



Selección de Resúmenes de Menopausia

Semana del 23 al 29 de mayo de 2018

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

Climacteric. 2018 May 23;1-6. doi: 10.1080/13697137.2018.1463982. [Epub ahead of print]

Non-clinical studies of progesterone.

Sitruk-Ware R.

Progesterone is a steroid hormone that is essential for the regulation of reproductive function. Progesterone has been approved for several indications including the treatment of anovulatory menstrual cycles, assisted reproductive technology, contraception during lactation and, when combined with estrogen, for the prevention of endometrial hyperplasia in postmenopausal hormonal therapy. In addition to its role in reproduction, progesterone regulates a number of biologically distinct processes in other tissues, particularly in the nervous system. This physiological hormone is poorly absorbed when administered in a crystalline form and is not active when given orally, unless in micronized form, or from different non-oral delivery systems that allow a more constant delivery rate. A limited number of preclinical studies have been conducted to document the toxicity, carcinogenicity and overall animal safety of progesterone delivered from different formulations, and these rather old studies showed no safety concern. More recently, it has been shown in animal experiments that progesterone, its metabolite allopregnanolone and structurally related progestins have positive effects on neuroregeneration and repair of brain damage, as well as myelin repair. These recent preclinical findings have the potential to accelerate therapeutic translation for multiple unmet neurological needs.

Arch Osteoporos. 2018 May 22;13(1):61. doi: 10.1007/s11657-018-0458-0.

The effect of cholecystectomy on 25-hydroxyvitamin D levels and bone mineral density in postmenopausal women.

Polat HB, Beyazal MS.

PURPOSE: The influence of bile salts on vitamin D absorption is well-known, and increased incidence of vitamin D deficiency has been reported in patients with gastrointestinal disorders. Little is known on the potentially deleterious effect of cholecystectomy on vitamin D levels and osteoporosis. Herein, we aimed to investigate the effects of cholecystectomy on vitamin D levels and osteoporosis in postmenopausal women. **METHODS:** The study group comprised 50 postmenopausal women who had previously undergone cholecystectomy; the control group comprised 50 age-matched postmenopausal women. Serum vitamin D, calcium, and phosphorus levels were determined. Bone mineral density (BMD) was determined using dual-energy X-ray absorptiometry. **RESULTS:** The study group had significantly higher parathyroid hormone levels (94.4 ± 45.1 vs. 69.2 ± 37.5 , $p < 0.001$) but significantly lower 25-hydroxyvitamin D levels (16.3 ± 7.6 vs. 19.8 ± 8.7 , $p = 0.03$). Compared with the control group, the BMDs of both the lumbar spine (-1.5 ± 1.0 vs. -0.9 ± 1.0 , $p = 0.004$) and femur (-0.5 ± 0.8 vs. 0.19 ± 1.1 , $p = 0.001$) were significantly lower in the study group. Body mass index [$B = 0.81$ (CI 0.67-0.98), $p = 0.03$] and prior cholecystectomy [$B = 7.9$ (CI 1.0-71.7), $p = 0.04$] were independent predictors of osteoporosis. **CONCLUSION:** In postmenopausal women, prior cholecystectomy is associated with lower serum 25-hydroxyvitamin D levels and BMD.

Korean J Fam Med. 2018 May;39(3):155-160. doi: 10.4082/kjfm.2018.39.3.155. Epub 2018 May 18.

Effects of Age at First Childbirth and Other Factors on Central Obesity in Postmenopausal Women: The 2013-2015 Korean National Health and Nutrition Examination Survey.

Lee WJ, Yoon JW, Lee JH, Kwag BG, Chang SH, Choi YJ.

BACKGROUND: Waist circumference is one of the key components of metabolic syndrome. Recent studies demonstrated that the reproductive profile was associated with metabolic syndrome in postmenopausal women. This study focused on the association between central obesity and age at first childbirth. It also considered other factors associated with central obesity in postmenopausal women. **METHODS:** This study was based on the 2013-2015 Korean National Health and Nutrition Examination Survey and involved 3,143 naturally postmenopausal women. These women were divided into three groups according to their age at first childbirth: 19 years or younger ($n=252$), 20-29 years ($n=2,695$), and 30 years or older ($n=196$). Multivariate analysis using logistic regression was performed to evaluate the

effects of various reproductive factors, including other confounding factors. RESULTS: During adjustment for confounding factors, in the early age at first childbirth group, odds ratios (95% confidence intervals) for central obesity decreased. In the final model, younger age at first childbirth was not significantly related to central obesity (waist circumference more than 85 cm) in naturally postmenopausal women after adjusting for other confounding factors. CONCLUSION: Younger age at first childbirth was not significantly associated with central obesity after adjustment for confounding factors.

J Natl Cancer Inst. 2018 May 18. doi: 10.1093/jnci/djy040. [Epub ahead of print]

The Effects of Metformin and Weight Loss on Biomarkers Associated With Breast Cancer Outcomes.

Patterson RE, Marinac CR, Sears DD, Kerr J, Hartman SJ, Cadmus-Bertram L, Villaseñor A, Flatt SW, Godbole S et al. Background: This study investigated the effects of metformin and weight loss on biomarkers associated with breast cancer prognosis. Methods: Overweight/obese postmenopausal breast cancer survivors (n = 333) were randomly assigned to metformin vs placebo and to a weight loss intervention vs control (ie, usual care). The 2 × 2 factorial design allows a single randomized trial to investigate the effect of two factors and interactions between them. Outcomes were changes in fasting insulin, glucose, C-reactive protein (CRP), estradiol, testosterone, and sex-hormone binding globulin (SHBG). The trial was powered for a main effects analysis of metformin vs placebo and weight loss vs control. All tests of statistical significance were two-sided. Results: A total of 313 women (94.0%) completed the six-month trial. High prescription adherence (ie, ≥80% of pills taken) ranged from 65.9% of participants in the metformin group to 81.3% of those in the placebo group (P < .002). Mean percent weight loss was statistically significantly higher in the weight loss group (-5.5%, 95% confidence interval [CI] = -6.3% to -4.8%) compared with the control group (-2.7%, 95% CI = -3.5% to -1.9%). Statistically significant group differences (ie, percent change in metformin group minus placebo group) were -7.9% (95% CI = -15.0% to -0.8%) for insulin, -10.0% (95% CI = -18.5% to -1.5%) for estradiol, -9.5% (95% CI = -15.2% to -3.8%) for testosterone, and 7.5% (95% CI = 2.4% to 12.6%) for SHBG. Statistically significant group differences (ie, percent change in weight loss group minus placebo group) were -12.5% (95% CI = -19.6% to -5.3%) for insulin and 5.3% (95% CI = 0.2% to 10.4%) for SHBG. Conclusions: As adjuvant therapy, weight loss and metformin were found to be a safe combination strategy that modestly lowered estrogen levels and advantageously affected other biomarkers thought to be on the pathway for reducing breast cancer recurrence and mortality.

J Clin Endocrinol Metab. 2018 May 18. doi: 10.1210/jc.2018-00579. [Epub ahead of print]

Reproductive Hormones and Subclinical Cardiovascular Disease in Midlife Women.

Thurston RC, Bhasin S, Chang Y, Barinas Mitchell E, Matthews KA, Jasuja R, Santoro N.

Reproductive hormones are understood to be important to the pathophysiology of cardiovascular disease (CVD) in women. However, standard estradiol (E2) and testosterone (T) assays lack sensitivity at the levels of postmenopausal women. Objective: Investigate relations of mass spectrometry-assessed estrone (E1), estradiol (E2), and testosterone (T), and sex hormone binding globulin (SHBG) and subclinical CVD in women. Design, Setting, Participants: 304 peri- and postmenopausal women, aged 40-60 years, and free of clinical CVD underwent subclinical CVD measurements. E1, E2, and T were assayed using liquid chromatography-tandem mass spectrometry; Free T (FT) was estimated using ensemble allosteric models. Associations between hormones and outcomes were analyzed using regression models adjusting for CVD risk factors. Main Outcome Measures: Carotid artery intima media thickness (IMT), inter-adventitial diameter (IAD), plaque; brachial flow mediated dilation (FMD). Results: Higher E1 was related to higher FMD [b(SE)=-.77(.37), p=.04], indicating better endothelial function. Higher E2 was related to lower IAD [b(SE)=-.07(.02), p=.004], indicating less carotid remodeling. Higher SHBG was related to higher FMD [b(SE)=1.31(.40), p=.001], yet higher IAD [b(SE)=.15(.06), p=.02] and carotid plaque [OR (95%CI)=1.84(1.16-2.91), p=.009]. Higher FT was associated with lower FMD [b(SE)=-1.58(.52), p=.003], yet lower IAD [b(SE)=-.19(.08), p=.01] and carotid plaque [OR(95%CI)=.49(.28-.88), p=.02]. Thus, higher SHBG and lower FT was associated with better endothelial function, yet greater carotid remodeling and plaque. Main Conclusions: Endogenous E1 levels were related to endothelial function and E2 to vascular remodeling, suggesting distinct roles of these estrogens. SHBG and free testosterone have a complex role and depend on the vessel under study.

Menopause. 2018 May 21. doi: 10.1097/GME.0000000000001137. [Epub ahead of print]

Physical performance in relation to menopause status and physical activity.

Bondarev D, Laakkonen EK, Finni T, Kokko K, Kujala UM, Aukee P, Kovanen V, Sipilä S.

OBJECTIVE: The aim of this study was to examine differences in physical performance (muscle power, muscle strength, aerobic capacity, and walking speed) across menopausal stages and potential of leisure physical activity (PA) to modify the impact of menopause on physical performance. **METHODS:** In this cross-sectional study, women aged 47 to 55 were randomly selected from the Finnish National Registry and categorized as premenopausal (n=233), perimenopausal (n=381), or postmenopausal (n=299) based on serum concentrations of follicle-stimulating hormone and bleeding diary. Physical performance was measured by knee extension force, handgrip force, vertical jumping height, maximal walking speed, and 6-minute walking distance. PA level was assessed by self-report and categorized as low, moderate, or high. Multivariate linear regression modeling was used for data analysis. **RESULTS:** After including fat mass, height, PA, and education in the model, the postmenopausal women showed 12.0N weaker ($P<0.001$) handgrip force and 1.1cm lower ($P<0.001$) vertical jumping height than the premenopausal women. There was no significant interaction between menopausal stage and PA on physical performance. The peri- and postmenopausal women with a high PA, however, showed better performance in the maximal knee extension strength and 6-minute walking test, and showed greater lower body muscle power than those with a low PA. **CONCLUSIONS:** Menopause status is associated with muscle strength and power, whereas the association between menopause status and mobility/walking is clearly weaker. A high leisure PA level provides more capacity to counteract the potential negative influence of menopausal factors on muscle function

Menopause. 2018 May 21. doi: 10.1097/GME.0000000000001136. [Epub ahead of print]

Metabolic syndrome and its components in premenopausal and postmenopausal women: a comprehensive systematic review and meta-analysis on observational studies.

Hallajzadeh J, Khoramdad M, Izadi N, Karamzad N, Almasi-Hashiani A, Ayubi E, Qorbani M, Pakzad R, et al.

OBJECTIVES: To perform a meta-analysis on the global prevalence of metabolic syndrome (MetS) in postmenopausal women. The meta-analysis also sought to measure the relationship menopause status has with MetS and its components. **METHODS:** The Web of Science, Medline, PubMed, Scopus, Embase, CINAHL, DOAJ, and Google Scholar were all searched using the relevant keywords. Articles published during the period 2004 to 2017 that met our inclusion criteria and reported the prevalence of MetS among premenopausal and postmenopausal women were included. In the presence of heterogeneity, random-effects models were used to pool the prevalence and odds ratios (ORs), as measures of association in cross-sectional and comparative cross-sectional studies, respectively. **RESULTS:** The prevalence of MetS among postmenopausal women (119 studies [n=95,115]) and the OR comparing the prevalence of MetS among postmenopausal and premenopausal women (23 studies [n=66,801]) were pooled separately. The pooled prevalence of MetS among postmenopausal women was found to be 37.17% (95% confidence interval [CI] 35.00%-39.31%), but varied from 13.60% (95% CI 13.55%-13.64%) to 46.00% (95% CI 1.90%-90.09%), depending upon the diagnostic criteria used. The overall pooled OR for MetS in postmenopausal women, compared with premenopausal women, was OR 3.54 (95% CI 2.92-4.30), but this ranged from OR 2.74 (95% CI 1.32-5.66) to OR 5.03 (95% CI 2.25-11.22), depending upon the criteria used. Furthermore, the odds of high fasting blood sugar (OR 3.51, 95% CI 2.11-5.83), low high-density lipoprotein cholesterol (OR 1.45, 95% CI 1.03-2.03), high blood pressure (OR 3.95, 95% CI 2.01-7.78), high triglycerides (OR 3.2, 95% CI 2.37-4.31), and high waist circumference (OR 2.75, 95% CI 1.80-4.21) were all found to be higher in postmenopausal women than in premenopausal women. **CONCLUSIONS:** The prevalence of MetS is relatively high in postmenopausal women and was more prevalent among postmenopausal than premenopausal women. Menopausal hormone therapy should be used with caution in patients with MetS, as its safety has not yet been evaluated among MetS patients and meticulous evaluation of each individual patient before starting MHT is needed.