

A.10e Calcium and phosphorous supplementation

Recommendation and remarks

NO RECOMMENDATION

Remark

- The GDG decided not to make a recommendation on calcium or phosphorous supplementation as there was little evidence of benefits or harms on any critical outcome.

Background and definitions

Preterm and LBW infants have low skeletal stores of calcium and phosphorus (123). Previous systematic reviews have reported that calcium and phosphorous supplements given to human-milk-fed preterm or LBW infants had no effect on growth (weight, length,

head circumference) but improved bone biomarkers (serum alkaline phosphatase) (123,124). No effects have been reported on mortality, morbidity or neurodevelopment and no evidence was found on the optimal dose or timing of initiation.

Summary of the evidence

OVERVIEW	A.10e Calcium and phosphorous supplementation
PICO	<p>Population – Preterm or LBW infants who are fed mother’s own milk or donor human milk</p> <p>Intervention – Calcium and phosphorous supplementation</p> <p>Comparator – No calcium and phosphorous supplementation</p> <p>Outcomes – All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up</p>
Timing, setting, subgroups	<p>Timing of the intervention – Birth to 6 months of age</p> <p>Setting – Health-care facility or home in any country or setting</p> <p>Subgroups</p> <ul style="list-style-type: none"> Gestational age at birth (< 32 weeks, ≥ 32 weeks) Birth weight (< 1.5 kg, ≥ 1.5 kg)

Effectiveness: Comparison – Calcium and phosphorous supplementation versus no calcium or phosphorous supplementation

Sources and characteristics of the evidence

The effectiveness evidence was derived from a systematic review of three trials (2 RCTs and 1 non-randomized trial) reporting on a total of 162 preterm and/or LBW infants from two countries (the Islamic Republic of Iran and the United Kingdom) (125). Most babies in the trials had birth weight below 1.5 kg and/or had been born before 32 weeks’ gestation.

Two trials assessed the effect of phosphorus supplementation only (dose of 15 mg/kg per day in 1 trial and 25 mg/kg per day in 1 trial) and the third trial assessed the effect of supplementation with calcium and phosphorous combined (calcium 45 mg/kg per day, phosphorus 25 mg/kg per day). All three trials gave supplements enterally, via naso- or orogastric tubes. Supplementation commenced between birth and 10 days chronological age in all three trials. The duration of supplementation was between 10 and 42 days in one trial and it could not be assessed in the other two.

Critical outcomes

For calcium and phosphorous supplementation compared with no calcium or phosphorous supplementation, three trials reported morbidity (2 reported rickets, 1 osteopenia) and one trial reported growth (length and head circumference). No trials reported all-cause mortality or neurodevelopment, and no trials reported on serious adverse events. (Full details are provided in GRADE Table A.10e, in the Web Supplement.)

Morbidity: Very-low-certainty evidence from three trials totalling 159 participants suggests a decrease in osteopenia or rickets at latest follow-up (mean 38.3 weeks) (RR 0.68, 95% CI 0.46 to 0.99).

Growth: Very-low-certainty evidence from one trial with 40 participants suggests little to no effect on weight (in grams) at 6 weeks of age (MD 138.5, 95% CI -82.16 to 359.16). Very-low-certainty evidence from one trial with 40 participants suggests little to no effects on length (in centimetres) at 6 weeks of age (MD 0.77, 95% CI -0.92 to 2.46). Very-low-

certainty evidence from one trial with 40 participants suggests little to no effect on head circumference (in centimetres) at 6 weeks of age (MD 0.33, 95% CI -0.3 to 0.96).

Other outcomes

There was little or no effect on serum alkaline phosphatase (IU/L) at 6 weeks of age (MD -126.11, 95% CI -298.5 to 46.27; 2 trials, 122 participants), serum calcium (mg/dl) at 6 weeks of age (MD 0.54, 95% CI -0.19 to 1.27; 1 trial, 40 participants), or serum phosphorus (IU/L) at 6 weeks of age (MD 0.07, 95% CI -0.22 to 0.36; 1 trial, 40 participants).

Subgroup analyses

The effect of gestational age and birth weight could not be assessed as there were insufficient trials reporting on any critical outcome.

Values and acceptability

The systematic review about what matters to families about the care of the preterm or LBW infant (see Table 1.1) reported that families want to be involved in delivering care to infants, including supporting nutrition, and want to take an active role in deciding what interventions are given to infants, including what and how they are fed (14). There was no specific evidence available about whether families value calcium and phosphorous supplements for their preterm or LBW baby or whether they find them acceptable.

Summary of judgements

Comparison: Calcium and phosphorous supplementation vs no calcium or phosphorous supplementation (A.10e)

- Justification**
- Evidence of small benefit: decreased osteopenia, rickets (*very-low-certainty evidence*)
 - Evidence of little or no effect on weight, length, head circumference (*very-low-certainty evidence*)
 - No evidence on other critical outcomes

Evidence-to-Decision summary

Benefits	Unknown
Harms	Unknown
Certainty	Very low
Balance	Does not favour calcium and phosphorous supplementation
Values	Uncertainty or variability about outcomes
Acceptability	Probably acceptable
Resources	Low to moderate
Feasibility	Probably feasible
Equity	Probably equitable

Resources required and implementation considerations

Organization of care

The supplements can be provided in the health-care facility or at home. The family needs accurate information on the dose and how to administer the supplement. National or local guidance for health-care facilities should be used.

Infrastructure, equipment and supplies

Common methods of providing enteral calcium and phosphorous for preterm and LBW infants include a 5 ml suspension containing 125 mg of calcium, 55 mg of phosphorus and 200 IU of vitamin D, which is given three times a day at a dose of 2 ml/kg. Droppers or syringes can be used to administer the supplement to the infant. National or local guidance for health facilities should be used.

Workforce, training, supervision and monitoring

Health workers at all levels can support mothers and families. Standardized packages are needed for training, supervision and monitoring. Dispensing needs to be documented in clinical records.

Feasibility and equity

There was no specific evidence available about the feasibility and equity of providing calcium and phosphorous supplements to preterm or LBW babies.