Clin Nutr Res. 2020 Jul;9(3):163-170
https://doi.org/10.7762/cnr.2020.9.3.163
pISSN 2287-3732·eISSN 2287-3740

CLINICAL NUTRITION RESEARCH

Original Article

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The Association between Dietary Vitamin A and C Intakes and Cataract: Data from Korea National Health and Nutrition Examination Survey 2012

Jeong-Hwa Choi [1], **Eunkyung Lee** [2], **Young-Ran Heo** [2]

[1]Department of Food Science and Nutrition, Keimyung University, Daegu 42601, Korea
[2]Department of Food and Nutrition, Research Institute for Human Ecology, Chonnam National University, Gwangju 61186, Korea

Received: Jun 23, 2020
Revised: Jul 10, 2020
Accepted: Jul 12, 2020

Correspondence to
Young-Ran Heo
Department of Food and Nutrition, Research Institute for Human Ecology, Chonnam National University, 77 Yongbong-ro, Buk-gu, Gwangju 61186, Korea.
E-mail: yrhuh@jnu.ac.kr

ORCID iDs
Jeong-Hwa Choi
https://orcid.org/0000-0003-4730-6544
Eunkyung Lee
https://orcid.org/0000-0002-5619-5009
Young-Ran Heo
https://orcid.org/0000-0001-5476-3714

Conflict of Interest
The authors declare that they have no competing interests.

ABSTRACT

Oxidative stress in eye lens is one of the main causes of the cataract. Dietary antioxidants including vitamin A and C are therefore known to be associated with the risk of the disease. However, evidences are still lacking in Koreans. This study aimed to examine whether dietary vitamin A and C levels are associated with the cataract, using data of Korea National Health and Nutrition Examination Survey 2012. A total of 3,344 individuals (599 cases and 2,745 controls) were analyzed in the study. Dietary data was classified into 3 groups following Dietary Reference Intakes for Koreans 2015: 1) ≤ estimated average requirements (EAR), 2) EAR-recommended nutrient intake (RNI), and 3) ≥ RNI. Findings suggested normal subjects (controls) had better vitamin A and C nutritional status. Vitamin A and C intakes of normal subjects were significantly higher than those of cataract cases ($p < 0.001$, respectively). Ratio of subjects who consumed vitamin A and C lower than EAR was higher in cataract cases compared to normal subjects ($p < 0.001$, respectively). These antioxidant intake levels predicted that having lower level of vitamins lower than EAR increased the odd ratios (ORs) for cataract [for vitamin A: OR, 1.89; 95% confidence interval (CI), 1.55–2.31 and for vitamin C: OR, 2.06; 95% CI, 1.69–2.51]. However, such associations were not retained, when the subjects' demographic and lifestyle factor were adjusted. In conclusion, vitamin A and C showed a protective effect against cataract. However, subjects' life style and demographic factors nullified the association. More studies are required to verify the true association between dietary antioxidants and risk of cataract in Koreans.

Keywords: Cataract; Nutrition Surveys; Koreans; Vitamin A; Vitamin C

INTRODUCTION

Cataract is the common eye disorder that the turbidity of crystalline lens in eyes is deteriorated [1]. There are 2 types of cataract that congenital and acquired ones, and the age-related cataract is the most commonly evident in acquired type [2]. Although the precise etiology of cataract has not been proved yet, age-related decreased and/or altered composition of aqueous proteins has known to be associated with the increase of turbidity of crystalline lens, and, consequently lead to development of cataract [2]. In Korea, growing numbers of the elderly who received cataract operation is evident since 2006. In 2016, approximately 841 (per 100,000 persons) cataract operations were performed, which made that is the most commonly performed surgery in Korean elderly [3]. This suggests that the prevalence of cataract would be increasing with the population aging.

Earlier studies suggested that multiple factors including age, sex, ultraviolet light, medicine, smoking, alcohol drinking, nutrition, diet and oxidative stress modify the risk of cataract [1]. Among the dietary factors, vitamin intakes have been drawing the attention in a relation with oxidative stress in the risk for cataract [4,5]. Vitamin A and C are a common type of antioxidants, which scavenge reactive oxygen species. Vitamin A is a critical compound in the maintaining of cornea clarity and eye vision [5]. Vitamin A and carotenoids are known to attenuate the UV-induced oxidative stress by reducing of reactive oxygen. This neutralizing effect of vitamin A and carotenoids is therefore protective against eye disorders, especially cataract [6]. Studies suggested that higher serum level of retinol significantly reduced the risk of cataract [5]. Vitamin C also functions as a major coenzyme involved in multiple physiological mechanisms [7]. Concentrations of the vitamins in aqueous humor and lens are approximately 15 times higher than those in plasma. However, the level of vitamin C in aqueous humor of cataract cases was significantly reduced with the age [8]. Furthermore, in patients with other types of ophthalmic disorders, level of vitamin C in the anterior chamber was commonly observed, compared to normal subjects. Therefore, studies explored the association between dietary vitamin C intake and eye diseases [9]. Findings suggested that having more vitamin C was evident to significantly reduce the risk of the eye problem, cataract [10]. Additionally, consumption of high intake of anti-oxidative nutrients could decrease the risk of cataract approximately by 79% [11].

The Korea National Health and Nutrition Examination Survey (KNHANES), the largest nation-wide health and nutritional surveillance system in Korea, suggested that vegetables and fruits are the most common sources of vitamin A and C [12]. Our earlier analyses confirmed that the sufficient total intake of vegetables and fruits reduced the risk of cataract, regardless of the type of consumption or cooking methods [13]. However, epidemiological evidences for the association between dietary intake of antioxidant nutrients vitamin A and C and the prevalence of cataract are still lacking in a Korean population.

Cataract is the major degenerative disease following the physiological aging. For better quality of life, the prevention of the disease is important. Therefore, the modifying effect of vitamin A and C intake on the risk of cataract is required to be ascertained. This study aimed to analyze the association between antioxidants vitamin A and C intakes and the cataract in Koreans using data of KNHANES 2012. Dietary intake references (DRIs) of these 2 vitamins are established [14]. For better understanding and applying of study findings, this study employed the DRIs to stratify the nutritional intake level.

MATERIALS AND METHODS

Study subject selection

The present study was conducted with the data from KNHANES 2012. From the total of 8,058 subjects of KNAHNES 2012, subjects who did not meet the following criteria were excluded: whom under 40 years of age, with any missing descriptive, diagnosing cataract information and dietary data, implausible total energy intake and excessive vitamin A intake (> 3,000 μg retinol activity equivalent [RAE], tolerable upper intake level of vitamin A). Finally, a total

https://doi.org/10.7762/cnr.2020.9.3.163

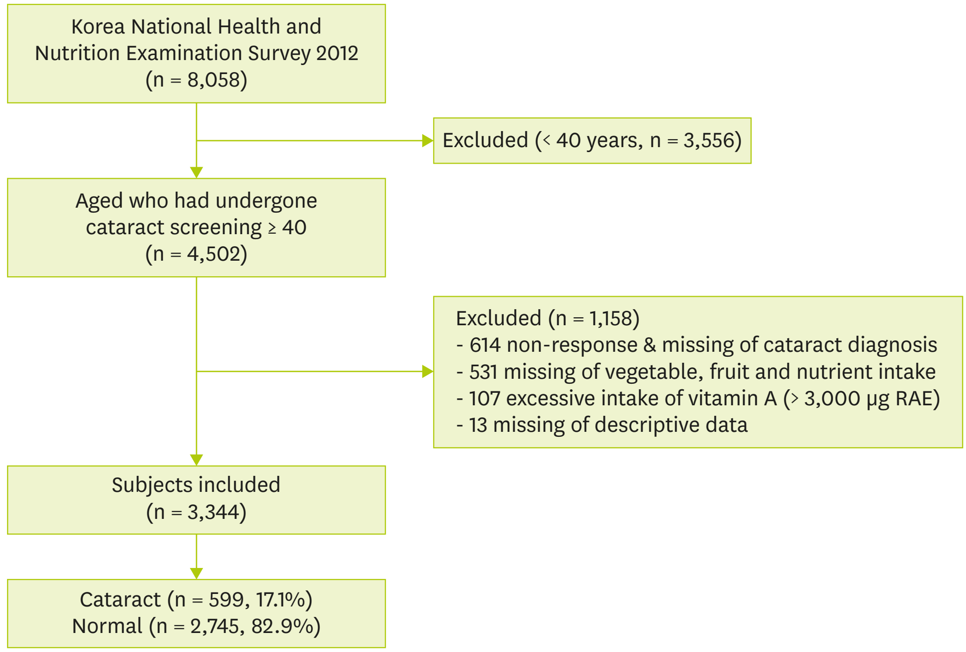

Figure 1. Simplified flow chart for study subject selection procedure.
RAE, retinol activity equivalent.

of 3,344 subjects, 599 cataract cases and 2,745 controls (normal subjects), were included in the study (**Figure 1**). Ethical approval of KNAHNES 2012 was given from Korea Centers for Disease Control and Prevention (2012-01EXP-01-2C). Ethics of current study was also approved by Institutional Review Board (1040198-160921-HR-087-01).

General and dietary data collection

General characteristics and dietary data were obtained from the KNAHNES 2012. The details of classification and analyses were described earlier. Simply, the level of education was grouped into 4 (less than elementary graduates, middle school graduates, high school graduates, and college graduates and more), level of income was also categorized into 4 groups taken into account of standard household income quartiles (low, low-mid, mid-high, and high). Practicing of regular exercise was also determined by 2 levels (high and low), and 'high' was defined as if the participant was engaged into physically heavy work or rigorous exercise including running, climbing, riding bicycle, swimming, football, basketball, for 3 times per week, for 20 minutes more per each session. The cigarette smoking status was grouped into 2 levels (yes and no), and 'yes' was defined as the subject was life time smoker. The alcohol drinking status was also classified into 2 levels (yes and no), and 'yes' was estimated if the participant regularly has more than 1 alcohol drink every month for last 12 months. The level of obesity was defined for 3 groups, using body mass index (kg/m^2). Lastly, if the subject was diagnosed for diabetes mellitus by specialist, then the subject was defined for 'yes'.

Dietary intake data of the KNAHNES 2012 was collected using 24-recall method. Nutrient intake was estimated using Korean Food Composition Table (7th edition). To estimate the association between dietary vitamin intake levels and cataract, the vitamin consumption levels was classified into 3 groups: 1) ≤ estimated average requirements (EAR), 2) EAR-recommended nutrient intake (RNI), and 3) ≥ RNI, following DRIs for Koreans (KDRIs) 2015, taking account of sex and age [14].

https://doi.org/10.7762/cnr.2020.9.3.163

Statistical analysis

To estimate the differences in general characteristics between cataract cases and normal subjects, χ^2 tests were applied. The comparisons for dietary vitamin intake levels were performed using Student's t-tests and χ^2 tests. The associations between cataract and dietary vitamin intake levels were estimated using logistic regression models. Two independent models were established with the presence or absence of covariates. The results were presented using odds ratios (ORs) and 95% confidence intervals (CIs). A 2-tailed p value < 0.05 was accepted for statistically meaningful. All statistical analyses were performed using SPSS (version 22.0, IBM Corp., Foster City, CA, USA).

RESULTS

Descriptive information

The general characteristics of cataract cases and normal subjects were presented in **Table 1**. The prevalence of cataract did not differ by sex, smoking status and obesity status. However, subjects' age, education years, economic status, physical activity level, and alcohol drinking status, and prevalence of diagnosed diabetes mellitus were different between cataract cases and normal subjects. Cataract cases were more likely older, less educated and were also in lower income and lower physical activity group. Cataract cases were however less likely to be alcohol drinkers, compared to normal subjects. More diabetes mellitus cases were evident in cataract cases. Those patterns were assumed to be associated with cataract in this Korean population, therefore, were adjusted as covariates in the statistical models later.

Dietary vitamin A and C intakes of subjects

The differential intake levels of vitamin A and C between cataract cases and normal subjects were compared using 2 independent approaches (**Table 2**). Cataract cases consumed less vitamin A and C, compared to normal subjects. The mean intake level of vitamin A in cataract cases and normal subjects were 311.3 ± 268.6 and 421.0 ± 314.9 μg RAE/day, respectively ($p < 0.001$). The mean dietary vitamin A intake per 1000 kcal was also significantly higher in normal subjects than in cataract cases ($p < 0.001$). The mean intake levels of vitamin C in cataract cases and normal subjects were 83.7 ± 68.5 and 114.4 ± 96.9 mg/day, respectively ($p < 0.001$). The intake level of vitamin C per 1,000 kcal was also higher in normal subjects, compared to cataract cases ($p < 0.001$). When the subjects were classified by the level of vitamin intake according to the DRI level, the distribution of subjects were significantly different between cataract cases and normal subjects ($p < 0.001$, respectively). Compared to cataract cases, normal subjects had higher ratio of taking the dietary intake above the RNI: for vitamin A, cataract and normal subjects were 32.9% and 45.9%, and, for vitamin C, those were 44.2% and 29.0%, respectively. In contrast, cataract cases were more evident to consume vitamins less than EAR: for vitamin A, cataract and normal subjects were 50.8% and 37.2%, and, for vitamin C, those were 56.9% and 42.0%, respectively.

Association of vitamin A and C intakes with cataract by ORs

The logistic regression analysis models were used to ascertain the association between the vitamin A and C intakes and cataract. The RNI level was used for reference intake. Model I predicted that, compared to consuming vitamin A at or above RNI, consuming vitamin A between EAR and RNI (OR, 1.34; 95% CI, 1.03–1.75), and less than EAR (OR, 1.89; 95% CI, 1.55–2.31) increased the ORs for cataract. However, such ORs for cataract due to the decreased consumption vitamin A was not statistically significant when the subjects'

https://doi.org/10.7762/cnr.2020.9.3.163

Table 1. General characteristics of study subjects

Characteristics	Cataract (n = 599)	Normal (n = 2,745)	χ^2	p value*
Sex			2.1	0.138
Male	222 (37.1)	1,115 (40.4)		
Female	377 (62.9)	1,635 (59.6)		
Age			638.0	< 0.001
40–49	11 (1.8)	735 (26.8)		
50–59	39 (6.5)	827 (30.1)		
60–69	172 (28.7)	700 (25.5)		
≥ 70	377 (62.9)	483 (17.6)		
Education			146.1	< 0.001
≤ Elementary	355 (59.3)	915 (33.3)		
Middle	70 (11.7)	395 (14.4)		
High	112 (18.7)	842 (30.7)		
≥ College	62 (10.4)	593 (21.6)		
Income			209.2	< 0.001
Low	281 (46.9)	564 (20.5)		
Low-mid	157 (26.2)	703 (25.6)		
Mid-high	83 (13.9)	683 (24.9)		
High	78 (13.0)	795 (29.0)		
Physical activity level			19.3	< 0.001
Low	563 (94.0)	2,405 (87.6)		
High	36 (6.0)	340 (12.4)		
Smoking status			0.8	0.347
Smoking	234 (39.1)	1,016 (37.0)		
Non-smoking	365 (60.9)	1,729 (63.0)		
Alcohol drinking			39.2	< 0.001
No	406 (67.8)	1,473 (53.7)		
Yes	193 (32.2)	1,272 (46.3)		
BMI			0.4	0.787
< 18.5	14 (2.3)	77 (2.8)		
18.5–25	383 (63.9)	1,731 (63.1)		
> 25	202 (33.7)	937 (34.1)		
Diabetes mellitus			106.1	< 0.001
No	454 (75.8)	2,495 (90.9)		
Yes	145 (24.2)	250 (9.1)		

Numbers in brackets present percentage of subjects.
*The p values are from χ^2 tests.

Table 2. Daily dietary intakes of vitamin A and C in subjects

Variables	Cataract (n = 599)	Normal (n = 2,745)	t/χ^2	p value*
Vitamin A (μg RAE)				
Mean	311.3 ± 268.6	421.0 ± 314.9	8.8	< 0.001
Mean/1,000 kcal	191.3 ± 157.5	228.1 ± 163.4	5.0	< 0.001
< EAR	304 (50.8)	1,022 (37.2)	41.7	< 0.001
EAR-RNI	98 (16.4)	464 (16.9)		
≥ RNI	197 (32.9)	1,259 (45.9)		
Vitamin C (mg)				
Mean	83.7 ± 68.5	114.4 ± 96.9	9.1	< 0.001
Mean/1,000 kcal	52.2 ± 41.6	61.9 ± 47.2	5.1	< 0.001
< EAR	341 (56.9)	1,152 (42.0)	52.8	< 0.001
EAR-RNI	84 (14.0)	380 (13.8)		
≥ RNI	174 (29.0)	1,213 (44.2)		

Digits for mean are presented mean ± standard deviation, otherwise all other numbers are presented numbers of subjects (%).
EAR, estimated average requirement; RNI, recommended nutrient intake.
*The p values for mean from Student's t-tests, otherwise χ^2 tests.

socioeconomic and life style factors were considered. The association between vitamin C intake and cataract were also analyzed. In the crude model (model I), ORs for cataract was significantly increased according to vitamin C intake, the subjects had vitamin C between

Table 3. Association between vitamin A and C intakes and cataract

Variables	Model I*		Model II†	
	OR (95% CI)	p value	OR (95% CI)	p value
Vitamin A				
≥ RNI	1.00 (reference)		1.00 (reference)	
EAR-RNI	1.34 (1.03–1.75)	0.027	1.28 (0.95–1.73)	0.522
< EAR	1.89 (1.55–2.31)	< 0.001	1.07 (0.85–1.35)	0.103
Vitamin C				
≥ RNI	1.00 (reference)		1.00 (reference)	
EAR-RNI	1.54 (1.15–2.04)	0.003	1.34 (0.96–1.84)	0.080
< EAR	2.06 (1.69–2.51)	< 0.001	1.21 (0.96–1.53)	0.100

OR, odds ratio; CI, confidence interval; EAR, estimated average requirement; RNI, recommended nutrient intake.
*Model I: unadjusted; †Model II: adjusted for sex, age, education, income, physical activity, smoking, alcohol drinking and diabetes mellitus.

EAR-RNI (OR, 1.54; 95% CI, 1.15–2.04), and less than EAR level (OR, 2.06; 95% CI, 1.69–2.51) had higher ORs for cataract, compared to those who consumed the vitamin C at or above the RNI level. However, again, when the covariates were considered, the estimated ORs for cataract by vitamin C intakes was not retained (**Table 3**).

DISCUSSION

Cataract is the consequence of corruption of proteins in the crystalline lens. Chronic oxidative stress and the insufficient nutrition intake are known to be associated with such altered protein level, hence, the development and the progression of the disease [15]. The present study examined whether the vitamin A and C intakes are associated with cataract in Koreans.

In this study, normal subjects were in better vitamin A and C nutritional status, compared to cataract cases. Approximately 46% of normal subjects and 33% of cataract cases consumed vitamin A at or above the RNI level. Mean value of vitamin intake A in cataract cases was significantly lower than that in normal subjects. Additional analyses supported that consuming the vitamin lower than RNI level—even it is not a significantly lower intake level—increased the ORs for cataract by 1.8 times. However, this negative modifying effect of lower vitamin A intake on the risk of cataract was not retained, when the subjects' socioeconomic and other life style factors were adjusted. These may suggest that vitamin A intake was not significantly associated with cataract in Korean population. However, another earlier Korean study reported that cases' serum beta-carotene level was significantly lower than controls [16]. A meta-analysis provided the comprehensive evidence that consuming sufficient amount of vitamin A reduced the risk of cataract by 17% (95% CI, 0.757–0.913) [4]. Another recent meta-analysis also reported the significantly reduced risk of cataract by the consumption of vitamin A and carotenoids: for vitamin A (relative risk [RR], 0.81; 95% CI, 0.71–0.92), and for beta-carotene (RR, 0.90; 95% CI, 0.83–0.99) [6].

The trend towards for the association between vitamin C intake and cataract by ORs in this study was similar to the results shown in vitamin A intake. The individuals who consumed vitamin C lower than EAR level had 2 times higher ORs for cataract than those who consumed it above RNI level. However, again, the statistical significance disappeared after the adjustments of covariates. Although current findings suggested that vitamin C intake was not associated with the cataract, other studies still supported the modifying effect of vitamin C on this eye disorder. In the study with Mediterranean population, consuming vitamin C > 135 mg/day decreased the risk of cataract [17]. Another study in Indians also suggested

https://doi.org/10.7762/cnr.2020.9.3.163

that consumption of vitamin C above 66.4 mg/day was less likely to have the cataract approximately 22%, compared to the individuals consuming vitamin C less than 10.8 mg/day [18]. Meta-analyses also confirmed such protective effect of vitamin C in Asian and US populations [19], and, in randomized controlled trials [6].

In current study, beneficial effect of antioxidative vitamin A and C against cataract seemed not to be significant in Koreans. However, the results are different from those provided by other studies. First, current study focused on the consumption of vitamin A and C from dietary intake, but did not consider the use of dietary supplements, and total intake of other antioxidative compounds in diets for the statistical analyses. Furthermore, recent publications suggested that other nutritive compounds including fatty acid, sterols, and vitamin D, B6 and B12 have shown the potential association of cataract prevalence [20-23]. Carbohydrates as a form of total carbohydrate intake and high glycemic index also independently predicted the incident of cataract [24]. Further studies for the comprehensive effect of dietary intake on the incidence of cataract should be required. Nevertheless, this study is meaningful to examine the estimated effect of vitamins A and C on the risk of cataract. Second, subject's socioeconomic and life styles factors may modify the protective effect of those antioxidants. Furthermore, this study did not consider the individual's genetic characteristics relevant to cataract etiology. These limitations may modify the association between dietary vitamin A and C, and cataract, which was confirmed in crude statistical models as well as other earlier studies. However, the beneficial effect of vitamin A and C consumption on the cataract should not be dismissed: numbers of meta-analyses and epidemiological studies, and experimental studies have been reporting the importance of dietary intake of those antioxidants. In line with this, dietary intake of vitamin A and C in Koreans need to be improved: Approximately 37% to 57% of Koreans had their vitamin A and C lower than EAR level. Better approaches including nutritional education and campaigns as well as health initiatives are required to increase the consumption level of those nutrients, and, further, for the prevention of cataract.

In conclusion, lower intakes of vitamin A and C seemed to increase ORs for the risk of cataract in Koreans, however the protective effect of dietary vitamin A and C were attenuated by other socioeconomic and life styles factors. More observational and experimental studies are required to verify the true association between dietary vitamin intake and cataract occurrence.

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