

A.10b Zinc supplementation

Recommendation and remarks

RECOMMENDATION A.10b (UPDATED)

Enteral zinc supplementation may be considered for human milk-fed preterm or low-birth-weight infants who are not receiving zinc from another source. (*Conditional recommendation, low-certainty evidence*)

Remarks

- The GDG noted that the evidence on harms (decreased neurodevelopment) was uncertain due to very-low-certainty evidence and imprecision.
- The recommendation is conditional on shared decision-making with parents; this includes informing parents about the benefits and risks and the need for further research.
- The GDG noted that there were limited data on the dose, timing of initiation and duration of supplementation. Based on most trials included in the evidence review, the GDG suggests a daily dose of 1–3 mg/kg per day of elemental zinc. The GDG also suggests that zinc may be initiated when enteral feeds are well established, and may be continued until the infant receives zinc from another source.

Background and definitions

Zinc is a trace element essential for physiological functions of the human body (103). Zinc deficiency is associated with dysfunction in epidermal, gastrointestinal, central nervous, immune, skeletal and reproductive systems (104,105). Human milk may not be able to meet the nutritional requirements of preterm or LBW infants because of their low zinc stores and catch-up growth (104–106). A recent (2021) Cochrane review of enteral zinc supplementation in hospitalized preterm infants

fed any type of milk (i.e. infant formula or human milk) reported that zinc supplementation reduced all-cause mortality and was associated with a probable improvement in short-term weight gain and linear growth, but had little or no effect on common morbidities of prematurity (107). However, there have been no recent systematic reviews of zinc supplementation in babies born at home or in the hospital or on babies fed human milk only. The optimal dose and timing of initiation are also unclear.

Summary of the evidence

OVERVIEW	A.10b Zinc supplementation
PICO	Population – Preterm or LBW infants who are fed mother’s own milk or donor human milk Intervention – Zinc supplementation Comparator – No zinc supplementation Outcomes – All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up
Timing, setting, subgroups	Timing of the intervention – Birth to 6 months of age Setting – Health-care facility or home in any country or setting Subgroups • Gestational age at birth (< 32 weeks, ≥ 32 weeks) • Birth weight (< 1.5 kg, ≥ 1.5 kg) • Dose of elemental zinc (< 3 mg/day, 3–5 mg/day and > 5 mg/day)

Effectiveness: Comparison – Zinc supplementation versus no zinc supplementation Sources and characteristics of the evidence

The effectiveness evidence was derived from a systematic review of 14 RCTs totalling 9940 preterm or LBW infants from 11 countries (Bangladesh, Brazil, Chile, Egypt, India, the Islamic Republic of Iran, Italy, the Republic of Korea, Nepal, Spain and the United

Republic of Tanzania) (108). Most infants had a birth weight of at least 1.5 kg or were born at 32 weeks’ gestation or later. Among these, two large RCTs assessed the effects of zinc supplementation in a total of 2748 term LBW infants in Brazil and India. Zinc supplementation dosages across all 14 RCTs ranged from 1 mg/day up to 10 mg/day and commenced between birth and 35 days of age. Most