

Short Communication

Exposure to Environmental Tobacco Smoke Is Associated with Lower Plasma β -Carotene Levels among Nonsmoking Women Married to a Smoker¹

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Abstract

We evaluated the association between exposure to environmental tobacco smoke (ETS) from husbands who smoke and plasma levels of antioxidant vitamins among nonsmoking women. A total of 1249 women from four areas in Italy answered a self-administered questionnaire, reported their diets on a food frequency questionnaire, had a medical examination, and gave their blood for α and β -carotene, retinol, L-ascorbic acid, α -tocopherol, and lycopene determinations. Urinary cotinine was used to evaluate the level of recent exposure to ETS. After adjusting for study center, age and education, we found no association between ETS exposure and daily nutrient intake of β -carotene, retinol, L-ascorbic acid, and α -tocopherol. However, we found an inverse dose-response relationship between intensity of current husband's smoke and concentrations of plasma β -carotene and L-ascorbic acid. The associations remained even after controlling for daily β -carotene and vitamin C intake and for other potential confounders (vitamin supplementation, alcohol consumption, and body mass index). Moreover, when urinary cotinine was considered as the exposure variable, a significant inverse association with plasma β -

carotene was found. The findings may be of interest to explain the biological mechanism that link ETS exposure with lung cancer and ischemic heart diseases.

Introduction

Cigarette smoke contains oxidant compounds and free radicals that cause oxidative damage and induce lipid peroxidation. Active cigarette smoking suppresses plasma levels of β -carotene and vitamin C (1, 2). It has been suggested that exposure to ETS⁴ could alter the redox status of ascorbic acid, leading to oxidative stress (3). In fact, reduced plasma ascorbic acid concentrations in passive smokers have been observed, and this reduction was not attributable to differences in vitamin C intake (4). A recent study found that exposure to passive smoking at home resulted in decreased circulating concentrations of carotenoids (5). However, dietary information was not available in this investigation, and the possibility of confounding from diet could not be excluded. There are indications that women whose spouses smoke have poorer diets than unexposed women. In particular, dietary intake of carotenoids seems to be lower in nonsmokers exposed to passive smoke at home than among those not exposed to ETS (6–9). We have recently reported that nonsmoking women married to a smoker do not differ for most of the risk factors linked with cardiovascular diseases and cancer but tend to eat less vegetables than those whose husbands are nonsmokers (10). To date, no human population study has evaluated the relationship between ETS exposure and plasma concentrations of various antioxidant vitamins, in particular β -carotene, controlling for several confounding factors, including diet. We examined the effects of ETS exposure on serum concentrations of antioxidant vitamins among nonsmoking women.

Materials and Methods

We have analyzed a sample of 1249 nonsmoking women (mean age, 47 years; range, 25–74 years) living in four areas of northern-central Italy, participating in a cross-sectional study aimed at evaluating the characteristics of women exposed and unexposed to ETS. The details of the study have been reported elsewhere (10). Briefly, all participants (76.7% response rate) answered a questionnaire about sociodemographic characteristics, passive smoking exposure, medical history, and preventive lifestyle behaviors. The Italian version of the European Prospective Investigation into Cancer and Nutrition food-frequency questionnaire (11) was used to evaluate dietary habits. Daily dietary intake of nutrients was then assessed according to a specific conversion program. All participants also attended a medical examination including measurement of standing height and weight according to standardized procedures. A blood

Received 12/14/00; revised 4/27/01; accepted 5/11/01.

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¹ This work was funded in part by Contracts 96-18 and 96-18A from the Center for Indoor Air Research (CIAR), Linthicum, MD.

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⁴ The abbreviation used is: ETS, environmental tobacco smoke.

Table 1 Urinary cotinine, dietary intake of antioxidants, and plasma levels of (pro-) vitamins by ETS exposure among nonsmoking women

	Exposure to husbands' smoking															P-trend
	Never Exposed			Previously Exp.			1–10 cig/day			11–20 cig/day			21+ cig/day			
	N	Mean	SD	N	Diff ^a	SE	N	Diff ^a	SE	N	Diff ^a	SE	N	Diff ^a	SE	
Cotinine (ng/ml)	460	7.95	7.4	460	0.62	0.65	122	5.2	0.98	137	7.2	0.94	56	11.7	1.40	<0.001
Dietary intake																
β -Carotene (μ g/day)	460	3429.1	2043.9	460	-5.3	136.2	122	-22.4	206.0	137	-275.1	198.2	56	-233.1	287.10	0.171
Retinol (μ g/day)	460	611.9	606.4	460	2.4	41.9	122	-37.1	63.4	137	5.5	61.0	56	42.2	88.40	0.873
L-ascorbic acid (mg/day)	460	151.0	90.2	460	-7.1	5.1	122	-5.2	7.7	137	-13.1	7.4	56	-9.6	10.70	0.082
α -Tocopherol (mg/day)	460	9.0	3.8	460	-0.12	0.25	122	0.01	0.38	137	-0.25	0.36	56	0.89	0.52	0.567
Plasma levels																
α -Carotene (ng/ml)	425	57.1	70.0	434	3.6	5.0	114	-7.8	7.6	134	-3.1	7.1	51	-16.0	10.66	0.143
β -Carotene (ng/ml)	436	345.6	351.3	445	-0.02	21.7	117	-32.0	32.9	136	-59.0	31.2	54	-96.5	45.70	0.007
Retinol (ng/ml)	433	523.0	292.7	449	-17.5	19.5	117	-13.4	29.5	136	-15.8	28.1	54	25.7	41.00	0.952
L-ascorbic acid (mg/dl)	408	0.94	0.36	425	-0.03	0.03	111	-0.06	0.04	122	-0.05	0.04	48	-0.08	0.05	0.050
α -Tocopherol (ng/ml)	437	10971.8	5023.9	449	82.3	337.4	117	-636.9	512.3	136	-383.7	486.8	54	-698.9	712.00	0.153
Lycopene (ng/ml)	395	357.4	221.9	396	23.5	20.2	111	32.7	30.0	121	42.0	29.2	44	-61.9	44.50	0.678
Plasma levels of β -carotene and L-ascorbic acid after additional adjustment for alcohol consumption, body mass index, dietary vitamin intake, and vitamin supplementation																
β -Carotene (ng/ml)	436	345.6	351.3	445	2.30	21.6	117	-40.0	32.7	136	-55.6	31.0	54	-93.9	45.50	0.008
L-ascorbic acid (mg/dl)	408	0.94	0.36	425	-0.03	0.02	111	-0.07	0.04	122	-0.05	0.04	48	-0.08	0.05	0.023

^aMean difference in exposed versus unexposed from linear regression analysis adjusted for center, age, and women's education.

sample was drawn in fasting conditions to determine α - and β -carotene, retinol, L-ascorbic acid, α -tocopherol, and lycopene using high-performance liquid chromatography (12, 13). A sample of urine was also collected to measure cotinine using radioimmunoassay (14). Informed consent was obtained.

We used the urinary cotinine to validate the nonsmoking status of the women. We excluded, as possible active smokers, 14 women having a value >100 ng/ml, thus leaving 1235 subjects for the analysis. We compared the mean daily dietary intake of β -carotene, retinol, L-ascorbic acid, α -tocopherol, as well as the mean serum concentrations of antioxidant (pro-) vitamins across five categories of ETS exposure from the husband (never exposed; previously exposed; and currently exposed to 1–10 cigarettes/day, 11–20 cigarettes/day, and >20 cigarettes/day.). Multivariate linear regression models were used to estimate the mean differences between exposed and unexposed after adjustment for center of recruitment (four categories), age (five classes), and women's education (four categories). We then evaluated the association between ETS exposure and serum concentration of β -carotene and of L-ascorbic acid after taking into account dietary intake of the same provitamins (tertiles), vitamin supplementation (9.9%), alcohol consumption (never drinkers, 23.7%; and tertiles among drinkers), and body mass index (tertiles). ETS exposure was included as an ordinal (0, 1, 2, 3, and 4) variable in the linear model to test for trend. Finally, we repeated all of the analyses considering urinary cotinine (classified as: <5, 5–9.9, 10–29.9, and 30–100 ng/ml) as an exposure variable.

Results

Table 1 reports the mean levels (and SDs) of urinary cotinine, daily nutrient intake, and serum (pro-) vitamin concentrations among women never exposed to husbands' smoking as well as adjusted differences (and SEs) among women in the four exposure categories. Urinary cotinine was higher among currently exposed women compared with unexposed subjects. There was a clear dose-response relationship between the number of cigarettes smoked by the husbands and the biological marker of exposure (P for trend <0.001). No clear association was found between ETS exposure and dietary intake of the four nutrients,

although dietary intake of both β -carotene and ascorbic acid was somewhat lower among those currently exposed to >20 cigarettes/day. When we examined the serum levels of provitamins, the concentration of β -carotene was lower among women in the two highest exposure categories, and a clear dose-response relationship was found (P for trend = 0.007). A similar but less evident pattern was seen for L-ascorbic acid (P for trend = 0.05). No other association was seen. After additional control for dietary intake of β -carotene, vitamin supplementation, alcohol consumption, and body mass index, the association between ETS exposure and serum level of β -carotene and L-ascorbic acid remained (P for trend = 0.008 and 0.023, respectively). Women exposed to >20 cigarettes/day had a 27% decrease (-94 ng/ml; 95% confidence interval = -183.1; -4.6) in β -carotene level and an 8.5% decrease in L-ascorbic acid level (-0.08 ng/ml; 95% confidence interval = -18.5; 0.03), compared with unexposed subjects. In a sensitivity analysis, we repeated the test for linear trend considering never-exposed women and previously exposed women as a single category: a stronger effect for β -carotene (P = 0.004) and a weaker effect for L-ascorbic acid (P = 0.05) were found. Finally, in an attempt to remove a possible residual confounding effect from diet, we controlled further for consumption of specific food items: vegetables (fresh vegetables and cooked vegetables, classified as <1/day, 1/day, and >1/day), β -carotene rich fruits (apricots, prunes, and peaches; <2/week, 2–4/week, and >4/week), and citrus fruits (oranges, tangerines, and kiwi; <2/week, 2–4/week, and >4/week). The estimates of the parameters and the strength of the association remained practically the same (P for trend = 0.010 for β -carotene and 0.021 for L-ascorbic acid).

Table 2 reports the association between urinary cotinine and β -carotene and L-ascorbic acid concentrations. The serum levels of β -carotene were lower among women exposed to ETS, and a dose-response relationship was found (P for trend = 0.026). No association was found for L-ascorbic acid level (P for trend = 0.227). Adjustment for alcohol consumption, body mass index, dietary vitamin intake, and supplementation did not alter the results.

Table 2 Association between urinary cotinine, indicator of ETS exposure, and plasma levels of β -carotene and L-ascorbic acid

	Urinary Cotinine												P-trend
	<5 ng/ml			5.0–9.9 ng/ml			10–29.9 ng/ml			30–100 ng/ml			
	N	Mean	SD	N	Diff ^a	SE	N	Diff ^a	SE	N	Diff ^a	SE	
Plasma levels													
β -carotene (ng/ml)	493	332.6	326.8	355	-8.22	22.5	382	-41.02	22.3	45	-85.0	49.9	0.026
L-ascorbic acid (mg/dl)	470	0.93	0.38	339	-0.02	0.03	345	-0.02	0.02	44	-0.07	0.06	0.227
Plasma levels after additional adjustment for alcohol consumption, body mass index, dietary vitamin intake, and vitamin supplementation													
β -carotene (ng/ml)	493	332.6	326.8	355	-5.67	22.4	382	-36.11	22.3	45	-85.7	49.7	0.039
Ascorbic acid (mg/dl)	470	0.93	0.38	339	-0.02	0.03	345	-0.01	0.03	44	-0.06	0.06	0.423

^a Mean difference in exposed versus unexposed from linear regression analysis adjusted for center, age, and women's education.

Discussion

We found an inverse association between the amount of cigarettes currently smoked by the husband and the serum level of β -carotene among nonsmoking women. The relationship remained when considering urinary cotinine as the exposure variable. The strength of the association, the clear dose-response relationship, the extensive control for several factors linked with antioxidant plasma levels, all make plausible a causal association. The results for L-ascorbic acid are also suggestive, but they are statistically weaker than those regarding β -carotene and not confirmed when using cotinine as a marker of exposure. Cotinine levels, on the other hand, reflect short-term (a few days) ETS exposure from all sources, whereas serum antioxidants are rather stable when in a steady state after several weeks from dietary modifications (15). Self-reported indicators of chronic exposure, like husband's current smoking, might better reflect the relevant time window for outcomes in biological equilibrium, such as serum (pro-) vitamins.

We have specifically addressed confounding from diet in this study. We have used a detailed and well-validated food-frequency questionnaire (11), and we were able to estimate dietary intake of vitamins. When adjustment was made for dietary intake of vitamins (in addition to other factors), only marginal changes in the parameter estimates were seen. No changes were seen when additional adjustment was done for individual dietary items. Because we found practically no confounding effect from the dietary variables that we were able to measure, it is unlikely that residual confounding from misclassification of diet could be responsible of the results.

The mechanism underlying the association of β -carotene with passive smoking is probably similar to what has been suggested for active smoking. Depressed plasma β -carotene concentrations have been reported in response to enhanced metabolic turnover resulting from smoking-induced oxidative stress (1). Several studies have indicated that exposure to ETS from spouses who smoke is associated with an increased risk of lung cancer among nonsmoking women (16, 17); the effect seems to be stronger among people with a lower intake of carotenoids, β -carotene, and retinol (18). Our findings may help to interpret the biological mechanism linking ETS exposure to lung cancer and cardiovascular diseases (13, 19).

Acknowledgments

We thank all those who participated in the design of the study, data collection, and data analysis. In particular, we thank Vittorio Krogh and Sabina Sieri for calculating nutrient intake.

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Cancer Epidemiol Biomarkers Prev 2001;10:907-909.

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