Micronutrient Forum

Istanbul, 16-18 April 2007

Integrating Biological and Epidemiological Research in Public Health Nutrition

Bruno de Benoist

Department of Nutrition for Health and Development

World Health Organization

- In the recent years, new scientific knowledge has accumulated, allowing us to enrich and refine the public health significance of major MN disorders and, therefore, to design strategies that are better adapted, more effective, and safer
- The main sources of information come from epidemiology and physiology. They are complementary and ideally should contribute equally to the conception of any strategy to control MN disorders
- In practice, it is not always the case because results of epidemiological surveys may call for a public health decision while biological knowledge is sometimes not available to interpret epidemiological information and assist in the decision

- WHO stresses the importance of strengthening research in both biology and epidemiology in order to advance the public health nutrition agenda
- To demonstrate this principle, this presentation reviews the essential strategic issues outlined in the WHO Technical Consultations that are needed to control MN disorders
- These Consultations covered several micronutrients, but the presentation only address: iron and iodine

World Health Organization

Assessing Iron Status of Populations

World Health Organization

Objectives and Review Process

- **Objectives**
  - To review indicators currently available to assess iron status in populations
  - To select the best indicators:
    - To assess iron status of populations
    - To evaluate the impact of iron interventions on iron status
- **Review process**
  - Five indicators were reviewed
    - Haemoglobin
    - Mean cell volume (MCV)
    - Zinc protoporphyrin (ZPP/H ratio)
    - Transferrin receptor (TfR)
    - Serum ferritin (SF)
  - The performance of the selected indicators were analysed from 10 double-blind randomized trials where iron was provided as supplements or fortified foods, representing 8 countries

Recommendations

- Indicators to assess prevalence and severity of iron deficiency in populations
  - Haemoglobin
  - Transferrin receptors (TfR) and serum ferritin (SF)
- Indicators to evaluate impact of interventions
  - Haemoglobin and serum ferritin
- Control of high serum ferritin in the presence of infection
  - To measure acute phase protein

Main Issues

- Performance of indicators and their interpretation need to be further documented and validated
  - No consensus on best indicators for assessing iron status
    - Haemoglobin is the most widely used, but is not specific
    - More specific indicators have limitations and need to be used in combination with others
  - No agreement on thresholds to identify deficiency and severity of deficiency. In these conditions, it is difficult:
    - To interpret and compare data
    - To generate estimates of the magnitude of iron deficiency
  - Interpretation of SF is difficult because of interactions between iron and infection

Research Needs

- Produce international reference material to standardize TfR assays
- Review of existing data to validate proposed thresholds for SF and TfR
  - Need to define/validate thresholds for all indicators of iron status in children aged 6-24 months
- Examine performance of indicators used to assess outcomes of iron interventions
  - Examine changes in body iron stores in response to iron interventions
- Review existing data on acute phase proteins (APP)
  - Select the best APP to interpret SF data during infection
  - Identify the thresholds to apply for APP and SF during infection
- Develop field methods
  - SF, TfR, APP

Control of Iron Deficiency in Malaria Endemic Areas in Children Less than 2 Years

World Health Organization

Objectives

- To review the scientific evidence of the safety and efficacy of different ways of administering Fe in children less than 2 years in malaria endemic areas

- To provide guidance on the safest, and most feasible and effective ways of delivering additional Fe to children less than 2 years in malaria endemic areas

World Health Organization

Recommendations

- Control of infectious diseases and malaria are critical components of health care
- Folic acid should not be included in micronutrient supplements in populations treated with antifolate antimalarial medications
  - To avoid the potential interference of folic acid supplementation with the action of such medications
- Control of iron deficiency in Children less than 2 years
  - At birth, delay cord clamping
  - Oral iron therapy
    - Targeted to children where ID is detected or with clinical symptoms of severe anemia
    - Exception: SGA and LBW infants who need iron supplements, even if ID is not detected, because their iron stores are low
  - Complementary foods fortified with iron in children after 6 months

Main Issues

- When bolus doses of iron are provided as oral doses, they may result in excessive free iron which can result in oxidative damage
  - If added to a single meal, the dose of iron (tablets, powder) may have a similar effect to a bolus of medicinal iron supplement
- Oral iron supplements can alter the gut flora and adversely affect the immune system
- Inflammation in response to infection induces dramatic changes in the handling of iron
- Thalassemias and hemoglobinopathies are protective against malaria and therefore may reduce the risk of severe adverse events due to Fe supplementation
- It is unclear whether the risks of Fe are specific to malaria or whether they apply to other infections as well
- Iron deficient children appear to benefit from iron supplementation and have fewer adverse effects than iron-replete children

Research Needs

- Impact of different types of iron preparations (*powders, tablets, fortified foods, fat-based spreads*), doses, duration and frequency of administration, and of different modalities of iron administration (with or without foods)
- Role of co-morbidity due to other infections in the adverse effects caused by iron administration in malaria
- Involvement of iron regulatory protein (hepcidin) in response to iron administration
- Interaction between iron and other micronutrients
- Identification of affordable and field-friendly tools to screen for iron deficiency in children less than 2 years

Control of Iodine Deficiency in Pregnant and Lactating Women, and Children Less Than 2 Years

World Health Organization

Objectives

- Objectives were to review in pregnant and lactating women, and children less than two years old:
  - Iodine requirements
  - Indicators to assess iodine nutrition status
  - Strategies to eliminate IDD

Recommendations

- Iodine requirements
  - Increased from 200µg/d to 250µg/d in pregnant and lactating women
  - Unchanged in children less than 2 years
- Indicators of iodine status
  - Median urinary iodine
  - Serum thyroid stimulating hormone (TSH) in neonates
- Strategies to control iodine deficiency
  - Household access to iodized salt >90%, no need for additional iodine intake
  - Household access to iodized salt <90%:
    - Additional iodine
      - Pregnant/lactating women: iodine supplements
      - 6-24 months: complementary foods fortified with iodine or iodine supplement
      - 0-6 months: protected by the supplemented mother
    - Salt iodization programmes should be strengthened

World Health Organization

Main Issues

- Iodine requirements
  - Because of the lack of data on sufficient intake, iodine requirements are estimated from iodine absorption, metabolic needs and daily losses
- Indicators
  - Median urinary iodine (UI)
    - Marker of recent dietary intake, but does not provide direct information about thyroid function
    - During lactation, UI may underestimate iodine intake as iodine is excreted in breast milk
    - Lack of data on UI in pregnant and lactating women, and children <2 years
  - Serum thyroid stimulating hormone (TSH) in neonates
    - Indicates a risk of brain damage
    - No standardization when and how to collect blood samples after birth,
    - Lack of data to establish a threshold for normal values

Research Needs

- Functional consequences of iodine deficiency
  - Impact of excessive iodine intake on thyroid function
  - Iodine concentration of breast milk
  - Impact of iodine deficiency on cognitive development
  - Interaction between iodine and other micronutrients in situation of iodine deficiency
- Indicators of iodine deficiency
  - More data on UI in pregnant and lactating women, and children less than 2 years from iodine sufficient populations
  - Define UI that corresponds to an excessive iodine intake in these groups
  - Standardize the measurement of serum TSH in neonates
  - Need more data on TSH in neonates from iodine sufficient populations
- Approaches to controlling iodine deficiency
  - Establish optimum dose of iodized oil to give to pregnant women and lactating women, and children less than 2 years
  - Develop new pharmaceutical preparations of iodine

Conclusions

- In order to improve micronutrient status of populations and prevent micronutrient disorders, it is important
  - To give more attention to research needs, especially those related to biological mechanisms
  - To better coordinate and integrate epidemiological and biological research in order to ensure that interpretation of epidemiological data are supported by biology

Acknowledgements

- Centers for Disease Control and Prevention
- International Council for Control of Iodine Deficiency Disorders
- UNICEF

World Health Organization