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Dietary intake of carotenoids and risk of type 2 diabetes

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Abstract *Background and aims:* Carotenoids may reduce diabetes risk, due to their antioxidant properties. However, the association between dietary carotenoids intake and type 2 diabetes risk is still unclear. Therefore, the objective of this study was to examine whether higher dietary carotenoid intakes associate with reduced type 2 diabetes risk.
Methods and results: Data from 37,846 participants of the European Prospective Investigation into Cancer and Nutrition- Netherlands study were analyzed. Dietary intakes of β-carotene, α-carotene, β-cryptoxanthin, lycopene, lutein & zeaxanthin and the sum of these carotenoids were assessed using a validated food frequency questionnaire. Incident type 2 diabetes was mainly self-reported, and verified against general practitioner information. Mean ±SD total carotenoid intake was 10 ± 4 mg/day. During a mean ±SD follow-up of 10 ± 2years, 915 incident cases of type 2 diabetes were ascertained. After adjustment for age, sex, diabetes risk factors, dietary intake, waist circumference and BMI, higher β-carotene intakes associated inversely with diabetes risk [Hazard Ratio quartile 4 versus quartile 1 (HR_{Q4}): 0.78 (95%CI:0.64,0.95), P-linear trend 0.01]. For α-carotene, a borderline significant reduced risk was observed, with a HR_{Q4} of 0.85 (95%CI:0.70,1.03), and P-linear trend 0.05. β-cryptoxanthin, lycopene, lutein & zeaxanthin, and the sum of all carotenoids did not associate with diabetes risk.
Conclusions: This study shows that diets high in β-carotene and α-carotene are associated with reduced type 2 diabetes in generally healthy men and women.

Introduction

Carotenoids are plant pigments that provide the yellow, orange and red pigments in fruits and vegetables [1]. Smaller quantities of carotenoids are also present in bread, eggs and oils [2]. Carotenoids have antioxidant functions, and may reduce type 2 diabetes risk by reducing oxidative stress, which plays an important role in the development of diabetes [3–5]. However, evidence from prospective studies on the associations of dietary carotenoids and diabetes risk is scarce and inconsistent.

So far, β-carotene has been studied most often, with two observational studies reporting an inverse association of dietary β-carotene with diabetes [6,7] and another reporting no association among male smokers [8]. In addition, studies that addressed serum or plasma β-carotene values in association with diabetes risk showed inconsistent results [6,9–11]. Randomized controlled trials with β-carotene supplementation consistently showed no effect on diabetes among women with a history of cardiovascular disease [12], generally healthy men [13] and among male smokers [14]. For dietary lycopene, three cohort studies showed no association with diabetes

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[7,8,15]. Very little research has been performed on other individual dietary carotenoids such as α-carotene, β-cryptoxanthin, lutein, zeaxanthin and the total of carotenoids, and therefore no conclusions can yet be drawn on such intakes [7,8].

Inconsistencies in results between studies performed thus far could be due to differences in study design, range of carotenoids intake, or population characteristics such as age and sex. Moreover, previous research suggests that smoking increases oxidative stress [16], and that smokers may need a higher intake of carotenoids in comparison with non-smokers to reduce their diabetes risk [9]. One study indeed found reduced diabetes risk with higher serum β-carotene and total carotenoid values in non-smokers only [9], and a study among male smokers reported no associations of dietary [8] or supplementary [14] β-carotene with diabetes risk. However, two other studies did not confirm such an interaction with dietary carotenoids [7] or supplementary β-carotene [12].

In the European Prospective Investigation into Cancer and Nutrition- Netherlands (EPIC-NL) cohort, we investigated associations of dietary intake of six carotenoids and incidence of type 2 diabetes. In addition, we explored whether smoking modified these associations.

Methods

Study population

EPIC-NL consists of the two Dutch contributions to EPIC, Prospect-EPIC and MORGEN-EPIC [17]. Both cohorts were set up simultaneously in 1993–1997 and were merged in 2007 according to standardized processes into one large Dutch EPIC cohort [17].

Prospect-EPIC includes 17,357 women aged 49–70 years at baseline, participating in the national breast cancer screening program, and living in the city of Utrecht and its surroundings [18]. The MORGEN-EPIC study includes 22,654 men and women aged 21–64 years selected from random samples of the Dutch population in three cities in the Netherlands (Amsterdam, Doetinchem, and Maastricht) [19]. All participants provided written informed consent before study inclusion. The study complied with the Declaration of Helsinki and was approved by local ethical committees.

After exclusion of prevalent diabetes cases (n = 615), participants without consent to linkage with disease registries (n = 1027), participants with abnormal high or low energy intake (n = 400) and missing data on carotenoid intake (n = 218), 37,846 participants were included in the analysis.

Dietary intake

Participants completed a self-administered validated food frequency questionnaire (FFQ), containing questions about the usual consumption frequency of 178 foods during the year preceding enrollment. The FFQ was administrated once at baseline. The Dutch food composition table was used to calculate energy and nutrient intakes [20]. All nutrient values were adjusted for total energy intake by the regression residual method. Nutritional intakes of carotenoids examined were β-carotene, α-carotene, β-cryptoxanthin, lycopene, lutein plus zeaxanthin, and the sum of these carotenoids.

The FFQ has been validated against twelve 24-h recalls [21]. Spearman correlations for carotenoids ranged from 0.16 for β-carotene to 0.31 for alpha-carotene for men, and from 0.17 for β-cryptoxanhin to 0.32 for lycopene for women (unpublished data).

Energy reporting

Basal metabolic rate (BMR) was estimated using the Schofield equations. Participants with an energy intake vs. BMR of <1.14 were defined as energy under-reporters, whereas those with an energy intake vs. BMR of >2.40 were classified as energy over-reporters, according to the Goldberg cut-offs [22]. Energy misreporters were defined as energy under-plus over-reporters. The remaining was defined as normal energy-reporters.

Type 2 diabetes

Ascertainment and verification of diabetes has been described elsewhere [23]. In summary, occurrence of diabetes during follow-up was obtained from self-report in two follow-up questionnaires and from linkage with hospital discharge diagnoses registries. Follow-up was complete until 1 January 2006. In the Prospect study, occurrence of diabetes was also obtained from a urinary glucose strip test for detection of glucosuria. Cases notified by any of these methods were verified against general practitioner or pharmacist information. Only cases confirmed by either the general practitioner or pharmacist were included in the analyses.

Other variables

At baseline, participants completed a general questionnaire containing questions on demographics, presence of chronic diseases, and chronic disease risk factors. Physical activity, assessed by validated questionnaire, was categorized using the Cambridge Physical Activity Score [24]. Blood pressure was measured twice in a supine position on the right arm using a Boso Oscillomat (Bosch & Son) (Prospect) or on the left arm using a random zero Sphygmomano-meter (MORGEN) from which the mean was taken. Hypertension was defined as: diastolic BP $>$ 90 mm Hg, and/or systolic BP $>$ 140 mm Hg, and/or self-report. Smoking was categorized into never, past and current. Body weight and waist circumference were measured, and BMI was calculated as weight divided by height squared (kg/m^2).

Data analysis

Baseline characteristics were presented according to quartiles of carotenoid intake. Pearson correlations were