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CAROTENOIDS : ELDERLY HEALTHY DIET MARKER

Editorial

Incidence of cardiovascular disease and cancer increases with aging. Preventive strategies are of utmost importance for healthy aging and quality of life. Among them, the reduction in oxidative damage appears to be an important strategy to reduce cancer and cardiovascular disease mortality.

Carotenoids are known to be powerful anti-oxidants and may be good candidates to protect against damage caused by oxidative stress, since epidemiologic studies suggest that a diet with high fruit and vegetable intake is protective against cancer and cardiovascular disease.

Carotenoids (alpha-carotene, beta-carotene, lycopene...) are present in a wide variety of fruits and vegetables. It is generally considered that plasma carotenoids are a valid biological marker for vegetable and fruit intake. Studying the relationship between plasma carotenoids and mortality may be of great interest, especially in older adults who are more prone to oxidative stress and in order to propose dietary guidelines for this population.

Sarcopenia is characterized by a loss of muscle mass, and loss of strength is a major hallmark for aging. It is also a main component of frailty and is predictive for disability. Developing strategies to fight against sarcopenia in the elderly is of utmost importance. Among various potential mechanisms, oxidative stress that can damage mitochondrial DNA may be a causal factor for sarcopenia. Therefore, results of studies developed to determine whether carotenoid intake may be protective against the decline in muscle mass and function may provide new perspectives.

Pr Bonnefoy
Department of Geriatric Medicine
Hospital Lyon-Sud (Pierre-Bénite) - France

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Plasma Carotenoids and Onset of Dysglycemia: Results from the EVA study

— Tasnime N. AKBARALY[1,2], Annick FONTBONNE[3]; Alain FAVIER[4], Claudine BERR[1] —

[1]INSERM, Université Montpellier I., France - [2]University College London, UK - [3]IRD, Montpellier, France - [4]CHU de Grenoble, France

Carotenoids are natural pigment found in food, especially in fruits and vegetables. Background has led to the hypothesis that carotenoids play a protective role in chronic diseases[1] and cancers. In this report[2], we investigated if carotenoids could have a role in diabetes incidence in the elderly, possibly through their antioxidant capacity. We explored the relationships between total plasma carotenoid at baseline and 9-year occurrence of type 2 diabetes or impaired fasting glucose (IFG) in a healthy elderly population: The EVA Study ("Epidemiology of Vascular Ageing").

The EVA Study is a nine-year longitudinal study[3] that, at baseline (EVA0, 1991-1993), included 1389 volunteers (574 men and 815 women) born between 1922 and 1932 (mean age = 65) who resided in the town of Nantes (Western France). The subsequent follow-up waves with biological measurements were EVA2 (2-year follow-up, n=1272), EVA3 (4-year follow-up, n=1188) and EVA6 (9-year follow-up, n=781). The present analyses carried on the 1165 participants who were normoglycemic at inclusion. Total plasma carotenoid was measured at baseline using a spectrophotometric assay and analysed by quartile. During the 9-year follow-up, cumulative incidence of dysglycemia (presence of IFG or diabetes status identified according to the WHO definition[4]) was considered.

Main finding

During the 9-year follow-up, 127 new cases of dysglycemia (including 27 cases of type 2 diabetes) occurred. Comparisons of survival distributions between quartiles of plasma carotenoids showed that the lower the quartile, the greater the occurrence of dysglycemia (Figure 1). After controlling for socio-demographic factors, smoking habits, alcohol intake, cardio-vascular disease history, blood pressure, BMI and lipid profile, Cox proportional hazards regression models showed that participants in the highest quartile of total plasma carotenoids had a reduced 9-year risk of dysglycemia compared to participants in the lowest quartile (Higher quartile vs. lower quartile : 0.42 [0.22;0.82], P=0.01). To take into account reversibility of IFG, sensitivity analyses with persistent IFG as an end point were performed and showed a similar graded association between quartiles of carotenoids and dysglycemia.

Discussion

To our knowledge, our study[2] is one of the few to explore longitudinally the relationship between carotenoid and dysglycemia.

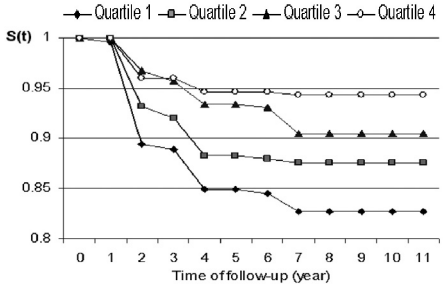

Figure 1: Non occurrence distributions for each total plasma carotenoid quartile groups [2].

The median and range values for each quartile were 1.42µmol/L, [0.21-1.82] for Q1 (<25th), 2.16µmol/L, [1.83-2.53] for Q2 (≥25th <50th), 2.90µmol/L, [2.55-3.43] for Q3 (≥50th <75th) and 4.14 µmol/L, [3.44-10.1] for Q4 (≥75th).

Currently, the mechanism of this potential relationship is still under debate and as described by Paiva et al., several hypotheses may explain this observation[5]. One of them involves the antioxidant properties of carotenoids. In our study, analyses were repeated after controlling on various antioxidative markers (TBARS, vitamin E, activity of glutathione peroxidases and superoxide dismutase), and our results remained unchanged suggesting that the association between total plasma carotenoids and diabetes observed in our cohort is independent of the oxidative stress status of subjects.

High plasma carotenoid is also a marker of fruits and vegetable consumption[7]. A reduced risk of type 2 diabetes with vegetables consumption was suggested in several studies[7, 8] but not all[9]. This possible protective effect of vegetables and fruits consumption in diabetes could result from the combined action of many protective compounds including antioxidants and could explain the controversial results in the literature between studies which were interested in blood measurement levels of carotenoids and those which were interested in consumption of carotenoid-rich vegetables and fruits.

Finally we cannot exclude that carotenoids might have been serving as markers for other protective lifestyle habits and health behaviours but are not acting as effective agents themselves.

In conclusion, our results bring support to a possible role of carotenoids in onset of IFG and type 2 diabetes in elderly people. Further studies are necessary to confirm this observation and to explore the mechanism which could explain the relationship, and hopefully design original measures which could help preventing dysglycemia.

REFERENCES

1. Hung, H.C., et al., Fruit and vegetable intake and risk of major chronic disease. J Natl Cancer Inst, 2004. 96(21): p. 1577-84.

2. Akbaraly, T.N., et al., Plasma carotenoids and onset of dysglycemia in an elderly population: results of the Epidemiology of Vascular Ageing Study. Diabetes Care, 2008. 31(7): p. 1355-9.

3. Akbaraly, N.T., et al., Selenium and mortality in the elderly: results from the EVA study. Clin Chem, 2005. 51(11): p. 2117-23.

4. World Health Organization, Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. 1999, World Health Organization: Geneva.

5. Paiva, S.A. and R.M. Russell, Beta-carotene and other carotenoids as antioxidants. J Am Coll Nutr, 1999. 18(5): p. 426-33.

6. Al-Delaimy, W.K., et al., Plasma carotenoids as biomarkers of intake of fruits and vegetables: individual-level correlations in the European Prospective Investigation into Cancer and Nutrition (EPIC). Eur J Clin Nutr, 2005. 59(12): p. 1387-96.

7. Feskens, E.J., et al., Dietary factors determining diabetes and impaired glucose tolerance. A 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study. Diabetes Care, 1995. 18(8): p. 1104-12.

8. Snowdon, D.A. and R.L. Phillips, Does a vegetarian diet reduce the occurrence of diabetes? Am J Public Health, 1985. 75(5): p. 507-12.

9. Hamer, M. and Y. Chida, Intake of fruit, vegetables, and antioxidants and risk of type 2 diabetes: systematic review and meta-analysis. J Hypertens, 2007. 25(12): p. 2361-9.

Low Total Plasma Carotenoids are Independent Predictors of Mortality Among Older Persons: the InCHIANTI Study

— Fulvio Lauretani[1], Stefania Bandinelli[2], and Luigi Ferrucci[3] —

[1]University Hospital of Parma, Italy - [2]Azienda Sanitaria Firenze, Florence, Italy - [3]NIA-NIH, USA

Background

Epidemiologic studies suggest that a diet high in fruit and vegetable intake is protective against cardiovascular disease, stroke, and cancer. Fruits and vegetables are high in bioactive compounds such as carotenoids, flavonoids, and other plant polyphenols. Carotenoids are powerful antioxidants and have been shown to protect against damage caused by oxidative stress. The reduction in oxidative damage is related to the decreased risk of all-cause, cancer, and cardiovascular disease mortality. Carotenoids act as free radical scavengers, modulate immune responses, and play an important role in the redox regulation involved in inflammation. Carotenoids (alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein, zeaxanthin, and lycopene) occur in a wide variety of fruits and vegetables. Plasma carotenoids can be reliable quantified and are considered a valid biological marker for vegetable and fruit intake.

The relationship between plasma carotenoids and mortality has not been well characterized.

We hypothesized that low plasma carotenoid concentrations were associated with increased mortality in older adults. In order to address this hypothesis, we examined the relationship between plasma carotenoid levels and mortality in the InCHIANTI study, a population-based cohort of older adults living in the community in Tuscany, Italy.

Methods

The study participants consisted of men and women, aged 65 and older, who participated in the Invecchiare in Chianti, "Aging in the Chianti Area" (InCHIANTI) study, conducted in two small towns in Tuscany, Italy. Briefly, in August 1998, 1270 people aged 65 years and older were randomly selected from the population registry of Greve in Chianti (pop. 11,709) and Bagno a Ripoli (pop. 4,704). Of 1256 eligible subjects, 1155 (90.1%) agreed to participate, and 1043 (90.3%) participated in the blood drawing. At the end of the field data collection, we collected data on mortality of the original InCHIANTI cohort, using data from the Mortality General Registry maintained by the Tuscany Region. During the eight-years of follow-up study, 310 participants died. Blood samples were collected in the morning after a 12-h fast. Aliquots of serum and plasma were immediately obtained and stored at -80° C. Aliquots of plasma were shipped on dry ice to Dr. Semba's laboratory for measurements of plasma carotenoids. Carotenoids were measured using high performance liquid chromatography (HPLC). Total carotenoids were calculated as the sum of alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein, zeaxanthin, and lycopene in Ìmol/L.

Results

Mean total carotenoid concentration was 1.80 (0.69) Ìmol/L. The mean plasma level of total carotenoids is significantly lower with aging (P for trend=0.0004) . During the eight years of follow-up, 310 (29.7%) of participants died. From the highest to the lowest tertile of total carotenoids, respectively, 74 (21.2%), 105 (30.2%) and 131 (37.8%) participants died after eight years of follow-up. In Cox Hazards Models adjusted for age and sex, participants with the highest tertile of plasma carotenoids at enrollment had lower mortality compared to those in the lowest tertile (Hazards Ratio = 0.63; 95% CI: 0.47-0.84; P=0.002). After adjusting for all covariates, adults in the highest tertile of plasma carotenoids at enrollment had lower mortality compared to those in the lowest tertile, although the association was slightly attenuated (Hazards Ratio obtained by considering carotenoids level as an ordinal variable = 0.81; 95% CI: 0.65-0.99; P for trend=0.046) .

Conclusion

The present study suggests that low total plasma carotenoids, a marker for fruit and vegetable intake, are an independent predictor of eight year, all-cause mortality among older persons. This work further shows the important relationship between antioxidant nutrients and mortality among older persons. Further work is needed to identify the sub-groups in the population which might be helped by interventions that reduce mortality in older populations.

REFERENCES

Lauretani F, et al. Eur J Nutr. 2008; 47:335-40.

Low Plasma Carotenoids and Skeletal Muscle Strength Decline over Six Years

— Luigi Ferrucci[1], Fulvio Lauretani[2,1], Stefania Bandinelli[3] —

[1]NIA-NIH, USA - [2]University Hospital of Parma, Italy - [3]Azienda Sanitaria Firenze, Florence, Italy

Sarcopenia, a condition characterized by loss of skeletal muscle mass and strength with aging, is considered a key factor in the disablement process. It is widely recognized that age-related sarcopenia is caused by a combination of intrinsic factors involving changes at the energetic molecular and cellular levels, and extrinsic or environmental factors such as nutrition and exercise.

Most studies looking at carotenoid intake or circulating levels and their relation with physical function have been cross-sectional. Thus, it is not known whether deficiency of carotenoids is a significant predictor of accelerated functional loss, or simply reflects a global deterioration of functional status, with little or no effect on the risk of losing physical function.

To address the hypothesis that low serum carotenoids may predict a greater decline in skeletal muscle strength, we examined the relationship between plasma total carotenoids at enrollment and the decline in hip, knee and grip muscle strength over a six-year interval among participants in the InCHIANTI study, a population-based study of older adult living in the Chianti region of Tuscany, Italy.

Subjects and Methods

The study participants consisted of men and women, aged 65 and older, who participated in the Invecchiare in Chianti, "Aging in the Chianti Area" (InCHIANTI) study, conducted in two small towns in Tuscany, Italy (www.inchiantistudy.net). Briefly, in August 1998, 1270 people aged 65 years and older were randomly selected from the population registry of Greve in Chianti and Bagno a Ripoli. The participants were seen again for a three-year follow-up visit (2001-2003) and a six-year follow-up visit (2004-2006).

Aliquots of serum and plasma were immediately obtained and stored at -80° C. Aliquots of plasma were shipped on dry ice to Dr. Semba's laboratory for measurements of plasma carotenoids. Carotenoids were measured using high performance liquid chromatography (HPLC). Total carotenoids were calculated as the sum of alpha-carotene, beta-carotene, beta-cryptoxanthin, lutein/zeaxanthin, and lycopene in Ìmol/L.

Results

Of the 1155 participants ≥65 years seen at enrollment, 1055 (91.3%) participated in the blood drawing. There were 948 (82.1%) participants at enrollment that had both plasma carotenoids and at least one of the three measures of strength (hip, knee, and/or grip strength) available for this analysis. There were 628 participants who had measurements of muscle strength conducted at the 6-year follow-up visit. Of 328 people who were not seen at the 6-year follow-up visit, 179 had died, 122 refused to participate, and 14 moved out of the study area.

Between enrollment and the 6-year follow-up visit, the overall mean declines (SD) in hip strength, knee strength and grip strength were -2.28 (5.24) kg (P <0.0001), -0.82 (5.60) kg (P <0.0001) and -1.44 kg (P <0.0001), respectively.

Adjusting for age, sex, education, body mass index, WHR, calf muscle density, CSAM, current smoking, total energy intake and physical activity, participants in the lowest quartile of total plasma carotenoids were at higher risk of developing poor hip strength (OR = 3.01; 95% CI: 1.44-6.31, P = 0.003), knee strength (OR = 2.94; 95% CI: 1.41-6.12, P = 0.004) and grip strength (OR = 1.87; 95% CI: 0.97-3.63, P = 0.07) compared to those in the highest quartile.

Discussion

This study shows that older community-dwelling men and women with low plasma carotenoid concentrations experience a greater decline in hip, knee and grip muscle strength over a period of six years compared to those with high plasma carotenoids. These findings support and expand the results of previous cross-sectional studies that showed low carotenoid intake and serum level of carotenoids, natural antioxidants, are independent correlates of poor skeletal muscle strength and impaired physical performance. In particular, our longitudinal analysis shows that older community-dwelling men and women with a total plasma carotenoids less than 1.37 Ìmol/L are at a higher risk of a decline in skeletal muscle strength over time.

REFERENCES

Lauretani F, et al. J Gerontol A Biol Sci Med Sci. 2008; 63:376-83