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Antioxidant Intake and Risk of Incident Age-related Nuclear Cataracts in the Beaver Dam Eye Study

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The relation of antioxidant nutrients to the incidence of nuclear cataracts was investigated in a cohort of adults aged 43–84 years in the Beaver Dam Eye Study (Beaver Dam, Wisconsin). Nuclear opacity was assessed on a five-point ordinal scale using lens photographs taken at baseline (1988–1990) and at follow-up (1993–1995). Of the 1,354 persons eligible, 246 developed a nuclear cataract (level 4 or 5 opacity) in at least one eye. Antioxidant intakes were assessed using a food frequency questionnaire administered at baseline for time points corresponding to intake during the year preceding baseline and 10 years before baseline (the distant past). Lutein-zeaxanthin was the only carotenoid, out of five examined, that was associated with nuclear cataracts. Persons in the highest quintile of lutein intake in the distant past were half as likely to have an incident cataract as persons in the lowest quintile of intake (95% confidence interval 0.3–0.8). In the overall group, nuclear cataracts were not significantly related to intake of vitamin C or vitamin E. However, vitamins C and E were inversely associated with opacities in persons who had some other risk factors for cataracts. While results of this short term follow-up study are consistent with a possible protective influence of lutein and vitamins E and C on the development of nuclear cataracts, the evidence in the present study provides weak support for these associations. *Am J Epidemiol* 1999;149:801–9.

age factors; antioxidants; ascorbic acid; carotenoids; cataract; diet; vitamin E

Opacification of the ocular lens, or cataractogenesis, is a multifactorial disease process that may be initiated by oxidative damage from photochemically or non-photochemically generated oxygen radicals (1). Vitamin C, vitamin E, and carotenoids may influence this process due to their being free radical scavengers. Although experimental animal models have shown that these vitamins can influence lens structure and function (2–5), the effect on human lens opacities is not known. Vitamin C, vitamin E as α-tocopherol and γ-tocopherol, and what appears to be the carotenoids lutein and zeaxanthin have been shown to be present in human lenses, with vitamin C being found at levels severalfold that seen in plasma (6–8).

To date, results from epidemiologic studies assessing dietary associations with opacities in the center nuclear region of the lens have been inconsistent. Prevalent nuclear cataracts were inversely associated with intakes of one or more antioxidant nutrients from foods or supplements in four previous studies (9–12) but not in three others (13–15). Both plasma vitamin E level and supplemental intake of vitamin E were recently reported to be related to the incidence of nuclear opacification in a longitudinal follow-up of participants in a case-control study (16). Additionally, results from two prospective observational studies provided some evidence of inverse associations between antioxidant vitamins and self-reported diagnosis or extraction of age-related cataracts (17, 18). In an intervention study in Linxian, China, the prevalence of nuclear cataracts was marginally lower among persons assigned to take a supplement containing vitamin C and molybdenum but not among those taking a supplement containing α-tocopherol, selenium, and β-carotene (19).

The purpose of this study was to determine whether intakes of nutrients with potential antioxidative functions were associated with age-related nuclear cataracts in a prospective population-based study in which lens opacities were assessed prior to cataract extraction. Our hypotheses were that 1) intakes of carotenoids, vitamin C, and vitamin E are inversely associated with the incidence of nuclear opacities and 2) important food sources of potential antioxidants are inversely associated with the incidence of nuclear opacities.

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Abbreviations: CI, confidence interval; OR, odds ratio.

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MATERIALS AND METHODS

Population

The Beaver Dam Eye Study is an ongoing study of middle-aged and older adults in a primarily Caucasian community in south-central Wisconsin. The entire population of persons aged 43–84 years residing in Beaver Dam were identified by private census and recruited for the study. Of the 5,925 persons eligible, 4,926 (83.1 percent) participated in the study at the baseline examination (1988–1990). A 50 percent random sample of noninstitutionalized persons (n = 2,429) was invited to take part in a nutrition study. Of these persons, 24 moved or died, six could not be located, and 23 were physically or mentally unable to be involved. Ninety-one percent (n = 2,152) of the remaining subjects participated in the nutrition study. Respondents were more likely than nonrespondents ($p < 0.05$) to be younger (a mean age of 61.5 years vs. 62.3 years), to be more educated (a mean of 12.0 years of schooling vs. 11.3 years), to report being in excellent or good health (84 percent vs. 76 percent), to have consumed alcoholic beverages during the past year (86 percent vs. 77 percent), and to engage in moderate exercise (27 percent vs. 20 percent). However, respondents and nonrespondents were similar with respect to gender, history of chronic diseases, smoking history, and vitamin supplement use (20). Seventy-nine percent of the baseline respondents were reexamined 5 years later. Of the subjects dropped from the study between the baseline and follow-up examinations, 29 could not be located or had moved, 202 had died, and 212 declined reevaluation. This study was approved by the University of Wisconsin Human Subjects Review Board, and informed consent was obtained from each participant.

Data collection

Physical examinations and lens photography were conducted at baseline, from 1988 through 1990, and at follow-up, from 1993 through 1995. Lens photographs were taken using a Topcon SL5 Slit Lamp camera (Paramus, New Jersey) with specially designed fixation targets for photographing the nuclear region of the lens. Procedures for photographing lenses in this study have been reported previously (21). Medical histories and information on demographic and behavioral characteristics were ascertained at baseline, using a standardized questionnaire administered in conjunction with the physical examinations. Characteristics evaluated for potential confounding are described in "Statistical methods."

Information on diet and the use of nutrient supplements was collected as part of a second, in-person interview approximately 1 month following the baseline examination. Participants were asked about their usual diet and use of supplements over the past year. The same information was solicited regarding dietary habits corresponding to 10 years before the interview. Diet was assessed using a 100-item modified form of the food frequency questionnaire developed by Block et al. (22). This questionnaire has been shown to rank persons' recent diets similarly to food records in the Beaver Dam population (23). For each supplement reported, information was collected on the brand, frequency of use, and amount of nutrient per pill.

Incidence of nuclear opacities

Nuclear opacities were graded from photographs on a five-step ordinal scale using a set of standard photographs for comparison. Procedures used to grade lenses have been described previously; they included independent assessments by two graders who were unaware of subject characteristics (21). The inter- and intragrader agreement and methods for assessing cataract incidence have been detailed elsewhere (24). A brief description is given here.

Nuclear opacification is a gradual and continuous process with no definitive point at which cataract is diagnosed. In this study, participants were classified as having an incident cataract if they were free of severe nuclear opacification (i.e., both lenses at levels 1–3) and had not had prior cataract surgery at baseline, and had at least one lens with severe nuclear opacification (level 4 or 5 opacity) at the follow-up examination. In secondary analyses, 26 persons who had cataract surgery during follow-up and had been graded on the basis of the lens in their other eye were reclassified as having a nuclear cataract. Because the main findings were not influenced when these additional participants were classified as cases, results are shown only for the former definition. Some subjects were ineligible for study of cataract incidence as follows: 218 because of a preexisting nuclear cataract at baseline; 50 because of cataract surgery prior to baseline; 85 with no lens to grade for reasons other than cataract surgery (e.g., trauma) or with photographs that were ungradable; and two who reported experiencing trauma to the lens in the past, which could have affected lens opacity.

Nutrient and food intake analyses

Intakes of nutrients from foods and supplements were combined to estimate total nutrient intakes. Nutrient intakes from food sources were determined from the food frequency questionnaire, using version 3.4 of the computer software and nutrient database (25). Carotenoid values (except for β-carotene) reflect

TABLE 1. Age-standardized characteristics of persons (n = 1,354) with low (quintile 1) and high (quintile 5) intakes of selected nutrients at baseline, Beaver Dam Eye Study (nutrition study subsample),* 1988–1990

	Lutein		Vitamin C		Vitamin E	
	Quintile 1	Quintile 5	Quintile 1	Quintile 5	Quintile 1	Quintile 5
Mean age (years)	56	58†	55	59†	57	59†
Geometric mean energy intake (MJ/day)	8.6	5.2	8.6	5.5	7.8	5.4
Gender (% women)	32	69†	23	70†	37	73†
Smoking of ≥25 pack-years (%)	40	24†	50	23†	35	21†
Alcohol intake of ≥91 g/week (%)	29	14†	35	13†	37	10†
Glycosylated hemoglobin level of ≥6.1% (%)	32	30	32	26	31	29
Hypertension (%)	25	31†	26	30†	30	27
Body mass index‡ ≥30 (%)	28	32	29	25	29	26

* Except for age, data were standardized to the age distribution of the nutrition study cohort. Quintiles of nutrient intake (per 4.18 MJ) were assigned separately for persons aged <65 years and ≥65 years.

† Differences across quintiles 1–5 were significant at $p \leq 0.05$ on the basis of analysis of variance (for age), analysis of covariance (for energy intake), or Cochran-Mantel-Haenszel χ^2 test for linear trend, adjusted for age (all other variables).

‡ Weight (kg)/height (m)^2.

intakes from foods alone, because supplements did not contain these carotenoids during the time periods studied. The nutrient database associated with the food frequency questionnaire was augmented with the most recent data available on carotenoid levels in fruits and vegetables (25, 26). Product labels from supplement containers were inspected at the interview to determine nutrient compositions. When this information was not available, nutrient composition was determined by contacting the manufacturer, by consulting the *Physicians' Desk Reference* (27, 28), or by assigning values from similar products. Food intakes were expressed in terms of "servings" that corresponded to the five food groups in the US Department of Agriculture's food guide pyramid (29). All nutrients and foods were expressed per 4.18 MJ (1,000 kcal).

Statistical methods

Participants were categorized into quintiles of intake for each nutrient and food. Risk of incident nuclear opacity was estimated for each quintile relative to the lowest quintile of intake, using odds ratios and 95 percent confidence intervals calculated from logistic regression models. Linear trends were evaluated by logistic regression analysis using quintile median intakes for foods and nutrients. Potentially confounding factors examined were: age, gender, smoking (never, past, and current smoking and pack-years of smoking), body mass index (weight (kg)/height (m)^2), alcohol consumption (total intake in grams per week, number of drinks of beer, wine, or hard liquor per week, and history of ever drinking more than four drinks per day), hemoglobin level, glycosylated hemoglobin level, and history of hypertension (systolic blood pressure ≥160 mmHg, diastolic blood pressure ≥95 mmHg, or reported history of hypertension with current use of antihypertensive medication). Interactions between potential confounders and nutrient intakes were tested using likelihood ratios in logistic regression analysis.

RESULTS

Table 1 shows how potential risk factors for nuclear cataracts differ between persons with low and high intakes of selected nutrients (data are not shown for carotenoids other than lutein). For all nutrients examined in this study, except lycopene, participants with higher nutrient densities (quintile 5) were, on average, older, less likely to be heavy smokers, and, with the added exception of vitamin E, more likely to have a history of hypertension than those with low nutrient intakes (quintile 1). In addition, persons with high nutrient intakes were more likely to be women and to be light drinkers or nondrinkers than those with low intakes. Age, total energy intake, pack-years of smoking, and total alcohol intake (g/week) altered odds ratios for nutrient intakes (quintile 5 vs. quintile 1) by ≥10

TABLE 2. Number and percentage of participants with incident nuclear cataract, by age and gender (n = 1,354), Beaver Dam Eye Study, 19883–1995

Gender and age (years)	N	Incident cataract	
		No.	%
Women			
43–64	528	60	11
65–84	185	76	41
Men			
43–64	471	42	9
65–84	170	68	40

percent, and therefore were retained in fully adjusted logistic regression models for nutrient intake analyses. Dietary intake of linoleic acid (expressed as percentage of total energy intake from linoleic acid) was included in the model for vitamin E, because of its influence on the physiologic need for vitamin E and because it affected odds ratios by more than 10 percent.

In the total nutrition study subsample, 1,354 persons were found to be at risk for incident cataract at the baseline examination, and 18.2 percent (n = 246) developed a nuclear cataract during the 5 years of follow-up. Older persons were less likely to be at risk for incident nuclear cataract (table 2), with 58.0 percent of persons aged ≥65 years at risk compared with 91.4 percent of younger persons. Nuclear cataracts occurred in 10.2 percent of persons aged <65 years (n = 102 of 999 at risk) and in 40.6 percent of persons aged ≥65 years (n = 144 of 355 at risk).

Associations between antioxidants and 5-year incidence of nuclear cataracts were similar for time periods coinciding with exposures at baseline and for retrospective recall of diet in the distant past (table 3).

TABLE 3. Odds ratios for incident nuclear cataract associated with intakes of vitamins C and E and carotenoids at baseline (1988–1990) and in the distant past (1978–1980), Beaver Dam Eye Study (nutrition study subsample), Beaver Dam, Wisconsin

Quintile of intake	Baseline* (1988–1990)					Distant past† (1978–1980)	
	Median intake	Age- and energy-adjusted OR‡	95% CI‡	Fully adjusted OR§	95% CI	Fully adjusted OR§	95% CI
			Vitamin C (mg/4.18 MJ)				
1	27	1.0		1.0		1.0	
2	51	0.9	0.5–1.5	1.0	0.6–1.7	0.8	0.5–1.4
3	78	0.9	0.5–1.5	1.0	0.6–1.7	1.3	0.8–2.2
4	117	0.9	0.5–1.5	1.0	0.6–1.7	1.2	0.7–2.0
5	281	0.8	0.5–1.3	0.9	0.5–1.5	0.8	0.5–1.4
p trend¶		0.45		0.47		0.42	
			Vitamin E (mg of α-TE‡/4.18 MJ)				
1	3.7	1.0		1.0		1.0	
2	4.7	0.6	0.4–1.0	0.6	0.4–1.1	1.0	0.6–1.8
3	5.7	0.9	0.6–1.5	0.9	0.5–1.5	1.4	0.8–2.5
4	10.0	1.1	0.7–1.7	1.0	0.6–1.8	1.1	0.6–2.2
5	28.3	0.7	0.4–1.1	0.7	0.4–1.1	0.8	0.4–1.4
p trend		0.23		0.22		0.08	
			α-Carotene (μg/4.18 MJ)				
1	66	1.0		1.0		1.0	
2	107	1.0	0.6–1.7	1.1	0.7–1.8	1.6	0.9–2.7
3	145	1.1	0.6–1.7	1.1	0.7–1.8	1.1	0.6–1.8
4	197	0.8	0.5–1.3	0.9	0.5–1.5	1.1	0.7–1.9
5	292	1.0	0.6–1.6	1.0	0.6–1.7	1.2	0.7–2.1
p trend		0.73		0.89		0.95	
			β-Carotene (μg/4.18 MJ)				
1	465	1.0		1.0		1.0	
2	704	1.1	0.6–1.8	1.1	0.6–1.8	1.0	0.6–1.7
3	928	1.3	0.8–2.1	1.4	0.8–2.3	1.0	0.6–1.8
4	1,217	0.9	0.5–1.6	1.0	0.6–1.7	0.9	0.5–1.6
5	1,939	1.0	0.6–1.8	1.1	0.6–1.8	0.9	0.5–1.5
p trend		0.77		0.82		0.47	
			Lutein (μg/4.18 MJ)				
1	298	1.0		1.0		1.0	
2	459	0.9	0.5–1.5	0.9	0.6–1.5	0.9	0.6–1.6
3	600	0.9	0.6–1.5	1.0	0.6–1.7	0.9	0.6–1.7
4	784	0.9	0.6–1.5	1.0	0.6–1.6	0.7	0.4–1.2
5	1,245	0.6	0.4–1.1	0.7	0.4–1.1	0.5	0.3–0.8
p trend		0.09		0.10		0.002	

Table continues

TABLE 3. Continued

Quintile of intake	Median intake	Baseline* (1988–1990) Age- and energy-adjusted OR‡	95% CI‡	Fully adjusted OR§	95% CI	Distant past† (1978–1980) Fully adjusted OR§	95% CI
			Lycopene (μg/4.18 MJ)				
1	477	1.0		1.0		1.0	
2	789	0.7	0.4–1.0	0.7	0.4–1.1	1.2	0.7–1.9
3	1,056	0.9	0.6–1.5	0.9	0.6–1.5	1.1	0.6–1.8
4	1,433	0.6	0.3–0.9	0.6	0.3–1.0	0.9	0.5–1.5
5	2,248	0.9	0.6–1.4	0.9	0.6–1.5	1.3	0.8–2.1
p trend		0.87		0.93		0.54	
			Cryptoxanthin (μg/4.18 MJ)				
1	2.3	1.0		1.0		1.0	
2	8.1	1.3	0.8–2.2	1.5	0.9–2.5	1.2	0.7–2.0
3	13.6	1.3	0.8–2.2	1.5	0.9–2.5	1.4	0.9–2.4
4	22.7	1.2	0.7–1.9	1.3	0.8–2.3	1.5	0.9–2.5
5	44.9	1.4	0.8–2.3	1.6	0.9–2.7	1.2	0.7–2.1
p trend		0.41		0.28		0.62	

* Of 1,354 participants, 246 had a nuclear cataract at the follow-up examination (1993–1995).

† Of 1,315 participants with nutrient intake data corresponding to 10 years before baseline, 233 had a nuclear cataract at the follow-up examination. One person with a cataract was not included in the fully adjusted models because information on alcohol use was not available.

‡ OR, odds ratio; CI, confidence interval; α-TE, α-tocopherol equivalents.

§ The fully adjusted models included age, energy intake, pack-years of smoking, reported amount of alcohol (g) consumed per week, and, in the vitamin E model, percentage of energy intake as linoleic acid. One person with a cataract was not included in the fully adjusted models because information alcohol use was not available.

¶ *p* value for linear trend using quintile medians.

Hence, while results presented in this paper focus on baseline exposures, we also describe relations with intakes in the distant past.

Vitamin C intake was not associated with the incidence of nuclear cataracts in the overall group (table 3). Subgroup analyses were undertaken to explore the meaning of several interaction effects seen in the logistic regression models (table 4). Consistently inverse trends were observed between vitamin C intake and opacities in subgroups with other possible risk factors for nuclear cataracts. Inverse trends were significant for heavy smokers and for persons with a history of hypertension. In contrast, vitamin C was directly associated with nuclear cataracts among persons with a glycosylated hemoglobin level in the top quartile (≥6.1 percent), although confidence intervals were wide and included 1.0.

Vitamin E intake was not significantly related to nuclear cataracts in the overall group (table 3). Intake of food sources of vitamin E (table 5) such as plant oils, nuts and seeds, and whole grains also was unrelated to nuclear cataracts. However, associations with vitamin E were apparent in some subgroups (table 4). Among persons with a history of hypertension or aged ≥65 years, a higher intake of vitamin E was associated with reduced odds for nuclear opacities.

Lutein was the only carotenoid of the five examined in this cohort that was associated with nuclear opacities (table 3), although this association was significant at the 95 percent confidence level only for diet in the more distant past. Intake of lutein at baseline was related to nuclear cataracts among younger persons (for quintile 5 vs. quintile 1, odds ratio (OR) = 0.4, 95 percent confidence interval (CI) 0.2–0.8) but not among older persons (for quintile 5 vs. quintile 1, OR = 0.8, 95 percent CI 0.4–1.7) (table 4). Additional analyses showed that relatively higher rates of mortality among older persons with low lutein intakes might have influenced the observed relation between lutein and the incidence of nuclear cataracts in older people. Odds ratios for mortality among older participants with lutein intakes in quintiles 2 through 5, relative to quintile 1, were 0.8, 0.8, 0.5, and 0.7 (95 percent CI 0.4–1.2), respectively (linear trend: $p = 0.13$).

Consumption of spinach and other dark leafy greens, which are the most concentrated source of lutein in the diet, was inversely associated with nuclear cataracts for persons with the highest intakes (table 5). The association with food sources of lutein was not limited to plant-based foods. In the younger age group, in which lutein intake at baseline was related to nuclear cataract, intakes of both spinach and eggs in the highest quintile

TABLE 4. Odds ratios for incident nuclear cataract associated with intakes of vitamins C and E and lutein at baseline, according to other potential risk factors for cataract, Beaver Dam Eye Study (nutrition study subsample), 1988–1990

Risk factor	No. of persons with incident nuclear cataract	Median intake: Quintile 1	Median intake: Quintile 5	Odds ratio*	95% confidence interval	p trend†	p for interaction
Vitamin C (mg/4.18 MJ)							
Age (years)							
<65	102	25	238	1.2	0.6–2.5	0.50	0.62
≥65	143	33	445	0.6	0.3–1.2	0.15	
Pack-years of smoking							
<25	165	33	315	1.0	0.5–1.9	0.76	0.04
≥25	80	19	236	0.3	0.1–0.8	0.01	
Weekly alcohol consumption (g)							
<91	207	30	310	0.8	0.4–1.4	0.33	0.12
≥91	38	20	186	0.4	0.1–1.4	0.37	
Hypertension							
No	154	25	272	1.4	0.7–2.7	0.20	<0.001
Yes	90	32	303	0.3	0.1–0.8	0.02	
Glycosylated hemoglobin (%)							
<6.1	161	28	274	0.6	0.3–1.1	0.03	0.08
≥6.1	83	25	291	1.5	0.6–3.7	0.15	
Vitamin E (mg of α-TE‡/4.18 MJ)							
Age (years)							
<65	102	3.7	26.6	0.7	0.3–1.4	0.54	0.02
≥65	143	3.8	31.0	0.5	0.3–1.1	0.04	
Pack-years of smoking							
<25	165	3.8	32.6	0.8	0.4–1.5	0.86	0.65
≥25	80	3.4	19.8	0.7	0.3–1.8	0.45	
Weekly alcohol consumption (g)							
<91	207	3.9	31.0	0.8	0.5–1.4	0.52	0.06
≥91	38	3.2	16.4	0.7	0.2–2.6	0.58	
Hypertension							
No	154	3.7	28.9	0.8	0.4–1.6	0.80	0.01
Yes	90	3.7	25.2	0.4	0.2–1.1	0.02	
Glycosylated hemoglobin (%)							
<6.1	161	3.7	28.0	0.7	0.4–1.4	0.41	0.24
≥6.1	83	3.7	29.5	0.5	0.2–1.3	0.36	
Lutein (μg/4.18 MJ)							
Age (years)							
<65	102	282	1,248	0.4	0.2–0.8	0.06	0.40
≥65	143	318	1,242	0.8	0.4–1.7	0.39	
Pack-years of smoking							
<25	165	323	1,268	0.7	0.4–1.3	0.17	0.85
≥25	80	257	1,167	0.6	0.2–1.5	0.37	
Weekly alcohol consumption (g)							
<91	207	319	1,284	0.8	0.4–1.4	0.37	0.004
≥91	38	257	1,079	0.1	0.02–0.6	0.01	
Hypertension							
No	154	283	1,240	0.6	0.3–1.2	0.26	0.05
Yes	90	322	1,252	0.7	0.3–1.7	0.11	
Glycosylated hemoglobin (%)							
<6.1	161	300	1,240	0.8	0.4–1.6	0.45	0.04
≥6.1	83	293	1,269	0.5	0.2–1.2	0.11	

* Odds ratio for quintile 5 versus quintile 1, adjusted for age, energy intake, pack-years of smoking, reported amount of alcohol (g) consumed per week, and, in the vitamin E model, percentage of energy intake as linoleic acid.

† *p* value for linear trend using quintile medians.

‡ α-TE, α-tocopherol equivalents.

TABLE 5. Odds ratios for incident nuclear cataract associated with intakes* of selected foods at baseline, Beaver Dam Eye Study (nutrition study subsample), 1988–1990

Food	Odds ratio†	95% confidence interval	p trend‡
Fruits	1.8	1.0–3.3	0.07
Vegetables	0.7	0.4–1.2	0.39
Spinach and greens	0.6	0.4–0.9	0.02
Eggs	0.7	0.5–1.2	0.32
Fats and oils of plant origin	1.2	0.7–1.9	0.92
Nuts and seeds	1.4	0.9–2.3	0.20
Whole grains	0.8	0.5–1.3	0.15

* Food intakes were assessed in terms of number of servings per 4.18 MJ.

† Odds ratio for quintile 5 relative to quintile 1. The logistic regression models included age, energy intake, and pack-years of smoking.

‡ *p* value for linear trend based on quintile medians.

versus the lowest were related to lower risk for nuclear cataract (for spinach, OR = 0.6, 95 percent CI 0.3–1.0, p trend = 0.05; for eggs, OR = 0.4, 95 percent CI 0.2–0.9, p trend = 0.004), despite a lack of correlation between spinach intake and egg intake (Pearson's r = −0.02).

DISCUSSION

To our knowledge, this is the first prospective population-based study to report relations between nutrient intakes and the incidence of nuclear cataracts. A strength of this study is that nutrient intakes corresponded to a time point before follow-up began, and lens changes were considered only for participants who were free of cataracts (including cataract surgery) at the outset. Consequently, nutrient intakes were less likely to have been influenced by the presence, diagnosis, or surgical removal of cataracts. Furthermore, both food sources and supplemental sources were accounted for in estimating intakes of β-carotene and vitamins C and E.

Lutein-zeaxanthin has been shown to be present in lens tissue (6, 8) and therefore is a plausible etiologic factor for cataracts. In this study, dietary intakes of lutein were inversely associated with the incidence of nuclear cataracts, especially intakes in the distant past. At baseline, lutein intake was associated with the incidence of cataracts in younger persons but not in older persons. Selective mortality is one possible explanation for the lack of a significant inverse association between lutein intake at baseline and nuclear cataracts among persons aged ≥65 years. Klein et al. (30) showed previously that the severity of nuclear cataracts was associated with decreased survival in this cohort. Moreover, lutein intake was inversely, though nonsignificantly, related to mortality among participants aged ≥65 years.

Previously in this cohort, intakes of lutein assessed by the participant's recollection of diet 10 years before baseline were shown to be associated with the severity of nuclear cataracts measured cross-sectionally at baseline (10). Additionally, associations between intake of spinach, the most concentrated source of lutein, and extraction of any type of cataract have been reported by other investigators (17, 31). In this study, the incidence of nuclear cataracts was inversely related to both plant and animal sources of lutein. Eggs are a type of food that is distinctly different from vegetable sources of lutein; this reduces the likelihood that some other constituent of plant foods is responsible for the apparent association with lutein intakes. Despite the fact that eggs have a moderate concentration of lutein, they are a relatively commonly consumed food, and they constituted 15 percent of the average lutein intake in the Beaver Dam Eye Study. On the basis of results from this study and other studies, dietary sources of lutein appear to be a consistently reported link between diet and nuclear cataracts.

The finding of stronger associations between nuclear cataracts and lutein intake in the distant past as compared with the recent past (baseline) is consistent with results of other studies (11, 16) in which longer term intake of other antioxidants was more strongly associated with nuclear cataract than short term intake. Because errors in recalling diet in the distant past are expected to be larger than errors in recalling recent diet, associations with diet in the more distant past would be expected to be weaker rather than stronger. Stronger associations with past diet in this study may reflect an influence of diet on early biochemical events that precede the development of observable opacities in the nuclear region of the lens. If this is the case, nutrient intake in middle age may influence the development of cataracts far into older age. Alternatively, stronger relations between incident nuclear cataracts and diet in the distant past could be due to a bias in recalling diet, such that people who develop nuclear opacities recall their diets as being lower in leafy greens and eggs than they actually were in the distant past. Longer term prospective studies could provide insights regarding this potential bias and the critical window of exposure in the natural history of nuclear cataract development.

Results from this study did not confirm previously reported associations with α-carotene and lycopene in the Beaver Dam cohort. Previously, the severity of nuclear opacities at baseline was shown to be inversely associated with α-carotene intake and directly associated with lycopene intake, based on the subjects' recollection of their diets 10 years before baseline (10). Even when data were stratified by gender to match these previous analyses, the 5-year incidence of nuclear cataract was unrelated to self-reported intakes of α-carotene and lycopene (data not shown). Although epidemiologic studies examining cataracts of all types combined have suggested a protective relation for carotenoids (17, 32, 33), β-carotene has not been shown to be related to nuclear cataracts (9, 14, 19). Furthermore, recent findings show that α-carotene, β-carotene, lycopene, and cryptoxanthin are not present in measurable levels in human lens tissue (6, 8). Therefore, to have an effect on nuclear cataracts, these carotenoids probably would need to affect lens opacification indirectly via a systemic mechanism. Results from this study do not support such an effect for these carotenoids.

Vitamin E status was inversely associated with nuclear cataracts in the Baltimore Longitudinal Study of Aging (14) and in the Lens Opacities Case-Control Study (9, 16, 34) but not in three other epidemiologic studies (13, 15, 35). Previously in the Beaver Dam cohort, associations with the severity of nuclear cataracts measured cross-sectionally at baseline differed depending on the method used to assess α-tocopherol status. Among men, the severity of nuclear opacities was inversely related to dietary intakes of α-tocopherol corresponding to a time point 10 years before the baseline examination (10) but was directly related to serum α-tocopherol concentrations measured at baseline (36). Both the Baltimore Longitudinal Study of Aging (14) and the Beaver Dam Eye Study (36) have reported differences in associations with α-tocopherol status depending on the time point at which status was assessed relative to determination of lens status. This problem was minimized in this study because nutrient intakes were assessed before follow-up and persons were included only if they were free of cataracts at baseline. Results reported here do not strongly support an inverse association between vitamin E and nuclear cataracts, except possibly among persons susceptible to cataracts due to the presence of other risk factors. However, the limited statistical power in this short term prospective study would impair the ability to detect a modest association between vitamin E and nuclear cataracts, particularly considering the influence of error in assessing levels of vitamin E in the diet. Two recent prospective studies (16, 37), one carried out in a subsample of Beaver Dam Eye Study participants, have observed a lower risk for incident nuclear opacities in people with high levels of vitamin E in serum. Although the administration of supplements containing vitamin E for 5 years did not influence the prevalence of nuclear cataracts in the Linxian study (19), longer time periods may be necessary for vitamin E to influence the process of nuclear lens opacification. Overall, the body of evidence at this time indicates that a potentially protective influence of vitamin E on the incidence of nuclear lens opacities cannot be ruled out.

As with vitamin E, associations with vitamin C intake were not significant in the overall group of participants, but there was evidence that vitamin C may be inversely associated with nuclear cataracts for persons with other suspected risk factors for nuclear cataracts. Use of vitamin C supplements, particularly of long duration, was recently reported to be associated with a lower prevalence of mild and moderate opacities in a subsample of participants in the Nurses' Health Study (11). Thus, a protective effect of vitamin C on nuclear lens opacification remains possible.

However, in contrast to the generally inverse relation between nuclear cataracts and vitamin C intake among susceptible persons in this study, findings also suggested that the potentially glycating effect of ascorbic acid (38) may be amplified in the presence of elevated glucose levels. Furthermore, an increased level of particular DNA adducts in people administered high doses of vitamin C supplements indicates that a prooxidant effect of vitamin C may be possible in humans taking vitamin C supplements (39). The potentially adverse association between the intake of high doses of vitamin C and lens opacification should be investigated further before widespread supplementation is advocated.

Limitations in our study design may have prevented us from observing stronger or more consistent associations with the antioxidant nutrients considered in this study. For example, the length of time to follow-up may have been too short to detect significant changes in cataract status, especially among the younger participants, who were less likely to reach level 4 or 5 opacity. Future studies of longer duration and with larger sample sizes are needed to further investigate associations between nuclear cataracts and lutein, vitamin C, and vitamin E, particularly among persons with other suspected risk factors for cataracts. Because subgroup analyses in this study were not based on a prior hypothesis, potentially stronger relations with intakes of vitamins E and C in subgroups with other risk factors for cataract need to be evaluated in larger and long term prospective studies.

In summary, data from the present short term prospective study are consistent with potentially protective influences of vitamins E and C and lutein on the development of cataract in the lens nucleus. However, strong inverse relations for intake of these nutrients were not observed. Data from longer term prospective studies and from clinical trials currently under way will be useful in further evaluating these associations.

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