Selección de Resúmenes de Menopausia

Semana del 25 de Noviembre al 1 de Diciembre de 2015

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chil

J Bone Miner Res. 2015 Nov 28. doi: 10.1002/jbmr.2757. [Epub ahead of print]

Hydrogen Sulfide Is a Novel Regulator of Bone Formation Implicated in the Bone Loss Induced by Estrogen Deficiency.

Grassi F, Malik Tyagi A, Calvert JW, Gambari L, Walker LD, Yu M, Robinson J, Li JY, Lisignoli G, et al.

Hydrogen sulfide (H2 S) is a gasotransmitter known to regulate bone formation and bone mass in unperturbed mice. However, it is presently unknown whether H2 S plays a role in pathologic bone loss. Here we show that ovariectomy (ovx), a model of postmenopausal bone loss, decreases serum H2 S levels and the bone marrow (BM) levels of two key H2 S-generating enzymes, cystathione β-synthase (CBS) and cystathione γ-lyase (CSE). Treatment with the H2 S-donor GYY4137 (GYY) normalizes serum H2 S in ovx mice, increases bone formation and completely prevents the loss of trabecular bone induced by ovx. Mechanistic studies revealed that GYY increases murine osteoblastogenesis by activating Wnt signaling through increased production of the Wnt ligands Wnt16, Wnt2b, Wnt6 and Wnt10b in the BM. Moreover, in vitro treatment with 17β-estradiol upregulates the expression of CBS and CSE in human BM stromal cells (hSCs), while a H2 S-releasing drug induces osteogenic differentiation of hSCs. In summary, regulation of H2 S levels is a novel mechanism by which estrogen stimulates osteoblastogenesis and bone formation in mice and human cells. Blunted production of H2 S contributes to ovx induced bone loss in mice by limiting the compensatory increase in bone formation elicited by ovx. Restoration of H2 S levels is a potential novel therapeutic approach for postmenopausal osteoporosis.

Maturitas. 2015 Nov 10. pii: S0378-5122(15)00808-7. doi: 10.1016/j.maturitas.2015.11.003. [Epub ahead of print]

EMAS position statement: Testosterone replacement therapy in the aging male.

Dimopoulou C, Ceausu I, Depypere H, Lambrinoudaki I, Mueck A, Pérez-López FR, Rees M, et al.

INTRODUCTION: Late-onset hypogonadism (LOH) represents a common clinical entity in aging males, characterized by the presence of symptoms (most usually of a sexual nature, such as decreased libido, decreased spontaneous erections and erectile dysfunction) and signs, in combination with low serum testosterone concentrations. Whether testosterone replacement therapy (TRT) should be offered to those individuals is still under extensive debate. AIMS: The aim of this position statement is to provide and critically appraise evidence on TRT in the aging male, focusing on pathophysiology and characteristics of LOH, indications for TRT, available therapeutic agents, monitoring and treatment-associated risks. MATERIALS AND METHODS: Literature review and consensus of expert opinion. RESULTS AND CONCLUSIONS: Diagnosis and treatment of LOH is justified, if a combination of symptoms of testosterone deficiency and low testosterone is present. Patients receiving TRT could profit with regard to obesity, metabolic syndrome, type 2 diabetes mellitus, sexual function and osteoporosis and should undergo scheduled testing for adverse events regularly. Potential adverse effects of TRT on cardiovascular disease, prostate cancer and sleep apnea are as yet unclear and remain to be investigated in large-scale prospective studies. Management of aging men with LOH should include individual evaluation of co-morbidities and careful risk versus benefit assessment.

Clin Cases Miner Bone Metab. 2015 May-Aug;12(2):139-141. Epub 2015 Oct 26.

Vascular calcification and fracture risk.

Szulc P.

Osteoporosis and cardiovascular diseases are public health problems. Fragility fractures are associated with high risk of cardiovascular event and patients with cardiovascular diseases have higher risk of fracture. Severe abdominal aortic calcification (AAC) is associated with higher cardiovascular mortality and morbidity. Severe AAC is associated with higher risk of fracture. In cross-sectional studies severe AAC was associated with greater prevalence, higher number and greater severity of vertebral fractures after adjustment for confounders including bone mineral

density (BMD). Prospective studies confirm the association between baseline AAC severity and prospectively assessed fracture risk in both sexes. Data on the link between AAC and BMD are discordant. Age, smoking, hypertension, diabetes mellitus, and low grade systemic inflammation are possible risk factors of severe AAC and fracture risk. However, in clinical studies, the link between AAC and fracture was significant after adjustment for these factors. Data on the association between calcification in other vascular beds and BMD are limited and discordant.

Cancer Prev Res (Phila). 2015 Nov 24. pii: canprevres.0284.2015. [Epub ahead of print]

Inflammatory marker changes in postmenopausal women after a year-long exercise intervention comparing high versus moderate volumes.

Friedenreich CM, O'Reilly R, Shaw E, Stanczyk FZ, Yasui Y, Brenner DR, Courneya KS.

This randomized dose comparison trial examined if higher exercise volume decreased inflammatory biomarkers, associated with postmenopausal breast cancer risk, more than moderate exercise volume. The Breast Cancer and Exercise Trial in Alberta (BETA) was a two-center, two-armed randomized trial in 400 inactive, healthy, postmenopausal women, aged 50-74 years, with a body mass index of 22-40 kg/m2. Participants were randomized to high (300 minutes/week) or moderate (150 minutes/week) volumes of aerobic exercise while maintaining usual diet. Fasting blood concentrations of C-reactive protein (CRP), interleukin-6 (IL-6), and tumour necrosis factor-alpha (TNF-α), were measured at baseline, six, and 12-months. Intention-to-treat analysis was performed using linear mixed models adjusted for baseline biomarker concentrations. Intention-to-treat analyses of 386 (97%) participants showed no statistically significant group differences for changes in biomarker levels at 6 and 12 months. Additionally, we did not observe any modification of this effect by baseline characteristics of participants. In post hoc analyses based on self-selected exercise level (measured in minutes/week) , CRP decreased by 22.45% for participants who exercised >246 minutes/week (highest quintile) and increased by 0.07% for those who exercised <110 minutes/week (lowest quintile, P-trend=0.04), adjusted for baseline covariates. When this analysis was restricted to include exercise time in the target heart rate zone only, statistically significant trends were observed for both CRP (P<0.01) and IL-6 (P=0.04). Prescribing 300 minutes/week of moderate-to-vigorous aerobic exercise did not improve inflammatory markers compared to 150 minutes/week in postmenopausal women. Decreases in CRP were observed with higher self-selected exercise volume.

Int J Cancer. 2015 Nov 24. doi: 10.1002/ijc.29942. [Epub ahead of print]

Menopausal Hormone Therapy use and breast cancer risk in Australia: Findings from the New South Wales Cancer Lifestyle and EvAluation of Risk (CLEAR) study.

Salagame U, Banks E, Sitas F, Canfell K.

Randomised controlled trials and large scale observational studies have found that current use of Menopausal Hormone Therapy (MHT) is associated with an increased risk of breast cancer; this risk is higher for oestrogen-progestagen combination therapy than for oestrogen only therapy. The current study was designed to estimate MHT-associated breast cancer risk in a population of Australian women. Data were analysed for postmenopausal women with self-reported incident invasive breast cancer (n=1,236) and cancer-free controls (n=862), recruited between 2006 and 2014 into a large case-control study for all cancer types, the NSW CLEAR study. Information on past and current MHT use was collected from all participants, along with other lifestyle and demographic factors, using a self-administered questionnaire. Unmatched multivariable logistic regression was performed, adjusting for socio-demographic, reproductive and health behaviour variables, body mass index and breast screening history. Compared to never-users of MHT, the adjusted odds ratio (aOR) for breast cancer in current users of any type of MHT was 2.09(95%CI: 1.57-2.78; p<0.0001) and for past users of any type of MHT the aOR was 1.03(0.82-1.28; p=0.8243). For current users of oestrogen-only and oestrogen-progestagen therapy, aORs were 1.80(1.21-2.68; p=0.0039) and 2.62(1.56-4.38; p=0.0003), respectively. These findings are consistent with those from other international observational studies, that current, but not past, use of MHT is associated with a substantially increased risk of breast cancer.

Gynecol Oncol. 2015 Nov 17. pii: S0090-8258(15)30190-6. doi: 10.1016/j. [Epub ahead of print]

Sexual activity and functioning after risk-reducing salpingo-oophorectomy: impact of hormone replacement therapy.

Johansen N, Liavaag AH, Tanbo TG, Dahl AA, Pripp AH, Michelsen TM.

OBJECTIVE: To examine sexual activity and functioning in women after risk-reducing salpingo-oophorectomy (RRSO) compared with the general population (NORM). METHODS: Retrospective cohort study. 294 women who underwent RRSO and 1228 women from the NORM group provided written information based on mailed questionnaires. Sexual pleasure and discomfort scores and frequency of sexual activity were evaluated using the Sexual Activity Questionnaire. RESULTS: The RRSO group reported less sexual pleasure (10.5 vs 11.9, P = 0.009), more discomfort (1.9 vs 0.83, P < 0.001), and less frequent sex than did the controls. Significant associations were observed between a lower pleasure score and being in the RRSO group, older age, history of cancer, low body image, high level of role functioning, and low level of global quality of life (QoL). Further, significant associations were detected between more discomfort and being in the RRSO group, older age, history of cancer, poor body image, and low level of global QoL. Hormone replacement therapy (HRT) use had no impact on pleasure or discomfort score in regression analyses among all the sexually active women. However, in subanalyses of the RRSO group, users of systemic HRT reported less discomfort (1.2 vs 2.4, P = 0.001) than did the nonusers. CONCLUSIONS: After RRSO, women reported significantly less sexual pleasure, more discomfort, and less frequent sex compared with the controls. In the RRSO group, systemic HRT users reported less discomfort than did the nonusers. Health care providers should be attentive to these issues when counseling before and after prophylactic surgery.

Eur J Cancer. 2015 Nov 17. pii: S0959-8049(15)00845-X. doi: 10.1016/j.ejca.2015.08.028. [Epub ahead of print]

A phase II trial of low-dose estradiol in postmenopausal women with advanced breast cancer and acquired resistance to aromatase inhibition.

Zucchini G, Armstrong AC, Wardley AM, Wilson G, Misra V, Seif M, Ryder WD, Cope J, Blowers E, Howell A, Palmieri C, Howell SJ.

BACKGROUND: High-dose oestrogen (HDE) is effective but toxic in postmenopausal women with advanced breast cancer (ABC). Prolonged oestrogen deprivation sensitises BC cell lines to estrogen and we hypothesised that third-generation aromatase inhibitors (AIs) would sensitise BCs to low-dose estradiol (LDE). METHODS: A single-arm phase II study of LDE (2 mg estradiol valerate daily) in postmenopausal women with estrogen receptor-positive (ER+) ABC. The primary end-point was clinical benefit (CB) rate. If LDE was ineffective, HDE was offered. If LDE was effective, retreatment with the pre-LDE AI was offered on progression. RESULTS: Twenty-one patients were recruited before the trial was closed early due to slow accrual; 19 were assessable for efficacy and toxicity. CB was seen in 5 in 19 patients (26%; 95% confidence interval 9.1-51.2%), all with prolonged SD (median duration 16.8 months; range 11.0-29.6). Treatment was discontinued for toxicity in 4 in 19 patients (21%) and 8 in 11 women without hysterectomy experienced vaginal bleeding (VB). After primary LDE failure, three patients received HDE and one achieved a partial response (PR). Following CB on LDE, four patients restarted pre-LDE AI and three achieved CB including one PR. Those with CB to LDE had a significantly longer duration of first-line endocrine therapy for ABC than those without (54.9 versus 16.8 months; p < 0.01) CONCLUSION: LDE is an effective endocrine option in women with evidence of prolonged sensitivity to AI therapy. LDE is reasonably well tolerated although VB is an issue. Re-challenge with the pre-LDE AI following progression confirms re-sensitisation as a true phenomenon.