may be associated with adverse effects, specifically increased risk of hospitalization (primarily due to malaria and infectious disease), and mortality. The results of this trial suggest also that the risk of adverse health effects may not be distributed uniformly across the whole sample of children. The trial in Nepal did not provide evidence of a difference in mortality between children receiving iron and folic acid and those receiving placebo.

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The data from the Zanzibar trial raised concerns about the efficacy and safety of iron supplementation at a population level. A meeting was convened by WHO in April 2004 to critically review the data available from both trials and to assess the possible public health implications (4). The main conclusions of that meeting were:

- The current WHO recommendations for iron supplementation of young children are based on the known physiology of iron metabolism as well as clinical practices at the time the recommendations were formulated, and apply to otherwise healthy children (5,6).
- Numerous efficacy trials have demonstrated that it is possible to significantly reduce the prevalence of iron deficiency with iron supplementation or food fortification.
- Caution should be exercised in altering policy on the basis of a single set of observations, and at the present time WHO policy with regard to prevention and treatment of iron deficiency anaemia remains unchanged (7).
- The findings of the trial in Zanzibar suggest that caution should be exercised in settings where the prevalence of malaria and other infectious diseases is high. Until the WHO recommendations are revised it is advised that iron and folic acid supplementation be targeted to those who are anaemic and at risk of iron deficiency. They should receive concurrent protection from malaria and other infectious diseases through prevention and effective case management.
- In cases of severe undernutrition, iron supplementation should be delivered in accordance with the WHO guide-

lines, which state that supplementation be withheld until the acute problems related to infection have been effectively treated, and growth has resumed (8).

- The findings from the Zanzibar trial should be considered specific to iron and folic acid supplementation of young children in regions of the world where malaria transmission is intense and infectious disease highly prevalent. The extent to which they may be more widely applied to recommendations in other environments is not clear. In Nepal, although the rates of morbidity and mortality did not differ between treatment and placebo groups, iron and folic acid supplementation was associated with a lower prevalence of severe and moderate anaemia.
- These conclusions should not be extrapolated to fortification or food-based approaches for delivering iron, where the patterns of iron absorption and metabolism may be substantially different.
- While iron deficiency is frequently the primary factor contributing to anaemia, it is important to recognize that the control of anaemia requires a multisectorial approach which, through integrated interventions, addresses the various factors that play a significant role in producing anaemia in a given community. In addition to iron deficiency, infectious diseases such as malaria, helminth infections, other chronic infections, particularly HIV/AIDS and tuberculosis, as well as other nutritional deficiencies, are especially important. It is necessary to take the health environment into account when designing iron supplementation programmes as public health measures so that the benefits can be optimized without incurring significant risk.

Additional research and evaluation of existing programmes are urgently needed to develop the most effective strategies for controlling iron deficiency and anaemia in regions where malaria transmission is intense and the prevalence of infection high. They should aim at ensuring that children in these regions, especially low birth weight infants, gain the benefits of iron supplementation during the first year of life without being exposed to any adverse health risks. Research should be designed to answer the following questions:

- What is the optimal dose of an iron supplement that is both safe and effective?
- What is the optimal duration of iron supplementation?
- What it is the optimal mode of iron supplement delivery?
- What is the pathophysiological basis for the increase in adverse events among iron sufficient children who are exposed to malaria and infectious diseases?
- Are there important interactions between iron and other micronutrients, especially zinc?
- Does iron supplementation affect the course of other potentially fatal infectious disorders such as HIV/AIDS and tuberculosis?

WHO CONSULTATION

WHO is currently planning to convene a consultative meeting to review the public health implications of these trials and other relevant studies and to formulate a detailed research agenda.

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ACKNOWLEDGEMENTS

This statement was prepared by the following Departments of the World Health Organization, Geneva, Switzerland: Child and Adolescent Health and Development (CAH), Control of Neglected Tropical Diseases (NTD), Nutrition for Health and Development (NHD), Roll Back Malaria (RBM) and with the input of the Nutrition and Health Section of UNICEF, New York, United States of America.