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Cancer Epidemiology, Biomarkers & Prevention

Null Results in Brief

Plasma Coenzyme Q10 Levels and Prostate Cancer Risk: The Multiethnic Cohort Study

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Abstract

Background: Coenzyme Q10 (CoQ10) is considered to be a potential anticancer agent, but epidemiologic evidence regarding CoQ10 and prostate cancer risk is lacking. We examined the association of circulating CoQ10 levels with prostate cancer risk, using prediagnostic blood samples.

Methods: Each of the 307 cases was individually matched to approximately 2 controls, for a total of 596 controls, on age, ethnicity, geographic location, date/time of specimen collection, and hours of fasting. Logistic regression was used to compute ORs and 95% CIs.

Results: There was no overall statistically significant association of plasma CoQ10 levels with prostate cancer risk ($P_{trend} = 0.50$). However, after matched sets in which controls who had possible undiagnosed prostate cancer (prostate specific antigen value >4.0) were excluded, the ORs for quintiles 2 to 5 were all less than 1.0.

Conclusions: The results suggest the possibility that moderate levels of circulating CoQ10 may be optimal for the reduction of prostate cancer risk; however, the findings were weak and not statistically significant. Because this is the first epidemiologic study of the association between CoQ10 and prostate cancer, further research on this topic is needed.

Impact: If a nutritional factor such as CoQ10 were determined to reduce prostate cancer risk, it would have considerable public health significance because of the very high incidence of this cancer. *Cancer Epidemiol Biomarkers Prev; 20(4); 708–10. ©2011 AACR.*

Introduction

Coenzyme Q10 (CoQ10) is a component of the mitochondrial respiratory chain and is considered an important cellular antioxidant (1, 2); consequently, it plays a critical role in immunity, cell growth, and apoptosis. A few clinical studies of CoQ10 supplementation in prostate cancer patients have been reported (3, 4), but the relationship of CoQ10 to the development of prostate cancer has not been studied. To determine whether CoQ10 affects prostate cancer risk, we examined the association between prediagnostic plasma CoQ10 levels and prostate cancer in the Multiethnic Cohort Study (MEC).

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Materials and Methods

We conducted a nested case–control study of prostate cancer from the biospecimen subcohort of the MEC as previously described (5, 6). Cases of prostate cancer, diagnosed after blood collection, were identified through a linkage of the MEC with the Hawaii and California population-based SEER (Surveillance Epidemiology and End Results) cancer registries. For the cases, the years of diagnosis ranged from 1995 to 2005 and the average time between blood collection and cancer diagnosis was 1.9 years. Advanced prostate cancers were defined as (1) having either regional or distant spread and/or (2) having a Gleason score 7 or more irrespective of tumor stage. Approximately 2 controls for each case were randomly chosen from men in the biospecimen subcohort who were alive and free of prostate cancer at the age of the case's diagnosis and who matched the case on birth year (±1 year), race/ethnicity (African American, Japanese American, Native Hawaiian, Latino, or white), location (Hawaii or California), date (±6 months) and time (±2 hours) of blood draw, and fasting hours (0 to <6, 6 to <8, 8 to <10, and 10+ hours). Plasma concentrations of total CoQ10 were analyzed by high-pressure liquid chromatography as previously described (7). Data analyses were done on 307 cases (54 advanced cases) and 596 matched

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controls with complete data on CoQ10 and the adjustment variables described in the following text.

Conditional logistic regression, with matched sets as strata, was used to compute ORs and 95% CIs. CoQ10 levels were categorized into quintiles on the basis of the distribution of the overall study population, and a trend variable was created by assigning the median value of the appropriate category. The full model was adjusted for body mass index (BMI), family history of prostate cancer, and education, with additional adjustment for age at blood draw and fasting hours prior to blood draw as continuous variables to account for any possible systematic differences within matched sets. In addition, the model was run including only advanced prostate cases and their matched controls. Finally, as prediagnostic prostate specific antigen (PSA) was measured on all sets, we also repeated the analyses excluding matched sets in which the controls had high PSA values (>4.0 ng/mL) to reduce disease misclassification in the control group. Separate analyses were done for subgroups defined by ethnicity, BMI, and smoking status. All analyses were conducted using SAS (Version 9.1; SAS Institute).

Results

Cases were similar to controls for most baseline characteristics, except that cases were more likely to have a family history of prostate cancer (Table 1).

Overall, no significant association between plasma CoQ10 levels and prostate cancer risk was observed for all cases ($P_{trend} = 0.50$; Table 2) or for cases with advanced tumors ($P_{trend} = 0.73$; data not shown). After excluding matched sets in which controls had PSA levels of more than 4.0 ng/mL, the ORs for quintiles 2 to 5 were all less than 1.0, with the lowest OR in the middle quintile (Table 2). However, none of these ORs was statistically significant. Stratification by ethnicity, BMI, and smoking status had little influence on the relation of CoQ10 with prostate cancer risk (data not shown).

Discussion

This study is the first epidemiologic study of which we are aware to assess the relation between circulating CoQ10 levels and prostate cancer risk. Our results showed no statistically significant association between prediagnostic CoQ10 and the subsequent occurrence of prostate cancer. However, the consistent inverse associations observed in quintiles 2 to 5 when the sets were limited to those in which the controls had PSA levels of 4.0 or less suggest the possibility that there may be an optimal level of circulating CoQ10, at least with regard to prostate cancer risk reduction.

There is *in vitro* evidence that CoQ10 suppresses the growth of prostate cancer cells (8). Two clinical studies examined the effect of CoQ10 in combination with other antioxidants in prostate cancer patients. One study found

Table 1. Baseline characteristics of prostate cancer cases and controls in the MEC[a]

	Cases ($N = 307$)	Controls ($N = 596$)
Age at blood draw, mean (SD)[b], y	69.0 (7.1)	68.9 (7.2)
Fasting hours prior to blood draw, mean (SD)[b]	13.6 (2.5)	13.8 (2.6)
Ethnicity, *n* (%)[b]		
African American	124 (40.4)	239 (40.1)
Japanese American	70 (22.8)	137 (23.0)
Latino	49 (16.0)	95 (15.9)
Native Hawaiian	12 (3.9)	22 (3.7)
White	52 (16.9)	103 (17.3)
Smoking status, *n* (%)		
Never	102 (33.2)	186 (31.3)
Former	162 (52.8)	341 (57.3)
Current	43 (14.0)	68 (11.4)
Years of education, mean (SD)	14.0 (2.7)	13.9 (2.9)
Family history of prostate cancer, *n* (%)	38 (12.4)	52 (8.7)
BMI, mean (SD), kg/m^2	26.1 (3.9)	26.2 (4.0)
METs of activity per day, mean (SD), h	1.6 (0.3)	1.6 (0.3)
Alcohol consumption (% total energy), mean (SD)	3.7 (7.4)	4.1 (7.2)

Abbreviation: MET, metabolic equivalent.

[a]Cases and controls were matched on geographic location (California or Hawaii), ethnicity (African American, Japanese American, Latino, Native Hawaiian, or white), year of birth (±1 year), date (±6 months) and time (±2 hours) of specimen collection, fasting status (0 to <6, 6 to <8, 8 to <10, and 10+ hours).

[b]Matching variables.

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Table 2. OR and 95% CI for risk of prostate cancer across quintiles of plasma coenzyme Q10 (CoQ10)

	CoQ10 quintiles, ng/mL	Cases	Controls[a]	OR[b] (95% CI)	P_{trend}[c]
All cases	Q1 (≤1,017)	64	117	1.00	
	Q2 (1,017–1,288)	61	120	0.93 (0.59–1.47)	
	Q3 (1,288–1,623)	52	128	0.73 (0.44–1.18)	
	Q4 (1,623–2,106)	66	115	1.13 (0.69–1.80)	
	Q5 (≥2,106)	64	116	1.05 (0.63–1.75)	0.50
Excluding matched sets in which controls had PSA > 4.0 ng/mL	Q1 (≤1,017)	43	71	1.00	
	Q2 (1,017–1,288)	43	76	0.88 (0.49–1.58)	
	Q3 (1,288–1,623)	34	87	0.56 (0.30–1.05)	
	Q4 (1,623–2,106)	41	82	0.78 (0.43–1.43)	
	Q5 (≥2,106)	44	80	0.89 (0.47–1.69)	0.95

[a]Controls were men matched to cases on geographic location (California or Hawaii), ethnicity (African American, Japanese American, Latino, Native Hawaiian, or white), year of birth (±1 year), date (±6 months) and time (±2 hours) of specimen collection, fasting status (0 to <6, 6 to <8, 8 to <10, and 10+ hours).

[b]Estimated by conditional logistic regression with matched sets as strata, with additional adjustment for age at blood draw, fasting hours prior to blood draw and years of education as continuous variables, as well as family history of prostate cancer and BMI.

[c]Linear dose–response in the logit of risk was estimated by a Wald test for CoQ10 modeled as a trend variable assigned the median value of the appropriate category.

that CoQ10 administered in combination with other antioxidants improved survival in patients with advanced prostate cancer (3). The second study was a randomized, placebo-controlled trial in which the authors found no effect of a combination of CoQ10, vitamin E, vitamin C, and selenium on PSA or hormonal levels in prostate cancer patients (4). A recent analysis within the MEC also found no associations between serum concentrations of antioxidants (carotenoids, tocopherols, selenium) and prostate cancer risk; however, CoQ10 was not examined in that study (6).

The major strengths of our study were the prospective design and reasonable statistical power due to the relatively large overall sample size. Although this investigation had some limitations, including a relatively short follow-up time (average duration: 1.9 years) and a small number of advanced cases, the results suggest that further studies are needed to assess a possible protective effect of higher circulating CoQ10 levels on the risk of developing prostate cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References

1. Crane FL. Biochemical functions of coenzyme Q10. J Am Coll Nutr 2001;20:591–8.
2. Ernster L, Dallner G. Biochemical, physiological and medical aspects of ubiquinone function. Biochim Biophys Acta 1995;1271:195–204.
3. Hertz N, Lister RE. Improved survival in patients with end-stage cancer treated with coenzyme Q(10) and other antioxidants: a pilot study. J Int Med Res 2009;37:1961–71.
4. Hoenjet KM, Dagnelie PC, Delaere KP, Wijckmans NE, Zambon JV, Oosterhof GO. Effect of a nutritional supplement containing vitamin E, selenium, vitamin C and coenzyme Q10 on serum PSA in patients with hormonally untreated carcinoma of the prostate: a randomised placebo-controlled study. Eur Urol 2005;47:433–9; discussion 439–40.
5. Kolonel LN, Henderson BE, Hankin JH, Nomura AM, Wilkens LR, Pike MC, et al. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. Am J Epidemiol 2000;151:346–57.
6. Gill JK, Franke AA, Steven Morris J, Cooney RV, Wilkens LR, Le Marchand L, et al. Association of selenium, tocopherols, carotenoids, retinol, and 15-isoprostane F(2t) in serum or urine with prostate cancer risk: the multiethnic cohort. Cancer Causes Control 2009;20:1161–71.
7. Franke AA, Morrison CM, Bakke JL, Custer LJ, Li X, Cooney RV. Coenzyme Q10 in human blood: native levels and determinants of oxidation during processing and storage. Free Radic Biol Med 2010;48:1610–7.
8. Quiles JL, Farquharson AJ, Ramirez-Tortosa MC, Grant I, Milne L, Huertas JR, et al. Coenzyme Q differentially modulates phospholipid hydroperoxide glutathione peroxidase gene expression and free radicals production in malignant and non-malignant prostate cells. Biofactors 2003;18:265–70.

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