Zinc deficiency: what are the most appropriate interventions?

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Clinical review

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Zinc deficiency is one of the ten biggest factors contributing to burden of disease in developing countries with high mortality.[1] Since the problem was highlighted in the *World Health Report 2002*, calls have increased for supplementation and food fortification programmes.[2 3] Zinc interventions are among those proposed to help reduce child deaths globally by 63%.[4] Populations in South East Asia and sub-Saharan Africa are at greatest risk of zinc deficiency; zinc intakes are inadequate for about a third of the population and stunting affects 40% of preschool children.[5] Zinc is commonly the most deficient nutrient in complementary food mixtures fed to infants during weaning.[6]

Improving zinc intakes through dietary improvements is a complex task that requires considerable time and effort.[7] The case for promoting the use of zinc supplements and for fortifying foods with zinc, especially those foods commonly eaten by young children, therefore seems strong. However, global policies or recommendations for zinc interventions are few. The World Health Organization recommends zinc only as a curative intervention, either as part of the mineral mix used in the preparation of foods for the treatment of severe malnutrition, or more recently in the treatment of diarrhoea.[8] We review current evidence that improving zinc intake has important preventive or curative benefits for mothers and young children and examine the programme implications for achieving this in developing countries.

Summary points

- Zinc deficiency is common in developing countries with high mortality
- Regular zinc supplements can greatly reduce common infant morbidities in developing countries
- Zinc is also an effective adjunct treatment for diarrhoeal disease
- Zinc deficiency commonly coexists with other micronutrient deficiencies including iron, making single supplements inappropriate
- Until the results of trials of multiple micronutrient interventions are available, zinc supplements should be given to children with infections

Sources and selection criteria

We searched PubMed and the databases of WHO and Unicef for information on zinc supplementation and zinc fortification. We examined existing reviews of the evidence for benefits of zinc supplementation and zinc fortification and recent papers reporting the results of randomised controlled trials. These findings were further considered in the light of international policy recommendations for supplementation and fortification of other micronutrients such as iodine, iron, and vitamin A and reviews of experience in the implementation of these programmes.

Zinc supplementation

Strong evidence exists that zinc supplements improve the prognosis of children being treated for diarrhoeal disease. A pooled analysis of randomised controlled trials of therapeutic zinc in children with diarrhoea showed that children with acute diarrhoea given zinc supplements had a 15% lower probability of continuing diarrhoea on a given day compared with those in the control group; children with persistent diarrhoea had a 24% lower probability of continuing diarrhoea. In addition, children with persistent diarrhoea had a 42% lower rate of treatment failure or death if given zinc supplements.[9]

The most effective way to deliver zinc supplements in diarrhoeal disease control programmes is not yet clear. Since zinc supplementation reduces the duration and severity of diarrhoeal episodes it might be beneficial to add zinc to oral rehydration solution; one of the shortcomings of oral rehydration therapy is that the frequency and volume of stools is not reduced. However, studies of the efficacy of including zinc in oral rehydration solutions are not conclusive.[10] In addition, many countries promote the use of home made fluids.

WHO and Unicef propose to distribute blister packs of 10 dispersible tablets of 20 mg zinc for daily

References w1-w29 are on bmj.com

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consumption as the part of the treatment of diarrhoea. The use of zinc as an adjunct therapy significantly improves the cost effectiveness of standard management of diarrhoea.[11] Achieving and maintaining high levels of coverage of current interventions for diarrhoeal disease, such as oral rehydration therapy, are already proving difficult.[12] The challenge of promoting zinc supplements to treat diarrhoea is therefore considerable.

Preventive action

Regular zinc supplements have been shown to prevent disease. Supplementation seems to be most beneficial in children with lower birth weights and those with stunted growth or zinc deficiency. The supplementation of low birthweight infants in Brazil from birth for 8 weeks reduced both diarrhoea and coughs by a third in the first six months of life.[w2] Pooled analysis of randomised control trials found that zinc supplements reduced diarrhoeal diseases by 18% and pneumonia by 41% in preschool children.[13] The results for pneumonia are remarkable considering the challenge that pneumonia presents from a child health perspective.[14] Zinc supplementation has also been shown to reduce cases of falciparum malaria presenting at health centres in Africa and Papua New Guinea.[w3 w4] Zinc supplementation of babies with low birth weight in India reduced mortality during infancy by a third.[15] Maternal zinc supplementation during pregnancy improves neonatal immune status, early neonatal morbidity, and infant infections but not birth weight.[w1]

Zinc supplementation may also prevent failure of child growth, although the evidence is weaker than for prevention of disease. A meta-analysis of randomised controlled trials of the effects of supplemental zinc on growth of prepubertal children found that height and weight growth were only moderately improved, and the greatest responses were shown by children who were initially underweight or stunted.[16] Zinc supplementation trials in infants with birth weights >2.5 kg have shown little effect on preventing growth faltering in the second half of infancy in Indonesia.[w5 w6] In Ethiopia, zinc supplements increased length growth of stunted infants, but these infants were not selected on birthweight criteria.[w7] Trials in infants from birth to 6 months in Bangladesh showed growth effects only in those with initial low zinc status.[w8]

CAROLINE PENN/PANOS

Adding zinc to treatment for diarrhoeal disease is the first step to tackle deficiency

Administering supplements

Consensus is growing that zinc should not be promoted as a single nutrient supplement for preventing zinc deficiency in young children and their mothers. This is because many people have multiple micronutrient deficiencies. Anaemia is a marker for both iron and zinc deficiency. The use of iron and folate supplements to treat and prevent anaemia during pregnancy and lactation has been recommended for three decades,[w9] and iron for the treatment of anaemia in young children for almost a decade.[w10] Progress in reducing anaemia in developing countries has, however, been disappointing,[w11] largely because of poor execution of programmes, especially the inadequate preparation of health staff and systems to deliver the supplements.[17 w12] In addition, only a half of anaemia is thought to be solely due to iron deficiency; other micronutrients, such as vitamin A and vitamin C, are implicated as well as infection and blood loss.[w13] The diets of anaemic women in developing countries are more often deficient in micronutrients than they are deficient in energy.[18 w14 w15] Infant diets also commonly have inadequacies in zinc and iron as well as B vitamins.[19]

Zinc, iron, vitamin A, and copper all potentially interact and interfere with each other's absorption and metabolism when used as single nutrient supplements.[20 21 w16] Trials are ongoing of a multiple micronutrient supplement formulated by WHO, Unicef, and United Nations University for mothers during pregnancy and lactation[w17 w18]; this supplement could eventually replace iron and folate if proved effective. Various trials of multiple micronutrients as preventive supplements during infancy and childhood have been carried out or are under way.[w19 w20 w21 w22] The results of this research need to be brought together to determine whether to promote multiple micronutrient supplementation programmes during pregnancy, lactation, and infancy.

Zinc fortification

The case for promoting fortification of foods with zinc in developing countries may seem strong, but experience of how best to do it is limited and it may not be a suitable approach in many countries. Most experience in food fortification comes from industrialised countries, where few governments mandate zinc fortification. Food fortification with micronutrients in developing countries is largely limited to iodine, with over 70% of households consuming adequately iodised salt in 2000 compared with less than 20% in 1990.[w23] Developing countries in the Latin American region have the greatest experience of iron fortification, which is mandated for wheat flour in most of the region, although the effectiveness of these interventions has not been verified.[w24 w25] Research into zinc fortification either as a single nutrient or as part of a multimicronutrient approach is incipient.[22] Innovative approaches will be needed to achieve fortification of foods with zinc in developing countries with the highest mortalities. These include the development of small scale community approaches for multiple micronutri-

Additional educational resources

WHO/UNICEF Joint statement on clinical management of acute diarrhoea (www.unicef.org/publications/files/ENAcute_Diarrhoea_reprint.pdf)—Explains the latest management recommendations

International Zinc Nutrition Consultative Group (www.izincg.ucdavis.edu/publications/default.html)—The website contains information on the public health importance of zinc and many of the references used in this article are available there as pdf files

ent fortification, using hammer mills, and the use of condiments, fish paste, and bouillon cubes.[w26 w27]

Independent of the food vehicle, the risks of interactions in food fortificants are still unknown. For example, zinc and iron are known to have interactions[w28 23] that are likely to be compounded by variations in the adequacy of nutritional status for other nutrients such as vitamin B6.[w29] Research is ongoing into the appropriate dose and form of zinc to fortify foods.

Dietary diversification

Increased consumption of foods with a high content of absorbable zinc is the long term sustainable solution to problems of zinc deficiency. Strategies are being developed that target agricultural and food production, household food processing, and dietary modification.[5] Zinc is highly correlated with the protein content of foods, but the availability of zinc in protein rich plant foods is much less than that in animal protein foods. Plant breeding efforts aim to produce new cereal varieties with higher zinc concentrations that are more available by reducing concentrations of inhibitors such a phytate and increasing enhancers of absorption such as the sulphurous amino acids. At the household level, food processing methods for increasing the availability of zinc in cereal grains and legumes include sprouting, fermenting, and soaking. These programme interventions are complex and require considerable investment in behaviour change, which takes time. As yet no evidence exists of their effectiveness for preventing zinc deficiency, especially in mothers and young children.

Conclusions

Zinc intakes are commonly inadequate, especially in the populations of developing countries with the highest mortality. Correcting this situation will have dramatic impact on the morbidity and mortality of young children and modest effects on their growth. Tackling zinc deficiency in isolation, however, is inappropriate. In particular, it is important to avoid any further fragmentation of health interventions by creating an additional zinc programme. Including zinc in multiple micronutrient supplementation and fortification interventions and promoting their use through existing programmes aimed at tackling anaemia will be less disruptive. But these approaches are still being researched. In the mean time, the use of zinc to treat diarrhoeal disease is the most appropriate entry point for zinc supplementation efforts. The cost of the micronutrient supplements is miniscule compared with the cost of the delivery system, and the greatest challenge for programmes will continue to be achieving high levels of coverage. If these challenges can be met, the chances of achieving the millennium development goals for child survival will be considerably enhanced.

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Endpiece

Common sense

Doctors will get off their pedestals when patients get off their knees.

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