EDITORIAL

Healthy Growth is More Than Zinc

TOR A STRAND
Professor, Department of Research, Innlandet Hospital Trust, Lillehammer; and Centre for Intervention Science in Maternal and Child Health, Centre for International Health, University of Bergen, Bergen; Norway.
tor.strand@uib.no

Zinc is an essential micronutrient required for proper immune function and growth [1]. Almost 50 years ago, it was discovered that the rare inherited disorder Acrodermatitis enterophatica was caused by impaired zinc absorption and that it could be effectively treated with large doses of oral zinc [2]. Key features of this illness are increased risk of infections and stunted growth. Stunting and a high burden of infectious diseases seen in many marginalized populations were then linked to poor zinc nutriture, recognizing possible public health importance of zinc deficiency [3]. Several randomized controlled trials (RCTs) on the effect of zinc in preventing infections and improving growth was subsequently undertaken [4]. Two decades ago, the initial efforts to summarize the effect of these trials confirmed a public health relevance of zinc deficiency [5]. The initial evidence linking stunting and zinc deficiency was so convincing that the prevalence of stunting in a population was suggested as a proxy for zinc deficiency [6].

In this issue, Gera and colleagues present the most comprehensive meta-analysis on the effect of routine zinc supplementation on growth [7]. Their analyses include data from almost 30,000 children under five years of age that participated in 63 different RCTs. The results are in line with most other meta-analyses that demonstrate no, or a negligible effect of zinc on linear growth. One of the outcomes they summarized were attained linear growth at the end of the study periods. For this important outcome, the authors found no effect of zinc whatsoever (Standardized effect size of 0.00; 95% CI -0.07, 0.07). They also demonstrated no or minimal effects on other anthropometric indices such as head circumference, weight, and mid-upper arm circumference. Similar to the previous systematic reviews, this review also demonstrated substantial heterogeneity between the studies. In other words, the effect of zinc on growth varies significantly between the RCTs. This variability is expected, as the impact of nutrient interventions likely vary according to the preexisting nutrient status of the populations or the degree to which the community is affected by the outcome of interest. It is therefore noteworthy that the observed heterogeneity of zinc cannot be explained by preexisting zinc status or the prevalence of stunted growth. Furthermore, micronutrient deficiencies often coexist and supplementing with one growth-limiting nutrient is unlikely to work if other nutrients necessary for growth is lacking.

Zinc supplementation reduces the risk and duration of infections [4], and frequent and persistent infections may hamper growth. The effect of zinc seen in some studies may accordingly be mediated through its impact on preventing or curbing infections. This potential indirect effect of zinc on growth depends on the nature and burden of infections and availability of the health services for the study population. These background variables could partly explain the heterogeneity between the different RCTs but such effect is not easy to measure.

It should be noted that a lack of a consistent beneficial effect of zinc supplementation on growth does not undermine the importance of this nutrient on human health. Nor does the results of this meta-analysis rule out zinc deficiency as one of many causes of stunted growth. However, the conclusion to not advocate zinc supplementation "as a public health measure to improve growth" is well justified in light of their findings and the expected costs of zinc supplementation programs. Another important point made by the authors is that the multifaceted origin of stunting and the limited effect of zinc question the use of stunting as a proxy for zinc deficiency.

We should continue our efforts to identify modifiable risk factors for stunted growth in marginalized populations. Zinc is one of these factors but seemingly not as important as previously assumed. However, despite the limited effect on growth, adequate intake of this essential micronutrient should be encouraged.

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