Selección de Resúmenes de Menopausia

Semana del 25 de Febrero al 3 de Marzo de 2015

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

Steroids. 2015 Feb 25. pii: S0039-128X(15)00071-9. doi: 10.1016/j.steroids.2015.02.015. [Epub ahead of print]

Epidemiologic Studies of Estrogen Metabolism and Breast Cancer.

Ziegler RG, Fuhrman BJ, Moore SC, Matthews CE.

Early epidemiologic studies of estrogen metabolism measured only 2-hydroxyestrone and 16α-hydroxyestrone and relied on direct enzyme immunoassays without purification steps. Eight breast cancer studies have used these assays with prospectively collected blood or urine samples. Results were inconsistent, and generally not statistically significant; but the assays had limited specificity, especially at the low concentrations characteristic of postmenopausal women. To facilitate continued testing in population-based studies of the multiple laboratory-based hypotheses about the roles of estrogen metabolites, a novel liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay was developed to measure concurrently all 15 estrogens and estrogen metabolites in human serum and urine, as unconjugated and total (glucuronidated+sulfated+unconjugated) concentrations. The assay has high sensitivity (lower limit of quantitation ~1-2 pmol/L), reproducibility (coefficients of variation generally ⩽5%), and accuracy. Three prospective studies utilizing this comprehensive assay have demonstrated that enhanced 2-hydroxylation of parent estrogens (estrone+estradiol) is associated with reduced risk of postmenopausal breast cancer. In the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO) cohort, the serum ratio of 2-hydroxylation pathway metabolites to parent estrogens was associated with a 28% reduction in breast cancer risk across extreme deciles (p-trend=.05), after adjusting for unconjugated estradiol and breast cancer risk factors. Incorporating this ratio into a risk prediction model already including unconjugated estradiol improved absolute risk estimates substantially (by ⩾14%) in 36% of the women, an encouraging result that needs replication. Additional epidemiologic studies of the role of estrogen metabolism in the etiology of hormone-related diseases and continued improvement of estrogen metabolism assays are justified.

J Endocrinol Invest. 2015 Feb 27. [Epub ahead of print]

Surgical menopause versus natural menopause and cardio-metabolic disturbances: A 12-year population-based cohort study.

Farahmand M, Ramezani Tehrani F, Bahri Khomami M, Noroozzadeh M, Azizi F.

PURPOSE: Menopausal status exposes women to increased risk of cardiovascular disease. This study was performed to compare the effect of menopausal types, including surgical and natural, on metabolic syndrome and other metabolic disorders 3 years before and after menopause. METHODS: Of 437 postmenopausal women, who participated in the Tehran Lipid and Glucose Study, 13 women with surgical menopause and 39 age-matched controls with natural menopause were selected. During the follow-up period, changes in metabolic and biochemical profiles were compared between surgical and natural menopause women. RESULTS: Odds of incidence of metabolic syndrome in surgical menopause women, compared to natural menopause women, was 9.7 (95 % CI 1.8-51.8). CONCLUSIONS: Metabolic disturbances after menopause are highly influenced by type of menopause and are more prevalent in those undergoing surgical menopause.

J Clin Endocrinol Metab. 2015 Feb 26:jc20144367. [Epub ahead of print]

Serum 25 Hydroxyvitamin D, Bone Mineral Density and Fracture Risk Across the Menopause.

Cauley JA, Greendale GA, Ruppert K, Lian Y, Randolph JF Jr, Lo JC, Burnett-Bowie SA, Finkelstein JS.

Context: Low levels of serum 25 Hydroxyvitamin D (25(OH)D) have been linked to greater fracture risk in older women. Objective: To determine if higher 25(OH)D is associated with slower loss of bone mineral density (BMD) and lower fracture risk during the menopausal transition (MT). Design, Setting and Participants: Prospective cohort study at 5 US clinical centers. Mean age, 48.5 ± 2.7 years. The fracture analysis included 124 women with an incident traumatic fracture, 88 with incident non-traumatic fracture and 1532 women without incident fractures; average follow-up of 9.5 years. BMD analysis included 922 women with a documented final menstrual period. Main

Outcome Measures: Serum 25(OH)D was measured by liquid chromatography tandem mass spectrometry at the third annual clinic visit. BMD was measured and incident fractures ascertained at each annual visit. Results: The mean 25(OH)D was 21.8 (ng/mL); 703 (43%) of the women had 25(OH)D values <20ng/mL. There was no significant association between 25(OH)D and traumatic fractures. In multivariable adjusted hazards models, the hazard ratio (HR) for non-traumatic fractures (95% confidence interval) was 0.72 (0.54, 0.95) for each 10 ng/mL increase in 25(OH)D. Comparing women whose 25(OH)D was ≥20 vs <20 ng/mL, the HR for fracture was 0.54 (0.32, 0.89). Changes in lumbar spine and femoral neck bone mineral density across menopause were not significantly associated with serum 25(OH)D level. Conclusion: Serum 25(OH)D levels are inversely associated with non-traumatic fracture in mid-life women. Vitamin D supplementation is warranted in midlife women with 25(OH)D levels below 20 ng/mL.

Cancer Prev Res (Phila). 2015 Feb 26. pii: canprevres.0243.2014. [Epub ahead of print]

Menopause is a Determinant of Breast Adipose Inflammation.

Iyengar NM, Morris PG, Zhou XK, Gucalp A, Giri D, Harbus MD, Falcone DJ, Krasne MD, Vahdat LT, et al.

Chronic inflammation is recognize as a risk factor for the development of several malignancies. Local white adipose tissue (WAT) inflammation, defined by the presence of dead or dying adipocytes encircled by macrophages which form crown-like structures (CLS), occurs in the breasts (CLS-B) of most overweight and obese women. Previously, we showed that the presence of CLS-B is associated with elevated tissue levels of proinflammatory mediators and aromatase, the rate-limiting enzyme for estrogen biosynthesis. The associated increased levels of aromatase in the breast provide a plausible mechanistic link between WAT inflammation and estrogen-dependent breast cancers. Thus, breast WAT inflammation could be relevant for explaining the high incidence of estrogen-dependent tumors with aging despite diminished circulating estrogen levels after menopause. To explore this possibility, we determined whether menopause in addition to body mass index (BMI) is associated with breast WAT inflammation among 237 prospectively enrolled women. The presence of CLS-B and its severity (CLS-B/cm2) as indicators of WAT inflammation correlated with menopausal status (P=0.008 and P<0.001) and BMI (P<0.001 for both). In multivariable analyses adjusted for BMI, the postmenopausal state was independently associated with the presence (P=0.03) and severity of breast WAT inflammation (P=0.01). Mean adipocyte size increased in association with CLS-B (P<0.001). Our findings demonstrate that breast WAT inflammation, which is associated with elevated aromatase levels, is increased in association with the postmenopausal state independent of BMI. Breast WAT inflammation, a process that can potentially be targeted, may help to explain the high incidence of estrogen-dependent tumors in postmenopausal women.

Menopause. 2015 Mar;22(3):267-74.

Consistent ovulation may not be enough to make women healthy when approaching menopause: an update from the Study of Women's Health Across the Nation.

Allshouse AA, Polotsky A, Crawford S, Chen HY, El Khoudary SR, Santoro N.

OBJECTIVE: This study aims to test the hypothesis that consistently ovulatory premenopausal/perimenopausal women have a more favorable cardiometabolic profile than anovulatory women. METHODS: The first four collections from the Study of Women's Health Across the Nation Daily Hormone Study (DHS) were used. DHS enrollees annually completed a daily collection of first morning voided urine for an entire menstrual cycle or up to 50 days (whichever comes first). A woman was categorized as consistently ovulatory annually (COA) if four ovulatory cycles or two to three ovulatory cycles followed by the final menstrual period (FMP) were observed. A woman was categorized as not consistently ovulatory annually (nCOA) if at least one anovulatory year was observed. Cross-sectional and longitudinal differences were compared between COA and nCOA women. Data were centered at FMP and adjusted for age and body mass index (BMI). RESULTS: Six hundred thirty-six DHS participants (mean [SD] age, 47.3 [2.5] y; mean [SD] BMI, 27.4 [7.1] kg/m) were included. Thirty-six percent of the DHS participants were COA women. On the fourth follow-up collection, COA women had lower high-density lipoprotein than nCOA women (mean [95% CI], 55.7 [54.0-57.4] vs 59.5 [57.9-61.0] mg/dL, P = 0.002, respectively), which persisted after adjustment. Among 460 women with FMP, 39% were COA women. COA women were slightly older (52.9 vs 52.0 y, P = 0.002) and had lower BMI (geometric mean, 26.1 vs 27.5 kg/m, P = 0.06) than nCOA women at FMP. Other

cardiometabolic factors did not significantly differ by COA status through FMP. CONCLUSIONS:Consistent ovulation across the menopausal transition does not seem to reflect cardiometabolic health.

Menopause. 2015 Feb 20. [Epub ahead of print]

Moderate to severe vasomotor and sexual symptoms remain problematic for women aged 60 to 65 years.

Gartoulla P[1], Worsley R, Bell RJ, Davis SR.

OBJECTIVE: This study aims to determine the prevalence and severity of menopausal symptoms in lder postmenopausal women and, hence, the need for treatment options for women of this age. **METHODS:** This is a cross-sectional questionnaire-based study conducted between October 2013 and March 2014 among 2,020 women aged 40 to 65 years and living independently across Australia. The main outcome measures were the prevalence of moderate to severe vasomotor symptoms (VMS), as measured by the Menopause-Specific Quality of Life Questionnaire, and the current use of prescription therapy for menopausal symptoms. **RESULTS:** The prevalence of moderate to severe VMS was as follows: 2.8% in premenopausal women, 17.1% in perimenopausal women, 28.5% in postmenopausal women younger than 55 years, 15.1% in postmenopausal women aged 55 to 59 years, and 6.5% in postmenopausalwomen aged 60 to 65 years. Prescription therapy for menopausal symptoms was used by 135 women: 120 (5.9%) women using hormone therapy and 15 (0.7%) women using nonhormonal medication. The factors positively associated with moderate to severe VMS were smoking (odds ratio, 1.6; 95% CI, 1.1-2.3; $P < 0.05$) and a body mass index of 25 to 29.9 kg/m (odds ratio, 1.7; 95% CI, 1.1-2.5; $P < 0.05$); education beyond high school was inversely associated (odds ratio, 0.7; 95% CI, 0.5-0.9; $P < 0.05$). **CONCLUSIONS:** In this large, representative, community-based sample of women, there is a high prevalence of untreated moderate to severe VMS even in women aged 60 to 65 years. The use of vaginal estrogen and nonhormonal prescription therapy with proven efficacy for treatment of menopausal symptoms is strikingly low, suggesting that menopause remains an undertreated condition.

Am J Epidemiol. 2015 Feb 18. pii: kwu347. [Epub ahead of print]

Hormone Therapy and Young-Onset Breast Cancer.

O'Brien KM, Fei C, Sandler DP, Nichols HB, DeRoo LA, Weinberg CR.

Estrogen plus progestin hormone therapy (HT) is associated with an increased risk of postmenopausal breast cancer, but few studies have examined the impact of HT use on the risk of breast cancer in younger women. We assessed the association between estrogen plus progestin HT or unopposed estrogen HT and young-onset breast cancer using data from the Two Sister Study (2008-2010), a sister-matched study of 1,419 cases diagnosed with breast cancer before the age of 50 years and 1,665 controls. We assessed exposures up to a family-specific index age to ensure comparable opportunities for exposures and used propensity scores to control for birth cohort effects on HT use. Ever HT use was uncommon (7% and 11% in cases and controls, respectively). Use of estrogen plus progestin was not associated with an increased risk of young-onset breast cancer (odds ratio = 0.80, 95% confidence interval: 0.41, 1.59). Unopposed estrogen use was inversely associated with the risk of young-onset breast cancer (odds ratio = 0.58, 95% confidence interval: 0.34, 0.99). Duration of use, age at first use, and recency of use did not modify these associations.