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Ardell S, Offringa M, Ovelman C, Soll R. Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates. *Cochrane Database of Systematic Reviews* 2018, Issue 2. Art. No.: CD008342. DOI: 10.1002/14651858.CD008342.pub2.

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[Intervention Review]

Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates

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Editorial group: Cochrane Neonatal Group. **Publication status and date:** New, published in Issue 2, 2018.

Citation: Ardell S, Offringa M, Ovelman C, Soll R. Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates. *Cochrane Database of Systematic Reviews* 2018, Issue 2. Art. No.: CD008342. DOI: 10.1002/14651858.CD008342.pub2.

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ABSTRACT

Background

Vitamin K is necessary for the synthesis of coagulation factors. Term infants, especially those who are exclusively breast fed, are deficient in vitamin K and consequently may have vitamin K deficiency bleeding (VKDB). Preterm infants are potentially at greater risk for VKDB because of delayed feeding and subsequent delay in the colonization of their gastrointestinal system with vitamin K producing microflora, as well as immature hepatic and hemostatic function.

Objectives

To determine the effect of vitamin K prophylaxis in the prevention of vitamin K deficiency bleeding (VKDB) in preterm infants.

Search methods

We used the standard search strategy of Cochrane Neonatal to search the Cochrane Central Register of Controlled Trials (CENTRAL 2016, Issue 11), MEDLINE via PubMed (1966 to 5 December 2016), Embase (1980 to 5 December 2016), and CINAHL (1982 to 5 December 2016). We also searched clinical trials databases, conference proceedings, and the reference lists of retrieved articles.

Selection criteria

Randomized controlled trials (RCTs) or quasi-RCTs of any preparation of vitamin K given to preterm infants.

Data collection and analysis

We evaluated potential studies and extracted data in accordance with the recommendations of Cochrane Neonatal.

Main results

We did not identify any eligible studies that compared vitamin K to no treatment.

One study compared intravenous (IV) to intramuscular (IM) administration of vitamin K and compared various dosages of vitamin K. Three different prophylactic regimes of vitamin K (0.5 mg IM, 0.2 mg vitamin K₁, or 0.2 mg IV) were given to infants less than 32 weeks' gestation. Given that only one small study met the inclusion criteria, we assessed the quality of the evidence for the outcomes evaluated as low.

Intramuscular versus intravenous

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There was no statistically significant difference in vitamin K levels in the 0.2 mg IV group when compared to the infants that received either 0.2 or 0.5 mg vitamin K IM (control) on day 5. By day 25, vitamin K₁ levels had declined in all of the groups, but infants who received 0.5 mg vitamin K IM had higher levels of vitamin K₁ than either the 0.2 mg IV group or the 0.2 mg IM group.

Vitamin K_1 2,3-epoxide (vitamin K_1 O) levels in the infants that received 0.2 mg IV were not statistically different from those in the control group on day 5 or 25 of the study. All of the infants had normal or supraphysiologic levels of vitamin K_1 concentrations and either no detectable or insignificant amounts of prothrombin induced by vitamin K absence-II (PIVKA II).

Dosage comparisons

Day 5 vitamin K₁ levels and vitamin K₁O levels were significantly lower in the 0.2 mg IM group when compared to the 0.5 mg IM group. On day 25, vitamin K₁O levels and vitamin K₁ levels in the 0.2 mg IM group and the 0.5 mg IM group were not significantly different. Presence of PIVKA II proteins in the 0.2 mg IM group versus the 0.5 mg IM group was not significantly different at day 5 or 25 of the study.

Authors' conclusions

Preterm infants have low levels of vitamin K and develop detectable PIVKA proteins during the first week of life. Despite being at risk for VKDB, there are no studies comparing vitamin K versus non-treatment and few studies that address potential dosing strategies for effective treatment. Dosage studies suggest that we are currently giving doses of vitamin K to preterm infants that lead to supraphysiologic levels. Because of current uncertainty, clinicians will have to extrapolate data from term infants to preterm infants. Since there is no available evidence that vitamin K is harmful or ineffective and since vitamin K is an inexpensive drug, it seems prudent to follow the recommendations of expert bodies and give vitamin K to preterm infants. However, further research on appropriate dose and route of administration is warranted.

PLAIN LANGUAGE SUMMARY

Prophylactic vitamin K for the prevention of vitamin K deficiency bleeding in preterm neonates

Review question

Is vitamin K prophylaxis effective in preventing vitamin K deficiency bleeding (VKBD) in preterm infants?

Background

Preterm infants are potentially at greater risk for VKBD because of delays in feeding and, therefore, delays in colonization of the intestine with vitamin K producing bacteria as well as immaturity of liver function and clotting function of the blood. Preterm infants are routinely given prophylactic vitamin K through intravenous or intramuscular routes.

Study characteristics

In searches completed up to 5 December 2016, we found no studies in preterm infants that compare prophylactic vitamin K to non treatment and one study that compared dosage and route of vitamin K administration.

Key results

One study met the inclusion criteria compared dosage and route of administration. This study suggests that both intravenous and intramuscular routes are adequate in achieving measurable vitamin K levels and that doses as low as 0.2 mg lead to measurable levels of vitamin K without evidence of the protein induced by vitamin K deficiency. More high-quality studies are needed to determine the best dose and route to give preterm infants vitamin K.

Quality of evidence

Low quality evidence.