AMERICAN ACADEMY OF PEDIATRICS

POLICY STATEMENT

Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of All Children

Committee on Fetus and Newborn

Controversies Concerning Vitamin K and the Newborn

ABSTRACT. Prevention of early vitamin K deficiency bleeding (VKDB) of the newborn, with onset at birth to 2 weeks of age (formerly known as classic hemorrhagic disease of the newborn), by oral or parenteral administration of vitamin K is accepted practice. In contrast, late VKDB, with onset from 2 to 12 weeks of age, is most effectively prevented by parenteral administration of vitamin K. Earlier concern regarding a possible causal association between parenteral vitamin K and childhood cancer has not been substantiated. This revised statement presents updated recommendations for the use of vitamin K in the prevention of early and late VKDB.

ABBREVIATION. VKDB, vitamin K deficiency bleeding.

BACKGROUND

Vitamin K deficiency may cause unexpected bleeding (0.25%–1.7% incidence) during the first week of life in previously healthy-appearing neonates (early vitamin K deficiency bleeding [VKDB] of the newborn [formerly known as classic hemorrhagic disease of the newborn]). The efficacy of neonatal vitamin K prophylaxis (oral or parenteral) in the prevention of early VKDB is firmly established. It has been the standard of care since the American Academy of Pediatrics recommended it in 1961.[1]

Late VKDB, a syndrome defined as unexpected bleeding attributable to severe vitamin K deficiency in infants 2 to 12 weeks of age, occurs primarily in exclusively breastfed infants who have received no or inadequate neonatal vitamin K prophylaxis. In addition, infants who have intestinal malabsorption defects (cholestatic jaundice, cystic fibrosis, etc) may also have late VKDB. The rate of late VKDB (often manifesting as sudden central nervous system hemorrhage) ranges from 4.4 to 7.2 per 100 000 births, according to reports from Europe and Asia.[2,3] When a single dose of oral vitamin K has been used for neonatal prophylaxis, the rate has decreased to 1.4 to 6.4 per 100 000 births. Parenteral neonatal vitamin K prophylaxis prevents the development of late VKDB in infants, with the rare exception of those with severe malabsorption syndromes.[2]

Oral administration of vitamin K has been shown to have efficacy similar to that of parenteral administration in the prevention of early VKDB.[4–6] However, several countries have reported a resurgence of late VKDB coincident with policies promoting the use of orally administered prophylaxis, even with multiple-dose regimens. In a 1997 review of these experiences by Cornelissen et al,[7] surveillance data from 4 countries revealed oral prophylaxis failures of 1.2 to 1.8 per 100 000 live births, compared with no reported cases after intramuscular administration. Newborns receiving incomplete oral prophylaxis tended to have a higher risk of developing VKDB, with rates of approximately 2 to 4 per 100 000. Small daily oral doses, as practiced in the Netherlands, may decrease the risk of late VKDB[8] and approach the efficacy of the parenteral route; however, this needs to be better studied.

Draper and Stiller,[9] using other data from Great Britain, have questioned the results of earlier studies of Golding et al[10,11] that attempted to show an association between intramuscular vitamin K administration in newborns and an increased incidence of childhood cancer. Using data from the National Registry of Childhood Tumors, they estimated the cumulative incidence of childhood leukemia. Three sources of data, including the estimates from Golding et al, provided rates of intramuscular vitamin K use over the same time frame. Their analyses failed to show a correlation between increased use of intramuscular vitamin K and the incidence of childhood leukemia.

The Vitamin K Ad Hoc Task Force of the American Academy of Pediatrics[12] reviewed the reports of Golding et al and other information regarding the US experience[13] and concluded that there was no association between the intramuscular administration of vitamin K and childhood leukemia or other cancers.

Additional studies that have since been conducted by other investigators have not supported a clinical relationship between newborn parenteral administration of vitamin K and childhood cancer. Ross and Davies[14] published a review of the evidence in 2000. They found no randomized or quasi-randomized evidence of an association between parenteral vitamin K prophylaxis and cancer in childhood. Ten case-control studies were identified, of which 7 found no relationship and 3 found only a weak relationship of neonatal administration of intramuscular or intravenous vitamin K with the risk of solid childhood tumors or leukemia.

PEDIATRICS (ISSN 0031 4005).

Recent research on the pathogenesis of childhood leukemia additionally weakens the plausibility of a causal relationship between parenteral administration of vitamin K and cancer. Investigations by Wiemels et al[15] suggest a prenatal origin of childhood leukemia. They found an acute lymphocytic leukemia-associated gene in 12 children with newly diagnosed acute lymphocytic leukemia and postulated that an in utero chromosomal translocation event combined with a postnatal promotional event results in clinical leukemia. Although intramuscular administration of vitamin K could conceivably be a postnatal promotional event, a genetic etiologic explanation further lessens the likelihood of a clinically significant relationship between intramuscular administration of vitamin K and leukemia.

There is concern that adequate vitamin K prophylaxis be provided to the increasing numbers of newborns who are breastfed exclusively to avoid an increased risk of late VKDB with its associated intracranial hemorrhage.[7]

RECOMMENDATIONS

Because parenteral vitamin K has been shown to prevent VKDB of the newborn and young infant and the risks of cancer have been unproven, the American Academy of Pediatrics recommends the following:

1. Vitamin K_1 should be given to all newborns as a single, intramuscular dose of 0.5 to 1 mg.[16]
2. Additional research should be conducted on the efficacy, safety, and bioavailability of oral formulations and optimal dosing regimens of vitamin K to prevent late VKDB.
3. Health care professionals should promote awareness among families of the risks of late VKDB associated with inadequate vitamin K prophylaxis from current oral dosage regimens, particularly for newborns who are breastfed exclusively.

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Pediatrics 2003;112;191