

Is there a relationship between α -linolenic acid and prostate cancer?

NM Attar-Bashi, D Li, AJ Sinclair

Department of Food Science, RMIT University, VIC, 3001

A number of studies have suggested there is a positive association between diet or plasma α -linolenic acid levels and the incidence of prostate cancer (1, 2), however other studies have not supported this association (3, 4).

The lack of consistency in findings from these studies might be due to a number of reasons including methodological limitations related to measurement error in estimating past dietary exposure of a nutrient like α -linolenic acid from food frequency questionnaires, measurement of α -linolenic acid levels in plasma which might not represent long-term dietary intake, the assumption that α -linolenic acid levels in plasma is representative of α -linolenic acid levels in the prostate tissue, and the sample size of the studies which might have been too small in some studies.

To shed light on the relationship between fatty acid exposure and the invasiveness and metastatic potential of prostate cancer, one study (4) examined prostatic levels of individual fatty acids in relation to histopathological characteristics of cancer in men undergoing radical prostatectomy for localised disease. The results of the study showed that prostatic α -linolenic acid levels tended to be lower in cases than in control subjects with significantly lower levels when tumours extended to an anatomical or surgical margin. Measuring prostatic levels of fatty acids, as in this study, offers advantages over self-reported usual dietary intake, since it provides an estimate of exposure at the target organ level, where the concentrations likely reflect long-term dietary intake.

We have been investigating the effect of α -linolenic acid and other fatty acids on the growth of PC-3 human prostate cancer cell lines. Concentrations of fatty acids tested ranged between 10-200 $\mu\text{g}/\text{mL}$. Cells were plated out at a density of $10^4/100 \mu\text{l}/\text{well}$ in a 96-well plate and allowed an overnight period for attachment. Different concentrations of fatty acids were then added in parallel and incubated for 24, 48, or 72 hours in a 37°C and 5% CO_2 incubator. Effects of fatty acids on cells was determined using a colorimetric MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide) assay. The results showed that α -linolenic acid and other polyunsaturated fatty acids (PUFA) such as DHA and EPA significantly ($P < 0.05$) reduced the growth rate of the tumour cells at the high concentrations. Current studies are looking at mechanisms of fatty acids effects on tumour cells which might include fatty acid peroxidation, where spontaneous oxidation of PUFA yields reactive aldehydes and other products of lipid peroxidation that are potentially toxic to cells and may also signal apoptosis. Also fatty acids can exert their effect by interfering with the lipoxygenase enzyme activity. The present results indicate that PUFA, including ALA, are effective at reducing the growth of PC-3 human prostate cancer cell lines. However, mechanisms of action are not yet understood and require further investigation.

References

1. Giovannucci E, Rimm EB, Colditz GA, Stampfer MJ, Ascherio A, Chute CC, Willett WC. A prospective study of dietary fat and risk of prostate cancer. *J Natl. Cancer Inst.* 1993; 85: 1571-1579.
2. Gann PH, Hennekens CH, Sacks FM, Grodstein F, Giovannucci EL, Stampfer M. Prospective Study of plasma fatty acids and risk of prostate cancer. 1994; 86: 281-286.
3. Schuurman AG, van den Brandt PA, Dorant E, Brants HA, Goldbohm RA. Association of energy and fat intake with prostate carcinoma risk: results from The Netherlands Cohort Study. *Cancer.* 1999; 86: 1019-27.
4. Freeman V, Meydani M, Yong S, Pyle J, Flanigan R, Waters B, Wojcik E. Prostatic levels of fatty acids and the histopathology of localized prostate cancer. *The Journal of Urology* 2000; 164: 2168-72.

Key words: prostate cancer, α -linolenic acid