18. Vitamin K

Physiology

Vitamin K activity is shown by a number of compounds containing the 2-methyl-1,4-naphthoquinone structure. They include phylloquinone (the major dietary source), which occurs in plants, and the menaquinones, synthesized by bacteria [1].

Knowledge of the physiology of vitamin K has lagged behind that of the other fat-soluble vitamins mainly because of the difficulty of quantifying the various forms. The best dietary sources are green leafy vegetables. Much smaller but nevertheless significant amounts are found in other foodstuffs of both plant and animal origin [1]. It is uncertain to what extent the intestinal bacteria contribute vitamin K to the body [2,3,4].

Vitamin K is reasonably well absorbed from the small intestine, but only poorly from the colon. Like all fat-soluble vitamins its absorption in substantial amounts depends upon normal production of bile acids and pancreatic enzymes. It is enhanced by dietary fat. In malabsorption syndromes uptake from the diet is very poor [1].

There is little storage of vitamin K in the body and there appears to be a fairly rapid turnover, so a continual supply is necessary in the diet.

Vitamin K operates as an essential cofactor for a carboxylase enzyme catalysing the postranslational carboxylation of specific glutamyl residues in some proteins to the γ-carboxyglutamic form [2]. The best known such proteins are prothrombin and at least five other proteins involved in blood clotting. More recent work has shown that a number of other proteins containing γ-carboxyglutamic acid require vitamin K for their biosynthesis, notably osteocalcin in bone [3].

Deficiency and excess

Vitamin K deficiency results in a bleeding syndrome consequent upon a lack of clotting factors. No deficiency signs have been reported as a result of inadequate production of other vitamin K-dependent proteins.

Clinical features may range from mild bruising to severe life-threatening haemorrhage. Deficiency can occur in infants, who are born with low reserves and no gut flora, as breast milk is not a good source of the vitamin.

Clinical vitamin K deficiency is never seen after the first few months of life, except as a consequence of disease states, e.g. malabsorption, the use of vitamin K antagonists as anticoagulant drugs, long-term treatment with some antibiotics, parenteral nutrition without vitamin K [4].

No adverse signs have ever been reported from large oral doses of vitamin K [5]. Menadione, a synthetic water-soluble compound with vitamin K activity, may induce haemolytic anaemia, hyperbilirubinaemia and kernicterus in the newborn; these are not manifestations of hypervitaminosis K, but are side effects of an unphysiological form [5].

Requirements

It is not easy to estimate human requirements because of the difficulty of inducing vitamin K deficiency in normal subjects. Vitamin K status has usually been assessed from the plasma concentration of prothrombin, measured from the clotting time in standardized conditions (prothrombin time). New more sensitive procedures are now being used to measure decreased activity of vitamin K-dependent clotting factors, lowered serum concentration of vitamin K and decreased urinary excretion of γ-carboxyglutamic acid [6].

In one experiment young healthy subjects consumed a diet, from which foods rich in vitamin K had been removed, to give approximately 50 µg phylloquinone/d. Blood clotting appeared normal, but there were signs that prothrombin biosynthesis was not optimal, and there was a decrease in γ-carboxyglutamic acid excretion. Supplements of 50 µg phylloquinone/d restored these indices to normal [7].

These findings are consistent with earlier work indicating that the requirement for dietary vitamin K is about 1 µg per kg body weight per day [2,7].

Considering the difficulty of inducing vitamin K deficiency in healthy subjects, the problem of monitoring vitamin K status sensitively and reliably, the uncertainty of how much might be supplied by intestinal bacteria and the lack of accurate values for the amount of dietary K just sufficient to maintain normal function, the Committee decided to make no recommendation for vitamin K. An intake of 1 µg per kg body weight per day appears adequate and would be provided by a normal mixed diet.

References

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