Journal Scan

Combined Estrogenic and Antiestrogenic Properties of Estetrol on Breast Cancer may provide a Safe Therapeutic Window for the Treatment of Menopausal Symptoms

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ABSTRACT

Increased risk of breast cancer is a critical side-effect associated with the use of a menopausal hormone therapy (MHT). Estetrol (E4) is a natural estrogen produced by the human fetal liver and is a promising compound for clinical use in MHT. However, its impact on breast cancer is controversial and poorly defined. In this preclinical study, we show that E4 acts as a weak estrogen by stimulating the growth of hormone-dependent breast cancer only at concentrations exceeding menopausal therapeutic needs. Estetrol (E4) presents also an antitumor activity by decreasing the strong proliferative effect of estradiol (E2). While estrogen receptor alpha (ERα) is the predominant receptor mediating its effects, the dual weak-estrogenic/antiestrogenic feature of E4 results from differential signaling pathways activation. Both nuclear and rapid extranuclear signaling pathway are necessary for a complete estrogenic effect of E4. However, the antitumor action of E4 is not due to a capacity to antagonize E2-induced nuclear activity. Altogether, our results highlight that E4 has a limited impact on breast cancer and may offer a safe therapeutic window for the treatment of menopausal symptoms.

Mediterranean Diet and Risk of Endometrial Cancer: A Pooled Analysis of Three Italian Case-control Studies

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ABSTRACT

Background: Some components of the mediterranean diet have favorable effects on endometrial cancer, and the mediterranean diet as a whole has been shown to have a beneficial role on various neoplasms.

Methods: We analyzed this issue pooling data from three case-control studies carried out between 1983 and 2006 in various Italian areas and in the Swiss Canton of Vaud. Cases were 1,411 women with incident, histologically confirmed endometrial cancer, and controls were 3,668 patients in hospital for acute diseases. We measured the adherence to the mediterranean diet using a Mediterranean Diet Score (MDS), based on the nine dietary components characteristics of this diet, that is, high intake of vegetables, fruits/nuts, cereals, legumes, fish; low intake of dairy products and meat; high monounsaturated to saturated fatty acid ratio and moderate alcohol intake. We estimated the odds ratios (OR) and the corresponding 95% confidence intervals (CI) for increasing levels of the MDS (varying from 0, no adherence, to 9, maximum adherence) using multiple logistic regression models, adjusted for major confounding factors.

Results: The adjusted OR for a 6 to 9 components of the MDS (high adherence) compared with 0 to 3 (low adherence) was 0.43 (95% CI 0.34–0.56). The OR for an increment of one component of MDS diet was 0.84 (95% CI 0.80–0.88). The association was consistent in strata of various covariates, although somewhat stronger in older women, in never oral contraceptive users and in hormone-replacement therapy users.

Conclusion: Our study provides evidence for a beneficial role of the mediterranean diet on endometrial cancer risk, suggesting a favorable effect of a combination of foods rich in antioxidants, fibers, phytochemicals and unsaturated fatty acids.

Primary Ovarian Insufficiency: The Paradox of Menopause in Young Women

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ABSTRACT

Primary ovarian insufficiency (POI) refers to the loss of ovarian function in young women. It can lead to primary or secondary amenorrhea. The loss of ovarian function is usually permanent akin to menopause. Resultant hypoestrogenemia has systemic adverse effects particularly on the bone health. Primary ovarian insufficiency is diagnosed on the basis of raised serum follicle stimulating hormones levels. Most of the cases are idiopathic. Hypothyroidism is the most common associated disorder suggesting autoimmune etiology in some of the cases. Karyotypic abnormalities (mostly monosomy X— Turner syndrome) should be excluded in cases presenting with primary amenorrhea or early onset secondary amenorrhea. Treatment involves long-term estrogen-progesterone replacement therapy which provides regular withdrawal bleed and prevents systemic effects of hypoestrogenemia.

Menopausal Symptoms in Women with Chronic Kidney Disease

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ABSTRACT

Objective: This study aims to determine whether menopausal symptoms differed between women with chronic kidney disease (CKD) and women without CKD, and whether CKD modified associations of late vasomotor symptoms (VMS) with mortality and/or cardiovascular events.

Methods: Chronic kidney disease defined as estimated glomerular filtration rate lower than 60 ml/minute/1.73 m^2 (using the CKD epidemiology collaboration equation), was determined in 17,891 postmenopausal women, aged 50 to 79 years at baseline, in the multiethnic Women's Health Initiative cohort. Primary outcomes were presence, severity and timing/duration of VMS (self-reported hot flashes and night sweats) at baseline. We used polytomous logistic regression to test for associations among CKD and four VMS categories (no VMS; early VMS—present before menopause but not at study baseline; late VMS—present only at study baseline; persistent VMS—present before menopause and study baseline) and Cox regression to determine whether CKD modified associations between late VMS and mortality or cardiovascular events.

Results: Women with CKD (1,017 of 17,891; mean estimated glomerular filtration rate, 50.7 ml/min/1.73 m^2) were more likely to have had menopause before age 45 years (26 *vs* 23%, p = 0.02) but were less likely to experience VMS (38 *vs* 46%, p < 0.001) than women without CKD. Women with CKD were not more likely than women without CKD to experience late VMS. Late VMS (hazard ratio, 1.16; 95% CI, 1.04–1.29) and CKD (hazard ratio, 1.74; 95% CI, 1.54–1.97) were each independently associated with increased risk for mortality, but CKD did not modify the association of late VMS with mortality (pinteraction = 0.53), coronary heart disease (pinteraction = 0.12) or stroke (pinteraction = 0.68).

Conclusion: Women with mild CKD experience earlier menopause and fewer VMS than women without CKD.

Translation and Validation of the Utian Quality of Life Scale in Serbian Peri- and Postmenopausal Women

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ABSTRACT

Objective: This study aimed to translate the Utian Quality of Life Scale (UQOL) into the Serbian and to assess its validity and psychometric properties in Serbian peri- and postmenopausal women.

Methods: This survey included 200 peri- and postmenopausal women. Women were approached after their regular gynecological checkup in two community health centers (city center and outskirts) in the capital city Belgrade. The following instruments were used: general questionnaire (sociodemographics, habits and medical history) UQOL, Short Form-36, and Beck Depression Inventory. The UQOL was translated according to the recommended methodology for translating questionnaires, and its psychometric properties (internal consistency, factor analysis, discriminant validity construct validity, and criterion validity) were tested.

Results: The mean (SD) UQOL total score was 80.5 (13.5). The Cronbach's (alpha) coefficient for the entire scale was 0.83 [occupational, (alpha) = 0.76; health-related, (alpha) = 0.72; emotional, (alpha) = 0.36; sexual, (alpha) = 0.66]. All corrected item-total correlation coefficients were greater than 0.40, confirming that all items were appropriate parts of the UQOL. On exploratory factor analysis, we obtained six factors (five items formed two new clusters: physical fitness and professional recognition) that explained 85.7% of the total variance. The UQOL total score was significantly negatively correlated with Beck depression inventory score (p = 0.001) and significantly positively correlated with all Short Form-36 domains (p = 0.001). In addition, significant intercorrelations of UQOL domains also indicated good criterion validity.

Conclusion: The Serbian version of the UQOL demonstrates satisfactory reliability and validity in the assessment of quality of life among peri- and postmenopausal women. The Serbian version of the UQOL is an adequate quality-of-life instrument in the Serbian language that can be applied in the everyday clinical setting.

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