Selección de Resúmenes de Menopausia

Semana del 23 al 29 de agosto de 2017

Juan Enrique Blümel. Departamento Medicina Sur. Universidad de Chile

Stem Cell Res. 2017 Aug 18;24:69-76. doi: 10.1016/j.scr.2017.08.012. [Epub ahead of print]

Epidermal growth factor as a mechanosensitizer in human bone marrow stromal cells.

Müller-Deubert S, Seefried L, Krug M, Jakob F, Ebert R.

Epidermal growth factors (EGFs) e.g. EGF, heparin-binding EGF and transforming growth factor alpha and their receptors e.g. EGFR and ErbB2 control proinflammatory signaling and modulate proliferation in bone marrow stromal cells (BMSC). Interleukin-6 and interleukin-8 are EGF targets and participate in the inflammatory phase of bone regeneration via non-canonical wnt signaling. BMSC differentiation is also influenced by mechanical strain-related activation of ERK1/2 and AP-1, but the role of EGFR signaling in mechanotransduction is unclear. We investigated the effects of EGFR signaling in telomerase-immortalized BMSC, transfected with a luciferase reporter, comprising a mechanoresponsive AP1 element, using ligands, neutralizing antibodies and EGFR inhibitors on mechanotransduction and we found that EGF via EGFR increased the response to mechanical strain. Results were confirmed by qPCR analysis of mechanoresponsive genes. EGF-responsive interleukin-6 and interleukin-8 were synergistically enhanced by EGF stimulation and mechanical strain. We show here in immortalized and primary BMSC that EGFR signaling enhances mechanotransduction, indicating that the EGF system is a mechanosensitizer in BMSC. Alterations in mechanosensitivity and -adaptation are contributors to age-related diseases like osteoporosis and the identification of a suitable mechanosensitizer could be beneficial. The role of the synergism of these signaling cascades in physiology and disease remains to be unraveled.

Microbiol Spectr. 2017 Aug;5(4). doi: 10.1128/microbiolspec.BAD-0015-2016.

The Potential of Probiotics as a Therapy for Osteoporosis.

Collins FL, Rios-Arce ND, Schepper JD, Parameswaran N, McCabe LR.

Osteoporosis, characterized by low bone mass and micro-architectural deterioration of bone tissue with increased risk of fracture, can be categorized into two forms: primary and secondary, depending on whether it occurs as part of the natural aging process (estrogen deficiency) or as part of disease pathology. In both forms bone loss is due to an imbalance in the bone remodeling process, with resorption/formation skewed more toward bone loss. Recent studies and emerging evidence consistently demonstrate the potential of the intestinal microbiota to modulate bone health. This review discusses the process of bone remodeling and the pathology of osteoporosis and introduces the intestinal microbiota and its potential to influence bone health. In particular, we highlight recent murine studies that examine how probiotic supplementation can both increase bone density in healthy individuals and protect against primary (estrogen deficiency) as well as secondary osteoporosis. Potential mechanisms are described to account for how probiotic treatments could be exerting their beneficial effect on bone health.

Korean J Intern Med. 2017 Aug 25. doi: 10.3904/kjim.2016.205. [Epub ahead of print]

Aromatase inhibitor use is a risk factor of carotid plaque presence in endocrine-responsive breast cancer patients.

Seo DH, Cho Y, Lee S, Park S, Kim SI, Park BW, Rhee Y.

Background/Aims: The aromatase inhibitors (AIs) are well known anti-hormonal therapy in endocrine-responsive breast cancer patients. It can lead to dyslipidemia and be the risk factor of cardiovascular disease due to low estrogen level. However, some recent studies comparing AIs with placebo have shown controversial results. The aim of this study was to investigate lipid profiles, measurement of carotid intima-media thickness (IMT) and the presence of plaque among endocrine-responsive breast cancer treated with AIs compared to ones that were not treated with AIs.
Methods: A total of 85 postmenopausal women, who underwent breast cancer surgery during the age of 50 to 64 without history of statin use were included. There were 42 patients who were treated with AIs over 1 year (group 1) and 43 patients without AIs use (group 2). Serum total cholesterol, high density lipoprotein cholesterol, triglycerides, fasting blood glucose, carotid IMT, and presence of plaque were assessed. Results: The baseline characteristics were

similar between two groups and there was no significant difference in carotid IMT irrespective of AIs administration. However, ultrasonographic evaluation of carotid artery revealed that the presence of plaque in AI users was significantly higher than in non-AI users (66.7% vs. 41.9%, p = 0.02; odds ratio, 4.21 in adjusted model; p = 0.01). History of diabetes was also the significant risk factor for the plaque formation. Conclusions: There was no significant difference in lipid profile itself between two groups, but more importantly the presence of the plaque was much higher indicating possible detrimental effect of AI on cardiovascular system.

PLoS One. 2017 Aug 24;12(8):e0182383. doi: 10.1371/journal.pone.0182383. eCollection 2017.

Development of a tool for prediction of ovarian cancer in patients with adnexal masses: Value of plasma fibrinogen.

Seebacher V, Aust S, D'Andrea D, Grimm C, Reiser E, Tiringer D, Von Mersi H, Polterauer S, Reinthaller A, et al.

OBJECTIVE: To develop a tool for individualized risk estimation of presence of cancer in women with adnexal masses, and to assess the added value of plasma fibrinogen. STUDY DESIGN: We performed a retrospective analysis of a prospectively maintained database of 906 patients with adnexal masses who underwent cystectomy or oophorectomy. Uni- and multivariate logistic regression analyses including pre-operative plasma fibrinogen levels and established predictors were performed. A nomogram was generated to predict the probability of ovarian cancer. Internal validation with split-sample analysis was performed. Decision curve analysis (DCA) was then used to evaluate the clinical net benefit of the prediction model. RESULTS: Ovarian cancer including borderline tumours was found in 241 (26.6%) patients. In multivariate analysis, elevated plasma fibrinogen, elevated CA-125, suspicion for malignancy on ultrasound, and postmenopausal status were associated with ovarian cancer and formed the basis for the nomogram. The overall predictive accuracy of the model, as measured by AUC, was 0.91 (95% CI 0.87-0.94). DCA revealed a net benefit for using this model for predicting ovarian cancer presence compared to a strategy of treat all or treat none. CONCLUSION: We confirmed the value of plasma fibrinogen as a strong predictor for ovarian cancer in a large cohort of patients with adnexal masses. We developed a highly accurate multivariable model to help in the clinical decision-making regarding the presence of ovarian cancer. This model provided net benefit for a wide range of threshold probabilities. External validation is needed before a recommendation for its use in routine practice can be given.

J Clin Psychiatry. 2017 Aug 22. pii: 16m11276. doi: 10.4088/JCP.16m11276. [Epub ahead of print]

Association Between Bone Mineral Density and Depressive Symptoms in a Population-Based Sample.

Hlis RD, McIntyre RS, Maalouf NM, Van Enkevort E, Brown ES.

OBJECTIVE: This analysis was conducted to determine the relationship between bone mineral density (BMD) and depressive symptoms in a population-based cohort. METHODS: Data were extracted from the second phase of the Dallas Heart Study (DHS-2), a large, multiethnic population sample in Dallas County, Texas, from September 1, 2007, to December 31, 2009. Depressive symptom severity was measured with the 16-item Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR_{16}), which is derived from DSM-IV major depressive disorder criteria. BMD was measured using dual-energy x-ray absorptiometry. Multiple linear regressions examined the relationship between QIDS-SR_{16} score and BMD controlling for age, body mass index, sex, ethnicity, smoking status, alcohol use status, serum 25-hydroxyvitamin D concentration, antidepressant use, and physical activity as measured by total vigorous and moderate metabolic equivalents. Subgroup analyses explored differences related to age. RESULTS: QIDS-SR_{16} score was not a significant predictor of either lumbar spine or total hip T-score (β = -0.01, P = .61 and β = -0.02, P = .39) in the overall population (n = 2,285). There was a significant negative interaction term between age and QIDS-SR_{16} group (β = -0.01, P = .01). In participants aged 60 years or older (n = 465), QIDS-SR_{16} score was a significant predictor of BMD at the lumbar spine and total hip (β = -0.14, P = .003 and β = -0.12, P = .006, respectively). CONCLUSIONS: QIDS-SR_{16} score did not significantly predict BMD in the overall DHS-2 sample. There was, however, a significant association observed in participants aged $\geq$ 60 years. Results suggest that diagnosis and treatment of depressive symptoms may be of clinical importance in older individuals, a subgroup at high risk for osteoporosis and fractures.

Stem Cells Transl Med. 2017 Aug 18. doi: 10.1002/sctm.17-0054. [Epub ahead of print]

Concise Review: Musculoskeletal Stem Cells to Treat Age-Related Osteoporosis.

Kiernan J, Davies JE, Stanford WL.

Age-related (type-II) osteoporosis is a common and debilitating condition driven in part by the loss of bone marrow (BM) mesenchymal stromal cells (MSC) and their osteoblast progeny, leading to reduced bone formation. Current pharmacological regiments targeting age-related osteoporosis do not directly treat the disease by increasing bone formation, but instead use bisphosphonates to reduce bone resorption-a treatment designed for postmenopausal (type-I) osteoporosis. Recently, the bone regenerative capacity of MSCs has been found within a very rare population of skeletal stem cells (SSCs) residing within the larger heterogeneous BM-MSC pool. The osteoregenerative potential of SSCs would be an ideal candidate for cell-based therapies to treat degenerative bone diseases such as osteoporosis. However, to date, clinical and translational studies attempting to improve bone formation through cell transplantation have used the larger, nonspecific, MSC pool. In this review, we will outline the physiological basis of age-related osteoporosis, as well as discuss relevant preclinical studies that use exogenous MSC transplantation with the aim of treating osteoporosis in murine models. We will also discuss results from specific clinical trials aimed at treating other systemic bone diseases, and how the discovery of SSC could help realize the full regenerative potential of MSC therapy to increase bone formation. Finally, we will outline how ancillary clinical trials could be initiated to assess MSC/SSC-mediated bone formation gains in existing and potentially unrelated clinical trials, setting the stage for a dedicated clinical investigation to treat age-related osteoporosis.

Menopause. 2017 Aug 21. doi: 10.1097/GME.0000000000000971. [Epub ahead of print]

Effects of oral versus transdermal menopausal hormone treatments on self-reported sleep domains and their association with vasomotor symptoms in recently menopausal women enrolled in the Kronos Early Estrogen Prevention Study (KEEPS).

Cintron D, Lahr BD, Bailey KR, Santoro N, Lloyd R, Manson JE, Neal-Perry G, Pal L, Taylor HS, et al.

OBJECTIVE: This study determined whether two different formulations of hormone therapy (HT): oral conjugated equine estrogens (o-CEE; 0.45 mg/d, n=209), transdermal 17β-estradiol (t-E2; 50 μg/d, n=201) plus cyclic progesterone (Prometrium, 200 mg) or placebo (PBO, n=243) affected sleep domains in participants of the Kronos Early Estrogen Prevention Study. METHODS: Participants completed the Pittsburgh Sleep Quality Index at baseline and during the intervention at 6, 18, 36, and 48 months. Global sleep quality and individual sleep domain scores were compared between treatments using analysis of covariance, and correlated with vasomotor symptom (VMS) scores using Spearman correlation coefficients. RESULTS: Global Pittsburgh Sleep Quality Index scores (mean 6.3; 24% with score >8) were similar across groups at baseline and were reduced (improved sleep quality) by both HT (average change -1.27 [o-CEE] and -1.32 [t-E2]) when compared with PBO (-0.60; P=0.001 [o-CEE vs PBO] and P=0.002 [t-E2 vs PBO]). Domain scores for sleep satisfaction and latency improved with both HT. The domain score for sleep disturbances improved more with t-E2 than o-CEE or PBO. Global sleep scores significantly correlated with VMS severity (rs=0.170, P<0.001 for hot flashes; rs=0.177, P<0.001 for night sweats). Change in scores for all domains except sleep latency and sleep efficiency correlated with change in severity of VMS. CONCLUSIONS: Poor sleep quality is common in recently menopausal women. Sleep quality improved with both HT formulations. The relationship of VMS with domains of sleep suggests that assessing severity of symptoms and domains of sleep may help direct therapy to improve sleep for postmenopausal women.