

# Effects of vitamin k analogues on blood clotting

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**ABSTRACT:** Vitamin k is an essential nutrient associated with clotting cascade and also has an anti cancer potential. Vitamin k antagonistic warfarin is an agent of choice for long term management of thromboembolic conditions. It is administered orally.

**Keywords:** Warfarin, oral drugs, anticoagulants

## INTRODUCTION –

Vitamin K is a fat soluble blood clotting vitamin. It is a crucial protein involved in the production of many proteins in the process of blood coagulation. It is integral in the synthesis of coagulants and anticoagulants such as factors prothrombin, proconvertin, christmas factor, stuartrower factor and protein c,s. Administration of vitamin k shortly after birth prevents the neonatal morbidity and mortality related to haemorrhage. Vitamin k is necessary for the post translation gamma carboxylation of coagulants and protein c and protein s. K quinolone, the reduced form of vitamin k is used for the reaction to occur in the endoplasmic reticulum such as calcium binding and gamma carboxylation.

## DISCUSSION –

Vitamin K is a group of structurally similar, fat-soluble vitamins the human body requires for complete synthesis of certain proteins that are prerequisites for blood coagulation and which the body also needs for controlling binding of calcium in bones and other tissues (1).

The vitamin K-related modification of the proteins allows them to bind calcium ions, which they cannot do otherwise. Without vitamin K, blood coagulation is seriously impaired, and uncontrolled bleeding occurs. Preliminary clinical research indicates that deficiency of vitamin K may weaken bones, potentially leading to osteoporosis, and may promote calcification of arteries and other soft tissues (2).

Newborn infants are susceptible to bleeding disorders causes due to the deficiency of vitamin k. It is known as the haemorrhagic disease of the newborn. Low molecular weight is used in coagulation monitoring because of its reduced levels of plasma binding proteins. It has to be administered parenterally only. Phylloquinone or menaquinone are capable of reversing the anticoagulant activity of the powerful anticoagulant warfarin. The newer anticoagulants dabigatran and rivaroxaban have different mechanisms of action and are generally taken with supplemental vitamin k. It is used to reverse the effects of "blood thinning" medications and to prevent clotting problems in the new born who don't have enough vitamin k. It treats bleeding caused by medications including salicylates, sulphonamides, quinine, quinidine, or antibiotics. Vitamin k is used to reduce the risk of bleeding in liver diseases. It helps to treat and prevent low levels of unusual bleeding by increasing the body's production of blood clotting factors.

This article concerning the pharmacokinetics and pharmacodynamics of vitamin K antagonists (VKAs) is part of the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). It describes the antithrombotic effect of the VKAs, the monitoring of anticoagulation intensity, and the clinical applications of VKA therapy and provides specific management recommendations. Grade 1 recommendations are strong and indicate that the benefits do or do not outweigh the risks, burdens, and costs. Grade 2 recommendations suggest that the individual patient's values may lead to different choices.

The article also includes several specific recommendations for the management of patients with nontherapeutic INRs, with INRs above the therapeutic range, and with bleeding whether the INR is therapeutic or elevated. For the use of vitamin K to reverse a mildly elevated INR, we recommend oral rather than subcutaneous administration (Grade 1A). For patients with life-threatening bleeding or intracranial hemorrhage, we recommend the use of prothrombin complex concentrates or recombinant factor VIIa to immediately reverse the INR (Grade 1C). For most patients who have a lupus inhibitor, we recommend a therapeutic target INR of 2.5 (range, 2.0 to 3.0) [Grade 1A]. We recommend that physicians who manage oral anticoagulation therapy do so in a systematic and coordinated fashion, incorporating patient education, systematic INR testing, tracking, follow-up, and good patient communication of results and dose adjustments [Grade 1B]. In patients who are suitably selected and trained, patient self-testing or patient self-management of dosing are effective alternative treatment models that result in improved quality of anticoagulation management, with greater time in the therapeutic range and fewer adverse events. Patient self-monitoring or self-management, however, is a choice made by patients and physicians that depends on many factors. We suggest that such therapeutic management be implemented where suitable (Grade 2B).

The antithrombotic effect of VKAs has conventionally been attributed to their anticoagulant effect, which in turn is mediated by the reduction of four vitamin K-dependent coagulation factors. Evidence suggests, however, that the anticoagulant and anti-thrombotic effects can be dissociated and that the reduction of prothrombin and possibly factor X are more important than the

reduction of factors VII and IX for the antithrombotic effect. This evidence is indirect and has been derived from the following observations.

First, the experiments of Wessler and Gitel (3) more than 40 years ago using a stasis model of thrombosis in rabbits showed that the antithrombotic effect of warfarin requires 6 days of treatment, whereas an anticoagulant effect develops in 2 days. The antithrombotic effect of warfarin requires the reduction of prothrombin (factor II), which has a relatively long half-life of about 60 to 72 h compared with 6 to 24 h for other vitamin K-dependent factors that are responsible for the more rapid anticoagulant effect.

Second, in a rabbit model of tissue factor- induced intravascular coagulation, (4) the protective effect of warfarin was mainly a result of lowering prothrombin levels.

Third, Patel and associates (5) demonstrated that clots formed from umbilical cord plasma containing about half the prothrombin concentration of plasma from adult control subjects generated significantly less fibrinopeptide A than clots formed from maternal plasma. The view that warfarin exerts its antithrombotic effect by reducing prothrombin levels is consistent with observations that clot-bound thrombin is an important mediator of clot growth and that reduction in prothrombin levels decreases the amount of thrombin generated and bound to fibrin, thereby reducing thrombogenicity (6).

#### CONCLUSION-

The suggestion that the antithrombotic effect of warfarin is reflected in lower levels of prothrombin forms the basis for overlapping the administration of heparin with warfarin until the PT or INR is prolonged into the therapeutic range during the treatment of patients with thrombosis. Because the half-life of pro- thrombin is about 60 to 72 h, at least 4 days of overlap is necessary. Furthermore, the levels of native pro- thrombin antigen during warfarin therapy more closely reflect antithrombotic activity than the PT.

#### REFERENCES -

1. "Vitamin K". Micronutrient Information Center, Linus Pauling Institute, Oregon State University, Corvallis, OR. July 2014. Retrieved 20 March 2017.
2. Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin k antagonists: American college of chest physicians evidence-based clinical practice guidelines (8th edition). *Chest* 2008;133:160S-98S. Rombouts EK, Rossendaal FR, Van Deer Meer FJ. Daily vitamin k supplementation improves anticoagulant stability. *J ThrombHaemost* 2007;25:1746-51. Sconce E, Khan T, Mason J, et al. Patients with unstable control have poor dietary intake of vitamin k compared to patients with stable control of anticoagulation. *ThrombHaemost* 2005;93:8872-5.
3. Wessler S, Gitel SN. Warfarin: from bedside to bench.
4. *N Engl J Med* 1984; 311:645– 652
5. Patel P, Weitz J, Brooker LA, et al. Decreased thrombin activity of fibrin clots prepared in cord plasma compared to adult plasma. *Pediatr Res* 1996; 39:826 – 830
6. Zivelin A, Rao VM, Rapaport SI. Mechanism of the antico- agulant effect of warfarin as evaluated in rabbits by selective depression of individual procoagulant vitamin-K dependent clotting factors. *J Clin Invest* 1993; 92:2131–214