Routine administration of vitamin K to newborns

A joint position statement of the Fetus and Newborn Committee, Canadian Paediatric Society (CPS),
and the Committee on Child and Adolescent Health, College of Family Physicians of Canada

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Hemorrhagic disease of the newborn (HDNB) was first identified over 100 years ago by Townsend (1); it presents as unexpected bleeding, often with gastrointestinal hemorrhage and ecchymosis, and, in many cases, intracranial hemorrhage. In 1961, the Committee on Nutrition of the American Academy of Pediatrics (AAP) recommended that vitamin K_1 (hereafter referred to as vitamin K, the only form of vitamin K_1 used in neonates) 0.5 to 1.0 mg be administered intramuscularly to all newborns shortly after birth to prevent this problem (2). In 1988, the Canadian Paediatric Society (CPS) indicated that 2.0 mg of vitamin K administered orally within 6 h of birth was an acceptable alternative (3). This was before the suggestion that the risk of childhood cancer increases after intramuscular vitamin K shortly after birth (4,5), a suggestion which has subsequently been shown invalid (6). Although other countries joined Canada in recommending the alternative oral administration of vitamin K, the AAP has continued to advocate sole use of the intramuscular route, noting that an approved oral form is not available (6). The CPS believes that, on the basis of available information, their recommendations should be modified.

The current status of administration of vitamin K to newborns has recently been reviewed (7). Clinical decisions must be made on the best available evidence, despite controversy and a lack of definitive answers to many clinical questions. Potential harm to the baby must also be considered.

Although no significant complications after 420,000 intramuscular injections of vitamin K to newborns were reported (8), the psychological effects of intramuscular injections on newborn infants and their parents are unknown. It has been reported that pain experienced during the neonatal period may have long term effects (9,10). However, the benefits of routine vitamin K administration have been clearly shown, and it is important that this be given in the most effective manner (11). The 1988 CPS recommendations aimed to obtain the benefit of vitamin K for newborns without incurring pain (3). These recommendations supported

the oral route of administration of vitamin K with a formulation designed for parenteral use, a regimen reported to be effective, practical and economical (12).

To prevent early HDNB (which occurs during the first 24 h of life), the CPS also recommended administration of vitamin K to expectant mothers who take drugs that impair vitamin K metabolism (3). Classic HDNB (occurring in the first week of life) is rarely seen when vitamin K is given to newborn infants (11). Late HDNB (at three to eight weeks of age), which occurs almost exclusively among infants who are breastfed, has emerged as a more serious concern in Germany (13), Britain (14), Sweden (15,16) and Australia (17,18). In these countries the incidence of this problem increased at the same time as the implementation of the use of oral rather than intramuscular administration of vitamin K occurred. Although intramuscular administration of vitamin K appears to be superior to oral administration (4,13-15), repeated oral doses of vitamin K have also been suggested (15,19). In the absence of adequate amounts of vitamin K, an induced protein (PIVKA-II) may be measured in the blood; this protein disappears by five days after oral administration of 1.0 mg of vitamin K at birth (20). At five days of age, there appears to be no difference whether vitamin K was administered orally or intramuscularly (21). However, at age four to six weeks, biochemical signs of vitamin K deficiency are observed in up to 19% of infants given 2.0 mg of vitamin K orally at birth; by comparison, only 5.5% of those given 1.0 mg intramuscularly have biochemical signs of vitamin K deficiency (22). A mixed-micelle form of vitamin K may be better absorbed. However, a study showed that, even with this formulation, there is a greater incidence of vitamin K deficiency when vitamin K is given orally than when it is administered intramuscularly (23). The problem common to all of these studies is the poor clinical correlation of these biochemical indicators to abnormal bleeding in infants.

An epidemiological study from Germany by von Kries (8) showed a failure rate (occurrence of late HDNB) after intramuscular administration of 0.25 per 100,000 infants, compared with a rate of 1.4 per 100,000 infants after oral administration. In other countries in which oral administration is the primary form of vitamin K deficiency prophylaxis, the incidence of late HDNB varied – 1.5 (Britain), 6.0 (Sweden) and 6.4 (Switzerland) per 100,000 infants (8,18). Some of these infants could have had underlying disorders that affected vitamin K metabolism (24). The specific incidence of late HDNB in Canada after oral or intramuscular administration of vitamin K is unknown, although addition of HDNB to reports to the Canadian Paediatric Surveillance Program may provide further information. (In the first six months of 1997, there were two confirmed reports of HDNB – one in a baby who received no vitamin K following birth and one who received oral vitamin K.)

A meta-analysis of cohort studies comparing babies who receive a single oral dose of vitamin K with those who receive a single intramuscular dose of vitamin K after birth indicates a relative risk of HDNB of 13.82 (Table 1) (14,25,26). Even excluding babies with liver disease, which usually cannot be determined at birth, the relative risk is 8.15 (95% CI 1.32 to 28.63). Although there are reports of successful experience using oral vitamin K prophylaxis in neonates (27), analysis of the reported scientific data supports the use of intramuscular rather than oral vitamin K after birth.

TABLE 1: Incidence of hemorrhagic disease of the newborn

Study (reference)	Single oral dose n/N	Single intramuscular dose n/N	Weight %	Relative risk*	95% CI
McNinch (14)	7/493,000	0/945,000	23.9	28.75	1.64 to 503.45

Tönz (26)	8/108,820	0/75,620	41.1	11.81	0.68 to 204.68
von Kreis (25)	2/140,250	1/418,500	35.0	5.97	0.54 to 65.82
Total	17/742,070	1/1,439,120	100.0	13.82	2.88 to 66.19

** Relative risk oral compared with intramuscular.*
n Number of babies with hemorrhagic disease of the newborn; N Number of babies given vitamin K after birth.
χ^2 *= 0.80 (df=2) Z=3.12*

Reasons for increased benefit with intramuscular administration of vitamin K following birth are not clear (possibly storage with slow release). Because risks of late HDNB are greatest in breastfed babies, it has been suggested that there may be benefit to giving lactating mothers vitamin K (28,29). Although one study from Denmark reported that a program of weekly oral vitamin K for babies until three months of age reduced the incidence of late HDNB compared with a single oral dose (30), a repeated oral dose regimen may not be practical because of poor patient compliance (31). An epidemiological study, which included the Netherlands, Germany, Switzerland and Australia, confirmed that three oral doses of 1 mg vitamin K are less effective than intramuscular vitamin K prophylaxis in neonates, although a daily oral dose of 25 mg after an initial dose of 1 mg vitamin K may be as effective (32).

It is important to note that intramuscular administration of vitamin K does not provide complete protection from HDNB, especially in breastfed infants whose oral intake of vitamin K is low. Physicians should also consider the possibility of vitamin K deficiency at an early stage in the evaluation of any bleeding that occurs during the first six months of life. Appropriate therapy with vitamin K should be instituted when required. (It is reasonable to consider administering further doses of vitamin K to infants at a high risk of HDNB: those who fail to thrive, have liver disease or have long term diarrhea.)

The large number of newborn infants required to conduct a prospective study comparing the efficacy of intramuscular and oral administration of vitamin K (with or without repeated doses) make it unlikely that such a study will be carried out. Furthermore, given the higher risk of late HDNB after a single oral dose of vitamin K after birth compared with vitamin K administered intramuscularly and the 50% chance that infants with late HDNB may have serious intracranial hemorrhage (22), administration of vitamin K by the intramuscular route seems most prudent. Repeated oral doses should be reserved for infants whose parents refuse intramuscular administration of vitamin K following birth.

Recommendations

Vitamin K_1 should be given as a single intramuscular dose of 0.5 mg (birthweight 1500 g or less) or 1.0 mg (birthweight greater than 1500 g) to all newborns within the first 6 h after birth following initial stabilization of the baby and an appropriate opportunity for maternal (family)-baby interaction.

For newborn infants whose parents refuse an intramuscular injection, the physician should recommend an

oral dose of 2.0 mg vitamin K_1 at the time of the first feeding. (A minority of committee members believe that physicians should have the option to recommend oral administration of vitamin K for newborns under their care.) Use of the parenteral form of vitamin K for oral administration is all that is currently available. This should be repeated at two to four weeks and six to eight weeks of age. Parents should be advised of the importance of the baby receiving follow-up doses and be cautioned that their infants remain at an increased risk of late HDNB (including the potential for intracranial hemorrhage) using this regimen.

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This paper was critically reviewed and evaluated by the College of Family Physicians of Canada's Committee on Child and Adolescent Health (Chair, Dr Carol Herbert)

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