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A prospective study of vitamin intake and the risk of hearing loss in men

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Abstract

Objective—Hearing loss is the most common sensory disorder in the US, afflicting over 36 million people. Higher intakes of vitamins C, E, beta carotene, B12 and folate have been proposed to reduce the risk of hearing loss.

Study Design—We prospectively evaluated the association between intake from foods and supplements of vitamins C, E, beta carotene, B12, and folate and the incidence of hearing loss.

Setting—Health Professionals Follow-up Study

Subjects and Methods—26,273 men aged 40–75 years at baseline in 1986. Participants completed questionnaires about lifestyle and medical history every two years and diet every four years. Information on self-reported professionally diagnosed hearing loss and year of diagnosis was obtained from the 2004 questionnaire and cases were defined as hearing loss diagnosed between 1986 and 2004. Cox proportional hazards multivariate regression was used to adjust for potential confounders.

Results—There were 3,559 cases of hearing loss identified. Overall, there was no significant association between vitamin intake and risk of hearing loss. Among men 60 years and older, total folate intake was associated with a reduced risk of hearing loss; the relative risk for men ≥ 60 years old in the highest compared to the lowest quintile of folate intake was 0.79 (95% confidence interval 0.65–0.96).

Conclusions—Higher intake of vitamin C, E, B12, or beta carotene does not reduce the risk of hearing loss in adult males. Men 60 years of age and older may benefit from higher folate intake to reduce the risk of developing hearing loss.

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Background

Hearing loss is the most common sensory disorder afflicting US adults, with over 36 million Americans suffering from this condition.[1] The highest prevalence of hearing loss is in the older adult population, with over half of the cases found in people over the age of 65.[2] Among individuals with no hearing loss, the 5-year incidence of developing hearing loss in adults aged 48 and above is 21%.[3] Even mild degrees of hearing loss can compromise the ability to process speech in the presence of background noise or multiple speakers, leading to social isolation, depression, diminished cognitive function, and poorer quality of life.[4,5] Cross-sectional studies have evaluated the relation between a limited number of risk factors and the prevalence of hearing loss, however there is scant prospective human information on potential modifiable risk factors for hearing loss.[2,6]

Dietary factors may play an important role in the pathogenesis of many auditory disorders.7 Several vitamin groups have been implicated in different hearing loss etiologies. Numerous animal studies have shown the otoprotective effects of free radical scavengers, and the antioxidant properties of vitamins C, E, and beta carotene have been demonstrated to protect from inner ear damage caused by aminoglycosides, cisplatin, acoustic trauma, noise exposure, and presbycusis.8,[9] Prospective data in humans are limited. For example, one 16 week human trial showed that daily vitamin C supplementation (600mg/day) in 23 individuals with presbycusis resulted in an average 3.8 dB audiometric threshold improvement in hearing sensitivity ($p<0.01$).[9]

Other micronutrients, including folate and vitamin B12, may also play a role in auditory function. Deficiencies of these vitamins are common in the elderly population, becoming most apparent in those over 60 years of age;[10] 5–15% are vitamin B12 deficient and 2–20% folate deficient.[11] Folate and B12 deficiency have been implicated neuronal and vascular function.[12] In a 2007 randomized controlled trial, folate supplementation demonstrated the potential to slow hearing deterioration in older adults.[13]

The potential relation between intake of these vitamins and development of hearing loss is yet to be definitively determined in human subjects. The significance of a nutritional-auditory relation is great because dietary intake represents a modifiable factor that might prevent hearing loss. Therefore, we prospectively evaluated the association between vitamin intake and development of hearing loss in a large adult male cohort.

Methods

Participants

The Health Professionals Follow-up Study enrolled 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists, and veterinarians who were 40–75 years of age at baseline in 1986. Participants filled out a detailed questionnaire about diet, medical history, and medication use. These questionnaires have been administered every other year, and the 20-year follow-up exceeds 90%. The 2004 long form questionnaire included a question regarding whether the participant had been professionally diagnosed with hearing loss, and if so, the date of diagnosis. Of the 34,884 men who responded to the long form questionnaire, 7092 (20.3%) reported a diagnosis of hearing loss. Those who reported hearing loss diagnosed before 1986 (n=2445) or cancer other than non-melanoma skin cancer were excluded from the analysis. Recent data from NHANES demonstrated that 43% of white men aged 60–69 exhibit hearing loss in the low-mid frequency range, and 93% exhibit high frequency hearing loss.[2] Thus, because age is such a strong risk factor and the prevalence of hearing loss is so high among the elderly, we also excluded men as they reached age 75 during follow-up. Men were also excluded if they provided incomplete diet information (omitted 70 or more of the 131 dietary questions on a dietary questionnaire).

Ascertainment of Vitamin Intake

A semiquantitative food frequency questionnaire (SFFQ) was administered in 1986, 1990, 1994, 1998, and 2002. The baseline SFFQ contained a list of 131 food and beverage items, including 15 fruit, 30 vegetable and 3 potato items. Nine mutually exclusive response possibilities were provided for average frequency of intake over the previous year, with choices ranging from "almost never or less than once per month" to "six or more times per day." In addition, every 2 years the respondents were asked about use of vitamin supplements, including the type, dose, duration and specific brand. Total intake for each nutrient was computed by multiplying the consumption frequency of each food by the nutrient content of the specified portion size, using composition values from US Department of Agriculture (USDA) sources and additional information from food manufacturers and then adding the amount from supplement intake. We considered missing values for individual items within SFFQs that were substantially complete to imply no intake (<1% of the data for most items). The calculations for vitamin E intake, expressed as mg of alpha-tocopherol, took into account the lower activity of synthetic vitamin E often used in supplements. Intake data for vitamin E was not available from the 2002 questionnaire and data obtained from the previous questionnaire was used to quantify vitamin E intake during this time period. Carotenoid values were based on the USDA-National Cancer Institute database and carotenoid content of foods was updated from the USDA. For multivitamins, a comprehensive multivitamin preparation database, which includes the dose of individual vitamins in each preparation, has been developed and updated biennially by the HPFS team. Participants who reported using supplements but did not report the dose or duration were assigned the median values for dose and duration observed among the users. The reproducibility and validity of the SFFQ have been demonstrated, and questionnaire derived information has been validated for the covariates by comparison to detailed diaries,[14] with correlation coefficients of 0.92 for intake of vitamin C, 0.92 for vitamin E, 0.64 for carotene, 0.77 for folate, 0.56 for vitamin B12, and 0.86 for alcohol intake.

Exposure was quantified as the energy adjusted total as well as dietary (without supplements) intake of vitamin C, vitamin E, beta carotene, vitamin B12, and folate.

Ascertainment of Outcome

The primary outcome, self-reported professionally diagnosed hearing loss, was defined as a "yes" response to the question "Have you ever had professionally diagnosed hearing loss?" Those who answered "yes" were additionally asked for the year of first diagnosis (before 1986, 86–87, 88–89, 90–91, 92–93, 94–95, 96–97, 98–99, 00–01, 02, 03, 04).

Ascertainment of Covariates

Covariates considered in the multivariate analysis included: age, race, body mass index (BMI), regular analgesic use (aspirin, acetaminophen, or NSAID) use, alcohol intake, smoking, hypertension (HTN), and diabetes mellitus (DM).

Age and race were obtained from the biennial questionnaires. Height and weight were obtained on the baseline questionnaire and self-reported weight has been updated every two years. BMI was calculated as weight in kilograms divided by the square of height in meters. Information on smoking status was updated every two years. Regular analgesic use was updated every two years and defined as taking aspirin, acetaminophen, or NSAIDs two or more times per week. Alcohol intake was calculated from SFFQs that were mailed to participants every 4 years. Information on other covariates was available from the biennial questionnaires, including diagnoses of HTN and DM.

Statistical Analyses

All analyses were prospective, using information on nutrient intake that was collected prior to the diagnosis of hearing loss. For the primary analyses, the calorie-adjusted total intake of each of the nutrients was subdivided into quintiles with the lowest quintile set as the reference group. The data on dietary intake (without supplements) of each of the nutrients was also similarly subdivided and analyzed.

For each participant, person-time was allocated based on the response to the nutritional intake questions at the beginning of each follow-up period. Participants were censored at the date of diagnosis of hearing loss, age 75, or the date of death, whichever came first. Age and multivariable-adjusted hazard ratios (HRs) were calculated using Cox proportional hazards regression models. Multivariable models were adjusted for potential confounders listed above as well as simultaneously for use of the other vitamins.

To examine whether the relation between vitamin intake and hearing loss varied by age, we performed analyses stratified by age <60 years and 60 and older. In addition, the relation between folate and vitamin B12 intake and incident hearing loss was analyzed by stratifying for levels of alcohol intake, by low (<10g/day), medium (10–30g/day) and high (>30g/day) intake. For all HRs, we calculated 95% confidence intervals (CIs). All P values are two-tailed. Statistical tests were performed using SAS statistical software, version 9 (SAS Institute Inc, Cary, NC).

IRB approval by Partners Human Research Committee at Brigham and Women's Hospital, Boston MA on 2/25/09.

Results

Characteristics of the participants according to vitamin intake in the year 1994 are shown in Table 1. Although updated information was used for the analysis, the characteristics presented are from the approximate midpoint of follow-up to provide representative values. Men in the highest intake quintile for the studied vitamins were 3–4 years older than those in the lowest quintile. There was no difference in prevalence of diabetes, hypertension, smoking, or alcohol intake or BMI.

During 387,890 person-years of follow-up, 3559 cases of hearing loss were documented. Overall, intake of vitamins C, E, B12, or beta carotene was not associated with risk of hearing loss (Table 2). After adjusting for age, race, BMI, alcohol intake, smoking, hypertension, diabetes and all of the vitamins of interest, there were no significant associations between the different quintiles of intake (dietary or total) and risk of hearing loss. Compared to men in the lowest quintile of total folate, those in the highest quintile had a marginally decreased risk of hearing loss (HR=0.88; 95% CI 0.76–1.02) (p, trend=0.39). Adjusting for regular analgesic use did not affect the results (data not shown).

Given the age-related differences in absorption and biological interactions,[11] we examined whether the relation between vitamin intake and hearing loss varied by age. The association between hearing loss and intake of vitamins C, E, B12 and beta carotene did not vary significantly by age (Table 3). For folate, there was no association in men younger than 60 years of age; however, men aged 60 or older in the highest quintile of folate intake had a 21% lower risk of developing hearing loss (HR=0.79; 95% CI 0.65–0.96) (p, interaction=0.50).

Stratification by alcohol intake did not affect the relation between intake of vitamin C, E, beta carotene or folate and incident hearing loss (data not shown). Among those with the highest alcohol intake, higher intake of vitamin B12 was marginally associated with a reduced risk of hearing loss (HR= 0.67; 95% CI 0.44–1.01, p=0.06) (p, interaction=0.05).

Discussion

Numerous animal studies have suggested protective properties of certain vitamins in various pathologic cochlear processes,[8] but there has been scant human data. This is the first large epidemiologic human study of the association between these vitamins with hearing loss. Overall, our study found no prospective association between vitamin C, E, beta carotene, B12 or folate intake and incident hearing loss. Higher intake of folate however, was associated with a 21% risk reduction for hearing loss in men 60 years and older. The relation between folate intake and incident hearing loss did not vary by alcohol intake. However, the lower risk of hearing loss among men with higher vitamin B12 intake was only observed in those with the highest alcohol intake.

Reactive oxygen metabolites may cause cochlear damage. Vitamins C, E, and beta carotene have shown promising otoprotection in animal studies, possibly due to their antioxidant properties.[8] A 16 week randomized trial of vitamin C supplementation (600 mg/day) in 23 participants with presbycusis showed a small hearing threshold improvement.[9] Our study, however, found no association between these vitamins and the overall incidence of hearing loss. The range of vitamin intake in our study included the ranges described in previous studies, and in the case of vitamin C, the 5th quintile of intake in our cohort (1247mg/day) was considerably higher than that described in the previously mentioned trial. Nevertheless, we cannot exclude the possibility that an association may be seen with even higher levels of antioxidant intake. However, the negative results in our study are only indicative of the relation between specific vitamin intake in the ranges consumed and hearing loss in adult males.

The association between folate intake and incident hearing loss in our cohort is consistent with previous data showing that folic acid supplementation slowed the decline in low frequency hearing in older adults.[13] A possible explanation for the impact of age on the relation between folate intake and hearing loss is the increased prevalence of folate malabsorption and folate depletion in the older age group.[11] Higher folic acid intake may be necessary to meet the optimal folate needs in this age group. In men 60 years and older, the significant association with hearing loss risk was seen starting in the 4th quintile of intake, which represented a total folate intake of at least 800 mcg/day. This level of folate intake is considerably higher than the current recommended minimum intake of 400 mcg/day for this age group.[15] Although ethanol is known to impede the bioavailability of dietary folate as well as several folate-related biochemical reactions,[16] it did not alter the relation between folate intake and hearing loss in our cohort.

Although there is no direct evidence in the literature that age-related hearing loss is associated with vitamin B12 deficiency, its role in neuronal and cellular metabolism may make vitamin B12 an important factor in cochlear pathology.[7] Previous cross-sectional data have suggested a possible association between vitamin B12 status and hearing loss, as a study of 55 healthy women found that women with hearing impairment had a 38% lower serum vitamin B12 level than those with normal hearing.[7] Our data did not support this finding, possibly due to the different methods used to measure vitamin B12 status. The SFFQ used in our study is a reliable measure of long term dietary intake, while serum biomarkers often provide information on the dietary status at a particular time point. While folate storage is limited, with deficiency occurring after just weeks of poor intake, vitamin B12 stores are often sufficient to prevent vitamin B12 deficiency for years in conditions of malabsorption.[11] Ethanol, however, decreases hepatic B12 storage and can cause vitamin B12 deficiency.[16] In these cases, a greater vitamin B12 intake is required to meet the physiologic requirements. This may explain the inverse association between vitamin B12 intake and incident hearing loss in men with higher alcohol intake.

Our study has limitations. Assessment of hearing loss was based on self-report of professionally diagnosed hearing loss and individuals who did not report hearing loss were considered not to be hearing impaired. Therefore, it is likely that cases of hearing loss were underreported. Although standard pure-tone audiometry is generally considered the gold standard of hearing loss evaluation, self-reported hearing loss has been demonstrated to be a reliable assessment.[17] Nevertheless, the sensitivity of the questionnaire in identifying cases of hearing loss is likely to be lower than that of an audiogram. Given the high prevalence of hearing loss in this population,[2] misclassification of outcome would likely bias the results toward the null.

The outcome analyzed in this study does not distinguish among different hearing loss etiologies. While sensorineural, age-related hearing loss is likely to be the dominant pathologic process in this cohort, we were not able to quantify other common entities such as noise induced hearing loss. We did not have information on noise exposure or reasons for vitamin use. Although noise exposure can cause both mechanical and metabolic cochlear damage,[18] as well as increase the vulnerability to hearing loss related to age,[19] there is no evidence that it is associated with variation in vitamin intake. It is therefore unlikely to be a confounder in this study.

The SFFQ has been validated and used to demonstrate numerous associations between our exposures of interest and other disease outcomes.[14,20] This instrument quantifies vitamin intake from food as well as multivitamin supplement sources. This has allowed us to adjust the intake of each individual vitamin to the intakes of the other vitamins of interest in our multivariate analyses and to update the intake every four years. We cannot, however, exclude the possibility that one of the numerous possible combinations between the intakes of our vitamins of interest is associated with hearing loss risk. Since the increased folic acid supplementation of the food supply that began in the mid 1990's, intake in our cohort has increased, and this change has been sufficiently quantified in the total folate intake calculation. While other hearing loss studies have used biomarkers as a method to quantify nutrient intake,[13] a validated SFFQ is generally a more accurate method of assessing long-term dietary intake.

The participants in this cohort are not representative of the adult population in the U.S., but the follow-up rates are high and the information provided is reliable. The observed associations are likely to apply to other groups inasmuch as the underlying biologic and pharmacologic mechanisms are likely to be similar. However, additional studies are needed to examine these relations in women and younger men.

In conclusion, vitamin intake was not associated with the development of hearing loss. However, our study suggests that specific groups may benefit from increased folate or vitamin B12 intake to reduce the risk of hearing loss. Men aged 60 years and older may benefit from increased folate intake. Given the aging of the population and the high prevalence of hearing loss, identification of modifiable factors to reduce the burden of this common condition should be an important public health priority.

Acknowledgments

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Table 1

Characteristics of Men According to Vitamin Use in 1994

		Vitamin E		Vitamin C		Beta Carotene		Folate		B12	
	Quintile of Intake	**1st**	**5th**	**1st**	**5th**	**1st**	**5th**	**1st**	**5th**	**1st**	**5th**
	n	**4455**	**4143**	**4549**	**4287**	**4468**	**4132**	**4541**	**4016**	**4503**	**3827**
Median Daily Intake											
Vitamin E, mg		8	232	9	195	11	192	9	124	10	46
Vitamin C, mg		124	740	104	1247	144	689	116	633	173	447
Beta Carotene, mcg		2851	7416	2829	7560	2173	13162	2872	6794	4024	5569
Folate, mcg		265	639	267	668	312	651	232	860	304	686
Vitamin B12, mcg		5	11	6	12	7	10	5	14	4	22
Calories		1719	1762	1922	1907	2005	1976	1893	1850	1909	1935
Alcohol, g/d		11	11	12	11	12	10	12	10	12	11
Demographic Factors*											
Age, yr		55	59	55	58	55	59	55	59	56	59
Race, %											
African-American		0.6	0.4	0.7	0.5	0.8	0.6	0.7	0.6	0.7	0.5
Asian		1.8	1.2	1.8	1.5	1.6	1.5	2.1	1.3	1.7	1.4
BMI (kg/m^2)		26	26	26	26	26	26	26	25	26	26
Hypertension, %		27	29	26	28	26	29	27	27	27	28
Diabetes, %		3.1	3.5	4	3	3.1	3.6	3	3.5	2.5	4.1
Smoking Never %		47	46	43	47	47	47	44	47	47	45
Smoking Past %		41	45	43	44	40	43	42	43	43	44
Smoking Current %	1–4cig/d	5	5	5	5	5	5	5	5	5	5
	5–14cig/d	7	4	9	4	8	4	9	4	5	6
	15+cig/d	0.4	0.5	0.4	0.3	0.03	0.5	0.4	0.6	0.2	0.7

* All values are median except where specified

Table 2

Multivariate-Adjusted* Hazard Ratios for Vitamin Intake and Incident Hearing Loss

Variable	Quintile				
	1	2	3	4	5
Total Vitamin C	1 (ref)	1.10 (0.98–1.24)	1.05 (0.92–1.19)	1.10 (0.97–1.25)	1.07 (0.94–1.23)
Dietary Vitamin C	1 (ref)	1.01 (0.91–1.13)	0.97 (0.86–1.09)	0.94 (0.83–1.07)	0.91 (0.79–1.05)
Total Vitamin E	1 (ref)	0.98 (0.87–1.10)	1.09 (0.96–1.24)	1.06 (0.93–1.22)	1.06 (0.92–1.22)
Dietary Vitamin E	1 (ref)	1.12 (1.00–1.25)	1.08 (0.96–1.21)	1.05 (0.93–1.18)	1.05 (0.93–1.19)
Total Beta Carotene	1 (ref)	1.06 (0.95–1.19)	1.04 (0.93–1.16)	1.01 (0.90–1.14)	1.00 (0.88–1.13)
Dietary Beta Carotene	1 (ref)	0.97 (0.87–1.09)	0.99 (0.88–1.11)	1.03 (0.92–1.16)	0.93 (0.82–1.06)
Total Folate	1 (ref)	0.98 (0.87–1.10)	0.97 (0.86–1.10)	0.88 (0.76–1.00)	0.88 (0.76–1.02)
Dietary Folate	1 (ref)	1.08 (0.96–1.21)	1.00 (0.88–1.14)	1.12 (0.98–1.27)	0.99 (0.85–1.15)
Total Vitamin B12	1 (ref)	1.03 (0.93–1.15)	1.10 (0.98–1.23)	1.17 (1.04–1.33)	1.07 (0.94–1.21)
Dietary Vitamin B12	1 (ref)	1.08 (0.97–1.20)	0.99 (0.89–1.11)	1.12 (0.98–1.16)	1.07 (0.96–1.20)

* Adjusted for age, BMI, alcohol, smoking, hypertension, diabetes, race, vitamins C, E, beta carotene, folate and B12

Table 3

Multivariate-Adjusted* Hazard Ratios for Total Vitamin Intake and Incident Hearing Loss Stratified by Age

	HR (95% CI)	
Nutrient	<60 yr (1475 cases)	≥60 yr (2084 cases)
Vitamin C		
Quintile 1	1 (ref)	1 (ref)
2	0.98 (0.82–1.17)	1.21 (1.04–1.42)
3	1.00 (0.82–1.20)	1.10 (0.93–1.31)
4	1.00 (0.82–1.22)	1.19 (1.00–1.42)
5	0.96 (0.78–1.18)	1.17 (0.97–1.41)
Vitamin E		
Quintile 1	1 (ref)	1 (ref)
2	0.95 (0.80–1.13)	1.00 (0.85–1.18)
3	1.07 (0.89–1.29)	1.10 (0.93–1.31)
4	1.15 (0.94–1.41)	1.00 (0.84–1.20)
5	1.07 (0.86–1.33)	1.05 (0.87–1.27)
B Carotene		
Quintile 1	1 (ref)	1 (ref)
2	1.04 (0.89–1.23)	1.07 (0.93–1.25)
3	1.04 (0.88–1.23)	1.04 (0.89–1.21)
4	1.05 (0.88–1.25)	1.00 (0.85–1.16)
5	0.98 (0.81–1.18)	1.01 (0.86–1.18)
Folate		
Quintile 1	1 (ref)	1 (ref)
2	1.09 (0.91–1.29)	0.91 (0.78–1.06)
3	0.95 (0.78–1.15)	0.98 (0.84–1.15)
4	1.00 (0.81–1.23)	0.79 (0.66–0.95)
5	1.01 (0.80–1.8)	0.79 (0.65–0.96)
B12		
Quintile 1	1 (ref)	1 (ref)
2	1.08 (0.92–1.27)	0.99 (0.85–1.14)
3	1.10 (0.92–1.31)	1.10 (0.93–1.26)
4	1.13 (0.93–1.36)	1.20 (1.02–1.40)
5	1.01 (0.83–1.24)	1.10 (0.93–1.30)

*Adjusted for age, BMI, alcohol, smoking, hypertension, diabetes, race, vitamins C, E, beta carotene, folate and B12

Folate (p, interaction=0.50)