Vitamin K Deficiency in the Hospitalized Patient-- Are we Underestimating the Prevalence?

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Editorial

Bleeding diathesis purely from vitamin K deficiency is rarely seen in adults. However mild vitamin K deficiency in the form of a slightly prolonged prothrombin time (PT) is commonly seen in hospitalized patients due to the poor oral intake, fat malabsorptive disorders, malignancy, broad spectrum antibiotic use especially cephalosporins and liver or renal disease.

Vitamin K is necessary for synthesis of coagulation factors II (prothrombin), VII, IX and X in the liver. In the absence of vitamin K, the liver will synthesize inactive precursor proteins known as proteins induced by the absence of vitamin K (PIVKA's). Because vitamin K is fat-soluble, it can only be absorbed from the intestine in the presence of bile salts. The body's capacity to store vitamin K is very low and the half-life of the vitamin K-dependent coagulation factors is short [1]. Because of this, deficiency can occur quickly if the intake is not sufficient.

Dietary sources of vitamin K, which occur mainly in the form of phylloquinone, include vegetables, particularly green leafed, broccoli, cabbage, lettuce, spinach, sprouts, potatoes, tomatoes and beans. Milk and dairy products, meats, eggs, cereals, fruit, pastry, some oils and salad dressings also contain some vitamin K [2].

Subclinical Vitamin K deficiency has been induced in healthy adults fed a diet providing about 10 micrograms of phylloquinone per day [3]. Vitamin K1 depletion dramatically and significantly decreased plasma vitamin K1 levels (P<0.0001) to values 13-18%. The vitamin K1 depletion period had no significant effect on either prothrombin and activated partial thromboplastin times. However, decarboxy prothrombin was found to increase slightly but significantly (P<0.05) as a consequence of the low vitamin K1 diet.

The use of broad spectrum antibiotics in the hospitalized patients is becoming increasingly common. Their use has been associated with hypoprothrombinemia. The two postulated mechanisms implicate either direct inhibition of biosynthesis of the vitamin K-dependent clotting factors by the N-methylthiotetrazole (NMTT) moiety found in certain antimicrobial agents or eradication of vitamin K-producing intestinal microflora in patients with reduced oral intake of vitamin K [4]. NMTT has been implicated in cephalosporin associated hypoprothrombinemia.

Measurements of prothrombin time, Echis time and plasma concentrations of under-carboxylated prothrombin (proteins induced in vitamin K absence or antagonism, PIVKA-II) have been used to measure Vitamin K deficiency and raised PIVKA-II are suggestive that vitamin K stores may be insufficient to maintain full gamma-carboxylation of prothrombin and emphasize the need to anticipate vitamin K deficiency in the intensive care unit by appropriate supplementation [5]. However, in clinical practice, an elevated PT without evidence of DIC is suspicious of Vitamin K deficiency and supplementation is usually given to correct it even if there is no evidence of bleeding. This probably has prevented severe Vitamin K deficiency and therefore bleeding diathesis secondary to it.

In this issue of the Journal of Blood and Lymph, Kasireddy and colleagues report a case of acute gastrointestinal bleeding due to acute on chronic Vitamin K deficiency. In the report, an elderly gentleman with poor nutritional status (prealbumin was 8) who came in with mild abdominal discomfort. His coagulation profile was normal at admission. He then went to develop a life threatening recto-sigmoid bleed after being placed on broad spectrum antibiotics for 4 days. At that time, his Prothrombin time (PT) and Activated partial thromboplastin time (APTT) were extremely elevated. Disseminated Intravascular bleeding (DIC) was ruled out by normal platelets, d-dimers and fibrinogen. The patient had no evidence of liver disease. However, he had a mild renal insufficiency. The PT and APTT corrected after patient was treated with fresh frozen plasma and IV Vitamin K and bleeding was controlled.

In summary, the case report shows that hospitalized patients, especially elderly with poor nutritional statuses those who are on broad spectrum antibiotics are at increased risk of Vitamin K deficiency. Vitamin K supplementation in these patients who have mildly elevated or even normal prothrombin times can prevent catastrophic bleeding.

References

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