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[Intervention Review]

Vitamin E supplementation for prevention of morbidity and mortality in preterm infants

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ABSTRACT

Background

Treating very low birth weight (VLBW) infants with pharmacologic doses of vitamin E as an antioxidant agent has been proposed for preventing or limiting retinopathy of prematurity, intracranial hemorrhage, hemolytic anemia, and chronic lung disease. However, excessive doses of vitamin E may result in concerning side effects.

Objectives

To assess the effects of vitamin E supplementation on morbidity and mortality in preterm infants.

Search methods

MEDLINE (October 2002), EMBASE (March 2002), the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2003), and personal files for clinical trials assessing vitamin E in preterm infants were searched. The MEDLINE and CCTR searches were updated in March 2007.

Selection criteria

Trials analyzing primary outcomes (mortality or combined long-term morbidity) or secondary outcomes (other morbidity) in infants with gestational age less than 37 weeks or birth weight less than 2500 grams were selected. The intervention was allocation to routine supplementation with vitamin E in the treatment group versus placebo, no treatment or another type, dose or route of administration of vitamin E.

Data collection and analysis

The standard methods of the Cochrane Collaboration and of the Cochrane Neonatal Review Group were used.

Main results

Twenty-six randomized clinical trials fulfilled entry criteria. No study assessed combined long-term morbidity. Routine vitamin E supplementation significantly increased hemoglobin concentration by a small amount. Vitamin E significantly reduced the risk of germinal matrix/intraventricular hemorrhage and increased the risk of sepsis; however, heterogeneity limits the strength of these latter two inferences. Vitamin E did not significantly affect other morbidity or mortality. In VLBW infants, vitamin E supplementation significantly increased the risk of sepsis, and reduced the risk of severe retinopathy and blindness among those examined.
Subgroup analyses demonstrated (1) an association between intravenous, high-dose vitamin E supplementation and increased risk of sepsis and of parenchymal cerebral hemorrhage; (2) an association between vitamin E supplementation by other than the intravenous

route and reduced risk of germinal matrix-intraventricular hemorrhage and of severe intraventricular hemorrhage; and (3) an association between serum tocopherol levels greater than 3.5 mg/dl and increased risk of sepsis and reduced risk for severe retinopathy among those examined.

Authors' conclusions

Vitamin E supplementation in preterm infants reduced the risk of intracranial hemorrhage but increased the risk of sepsis. In very low birth weight infants, vitamin E increased the risk of sepsis, and reduced the risk of severe retinopathy and blindness among those examined. Evidence does not support the routine use of vitamin E supplementation by intravenous route at high doses or aiming at serum tocopherol levels greater than 3.5 mg/dl.

PLAIN LANGUAGE SUMMARY

Vitamin E supplementation for prevention of morbidity and mortality in preterm infants

Giving extra vitamin E to preterm babies can provide some benefits, but it increases the risk of life-threatening infections. Preterm babies (born before 37 weeks) can develop a range of problems because their organs are not mature. Vitamin E may be able to help prevent or limit some of these problems, but it can potentially also have harmful effects. Breast milk of a woman who has given birth prematurely has higher than usual levels of vitamin E. Preterm babies can be given extra vitamin E as vitamin drops, in vitamin E-enriched formula, in intravenous fluids, or by injection into their muscles. This review of studies of vitamin E supplements found that while extra vitamin E reduces the chances of some complications (including disease of the retina), the risk of life-threatening infection is increased. The risk of bleeding in the brain is increased when extra vitamin E is given by vein but decreased when the extra vitamin E is given by other routes.