ZINC *Protects!*

Zinc and Human Health

Recent Scientific Advances and Implications for Public Health Programs

Conclusions of the International Conference, Stockholm – June 2000

IZiNCG

IZiNCG – The International Zinc Nutrition Consultative Group – was established in 2000 by the Nutrition Programme of the United Nations University and the International Union of Nutrition Scientists. Its purpose is to promote improved zinc nutriture in vulnerable populations in low-income countries and to provide related technical assistance to governments and international agencies.

The IZiNCG Steering Committee is currently preparing guidelines on available ways to assess the zinc status of different populations, and methods to control zinc deficiency.

IZiNCG is supported by UNICEF, the United Nations University, the International Nutrition Foundation and International Zinc Association.

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Conference on Zinc and Health Stockholm, June 2000

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Juan Rivera Dommarco	Instituto Nacional de Salud Publica	Mexico
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Manuel Ruz	University of Chile	Chile
Janet King	Western Human Nutrition Research Center	USA
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Rosalind S. Gibson	University of Otago	New Zealand
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Zinc and Human Health

Recent Scientific Advances and Implications for Public Health Programs

The international conference on Zinc and Human Health, held in Stockholm on June 12-14, 2000, brought together some 130 researchers, nutritionists and healthcare specialists from 37 countries to review the latest research findings on zinc's health benefits and the implications for public health policy. This issue of 'Zinc Protects' looks at the conclusions of the conference.

Zinc Deficiency - Global Prevalence and Assessment

The Stockholm conference first addressed three underlying aspects of zinc nutriture: the determination of zinc requirements; the assessment of zinc status at the individual and population level; and national and global data on the prevalence of zinc deficiency.

The determination of requirements for zinc has been aided by the increasing use of zinc stable isotope techniques. The application of these techniques allows the measurement of the proportion of zinc absorbed across the intestine, the size of exchangeable zinc pools within the body, and the amount of zinc lost from the body each day. From such data, zinc requirements can be estimated. The US and Canadian RDAs[1] for zinc are currently being revised and will represent the most up-to-date estimates for zinc requirements and recommended intakes. Nonetheless, there are still gaps in our knowledge of zinc requirements for specific populations and the need continues for basic research in this area.

A single specific biochemical measure of individual zinc status is currently lacking. Potential new tools and approaches to assess zinc status include the measurement of: rapidly exchangeable zinc pools using stable isotope techniques; erythrocyte metallothionein concentrations; and monocyte metallothionein mRNA. There is a need for methods that assess the bioavailability and status of micronutrients concurrently, and for the combined evaluation of risk factors (dietary + stunting/low birth weight + morbidity).

[1] Recommended Daily Allowance

At the population level, the prevalence of conditions that are typically improved by zinc supplementation in low income countries may be used as indirect indicators of a population's risk of zinc deficiency. In populations where stunting is prevalent, growth of stunted children is most often significantly improved following zinc supplementation. Thus the prevalence of growth-stunting may be a useful indicator of poor zinc status in the population. The incidence of low birth weight may also be used as a proxy for a population's risk of zinc deficiency, as this condition can be responsive to prenatal zinc supplementation. Although mean plasma zinc concentrations can be difficult to interpret when infections are present, this may only be a concern with more severe infections. Results from most studies support the usefulness of mean plasma zinc concentration as a marker for zinc status at the population level. Biochemical assessment useful at the population level may extend to the analysis of other tissues such as hair and cellular elements, enzymatic changes, and possibly other markers such as the biochemical status of iron and vitamin A, although more research in this area is needed.

National food balance data may also be used to identify populations at high risk of zinc deficiency. Per capita estimates for zinc availability in the food supply are 9-12 mg/d for total zinc in food and 1-3 mg/d for absorbable zinc. Due to the heavier reliance on plant foods as a source of zinc in low-income countries, and the relatively poorer bioavailability of this zinc as compared to that from animal source foods, the amount of absorbable zinc among low-income populations is approximately one-third of that in industrialized nations. Based on this global intake data, an estimated 49% of the global population is at risk of inadequate zinc in their food supply.

Zinc Absorption, Metabolism and Status during Pregnancy, Lactation and Early Infancy

The conference concluded that pregnancy and lactation may be influenced by maternal zinc depletion, although the available human data are inconsistent. The evidence presented suggested that outcomes that respond to zinc interventions vary among populations. Available survey data indicate positive relationships between maternal zinc status and

birthweight in 20 out of 38 surveys, while 5 out of 13 surveys indicated a positive relationship with maternal outcomes. Of the 11 zinc supplementation trials identified, 6 of these reported improved birth or maternal outcomes. It was concluded that there is a very complex interaction between habitual diet, other environmental issues, and possibly genetic factors, and that further research is required to define the situations in which maternal and birth outcomes will benefit from improved zinc nutriture.

The first six months of life are a period of rapid growth, however the relatively high zinc requirements during this period can be met satisfactorily from breastmilk alone. The breast-fed, low birth weight infant, however, is at risk for zinc deficiency due to increased requirements, potentially lower intake and/or lower absorption efficiency. The positive association between net absorption of zinc and growth in low birth weight infants has been observed in several trials. From six months to two years of age, adequacy of zinc intake becomes highly dependent on the amount and bioavailability of zinc from complementary foods. Based on information to date, the following recommendations can be made:

1) promote exclusive breast-feeding up to six months,
2) identify complementary foods that ensure adequate intake of zinc (and other micro-nutrients) from six months onwards, and
3) explore ways to enhance the intake and absorption of zinc, and other nutrients, by young children.

Consequences of Zinc Deficiency

Various aspects of human health associated with zinc deficiency were examined during the conference. From the results of a series of randomised trials, it is evident that zinc supplementation enhances linear growth. Stunted children benefit more than non-stunted children, and children of up to 24 months benefit more than older children.

In populations with evidence of dietary zinc deficiency and with high rates of stunting and/or low plasma zinc concentrations, zinc supplementation should be implemented to promote children's growth, particularly for children under 24 months of age. There is a need for more

zinc supplementation trials in Africa and Asia, and a pooled analysis is required to identify effect modifiers better.

On the issue of nutrition rehabilitation, trials have shown that zinc-supplemented malnourished children gain weight more rapidly, with a significant reduction in anaemia, morbidity and fatality rates. Malnourished children need to receive adequate amounts of zinc, though high doses may be associated with adverse effects such as suppression of cellular immune response. There is a need to research an appropriate range of zinc intake in the treatment of malnourished children.

Zinc deficiency may compromise foetal immune development in utero as well as many aspects of immune function in childhood. For example, zinc supplementation of women during pregnancy may reduce the risk of diarrhoeal disease in their infants. There is a need for research into the role of zinc in immune responses to vaccines, and into specific mechanisms of protection from infectious disease that are influenced by zinc. The role of zinc during pregnancy in foetal immune development, and the duration and reversibility of compromise in infancy, are other topics in need of further study.

Zinc supplementation reduces the incidence of childhood diarrhoeal disease. Implementation of interventions to improve zinc status is advised in populations with high rates of diarrhoea and evidence of zinc deficiency. Further research is called for in this area.

Supplementation is also an important factor in diarrhoea therapy, reducing the severity and duration of the illness.

The incidence of both pneumonia and malaria may be reduced in childhood by zinc supplementation, while supplementation in pregnancy may reduce pneumonia incidence in childhood. Further research is needed in both these areas. There is also circumstantial evidence that zinc supplementation may reduce mortality in children born small-for-gestational-age.

Research is also needed into the role of zinc in other areas of child development, notably foetal development, motor development and cognitive development.

Zinc Intervention Programs

It is unlikely that a single conceptual solution for the eradication of zinc deficiency will be universally applicable to all countries: the fundamental ecological backgrounds and the available infrastructures of developing countries are simply too diverse, and there are major geographical variations in the underlying dietary patterns of each of them.

Two generalised dietary patterns are likely to be major factors in the aetiology of dietary zinc deficiency:

1) Cereal and legume-based diets which are not fermented are potentially high in phytic acid, a potent inhibitor of zinc absorption, and thus reduce the amount of absorbable zinc from the diet;

2) Diets based on starchy roots and tubers have a low total zinc content. When these diet types are combined with a low intake of meat, poultry or fish, as is common in many low-income countries, the intake of absorbable zinc is likely to be inadequate. These dietary patterns may be used to identify populations who are at risk of inadequate zinc nutriture.

Some of the most attractive options may be those based on modifications to the plant-based staples. A wide spectrum of possibilities exists, from introducing new crops to manipulating the soil with natural and artificial fertilisers in areas where zinc content is very low, to using plant-breeding techniques to generate cereals that are zinc-rich and/or high in sulphur amino acids that promote zinc absorption. An alternative approach is to reduce the phytate content of cereal staples by more than 50% using cross-breeds low in phytate, or by using genetic modification techniques to incorporate heat-stable phytase enzymes into cereals. This inevitably implies fundamental changes in farming practice.

Household interventions can also be used to increase the zinc content and/or reduce the phytate content of diets. Germination and fermentation are used in India to reduce the phytate content of legumes, and soaking may be a practical strategy for removing water-soluble phytate from maize in African countries such as Malawi.

Fortification with micronutrients is a technique that is introduced effectively in countries as far apart as Mexico and Indonesia. Here, more work needs to be done to establish the optimum levels and chemical form of the zinc fortificant.

The evidence suggests that single-element micronutrient deficiencies are the exception rather than the rule. It would therefore seem logical to develop multi-micronutrient interventions, subject to a better understanding of the interactions involved.

Implications for Public Health Programs

With new information being compiled from recent research on zinc and human health, we have increased our ability to define the public health concerns associated with poor zinc status, the magnitude of those concerns, and the actions required to improve global zinc status. It is nonetheless recognized that, due to the nature of zinc metabolism in humans, there are special challenges in assessing human zinc status, and thus in identifying individuals and populations who are at risk of zinc deficiency. These challenges have previously hampered recognition of the importance of zinc in public health and must continue to be met through advances in science.

Critical consequences of zinc deficiency include childhood growth retardation, impaired immune function, increased rates of infections such as diarrhoea and pneumonia, possibly increased rates of mortality as a result of those infections, adverse outcomes of pregnancy, and abnormal neuro-behavioural development. Those at highest risk from the adverse outcomes of zinc deficiency are infants, young children, and pregnant and lactating mothers - this is largely because of their relatively high requirements for zinc. Infants born with a low birth weight, and children with frequent or persistent diarrhoea, are particularly vulnerable to zinc deficiency. Not only can zinc deficiency contribute to these conditions, but the conditions themselves result in increased needs for zinc.

National food balance data indicate that as much as one half of the world's population is at risk of inadequate zinc intake. Diets based exclusively or predominantly on plant products have relatively low zinc contents and poor absorption of zinc. Populations in low-income countries are largely dependent on plant-based diets, and are therefore at increased risk of inadequate zinc nutriture. At-risk regions include South and Southeast Asia, sub-Saharan Africa, Northern Africa and the Eastern Mediterranean and some countries of Latin America. Growth stunting, a condition that is often responsive to increased intake of zinc, is also highly prevalent in these regions; national growth surveillance data indicate that 33% of preschool children in low-income countries have stunted growth. While

neither of these indicators can conclusively identify zinc deficiency in a population, they strongly suggest that a substantial proportion of the world's population is at risk.

Several strategies exist which can be used to alleviate zinc deficiency in affected populations. Dietary diversification and/or modification strategies to improve the amount of zinc in the food supply or the absorbability of zinc in the food supply represent long-term approaches to the prevention of inadequate zinc intake. Programs to provide zinc supplements to high-risk groups may provide the most rapid method of correcting and preventing zinc deficiency and its consequences. Fortification of foods with zinc is another approach that could be effective and sustainable where suitable, centrally-processed foods are consumed by the population at risk.

When possible, policy makers should identify opportunities to integrate zinc interventions into ongoing primary health care and into existing nutrition and public health programs rather than attempt to establish new, independent programs to control zinc deficiency. To stimulate this process, efforts should be undertaken to assist countries in assessing the zinc status of their populations, and developing suitable intervention programs.

The Stockholm Zinc and Health Conference was sponsored by International Zinc Association, the International Atomic Energy Agency, the Society for International Nutrition Research and Sweden's International Development Cooperation Agency.

The conference abstracts and other zinc and health information are available at www.zinc-health.org

IZA wishes to thank Richard Hill, Holger Nilén, Christine Hotz and Kenneth Brown for compiling and editing these conference conclusions.

Statement

by Dr. Bruno de Benoist,
Department of Nutrition for Health and Development,
World Health Organization (WHO)
at the Conference on Zinc and Human Health,
Stockholm, 14th June 2000

"First of all, let me congratulate the organizers, especially the International Zinc Association, for holding this important Conference on zinc and human health and thank them for inviting WHO.

Zinc is indeed an essential micronutrient. Over the last few years, a great deal of work has been carried out in both the industrialized and non-industrialized countries of the world, which shows that zinc deficiency is likely to be a public health problem both in terms of its magnitude and its health consequences. Furthermore, the evidence suggests that zinc deficiency affects the most vulnerable segments of a population - pregnant women and young children, especially in developing countries. For the health consequences, zinc deficiency affects a range of functions, chiefly, reproduction, growth, immunity and brain development.

Therefore, it is legitimate to raise the question 'Has the time come to draw some lessons from the accumulated scientific information we have at hand and initiate interventions to control zinc deficiency?' However before we can answer this, certain issues needs to be clarified:

While the magnitude of zinc deficiency is likely to be significant, we still do not have data to estimate how many people are affected. We also do not know its geographical distribution. Zinc deficiency is not universal - it does not affect every country equally, or every population within those countries equally. And this is a key point. For any public health intervention to be successful and to target programs efficiently and effectively, it is essential to first set up criteria to define exactly who should benefit and the level of public health significance from which an intervention could be triggered.

Secondly, indicators, which are practical in the field, need to be developed to identify those risks and which also can assess and monitor the impact and progress a program is making. We have to be realistic. The identification of such indicators is not likely to be imminent. An interim answer would be to agree on a battery of indirect indicators which measures a number of bio-chemical and functional outcomes and to standardize its use. In this case for example, prevalence rates of low plasma zinc concentration, dietary indices, prevalence rates of stunting and acute diarrhea. This type of approach is currently used to decide whether to instigate a vitamin A supplementation campaign where data on xerophtalmia or retinol status are missing.

With regard to the functional consequences of zinc deficiency, controlled trials have shown that zinc supplementation is associated with improved growth, particularly among stunted children and also reduces the severity and duration of diarrhea, whether it is acute or prolonged diarrhea. On an individual treatment basis WHO already recommends giving zinc supplements

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as part of the management schedule of severe protein energy malnutrition and persistent diarrhea.

Evidence also exists that zinc supplementation may interfere with the course of some other childhood infectious diseases, in particular pneumonia and malaria, although the association is less clear. Protein energy malnutrition and infection are two of the main driving forces behind high childhood mortality rates: if zinc supplementation therefore reduces child mortality - it would clearly make a decisive argument to justify zinc supplementation programs. WHO is currently carrying out two studies together with Johns Hopkins University and UNICEF with support from the UN Foundation and USAID to address this issue.

Another issue is that of multiple micronutrient deficiencies. It is very likely that populations deficient in zinc are also deficient in other micronutrients, especially population groups where micronutrient requirements are relatively high, in other words pregnant women and young children. In a micronutrient supplementation program the cost of adding another micronutrient to the mixture is low and, in any case, much less than the cost of distributing the supplement. It therefore makes sense to piggy-back zinc supplements onto existing supplementation programs.

This is an area of work which WHO and UNICEF are currently collaborating on which will test a multiple micronutrient mixture for pregnant women in 11 countries. This is an exciting new area, but like the zinc arena, it also raises important questions before it can be scaled up to larger operations.

As with other micronutrients, any strategy to combat zinc deficiency should not be limited to supplementation alone. Fortification and dietary diversification are also key prongs WHO has consistently advocated. In practice, these three approaches should be combined - their respective importance depends on local conditions and the severity of zinc deficiency.

In conclusion, zinc deficiency is a public health problem that may have been underestimated. However, we need to identify the tools to define the epidemiological profile of the target population before we start any intervention and focus interventions on populations with zinc deficiency or at risk of zinc deficiency.

Moreover, during this meeting, the relationship between zinc and other micronutrients were brought up on several occasions. So it would be sensible and logical to consider the control of zinc deficiency not in isolation, but in the broader context of multiple micronutrient deficiencies. From this standpoint, dietary approaches should be considered as complementary to supplementation and fortification are ideal as they ensure a balanced and sustainable intake of micronutrients in the long term.

Lastly, the beneficial effects of zinc supplementation on health have been extensively demonstrated. The next step now is to look for the additional information required to provide countries with guidance on how to alleviate zinc deficiency."

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For more information about zinc and health, please visit

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