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Jochanan E. Naschitz *

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Research Article

Enteral feeding deficient in vitamin K. Is there a related substantial bleeding risk?

Natalia Zaigraykin, Elena Zlotover, Faisal Neime, Natalia Starikov, Ygor Yalonetski, Gregory Leibovitz, Jochanan E. Naschitz*

Bait Balev Nesher and the Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel.

***Corresponding Author:** Jochanan E. Naschitz, Bait Balev Nesher and the Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel.

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Abstract

Vitamin K is essential for clotting factors II, VII, IX and X to be released in their active form. Under vitamin K deficiency a coagulopathy may develop that is marked by prolongation of the prothrombin time (PT). Patients receiving enteral feeding which does not cover the daily vitamin K requirements might be predisposed to develop a bleeding diathesis. Yet, current guidelines do not recommend monitoring the PT in patients receiving enteral feeding. In the present cross-sectional study, we assessed the prevalence of a prolonged PT in patients receiving long-term enteral feeding with one or a combination of the enteral formulas Osmolite®, Jevity®, Easymilk®. Sixty residents in long-term geriatric care received exclusively enteral feeding for a median 27 months (average 34.7, SD 29). The median daily vitamin K supplied by enteral feeding was 63.5 mcg (average 8.3, SD 17.2), i.e. less than the 150 mcg recommended by the Food and Drug Administration. In 57 patients the PT-INR was 0.9 - 1.2 (normal); the PT-INR was prolonged to 1.4 in 3 patients. There were 6 episodes of major bleeding and 4 episodes of minor bleeding during the study period, unrelated to prolonged PT and distributed at random along the time of enteral feeding. Accordingly, long-term vitamin K-deficient enteral nutrition did not affect vitamin K-dependent coagulation. This may argue against the need to regularly monitor the PT in patients receiving long-term enteral nutrition

Key words: vitamin k; enteral feeding; bleeding; prothrombin time

Introduction

Vitamin K deficiency occurs when the vitamin K content in the diet is persistently low or when the absorption of vitamin K is defective. Patients receiving enteral nutrition which is not adequately fortified with vitamin K may develop vitamin K deficiency [1]. The requirements of the Food and Drug Administration for an adult parenteral multivitamin drug product recommend 150 microg of vitamin K [2]. However, none among 60 in common enteral nutrition formulas supplied the daily vitamin K requirements [3].

Vitamin K is essential for carboxylation of clotting factors II, VII, IX and X to be released in their active form [4]. Under vitamin K deficiency a coagulopathy may develop that is marked by prolongation of the prothrombin time (PT). Based on this principle the prothrombin time (PT) is traditionally used as an indicator of the bodily vitamin K status assuming that timely detection and correction of vitamin K deficiency can protect against bleeding. Scrutiny the literature about the need for monitoring the PT in patients receiving enteral feeding did not provide convincing data. WE addressed this question in a pilot study including 23 patients who received exclusively enteral feeding. The daily vitamin K supplied by enteral feeding did not satisfy the 150 mcg required by the Food and Drug Administration. Yet, a long-time vitamin K-deficient nutrition did not affect the vitamin K-dependent coagulation in these subjects (5). The present study expands the survey to a large and diverse patient population of residents in comprehensive nursing and palliative care, and receiving solely enteral nutrition.

Methods

Our institution is a university affiliated geriatric hospital located in Northern Israel. The present retrospective, cross-sectional study was approved by the Institutional Review Board (decision 0014-21-BBL) waiving the need to obtain patient informed consent. Residents of four departments receiving exclusively enteral feeding for at least three months were included. Excluded were residents having enteral feeding supplemented with oral meals. The following patient data were recorded: age, gender, length of enteral feeding, daily dose of enteral formulas and their vitamin K content, minor and major bleeding events, bariatric surgery, chronic diarrhea, arterial hypertension, ischemic heart disease, congestive heart failure, diabetes mellitus, COPD, cancer, liver disease, antiphospholipid antibody syndrome, systemic lupus erythematosus, tracheostomy, mechanical ventilation, use of anticoagulant medications. Bleeding events were classified according to the Bleeding Academic

Research Consortium (BARC) guidelines. Data of routine coagulation tests were available and were reviewed.

The following enteral feeding formulas were in use: Osmolite HT® (Abbott nutrition, USA) which provides 61 mcg/L vitamin K, Jevity® (Abbott nutrition, USA) which provides 61 mcg/L vitamin K, Easymeal-k2® (Easyline, Israel) which provides 110 mcg/L vitamin K. The duration of enteral feeding was assessed, and the daily vitamin K supplied by the feeding formulas was calculated and referred to the recommended dose [2]. The PT-INR and activated partial prothrombin time (APTT) were assessed according to the standard method with PT-INR 1 to 1.2 accepted as normal [4].

Sixty patients constitute the study group, 34 women and 26 males, median age 68.5 years, 28 in unaware wakefulness state, 11 with severe dementia, 54 had tracheostomy, and 48 received long-term mechanical ventilation. None had chronic diarrhea, none was diagnosed with a malignant neoplasia. Four patients were receiving low dose enoxaparin for secondary thromboprophylaxis, and 2 patients having chronic atrial fibrillation received apixaban. Enteral feeding consisted of Jevity® in 27 patients, Osmolite HT® in 14, Easymeal® in 8, or a combination of two of the feeding formulas in 16 patients. The median duration of exclusively enteral feeding was 27 months. The median daily vitamin K supplied by enteral feeding was 68 mcg (Table 1). One patient received 169 mcg vitamin K/day and another 176 mcg vitamin K/day. Fifty-eight patients received less than the 150 mcg of vitamin K required by the Food and Drug Administration [2].

Variables	
Subjects	60
Females/males	34/26
Age, years (avg, SD)	67.7 (12.3)
Enteral feeding, months (avg, SD)	34.7 (29)
Bleeding events	10
Anticoagulant treatment, patients	6
PT-INR >1.2, patients	3
Vitamin K supplied by enteral formulas, daily, mcg (avg, SD)	63.5 (17.2)

Table 1: *Daily vitamin K provided, PT-INR, and bleeding events.*

In 57 patients the PT-INR was 0.9 - 1.2 (normal 1 - 1.2). It was prolonged in 3 patients. In one case, prolongation of the PT-INR was not confirmed on duplicating the test without having supplemented vitamin K. One patient having repeatedly PT-INR 1.4 (and a normal APTT) administration of vitamin K did not correct the PT; there were neither signs of infection, systemic lupus erythematosus, other rheumatic disorders, nor malabsorption. This patient's general condition did not allow a detailed work-up, but a prolonged PT which was not corrected by administration of vitamin K could not be attributed to vitamin K deficiency. The third patient entered the end-of-life condition and further testing was declined.

During their residence in our institution 4 patients had one minor bleeding event consistent with BARC type 2 criteria, which occurred during time periods of 4, 48, 48 and 72 months. There were 6 episodes of major bleeding in 5 patients, i.e. overt bleeding and hemoglobin drop of 3-5 g/dL, which events occurred 5, 8, 10, 18 and 50 months after admission (one patient bled from the thyroidal artery and once he had melena while receiving apixaban). The bleeding events were distributed at random during the months of enteral feeding and there was no correlation between bleeding events and the amount of vitamin K supplied by enteral feeding (Figure 1).

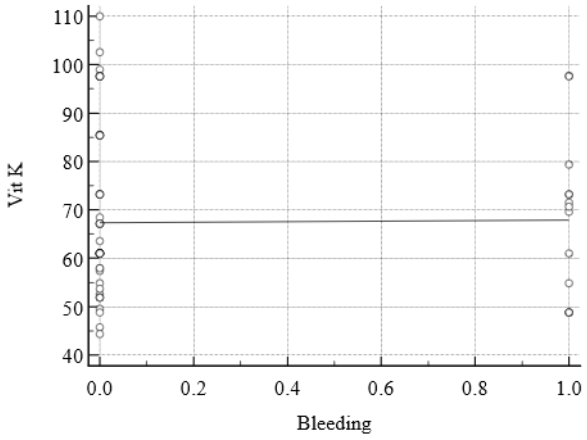

Figure 1: *Bleeding events related to the daily vitamin K supplied by enteral feeding (r = -0.27, p NS)*

Discussion

Long-term vitamin K-deficient enteral nutrition did not affect vitamin K-dependent coagulation in the study population. This data is contra-intuitive since vitamin K deficiency develops when the vitamin K content

in the diet is persistently low or when the absorption of vitamin K is defective. The latter occurs in obstructive jaundice [6], in malabsorptive states [7,8], or after bariatric surgery [9], neither being pertinent to patients of this study. The dissociation between a deficient vitamin K status and the normal PT might be explained by the "triage theory" which states that during a poor dietary supply vitamins are preferentially utilized for functions that are essential for immediate survival [10]; such is synthesis of coagulation proteins. Traditionally the PT and APTT are the recommended tests in screening for a bleeding diathesis [11]. Yet, as shown in the present study, the PT appears not to be useful for detecting a bleeding tendency under vitamin K deficiency. The ideal indicator of the bodily vitamin K status is by measuring undercarboxylated prothrombin [12,13]. The latter is not accessible in common clinical use.

There are limitations to our study, inherent to the cross-sectional design and unavailability of high-sensitivity vitamin K assays. The strength of our study consists in recruiting the most severe patients, long duration of enteral feeding, and the confident assessment of the amount of vitamin K supplied. While conventional dietary recommendations are based on the dose of vitamin K required to prevent bleeding, novel data suggest higher doses of the vitamin should be provided for the benefit of several chronic conditions, especially among elderly people. So, vitamin K activates matrix Gla protein an inhibitor of vascular calcification, it carboxylates Gas6 protein which is protective against neurodegeneration, it exerts antiproliferative effects associated with a reduced risk of cancer [9].

In concluding, the PT in chronically enteral fed subjects correlated neither with a history of bleeding nor with the deficient vitamin K status. Accordingly, monitoring the PT in patients receiving enteral feeding appears not to be a practical means to prevent bleeding. Rather, the patients might benefit from fortifying the feeding formulas with higher doses of vitamin K in virtue of the numerous beneficial effects of this vitamin.

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