Vitamin K and the Breast-Fed Infant

Samuel J. Fomon

Department of Pediatrics, College of Medicine, University of Iowa, Iowa City, Iowa

Chemical methods for determining concentrations of vitamin K in milk and other body fluids have been developed and improved during the past 10 to 15 years. These methods are a major advance over the earlier biologic assays and permit new interpretations of available data as well as opportunities for answering a number of questions about vitamin K deficiency of infants. The requirement for vitamin K must be considered separately for the first few days of life and for somewhat older infants.

REQUIREMENT FOR VITAMIN K DURING THE FIRST FEW DAYS AFTER BIRTH

In 1967, Sutherland et al. (1) summarized earlier literature and provided additional data supporting the conclusion that vitamin K deficiency manifested clinically as hemorrhagic disease of the newborn is almost exclusively a disorder of breast-fed infants. The time of greatest risk is the second and third days of life (2). In nearly all instances, the disorder can be prevented by administration of 1 mg vitamin K$_1$ oxide intramuscularly in the first few hours after birth. Recent evidence suggests that oral administration of vitamin K$_1$ oxide may also be effective in preventing hemorrhagic disease of the newborn (3).

A number of reports strongly suggest that many infants are born with marginally adequate body stores of vitamin K. The report of Keenan et al. (4) is particularly instructive in this respect. The investigators determined prothrombin times of infants approximately 24 hr after the initiation of feeding, and it appears that feedings were begun at about 12 hr of age. Thus, the prothrombin times were probably determined at about 36 hr of age. Infants given only glucose and water and infants who were breast-fed or fed pooled human milk by bottle demonstrated prolonged prothrombin times (Table 1). Since prolongation of prothrombin times could be prevented by
TABLE 1. Prothrombin time at age 36 hr*

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Prothrombin time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin Kb</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Evaporated milk formula</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>Breast-fed</td>
<td>16</td>
<td>22c</td>
</tr>
<tr>
<td>Pooled human milk</td>
<td>16</td>
<td>20c</td>
</tr>
<tr>
<td>Water</td>
<td>8</td>
<td>27c</td>
</tr>
</tbody>
</table>

* Approximately 24 hr after initiation of feeding; data from ref. 4.

b Received an intramuscular injection of 1 mg water-soluble analog of menadione (various feedings).

c Significantly less (p < 0.001) than for the group given vitamin K.

administration of a dose of a substance with vitamin K activity (a water-soluble analog of menadione), it is evident that body stores were low.

As indicated in Table 1, there was little difference in prothrombin times of infants who had received an injection of the vitamin K-active substance and those fed a formula prepared from evaporated milk. From these findings and recent data on vitamin K concentrations of cow’s milk and human milk, a crude estimate of the requirement for vitamin K during the first 36 hours of life may be made. For this purpose, I have assumed that the intake of the evaporated milk formula or of human milk fed by bottle was 150 ml between 12 and 36 hr of age. This intake of evaporated milk formula would be equivalent to an intake of 100 ml of whole cow’s milk. Fournier et al. (5) have reported that mean concentrations of vitamin K in cow’s milk range from 7.5 µg/liter in winter to 35 µg/liter in summer. Thus, 100 ml milk would provide between 0.75 and 3.5 µg vitamin K. We do not know whether any of the evaporated milk was actually prepared from milk with vitamin K at the lowest end of the range, but it seems likely that the requirement is no more than 3.5 µg in the first 36 hr.

The data of Fournier et al. (5) indicate that median concentrations of vitamin K in human milk at 3, 8, and 21 days of lactation are 5.2, 8.9, and 9.2 µg/liter, respectively. If the pooled human milk fed by Keenan et al. (4) consisted of milk collected from women during the early days of lactation, intake of vitamin K may have been about 0.8 µg in the first 36 hr of life (5.2 µg/liter × 0.15 liter = 0.8 µg).

The requirement for vitamin K during the first 36 hr of life is thus likely to lie between 0.8 µg (which appears to result in prolonged prothrombin times) and 3.5 µg (the upper limit of the range probably consumed by the infants fed evaporated milk formulas).
REQUIREMENT FOR VITAMIN K AFTER THE IMMEDIATE NEWBORN PERIOD

Clinical manifestations of vitamin K deficiency are sometimes observed in breast-fed infants beyond the newborn period (6–10). Bleeding is then most likely to occur at 4 to 6 weeks of age in infants who did not receive vitamin K prophylaxis at the time of birth.

Even among infants who fail to receive a dose of vitamin K in the newborn period, relatively few develop clinical manifestations of vitamin K deficiency. Thus, if the median concentration of vitamin K in mature human milk is about 9 μg/liter (5) and daily intake of human milk is generally no more than 0.15 liter/kg, the average daily requirement for vitamin K is probably no more than 1.4 μg/kg.

Infants who fail to receive vitamin K prophylaxis in the newborn period and develop late clinical manifestations of vitamin K deficiency probably fall into one or more of the following three categories: (a) intakes of vitamin K from human milk are less than 1.4 μg/kg/day; (b) requirement for vitamin K is greater than 1.4 μg/kg/day; (c) bacterial synthesis of vitamin K in the intestine provides a smaller contribution to vitamin K nutritional status than is the case with other infants. The third category must be considered, even though there is no convincing evidence that vitamin K synthesized by intestinal bacteria is absorbed in appreciable amounts by human infants.

EXPECTATIONS FOR THE NEXT FEW YEARS

With more satisfactory methods for analysis of vitamin K now available, we can anticipate rapid accumulation of additional data, including more extensive information on the range of concentrations of vitamin K in human milk. We need to learn whether concentrations of vitamin K in milk of some women are consistently low and, if so, whether the diets of these women differ substantially from diets of other women. Clinical trials to determine the effect of vitamin K intake of lactating women on vitamin K concentration of milk seem desirable. We need also to determine whether among breast-fed infants who did not receive an initial injection of vitamin K there is a correlation between laboratory indices of vitamin K nutritional status and concentration of vitamin K in maternal milk. Finally, it will be important to determine whether concentrations of vitamin K are consistently low in the milk of women whose infants develop late manifestations of vitamin K deficiency.

We need to increase our efforts to assure that all infants receive a dose of vitamin K soon after birth; however, efforts in preventing vitamin K deficiency should not be directed exclusively toward the newborn period.
Health workers should routinely ascertain whether breast-fed infants less than 2 months of age received an initial dose of vitamin K and, if not, should arrange for a dose to be given. Oral administration is probably adequate.

REFERENCES