

5 May 1998

Dear Colleagues

VITAMIN K FOR NEWBORN BABIES

Additional vitamin K is widely used for prevention of vitamin K deficiency bleeding in newborn babies. Concerns about its use have focused on the safety and effectiveness of differing regimes. In 1992 we issued guidance about vitamin K and now, in the light of further information, we are in a position to update our advice which is attached to this letter.

We would be grateful if GPs could bring this letter to the attention of the nurses, midwives and health visitors associated with their practices, and if Chief Executives of NHS Trusts could arrange for it to be circulated among nursing and midwifery staff working in maternity and paediatric departments in hospitals and nurses, midwives and health visitors employed by community trusts. Also Health Authority Pharmaceutical Advisers are advised to bring this letter to the attention of community pharmacists.

Those with responsibilities for the care of newborn babies will wish to take account of this guidance when reviewing and agreeing local policies.

Sir Kenneth Calman **Mrs Y Moores**
Chief Medical Officer **Chief Nursing Officer**



From the Chief Medical Officer and Chief Nursing Officer

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PL/CMO/98/3
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Vitamin K for newborn babies

For information

- General Practitioners
- Paediatricians
- Obstetricians
- Chief Executives of Health Authorities
- Chief Executives of NHS Trusts
- Medical Directors of NHS Trusts
- Regional Directors
- Regional Directors of Public Health
- District Directors of Public Health
- Regional Nurse Directors
- Trust Nurse Executive Directors
- Midwives
- Health Visitors
- Regional Pharmaceutical Advisers

- Regional Drug Information Pharmacists
 - Trust Chief Pharmacists
 - Health Authority Pharmaceutical Advisers
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Sources of further information

A review by Drs S. Logan and R. Gilbert " Vitamin K prophylaxis for VKDB : an appraisal of the effectiveness of oral regimes" is expected to be published later in 1998. The following recent publications may prove helpful:

Reviews

McNinch A, Draper G. Vitamin K for neonates: the controversy. *BMJ* 1994; **308**:867-8.

Passmore SJ, McNinch A. Vitamin K in infancy. *Current Paediatrics* 1995; **5**:36-8.

McNinch A. The vitamin K story. *Midwives* 1997; **110**:56-8.

McNinch A. Vitamin K deficiency bleeding in the newborn infant. *Health Visitor* 1997; **70**:161-163.

Von Kries R. Neonatal vitamin K prophylaxis: the Gordian knot still awaits untying. *BMJ* 1998; **316**:161-2.

Which vitamin K preparation for the newborn ? *Drug and Therapeutics Bulletin* 1998; **36**:17-19.

International practice

Darlow B, Harding J. Vitamin K prophylaxis in the new born. *New Zealand Medical Journal* 1995; **108**: 514.

Cornelissen M, von Kries R, Loughnan P, Schubiger G. Prevention of vitamin K deficiency bleeding: efficacy of different multiple oral dose schedules of vitamin K. *Eur J Pediatr* 1997; **156**: 126-130.

Controversies concerning vitamin K and the newborn. Vitamin K ad hoc task force recommendations. *Pediatrics* 1993; **91**:1001-3.

Norgaard-Hansen-K; Ebbesen-F. Neonatal vitamin K prophylaxis in Denmark: Three years' experience with oral administration during the first three months of life compared with one oral administration at birth. *Acta-Paediatrica* 1996; **85**:1137-9.

Joint Statement and Interim Recommendations on Vitamin K Prophylaxis for Haemorrhagic Disease in Infancy. National Health and Medical Research Council, The Australian College of Paediatrics and The Royal Australian College of Obstetricians Gynaecologists. *Journal of Paediatrics and Child Health* 1993; **29**:182.

McMillan DD. Administration of Vitamin K to newborns: implications and recommendations. *Can Med Assoc J* 1996 ; **154**:347-9.

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VITAMIN K FOR NEWBORN BABIES AND VITAMIN K DEFICIENCY BLEEDING (VKDB)

◆ Do all babies need additional vitamin K?

- we recommend that all new born babies should receive an appropriate vitamin K regime to prevent the rare but serious and sometimes fatal disorder of VKDB.
- all should be offered one of the available regimes after an informed discussion with parents in the antenatal period.

◆ Could vitamin K be harmful?

- A joint Medicines Control Agency, Committee of Safety of Medicines and Department of Health expert group has concluded that overall, the available data do not support an increased risk of cancer caused by vitamin K but due to limitations of the data it is not possible to exclude a small increase in leukaemia.

◆ How can vitamin K be given?

- Either by intramuscular (i.m.) injection or using an oral regime. Parents should be fully informed about benefits and possible disadvantages of the regimes and be involved in the decision about the one chosen.
- i.m. Vitamin K effectively prevents VKDB in virtually all babies following a single dose given at birth, using Konakion (Roche) in a dosage of 1 mg.
- Oral regimes for additional doses of vitamin K can also be effective, but doses must be repeated. Arrangements must be in place to ensure that all recommended oral doses are given at the appropriate ages. Doses of vitamin K given at and shortly after birth should suffice for formula fed babies who then continue to receive vitamin K because it is added to formula milk. Breast milk is the ideal nutrition for babies and, as for formula fed, breast feeding babies need to receive additional vitamin K.

◆ Which babies are at greater risk of bleeding?

VKDB occurs unpredictably in some babies but others are at higher risk:

- *For early or classic VKDB:* babies who are premature, or are failing to take or absorb feeds, or had a complicated delivery or are ill or, if their mothers have been receiving medication associated with a higher risk of bleeding in the newborn period (e.g. anticonvulsant drugs).
- *For late VKDB :* babies with liver disease which may manifest as prolonged jaundice or with other symptoms e.g. pale stools and or dark urine, or, babies who have bleeding or spontaneous bruising in early infancy or who are ill from other causes.

The issues

For some time there have been professional concerns about administration of vitamin K to new born babies to prevent vitamin K deficiency bleeding (VKDB). VKDB may occur in the first 24 hours when it is classified as early, during age 2 to 7 days (classic) or after 7 days (late). The concerns have focused firstly, on whether all babies should receive additional vitamin K - especially in view of a possible though disputed association with childhood cancers which was suggested by research published in 1990 and 1992 - or secondly, on the best way to provide it. The following guidance is based on advice provided in the autumn of 1997 by two ad hoc expert working groups of the Department of Health and an expert advisory group convened by the Medicines Control Agency (MCA) on behalf of the MCA, the Committee on the Safety of Medicines (CSM) and the Department of Health.

The following questions are considered:

- ◆ **Do all babies need additional vitamin K?**
- ◆ **Could vitamin K be harmful?**
- ◆ **How can vitamin K be given?**
- ◆ **Which babies are at greater risk of bleeding?**

◆ Is it necessary that all babies receive additional vitamin K?

In babies who do not receive additional vitamin K, the best estimate available is that vitamin K deficiency bleeding (VKDB) occurs in approximately 1 in 10,000 babies. Studies also indicate that in half of the babies affected, bleeding occurs late, that is after the first week of life. In babies with late VKDB, about half suffer bleeding into the brain leading to death in about one fifth of these babies, or to brain damage in many of those surviving. Vitamin K is already added to formula milk to provide approximately 50 mcg daily. There is insufficient vitamin K in breast milk to prevent VKDB in a minority of babies, and multiple doses are needed to supplement the baby's natural stores of vitamin K throughout the period of exclusive breastfeeding. Thus since there is convincing evidence that VKDB can be prevented by administration of vitamin K, additional vitamin K should be offered to all newborn babies. A selective policy for high or low risk infants is not feasible as bleeding occurs unpredictably in some babies and confident categorisation of risk is not achievable. Late bleeding, which is more frequent in exclusively breast fed babies, occurs particularly in babies who have liver disease or other illness or who fail to absorb sufficient vitamin K from the gut. Many who suffer severe late VKDB have minor warning bleeds in the preceding few days. In about one third of instances the bleeding occurs without evident cause or risk factor.

If vitamin K were not given to other than high risk babies (described on page 7), it can be estimated that among the 800,000 or so annual births in the UK, there might be

- 60-80 babies who suffered a bleed
- 15-20 babies suffering an intra cranial bleed particularly with late VKDB
- 4-6 babies who may die from an intra cranial bleed
- 10-20 babies who may be brain damaged as a result of an intra cranial bleed

◆ Is vitamin K harmful?

In 1990 and 1992, studies from Bristol raised concern about a possible association between childhood cancer and intramuscular (i.m.) vitamin K given to newborn babies. Then the Department of Health undertook to commission further research aimed at resolving the uncertainties that have been raised by this reported association. This evidence together with other published papers was considered by an expert group convened in October 1997 by the Medicines Control Agency on its own behalf and for the Department of Health and Committee of Safety of Medicines. They reported :

"i. The Working Group considered all the evidence presently available from epidemiological studies which have examined the risks of childhood cancer after exposure to neonatal vitamin K. These included seven published and four unpublished papers¹, describing twelve studies; eight were case-control and four ecological in design. Further data are expected from the UK Childhood Cancer Study. The Working Group took into account the limitations of the evidence, particularly in the recording of exposure (whether vitamin K was given, the product, dose and route of administration) and in the comparability of control groups in some studies.

ii. The Working Group considered that the evidence suggests that there is no increased risk of solid tumours in association with vitamin K. There are fewer data relating to the risk of leukaemia and the findings of the epidemiological studies, some of which suggest the possibility of an increased risk, are inconsistent. This means that an increase in the risk of leukaemia overall or in particular subgroups such as acute lymphoblastic leukaemia (ALL) or ALL at ages 12 to 71 months, cannot be excluded. Nonetheless the Working Group considered that all the observed results were compatible with the play of chance.

iii. *The Working Group also considered ways in which vitamin K itself or 1 mg intramuscular (IM) Konakion might exert a carcinogenic effect, but did not identify a plausible mechanism for either.*

iv. *Working Group considered the efficacy of 1 mg IM Konakion to be well-established in the prevention of vitamin K deficiency bleeding in infants.*

v. *In the light of the above conclusions there is no basis for recommending a change to the current licensing position of Konakion."*

¹ The unpublished papers referred to were published in the BMJ on 17th January 1998

Summary

- (a) Some epidemiological studies have found an increased risk of childhood cancer in children receiving i.m. vitamin K but others have not confirmed this. An increased risk of cancers other than leukaemia is virtually excluded by the evidence.
- (b) The evidence on the risk of leukaemia associated with the use of i.m. vitamin K is inconsistent. Overall, it does not clearly indicate an increased risk but it is not possible to exclude a small increase in leukaemia due to limitations of the data.
- (c) A joint MCA, CSM and DH expert group has concluded that overall, the available data do not support an increased risk of cancer, including leukaemia, caused by vitamin K.

◆ How can vitamin K be given?

The choice of regime for administration of vitamin K lies between intramuscular (i.m.) injection or oral regimes.

Intramuscular vitamin K effectively prevents VKDB in virtually all babies following a single dose given at birth, using Konakion (Roche) in a dosage of 1 mg. Lower doses, e.g. 0.5 mg., given i.m. offer some protection but only the dose of 1 mg is licensed in UK for this purpose. The efficacy of the new mixed micelle Konakion MM given by a single i.m. injection is yet to be established.

Oral doses of vitamin K have been shown to be effective, but must be repeated to achieve equivalent effect to intramuscular usage. One dose of vitamin K given at birth may suffice for formula fed babies (though a second dose in the first week is advised) this is because all formula fed babies will continue to receive vitamin K which is added to formula milk.

Breast feeding remains the ideal nutrition for babies and like formula fed babies, they also need to receive vitamin K though as a supplement if i.m vitamin K has not been given.

An advantage of oral regimes is that the need to inject babies is avoided. Arrangements must, however, be in place to ensure that all recommended oral doses are given at the appropriate ages to all babies in order to ensure prevention of VKDB.

An oral preparation of vitamin K in a mixed micelle preparation enabling improved absorption is available in the form of Konakion MM (Roche). This is licensed for oral use in 2 doses of 2 mg to be given in the first week for all babies and, for exclusively breast feeding babies, a third dose of 2 mg is to be given at one month of age. This regime should be effective in prevention of VKDB providing that all recommended doses are given. The second dose in the first week is advised for formula fed babies to compensate for any failure to take or absorb the dose on the first day. For breast feeding babies the second and subsequent doses are necessary in order to maintain sufficient levels of vitamin K which are achieved in formula fed babies through the vitamin K added to the formula. Konakion MM is formulated in glass ampoules and currently it is necessary for a health care professional to administer the doses. Arrangements will need to be in place to ensure timely compliance with this regime. The involvement of health care professionals in giving the one month dose advised for exclusively breast fed babies is an organisational issue and arrangements should be agreed locally. They may include use of baby clinics or use of other contacts, such as home visits, during professional support offered to breast feeding mothers by health visitors and other healthcare professionals.

Other preparations of vitamin K, including frequent low dose regimes, are in use in breast feeding babies in this and other countries but no licensed preparation is available for this purpose in the United Kingdom. Advised nutritional requirements are for similar amounts of vitamin K. Formula feeds include extra vitamin K at this level.

Parents should be involved in the decision about giving vitamin K to their babies after they have been fully informed about the advantages and possible disadvantages of its use. Though breast feeding babies are at greater risk of vitamin K deficiency bleeding it is important that an impression is not given that breast milk is in some way deficient, rather that it is made clear that vitamin K is added to formula milk and that breast feeding babies require an alternative means of providing it. Information should be available to support the advice offered by professionals. Ideally the discussion with parents should take place in the antenatal period and preferably a decision about the regime to be adopted for their baby made then, recorded in the antenatal notes and confirmed at delivery.

◆ Which babies are at greater risk of bleeding?

Early VKDB is a particular risk to babies of mothers on certain drugs, for example, anticonvulsants. For classic and late VKDB, risks are higher in babies who are premature, who had a complicated delivery or who are ill or who have liver disease or difficulty absorbing feeds, especially if breast fed. Many babies who later suffer an intracranial bleed present with minor bleeds from the skin, nose or mouth. Any baby who is still jaundiced at 2 weeks of age needs specialist assessment particularly if the baby is failing to thrive or has features of obstructive jaundice (pale stools and yellow urine) or is ill in any way. If a jaundiced baby is formula fed, urgent investigation for obstructive jaundice is required. Breast feeding babies, if well, may be re-assessed at 3 weeks. If a baby remains jaundiced investigations should be carried out to identify the cause. At any time in the first 6 months of life minor bleeds should be investigated urgently, especially in breast feeding babies.

Parents may decide that their babies should not receive vitamin K or may prefer a modified course. In these circumstances, advice about features of higher risk of bleeding should be emphasised as is the need to be vigilant and to take action should minor warning bleeds or prolonged neonatal jaundice be present.

Conclusion

It is for professionals and services locally to agree which regimes should be available taking account of local circumstances and medical and social reasons which may affect the choice of regime in an individual baby. It is essential that a clear record is made for each baby on the dose, route and exact formulation of administration of vitamin K. When unlicensed preparations are prescribed, the responsibility lies with the prescribing doctor.