WHO/NMH/NHD/MNM/09.2

World Health Organization

WEEKLY IRON-FOLIC ACID SUPPLEMENTATION (WIFS) IN WOMEN OF REPRODUCTIVE AGE: ITS ROLE IN PROMOTING OPTIMAL MATERNAL AND CHILD HEALTH

WHO/AFRO GUBB L

PURPOSE

This position statement is based on the consensus of a World Health Organization (WHO) Global Consultation on Weekly Iron and Folic Acid Supplementation (WIFS) for Preventing Anaemia in Women of Reproductive Age held in Manila, Philippines, 25-27 April 2007 and summarizes recommendations based on a desk review commissioned by the WHO Regional Office for the Western Pacific (WPRO) and additional evidence presented and discussed in the expert consultation. It is intended for a wide audience including program implementing partners, scientists and governments involved in the design and implementation of micronutrient programs as public health interventions.

BACKGROUND

Anaemia is a multi-factorial disorder that requires a multi-pronged approach for its prevention and treatment. Iron deficiency and infections are the most prevalent etiological factors. However other conditions may have a contributory role. They include nutritional deficiencies of vitamin A, vitamin B_{12}, folate and riboflavin as well as thalassemias and hemoglobinopathies. The global prevalence of anemia is estimated to be 30.2% in non-pregnant women rising to 47.4% during pregnancy (de Benoist B et al, 2008). Weekly iron supplementation, in synchrony with the turnover of mucosal cells, has been proposed as a more efficient preventive approach in public health programs (Viteri FE,1995; Viteri FE et al 1998). The approach is attractive because side effects are thought to be less prominent, and it may be both operationally easier to manage at the community level and more sustainable over extended time periods. Improving iron and folate nutrition of women of reproductive age could improve pregnancy outcomes as well as enhance maternal and infant health. The prudent pragmatic approach is therefore considered to be the recommendation of WIFS in appropriately selected settings where the necessary program monitoring is feasible. Additional short-term efficacy trials are unlikely to provide more useful information about potential long-term effectiveness. The findings of the first three pilot projects were reviewed at a previous meeting held at WPRO in October 2003, a report of which is available on the WPRO website (www.wpro.who.int). The findings, conclusions and recommendations of these projects were published in a supplement of the international journal *Nutrition Reviews*, December 2005, (II)S95-S108. To date, more than 30 papers have been published globally, reporting findings, conclusions and recommendations on the use of the WIFS approach for the prevention of iron deficiency and anaemia.

THE WHO GLOBAL EXPERT CONSULTATION

A WHO Global Expert Consultation on Weekly Iron and Folic Acid Supplementation for Preventing Anaemia in Women of Reproductive Age was convened in Manila, Philippines in 2007 to discuss the findings of a desk review and discuss the public health implications of the results, especially in developing countries. The consultation objectives included a formal assessment of the review, an analysis of all available evidence related to efficacy, effectiveness, safety and feasibility of preventive supplementation with WIFS programs in improving iron and folate status before and during the early months of pregnancy, a discussion on specific conditions under which WIFS may be implemented effectively and are most likely to have a significant impact on iron and folic acid status before and during pregnancy, and the identification and prioritization of knowledge gaps for which additional research is needed. The proceedings of the consultation, including conclusions and recommendations by the participants, are expected to be published in a special supplement of the *Food and Nutrition Bulletin* in 2009.

WEEKLY IRON AND FOLIC ACID SUPPLEMENTATION

WIFS is an approach that can be effective for ensuring adequate iron status of women, particularly before pregnancy and during the first trimester in communities where food-based strategies are not yet fully implemented or effective.
Short-and medium-term WIFS has been effective in reducing the prevalence of anaemia among women of reproductive age in several community settings where the necessary support, social marketing and interpersonal advocacy ensured adequate compliance.
Although the proven method for decreasing the risk for neural tube defects (NTDs) is through daily dosing with folic acid before pregnancy through the first trimester of pregnancy, WIFS provides an additional opportunity for ensuring adequate folate status before pregnancy and in the very early stages of pregnancy particularly for those who may become pregnant or do not know that they are already pregnant and are not covered by other programs. Many pregnancies are not planned. Various studies have demonstrated that WIFS can improve iron status in women of reproductive age when supplementation is continuous for periods from several months to two years (Beaton GH, McCabe GP, 1999). A current review (Margetts B, 2007) concluded that WIFS taken for at least 12 weeks improved iron status, as judged by increased hemoglobin and in some studies serum ferritin levels. The impact of weekly supplementation with 60 mg of iron was similar to daily supplementation except in severely anaemic women.

CONSULTATION RECOMMENDATIONS

The recommendations summarized here below represent the conclusions of the experts in the consultation.

- Strategies to combat both iron deficiency and anaemia, and to improve iron reserves and folate status in women of reproductive age should be integrated. Deworming, measures to prevent hookworm infections, the promotion of improved bioavailable iron intake, as well as interventions to control other prevalent causes of anemia, particularly malaria and other infections, and vitamin A deficiency need to be considered.
- In population groups where the prevalence of anaemia is above 20% among women of reproductive age and mass fortification programs of staple foods with iron and folic acid are unlikely to be implemented within 1-2 years, WIFS should be considered as a strategy for the prevention of iron deficiency, the improvement of pre-pregnancy iron reserves and the improvement of folate status in some women. If data on anaemia prevalence in women of reproductive age is not available, anaemia prevalence in other groups such as pregnant women (>40% anaemia prevalence) or children under 5 years of age may be used as a proxy. In the absence of such information, criteria such as dietary patterns and socioeconomic status may be considered. Women from low income groups who may not have access to processed iron-fortified food products and other sources of highly bioavailable iron could be considered a priority group for this intervention.
- The weekly supplement should contain 60 mg iron in the form of ferrous sulphate ($FeSO_4.7H_20$) and 2800 µg folic acid, although evidence for the effective dose of folic acid for weekly supplementation is very limited. Daily folic acid supplementation is effective for reducing the risk of NTDs (Botto LD et al, 1999). The recommendation for the weekly folic acid dosage is based on the participants' rationale of providing 7 times the recommended daily dose to prevent NTDs and the limited experimental evidence demonstrating that this dose can improve red blood cell folate concentrations to levels that have been associated with a reduced risk for NTDs. The iron dose recommended for WIFS may cause short-term gastrointestinal discomfort and black stool, but there is no reported risk of long-term toxicity. The participants also agreed that the recommended weekly folic acid dose has no known toxicity, although evidence for this was limited. Two published studies evaluating weekly folic acid supplementation were considered. In Mexico, women received 5.0 mg folic acid for 3 months, and their red blood cell folate levels were still in the range associated with a 50% lower risk of NTDs one week after the last tablet was consumed (Martinez-de Villarreal LE et al, 2001). They also showed a 50% decrease in the incidence of anencephaly and spina bifida cases, and a significant reduction in infant mortality and disability after two years (Martinez-de Villarreal LE et al, 2002). In New Zealand, a once a week supplement of 2.8 mg of folic acid taken for 12 weeks increased women's red blood cell folic acid levels to concentrations associated with a reduced risk of bearing a child with a NTD (Norsworthy B et al 2004).
- Two situations may necessitate supplementation with iron alone. Fortification of staple foods with folic acid has been shown to be very effective and is being widely implemented. Iron alone should be used in weekly supplementation programs where mandatory folic acid fortification has been introduced and shown to be effective if fortification with iron has not been implemented or is ineffective. Antifolate antimalarial treatment is employed in some malaria endemic regions. There is some evidence to suggest that the efficacy of these drugs may be reduced by folic acid supplementation. In these settings, it is considered prudent to provide iron only weekly supplements.
- Upon confirmation of pregnancy, women should receive standard antenatal care. The current WHO recommendation is to provide daily supplementation with 60 mg iron and 400 ug folic acid to women during pregnancy and the first 3 months postpartum.
- WIFS programs must be integrated with other efforts to control iron deficiency and anaemia and should be planned as long-term self-sustained interventions that women of reproductive age will utilize during their childbearing years.
- Successful implementation of WIFS programs will require motivation and creation of demand by women of reproductive age as the starting point for promoting this new approach, establishing adequate mechanisms to start and sustain programs, including adequate funding, community level support and public-private partnerships including nongovernmental organizations, an uninterrupted supply of good quality iron and folic acid supplements, the development and implementation of effective communication strategies with the media and other information channels, establishment of methods for promoting compliance by women of reproductive age, especially when consumption is not supervised, and integration with effective existing delivery systems in health, education and the private sector (e.g. in factories, markets, and local shops) as well as through community organizations.
- Baseline data are needed before launching WIFS interventions; programs must be monitored closely with regard to both processes and outcomes, during the first year, and then annually for the first 5 years. Monitoring and evaluation systems should be implemented to determine if the intended outcomes are being achieved.

SUMMARY OF STATEMENT DEVELOPMENT

This statement was prepared by the WHO Department of Nutrition for Health and Development in close collaboration with the Regional Office for the Western Pacific (WPRO). Dr. Juan Pablo Pena-Rosas (WHO) and Dr. Luca Tommaso Cavalli-Sforza (WPRO) summarized the conclusions and recommendations. This position statement is based on background documents, including a desk review commissioned to Professor Barrie Margetts and his team at the School of Public Health, University of Southampton (United Kingdom) in 2007 by WPRO. This review included all published work done on WIFS in women of reproductive age to better define the potential benefits of WIFS in preparing women of reproductive age for pregnancy. All available information related to WIFS was discussed at a global consultation held at WPRO jointly with WHO Headquarters in Manila, Philippines in 2007. The desk review provided the updated background for the expert consultation discussions. Studies considered in the review were identified through searching key databases, contacts with principal investigators, and contacts with a number of organisations and agencies that have been gathering literature in the relevant areas of work. Studies were a mix of efficacy and effectiveness designs. This was followed by four invited written commentaries by experts in the fields of iron and folic acid metabolism and public health. In making the recommendations, additional information gathered at the consultation was considered in conjunction with conclusions drawn from the review of both controlled and uncontrolled studies. The consensus conclusions and recommendations from the consultation were revised and summarized for this statement.

CONFLICTS OF INTEREST

All participants in the consultation were asked to submit and sign a Declaration of Interest statement which are on file. There were no known conflicts of interest disclosed among the participants and those developing this statement.

PLANS FOR UPDATE

It is anticipated that the recommendations in this position statement will remain valid until December 2010. The Department of Nutrition for Health and Development at WHO Headquarters in Geneva will be responsible for initiating a review following formal *WHO Handbook for Guideline Development* procedures at that time.

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Suggested citation

WHO. *Weekly iron–folic acid supplementation (WIFS) in women of reproductive age: its role in promoting optimal maternal and child health. Position statement*. Geneva, World Health Organization, 2009 (http://www.who.int/nutrition/publications/micronutrients/weekly_iron_folicacid.pdf, accessed [date]).

FOR FURTHER INFORMATION PLEASE CONTACT

Department of Nutrition for Health and Development (NHD)
World Health Organization
20, Avenue Appia, 1211 Geneva, Switzerland
Email: micronutrients@who.int
WHO home page: http://www.who.int