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Association of Dietary Vitamin K_1 Intake With the Incidence of Cataract Surgery in an Adult Mediterranean Population

A Secondary Analysis of a Randomized Clinical Trial

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Key Points

Go to:

Question

Is dietary vitamin K associated with a decreased risk of cataract among an elderly Mediterranean population?

Findings

In this secondary analysis of 5860 participants in a randomized clinical trial, participants in the highest tertile of dietary vitamin K_1 intake had a lower risk of cataract than those in the lowest tertile.

Meaning

These findings suggest that a high intake of dietary vitamin K_1 is associated with a reduced risk of cataract in an elderly Mediterranean population.

Abstract

Importance

Cataract, one of the most frequent causes of blindness in developed countries, is strongly associated with aging. The exact mechanisms underlying cataract formation are still unclear, but growing evidence suggests a potential role of inflammatory and oxidative processes. Therefore, antioxidant and anti-inflammatory factors of the diet, such as vitamin K_1, could play a protective role.

Objective

To examine the association between dietary vitamin K_1 intake and the risk of incident cataracts in an elderly Mediterranean population.

Design, Setting, and Participants

A prospective analysis was conducted in 5860 participants from the Prevención con Dieta Mediterránea Study, a randomized clinical trial executed between 2003 and 2011. Participants were community-dwelling men (44.2%) and women (55.8%), and the mean (SD) age was 66.3 (6.1) years.

Main Outcomes and Measures

Dietary vitamin K_1 intake was evaluated using a validated food frequency questionnaire. The time to the cataract event was calculated as the time between recruitment and the date of the occurrence to cataract surgery, the time to the last visit of the follow-up, date of death, or the end of the study. Hazard ratios and 95% CIs for cataract incidence were estimated with a multivariable Cox proportional hazards model.

Results

Go to:

Participants were community-dwelling men (44.2%; n = 868) and women (55.8%; n = 1086), and the mean (SD) age was 66.3 (6.1) years. After a median of 5.6 years follow-up, we documented a total of 768 new cataracts. Participants in the highest tertile of dietary vitamin K_1 intake had a lower risk of cataracts than those in the lowest tertile (hazard ratio, 0.71; 95% CI, 0.58-0.88; *P* = .002), after adjusting for potential confounders.

Conclusions and Relevance

Go to:

High intake of dietary vitamin K_1 was associated with a reduced risk of cataracts in an elderly Mediterranean population even after adjusting by other potential confounders.

Trial Registration

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isrctn.org: ISRCTN35739639

Introduction

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A cataract is a clouding of the crystalline lens that causes a decrease in the vision. Aging is its major predictor, but it is also associated with obesity, type 2 diabetes, diet, smoking, and alcohol, among others. Inflammation and oxidation could underlie the cataract formation. Because diet modulates these processes, the relationship between food or specific dietary components and cataractogenesis has been prospectively assessed. Meta-analyses of cohort studies showed that higher intakes of some vitamins were associated with a reduced cataract risk. Similarly, high intakes of fruit and vegetables are also associated with a lower prevalence of cataract or cataract surgery.

Because vitamin K has anti-inflammatory and antioxidant properties and is related to glucose and insulin metabolism, we hypothesize that dietary vitamin K_1 intake would be associated with a decreased risk of cataracts among an elderly Mediterranean population.

Methods

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The analysis was conducted in the Prevención con Dieta Mediterránea (PREDIMED) study, a parallel-group, randomized clinical cardiovascular prevention trial in participants at high cardiovascular risk (http://www.predimed.es). The detailed protocol was published elsewhere. All participants included in the study provided written informed consent according to a protocol approved by the institutional review boards of all the recruiting centers. At baseline and yearly thereafter, a food frequency questionnaire was administered, and data on energy and nutrient intake were obtained using Spanish food composition tables. Vitamin K_1 intake was estimated using the US Department of Agriculture nutrient database. Cataract was a prespecified secondary outcome defined as the occurrence of cataract surgery during the study. The outcome was externally confirmed by an independent adjudication committee. Traumatic cataracts and those that emerged after intraocular surgery were excluded. In cases of bilateral surgery in the same patient, only the first event was considered (eMethods in the Supplement).

Baseline descriptive data were presented as mean (SD) and percentages using analysis of variance and χ^2 test. Dietary variables were adjusted for total energy intake using the residuals method. We averaged food consumption from the baseline to the end of the follow-up or to the last follow-up food frequency questionnaire before the occurrence of cataract surgery. Multivariable Cox proportional hazard models were fitted to assess the association between dietary vitamin K_1 intake and the risk of cataract surgery. Follow-up time was calculated as the time between recruitment and the date of the event, death, or end of study, whichever came first. Hazard ratios (HRs) and 95% confidence intervals were calculated. A sensitivity analysis was conducted excluding all cataract surgeries that occurred during the first year of the trial. The level of significance was $P < .05$, and all P values were 2-sided. Statistical analyses were conducted using SPSS, version 19.0 (SPSS Inc) and Stata, version 14 (StataCorp).

Results

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We included 5860 participants in the analysis after excluding those with extremes of energy intake, incomplete dietary data at baseline, bilateral cataract, or for whom bilateral cataract could not be discarded at baseline.

During a median of 5.6 years of follow-up, 768 participants underwent cataract surgery. Baseline characteristics of study participants are shown in Table 1. Individuals in the highest tertile of mean energy-adjusted dietary vitamin K_1 intake had a lower waist circumference, were more physically active, and were less inclined to smoke. Baseline dietary intake is presented in the eTable in the Supplement. Participants in the highest tertile of the mean energy-adjusted dietary vitamin K_1 intake had a lower risk of cataract surgery than those in the lowest tertile (HR, 0.71; 95% CI, 0.58-0.88; $P = .002$) (Table 2). The survival curves and the number of participants at risk in each tertile are shown in Figure. The results of the sensitivity analysis did not differ from the general one, showing a lower risk of cataract surgery in the highest tertile of energy-adjusted dietary vitamin K_1 intake (HR in the 3rd tertile, 0.75; 95% CI, 0.60-0.92; $P = .02$).

Discussion

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These data suggest that higher intake of dietary vitamin K_1 is associated with a reduced risk of cataract. A lens is a complex tissue with a high protein content, minimum turnover, and a powerful antioxidant system. However, during the aging process, lens proteins are subject to posttranslational modifications, and the antioxidant system is compromised. Other chronic conditions, such as hyperglycemia and inflammation, also contribute to the cataract formation.

Several epidemiologic studies have shown an inverse association between diets rich in antioxidant and anti-inflammatory vitamins and the risk of cataract, although the results of clinical trials failed to establish any causal association. In this study, we found an inverse association between higher intake of dietary vitamin K_1 and the risk of cataract surgery. Our results could be partly explained by the antioxidant and anti-inflammatory properties attributed to this vitamin. Moreover, dietary vitamin K_1 intake has been also associated with lower circulating glucose levels and a delay in the insulin response to glucose infusion. In this regard, dietary vitamin K_1 intake was associated with a reduced risk of new-onset type 2 diabetes in the PREDIMED trial after 5.5 years of follow-up. A 51% lower risk of diabetes was reported in those participants who increased their vitamin K_1 intake during the follow-up. Similarly, a 2014 study conducted in diabetic rats demonstrated that the treatment with vitamin K_1 decreased blood and lens glucose concentrations and reduced the levels of lens sorbitol that could help prevent cataract formation. Therefore, the protective effect of vitamin K_1 intake on cataract surgery risk observed in our study helps to reinforce these findings in animals and extend them to the human population.

Limitations

Some limitations of this study should be mentioned. First, because food frequency questionnaires were used for the dietary assessment and vitamin K_1 contents were extracted from the US Department of Agriculture food composition database because no Spanish composition tables include the vitamin K contents of food, we cannot discard errors in the estimation of vitamin K_1 intake. However, although the food frequency questionnaire used was not specifically validated for vitamin K_1 intake, an intraclass correlation coefficient of 0.81 was found. Second, because we have no data on vitamin K_1 plasma levels, we cannot discard physiological conversions of dietary vitamin K_1 that do not account for the circulating active form of vitamin K. However, a high association between dietary vitamin K_1 intake and plasma vitamin K_1 levels has been demonstrated previously. Third, because the study was conducted in elderly participants at high cardiovascular risk living in a Mediterranean country, our findings may not be extrapolated to other populations. Finally, although we cannot completely discard a potential different access to healthier dietary habits according to the socioeconomic status, we have adjusted the Cox model by food groups to avoid the residual confounding. Likewise, in Spain, cataract surgery is included in the National Health System, thus removing any bias regarding access to the surgery procedures according to socioeconomic status. The strengths of this study include its longitudinal design, the use of repeated dietary measurements during follow-up, and the accurate assessment of incident cataract surgery.

Conclusions

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The results of this study suggest a protective role of high vitamin K_1 dietary intake on cataract incidence in a senior Mediterranean population even after adjusting by other potential confounders. Further studies and trials are required to confirm these results.

Notes

Go to:

Supplement.

eMethods.

eTable. Baseline Characteristics of 5860 PREDIMED Participants By Tertiles of Baseline Dietary Phylloquinone Intake

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Figures and Tables

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Table 1.

Baseline Characteristics of 5860 Prevención con Dieta Mediterránea Participants by Tertiles of Baseline Dietary Vitamin K_1 Intake

Variable	Energy-Adjusted Baseline Vitamin K_1 Intake, µg/d, No. (%)			*P* Value[a]
	T1 (n = 1953)	T2 (n = 1954)	T3 (n = 1953)	
Women	1001 (51.3)	1086 (55.6)	1182 (60.5)	<.001
Age, mean (SD), y	66.3 (6.3)	66.4 (6.0)	66.1 (5.9)	.41
BMI, mean (SD)	30.1 (3.9)	29.8 (3.8)	29.9 (4.1)	.07
Waist circumference, mean (SD), cm	101.3 (10.1)	100.0 (10.5)	100.1 (10.7)	<.001
Leisure-time physical activity, mean (SD), MET min/d	213.0 (224.7)	235.4 (239.6)	245.2 (248.4)	<.001
Glucose, mean (SD), mg/dL	119.3 (38.3)	120.5 (40.3)	123.1 (42.6)	.011
Total cholesterol, mean (SD), mg/dL	211.9 (37.8)	217.1 (44.4)	218.1 (40.3)	.007
Triglycerides, mean (SD), mg/dL	151.6 (103.0)	140.5 (75.8)	145.9 (85.1)	.09
HDL cholesterol, mean (SD), mg/dL	51.6 (13.1)	53.8 (14.8)	54.0 (13.3)	<.001
Diabetes	881 (45.1)	903 (46.2)	991 (50.7)	.001
Hypertension	1607 (82.3)	1655 (84.7)	1593 (81.6)	.03
Hypercholesterolemia	1414 (72.4)	1370 (70.1)	1453 (74.4)	.01
Smoking status				
Never	1115 (57.1)	1190 (60.9)	1217 (62.3)	
Current	342 (17.5)	299 (15.3)	240 (15.3)	<.001
Former	496 (25.4)	465 (23.8)	496 (25.4)	

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Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); EVOO, extra virgin olive oil; HDL, high-density lipoprotein; MET, metabolic equivalent of task; PREDIMED, Prevención con Dieta Mediterránea; T, tertile.

SI conversion factor: To convert HDL cholesterol to millimoles per liter, multiply by 0.0259; total cholesterol to millimoles per liter, multiply by 0.0259; glucose to millimoles per liter, multiply by 0.0555; triglycerides to millimoles per liter, multiply by 0.0113.

[a] *P* values are based on the difference between tertiles of mean energy-adjusted dietary vitamin K_1 intake (analysis of variance for the continuous variables and χ^2 test for categorical variables).

Table 2.

Adjusted HRs of Cataracts According to Tertiles of Vitamin K_1 Intake[a]

Variable	Energy-Adjusted Average Dietary Phylloquinone Intake, µg/d			*P* Value for Trend
	T1 (n = 1953)	T2 (n = 1954)	T3 (n = 1953)	
Vitamin K_1 intake, median (IQR), µg/d	249.4 (206.7-281.7)	353.6 (329.6-378.0)	496.7 (444.4-597.2)	NA
Cases/person-year, No.	10 420	11 203	11 204	NA
Crude model, HR (95% CI)	1 (Reference)	0.93 (0.79-1.10)	0.71 (0.60-0.85)	<.001
Model 1, HR (95% CI)[b]	1 (Reference)	0.96 (0.80-1.15)	0.71 (0.58-0.88)	.002

Abbreviatons: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HR, hazard ratio; IQR, interquartile range; MET, metabolic equivalent of task; NA, not applicable.

[a]Cox regression was used to evaluate the risk of cataracts according to tertiles of baseline dietary vitamin K intake and mean dietary energy-adjusted vitamin K intake.
[b]Model 1 was adjusted for sex, age, BMI, recruiting center, intervention group, smoking (never, current, past), leisure time activity (MET/d), education (primary education, secondary education, higher education), cataract event at baseline, diabetes at baseline, hypertension, hypercholesterolemia, and use of anticoagulant and for baseline dietary variables in energy-adjusted tertiles (vegetables, fruits, legumes, cereals, dairy, meat, fish, olive oil, and nuts), Vitamin C, alcohol, and alcohol squared in grams per day.

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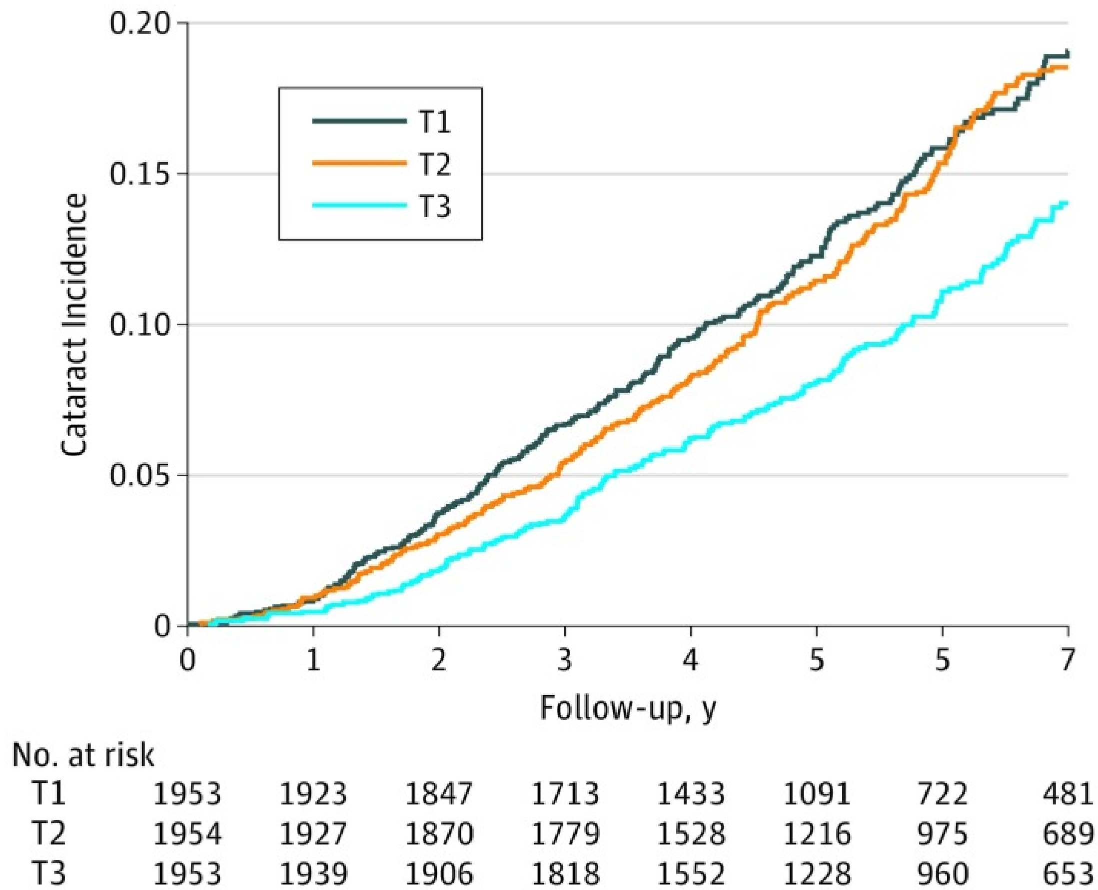
Figure.



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Nelson-Aalen Estimates of Incidence of Cataracts by Tertiles of Vitamin K_1 Intake