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A Case Control Study of Nutrient Intake Deficiencies in Patients Taking Warfarin

Philip Riley IV; Kim Lucas Day, MD; George M. Yousef, MD; Sirisha Devabhaktuni, MD; Ashley N. Gaing; and Lynne J. Goebel, MD

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A case control study of nutrient intake deficiencies in patients taking warfarin

Philip Riley IV MS-2[1], Kim Lucas Day MD[1], George Yousef MD[1], Sirisha Devabhaktuni MS-4[1], Ashley Gaing[2], and Lynne Goebel MD[1]

Authors affiliations:

1. Marshall University Joan C Edwards School of Medicine
2. Wellesley College

Authors have no conflict of interest and no financial disclosures

Corresponding author:

Lynne J Goebel, MD

Professor, Internal Medicine

Marshall University Joan C. Edwards School of Medicine

E-mail- goebel@marshall.edu

Abstract

Introduction: We previously published the case of a woman taking warfarin who was found to have scurvy, a disease caused by a deficiency of vitamin C. This led us to hypothesize that patients taking warfarin who consume a diet limited in vitamin K rich foods may be at risk for other nutrient deficiencies. To test our hypothesis, we studied dietary nutrient intake in patients taking warfarin compared to patients with heart disease not taking warfarin.

Methods: The warfarin (n=59) and control groups (n=24) comprised convenience samples of patients with heart disease over age 60 years. Patients completed a three-day food diary and reported use of supplements.

Results: Based on diet history, the most common deficiencies were vitamin D (100% both groups), vitamin E (93% warfarin, 92% control), vitamin A (71% warfarin, 71% control), vitamin K (66% warfarin, 58% control), vitamin C (58 % warfarin, 46% control) and pantothenic acid (69% warfarin, 71% control) with no significant differences in intake deficiencies between warfarin and control groups.

Conclusion**:** All of our patients had nutritional intake deficiencies. This may be due to Appalachian dietary habits and not the low vitamin K diet. It seems prudent to recommend multivitamins, however, universal multivitamin supplementation has not been supported by randomized controlled trials. More study is needed to determine the reason for poor nutritional intake in our Appalachian population and to determine whether similar results are evident in a larger sample

Keywords: nutrient, deficiency, vitamin, Appalachian, diet, warfarin

Introduction:

After diagnosing scurvy in a patient taking warfarin, we questioned the diets of patients taking the drug who carefully limit their vitamin K intake in order to prevent fluctuations in the drug's efficacy.[1] It is possible that patients taking warfarin eliminate vitamin K rich foods like leafy green vegetables from their diet, rather than eating a consistent amount of vitamin K rich foods as is the current recommendation because it is a simpler approach. Foods high in vitamin K are also high in other nutrients and avoiding these foods may put patients at risk for other nutritional deficiencies. To our knowledge, there are no studies looking at nutrient deficiencies in the diets of patients taking warfarin. We reviewed the diets of patients in our cardiology clinic taking warfarin and compared their diets to that of patients with heart disease not taking warfarin to see if the patients taking warfarin had more nutrient intake deficiencies.

Methods:

Study Design:

This was a case control study. All patients in both groups were over the age of 60 years. The warfarin group comprised 59 patients in the cardiology anticoagulation clinic who were taking warfarin for at least 3 months and completed a three-day food diary. We invited all (325) patients who were followed in the anticoagulation clinic to participate in the study. Two hundred eight patients were eligible for the study as they were over age 60 and on warfarin for at least 3 months. The control group comprised 24 cardiology clinic patients who were not taking warfarin. An attempt was made to enroll control participants who were similar to case participants in percent male and decile of age. All participants were from the outpatient clinic at Marshall Health, a university practice located in Huntington, West Virginia and signed consent to participate in the IRB approved study. The study was completed over a 1-year period beginning in May 2013.

Procedures:

We counseled participants on documenting their diet in a three-day food diary, noting their food and drink consumption with the quantities, brand names, and methods of preparation for three days during the following month. We also asked that they report the use of vitamins and other dietary supplements. Warfarin patients returned the diaries on their next monthly visit, while control patients returned their diaries in pre-addressed stamped envelopes. Using Foodworks software Version 13, we analyzed the diets for the following nutrients: kilocalories, protein, carbohydrates, fiber, calcium, copper, iron, magnesium, manganese, phosphorus, selenium, zinc, vitamin A, vitamin C, vitamin D, vitamin E, vitamin K, thiamine, riboflavin, niacin, pantothenic acid, folate, vitamin B6, and vitamin B12 and entered the data into an Excel spreadsheet. We averaged nutrient values over the three days and intake of less than 75% of the daily reference intake (DRI) was considered deficient.

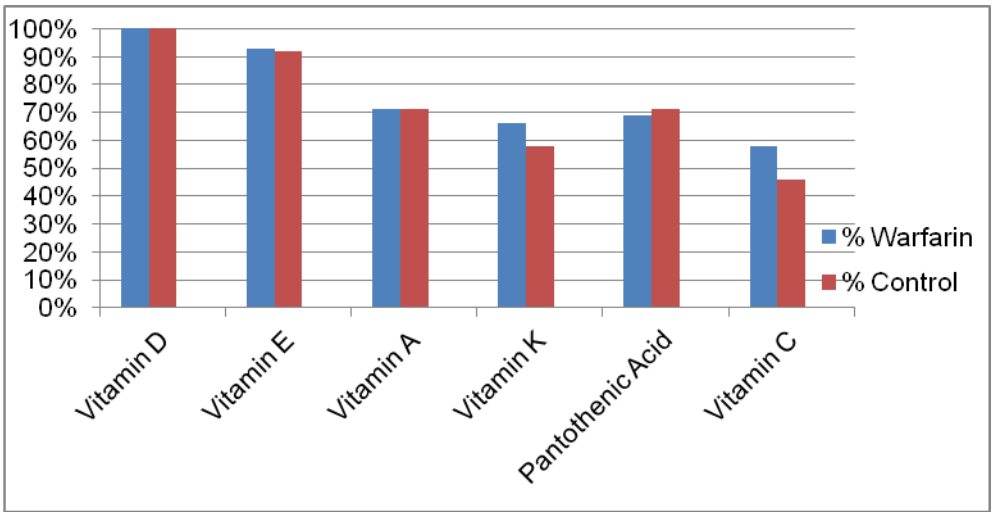
Statistical analysis:

We used Vassarstats website (www.vassarstats.net) Chi-square or Fisher exact test to compare the frequency of deficiencies among the warfarin and control groups with two tailed p values less than 0.05 being significant.[2]

Results:

The warfarin and control groups were comparable in average age (warfarin 73 years, control 72 years) and gender (warfarin 51% male, control 46% male). Based on their diets, each patient in the warfarin and control groups had nutrient intake deficiencies of less than 75% of the DRI. All of the patients in both groups were deficient in vitamin D intake. The most common other intake deficiencies were vitamin E (N=55, 93% warfarin; N=22, 92% control), vitamin A (N=42, 71% warfarin; N=17, 71% control), vitamin K (N=39, 66% warfarin; N=14, 58% control), vitamin C (N= 34, 58 % warfarin; N=11, 46% control) and pantothenic acid (N=41, 69% warfarin; N=17, 71% control) (Figure 1). Although there were many intake deficiencies, there were no statistically significant differences between warfarin and control groups.

Figure 1. Most common nutritional intake deficiencies



Many patients in both groups took nutritional supplements with 76% (N=45) of warfarin and 83% (N=20) of control patients taking at least one supplement. There was no significant difference in supplement use between the groups (Table 1). The most common supplements taken were multivitamins (N=17, 29% warfarin; N=8, 33% control), and vitamin D (N=17, 29% warfarin; N=9, 38% control).

Table 1. No significant difference in vitamin supplements in study groups.

	Control N(%)	Warfarin N(%)
At least one supplement	20(83%)	45(76%)
Multivitamin	8(33%)	17(29%)
Eye vitamin	3(13%)	2(3%)
Vitamin D	9(38%)	27(46%)
Calcium	5(21%)	17(29%)
Fish oil	7(29%)	10(17%)

Vitamin C	4(17%)	11(19%)
Vitamin B12	3(13%)	6(10%)
Vitamin E	1(4%)	4(7%)

Note: Some patients were more than one supplement.

Discussion:

In our convenience sample of two groups of cardiology clinic patients, one group taking warfarin and one group of control patients, we found an abundance of dietary nutrient intake deficiencies with no significant differences between the groups. Because of this finding, it seems reasonable to recommend multivitamin supplements to all of our cardiology patients.

However, randomized controlled trials do not support this practice. Daily multivitamin supplements did not reduce major cardiovascular events, myocardial infarction, stroke, and cardiovascular disease mortality following a decade of treatment in a group of U.S. male physicians.[3] A Cochrane review indicated that randomized controlled trials do not support universal multivitamin supplementation.[4] In fact, they report that beta carotene and vitamin E supplementation increase mortality. Further, the U.S. Preventive Services Task Force does not recommend the use of beta carotene or vitamin E supplements to decrease chances of cardiovascular disease or cancer as beta carotene increased the risk of cancer in smokers and vitamin E supplements showed no effect on cardiovascular disease, cancer, or death rates.[5] Not all published data on vitamin supplementation is negative. One study found that multivitamin use was associated with lower risk of colorectal adenoma, even for a short duration of use.[6] Another study, which reviewed data from ten trials, found multivitamins enhanced immediate free recall memory.[7] Of note, the randomized controlled trials that did not find benefit of multivitamin supplementation were not conducted using subjects with known nutritional intake deficiencies. Therefore, their conclusions may not apply to patients in our population all of whom had nutritional intake deficiencies.

People living in Appalachia may be predisposed to nutrient intake deficiencies due to local dietary habits. Although the Appalachian diet tends to be varied, it is high in fat due to daily preparation of fried foods, gravies, sauces, and fatty meats.[8] In addition, the consumption of vegetables in the Appalachian region is markedly low. In an Appalachian region in Ohio, adults have fruits and vegetables 17 times per week on average compared to 23.8 times per week on average nationally. Another study found that children in Appalachian Kentucky commonly displace basic food groups with foods high in saturated fat and sugar.[9] Low consumption of fruits and vegetables is common among Appalachian Kentucky youth with 17.1% of them eating 5 or more servings of fruits and vegetables per day compared to a national rate of 20.1%.[10] The 2013 West Virginia Youth Risk Behavior Survey indicated that 6% of high school students did not eat fruit or drink 100% fruit juices during the 7 days before the survey and that 7% did not eat vegetables during the 7 days before the survey.[11] A survey of southern rural people revealed the most common barriers to eating fruits and vegetables were fear of fresh fruits and vegetables spoiling before being used, restaurants they frequented did not serve fruits and vegetables, and the higher cost of purchasing them.[12] Brown and Wenrich reported that the food preparers in Appalachia tended to serve foods that are preferred by the family and attempts at changing food intake are not successful because of the overarching desire to please their family.[13] A focus group of Appalachian people in this study reported eating unhealthily when they were

emotionally stressed or as a reward. It is possible that low income plays a role with unhealthy eating patterns because it increases stress. Another focus group participant stated that social events at church that involve food are typically unhealthy, high fat foods. Most commonly, however, the unhealthy diet in Appalachia is blamed on socioeconomic factors such as inability to afford high quality food and geographic isolation making it harder to access fresh food.

Diet alone does not usually provide the recommended quantities of all vitamins and minerals. All of our patients were deficient in Vitamin D intake. According to the National Institute of Health Office of Dietary Supplements, for people between the ages of 1 and 70, the recommended daily allowance is 600 IU, and for those over 70, it is 800 IU.[14] Some foods containing significant amounts of vitamin D are: salmon (3 oz has 566 IU), orange juice (1 cup has 137 IU), milk fortified with vitamin D (1 cup has 115 IU), ready-to-eat cereal fortified with vitamin D (3/4 cup has 40 IU), and eggs (one large egg has 41 IU).[14] Although the daily requirement of vitamin D can be reached by eating a serving of salmon and three glasses of fortified milk, most people would not want to eat this every day. Vitamin D levels are also affected by sunlight exposure with just ten minutes of sunlight exposure daily fulfilling the requirement. However, for those who live north of Atlanta, the winter sun is not strong enough to enable the production of vitamin D by the skin. As an example, Constantini, et al. found that the prevalence of vitamin D insufficiency was higher among dancers (94%), basketball players (94%), and Tae Kwon Do fighters (67%) and among athletes from indoor versus outdoor sports (80% vs 48%; $P = 0.002$).[15]

Serious health issues result from some vitamin deficiencies. Vitamin A deficiency, one of the more common deficiencies found in our study population, can cause night blindness.[16] As we observed in the patient that inspired this study, deficiency in vitamin C intake led to scurvy. Approximately half of both of our study groups had insufficient intake of vitamin C. Vitamin C is required for the production of mature collagen so people who are deficient may present with bleeding gums and perifollicular hemorrhage due to defective collagen. Although a significant number of patients consumed diets deficient in both of these vitamins, many were taking vitamin supplements so clinical deficiency may not have occurred. We observed that over two thirds of our study patients had reduced intake of pantothenic acid. This vitamin is commonly included in multivitamin supplements. The daily requirement for adults is 5mg.[17] Pantothenic acid is found in highest amounts in the fortified cereals (1 cup has 10 mg), turkey breast (1 serving has 9 mg), shiitake mushrooms (1 cup has 5 mg), beef (6 oz has 3 mg), chicken breast (1 serving has 3 mg), Alaskan salmon (1 fillet has 3 mg), and avocado (1 cup cubed has 2 mg).[18] Deficiency causes fatigue and irritability secondary to low coenzyme A. Clinical deficiency of pantothenic acid is rarely reported, perhaps because clinicians do not think of it or check for it in the evaluation of patients with fatigue, a common complaint in outpatient practice. Further study with confirmation of deficiency by blood tests could determine whether pantothenic acid deficiency is a clinically significant problem.

There were a few limitations to this study. Besides having a small sample size, there is the possibility of inaccuracy of data recorded in the food diaries. Furthermore, we did not measure blood values of vitamins and minerals to confirm deficiency. In fact, many of the patients with deficient dietary intake were taking supplements that contained those nutrients so their blood levels might not have shown clinical deficiency. Instead, we used documented intake as measured by the food diaries and a computer program as a surrogate marker of dietary

deficiency. Although three-day diary reports may not perfectly represent someone's diet, three-days of diet histories are commonly used in nutritional studies and an analysis of cost-efficient design of diet validation studies revealed that more than 5 days is rarely necessary.[19-22]

Conclusion:

Patients taking warfarin did not have more nutrient intake deficiencies compared to other heart disease patients in our population. Given the high prevalence of vitamin intake deficiency among our sample of patients with heart disease from our clinic in West Virginia, it seems reasonable to recommend supplementation with a multivitamin. Healthcare providers should be aware that nutritional intake deficiencies may occur commonly in the Appalachian population, and have a high index of suspicion, especially among patients who present with symptoms suggestive of a clinical syndrome of nutrient deficiency and who are not already taking multivitamins. A larger study of people living in Appalachia could be performed to achieve a greater understanding of the prevalence of nutritional intake deficiency in this population. Nonetheless, we found profound intake deficiencies of vitamins that can be addressed by adequate and conscientious vitamin supplementation.

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