

Issue 73

In a nutshell

Despite epidemiological linking low vitamin A levels with prostate cancer, clinical trials of carotene or retinol supplements have consistently failed to show positive results, or even suggested a negative impact.

Clinical focus is now shifting to the possibility that a particular form of carotene may be more useful, and onto lycopene.

Vitamin A, lycopene and prostate cancer

Arbor Clinical Nutrition Updates 1999 (Oct)73:1-2 ISSN 1446-5450

ARCHIVES

The full list of archived issues can be found at www.arborcom.com/archives/. Some issues of our translated language editions are also available in archive, for Spanish, Portuguese and French.

COPYRIGHT, disclaimer and terms of use

This copy from our archives is for your private use only, and is NOT to be forwarded to any other party. Your use of these Updates constitutes your agreement to our disclaimer and terms of use: see section at the end of this publication.

NUTRITION RESEARCH REVIEW

Study one: Carotenes: case control

Subjects: 578 men from the Physicians Health Study who had developed prostate cancer during the 13 year follow-up period and 1,294 age- and smoking status-matched controls.

Method: Case-control study in which individual carotenes were assayed on the baseline blood sample (alpha-, beta-carotene, beta-cryptoxanthin, lutein, lycopene), together with retinol, and vitamin E.

As the original study had been a randomised, placebo-controlled intervention trial involving the giving of aspirin and beta-carotene, the current study group contained both those who had been given beta-carotene supplementation and those who had been given placebo.

Results: Lycopene was the only antioxidant found at significantly lower mean levels comparing cases with controls ($p = 0.04$ for all cases).

The results were stronger in the placebo treated group and for aggressive prostate cancers. For example, the odds ratio of having an aggressive prostate cancer in placebo treated group was $OR=0.40$ ($p = 0.006$ for trend) when comparing the highest quintile of plasma lycopene with the lowest.

These results were independent of possible confounders, such as age, smoking, body mass index, exercise, alcohol, use of multivitamins and plasma cholesterol.

Ref: *Cancer Res* 1999;59:1225-30

Study one: Carotenes: more case control

Subjects: 2,974 men from Basle, Switzerland.

Method: Prospective study in which plasma levels of vitamins C, E, retinol, and carotene were measured and subjects who were then followed up 17 years later.

Results: There were no significant differences related to retinol or carotene levels in prostate cancer cases compared to the other subjects.

Ref: *Prostate* 1999;38:189-98

Study three: Lycopene: case-control

Subjects: 12 patients with prostate cancer and 12 age-matched controls.

Method: Analysis of serum and prostatic tissue for major carotenoid concentrations and markers of lipid and protein oxidation.

Results: Lycopene levels were reduced in serum (44%, $p=0.04$) and in prostatic tissue (78%, $p=0.05$) in the prostate cancer patients compared with controls. There were no significant differences in relation to beta- and other major carotenoids.

Lipid peroxidation measures did not differ significantly between the cases and controls, but the serum protein thiol levels were higher in the prostate cancer subjects ($p=0.026$).

Ref: *Nutr Cancer* 1999;33:159-64

Study four: Intervention trial: ATBC trial

Subjects: 29,133 male smokers aged 50-69 years from southwestern Finland.

Method: Subjects were randomly assigned to receive either beta-carotene (20mg/day), alpha-tocopherol (50 mg/day), both or placebo for a median of 6.1 years.

Results: The beta-carotene supplemented subjects had a non-significantly higher level of prostate cancer development and mortality during follow-up compared to those not receiving it (which includes both those

taking vitamin E alone and those on placebo). The incidence of prostate cancer was 23% higher (95% CI = -4% to 59%) and mortality was 15% higher (95% CI = -30% to 89%).

(The vitamin E supplemented subjects had a significantly lower incidence of subsequent prostate cancer, (the detail of that part of the study is discussed in issue #74).

Ref: *JNCI* 1998;90:440-446

Comments

Background note: Beta-carotene is a provitamin A compound which can be converted to retinoid within the body. Lycopene is a carotenoid without any provitamin A activity, but which has strong antioxidant capacity.

Until recently, epidemiologic investigations on the relationship between vitamin A and carotenoids and prostate cancer have been divided almost equally between studies showing positive and inverse associations ¹.

However, as these latest studies suggest, this may be in part because of a lack of subtlety in differentiating between various types of carotenoid. After all, what was shown in many of the positive epidemiological studies were associations between high dietary intakes of certain fruits and vegetables that were rich in carotenoids, not necessarily a relationship with any specific carotenoid.

In some cases, the association was specifically with tomatoes rather than carotenoid-rich foods in general (e.g. see ²). On the other hand, a recently published case-control study from the USA failed to find any significant association between dietary lycopene intake and prostate cancer ³, and neither did a similar study from the UK ⁴.

However, both these last two studies were based on dietary history-taking at the time cancer was already present, and hence subject to the many limitations of this approach to assessing dietary intake.

The three epidemiological studies summarised above, on the other hand, use tissue levels as the marker of carotene status, and overall do seem to be pointing to

a possible relationship between lycopene specifically and prostate cancer.

When it comes to intervention trials, results of studies reported over the last few years have generally failed to show benefit in cancer risk situations from administration of vitamin A in various forms, including beta-carotene.

In some studies, results have even suggested a negative effect. For example, the ATBC study reported above in relation to beta-carotene.

Whilst this may have been disappointing to some, it is becoming clearer as further studies are conducted that the story is not over yet. It is obvious that retinol and the individual carotenoids are each a separate entity, and that what may be true for beta-carotene may not be true for other carotenoids.

So, whilst the focus in carotenoid trials has so far tended to be on beta-carotene, interest is now widening to include other carotenoids, particularly lycopene. In addition, there are some studies which suggest the cancer-related effects of carotenoid intake may depend on the levels of other antioxidants, including particularly vitamin E.

Clearly there is much still to consider before we can reach any definitive conclusions about the role of vitamin A and the carotenoids in prostate cancer.

References:

1. *Cancer Causes Control*, 7(1):83-44 1996
2. *Altern Med Rev* 1999;4:162-9
3. *Cancer Epidemiol Biomarkers Prev* 1999;8:25-34
4. *Br J Cancer* 1997;76:678-87

Disclaimer, copyright and terms of use

Your use of these Updates constitutes your agreement to our disclaimer and terms of use which can be found on our web site at: <http://arborcom.com/disclaim3.htm>. You can also obtain the disclaimer and terms of use by emailing us at: upD@arborcom.com.

© Copyright Arbor Communications PTL 1999. All rights reserved. This publication may NOT be forwarded onto others without our written permission.

If you want to receive the Clinical Nutrition Updates on an ongoing basis, please send us a request email to upD@arborcom.com. This is a FREE service to health professionals and students. Include details of your name, email address, which country you live in, institution you are associated with (if relevant) and professional background. The Updates are available in English, Spanish, Portuguese, Italian, French, Korean and Russian