Selección de Resúmenes de Menopausia

Semana del 15 al 21 de Octubre de 2014

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

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Effects of Estradiol and Venlafaxine on Insomnia Symptoms and Sleep Quality in Women with Hot Flashes.

Ensrud KE, Guthrie KA, Hohensee C, Caan B, Carpenter JS, Freeman EW, LaCroix AZ, Landis CA, Manson J, et al.

Study Objectives: Determine effects of low-dose estradiol and low-dose venlafaxine on self-reported sleep measures in menopausal women with hot flashes. **Design:** 3-arm double-blind randomized trial. Participants assigned in a 2:2:3 ratio to 17β estradiol 0.5 mg/day (n = 97), venlafaxine XR 75 mg/day (n = 96), or placebo (n = 146) for 8 weeks. **Setting:** Academic research centers. **Participants:** 339 community-dwelling perimenopausal and postmenopausal women with ≥2 bothersome hot flashes per day. **Measurements and Results:** Insomnia symptoms (Insomnia Severity Index [ISI]) and sleep quality (Pittsburgh Sleep Quality Index [PSQI]) at baseline, week 4 and 8; 325 women (96%) provided ISI data and 312 women (92%) provided PSQI data at baseline and follow-up. At baseline, mean (SD) hot flash frequency was 8.1/day (5.3), mean ISI was 11.1 (6.0), and mean PSQI was 7.5 (3.4). Mean (95% CI) change from baseline in ISI at week 8 was -4.1 points (-5.3 to -3.0) with estradiol, -5.0 points (-6.1 to -3.9) with venlafaxine, and -3.0 points (-3.8 to -2.3) with placebo (P overall treatment effect vs. placebo 0.09 for estradiol and 0.007 for venlafaxine). Mean (95% CI) change from baseline in PSQI at week 8 was -2.2 points (-2.8 to -1.6) with estradiol, -2.3 points (-2.9 to -1.6) with venlafaxine, and -1.2 points (-1.7 to -0.8) with placebo (P overall treatment effect vs. placebo 0.04 for estradiol and 0.06 for venlafaxine). **Conclusions:** Among perimenopausal and postmenopausal women with hot flashes, both low dose oral estradiol and low-dose venlafaxine compared with placebo modestly reduced insomnia symptoms and improved subjective sleep quality.

J Obstet Gynaecol. 2014 Oct 17:1-5. [Epub ahead of print]

Association between pelvic organ prolapse and bone mineral density in postmenopausal women.

Lee SW, Cho HH, Kim MR, You YO, Kim SY, Hwang YB, Kim JH.

Both pelvic organ prolapse (POP) and osteoporosis are age-related diseases in older aged women. Both POP and bone metabolism may be associated with collagen metabolism. Our study determined the relationship between POP and bone mineral density (BMD) of the lumbar spine and femur neck in postmenopausal women. We selected 554 postmenopausal women (aged 50-79 years) and divided them into two groups (moderate to severe POP and absent to mild POP). We compared the BMDs of the lumbar spine and femur neck between the moderate to severe POP and absent to mild POP groups. Lumbar spine BMD was inversely correlated with POP severity (p = 0.001). However, after adjusting for age, time since menopause, height, weight, body mass index (BMI), and vaginal delivery, the BMDs of both the lumbar spine and femur neck were not significantly different between the moderate to severe POP and absent to mild POP groups (p = 0.583 and p = 0.305, respectively). A lower BMD is associated with increased fracture risk and we postulated that women with severe POP would have an increased risk of osteoporotic fracture.

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Is postmenopausal hormone replacement therapy suitable after a cardio- or cerebrovascular event?

Windler E1, Stute P, Ortmann O, Mueck AO.

PURPOSE: Vascular disease is the leading cause of death in women. One-third of acute events affect women below age 60, when the prevalence of menopausal symptoms is high. This raises the question if hormone replacement therapy (HRT) may be an appropriate treatment for individual women although vascular disease is generally considered a contraindication. METHODS: Selective literature search was used for this study. RESULTS: In healthy women, HRT increases risks for venous thromboembolism and ischemic stroke, but for cardiovascular disease apparently only beyond 10 years after menopause or 60 years of age. Limited data in women with cardio or cerebrovascular disease have not demonstrated an increased risk for a vascular recurrent event, but for the first year after initiation. In HRT users affected by a cardiovascular event continuation of HRT has not been found to be associated with adverse outcome. Low dose

estradiol--preferentially as transdermal patches, if necessary combined with metabolically neutral progestins--appears to convey lower risk. CONCLUSIONS: Safety data on HRT in survivors of cardiovascular events or ischemic stroke are limited, but exceptionally increased risk appears to be excluded. If off-label use of HRT is considered to be initiated or continued in women with cardio- or cerebrovascular disease, extensive counseling on the pros and cons of HRT is mandatory.

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Comparison of Fracture Risk Prediction by the US Preventive Services Task Force Strategy and Two Alternative Strategies in Women 50-64 Years Old in the Women's Health Initiative.

Crandall CJ, Larson JC, Watts NB, Gourlay ML, Donaldson MG, LaCroix A, Cauley JA, Wactawski-Wende J, et al.

Context: The United States Preventive Services Task Force (USPSTF) recommends osteoporosis screening for women younger than 65 years whose 10-year predicted risk of major osteoporotic fracture (MOF) is at least 9.3% using the Fracture Risk Assessment Tool. In postmenopausal women age 50-64 years old, it is uncertain how the USPSTF screening strategy compares with the Osteoporosis Self-Assessment Tool and the Simple Calculated Osteoporosis Risk Estimate (SCORE) in discriminating women who will and will not experience MOF. Objective: This study aimed to assess the sensitivity, specificity, and area under the receiver operating characteristic curve of the three strategies for discrimination of incident MOF over 10 years of follow-up among postmenopausal women age 50-64 years. Setting and Design: Prospective study, 1993-2008 at 40 US Centers. Participants: Participants of the Women's Health Initiative Observational Study and Clinical Trials (n = 62 492), age 50-64 years, not taking osteoporosis medication. Main Outcome Measures: Ten-year (observed) incidence of MOF. Results: For identifying women with incident MOF, sensitivity of the strategies ranged from 25.8-39.8%, specificity ranged from 60.7-65.8%, and area under the curve values ranged from 0.52-0.56. The sensitivity of the USPSTF strategy for identifying incident MOF ranged from 4.7% (3.3-6.0) among women age 50-54 years to 37.3% (35.4-39.1) for women age 60-64 years. Adjusting the thresholds to improve sensitivity resulted in decreased specificity. Conclusions: Our findings do not support use of the USPSTF strategy, Osteoporosis Self-Assessment Tool, or SCORE to identify younger postmenopausal women who are at higher risk of fracture. Our findings suggest that fracture prediction in younger postmenopausal women requires assessment of risk factors not included in currently available strategies.

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Bisphosphonates in adjuvant setting for breast cancer: a review of the meta-analysis of bisphosphonates' effects on breast cancer recurrence presented in December 2013 at San Antonio Breast Conference.

Costa L.

PURPOSE OF REVIEW: Bisphosphonate therapy has been used as standard of care for patients with metastatic bone disease. As bisphosphonate had demonstrated antitumor effects in preclinical studies, it was natural to advance to the development of large phase 3 trials that would test the activity of bisphosphonate in the adjuvant setting. Surprisingly, the results of adjuvant breast cancer trials have shown either modest or contradictory effects. One of the most consistent results across the latest reports on this issue is that bisphosphonate shows benefit in the prevention of distant relapses in breast cancer women after menopause, but not before. We sought to comment on the most recent studies and to reflect on the possible practical recommendations for the use of bisphosphonate in this setting. RECENT FINDINGS: In the last San Antonio Breast Cancer Conference, the Early Breast Cancer Trialists' Collaborative Group's Bisphosphonate Working Group presented a meta-analysis of individual patient data from randomized trials. The main conclusions of this presentation were that all bisphosphonates (not only nitrogen-containing bisphosphonates) can decrease bone recurrence in postmenopausal women with early breast cancer. SUMMARY: The benefit of bisphosphonate use in an adjuvant setting is significant only in postmenopausal women. Further investigation into factors influencing the response to bisphosphonate treatment is needed.

Semin Reprod Med. 2014 Nov;32(6):454-62. doi: 10.1055/s-0034-1384629. Epub 2014 Oct 16.

Insights into the Epidemiology of Postmenopausal Osteoporosis: The Women's Health Initiative.

Jackson RD, Mysiw WJ.

Osteoporosis and its associated increased risk for fragility fracture is one of the most disabling consequences of aging in women. To successfully reduce the public health burden of this pervasive disease, it is necessary to develop strategies that permit the earlier identification of women at risk for fracture and ensure that preventive interventions to reduce the risk for fracture are both safe and effective. The Women's Health Initiative offers the unprecedented opportunity to systematically address both of these issues. Eleven clinically available risk factors (age, race/ethnicity, self-reported health, weight, height, physical activity, parental hip fracture, fracture history after age 54, current smoking, corticosteroid use, and history of treated diabetes), have been identified to predict 5-year hip fracture risk in white women. Two of these factors (age and fracture history) also predict risk for total fractures in women irrespective of race-ethnicity. Biomarkers including low vitamin D or bioavailable testosterone and/or high cystatin C, pro-inflammatory cytokines, osteoprotegerin and sex hormone-binding globulin also predict risk for hip fracture independent of clinical risk factors. Two cornerstones of therapy for postmenopausal osteoporosis-postmenopausal hormone therapy and calcium plus vitamin D supplementation- were rigorously studied. Estrogen with or without a progestin was effective at preventing bone loss and reducing risk for hip, clinical vertebral and total fractures but the balance of risks and benefits failed to show an overall benefit of taking estrogen-alone or estrogen plus progestin as a preventive strategy for skeletal health. Calcium plus vitamin D supplementation also demonstrated a small but significant favorable effect on hip bone density but in contrast, the modest effect did not translate into a significant reduction in the risk of fractures in intent-to-treat analyses. Data such as these have helped to lay a foundation for the more effective management of postmenopausal osteoporosis.

Neural Regen Res. 2012 Dec 15;7(35):2761-9. doi: 10.3969/j.issn.1673-5374.2012.35.003.

Activities of autonomic neurotransmitters in Meibomian gland tissues are associated with menopausal dry eye.

Li L, Jin D, Gao J, Wang L, Liu X, Wang J, Xu Z.

The secretory activities of meibomian glands are regulated by the autonomic nervous system. The change in density and activity of autonomic nerves in meibomian glands during menopause play an important role in the pathogenesis of dry eye. In view of this, we established a dry eye rat model by removing the bilateral ovaries. We used neuropeptide Y and vasoactive intestinal polypeptide as markers of autonomic neurotransmitters. Our results showed that the concentration of estradiol in serum significantly decreased, the density of neuropeptide Y immunoreactivity in nerve fibers significantly increased, the density of vasoactive intestinal polypeptide immunoreactivity in nerve fibers significantly decreased, and the ratio of vasoactive intestinal polypeptide/neuropeptide Y positive staining significantly decreased. These results suggest that a decrease in ovary activity may lead to autonomic nervous system dysfunction, thereby affecting the secretory activity of the meibomian gland, which participates in sexual hormone imbalance-induced dry eye.

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Effects of long-term alendronate treatment on postmenopausal osteoporosis bone material properties.

Hassler N, Gamsjaeger S, Hofstetter B, Brozek W, Klaushofer K, Paschalis EP.

Raman microspectroscopic analysis of iliac crest from patients that were treated with alendronate (ALN) for 10 years revealed minimal, transient alterations in bone material properties confined to actively forming bone surfaces compared to patients that were on ALN for 5 years. These changes were not encountered in the bulk tissue. INTRODUCTION: Alendronate (ALN) and other bisphosphonates (BPs) are the most widely prescribed therapy for postmenopausal osteoporosis. Despite their overall excellent safety record and efficacy in reducing fractures, questions have been raised regarding potential detrimental effects that may be related to prolonged bone turnover reduction, although no definite cause-effect relationship has been established to date. The purpose of the present study was to evaluate bone material properties in patients that were receiving ALN for 5 or 10 years. METHODS: Raman microspectroscopic analysis was used to analyze iliac crest biopsies from postmenopausal women with osteoporosis who had been treated with ALN for 5 years and were then re-randomized to placebo (PBO, N = 14), 5 mg/day ALN (N = 10), or 10 mg/day ALN (N = 6) for another 5 years. The parameters monitored and expressed as a function of tissue age were (i) the mineral/matrix ratio (MM), (ii) the relative proteoglycan content (PG), (iii) the relative lipid content (LPD), (iv) the mineral maturity/crystallinity (MMC), and (v) the relative pyridinoline content (PYD). RESULTS: The obtained data indicate that 10-year ALN use results in minimal, transient bone tissue composition changes compared to use for 5 years, confined to actively forming trabecular surfaces, implying potential differences in bone matrix maturation that

nevertheless did not result in differences of these values in bulk tissue. CONCLUSIONS: The data suggest that prolonged reduction in bone turnover during 10 years of therapy with ALN by itself is unlikely to be associated with adverse effects on bone material properties.