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Vitamin K and Thrombotest values in full term infants

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SUMMARY The vitamin K dependent clotting factors were measured by the 'Thrombotest' on the second day of life in 72 healthy full term babies, half of whom had received vitamin K at birth. Forty eight of these were breast fed, and those not given vitamin K had significantly lower Thrombotest values than those who had received vitamin K. By contrast, administration of vitamin K did not affect the Thrombotest values in bottle fed babies, the values in treated and untreated babies being the same and of the same order as the level in those breast fed babies treated with vitamin K.

Serial study of 18 normal breast fed babies tested at day 0 and day 2 showed a pronounced drop in the Thrombotest values in this period, which was prevented by one intramuscular dose of 1 mg vitamin K at birth. Although none of the neonates in this study showed haemorrhagic disease, nine of the 24 untreated breast fed infants had Thrombotest values below 10% on day 2, at which level bleeding has been reported.

Haemorrhagic disease of the newborn is a serious haemorrhagic disorder resulting from vitamin K deficiency that occurs most commonly in breast fed babies in the first few days of life.[1] The value of giving vitamin K prophylactically to neonates is controversial: it is not given routinely to all neonates in United Kingdom hospitals,[2] whereas the American Academy of Pediatricians recommends that 0·5–1·0 mg vitamin K is given to all newborn infants.[3] The weight of evidence for giving vitamin K is that it prevents haemorrhagic disease in the newborn, rapidly corrects bleeding in this condition, and has been shown to prevent low clotting factors associated with this disorder.[4] On the other hand, there is evidence to suggest that deficiency of vitamin K is not the cause of low level of vitamin K dependent factors in neonates and that liver immaturity may be responsible.[5 6]

Vitamin K dependent factors at birth are about one third of normal adult values[7] and can conveniently be measured by the 'Thrombotest' clotting test. This is a more specific and sensitive test for the measurement of the vitamin K dependent clotting factors than the previously used prothrombin time.[8] There is a postnatal fall in vitamin K clotting factors,[9] which may be responsible for haemorrhage, and a Thrombotest value of below 10% has been implicated as a dangerous level.[10] While it could be argued that the routine use of vitamin K is indicated in infants at risk because of complicated deliveries, its use in healthy neonates is open to question. The present study was therefore undertaken in normal full term infants to determine the effect of vitamin K on their clotting state and whether this differed in breast fed and bottle fed infants.

Patients and methods

The neonates studied were all born at the Princess Anne Hospital, Southampton. They were all healthy full term infants and were otherwise unselected. Those who were born by forceps or caesarean section were given vitamin K, in accordance with our normal practice; the rest were not given vitamin K. Permission to take blood samples from the babies was obtained from the parents, and the study was approved by the local ethical committee. The study was carried out on two separate groups of babies.

Group 1 (72 babies). Thirty six infants receiving vitamin K according to the criteria stated above were studied, together with a further 36 infants who did not receive vitamin K. Capillary samples were taken 48–60 hours after birth. Of the 72 babies, 48 were breast fed and 24 bottle fed.

Group 2 (18 babies). A further 18 babies, all of whom were breast fed, were studied twice, a cord blood sample being taken at birth followed by a

capillary blood sample 48–60 hours later. Ten of these babies were given vitamin K, and the other eight were untreated.

The Thrombotest (Nyegaard, Oslo) was used to assess the vitamin K dependent clotting factors according to the manufacturer's instructions. The coefficient of variation of replicated measurements on control blood was 1·4%. The results from 20 adult volunteers fell within the manufacturer's recommended normal range, and there was no significant difference between venous and capillary blood on paired samples.

The significance of differences between blood samples taken on day 0 and day 2 was analysed by Student's paired *t* test and for unpaired data by the non-parametric Mann-Whitney test for unpaired samples.

Results

Thrombotest values at day 2 in treated and untreated breast and bottle fed babies (group 1). Figure 1 shows a highly significant difference in the Thrombotest values in response to treatment with vitamin K in breast fed compared with bottle fed babies. Among the breast fed babies, the 24 who did not receive vitamin K at birth had significantly lower Thrombotest values ($p<0·001$) than those who were given the vitamin (mean values 15·2 and 39·1, respectively). Of the untreated babies nine (37·5%) had values below 10%. By contrast, in the bottle fed group none of the untreated babies had such low levels and the mean Thrombotest result was not significantly different in the untreated and treated babies (31·9 and 49·2, respectively). No bleeding manifestations were seen in any of these babies.

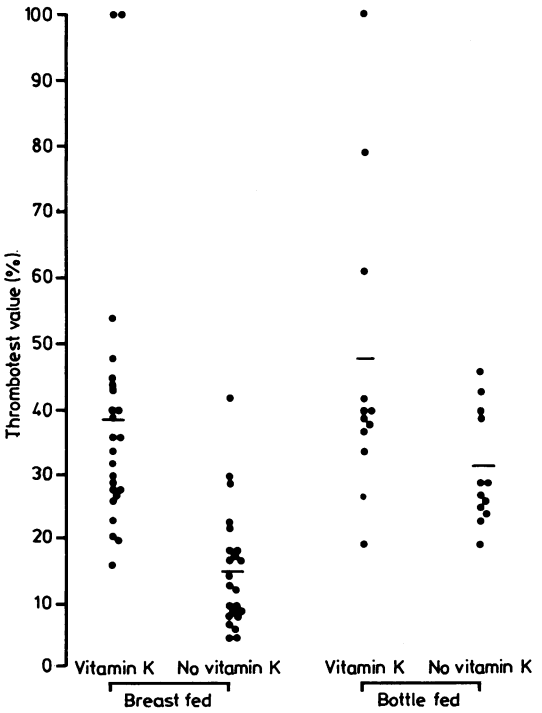

Fig. 1 *Thrombotest values at day 2 of life in 48 breast fed babies and 24 bottle fed babies (group 1), half of whom received vitamin K at birth (——=mean value).*

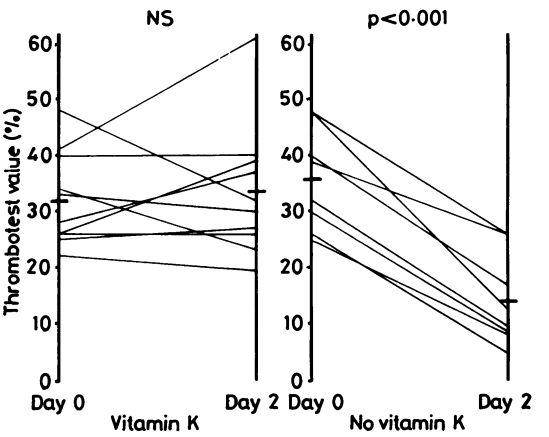

Fig. 2 *Change in thrombotest values between birth and day 2 in 10 full term breast fed babies (group 2) who received vitamin K at birth and in eight breast fed babies who did not receive vitamin K (——=mean value).*

Serial study of clotting state in treated and untreated breast fed babies (group 2). The change in Thrombotest values between day 0 and day 2 in the breast fed babies is shown in Figure 2 and clearly shows that vitamin K prevented the postnatal fall in Thrombotest values. Those given vitamin K showed no change with mean values of 32·5% and 33% for day 0 and 2, respectively, whereas those not given vitamin K showed a significant fall from 36% to 13·5% ($p<0·001$).

Discussion

This study confirms the reported decline in vitamin K dependent clotting factors during the first two days of life in breast fed full term babies, a decline preventable by the administration of vitamin K. Despite the finding of a Thrombotest value of less than 10% of the adult level in a third of the untreated breast fed babies, however, no haemor-

rhagic disease was seen. A mortality of 25% from haemorrhagic disease in babies with a Thrombotest value below 10% has been reported,[10] but these infants were premature and so liable to bleed from a number of other causes.[11 12] Extrapolating the results of this study, 800 babies a year in the Princess Anne Hospital could be expected to have a Thrombotest value below 10%, yet haemorrhagic disease is rare. Thus a low Thrombotest value alone is not diagnostic of this condition and factors other than low clotting levels must be important in its pathogenesis.

Our finding that the Thrombotest value was significantly greater in untreated bottle fed babies, none of whom had levels below 10%, compared with untreated breast fed babies is in keeping with the clinical observation that haemorrhagic disease is virtually unknown in bottle fed babies.[13] Treatment with vitamin K did not alter the clotting ability of bottle fed babies, there being no significant difference in treated or untreated infants. These contrasting results in breast and bottle fed infants support the concept of a protective effect of bottle feeding in preventing this disorder.

The increased risk of haemorrhagic disease in breast fed babies was thought to be due to a significantly lower vitamin K content in breast milk, but a new high performance liquid chromatography technique[14] has shown minimal quantities of vitamin K in both breast milk (2·1 μg/l) and artificial milk (4·2 μg/l). The readily observed difference between the stool of bottle and breast fed infants may be relevant; whereas *Escherichia coli*/coliforms that produce vitamin K flourish in the gut of the bottle fed baby, bifidobacteria predominate in the breast fed baby.[15] These flora, through differing capacities for production of vitamin K, may account for the differences in the reported haemorrhagic tendency in the two groups.

Our survey has shown that a number of breast fed babies born on our unit have levels of vitamin K dependent clotting factors that seem to be dangerously low. Although we have not seen clinical haemorrhagic disease of the newborn during this survey, a resurgence of this condition has been reported as the incidence of breast feeding has risen and with the gradual elimination of supplementary bottle feeding that may have protected some otherwise breast fed infants in the past.[2] Our present policy of giving vitamin K only to those with risk factors, such as prematurity, hypoxia, and delivery by forceps and caesarian section, now seems illogical, and a survey of our infants has shown that these criteria are not necessarily consistently applied. On our unit most women intend to breast feed, and it would not be easy to apply a different policy to breast fed and bottle fed babies. In conclusion, therefore, we feel bound to agree with the American Academy of Pediatrics that vitamin K should be given to all newborn infants.[3]

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