

*Review Article***Effect of Vitamin K on Mothers and Neonates****Beshoy T. Asaad*, Essa Mahmoud, Heba Hassan* and Reem A. Abdel Aziz****

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Introduction

Vitamin K was first discovered in the early 1930s by the Danish biochemist Henrik Dam who observed while studying cholesterol metabolism in chickens that chicks fed with a diet free of sterols and low in fat tended to develop subcutaneous and intramuscular hemorrhages.^[1] Current researches increasingly indicate that the antihemorrhagic vitamin has a considerable benefit in the prevention and treatment of bone and vascular disease.^[2] Vitamin K1 (phylloquinone) is more abundant in foods but less bioactive than the vitamin K2 (menaquinones).^[2] Phylloquinone (vitamin K1) and menaquinone (vitamin K2) are the two naturally occurring forms of vitamin K.^[3] The importance of vitamin K in hemostasis arises from the fact that all vitamin K-dependent coagulation factors require γ -carboxylation of glutamic acid residues at their Gla domains, to enable binding of calcium and attachment to phospholipid membranes.^[4] This enzymatic reaction is catalyzed by a microsomal, vitamin K-dependent enzyme, γ -glutamyl carboxylase, which in turn is linked to a cyclic salvage pathway known as the vitamin K epoxide cycle.^[5]

This carboxylation process necessarily requires a functional vitamin K cycle to produce the active vitamin K co-factor (vitamin K quinone) for the γ -carboxylase which post translationally modifies the precursors of the vitamin K-dependent proteins.

Seven vitamin K-dependent proteins are involved in blood coagulation: prothrombin (factor II), factors VII, IX, and X, and proteins C, S, and Z. Prothrombin and factors VII, IX, and X possess procoagulant activity, whereas proteins C and S act as anticoagulants. The physiologic function of protein Z is still unknown. The vitamin K-dependent coagulation proteins are typical secretory glycoproteins synthesized in the liver.^[6]

Protein S also has been shown to be present in protein extracts of human bone matrix and to be synthesized and secreted by osteoblasts in addition to its synthesis in liver.^[7]

Factors II, VII, IX, and X represent the classical vitamin K-dependent plasma clotting factors and participate in the cascade that results in the formation of the fibrin clot.^[8]

A key element in the formation of fibrin is the generation of thrombin from prothrombin by activated factor X. Vitamin K-dependent factors VII and IX activate factor X by extrinsic and intrinsic pathways.^[6]

In contrast to prothrombin and factors VII, IX, and X, proteins C and S are inhibitors of the procoagulant system. Protein C is a two-chain glycoprotein. It exerts its primary inhibitory activity by inactivating activated factors V and VIII, representing two rate-limiting steps of coagulation.^[9]

The roles of vitamin k dependent (Gla) proteins are shown in (table 1).^[10]

Protein C is known to possess significant fibrinolytic activity. In humans, protein C increases fibrinolysis by inactivating the major inhibitor of tissue plasminogen activator.^[11]

Protein S is a single chain glycoprotein found in plasma in the free form. Although protein S was observed to be a cofactor of protein C for inactivation of factor V and VIII, Protein S also serves as a cofactor for protein C enhancement of fibrinolysis.^{[12][13]}

Vitamin K has important actions in the nervous system. As a unique cofactor to the γ -glutamyl carboxylase enzyme, vitamin K contributes to the biological activation of proteins Growth arrest specific gene 6 (Gas6) and protein S.^[14]

The effect of vitamin K1 supplementation on insulin sensitivity and glycemic status has been examined by Rasekhi et al., (2015) among prediabetic and women population in india.^[15]

Vitamin K1 supplementation caused a significant decrease in fasting glucose, 2-h post-OGTT glucose and insulin concentrations, and an increase in insulin sensitivity index, but did not affect the insulin resistance.^[16]

Vitamin K deficiency leads to the synthesis of undercarboxylated proteins called PIVKA (protein induced by vitamin K absence), that are unable to bind calcium and therefore inactive. PIVKAs are released from the liver into the blood and their level increases with the severity of the deficiency.^[17]

Vitamin k deficiency can cause serious risks to pregnant women and their babies that may lead to hemorrhage, especially in the newborns. Hemorrhage occurs due to reduced levels of prothrombin which is a vitamin k dependent coagulation factor that slows down the blood clotting process and may result in excessive maternal or neonatal bleeding.^[18]

Nutritional requirements generally increase in pregnancy, the risks of clinically relevant deficiencies also escalate, especially among pregnant women with poor nutritional status.^[19]

It is largely unknown what type of crucial role vitamin K plays during pregnancy.^[20]

VKD in pregnant women causes intracranial hemorrhage (ICH) in fetuses. Fetal ICH frequently causes life-threatening and persistent neurological damage.^[21]

Levels of vitamin K-dependent factors (II, VII, IX, and X) are physiologically low in newborns, so parenteral vitamin k administration is routinely prescribed to babies born with inadequate vitamin k storage as they are at risk of developing vitamin k bleeding disorder (VKBD) which is a serious condition that can result in bleeding in the brain leading to brain damage.^[22]

Vitamin K supplementation during pregnancy is recommended if mothers are on anticonvulsant therapy or prolonged treatment with certain antibiotics such as B lactam antibiotics containing the methyltetrazole-thiol group. This group is present in cefamandole, latamoxef (moxalactam) and cefoperazone. Cefazolin and cefazedone, which predispose the neonate to bleeding tendency.^[23]

Evaluation of a bleeding neonate always begins with taking a detailed maternal and family history. It is important to obtain details about the mother's state of health during pregnancy and labor, including infections, maternal autoimmune disease, and platelet count. Other details about the labor and delivery itself, such as prolonged time between rupture of membranes and delivery, fetal distress, and chorioamnionitis are also important.^[24]

In an otherwise well infant, bleeding from a circumcision site, oozing from the umbilicus, bleeding into the scalp, large cephalhematomas, or ICH may point to coagulation factor deficiencies such as hemophilia or von Willebrand disease, or disorders of platelet numbers such as Neonatal Alloimmune Thrombocytopenia (NAIT).^[22]

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