Delayed introduction of progressive enteral feeds to prevent necrotising enterocolitis in very low birth weight infants

01 June 2015

RHL Summary

Key findings

- There is no clear evidence that delaying the introduction of progressive enteral feeds affected the risk of NEC or death
- Delaying the introduction of feeds results in a delay of one to three days until full enteral feeding is achieved. The clinical significance of this delay is unclear.

Evidence included in this review

Seven trials including a total of 964 infants with low birth weight (LBW) (<2000g) or preterm birth (gestational age <32 weeks). Trials compared risk of NEC in early enteral feeding to delayed enteral feeding. Trials were included from Qatar (1), the USA (3), Greece (1), the UK (1) Ireland (1), and Colombia (1). Feeding regimens differed between trials, and trials included infants classified as both very LBW as well as extremely LBW (few participants).

Quality assessment

The included trials were of moderate quality. Blinding of caregivers and clinical assessors to the intervention was not possible. Incomplete methodological reporting made the risk of either selection or attrition bias unclear in 5 of the 7 trials.

Clinical implications

There is not sufficient evidence to support delaying the introduction of progressive enteral feeding in preterm or very low birth weight infants beyond four days after birth for the purpose of preventing NEC.

The applicability of findings to lower-income countries is unclear, as data was collected in high- and middle-income countries with neonatal care centres.

Further research

Future trials should provide subgroup analyses of extremely LBW and extremely pre-term infants. Additionally, more precise assessment of the effects of different feeding regimes, and the implications of...
delayed feeding in low-income countries will be valuable.

**Cochrane review**

Citation: Morgan J, Young L, McGuire W. Delayed introduction of progressive enteral feeds to prevent necrotising enterocolitis in very low birth weight infants. *Cochrane Database of Systematic Reviews* 2014, Issue 12. Art. No.: CD001970. DOI:10.1002/14651858.CD001970.pub5

**Abstract**

The introduction of enteral feeds for very preterm (less than 32 weeks' gestation) or very low birth weight (VLBW; less than 1500 g) infants is often delayed for several days or longer after birth due to concern that early introduction may not be tolerated and may increase the risk of necrotising enterocolitis (NEC). However, delaying enteral feeding could diminish the functional adaptation of the gastrointestinal tract and prolong the need for parenteral nutrition with its attendant infectious and metabolic risks.

To determine the effect of delayed introduction of progressive enteral feeds on the incidence of NEC, mortality and other morbidities in very preterm or VLBW infants.

We searched the Cochrane Central Register of Controlled Trials (CENTRAL, 2014, Issue 8), MEDLINE (1966 to September 2014), EMBASE (1980 to September 2014), CINAHL (1982 to September 2014), conference proceedings and previous reviews.

We included randomised or quasi-randomised controlled trials that assessed the effect of delayed (more than four days after birth) versus earlier introduction of progressive enteral feeds on the incidence of NEC, mortality and other morbidities in very preterm or VLBW infants.

Two review authors independently assessed trial eligibility and risk of bias and undertook data extraction. We analysed the treatment effects in the individual trials and reported the risk ratio (RR) and risk difference for dichotomous data and mean difference for continuous data, with respective 95% confidence intervals (CI). We used a fixed-effect model in meta-analyses and explored the potential causes of heterogeneity in sensitivity analyses.

We identified nine randomised controlled trials in which 1106 infants participated. Few participants were extremely preterm (less 28 weeks' gestation) or extremely low birth weight (less than 1000 g). The trials defined delayed introduction of progressive enteral feeds as later than four to seven days after birth and early introduction as four days or less after birth. Meta-analyses did not detect statistically significant effects on the risk of NEC (typical RR 0.93, 95% CI 0.64 to 1.34; 8 trials; 1092 infants) or all-cause mortality (typical RR 1.18, 95% CI 0.75 to 1.88; 7 trials; 967 infants). Four of the trials restricted participation to growth-restricted infants with Doppler ultrasound evidence of abnormal fetal circulatory distribution or flow. Planned subgroup analyses of these trials found no statistically significant effects on the risk of NEC or all-cause mortality. Infants who had delayed introduction of enteral feeds took longer to establish full enteral feeding (reported median differences two to four days).
The evidence available from randomised controlled trials suggested that delaying the introduction of progressive enteral feeds beyond four days after birth did not reduce the risk of developing NEC in very preterm or VLBW infants, including growth-restricted infants. Delaying the introduction of progressive enteral feeds resulted in a few days' delay in establishing full enteral feeds but the clinical importance of this effect was unclear. The applicability of these findings to extremely preterm or extremely low birth weight was uncertain. Further randomised controlled trials in this population may be warranted.

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