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Correlates of Toenail Zinc in a Free-Living US Population

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Keywords

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INTRODUCTION

Zinc plays a crucial role in growth and cell division, insulin activity, and in prostate health (1,2). However, current dietary assessment tools do not adequately measure intake of zinc from the diet and supplements (3–6). Biomarkers of exposure to trace elements are potentially useful in epidemiologic studies, both as a measure of dietary intake and of nutritional status (7). The most often used biomarker of zinc exposure in population studies is serum zinc concentrations, but this method may be limited as a measure of zinc intake because plasma concentrations vary day-to-day, have a diurnal variation and are influenced by concurrent infection (8–10).

Toenail clippings may serve as a useful method for assessing zinc status because they are more convenient to collect and store than blood. Also, in contrast to serum, toenail clippings may provide a more stable measure of zinc status. Garland et al. reported good long-term reliability of toenail zinc measures, with a correlation of 0.58 across two toenail zinc samples taken 6 years apart (11).

Despite the fact that toenail zinc has potential for, and has been used as, a measure of zinc exposure in epidemiologic studies of cardiovascular disease and cancer (12–14), there are no prior studies to our knowledge that have examined how this marker varies with zinc intake from food or supplements and only one prior study of how this marker varies with other factors such as smoking, alcohol and body mass (13).

MATERIALS AND METHODS

Participants in this study were 106 men and 106 women, age 50–76 years, in Washington State without insulin-dependent diabetes who were randomly selected to be in the measurement sub-study (15) of the VITamins And Lifestyle (VITAL) cohort study. Of those randomly selected participants, 73% completed the study protocol.

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Participants completed the VITAL baseline mailed, self-administered questionnaire in 2000–01. Average daily supplemental zinc intake (current use for at least a year) was computed by dividing reported days per week by seven and multiplying by dose per day. This number was then summed for both individual zinc supplements and multivitamins. Dose of zinc in multivitamins was based on the selected brand or by the participant specifying the full content of their brand.

Diet over the previous year was assessed by a semi-quantitative food frequency questionnaire (FFQ) developed at the Hutchinson Cancer Center (16), which covers 120 foods or food groups. Nutrient intake was computed based on nutrient values from the Minnesota Nutrition Data System (17). Participants were excluded from the nutrient calculations if they failed quality control checks or had energy intake out of a plausible range (800 – 5000 kcal for men or 600 – 4000 kcal for women).

Participants were asked to clip their toenails from all 10 toes, which were collected during the measurement study home visit that occurred approximately 3– 5 months after the FFQ data was received. Toenail zinc concentrations in parts per million (ppm) were determined by instrumental neuron activation analysis at the University of Missouri Research Reactor Center (Columbia, Missouri) (11).

Linear regression was used to estimate associations of zinc intake from diet and supplements and other covariates with toenail zinc. All analyses were adjusted for demographic factors (age, gender and race as white/non-white) and the factors that were significant or borderline significant predictors of toenail zinc in a model with the demographic factors (body mass index (BMI), dietary zinc, vegetable intake, dietary fiber, and iron from diet).

RESULTS

Mean toenail zinc concentrations for men and women were 66.9 (s.d. 17.4 ppm) and 60.2 (s.d. 14.0 ppm), respectively.

Table 1 lists the crude and adjusted differences of toenail zinc concentrations by demographic and nutrient variables. Even after adjustment, toenail zinc concentration in men waps 5.8 ppm greater than in women ($p = 0.04$). BMI had borderline significant associations with toenail zinc (p for trend = 0.11). For all other demographic factors (age and race) and health-related behaviors (smoking and exercise (data not shown)), we did not find any statistically significant differences.

Zinc supplement use was not a significant predictor of toenail zinc, whereas higher intake of dietary zinc was associated with higher toenail zinc concentrations (p for trend = 0.03). The dietary zinc-toenail zinc association was stronger for men and weak for women (p for interaction = 0.05, data not shown). Animal protein, the major source of bioavailable zinc in the diet, was not associated with toenail zinc.

We specifically examined other dietary factors that have been found to negatively influence zinc absorption including phytic acid, vegetable and fiber intake (as surrogates of phytic acid), iron and calcium from food supplements and alcohol intake (8,18–20) (some data not shown). There was a borderline significant association between increased vegetable intake and decreased toenail zinc (p for trend = 0.08). Conversely, dietary fiber intake was associated with an increase in toenail zinc (p for trend = 0.04). We also investigated the potential effect modification of the dietary zinc-toenail zinc association by vegetable, fiber and iron intake, and there was no significant effect modification (data not shown).

DISCUSSION

To our knowledge, we are the first to demonstrate an association between dietary intake of zinc and toenail zinc concentrations. Observational studies of dietary zinc intake and plasma zinc, another biomarker of zinc status, have reported no association in a US population (21), while one in the UK found a positive association (22).

We found no association between supplemental zinc and toenail zinc, even though use of supplemental zinc was high in our study (66%) and despite evidence that our questionnaire accurately measures supplemental zinc (15). Reasons for our null association may be that zinc found in supplements is in the inorganic form (bound to chloride, sulfate, oxides, or propionate) which may not be well absorbed (23,24), and that zinc absorption from supplements may be low when dietary intake is sufficient (25). However, results from randomized clinical trials have shown that zinc supplementation positively affects zinc plasma levels (26–28).

A borderline statistically significant *inverse* association was seen for vegetable intake. Our results are consistent with studies which suggest that zinc in vegetables has poor bioavailability, and moreover, the phytate content of vegetables decreases the absorption of zinc from all sources (8,18).

Dinsmore et al. demonstrated lower absorption of zinc in alcoholics (29). We found alcohol intake was not associated with toenail zinc, nor was it in the study by Martin-Moreno et al. (12). Our results are also consistent with the latter study in that both found a small, non-significant increase in toenail zinc with increasing BMI and no association with smoking status.

In summary, our results suggest that toenail zinc may be a useful biomarker in epidemiologic studies, because it varies with dietary zinc intake, even in a healthy population with presumably little zinc deficiency.

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Table 1

Association of Demographic, Behavioral and Nutrient Factors with Toenail Zinc Concentrations

Factor	N[1]	Unadjusted Beta[2]	Adjusted Beta[2]
Sex			
Female	106	Ref	Ref
Male	106	6.70	5.82
p-value			0.04
Age (years)			
50–55	50	Ref	Ref
55–60	53	−1.98	0.40
60–65	36	1.84	3.97
65–70	29	−1.78	−0.23
70–77	44	−3.42	2.21
p-trend			0.56
Race			
White	201	Ref	Ref
Non-white	10	−6.34	−8.02
p-value			0.15
Body mass index (kg/m^2)			
Normal (18–24.9)	84	Ref	Ref
Overweight (25–30)	86	6.11	4.82
Obese (>30)	36	6.80	4.24
p-trend			0.11
Zinc supplement use (mg/day) (individual plus multivitamins)			
Non-User	72	Ref	Ref
0–15	86	1.34	2.92
15.01–122.5	51	2.40	2.84
p-trend			0.30
Dietary zinc (mg/day)[3]			
Q1 (0–8.76)	48	Ref	Ref
Q2 (8.77–11.96)	51	1.70	2.63
Q3 (11.97–15.14)	49	3.82	5.83
Q4 (15.15–35.32)	51	5.34	10.98
p-trend			0.03
Diet plus zinc supplement use (mg/day)[3]			
Q1 (0–14.69)			
Q2 (14.70–24.03)	48	Ref	Ref
Q3 (24.04–35.12)	49	3.75	3.93
Q4 (35.13–138.8)	49	2.60	0.51
p-trend	50	4.99	4.72
Animal protein (g/day)[3]			
Q1 (0–34.7)	51	Ref	Ref

Factor	N[1]	Unadjusted Beta[2]	Adjusted Beta[2]
Q2 (34.71–50.14)	51	2.04	−2.10
Q3 (50.15–65.47)	51	0.92	−2.93
Q4 (60.48–155.76)	51	4.02	−2.84
p-trend			0.48
Vegetable intake (servings/day)[3]			
Q1 (0–1.22)	50	Ref	Ref
Q2 (1.221–1.85)	50	6.10	5.13
Q3 (1.851–2.78)	49	−1.64	−2.60
Q4 (2.781–7.15)	49	−5.28	−6.51
p-trend			0.08
Dietary fiber (g/day)[3]			
Q1 (0–12.89)	50	Ref	Ref
Q2 (12.90–18.81)	48	−.25	2.19
Q3 (18.82–25.08)	50	2.15	9.97
Q4 (25.09–50.39)	51	−0.19	10.31
P-trend			0.04
Alcohol (g/day)[3]			
Q1 (0–0.053)	52	Ref	Ref
Q2 (0.531–2.35)	53	−2.43	−0.24
Q3 (2.35–11.25)	53	4.24	4.88
Q4 (11.26–102.36)	50	2.79	2.88
p-trend			0.19
Iron supplement (mg/day)			
Non-users	104	Ref	Ref
0–7.85	35	7.22	6.75
7.86–18	58	4.56	3.10
18.01–54	12	4.57	3.93
p-trend			0.17
Dietary iron (mg/day)[3]			
Q1 (0–10.84)	49	Ref	Ref
Q2 (10.85–14.40)	49	−2.18	−8.28
Q3 (14.41–18.94)	51	1.14	−4.47
Q4 (18.95–41.41)	50	0.73	−9.94
p-trend			0.26

[1] Number of subjects = 212. Numbers do not total 212 due to missing data.

[2] Beta coefficients represent the difference from the reference group in ppm of toenail zinc. Adjusted betas are adjusted for age, gender, race (white, non-white), BMI, dietary iron, dietary zinc, vegetable intake, and dietary fiber. All adjustment variables are continuous except for gender and race.

[3] Q1–Q4 = quartiles