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Conflict of Interest

The authors have no potential conflicts of interest to disclose.

Validity and Reliability of a Self-administered Food Frequency Questionnaire to Assess Vitamin K Intake in Korean Adults

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ABSTRACT

This study was conducted to validate a food frequency questionnaire (FFQ) to assess vitamin K intake in clinical and research settings based on data from the Fifth Korea National Health and Nutrition Examination Survey (KNHANES V). We collected a subset of data on informative food items using the 24-hour recall method from adults aged 19 to 64 years from KNHANES V. The cumulative percent contribution and cumulative multiple regression coefficients for vitamin K intake from each food were computed. Twenty-five foods items were selected for the FFQ to assess vitamin K intake. The FFQ was validated against intakes derived from a 5-day food record (5DR) (n = 48). To assess the reliability of the FFQ, participants completed the self-administered FFQ (FFQ1) and a second FFQ (FFQ2) after a 6-month period (n = 54). Data were analyzed using Pearson's correlation coefficients, the cross-classification method, and Bland-Altman plots. Mean intakes were similar for vitamin K between the FFQ and dietary records, with significant correlations observed ($r = 0.652$), and cross-classification analyses demonstrated no major misclassification of participants into intake quartiles. Bland-Altman plots showed no serious systematic bias between the administrations of the two dietary assessment methods over the range of mean intakes. FFQ reliability was high, with a Pearson's correlation coefficient of 0.560. This pilot study shows promising validation and reliability evidence for the use of this FFQ, which is focused on vitamin K intake in adults, as an efficient screening tool in clinical and research settings.

Keywords: Food frequency questionnaire; Vitamin K; Validity; Reliability; Korean adults

INTRODUCTION

Vitamin K is a fat-soluble vitamin existing mostly in nature and comprises vitamin K1 (phylloquinone), contained mostly in deep green vegetables, and vitamin K2 (menaquinone), found mainly in meats, dairy, fish, and fermented foods [1-3]. The classic role of vitamin K is as a cofactor for the enzyme gamma-glutamyl carboxylase, which converts glutamate residues to gamma-carboxy glutamate residues on vitamin K-dependent proteins such as coagulation factors II, VII, IX, and X; proteins C and S [4]; osteocalcin [5]; and matrix Gla protein [6]. In recent years, considerable evidence has reported that vitamin K has anticancer, anti-inflammatory, and metabolic disease preventive properties in addition to blood coagulation activities and bone health effects [7,8]. However, until now optimal vitamin K intake was

established as an adequate intake (AI) based only on the hepatic requirement for blood clotting factor synthesis. The US Institute of Medicine has established sufficient daily intakes of vitamin K of 120 µg for men and 90 µg for women [9], and the UK recommends vitamin K intakes of 1 µg per kg body weight for adults and 2 µg per kg body weight for children [10]. The AI of vitamin K is 75 µg for adult men and 65 µg for adult women in Korea [11].

Warfarin is a vitamin K antagonist widely prescribed as an oral anticoagulant medicine for the prevention and treatment of ischemic stroke, deep vein thrombosis, cardiovascular disease, and other thrombotic diseases. Warfarin-based anticoagulation therapies seek to maintain a patient's international normalized ratio (INR) within an appropriate treatment range between 2.0 and 3.0 [12]. However, this range is too narrow to be maintained at all times. If one's INR increases, his or her thrombosis risk decreases, but the risk of bleeding and other complications could increase. On the other hand, if INR decreases, one's bleeding risk decreases but thrombosis risk increases [13]. Therefore, maintenance of appropriate INR levels is important for people in taking warfarin, and assessments of dietary vitamin K intake are critical to stabilize anticoagulation therapy [14,15].

Various dietary assessment tools can be used in clinical practice and research to estimate vitamin K intake. The food record method has been widely used; however, it demands a great deal of time and expense to analyze data. Food frequency questionnaires (FFQ) are cost-effective and reliable methods of estimating usual dietary intakes in relation to health concerns. Some FFQs have been used to assess dietary vitamin K intake [16-18], but there is no tool to assess vitamin K intake in Korean individuals. Due to differences in dietary habits according to population, ethnically specific FFQs could be used in nutrition surveys. Each questionnaire should be validated and compared to a gold standard diet analysis technique for the specific population being studied. Thus, the purpose of this study was to validate an FFQ specifically developed to assess vitamin K intake in Korean adults.

MATERIALS AND METHODS

Food frequency questionnaire development

Data from the Fifth Korean National Health and Nutrition Examination Survey (KNHANES V) of 12,546 adults aged 19–64 years were utilized to develop the vitamin K-specific FFQ. Dietary intake was assessed by the 24-hour dietary recall method, and vitamin K contents were analyzed using the 475 food databases of Computer Aided Nutritional Analysis Program (Korean Nutrition Society, Seoul, Korea) and 76 United States Department of Agriculture food databases. To select vitamin K food source items to be included in the FFQ, a contribution analysis was used to determine the percent of vitamin K intake contributed by each food item [19]. Food items with larger variations in vitamin K intakes between individuals were analyzed via regression using daily vitamin K intake as the dependent variable and vitamin K intakes from each food as the independent variables for each research participant. The regression analyses also included foods with the accumulated total of model explanation power of 90% from the Stepwise regression analysis [20]. The rank of twenty-five food items that contributed cumulatively up to 90% of the total vitamin K intake were selected to develop the FFQ.

Validity and reliability of the food frequency questionnaire

The present study was approved by the Clinical Test Deliberation Commission of Institutional Review Board (IRB), Wonkwang University (WKIRB-201308-SB-003, WKIRB-201406-SB-038), and written informed consent was obtained from each subject. This research was performed from September to December 2013 and from May to June 2014. A total of 54 participants recruited voluntarily for the validity and reliability analyses study were free from diseases and aged between 19 and 64 years. For validity verification of the developed FFQ, we collected 5-day food records (including one weekend day) (5DR). On the first visit to the subjects, a trained dietitian recorded the first day food record through face-to-face interviews using the 24-hour recall method. The remaining four days of the 5DR were recorded by each subject. Participants were instructed to record their normal meals and to exclude dining-out, parties, or other special event meals from the food journals. A total of 6 subjects were excluded from the final validation analysis, as they had incomplete food records. For reliability verification of the FFQ, we compared each participant's first and second FFQ sets within an interval of about 6 months.

During FFQ administration, subjects were asked about the quantity and frequency of consumed food items. The reference quantities of food items were set based on one serving size of the Dietary Reference Intakes for Koreans (KDRIs), and relevant photographs were presented to identify serving size. For intake amounts, three different levels of portion size, such as half, same, and 1.5-times larger than the reference amount, were presented as options. Each food frequency was categorized into 9 items: hardly eat it, once a month, 2–3 times a month, once a week, 2–3 times a week, 4–6 times a week, once a day, two times a day, and three times a day. Vitamin K intake from each food item was computed based on the portion size, frequency of consumption, and amount per serving.

Statistical analysis

Results are reported as means (SD) or as percentages and 95% confidence intervals (CI). Vitamin K intake data were log-transformed because they were not normally distributed from both 5DR and FFQ. To examine the validity and reliability of the FFQ, the Student's paired t-test and Pearson's correlation were performed on vitamin K intakes in the FFQ versus the dietary records and FFQ1 versus FFQ2, respectively. We calculated an adjusted de-attenuated correlation coefficient between FFQ and 5DR to reduce random error in intra-individual variability. A cross-classification analysis was performed to compare the categorization of vitamin K intake into quartiles by the food records and FFQ. The overall percentages of subjects classified into the same, adjacent, or extreme quartiles were determined, and the coincidence levels between the two methods were calculated by Cohen's kappa coefficient. A Bland-Altman plot was used to assess measurement error of the log-transformed vitamin K intake levels between the 5DR and FFQ. All analyses were carried out using SPSS 19.0 for Windows (SPSS, Chicago, CA, USA) and the statistical significance level was set at $p < 0.05$.

RESULTS

The list of major vitamin K contributing food sources extracted from KNHANES V to develop the vitamin K-specific FFQ is shown in **Table 1**. Foods with the highest contribution to total vitamin K intake were spinach (15.00%), followed by kimchi (10.61%), radish leaves (7.20%), sesame leaves (5.89%), and laver (4.38%) (data not shown).

Table 1. List of food items included in the vitamin K-specific FFQ

Food group	Food item	Reference amount, g
Vegetables	Kimchi	40
	Yeolmukimchi	40
	Cucumber	70
	Lettuce	70
	Spinach	70
	Radish leaves	70
	Cabbage	70
	Chinese cabbage	70
	Chives	70
	Water celery	70
	Crown daisy	70
	Soybean sprouts	70
	Shepherd's purse	70
	Broccoli	70
	Sesame leaves	70
	Laver	2
	Sea mustard	30
Legumes	Soybean curd	80
Fruits	Tomato	70
	Kiwi	100
	Apple	100
Seasonings	Soybean oil	5
	Gochujang	15
	Cheongguk-jang	15
	Doenjang	15

Table 2. Vitamin K intakes in Korean adults estimated by the FFQ1, FFQ2, and 5-day food record (5DR)

Method	Mean (SD)	Median
FFQ1 (n = 61)	226.69 (172.65)	183.26
FFQ2 (n = 61)	194.51 (152.49)*	150.44
5DR (n = 56)	166.56 (88.85)†	159.00

*p = 0.116 by Student paired t-test between FFQ1 and FFQ2.

†p = 0.072 by Student paired t-test between FFQ1 and 5DR.

Women and men with a mean age (SD) of 35.43 years (13.46 years) participated in the study. Of the 54 subjects who agreed to participate in this study, 48 (88%) subjects completed 5DRs. Mean, SD, and median daily vitamin K intakes for FFQ1 and FFQ2 and the 5DR are shown in **Table 2**. Comparing FFQ1 to FFQ2, vitamin K intakes were 226.69 ± 172.65 $\mu\text{g}/\text{day}$ and 194.51 ± 152.49 $\mu\text{g}/\text{day}$, respectively, with no significant difference between the results of the two questionnaires. There were no significant differences in vitamin K intakes derived from the FFQ1 and 5DR ($p > 0.05$).

Table 3 describes the correlation of vitamin K intake between the FFQ and 5DR (validity) and the two FFQs (reliability). The Pearson's correlation coefficient between the FFQ and 5DR was 0.652, and the calorie-adjusted de-attenuated correlation was 0.740, indicating a strong correlation. The correlation between FFQ1 and FFQ2 was 0.560, representing a statistically significant difference ($p < 0.001$). The coincidence or proximity ratio of vitamin K intake between the FFQ and the 5DR was 83.6%, and the discordance ratio was 6.0%. Cohen's kappa coefficient was 0.519. Following the categorization of vitamin K intake from FFQ1 and FFQ2 into quartiles, and the coincidence or proximity ratio of vitamin K intake was 83.4, the discordance ratio was 5.6, and Cohen's kappa coefficient was 0.333.

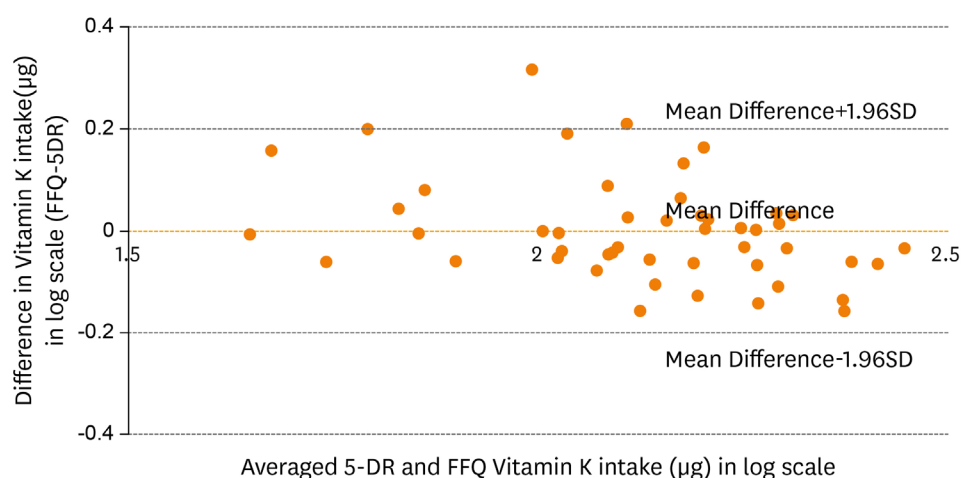


Figure 1. Bland-Altman plot of the difference in vitamin K intake as assessed by FFQ and the 5DR ($n = 48$). Values are log-transformed.

The coincidence of vitamin K intakes estimated under the log transformation based on the FFQ and the 5DR was analyzed with a Bland-Altman plot, and the outcomes are described in **Figure 1**. The log transformed mean difference between 5DR and FFQ methods was -0.002 , and limits of agreement being from -0.20 to 0.20 .

DISCUSSION

The present study was performed to develop a FFQ specifically designed to assess dietary vitamin K intake among the general population in Korean adults. A 25-item FFQ, which reflects the food intake patterns of Koreans, was developed and tested for validity and reliability. Our findings showed that a total of 25 food items contributes to 90% of vitamin K intake in Korean adults and vegetables account for a considerable percentage of vitamin K intake, and this phenomenon is likely due to the food sources and eating habits of Korean people [21].

In previous studies, the vitamin K intakes analysis by FFQ were significantly higher than those of 5DR and the difference of intakes between two methods were about $93 \mu\text{g/day}$ – $146 \mu\text{g/day}$ [16,17]. In our study, mean vitamin K intakes from the FFQ and 5DR were not significantly different; this result represents an improvement over previous studies in which the difference in vitamin K intake between the FFQ and the diet record method was relatively high. A generally acceptable correlation coefficient between an FFQ and the gold standard method is between 0.5 and 0.7. The correlation coefficient obtained from vitamin K intakes assessed by our FFQ and 5DR ($r = 0.652$) was comparable with results of the previous

Table 3. Cross-classification analysis of the vitamin K intake of Korean adults based on the FFQs and 5-day food record (5DR)

	Pearson's correlation coefficient r	De-attenuated correlation coefficient r (95% CI)	% classified into same or adjacent quartiles	% classified into opposite quartile	Cohen's kappa coefficient
FFQ1 versus 5DR	0.652 [*]	0.740 (0.553–0.849)	83.6	6.0	0.519
FFQ1 versus FFQ2	0.560 [†]	-	83.4	5.6	0.333

^{*}Indicated significant correlation between FFQ1 and 5DR, $p < 0.001$.

[†]Indicated significant correlation between FFQ1 and FFQ2, $p < 0.001$.

validation studies, where vitamin K intake from FFQs was moderately correlated to that from food records ($r = 0.53-0.83$) [17,22,23]. Therefore, this FFQ can be considered for estimating an individual's actual vitamin K intake. Generally, vitamin K intakes measured by the FFQ were higher than those estimated by food records. A possible reason for this discrepancy is that subjects might have included vitamin K-rich food items when responding to the FFQ but did not eat those foods during the diet recording periods. Another reason might be that the answers to the FFQ are fixed as multiple frequencies at presented intervals.

In clinical settings, the efficacy of an FFQ would be dependent on good relative agreement in a cross-classification of nutrient intake. Our FFQ showed a favorable ability to classify individuals into quartiles of vitamin K intake, with 83.6% of subjects being correctly classified into the same or adjacent quartiles compared to 5DR, and only 6.0% of subjects being grossly misclassified. The Cohen's kappa was 0.519, which was similar to that in an earlier trial [17]. A high degree of cross-classification coincidence was found between the two methods in our study. Developed vitamin K-specific FFQ consists of only 25 items, and then it takes only 10 to 15 minutes to complete. Therefore, the FFQ can be used as a clinical tool for the rapid assessment of vitamin K for dietary intervention [24].

From a reproducibility perspective, the questionnaire should be administered at two points with reasonable test interval to the same group of people. However, only less than 50% of reported papers regarding the FFQ development had been performed the test-retest reliability [25]. When study design was set, the reasonable time interval between repeated test performances should be contemplated. If the interval was short, the memory of a subject may affect his or her responses on the second FFQ, and if the interval was long, the subject's dietary pattern may have changed thereby reducing objective measurements of reliability. In our study, due to relatively short FFQ (25 items), the time interval between FFQ1 and FFQ2 was set at 6 months to limit errors. Our study showed good reproducibility of the FFQ, with a Pearson's correlation coefficient of 0.560. Cross-classification also showed a fair agreement, because 83.4% of subjects were classified into the same or adjacent quartile of intake for vitamin K.

The present study has several potential weaknesses. First, the utility of the FFQ in the general population must be considered due to the selection of subjects with similar ethnic backgrounds as well as the relatively small sample size, which limit generalizability. Second, the selection of the reference method that is mostly close to gold standard value is the key component of the validation process. It was suggested that recording more than three days is proper for a reference method in validation study for vitamin intake assessment [23]. In our study, 5DR were used as reference method to fulfill a sufficient length to reliably assess vitamin K intake by considering intra- and inter-personal variation. However, a large number of recording periods may result in lowering accuracy and changes in eating habits. To increase the validity of the results, further studies may require the inclusion of biomarker reference methods, such as serum vitamin K and percentage of uncarboxylated osteocalcin levels [26,27].

CONCLUSION

The vitamin K-specific FFQ presented in this study showed good relative correlation with dietary records, and therefore, it is a valid tool for assessing individuals' vitamin K intakes. This new FFQ represents a substantially lower burden to subjects than food records and will

be fruitfully used as a practical tool in the research field and disease prevention settings. The vitamin K-specific FFQ could also be clinically useful to identify adults with the greatest need of nutritional counseling, such as anticoagulation therapy patients with uncontrolled vitamin K intake or those at the highest risk of vitamin K inadequacy.

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