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Original Research

The Western dietary pattern is associated with increased serum concentrations of free estradiol in postmenopausal women: implications for breast cancer prevention

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ABSTRACT

Little is known about the possible influence of food consumption on the serum concentrations of endogenous sex hormones in postmenopausal women. We evaluated the relationships of the Western dietary pattern with serum concentrations of free estradiol and testosterone of postmenopausal women to test the hypothesis that a highly Western dietary pattern is associated with high serum concentrations of these hormones. We used data from a representative subsample of 305 women from the control group of a population-based case-control study conducted in Mexico from 2004 to 2007. A Western dietary pattern index value was compared with log natural serum concentrations of testosterone and estradiol using multiple linear regression models. The median values of serum concentrations of free estradiol and testosterone were 0.26 pg/mL (interquartile range, 0.14-0.43) and 0.40 pg/mL (interquartile range, 0.30-0.70), respectively. A multiple linear regression model showed that for each unit increase in the Western dietary pattern index, there was a 16.2% increase in the serum concentrations of free estradiol ($\beta = 0.15$; 95% confidence interval [CI], 0.01-0.29); for each additional serving per week of chicken eggs, the increase was 31.0% ($\beta = 0.27$; 95% CI, 0.106-0.441); for each additional serving per week of red meat, the increase was 64.9% ($\beta = 0.50$; 95% CI, 0.01-1.01). There was no relationship found between dietary patterns and serum concentrations of free testosterone. The present findings suggest that intake of a Western diet, particularly of chicken eggs and meat, increases serum concentrations of free estradiol; these results have implications for breast cancer prevention.

Abbreviations: AHEI, Alternate Healthy Eating Index; BMI, body mass index; CI, confidence interval; IQR, interquartile range; SHBG, sex hormone binding globulin.

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1. Introduction

High serum concentrations of free estradiol and testosterone have been associated with an increased risk of breast cancer in postmenopausal women [1] and other diseases such as cardiovascular disease, increased triglyceride concentrations and insulin resistance [2]. High serum concentrations of estradiol have been considered mutagenic for breast duct cell DNA [3]. In postmenopausal women, the synthesis of 17β-estradiol is produced from the aromatization of adrenal androgens, which are derived from cholesterol [4,5]. Adipose tissue is the primary storage site of the enzymes (aromatase and 17-hydroxysteroid dehydrogenases) that catalyze the synthesis of estrone, testosterone, and estradiol [6]. Testosterone may have an effect on breast cancer risk through estrogen synthesis or by a direct effect on breast tissue [2]. During postmenopause, women secrete more testosterone; therefore, serum concentrations of this hormone are higher in this period than during premenopause [4].

Dietary patterns have been used to assess the effects of a variety of foods on the risk of chronic diseases, including breast cancer [7–10]. Research on the association between individual foods or nutrients and several diseases has been difficult to interpret because of the strong correlations among them [7]. The consumption of meat and processed meat has been associated with the risk of colorectal cancer [11,12], and it has been suggested that diets high in tuna fish and processed meats increase the risk of breast cancer among Hispanic women, particularly in those with estrogen receptor–positive tumors [13]. Using dietary patterns reduces collinearity, and there is evidence of the synergistic and interactive effects of a variety of foods on the risk of chronic diseases, including cancer [7–10]. It has been shown that the Western dietary pattern increases the risk of breast cancer [14], and a higher estrogenic dietary pattern score has also been associated with an increased risk [15]. There is evidence that "prudent or healthy" dietary patterns have a protective effect on breast cancer; this is mainly attributed to the high content of fiber and antioxidants and fewer animal fats, carbohydrates, preservatives, and additives [14,16–18].

Little is known about the possible influence of food on the concentration of endogenous sex hormones in postmenopausal women. It has been observed that a high fiber intake [19,20] and a Mediterranean dietary pattern [21] are associated with lower serum concentrations of estradiol; in contrast, milk consumption has been associated with higher serum concentrations [22,23]. A dietary pattern known as *estrogenic food* with a high component of meat was positively correlated with serum estradiol [24]. In the Nurses' Health Study, it was found that in overweight postmenopausal women, the Alternate Healthy Eating Index (AHEI-2010) was associated with lower serum concentrations of estradiol; the authors suggested that there may be other combinations of foods that could have stronger associations [25]. The AHEI-2010 was proposed as a more accurate measure of diet quality and is based on high intakes, for example, vegetables, fruit, whole grains, nuts and legumes, and long-chain omega-3 fatty acids, among others [26,27]. Fung et al (2007) [25] compared the fifth and first quintiles of the AHEI score, and the geometric means of free estradiol were 0.08 and 0.12 pg/mL, respectively (P for trend < .0001). Regarding testosterone, in men, it has been observed that energy restriction in the diet lowers serum concentrations of free testosterone [28].

The association between Western dietary patterns and the risk of breast cancer could be explained, in part, by the correlation between this dietary pattern and serum concentrations of sex hormones. The hypothesis for this study was that a highly Western dietary pattern is associated with high serum concentrations of free estradiol and testosterone. In this context, the aim of this study was to assess the association of the Western dietary pattern with serum concentrations of free testosterone and estradiol in postmenopausal women.

2. Methods and materials

2.1. Design and study population

This study used data from the control group of a population-based case-control study conducted from 2004 to 2007 in Mexico City, Monterrey, and Veracruz, with a total of 1000 cases and 1074 controls [29]. The cases were patients with a new histologically confirmed diagnosis of breast cancer, with no previous treatment, such as radiotherapy, chemotherapy, or antiestrogens such as tamoxifen, during the previous 6 months. Controls were selected based on a probabilistic multistage sampling design and were frequency-matched to cases on 5-year age groups, health care system, and region. Of 1074 controls, 598 were postmenopausal women, and 305 had diet information and serum hormone determinations (Fig. 1). Briefly, all participants signed an informed consent letter. A nurse performed an in-person interview to obtain sociodemographic information as well as data on physical activity, diet, and health. In addition, anthropometric measurements (weight, height, and waist circumference) and blood samples for biochemical determinations were taken. The response rate for controls was 90.1% for Monterrey, 87.4% for Mexico City, and 97.6% for Veracruz. The study was approved by the National Institute of Public Health Institutional Review Board as well as by the equivalent committees from each of the participating hospitals [29].

In the present study, *postmenopausal women* were defined as those experiencing natural menopause (12 months or more since their last period), women with induced menopause (bilateral oophorectomy), and women with a history of hysterectomy who did not know if their ovaries had been removed but were older than 48 years, taking into consideration that the mean age at menopause in Mexico is 48 years [29–31].

2.2. Analysis of dietary patterns

Dietary data were obtained using a semiquantitative food-frequency questionnaire of 104 food components with 10 multiple-choice consumption frequency categories, as described by Willett [32] and adapted to the Mexican population [33].

To determine dietary patterns [34], all 104 foods included in the questionnaire were classified into groups according to their composition, with reference to tables of the Mexican system of food equivalents [35]. Seventeen food groups were obtained as a result (Supplemental Table 1). Subsequently, a