

Intervention Trial in Breast Cancer Primary Prevention: Diet and Risk Control

Sperimentazione di un Modello di Intervento di Prevenzione Primaria del Tumore della Mammella: Alimentazione e Controllo del Rischio

Barbara Ravazzolo

Cancer Registry of Palermo

Department of Hygiene and Microbiology, University of Palermo, Italy
Via del Vespro 133, 90127 Palermo Ph: +39 091 6553637 e-mail:barbara.rav@tiscali.it

Riassunto

Recenti studi prospettici hanno mostrato che il rischio di sviluppare un cancro della mammella nelle donne in post-menopausa è associato ai livelli di androgeni ed estrogeni. Pochi studi riportano, invece, l'influenza dell'alimentazione sugli estrogeni, e quindi sul rischio di cancro alla mammella. Nel presente articolo vengono riportati i risultati di un recente studio di intervento randomizzato (MeDiet¹), volto a valutare l'impatto potenziale dell'alimentazione sugli estrogeni endogeni, in donne sane in post-menopausa.

Keywords: breast cancer, mediterranean diet, estrogens, blocked randomization.

1. Introduction

The present paper reports results of a randomized dietary intervention study aimed to evaluate the potential impact of a diet on endogenous estrogens in healthy postmenopausal women. Evidence from both epidemiological and biomolecular studies clearly indicates that estrogens are primarily implicated in the development of human breast cancer, and that individual estrogen derivatives may have a distinct role in the development and clinical progression of breast cancer (Castagnetta LA et al., 2002). To evaluate the potential impact of a diet on endogenous estrogens (Carruba G et al., 2006), 310 healthy female volunteers were contacted and out of these women, 230 were found to be eligible and were enrolled in the study. Among these, 115 were selected based on serum testosterone levels, that has been shown to be a reliable predictor of breast cancer risk (Berrino F et al., 1996), equal or greater than median value.

The women were individually assigned to the dietary intervention or to the control group using a blocked randomization method and were stratified for pre-baseline parameters (including weight and serum testosterone) to achieve a balanced allocation of subjects in the two groups. Before and after the dietary intervention, all the women compiled a validated food frequency questionnaire. Fasting blood samples and 12-hour urine samples, and anthropometric measures were collected at the beginning and at the end of the study.

(¹) The present paper is supported by MeDiet Project working group: Experimental Oncology and Clinical Oncology, Department of Oncology, ARNAS-Civico, Palermo, Italy; Department of Preventive and Predictive Medicine, Istituto Nazionale Tumori, Milan, Italy; Department of Public Health, Epidemiology and Preventive Medicine, A.S.L. 6, Palermo, Italy.

Women in the intervention group adhered to a diet for six months, while women in the control group continued to follow their usual diet. The intervention group diet included Mediterranean food containing several biologically relevant anticancer agents. Furthermore, women were asked to avoid the use of refined carbohydrates and additional animal fat, to increase the consumption of mono- and poly-unsaturated fat, to increase the intake of fruits and vegetables, and to increase the intake of food rich in phytoestrogens.

Statistical analysis was conducted on the changes observed in urinary estrogen levels in both control and intervention groups at baseline and after six months. The changes in log-concentrations of individual estrogens were also measured as the difference between values after six months and at the beginning of the study comparing women of the two groups. Multivariate analysis of variance was used to assess the impact of potentially confounding variables (including glycaemia, cholesterol, testosterone, insulin, weight and body mass index). The compliance with dietary recommendations, were monitored using a validated food frequency questionnaire developed for EPIC study (Pisani P. et al., 1997) using a computer program (NAF) that converts questionnaire data into frequencies and average daily intake of foods, energy and nutrients.

2. Results

Intervention group reduced significantly the intake of both animal protein, fat (notably saturated fat), and showed a marked decrease of carbohydrate intake. Conversely, the control group did not show any significant change in their dietary nutrients.

At baseline, no significant difference was observed in urinary levels of individual estrogens between intervention and control women. After six months, women in the intervention group exhibited a significant decrease (over 40%) of total estrogen level, largely based upon the reduction of selected estrogen metabolites, while we did not observe a significant change in control women. The comparison among changes in total urinary estrogens of the two groups, after six months, showed significant differences.

References

- Castagnetta LA, Granata OM, Traina A, Ravazzolo B, et al. (2002) Tissue content of hydroxyestrogens in relation to survival of breast cancer patients. *Clin. Cancer Res.* 8, 3146-3155.
- Carruba G., Granata O., Pala V., Campisi I., Agostara B., Cusimano R., Ravazzolo B., Traina A. (2006) A traditional Mediterranean diet decreases endogenous estrogens in healthy postmenopausal women, *Nutr. Cancer*, 56(2), 253-259.
- Berrino F, Muti P, Micheli A, Bolelli G, Krogh V, et al. (1996) Serum sex hormone levels after menopause and subsequent breast cancer. *J. Natl. Cancer Inst.* 88, 291-296.
- Pisani P., Faggiano F., Krogh V., Palli D., Vineis P., and Berrino F. (1997) Relative validity and reproducibility of a food frequency dietary questionnaire for use in the Italian EPIC centres. *Int. J. Epidemiol.* 26, Suppl 1, S152-60.