Are Pediatricians Complicit in Vitamin K Deficiency Bleeding?

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abstract

The American Academy of Pediatrics recommends that all newborns receive a single dose of intramuscular vitamin K to prevent vitamin K deficiency bleeding. How should the clinician respond when parents decline vitamin K? Although vitamin K deficiency bleeding can have devastating sequelae, they are uncommon; therefore, parents are generally allowed to decline vitamin K after counseling is provided. When parents ask for a vitamin K preparation of unproven effectiveness, should the clinician honor that request? To address these questions, we present a case of a healthy newborn whose parents declined intramuscular vitamin K and requested an oral preparation. Two general pediatricians discuss the medical and ethical issues these situations pose, and the parents describe their experience.

Many parents refuse routine preventive treatments. The most widely publicized and contentious such refusal involves childhood immunizations. Recently, there have been cases in which parents have refused intramuscular vitamin K at birth and infants have developed hemorrhagic disease. Such parental refusals place pediatricians in a tough situation. The American Academy of Pediatrics (AAP) recommends that all infants receive intramuscular vitamin K. But, as with immunizations, there is no imminent life-threatening danger when infants do not receive this injection.

Here we present a case of this sort of disagreement. We were fortunate that the parents who were involved in this case were willing to share with us the reasons behind their decision. We also have comments from the pediatricians who were involved.

THE CASE

Evan Green was born by spontaneous vaginal delivery to a 34-year-old primiparous mother after an uncomplicated, full-term pregnancy. His mother took no medications apart from prenatal vitamins and planned to exclusively breastfeed her infant. His parents declined the vitamin K injection in the labor and delivery unit and signed a refusal form in the presence of a nurse.

AARON AND JOY GREEN, PARENTS OF EVAN GREEN, COMMENT:

We knew that it was standard practice to give most infants a vitamin K shot and that its purpose is to help with blood clotting. We had heard that the dose given is more than what is necessary. Also, more generally, we knew that shots are painful and the puncture is another point where germs/bacteria can enter the body. We were concerned that the dose may contain an ingredient other than vitamin K, such as metal, preservatives, etc. We thought oral vitamin K would be a better option because it does not have those concerns. We heard about oral vitamin K from our chiropractor, who is a natural health fan and a reader of Dr Joseph Mercola. She is also a little biased on this topic because she hates all shots. We did not discuss vitamin K with anyone else before delivery.

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Drs Weddle and Phillipi conceptualized and designed the ethics question, searched the literature for current evidence, and drafted portions of the initial manuscript; Drs Empey and Crossen drafted the initial ethical question in the manuscript; Mr Green and Ms Green drafted the parent perspective; Dr Empey coordinated and helped author the contribution from the parents; Drs Weddle, Empey, Crossen, and Phillipi critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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Because birth is a traumatic experience for the infant, we imagined bleeding could occur in any area, especially if there is a complication. The possibility of Evan having intracranial bleeding did not enter into our decision-making at the time. It was a long labor, but not a complicated one (from our perspective). Like all infants, he was very flexible, and because skull plates move around for the process of being born, we were not concerned about it.

No one had explained how brain bleeds could happen even weeks after childbirth. Most of the reading we did had general information like "to help with blood clotting." Nothing said where the bleeding was likely to occur or how long it could take to occur. Our preparation for birth class was likewise general—or at least not memorable on this topic. In it, there was a short segment about things that would take place after birth, like the antibiotic eye drops and the vitamin K shot. It did not necessarily state why it would happen, just that it would.

QUESTIONS TO CONSIDER

What steps should the pediatric team take to address this infant's risk for vitamin K deficiency bleeding (VKDB)? Should they offer oral vitamin K?

The pediatric resident and attending physician discuss how VKDB was recently publicized in the media after 4 cases of late VKDB were reported in Nashville, Tennessee.[1] In all 4 cases, the parents had refused the vitamin K injection at birth.

CARRIE PHILLIPI, MD, PHD, COMMENTS:

Newborn care clinicians are frequently faced with parents who decline intramuscular phytonadione (vitamin K) administration and request oral formulations instead. Sometimes parents have obtained or plan to administer oral vitamin K from another source. Parental concerns regarding intramuscular vitamin K include pain, exposure to preservatives, high dosing, excessive interventions, and (unsubstantiated) association with childhood cancer. A recent cluster of 4 cases of late VKDB in healthy newborns who did not receive vitamin K[1] reinforces anecdotal concerns from pediatric providers that parental refusal of intramuscular vitamin K is becoming more commonplace. In a Canadian cohort, 0.3% of children did not receive vitamin K owing to parental refusal.[2] Incidence of vitamin K refusal in the United States is unknown but likely varies by geography, delivery clinician, and delivery setting.

VKDB presents in 3 forms: early, classic, and late. Early bleeding occurs in the first 24 hours, is often severe, and is associated with maternal medications that inhibit vitamin K, such as anticonvulsants, antituberculous medications, some antibiotics (cephalexin), and vitamin K antagonists (warfarin, coumarin).[3] The classic form of VKDB occurs in the first week of life and can have a milder presentation, with bruising or bleeding from injection sites.[4] Late VKDB presents with severe bleeding, primarily in infants who are exclusively breastfed, and may occur many weeks after birth. Of infants with late VKDB, 50% have intracranial bleeding with resultant risk of neurologic injury; mortality rates are estimated at 20%.[4,5]

In 2003, the AAP published a policy statement recommending that all neonates receive a single intramuscular dose of 0.5 to 1 mg vitamin K for prevention of early, classic, and late VKDB.[6] According to the policy statement, oral formulations require more study. Oral vitamin K has been administered in a variety of regimens in countries outside the United States, and although they are effective based on surveillance data, they are not as effective as a single intramuscular dose.[7] Multiple oral doses are more efficacious than a single dose.[8] A more contemporary recommendation from the Canadian Paediatric Society suggests that oral vitamin K should be administered to those newborns whose parents decline intramuscular vitamin K in a multidose regimen (2 mg at birth and at 1 and 6 weeks).[9] The authors admit that "use of the parenteral form of vitamin K for oral administration is all that is currently available."

What do we know about the efficacy of vitamin K preparations available in the United States? Unfortunately, very little. The phytonadione 5 mg tablet is the only oral formulation approved by the US Food and Drug Administration and licensed in the United States.[10] Because administering crushed tablets to newborns is challenging, the only licensed injectable formulation is commonly given orally (Hospira, 1 mg/0.5 mL).[10] No other formulations are manufactured and approved for use in the United States, with the exception of unregulated over-the-counter supplements. No data on the oral bioavailability of these products exist, nor are data available regarding oral administration of the intramuscular formulation. Compounding pharmacies may prepare a 1-mg/mL suspension, but it must be stored under refrigeration and is stable for only a few days,[11] making repeated administration challenging for clinicians and families. Although compliance with multidose administration has not been studied in the United States, compliance with a 3-dose regimen in England was found to be poor.[12]

At Oregon Health & Science University, pediatric clinicians created a set of orders for oral vitamin K in the electronic health record. Reasoning that any vitamin K was likely to offer a benefit over none, clinicians could easily order oral vitamin K in a standardized fashion with the intramuscular formulation

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given orally at birth, and a prescription for 2 additional doses of crushed tablets after discharge. Despite being informed about the lack of evidence supporting this regimen, some families seemed to perceive it as equally effective to the intramuscular vitamin K. What initially seemed a good idea (delivery of a plausible but untested therapy) became troubling to clinicians, and the electronic order set was retired, although individual providers may still prescribe oral vitamin K.

Off-label use of drugs is common in children, especially those with rare diseases. In the AAP Committee on Drugs Report, off-label prescribing "does not imply an improper, illegal, contraindicated, or investigational use" when completed using professional judgment to benefit the individual patient.[13] However, this typically implies that no alternative option exists, which is not the case with vitamin K.

Our experience prompts the question: Armed with little, if any, information to support its efficacy, should pediatric providers in the United States recommend and prescribe oral vitamin K formulations in lieu of intramuscular formulations when parents decline? I argue they should not.

MELISSA WEDDLE, MD, MPH, COMMENTS:

This case poses 2 ethical questions: (1) What is the appropriate response when parents decline recommended treatment such as vitamin K? (2) Should clinicians offer oral vitamin K to newborns when families decline the recommended vitamin K injection?

The first question points to conflict between parent choice and child well-being. As physicians, our duty is to promote the well-being of our patients. In the case of vitamin K in the newborn period, we have a preventive intervention—a single injection of vitamin K—that is safe and effective in preventing a disease that is rare but has potentially devastating consequences. In the United States, clinicians have limited ability to interfere with parental decision-making; we respect the authority of parents to decide for their children unless a decision poses an unacceptably high or immediate risk.[14] Because VKDB is sufficiently uncommon (incidence of early and classic VKDB is 1/300,[15] and late VKDB, 4 to 10/100 000 infants[3,5,16]), parents are allowed to decline vitamin K.

However, for patients (or surrogates) to accept or reject recommended care, informed consent must occur. How information is delivered and the discussion that follows influences decision-making. Kon describes a continuum of shared decision-making, a model in which the parents (in this case) and physician reach a medical decision together.[17] At the patient-driven end of the spectrum, the physician presents factual information and available options, leaving parents to decide. This would be appropriate when there is more than one option with comparable effectiveness, not the case in our vitamin K scenario. At the physician-driven end of the spectrum, care is provided without discussion, as in life-threatening situations. Our vitamin K scenario falls somewhere in the middle, which leads to the next question: When a family declines the recommended care, how far can a clinician ethically go to promote a low-risk option with clear health benefit?

The clinician may attempt to persuade parents to give the more effective intramuscular vitamin K, as long as voluntariness is preserved.[18] Persuasion includes removal of biases,[19] a requisite step in negotiating recommended care. For example, if parents believe that an oral preparation is more natural and therefore more effective, the clinician appropriately gives best available information about efficacy. Using evidence and rational argument to influence others is considered the ideal in modern medical practice, and is compatible with respecting autonomy.[20] In many situations, a clinician would be morally blameworthy if he or she did not attempt to persuade the patient to consent to a medically indicated intervention.[21]

For those parents who refuse vitamin K altogether, we would follow an approach similar to that recommended for those who decline immunizations: respectfully elicit parent concerns, attempt to correct misinformation, and recommend intramuscular K while giving the reasons for it. As with families who decline immunizations, it is appropriate to provide written information to supplement the discussion, and ask parents to sign a document indicating that they have received information, had questions answered, and understand the risks of declining.[22]

Looking beyond our scenario, clinicians who care for newborns may need to ally with obstetric clinicians to inform expectant parents about newborn preventive health measures. In a recent study, 69% of expectant parents did not know the purpose for vitamin K,[23] indicating a need for education and counseling before delivery. A different study showed increased likelihood of vitamin K refusal among those who chose midwife delivery, suggesting a role for targeted prenatal counseling by trusted providers who care for those most likely to decline it.[2]

The second question central to this case is whether clinicians should offer or support oral vitamin K. We know oral vitamin K preparations used in Europe are effective in prevention of classic VKDB, but they are less effective in prevention of late VKDB.[24] In the United States, oral preparations include vitamin K

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intravenous solution, compounded vitamin K tablets, and a mail-order liquid preparation. There is no evidence that any of these formulations is effective in prevention of early, classic, or late VKDB.[10] Puckett and Offringa[25] conclude that a single dose of intramuscular vitamin K (1.0 mg) after birth is effective in the prevention of classic VKDB, and they note that intramuscular vitamin K has not been tested in randomized trials for effect on late VKDB. They also note that oral vitamin K, in either single or multiple doses, has not been tested in randomized trials for effect on either classic or late VKDB.[25] The World Health Organization recommends that all newborns be given 1 mg vitamin K intramuscularly after birth (strong recommendation, moderate-quality evidence).[26]

When parents decline the vitamin K injection at our institution, an oral dose of vitamin K intravenous solution is sometimes provided at parents' request. Physicians who order oral vitamin K follow the 3-dose recommendation made by the Canadian Paediatric Society[9]; other regimens are readily found by internet search (eg, http://newborns.stanford.edu/VitaminK.html).[27] A weekly oral regimen given over a 12-week period was recently suggested to be safer compared with 3-dose oral regimens.[28] Here in the Portland, Oregon metropolitan area, practice differs between medical centers, with not all hospitals offering oral vitamin K. Some parents at our hospital obtain oral vitamin K before admission, either purchasing an over-the-counter preparation or obtaining it through the mother's clinician.

Should we offer oral vitamin K to those families who are opposed to the injection? We have a responsibility to offer only treatments that have reasonable possibility of benefit to our patients (beneficence). When we offer a treatment, we imply that the option may have benefit. In the case of oral vitamin K, we have no evidence that the preparations used in the United States have any benefit in prevention of VKDB. Even when we counsel about uncertain benefit of a medication, its availability connotes acceptability. Our experience suggests that some families who would choose oral vitamin K when it is offered may choose the intramuscular form when the oral form is not available. I argue that although VKDB is rare, its severity and its complications, which include brain injury and death, warrant the use of effective prophylactic measures. The AAP has endorsed intramuscular vitamin K based on evidence and expert opinion and recommends additional research to evaluate oral vitamin K.[6] When a standard of care does not exist, as in the case of oral vitamin K, clinicians or institutions rightly may vary practice. When practice varies, it is incumbent on practitioners to base practice on an understanding of available evidence.

A thorough review of the medical literature caused our group to be concerned about increasing risk of VKDB in our newborns by offering a potentially ineffective medication for a disease with serious sequelae when a safe and effective medication exists. I believe that we should not offer oral vitamin K and that we should advise against use of the oral vitamin K preparations currently available in the United States until we have evidence of benefit.

AARON AND JOY GREEN COMMENT:

We decided to give Evan the vitamin K shot. We learned that even if Evan got more vitamin K than he needed, it is not toxic. The pain and risk for infection were things we considered, but ultimately not big factors in our decision. The largest concern to us was that the vitamin K dose would contain ingredients other than vitamin K. We both avoid injecting things like aluminum, mercury (including thimerosal), formaldehyde, animal DNA, etc, directly into our bloodstreams (as opposed to entering our body through the digestive tract). After we were assured that the vitamin K shot contained no other ingredients, we agreed to have it given to Evan.

JOHN D. LANTOS, MD, COMMENTS:

Studies of parents who refuse routine preventive treatments generally show that parents trust doctors more than they trust other sources of health information.[29] This case illustrates the importance of talking together about the reasons we recommend certain treatments. Talking takes time, but it is time well spent. It shows respect, illustrates the principle of respect for parental autonomy, and allows the physician to be not just a healer but an educator. We should encourage parents to question our recommendations, just as we encourage students to do, and welcome the opportunity to explain why we recommend the treatments that we recommend. Educated parents make the best child advocates.

ABBREVIATIONS

AAP: American Academy of Pediatrics
VKDB: vitamin K deficiency bleeding

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