Selección de Resúmenes de Menopausia

Semana del 9 al 15 de Junio 2021

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

Aging Clin Exp Res. 2021 Jun 12.doi: 10.1007/s40520-021-01894-z. Online ahead of print.

Vitamin D and coronavirus disease 2019 (COVID-19): rapid evidence review

Zahra Raisi-Estabragh 1 2 , Adrian R Martineau 3 , Elizabeth M Curtis 4 , Rebecca J Moon 4 , et al.

Background: The rapid global spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), has re-ignited interest in the possible role of vitamin D in modulation of host responses to respiratory pathogens. Indeed, vitamin D supplementation has been proposed as a potential preventative or therapeutic strategy. Recommendations for any intervention, particularly in the context of a potentially fatal pandemic infection, should be strictly based on clinically informed appraisal of the evidence base. In this narrative review, we examine current evidence relating to vitamin D and COVID-19 and consider the most appropriate practical recommendations. Observations: Although there are a growing number of studies investigating the links between vitamin D and COVID-19, they are mostly small and observational with high risk of bias, residual confounding, and reverse causality. Extrapolation of molecular actions of 1,25(OH)2-vitamin D to an effect of increased 25(OH)-vitamin D as a result of vitamin D supplementation is generally unfounded, as is the automatic conclusion of causal mechanisms from observational studies linking low 25(OH)-vitamin D to incident disease. Efficacy is ideally demonstrated in the context of adequately powered randomised intervention studies, although such approaches may not always be feasible. Conclusions: At present, evidence to support vitamin D supplementation for the prevention or treatment of COVID-19 is inconclusive. In the absence of any further compelling data, adherence to existing national guidance on vitamin D supplementation to prevent vitamin D deficiency, predicated principally on maintaining musculoskeletal health, appears appropriate.

Gynecol Oncol. 2021 Jun 8;S0090-8258(21)00442-X.doi: 10.1016/j.ygyno.2021.05.036. Online ahead of print.

What happens after menopause? (WHAM): A prospective controlled study of sleep quality up to 12 months after premenopausal risk-reducing salpingo-oophorectomy

Martha Hickey 1 , Katrina M Moss 2 , Efrosinia O Krejany 3 , C David Wrede 4 , Susan M Domchek 5 , et al

Objective: Sleep difficulties impair function and increase the risk of depression at menopause and premenopausal oophorectomy may further worsen sleep. However, prospective data are limited, and it remains uncertain whether Hormone Therapy (HT) improves sleep. This prospective observational study measured sleep quality before and up to 12 months after risk-reducing salpingo-oophorectomy (RRSO) compared to a similar age comparison group who retained their ovaries.Methods: Ninety-five premenopausal women undergoing RRSO and 99 comparisons were evaluated over a 12-month period using the Pittsburgh Sleep Quality Index (PSQI). Results: Almost half reported poor sleep quality at baseline. Overall sleep quality was not affected by RRSO until 12 months ($p = 0.007$). However, sleep disturbance increased by 3 months and remained significantly elevated at 12 months ($p < 0.001$). Trajectory analysis demonstrated that 41% had increased sleep disturbance after RRSO which persisted in 17.9%. Risk factors for sleep disturbance included severe vasomotor symptoms, obesity and smoking. Around 60% initiated HT after RRSO. Sleep quality was significantly better in HT users vs non users ($p = 0.020$) but HT did not restore sleep quality to baseline levels. Conclusions: Overall sleep quality is not affected by RRSO, but new onset sleep disturbance is common, particularly in those with severe vasomotor symptoms. Clinicians should be alert to new-onset sleep disturbance and the potential for HT to improve sleep quality.

Neurosci Lett. 2021 Jun 8;136038.doi: 10.1016/j.neulet.2021.136038. Online ahead of print.

Estrogen Pendulum in Schizophrenia and Alzheimer's Disease: Review of Therapeutic Benefits and Outstanding Questions

Renáta Androvičová 1 , James G Pfaus 2 , Saak V Ovsepian 3

Although produced largely in the periphery, gonadal steroids play a key role in regulating the development and functions of the central nervous system and have been implicated in several chronic neuropsychiatric disorders, with schizophrenia

and Alzheimer's disease (AD) most prominent. Despite major differences in pathobiology and clinical manifestations, in both conditions, estrogen transpires primarily with protective effects, buffering the onset and progression of diseases at various levels. As a result, estrogen replacement therapy (ERT) emerges as one of the most widely discussed adjuvant interventions. In this review, we revisit evidence supporting the protective role of estrogen in schizophrenia and AD and consider putative cellular and molecular mechanisms. We explore the underlying functional processes relevant to the manifestation of devastating conditions, with a focus on synaptic transmission and plasticity mechanisms. We discuss specific effects of estrogen deficit on neurotransmitter systems such as cholinergic, dopaminergic, serotoninergic, and glutamatergic. While the evidence from both, preclinical and clinical reports, in general, are supportive of the protective effects of estrogen from cognitive decline to synaptic pathology, numerous questions remain, calling for further research.

Curr Pharm Des. 2021 Jun 10.doi: 10.2174/1381612827666210610114029. Online ahead of print.

Metabolic syndrome and myocardial infarction in women

Djuro Macut 1 , Sanja Ognjanović 1 , Milika Ašanin 2 , Gordana Krljanac 2 , Tatjana Milenković 3

Metabolic syndrome (MetS) represents a cluster of metabolic disorders that arise from insulin resistance (IR) and adipose tissue dysfunction. As a consequence, there is an increased risk for type 2 diabetes mellitus and atherosclerotic cardiovascular disease (CVD). MetS is associated with a 2-fold increase in cardiovascular outcomes. Earlier population analyses showed a lower prevalence of MetS in women (23.9%) in comparison to men (27.8%), while later analyses suggested significantly reduced difference due to an increase in prevalence in women aged between 20 and 39. However, the prevalence of MetS in specific populations of women, such as in women with polycystic ovary syndrome, ranges from 16% to almost 50% in some geographic regions. Abdominal fat accumulation and IR syndrome are recognized as the most important factors in the pathogenesis of MetS. After menopause, a decline in insulin sensitivity corresponds to an increase in fat mass, circulating fatty acids, low-density lipoproteins, and triglycerides. Prevalence of MetS in acute coronary syndrome (ACS) is significantly more present in women (55.9%-66.3%) than in men (40.2%-47.3%) in different cohorts. Younger women with ACS had a higher mortality rate than younger men. Acute myocardial infarction (AMI) remains a leading cause of death in aging women. Women with AMI have significantly higher rates of prior congestive heart failure, hypertension history, and diabetes. The role of androgens in CVD pathogenesis in women has not yet been clarified. The current review aims to give an insight into the role of MetS components and inflammation for the development of atherosclerosis, CVD, and AMI in women.

Medicine (Baltimore). 2021 Jun 11;100(23):e26216.doi: 10.1097/MD.0000000000026216.

Variants translating reduced expression of the beta estrogen receptor gene were associated with increased carotid intima media thickness: A cross-sectional study in late postmenopausal women

Antonio-Jorge Cano-Marquina, Miguel-Ángel García-Pérez, Juan J Tarín, Alicia M Maceira, et al.

There is debate on the role of estrogens in modulating the risk for atherosclerosis in women. Our purpose was to investigate whether the size of the estrogenic impact was independently associated with variation of carotid intima-media thickness (IMT) in healthy late postmenopausal women. The levels of circulating estrogens have been used in previous studies but the influence of SNPs of the estrogen receptors (ER) α and β have not been investigated. We performed a crossed-sectional study of 91 women in a university hospital. We used a double approach in which, in addition to the measurement of estradiol levels by ultrasensitive methods, genetic variants (SNPs) associated with differing expression of the ER α and β genes were assessed. Multivariable analysis was used to examine the association of candidate factors with the value of IMT and plaque detection at both the carotid wall and the sinus. A genotype combination translating reduced gene expression of the ERβ was directly associated with IMT at both the carotid wall (P = .001) and the sinus (P = .002). Other predictors of IMT were the levels of glucose, positively associated with IMT at both the carotid wall (P < .001) and the sinus (P = .001), age positively associated with IMT at the sinus (P = .003), and levels of vitamin D, positively associated with IMT at the carotid wall (P = .04). Poorer estrogenic impact, as concordant with a SNP variant imposing reduced expression of the ERβ, was directly associated with IMT at both the carotid wall and the sinus. Glucose level, vitamin D only for the carotid wall, and age only for the sinus, also emerged as independent factors in the IMT variance.

Endocr Pract. 2021 Jun 7;S1530-891X(21)01077-6.doi: 10.1016/j.eprac.2021.05.012. Online ahead of print.

Switching to denosumab or bisphosphonates after completion of teriparatide treatment in women with severe postmenopausal osteoporosis

Tomaz Kocjan, Antonela Sabati Rajic, Andrej Janez, Gaj Vidmar, Nina Orehek, Janja Marc, Barbara Ostanek

Objective: We compared bone mineral density (BMD) changes after 12 months' treatment with denosumab or bisphosphonates in postmenopausal women with severe osteoporosis after stopping teriparatide therapy. Methods: We retrospectively analyzed 140 postmenopausal women (mean age 74.2 years) with severe osteoporosis who had been treated with teriparatide for 18–24 months at our outpatient clinic in a tertiary endocrine center between 2006 and 2015. After stopping teriparatide, they continued treatment with a bisphosphonate (alendronate, risedronate, ibandronate, or zoledronic acid) or denosumab, while receiving daily vitamin D and calcium. BMD at the lumbar spine (LS), total hip (TH), and femoral neck (FN) was measured by dual-energy X-ray absorptiometry when teriparatide was discontinued (baseline) and after 12 months of further treatment. Multivariate linear regression models were used to identify predictors of BMD gain. Results: After stopping teriparatide, 70 women continued treatment with bisphosphonates and 70 received denosumab. LS, but not TH or FN, BMD gain was significantly greater in the denosumab than the bisphosphonates group at 12 months. Multivariate analysis showed that BMD gain at the LS was negatively associated with bisphosphonate versus denosumab treatment, and positively associated with baseline serum total procollagen type 1 N-terminal propeptide (PINP). BMD gains at the FN were predicted by higher baseline serum urate levels. BMD gains at the TH and FN were negatively associated with pretreatment BMD gains at the same site.Co nclusions: Twelve months after stopping teriparatide, sequential denosumab treatment appears to yield higher additional LS BMD gain on average compared to bisphosphonates.

Sci Rep. 2021 Jun 9;11(1):10867.doi: 10.1038/s41598-021-90084-y.

Menopause impacts human brain structure, connectivity, energy metabolism, and amyloid-beta deposition

Lisa Mosconi, Valentina Berti, Jonathan Dyke, Eva Schelbaum, Steven Jett , Lacey Loughlin, Roberta Diaz Brinton.

All women undergo the menopause transition (MT), a neuro-endocrinological process that impacts aging trajectories of multiple organ systems including brain. The MT occurs over time and is characterized by clinically defined stages with specific neurological symptoms. Yet, little is known of how this process impacts the human brain. This multi-modality neuroimaging study indicates substantial differences in brain structure, connectivity, and energy metabolism across MT stages (pre-menopause, peri-menopause, and post-menopause). These effects involved brain regions subserving higher-order cognitive processes and were specific to menopausal endocrine aging rather than chronological aging, as determined by comparison to age-matched males. Brain biomarkers largely stabilized post-menopause, and gray matter volume (GMV) recovered in key brain regions for cognitive aging. Notably, GMV recovery and in vivo brain mitochondria ATP production correlated with preservation of cognitive performance post-menopause, suggesting adaptive compensatory processes. In parallel to the adaptive process, amyloid-β deposition was more pronounced in peri-menopausal and post-menopausal women carrying apolipoprotein E-4 (APOE-4) genotype, the major genetic risk factor for late-onset Alzheimer's disease, relative to genotype-matched males. These data show that human menopause is a dynamic neurological transition that significantly impacts brain structure, connectivity, and metabolic profile during midlife endocrine aging of the female brain.

Maturitas. 2021 May 24;S0378-5122(21)00075-X.doi: 10.1016/j.maturitas.2021.05.005. Online ahead of print.

The effect of exercise training on blood pressure in menopause and postmenopausal women: A systematic review of randomized controlled trials

Andrés F Loaiza-Betancur 1 , Iván Chulvi-Medrano 2 , Víctor A Díaz-López 1 , Cinta Gómez-Tomás 3

The prevalence of hypertension is higher in postmenopausal than in premenopausal women. Regular exercise training has been shown to be effective in addressing hypertension. The aim of this systematic review was to synthesize the effect of exercise training on systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) in menopausal and postmenopausal women. This review was reported according to the PRISMA statement and registered in PROSPERO. The literature search was done in MEDLINE, Embase, Cochrane CENTRAL and ClinicalTrials. Randomized controlled trials involving menopausal and postmenopausal women undergoing exercise training were included. Two blinded reviewers assessed risk of bias in the included studies by using the Cochrane Risk of Bias tool. A random-effects model was used for all analyses. Significance was set at $P < 0.05$. Compared with the control group, exercise training resulted in clinically significant reductions on SBP (MD -3.43 mmHg; 95% CI, -5.16, -

1.71; P < 0.0001), DBP (MD, -2.25 mmHg; 95% CI, -3.40, -1.11; P = 0.0001) and MAP (MD, -3.48 mmHg; 95% CI, -5.84, -1.11; P = 0.004). Aerobic training (AT) did not produce a significant reduction in SBP, DBP and MAP (P >0.05). Combined training (CT) generated larger reductions. Exercise training generated small but clinically relevant reductions in SBP, DBP and MAP in menopausal and postmenopausal women, younger or older than 65 years, with prehypertension or hypertension. AT did not lead to a clinically relevant improvement in blood pressure (BP) in this population. In addition, CT showed the largest reductions in SBP, DBP and MAP.

Ther Adv Endocrinol Metab. 2021 Apr 22;12:20420188211010052.doi: 10.1177/20420188211010052.

Should denosumab treatment for osteoporosis be continued indefinitely?

Jane A Noble 1 , Malachi J McKenna 2 , Rachel K Crowley 3

Denosumab was approved for the treatment of postmenopausal osteoporosis in 2010, based on the FREEDOM study, which indicated a benefit in terms of increased bone mineral density and reduced risk of major osteoporotic fracture. In the initial clinical studies it was noted that discontinuation of denosumab can lead to a rebound of bone turnover markers and loss of accrued bone mineral density. An increased risk of fractures (multiple vertebral fractures in particular) associated with discontinuation was noted after approval and marketing of denosumab. For many patients experiencing gain in bone mineral density and fracture prevention while taking denosumab, there is no reason to stop therapy. However, discontinuation of denosumab may happen due to non-adherence; potential lack of efficacy in an individual; where reimbursement for therapy is limited to those with bone mineral density in the osteoporosis range, when assessment reveals this has been exceeded; or patient or physician concern regarding side effects. This review paper aims to discuss these concerns and to summarize the data available to date regarding sequential osteoporosis therapy following denosumab cessation to reduce the risk of multiple vertebral fracture.

J Sex Med. 2021 Jun 5;S1743-6095(21)00427-6.doi: 10.1016/j.jsxm.2021.04.004. Online ahead of print.

Physical Activity and Female Sexual Dysfunction: A Lot Helps, But Not Too Much

Elisa Maseroli 1 , Giulia Rastrelli 2 , Vincenza Di Stasi 1 , Sarah Cipriani 1 , Irene Scavello 1 , ET AL.

Background: Research on the relationship between physical activity (PA) and female sexual dysfunction (FSD) is lacking. Aim: To investigate the clinical, psychological, and sexual correlates of PA in women with FSD. Methods: A non-selected series of n = 322 pre- and post-menopausal patients consulting for FSD was retrospectively studied. Regular involvement in PA and its frequency (<1 hour/week: sedentary, 1-3 hours/week: active, 4-6 hours/week: very active, >6 hours/week: extremely active) were investigated with a specific question. Outcomes: FSDs, including HSDD (Hypoactive sexual desire disorder) and FGAD (Female genital arousal disorder), were diagnosed according to a structured and clinical interview. Participants underwent a physical examination and a clitoral Doppler ultrasound, and were asked to complete the Female Sexual Function Index, Female Sexual Distress Scale-Revised, Body Uneasiness Test, and Middlesex Hospital Questionnaire. Results: At multivariate analysis, women engaging in PA (67.4%, n = 217) scored significantly higher in several Female Sexual Function Index domains - including desire, arousal and lubrication - and showed lower sexual distress and lower resistance of clitoral arteries, as compared to sedentary women. A significant, inverse association between PA and HSDD was observed. Mediation analysis demonstrated that the negative association between PA and HSDD was partly mediated by body image concerns (Body Uneasiness Test Global severity index), psychopathological symptoms (Middlesex Hospital Questionnaire total score) and sexual distress (Female Sexual Distress Scale-Revised score). These latter 2 factors also partly mediated the association between PA and a reduced risk of FGAD, whilst a lower BMI was a full mediator in the relationship between PA and FGAD. Finally, extreme PA was associated with significantly worse scores in several psychosexual parameters (i,e, sexual satisfaction and histrionic/hysterical symptoms), even compared to a sedentary lifestyle. Clinical implications: Women consulting for FSD may gain benefits on desire, arousal, lubrication and sex-related distress from regular PA; however, physicians should remain alert to the downsides of excessive exercise. Strengths & limitations: The main strength lies in the novelty of the findings. The main limitations are the cross-sectional nature, the clinical setting, the small sample size of the different PA groups, and the use of self-reported instruments for the evaluation of PA. Conclusion: In women with FSD, PA was associated with better sexual function and clitoral vascularization, lower sexual distress and reduced odds of HSDD and FGAD; the benefits of PA on sexuality were mediated by both psychological and organic determinants; excessive PA was related with a poor overall sexual function and with a low sexual satisfaction.