

Original**The Stability of Vitamin K in The Diet of Patients Using Oral Anticoagulant Vitamin K Antagonist (VKA) Drugs in Hanoi Medical University Hospital in 2021**

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ABSTRACT: The amount of vitamin K in the daily diet plays a pivotal role in the therapeutic effects of oral anticoagulant vitamin K antagonist (VKA) medicines. The study aims to describe the dietary and the stability of vitamin K in daily meals of patients who use oral anticoagulant VKA medicines. A longitudinal study was carried out on 26 patients, which shows that the average amount of vitamin K in the participant's diet was 237.8 µg, and 58.6% of the patient's diet did not meet the recommendation for vitamin K. The surveys had been conducted among two groups: patients who knew and patients who did not know about the nutritional knowledge when using oral anticoagulant VKA drugs. The results showed that the average amounts of vitamin K of the two groups were 183.4 µg and 292.2 µg, respectively. The variation in the amount of vitamin K in knowledgeable patients' groups was less than the figure for the non-knowledgeable patients' groups with the coefficient of variation (CV) being 1.01 and 1.19, respectively.

Key words: Vitamin K, oral anticoagulant vitamin K antagonist (VKA) drugs, Hanoi Medical University Hospital.

INTRODUCTION

Vitamin K antagonists (VKA) are a group of substances that reduce blood clotting by reducing the action of vitamin K. However, the risks of complications related to the usage of these substances are significant. According to some studies, the rate of hemorrhage is approximately 1% to 3% each year (1,2). World-wide, "Vitamin K antagonist medicines related to about 6.000 deaths in which about 4.000 cases can be avoided as well as 17.300 hospitalization cases can be avoided each year" (3). Recently, many pieces of evidence showed that uncontrolled-vitamin K diets are one of the most prevalence factors which have direct influences on these treatments (4,5). If the amount of vitamin K intake is too much, this can increase clotting factors and decrease the effect of these drugs. Whereas, if the amount of vitamin K intake is not enough, it will lead to clotting factor deficiency and the risks of hemorrhage. According to previous opinions, patients who use oral anticoagulant VKA medicines need to limit food containing a high amount of vitamin K. However, recent researches show that it is not necessary to constrain these food and more important thing is that patients have to maintain their daily diets with a stable amount of vitamin K (6,7).

In Vietnam, there are many common food, which are used in everyday meals that containing a high amount of vitamin K such as cruciferous vegetables, seasoning vegetables, amaranths, and morning glory water (8). In fact, vitamin K dietary intake is unstable because of seasonal vegetables and therefore making

it difficult to control the INR. In many Western and North American countries, patients are instructed to practice nutrition under the supervision of doctors, the proportion of patients who achieved the INR target was from 60% to 75% (9,10). In Vietnam, it is only 30% to 45% of patients using oral anticoagulant VKA drugs meet the INR target (11,12).

In the world, there are researches about the effect of diets relating to the result of INR (6,7). By contrast, in Vietnam, researches about nutrition for patients who used oral anticoagulant VKA drugs are extremely rare. Therefore, we conducted this study to describe the dietary vitamin K intake and the stability of vitamin K intake in diets of patients who used these medicines.

METHODS**Study setting and subjects**

This longitudinal study involved 26 inpatients in the Cardiovascular Center at Hanoi Medical University Hospital from January to May 2021. We used a non-probabilistic and purposive sampling method in this study and collected all inpatients who had the required criteria during the study period. Patients were chosen based on the criteria: people who were above 18 years, were treated with oral anticoagulant VKA drugs, and had agreed for the researcher to keep in contact to ask for 24-hour recall dietary meals after discharging from the hospital. The study excluded patients who were in serious conditions, had disabilities such as dumbness or deafness, or refused to take part in this study (figure 1).

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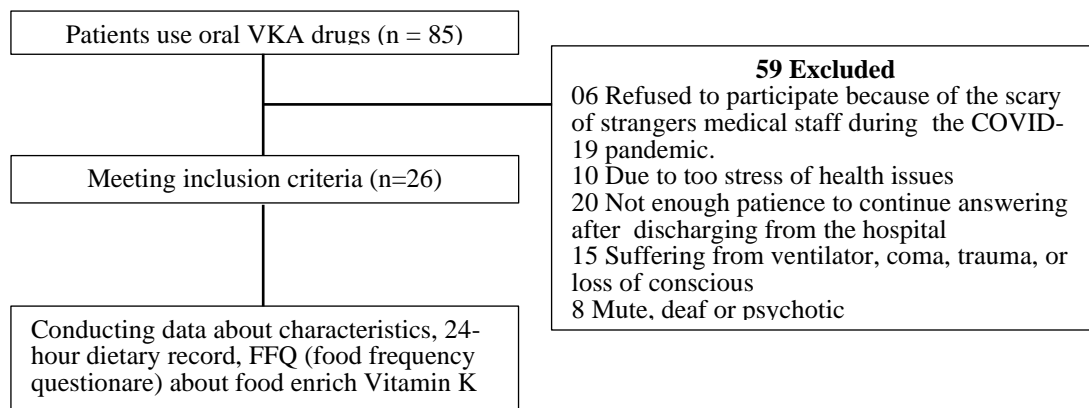


Figure 1. Diagram of study participants

Data collection

Demographic characteristics (gender, age, academic levels (primary/secondary/high school/college/university/postgraduate) and address (rural or urban areas)).

The average amount of vitamin K and the proportion of patients which achieve recommended vitamin K allowances of subjects.

The variation of vitamin K intake in groups with knowledge and without knowledge during the study period.

Knowledge of patients: Knowledgeable patients when they have been consulted directly by medical staff/ received nutritional leaflets/ self – educate information through media and then answering the correct answer about the name and the principle of using enriched vitamin K vegetables. Non-knowledge patients when they have not been consulted by medical staff or they have not learned by themselves about nutrition while using oral anticoagulant VKA drugs or have been consulted by medical staff but answered wrongly about the name and the principle of using enriched vitamin K vegetables.

The amount of vitamin K had been evaluated by the 24-hour recording method in three consecutive weeks. Each week, 24-hour dietary record in three consecutive days. The patient's dietary intake information was taken by face-to-face questionnaires during the hospital stay and by telephone interviews during the patient's discharge period from the hospital. General information of patients and the frequency of using food containing a high level of vitamin K in the past 12 months were gathered by using questionnaires. Food that contains a high level of vitamin K is divided into 3 main groups: the cruciferous vegetable group, the seasoning vegetable group, and other vegetables group. The cruciferous vegetable group includes: green cruciferous vegetables, watercress, spinaches; the seasoning vegetable group includes: cilantro, saw leaf, basil. Others include Morning glory, amaranth, and lettuces. Patients would be asked about the

frequency of using these food in a week in its season and out of season. The frequency of food was calculated by the total number of consumption in a week multiplied by the number of weeks in a season. Biases were controlled by using a single equipment tool and one researcher to collect the data for all subjects.

The assessing criteria about the amount of vitamin K in dietary

Based on the recommended vitamin K allowance for Vietnamese adults: Recommended vitamin K allowance for male and female: 150µg/day (13).

Currently, we have not referred to any recommendation in the amount of vitamin K daily for patients who use oral VKA drugs. The most important thing is that patients should keep on stability regularly.

Statistical analysis

The data were entered by using Microsoft Excel Workbook 2019 (Microsoft Corporation) and Stata 15.1 statistical software (StataCorp LLC) for analysing. The intergroup comparisons were performed using the Mann-Whitney test. Categorical and quantitative variables were expressed as the number of subjects (percentage), and mean (standard deviation), respectively. Statistical differences were considered significant at $p < 0.05$.

Ethics approval

The study has been approved by the research review board of Hanoi Medical University Hospital. All participants are fully informed about the purposes of the study.

RESULTS

The study was conducted on 26 patients who were treated with oral anticoagulant VKA drugs, the proportions of males and females were 26.9% and 73.1% respectively. The percentage of patients who had knowledge and patients did not know were the same, at 50%

Table 1: The amount of vitamin K in 24 - hour recall dietary of participants

	Groups	Mean \pm SD	Nutrients Recommendation (μ g)	Percentage (%)	
				Meet RDA	Did not meet RDA
Age	19-65 (n=16)	255.9 \pm 317.5	150	45.1	54.9
	> 65 (n=10)	227.4 \pm 316.4	150	33.3	66.7
Gender	Male (n=7)	176.1 \pm 254.1	150	33.3	66.7
	Female (n=19)	272.8 \pm 333.4	150	43.8	56.2
Address	Rural areas (n=15)	240.5 \pm 301.9	150	40	60
	Urban areas (n=11)	253.7 \pm 337.4	150	42.4	57.6
Academic level	Before high school (n=7)	215.1 \pm 267.4	150	41.6	58.4
	High school (n=8)	258.9 \pm 327.2	150	41.6	58.4
	College/university/postgraduate (n=11)	260.6 \pm 345.1	150	40	60
Knowledge	Knowledge (n=13)	183.4 \pm 209.4	150	37.6	62.4
	Non - knowledge (n=13)	292.2 \pm 349.7	150	46.2	53.8
Total (n=26)		237.8\pm292.7	150	41.4	58.6

Table 1 showed that the average amount of vitamin K intake of participants was 237.8 μ g per day, and the percentage of patients who meet recommended vitamin K allowance was 41.4%. The average amounts of vitamin K in dietary in groups of knowledgeable and non-knowledgeable groups were 183.4 \pm 209.4 μ g and 292.2 \pm 349.7 μ g respectively. The proportions of male and older people who meet the recommended vitamin K allowance were the lowest, at approximately 33.3%. The percentage of patients who meet the recommended vitamin K allowance was the highest in non- knowledgeable patients (46.2%). The average amount of vitamin K and the percentage of patients who meet the recommended allowance of vitamin K, which were classified by living areas and the education levels of subjects, showed no significant difference.

Figure 2 illustrated that the differences in the amount of vitamin K in the diet between two

consecutive investigation days of non-knowledgeable patients were mostly higher than that of knowledgeable patients. In terms of the non-knowledgeable group, the orange line was dramatic fluctuated between investigation days. To be specific, the amount of vitamin K was highest on the third investigation day at 513.3 μ g while the lowest figure on the sixth day was at 114.1 μ g. The coefficient of variation (CV) of vitamin K between investigation days in the group was 1.19. When it came to the knowledgeable group, the blue line slightly fluctuated between investigation days. To be specific, the amount of vitamin K was highest on the eighth investigation day at 269.3 μ g while the lowest figure on the sixth day was at 87.4 μ g. The coefficient of variation (CV) of vitamin K between investigation days in the group was 1.01. Therefore, the amount of vitamin K in the diet of knowledgeable patients was more stable than the figure for non-knowledgeable patients.

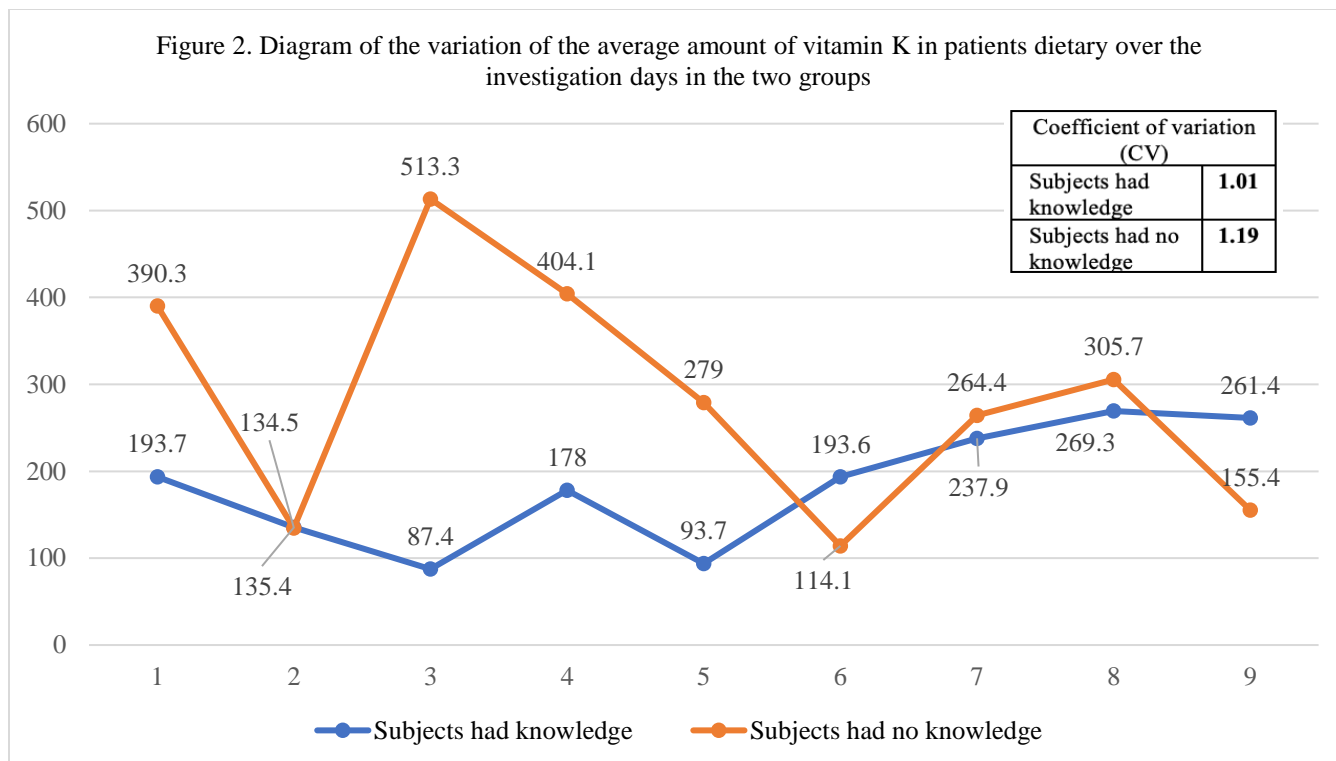


Figure 2. Diagram of the variation of the average amount of vitamin K in patients dietary over the investigation days in the two groups

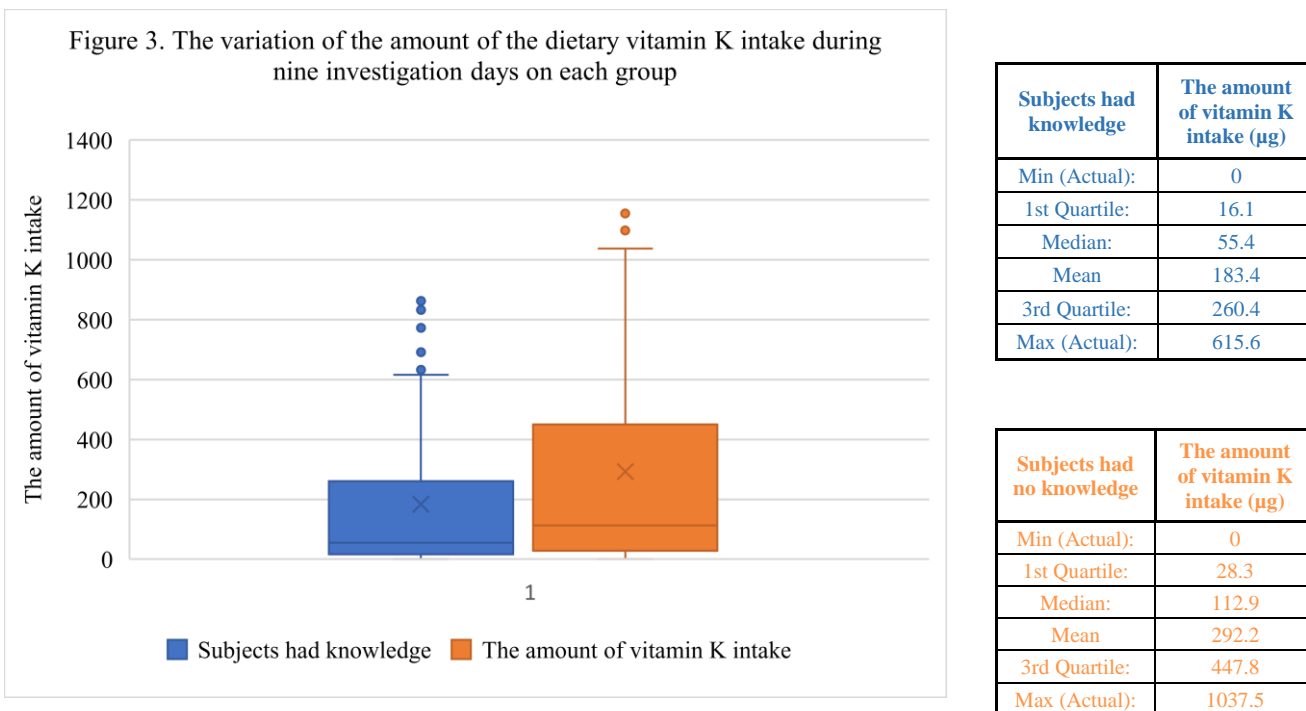


Figure 3. The variation of the amount of the dietary vitamin K intake during nine investigation days on each group

Figure 3 provided data on the variation of the amount of vitamin K between nine investigation days on two groups. In terms of the knowledgeable group, the average amount of vitamin K consumption and the median were 183.4 µg and 55.4 µg respectively. The data tended to toward the above of the mean. The interquartile range IQR = Q3 - Q1 = 244.3 µg. The difference between the highest and the lowest amount of vitamin K in the patients' diet was 866 µg. Regarding the non-knowledgeable group, the average amount of vitamin K consumption and the median were 292.2 µg and 112.9 µg respectively. The data had a tendency toward the above of the mean. The interquartile range IQR = Q3 - Q1 = 419.3 µg. The difference between the highest and the lowest amount of vitamin K in the patients' diet was 1171.6 µg. Thereby, there was a large variation in the amount of

vitamin K in patients' diets in both groups. But, the swing of the amount of vitamin K in the non-knowledgeable group was worse than the figure for the knowledgeable group.

Figure 4 showed that the frequency of using food that contains a high amount of vitamin K increased significantly in two seasons (winter and spring), especially in the cruciferous vegetable group (higher than that of summer and autumn for about six times). The frequency of using vegetable seasoning group showed little difference between seasons. Some types of vegetables that contain a high amount of vitamin K such as morning glory water or lettuce, were consumed much higher in summer and autumn. The consumption of these vegetables in winter and spring was only one-third.

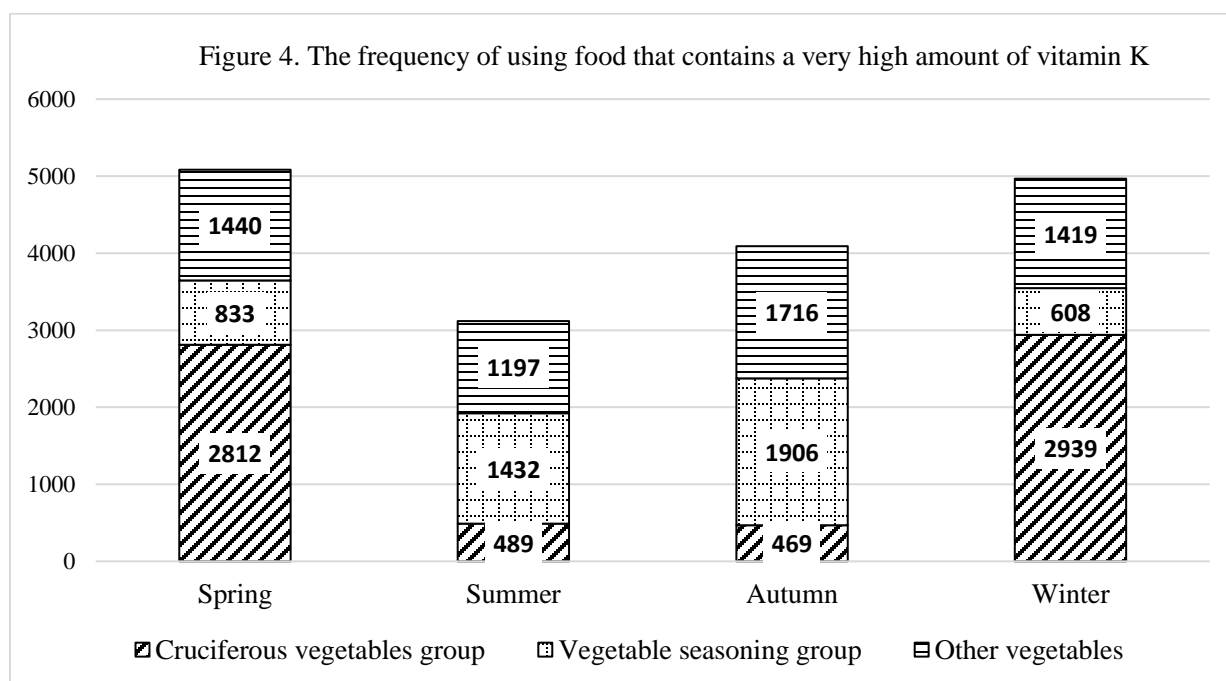


Figure 4. The frequency of using food that contains a very high amount of vitamin K in four seasons

DISCUSSION

In terms of the average amount of vitamin K, the result in the study was 237.8 µg per day, lower than the study of Pham Van Bac in Bac Ninh General hospital (346.6(µg)) and higher than the result of Kim K.H et al., 2010 in Korean (161.3µg), Lubetsky A in Israel (176 µg/day) or Custodio das Dores SM in Brazil (76-120 µg/day) (5,14,15,16). The result can be explained by eating habits and the availability of vitamin K-rich food in different countries. Other studies about the vitamin K diet in Vietnamese people showed that the average amount of vitamin K in the diet was higher than the recommended allowance. However, based on our study, the percentage of patients who did not achieve the recommended allowance as normal adults was still significantly high

(58.6%). The result shows that the amount of vitamin K intake in the patients' diet was unstable. Patients may much food enriched with a high amount of vitamin K on some days to make up for the other days, which could lead to a high average amount of vitamin K in general. The study also showed that the proportion of people who meet the recommended vitamin K in knowledgeable patients was lower than the figure for non-knowledgeable patients. This shows that instructing patients to eat limited foods containing vitamin K leads to unnecessary abstinence. And there should be more specific instructions to help patients maintain a diet with a stable vitamin K content.

To assess the stability of the amount of vitamin K in the patients' diet, we used the coefficient of variation (CV) and the interquartile range (IQR). The

CV of knowledgeable patients about nutrition relating to vitamin K was 1.01 while the figure for non-knowledgeable patients was 1.19. The coefficient of variation of knowledgeable patients was lower, which proved that the amount of vitamin K of the knowledgeable patient's diet was more stable than the figure for non-knowledgeable subjects. The result showed that it is important to consult nutritional information carefully for patients who use oral anticoagulant VKA drugs. However, this effect was not high enough and had not led to a significant difference in controlling the stability of vitamin K dietary intake of patients. This could show that consultation for these patients about the diet patterns was effective. The amount number of Vitamin K in knowledgeable patients' diets was less changing than the figure for non-knowledgeable patients' diets. However, this effect on these patients was not high and was not leading to many differences in controlling the stability of the amount of vitamin K in patients's diets. So it is necessary to establish an intensive intervention strategy, which could help patients to have a deep understanding of their diets and its importance. The limitation of our research is the basic in studying design, which only accessed patients' knowledge while using oral VKA drugs. Change in attitudes and practices is extremely hard. Therefore, there is a need for more new nutritional intervention patterns, which are not only focussing on knowledge but also on how to do the right practice.

Moreover, vitamin K dietary intake was also affected by the frequency of consumption and the availability of foods. With the development of technology and farming techniques, most of these food was available all year round. However, some types of food are not usually consumed because Vietnamese people have the tendency to eat a particular kind of food in its main season. Therefore, vitamin K dietary intake was indirectly affected by the seasonal nature of these food, especially in the group of vegetables and fruits. In addition, this group has the highest amount of vitamin K compared with other food groups. This was the main reason why we decided to survey the frequency of using types of vegetable which contains the highest amount of vitamin K in a year. The results showed that the frequency of using foods containing a high amount of vitamin K increased remarkably in the two seasons: winter and spring, especially in the group of cruciferous vegetables. The frequency of using cruciferous vegetables in winter and spring was about six times as many as in other seasons. The frequency of using seasoning vegetables had a little variation between each season of the year. Other food containing a very high level of vitamin K such as water spinaches, amaranths, lettuces, which had a frequency of use in summer and autumn was about three times as many as other seasons. The frequency of vegetable consumption with a very high amount of vitamin K was closely related to the patients' vitamin K intake mainly because even a small amount of these foods can contribute a significant part to the amount of vitamin K intake. It is clear that not every vegetable has vitamin K, so it is easy to point out the difference in the amount of vitamin K in the patients' diet.

CONCLUSION

The average amount of vitamin K intake of all patients was higher than the recommendation for vitamin K but there were 58.6% of patients' dietary did not meet the recommendation as normal adults. The study showed that the instability of vitamin K in patient's diets who used oral anticoagulant VKA drugs, and the amount of vitamin K in the diet of knowledgeable patients was more stable than the figure for non-knowledgeable patients. The amount of vitamin K in diet of the knowledgeable patients compared with non-knowledgeable patients showed that the intervention in order to raise the awareness of patients using oral anticoagulant VKA drugs was effective. The frequency of using vitamin K enriched food in winter and spring was significantly higher than in summer and autumn, which indirectly showed the instability of vitamin K in the patient's diet in different seasons.

GREATFUL THANKS

We would like to express our sincere thanks to Hanoi Medical University Hospital because of creating suitable conditions during the research process. We would also like to thank the patients who participated in the study for their tireless efforts to help us complete this study.

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