Effect of supplemental zinc on the growth and serum zinc concentrations of prepubertal children: a meta-analysis of randomized controlled trials

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Authors' objectives
To determine the effect of zinc supplements on physical growth and serum zinc concentrations.

Searching
MEDLINE was searched from 1966 to 2001 (completed May 14, 2001) using the keywords 'supplement' and 'children' and 'zinc' and 'growth'. The bibliographic citations from each of the studies were also checked for other relevant references. Several unpublished studies were located through personal communications with other investigators working in this field.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with a concurrent control group which included at least one of the major outcome measures of interest (change in height or weight) were eligible. RCTs only were included.

Specific interventions included in the review
The inclusion criteria specified that supplemental zinc had to be given for at least 8 weeks. The doses ranged from 1 to 50 mg/day. The authors report that, in most cases, the doses were given daily for 5 or 6 days per week.

Participants included in the review
The inclusion criteria specified children aged under 12 years, or specifically stated to be prepubertal, not premature infants and free from chronic diseases.

Outcomes assessed in the review
Change in height, weight and serum zinc concentration were assessed.

How were decisions on the relevance of primary studies made?
Each of the co-authors independently assessed the suitability of the papers for inclusion.

Assessment of study quality
The authors did not report the method used to assess quality, or how the quality assessment was performed.

Data extraction
The data were independently abstracted by each of the co-investigators and then summarised in a common database. Data were extracted on the study and country, the number of participants, intervention, baseline characteristics of the participants, and outcomes of the intervention.

All results were standardised as effect sizes. These were calculated as the mean change in nutritional outcome of the treatment group minus the mean change of the control group, divided by the pooled standard deviation of change for both groups. Each study was weighted in the analysis by considering the total number of participants in the study and the effect size.

Methods of synthesis
How were the studies combined?
The mean and 95% confidence interval (CI) for the weighted average effect size were calculated for each outcome.
variable.

How were differences between studies investigated?
The homogeneity of effect size was tested using the chi-squared statistic. When significant heterogeneity was found, a regression analysis was used to examine possible sources of heterogeneity. The authors also undertook a visual inspection of the mean effect sizes for subgroups of studies based on study design and participants.

Results of the review
Thirty-three RCTs with 2,945 children participating were included. Thirteen of the studies were from Latin America and the Caribbean, 8 from North America or Europe, 8 from Asia and the Middle East, and 4 from Africa. The studies ranged from 2 to 15 months in duration (mean: approximately 6 to 7 months) and included from 21 to 210 participants (mean: 89). The participants ranged in age from birth to 10 years (mean: 3.1 years).

Zinc supplementation produced significant positive responses in both height and weight increments, with effect sizes of 0.350 (95% CI: 0.189, 0.511) and 0.309 (95% CI: 0.178, 0.439), respectively. Heterogeneity was found for all three key variables: height, weight and serum zinc concentration. There was no significant effect of zinc on weight-for-height indexes (weighted mean effect size -0.018, 95% CI: -0.132, 0.097). There was a large increase in serum zinc concentration (effect size 0.820, 95% CI: 0.499, 1.14). Growth responses were greater in children aged above 6 months with a low initial height-for-age z score, and for those with a low initial weight-for-age z score.

Authors' conclusions
The authors believe that there is now sufficient information to indicate that, in those settings with high rates of stunting and/or low plasma zinc concentrations, programmes to enhance zinc status should be considered to improve children's growth. Successful delivery and absorption of zinc supplements can be measured by the population mean serum zinc concentration.

CRD commentary
The authors clearly state the research question and have listed inclusion and exclusion criteria for the review. The literature review was conducted using only MEDLINE and handsearches, and there remains the possibility that some studies have been missed. The authors did not state whether there were any language restrictions. The details of the review process, in particular the quality assessment, were limited. The initial studies are not reported in the review so the summaries of the study characteristics cannot be verified.

The studies were combined in a statistical analysis and the methods used were appropriate. However, significant heterogeneity was found; this was investigated in detail in the statistical analyses. The authors explored the possibility of publication bias and correlation between the number of participants and effect size; they concluded that there was no publication bias. The results from these studies should be viewed with caution because of the review's limitations.

This review is an update of a previous review and the key difference is the exclusion of nine previously included studies. Reasons for exclusion include the duration of the study, the inclusion of premature infants, the inclusion of severely malnourished children, and that some studies may have included some postpubertal participants.

Implications of the review for practice and research
Practice: The authors believe that programmes to enhance zinc status in settings with high rates of stunting and/or low plasma zinc concentrations should be considered to improve children's growth.

Research: The authors did not state any implications for further research.

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