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[Intervention Review]

Inositol in preterm infants at risk for or having respiratory distress syndrome

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ABSTRACT

Background

Inositol is an essential nutrient required by human cells in culture for growth and survival. Inositol promotes maturation of several components of surfactant and may play a critical role in fetal and early neonatal life.

Objectives

To assess the effectiveness and safety of supplementary inositol in preterm infants with or without respiratory distress syndrome (RDS) in reducing adverse neonatal outcomes.

Search methods

The Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*, MEDLINE, EMBASE, CINAHL, Clinicaltrials.gov and Controlled-trials.com were searched in September 2014. The reference lists of identified randomised controlled trials (RCTs), personal files and Web of Science were searched.

Selection criteria

All RCTs of inositol supplementation of preterm infants compared with a control group that received a placebo or no intervention were included. Outcomes of interest were neonatal death, infant death, bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), intraventricular haemorrhage (IVH), necrotizing enterocolitis (NEC) and sepsis.

Data collection and analysis

Data on neonatal outcomes were abstracted independently by the three review authors and any discrepancy was resolved through consensus. Outcomes were reported as relative risk (RR), risk difference (RD) and number needed to treat to benefit (NNTB) or to harm (NNTH).

Main results

Four published RCTs and one ongoing RCT were identified. Study quality varied and interim analyses had occurred in all trials of repeat doses of inositol that provided data for the outcomes of interest in this review. In these trials neonatal death was found to be significantly reduced (3 trials, 355 neonates; typical RR 0.53, 95% CI 0.31 to 0.91; typical RD -0.09, 95% CI -0.17 to -0.03; NNTB 11, 95% CI 6 to 33). Infant deaths were reduced (3 trials, 355 infants; typical RR 0.55, 95% CI 0.40 to 0.77; typical RD -0.18, 95% CI -0.27 to -0.08; NNTB 6, 95% CI 4

to 13). ROP stage ≥ 3 was significantly reduced (2 trials, 262 infants; typical RR 0.09, 95% CI 0.01 to 0.67; typical RD -0.08, 95% CI -0.13 to -0.03; NNTB 13, 95% CI 8 to 33) and IVH grade > II was significantly decreased (3 trials, 355 infants; typical RR 0.53, 95% CI 0.31 to 0.90; typical RD -0.09, 95% CI -0.16 to -0.02; NNTB 11, 95% CI 6 to 50). Neither sepsis nor NEC differed significantly between groups. One study (74 infants) that administered a single dose of inositol (60 or 120 mg/kg) found no significant differences in adverse outcomes using RR, but an increased RD for BPD at 36 weeks postmenstrual age (RD 0.23, 95% CI 0.03 to 0.43; NNTH 4, 95% CI 2 to 33). This result should be interpreted with caution as only one dose of inositol was given and only the RD, but not the RR, was significant. One ongoing large study of repeat doses of inositol in preterm infants was identified.

Authors' conclusions

Inositol supplementation results in statistically significant and clinically important reductions in important short-term adverse neonatal outcomes. A large size multi-centre randomised controlled trial is currently ongoing and the trial will likely confirm or refute the findings from this systematic review.

PLAIN LANGUAGE SUMMARY

Supplementing preterm babies who have respiratory distress with the nutrient inositol may reduce death and disability

Review question

Does the administration of supplementary inositol reduce adverse outcomes in preterm infants with or without respiratory distress syndrome (RDS)?

Background

Inositol is an essential nutrient for cells, with high concentrations in breast milk (particularly in the breast milk of mothers whose babies have been born early). A drop in inositol levels in babies with respiratory distress syndrome (RDS) can be a sign that their illness will be severe.

Study characteristics

Four published randomised controlled trials met our inclusion criteria.

Results

We found that the initial evidence regarding inositol supplementation in preterm babies with RDS is promising. Supplementation lowered rates of death and bleeding in the brain, with an important reduction in eye problems as well. Inositol did not have serious adverse effects. Further research is warranted to confirm these preliminary findings. Such research is currently ongoing in the USA.