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VITAMIN K PROPHYLAXIS IN NEWBORNS: BENEFITS, CURRENT RECOMMENDATIONS, AND CONTROVERSIES – A LITERATURE REVIEW

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ABSTRACT

Vitamin K prophylaxis is an essential component of routine newborn care and is used to prevent vitamin K deficiency bleeding (VKDB), a potentially severe and sometimes fatal bleeding disorder. Newborn infants have physiologically low vitamin K stores and are particularly vulnerable to bleeding during the first weeks of life. This narrative review aims to summarize the benefits, current recommendations, routes of administration, and controversies surrounding vitamin K prophylaxis in newborns. Intramuscular vitamin K administration has been shown to be highly effective in preventing VKDB, including late-onset disease. Oral vitamin K regimens may provide an alternative in selected settings but are less reliable, particularly for the prevention of late VKDB. Current international recommendations support routine vitamin K prophylaxis for all newborns, with intramuscular administration considered the most effective approach. Appropriate counseling of parents and adherence to standardized neonatal protocols remain essential to ensure effective prevention.

Keywords: Vitamin K; Newborn; Vitamin K deficiency bleeding; VKDB; Neonatal prophylaxis; Intramuscular vitamin K

1 INTRODUCTION

Vitamin K prophylaxis is one of the most established preventive interventions in neonatal care. It is routinely administered after birth to prevent vitamin K deficiency bleeding (VKDB), a potentially life-threatening condition that may occur during the neonatal period or early infancy [1,2].

Newborn infants have low vitamin K stores at birth because of limited placental transfer, low concentrations of vitamin K in breast milk, and the immature intestinal synthesis of vitamin K during the first weeks of life. As a result, newborns are particularly vulnerable to vitamin K deficiency and associated bleeding complications [2,3].

VKDB can be classified into early, classic, and late forms. Early VKDB occurs within the first 24 hours of life and is often associated with maternal medications or underlying disorders. Classic VKDB generally occurs during the first week of life, whereas late VKDB occurs from approximately the second week to several months of age and may present with severe intracranial hemorrhage [2,4].

The administration of vitamin K shortly after birth has markedly reduced the incidence of VKDB. Intramuscular administration is considered the most effective route because it provides reliable vitamin K exposure and better protection against late-onset disease compared with a single oral dose [1,2].

Despite the established benefits of prophylaxis, differences remain between countries regarding the preferred dose, route of administration, and oral regimens. In addition, parental concerns regarding the injection, potential adverse effects, and misinformation may contribute to refusal of prophylaxis [1,5].

This review aims to summarize the rationale, benefits, administration strategies, current recommendations, and remaining controversies regarding vitamin K prophylaxis in newborns.

2 METHODS

PubMed, Google Scholar, and the Cochrane Library. Articles published in English between 2000 and 2026 were considered. The search strategy included combinations of the following keywords: “vitamin K,” “newborn,” “neonate,” “vitamin K deficiency bleeding,” “VKDB,” “vitamin K prophylaxis,” “intramuscular vitamin K,” and “oral vitamin K.”

Relevant studies, including randomized controlled trials, observational studies, systematic reviews, clinical guidelines, and recommendations from international pediatric and neonatal organizations, were reviewed. Particular attention was given to studies evaluating the incidence and prevention of vitamin K deficiency bleeding, the efficacy of different routes and doses of vitamin K administration, and current recommendations for neonatal prophylaxis.

Articles were selected according to their relevance to the objectives of this review, with priority given to recent publications and evidence from major international guidelines. The available literature was analyzed narratively to summarize the benefits, administration strategies, current recommendations, and controversies surrounding vitamin K prophylaxis in newborns.

2.1 Vitamin K Deficiency and Vitamin K Deficiency Bleeding in Newborns

Vitamin K is essential for the synthesis of several coagulation factors, including factors II, VII, IX, and X, as well as proteins C and S. Newborn infants have naturally low vitamin K stores because of limited placental transfer, low vitamin K concentrations in breast milk, and the immature intestinal production of vitamin K during the first weeks of life [1,2].

Vitamin K deficiency bleeding (VKDB) is classified into three forms according to the time of onset. Early VKDB occurs within the first 24 hours of life and is usually associated with maternal medications or underlying maternal or neonatal conditions. Classic VKDB occurs during the first week of life and may present with gastrointestinal, skin, mucosal, or umbilical bleeding. Late VKDB occurs from approximately 2 weeks to 6 months of age and is particularly concerning because intracranial hemorrhage is common and may result in severe neurological complications or death [2,3].

Breastfed infants are at increased risk of late VKDB because breast milk contains relatively low concentrations of vitamin K compared with formula milk. Infants with unrecognized cholestatic liver disease or other conditions associated with impaired vitamin K absorption are also at increased risk [2,4].

Before routine vitamin K prophylaxis was introduced, VKDB was an important cause of preventable neonatal and infant bleeding. Administration of vitamin K shortly after birth has substantially reduced the incidence of both classic and late VKDB and has become a standard component of newborn preventive care [1,2].

The prevention of VKDB is particularly important because late-onset disease may occur in apparently healthy infants without preceding warning signs. Consequently, routine prophylaxis is recommended even in newborns who have no identifiable risk factors for vitamin K deficiency [1,2].

2.2 Benefits and Efficacy of Vitamin K Prophylaxis

Vitamin K prophylaxis is highly effective in preventing vitamin K deficiency bleeding (VKDB) in newborns. Administration of vitamin K shortly after birth significantly reduces the incidence of classic VKDB and provides important protection against late-onset disease, particularly intracranial hemorrhage [1,2].

Intramuscular vitamin K has been shown to provide more reliable and sustained protection than oral administration. A single intramuscular dose administered after birth is highly effective in preventing late VKDB, including in exclusively breastfed infants [2,5].

The benefits of prophylaxis are particularly important because late VKDB can occur several weeks after birth in infants who initially appear healthy. In many cases, intracranial bleeding is the first clinical manifestation and may lead to seizures, neurological impairment, or death [3,4]. Effective prophylaxis therefore represents an important preventive intervention in neonatal and infant care.

Several studies have demonstrated that routine vitamin K administration has dramatically reduced the incidence of VKDB compared with the pre-prophylaxis era [1,2]. The effectiveness of prophylaxis is also supported by population-based surveillance studies showing very low rates of late VKDB among infants who received appropriate intramuscular vitamin K at birth.

Oral vitamin K regimens can also reduce the risk of VKDB and may be considered in situations where intramuscular administration is declined or not feasible. However, oral prophylaxis requires multiple doses and strict adherence to the recommended schedule. Its effectiveness may also be reduced in infants with unrecognized cholestasis or impaired intestinal absorption [2,6].

Overall, the available evidence supports routine vitamin K prophylaxis for all newborns, with intramuscular administration providing the most consistent protection against both early and late VKDB.

2.3 Routes, Doses, and Administration Regimens

Vitamin K can be administered to newborns by intramuscular or oral routes. The choice of route and dosing regimen varies between countries and clinical guidelines, although intramuscular administration is generally considered the most reliable method for preventing VKDB [1,2].

For healthy term newborns, a single intramuscular dose of vitamin K administered shortly after birth provides effective and prolonged protection against vitamin K deficiency. Current recommendations generally use 1 mg of vitamin K given intramuscularly for newborns with a birth weight above 1500 g [1,2]. For very small preterm infants, lower doses may be recommended according to local protocols and the formulation available.

Oral vitamin K regimens have been developed as an alternative for parents who decline intramuscular injection or when intramuscular administration is not feasible. However, oral prophylaxis requires repeated administration to maintain adequate protection. Different schedules have been proposed, including an initial dose at birth followed by additional doses during the first weeks or months of life [2,6].

One of the main limitations of oral prophylaxis is the need for strict adherence to the complete regimen. Missed doses may reduce its effectiveness, particularly against late VKDB. In addition, oral vitamin K may be less effective in infants with cholestasis or other disorders associated with impaired intestinal absorption [2,4].

The intramuscular route therefore remains the preferred approach in most current recommendations because it provides reliable protection with a single administration. When oral prophylaxis is selected, parents should receive clear instructions regarding the complete dosing schedule and the importance of administering all recommended doses.

2.4 Current Recommendations and Controversies

Current international recommendations support routine vitamin K prophylaxis for all newborns because the risk of VKDB cannot be reliably predicted on the basis of clinical appearance alone [1,2]. Intramuscular administration shortly after birth is generally recommended because of its high efficacy and its ability to provide sustained protection against late-onset VKDB.

The main differences between guidelines concern the dose, timing of administration, and the use of oral regimens. While a single intramuscular dose is widely accepted, oral regimens vary between countries and generally require several doses. These differences reflect variations in available formulations, healthcare systems, and national policies [2,6].

One important issue is parental refusal of intramuscular vitamin K. Some parents may be concerned about the injection itself or may have encountered inaccurate information regarding the safety of vitamin K. Healthcare professionals should therefore provide clear and evidence-based information about the benefits of prophylaxis and the potentially severe consequences of VKDB.

Another controversy concerns the historical association between injectable vitamin K and childhood cancer. This concern originated from an observational study published several decades ago. Subsequent larger epidemiological studies failed to confirm an increased risk of leukemia or other childhood cancers following neonatal vitamin K administration [7,8]. Current evidence therefore does not support an association between vitamin K prophylaxis and childhood cancer.

Overall, the available evidence strongly favors routine neonatal vitamin K prophylaxis. Although oral administration may be an alternative in selected circumstances, intramuscular vitamin K remains the most effective and reliable strategy for preventing VKDB, particularly the late form of the disease.

3 DISCUSSION

Vitamin K prophylaxis has become a fundamental component of routine newborn care because it effectively prevents vitamin K deficiency bleeding (VKDB), a rare but potentially life-threatening condition. The physiological characteristics of newborn infants, including low vitamin K stores, limited placental transfer, low concentrations of vitamin K in breast milk, and immature intestinal synthesis, contribute to the increased susceptibility to vitamin K deficiency during early life [1–3].

The clinical importance of VKDB lies particularly in its late form, which may occur several weeks after birth in infants who initially appear completely healthy. Late VKDB frequently involves intracranial hemorrhage and may result in severe neurological sequelae or death [3,4]. A systematic review estimated that, in the absence of prophylaxis, the median incidence of late VKDB was approximately 35 cases per 100,000 live births, with substantially higher rates reported in low- and middle-income countries [5]. These findings emphasize the importance of universal prophylaxis, particularly in settings where access to specialized neonatal and pediatric care may be limited.

The effectiveness of vitamin K prophylaxis has been demonstrated in both clinical studies and population-based surveillance. Intramuscular administration has been associated with a marked reduction in the incidence of late VKDB compared with no prophylaxis, with observational evidence suggesting a substantial protective effect [5]. Earlier randomized studies also demonstrated a reduction in clinically significant bleeding following intramuscular vitamin K administration [6]. Although the absolute incidence of VKDB is low, the severity of potential complications makes prevention highly relevant from a public health perspective.

The route of administration remains an important consideration. Intramuscular vitamin K is generally considered the most reliable method because a single dose provides prolonged protection without requiring subsequent parental adherence [2,5]. In contrast, oral administration requires repeated doses and may be less reliable, particularly when doses are missed or when intestinal absorption is impaired. A systematic review found that a single oral dose was associated with a higher risk of VKDB than intramuscular prophylaxis, whereas multiple-dose oral regimens appeared to provide better protection [5].

This distinction is particularly relevant for late VKDB. Infants with unrecognized cholestatic liver disease may have impaired absorption of fat-soluble vitamins, including vitamin K. In such circumstances, oral administration may not provide adequate protection, whereas parenteral administration remains more reliable [3,7]. This is one of the principal reasons why international recommendations generally favor intramuscular prophylaxis as the preferred strategy.

Current recommendations are broadly consistent in supporting routine vitamin K administration to all newborns. The ESPGHAN Committee on Nutrition recommends that all newborn infants receive vitamin K prophylaxis and considers intramuscular administration the preferred route because of its efficacy and reliability [2]. Alternative oral regimens may be used in selected circumstances, but they require strict adherence to a schedule involving multiple doses [2]. Thus, the choice of regimen should take into account local practices, available formulations, healthcare resources, and the ability to ensure follow-up.

Parental acceptance is another important aspect of vitamin K prophylaxis. Although the intervention is well established, some parents may decline intramuscular vitamin K because of concerns regarding the injection, perceived lack of necessity, or exposure to inaccurate information. Refusal is clinically important because an infant who does not receive prophylaxis remains at risk for a preventable bleeding disorder, including severe intracranial hemorrhage. Clear communication and evidence-based counseling before or shortly after delivery are therefore essential components of neonatal care [2,8].

Safety concerns have also influenced the history of vitamin K prophylaxis. In the early 1990s, two observational studies raised concerns about a possible association between intramuscular vitamin K and childhood leukemia. These findings generated considerable debate and led to further epidemiological investigations [9]. However, subsequent studies did not confirm a convincing association. A large case-control analysis found no significant increase in childhood cancer following neonatal vitamin K administration [10]. Similarly, a pooled analysis of individual patient data from six case-control studies found no convincing evidence that intramuscular vitamin K was associated with childhood leukemia [11]. Current evidence therefore does not support withholding vitamin K prophylaxis because of a presumed cancer risk.

Another consideration is the administration of vitamin K to preterm and low-birth-weight infants. These infants may have an increased vulnerability to bleeding and may require dose adjustments according to birth weight, gestational age, and the specific formulation used. Although international recommendations differ somewhat regarding dosing in very small preterm infants, there is broad agreement that they should receive prophylaxis and that dosing should follow established neonatal protocols [2,12].

Overall, the evidence accumulated over several decades strongly supports routine vitamin K prophylaxis in newborns. The intervention is inexpensive, simple to administer, and highly effective in preventing a potentially devastating condition. Intramuscular administration remains the preferred approach because of its reliability and superior protection against late VKDB, while oral regimens may represent an alternative when intramuscular administration is declined or unavailable. Continued education of healthcare professionals and parents is essential to maintain high prophylaxis coverage and prevent avoidable cases of severe neonatal and infant bleeding.

4 CONCLUSION

Vitamin K prophylaxis is a simple, safe, and highly effective intervention for the prevention of vitamin K deficiency bleeding in newborns. Its administration shortly after birth markedly reduces the risk of both classic and late-onset VKDB, including potentially life-threatening intracranial hemorrhage.

Intramuscular administration remains the preferred method because it provides reliable and sustained protection, particularly against late-onset disease. Although oral regimens may be considered in selected circumstances, they require repeated administration and adequate adherence.

Current evidence does not support an association between neonatal vitamin K administration and childhood cancer. The benefits of prophylaxis clearly outweigh the potential concerns surrounding its use.

Vitamin K prophylaxis should therefore remain an integral component of standard newborn care. Appropriate parental counseling, correction of misconceptions, and adherence to evidence-based neonatal protocols are essential to ensure optimal prevention of VKDB and its potentially severe complications.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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