Zinc supplementation: Time for public health intervention


SUMMARY

This meta-analysis provides robust information on the effect of supplemental zinc on growth (height, weight and weight-for-height index) and serum zinc concentrations in prepubertal children. The authors scrutinized more than 400 articles and, of these, 33 studies (1976–2001) were included in the final analysis. The inclusion and exclusion criteria were explicitly defined and this ensured uniform methodological quality of the studies. These 33 studies were randomized, placebo-controlled intervention trials of zinc supplementation in children <12 years of age. The trials on premature infants, hospitalized subjects, children with chronic diseases or with <8 weeks of supplementation were excluded. The data on growth and serum zinc levels were converted to effect sizes that were calculated as the difference between the means of the zinc and the control groups divided by their pooled SD. The overall effect size for each outcome was estimated from the random-effects model, and random-effects meta-regression analyses were carried out. Moreover, formal analyses were done to detect publication bias (file-drawer problem: negative studies are less likely to be published and thus published literature will have a positive bias in favour of the intervention) by assessing correlation between effect sizes and sample sizes. This was further explored by calculating the hypothetical number of non-significant studies that would be required to neutralize any significant finding from the current analysis. Eventually, the data sets provided information from 2945 children with most of the studies having <100 subjects. The studies originated from all parts of the world including 8 from Asia. The average dose of elemental zinc supplement was 1–20 mg/day and the duration of supplementation lasted from 8 weeks to 15 months. The results showed highly significant positive responses in height and weight increments with effect sizes of 0.35 (95% CI: 0.189–0.511) and 0.309 (95% CI: 0.178–0.439). Zinc supplementation caused a large increase in serum zinc levels with an effect size of 0.820. The growth response was more pronounced in children who were lagging behind at enrolment.

COMMENT

Malnutrition increases morbidity and mortality in all settings. Moreover, it has profound adverse effects on physical growth and development in children. It is likely that some of the deleterious effects of malnutrition stem from specific micronutrient deficiencies, e.g. iron, iodine, zinc, selenium and a host of vitamin deficiency states. Micronutrient deficiency is a serious public health concern in most developing countries. While the problems of iron and vitamin A deficiency, and iodine deficiency disorders have been highlighted till recently, attention is now being focused on other micronutrients such as zinc. Rauling discovered zinc as an essential trace element in 1869. It is required for the metabolic activity of over 200 body enzymes and is considered essential for cell division, synthesis of DNA and proteins. It has an unquestionable role in gene expression. Though at present our knowledge on optimal micronutrient levels for genomic stability is scanty and disorganized, there is already sufficient evidence to suggest that marginal deficiencies in folate, vitamin B12, niacin and zinc impact significantly on the spontaneous chromosome damage rate. This has far-reaching consequences right from the periconceptional period to ageing-related states. Studies have suggested that zinc plays a vital role in the growth and development of children. It has been shown to reduce the incidence and severity of common childhood infections. It has a favourable impact on the host’s immune response. Deficiency of zinc during pregnancy has been linked to a higher incidence of foetal malformations such as neural tube defects, and it may lead to foetal resorption.

Numerous studies have been published on the effect of zinc supplementation in children. This study lends a strong argument...
in favour of zinc supplementation in children for optimizing growth and development. The effect size of 0.39 SD for height translates into a 0.72 cm mean increase in height for children with a mean age of 2.8 years when they receive a mean of 6.8 months of zinc supplementation. While meta-analyses have their limitations, the current study seems reliable and valid. The analysis for publication bias revealed an insignificant correlation between effect sizes and sample sizes of individual studies. Also, it was estimated that more than 500 zero effect studies would be needed to invalidate the conclusions of the current findings. The accompanying editorial calculated that 83 studies would be required to reduce the effect size for height to a level below which the results are considered clinically inconsequential. These numbers clearly suggest an absence of publication bias. The larger effect size for stunted children adds strength to a possible biological association between zinc deficiency and growth. The stringent inclusion criteria and explicit description of methodology lend credibility to the results. A visual inspection of all the charts plotting individual study mean effect sizes and confidence intervals reveals that most of the 95% confidence intervals do not include zero and the results of pooling were not being driven by outliers.

The population included for analysis allows for a wide generalization of results to the general population and thus will have an impact on public health policy measures. Height and weight are gross markers of development and it is likely that zinc deficiency may have an impact on more subtle end-points such as cognitive functions, ageing, immunity, etc. The available data for zinc are promising with regard to the prevention of diarrhoea and pneumonia. The combined effect of these benefits makes a strong case for a favourable impact of zinc supplementation. The present study also highlights that a mean serum zinc level is a useful indicator of the successful delivery of a supplement and it can be used for the assessment of public health interventions. The National Pilot Programme on Control of Micronutrient Malnutrition (India), launched in 1995, found that mean dietary zinc intakes in all the surveyed districts were much lower than the recommended dietary allowance (RDA). For a developing nation such as India, where a sizeable population of those <12 years is stunted, these results could have far-reaching consequences. While a comprehensive policy for initiating a programme for zinc supplementation will need more data on safe and efficient delivery systems, burden of zinc deficiency states and a cost–benefit analysis, the stage is set for some formal recommendations to be made by professional bodies or policymakers.

REFERENCES


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Obituaries

Many doctors in India practise medicine in difficult areas under trying circumstances and resist the attraction of better prospects in western countries and in the Middle East. They die without their contributions to our country being acknowledged.

The National Medical Journal of India wishes to recognize the efforts of these doctors. We invite short accounts of the life and work of a recently deceased colleague by a friend, student or relative. The account in about 500 to 1000 words should describe his or her education and training and highlight the achievements as well as disappointments. A photograph should accompany the obituary.

—Editor