Selección de Resúmenes de Menopausia

Semana del 10 al 16 de Junio de 2015

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Hypothyroidism Is a Risk Factor for New-Onset Diabetes Mellitus: A Cohort Study.

Gronich N, Deftereos SN, Lavi I, Persidis AS, Abernethy DR, Rennert G.

OBJECTIVE: To identify risk factors for the development of statin-associated diabetes mellitus (DM). RESEARCH DESIGN AND METHODS: The study was conducted in two phases. Phase one involved high-throughput in silico processing of a large amount of biomedical data to identify risk factors for the development of statin-associated DM. In phase two, the most prominent risk factor identified was confirmed in an observational cohort study at Clalit, the largest health-care organization in Israel. Time-dependent Poisson regression multivariable models were performed to assess rate ratios (RRs) with 95% CIs for DM occurrence. RESULTS: A total of 39,263 statin nonusers were matched by propensity score to 20,334 highly compliant statin initiators in 2004-2005 and followed until the end of 2010. Within 59,597 statin users and nonusers in a multivariable model, hypothyroidism and subclinical hypothyroidism carried an increased risk for DM (RR 1.53 [95% CI 1.31-1.79] and 1.75 [1.40-2.18], respectively). Hypothyroidism increased DM risk irrespective of statin treatment (RR 2.06 [1.42-2.99] and 1.66 [1.05-2.64] in statin users and nonusers, respectively). Subclinical hypothyroidism risk for DM was prominent only upon statin use (RR 1.94 [1.13-3.34] and 1.20 [0.52-2.75] in statin users and nonusers, respectively). Patients with hypothyroidism treated with thyroid hormone replacement therapy were not at increased risk for DM. CONCLUSIONS: Hypothyroidism is a risk factor for DM. Subclinical hypothyroidism-associated risk for DM is prominent only upon statin use. Identifying and treating hypothyroidism and subclinical hypothyroidism might reduce DM risk. Future clinical studies are needed to confirm the findings.

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Parathyroid hormone plus alendronate in osteoporosis: a meta-analysis of randomized controlled trials.

Zhang Q, Qian J, Zhu Y.

BACKGROUND: Parathyroid hormone (PTH) increases both bone formation (BMD) and bone resorption, whereas alendronate reduces bone resorption. It is possible that the combination therapy of PTH with alendronate will enhance their effects on BMD. Therefore, we conducted this meta-analysis to evaluate the efficacy of the combination therapy of PTH with alendronate in the treatment of patients with osteoporosis. METHODS: A comprehensive literature search of PubMed, Embase, and Web of Science was conducted to identify relative studies. Eligible studies were randomized controlled trials (RCT), which assessed the efficacy of combination therapy in patients with osteoporosis. The outcomes included the mean percent increases in BMD of lumbar spine, femoral neck, total hip, and distal radius. Weighted mean difference (WMD) with 95% confidence intervals (CIs) were calculated using of random-effects or fixed-effects model, depending on the heterogeneity between the included studies. RESULTS: Six RCTs with a total number of 833 patients were included in this meta-analysis. The pooled estimates showed that, the combination therapy of PTH with alendronate resulted in a higher mean percent change of increased BMD in distal radius (WMD = 2.45, 95% CI: 1.58, 3.31; P = 0.000), but not in lumbar spine (WMD = -0.83, 95% CI: -3.48, 1.81; P = 0.538), femoral neck (WMD = -0.99, 95% CI: -2.04, 0.07; P = 0.068), and total hip (WMD = -0.06, 95% CI: -0.93, 0.81; P = 0.892). The subgroup analysis based on the dosage and schedule of PTH, study duration, gender of patients, and anabolic agents, were conducted. And results revealed that among the patients in the combination therapy group, greater increases in the spine BMD were observed when the PTH was administered with a dosage of 20 μg (WMD = 2.33, 95% CI: 1.24, 3.43; P = 0.000), or the treatment duration lasted more than 12 months (WMD = 2.23, 95% CI: 1.00, 3.47; P = 0.000), or the combination therapy was used in osteoporosis women (WMD = 1.58, 95% CI: 0.63, 2.53; P = 0.001). However, the combination of PTH of 40 μg with alendronate produced a decrease in the BMD at spine (WMD = -4.56, 95% CI: -7.56, -1.56; P = 0.003) and femoral neck (WMD = -5.82, 95% CI: -9.91, -1.72; P = 0.005). CONCLUSION: Our findings indicated that the addition of alendronate to PTH in the treatment of osteoporosis, reduced the ability of PTH therapy to increase the BMD at the lumbar spine, femoral neck, and total hip.

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Treatment of menopausal symptoms with three low-dose continuous sequential 17β-estradiol/progesterone parenteral monthly formulations using novel non-polymeric microsphere technology.

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OBJECTIVE: To analyze the short-term efficacy and safety over menopausal symptoms of three low-dose continuous sequential 17β-estradiol (E)/progesterone (P) parental monthly formulations using novel non-polymeric microspheres. METHODS: This was a multicenter, randomized, single blinded study in which peri- and postmenopausal women were assigned to receive a monthly intramuscular injection of 0.5 mg E + 15 mg P (Group A, n = 34), 1 mg E + 20 mg P (Group B, n = 24) or 1 mg E + 30 mg P (Group C, n = 26) for 6 months. Primary efficacy endpoints included mean change in the frequency and severity of hot flushes and the effect over urogenital atrophy symptoms at 3 and 6 months. Safety variables included changes in the rate of amenorrhea, endometrial thickness and histopathology, and local and systemic adverse events. RESULTS: Compared to baseline at month 6, the three treatment schemes significantly decreased the rate of urogenital atrophy symptoms and the frequency (mean number per day) and severity (mean number graded as moderate and severe per month) of hot flushes. No differences in studied efficacy parameters were observed between studied groups at baseline or at the end of the study. For all groups the most frequent adverse event was pain at the injection site; however they were all rated as mild. At the end of the study peri- and postmenopausal women displayed no significant changes in endometrial thickness or histopathology in all treated groups. The rate of amenorrhea at the end of the study decreased for all studied groups yet was less evident among postmenopausal women as compared to perimenopausal ones. CONCLUSIONS: The three low-dose continuous sequential intramuscular monthly treatments of E/P using novel microsphere technology were effective at reducing menopausal symptoms at short-term with a low rate of adverse events. More long-term and comparative research is warranted to support our positive findings.

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Comparing clinical and economic outcomes of biologic and conventional medications in postmenopausal women with osteoporosis.

Hernandez I, Zhang Y.

RATIONALE, AIMS AND OBJECTIVES: Biologics are substantially more expensive than their conventional counterparts but it is unclear whether extra costs deliver better health outcomes. We compare clinical and economic outcomes between teriparatide (monthly costs $1120) and bisphosphonates (monthly costs $14) among postmenopausal women with osteoporosis. METHODS: From a 5% random sample of Medicare beneficiaries, we selected women newly diagnosed with osteoporosis between 1 January 2007 and 31 December 2011 and who initiated teriparatide or bisphosphonates after the diagnosis. We followed them up until one of these events: switching osteoporosis treatment, death, or the end of study period - 31 December 2011. Clinical outcomes included hip fracture, vertebral fracture, fracture of radius, ulna or carpal bones, other upper limb fractures, other lower limb fractures and any fracture. Economic outcomes included medical costs, pharmacy costs, and total costs associated with osteoporosis. Using conventional propensity score, high-dimensional propensity score and instrumental variable analysis, we constructed Cox proportional hazards models to evaluate the risk of fracture and two-part models to compare costs. RESULTS: Teriparatide users had higher risk of fracture and higher costs, compared with similar bisphosphonates users. The hazard ratios of fracture for teriparatide relative to bisphosphonates ranged from 1.37 to 2.12, depending on methods. There was no difference in the risk of hip fracture between treatment groups. Total annual costs related to osteoporosis were between $2733 and $3352 higher for teriparatide users. CONCLUSIONS: The biological agent, teriparatide, is more expensive yet less effective than conventional treatment,

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Duration of ovarian hormone exposure and atherosclerotic cardiovascular disease in Korean women: the Korean Heart Study.

Jung KJ, Kim MR, Yun YD, Kim HC, Jee SH.

OBJECTIVE: Although reproductive and hormonal factors, such as menarche and menopause, have been reported as independent risk factors for atherosclerotic cardiovascular disease (ASCVD), few studies have examined these factors in East Asian populations. In the Korean Heart Study, ASCVD risk related to duration of ovarian hormone exposure was examined in a cohort of 66,104 Korean women. METHODS: Study members were recruited from participants of routine

health examinations at health promotion centers across South Korea in 1996-2004. Ovarian hormone exposure was defined as duration between menarche and menopause. Incidence rates for ASCVD, stroke, and ischemic heart disease were examined in relation to ovarian hormone exposure. RESULTS: The mean duration of ovarian hormone exposure at study baseline was 33.7 years, and risk for ASCVD was negatively associated with duration. Women with shorter ovarian hormone exposure (<30 y) had a higher risk of developing ASCVD (hazard ratio [HR], 1.30; 95% CI, 1.01-1.68) than women with longer ovarian hormone exposure (35-35 y). In similar comparison groups, women with ovarian hormone exposure shorter than 30 years were at increased risk for developing total stroke (HR, 1.18; 95% CI, 1.00-1.38), thrombotic stroke (HR, 1.30; 95% CI, 1.05-1.61), ischemic heart disease (HR, 1.40; 95% CI, 1.19-1.63), and acute myocardial infarction (HR, 1.73; 95% CI, 1.08-2.47). CONCLUSIONS: Our study provides further confirmation of increased cardiovascular risk with shorter reproductive years. Therefore, women with reduced lifetime ovarian hormone exposure should focus on minimizing ASCVD risk by lifestyle modifications such as smoking avoidance or increased physical activities.

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Combined exercise ameliorates ovariectomy-induced cognitive impairment by enhancing cell proliferation and suppressing apoptosis.

Kim TW, Kim CS, Kim JY, Kim CJ, Seo JH.

OBJECTIVE: Estrogen plays an important role in cognitive function, including attention, learning, and memory, and affects the structure and function of brain areas. We investigated the effects of combined exercise on memory deficits induced by ovariectomy (OVX) in relation to cell proliferation and apoptosis in the hippocampus. METHODS: Rats were randomly divided into four groups: sham, sham and exercise, OVX, and OVX and exercise. Rats in combined exercise groups were subjected to 3 days of resistance training and 3 days of running (for a total of 6 d/wk) for eight consecutive weeks. Rats were tested in step-down avoidance task and Morris water maze task to verify the effects of OVX on short-term and spatial working memory. RESULTS: In the present study, the number of BrdU-positive and doublecortin-positive cells and expression of brain-derived neurotrophic factor, TrkB, and Bcl-2 decreased; expression of Bax and the number of caspase-3-positive and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling-positive cells increased; and short-term and spatial working memory decreased in the OVX group compared with the sham group. Conversely, when the combined exercise group was compared with the OVX group, the number of BrdU-positive and doublecortin-positive cells and expression of brain-derived neurotrophic factor, TrkB, and Bcl-2 increased; expression of Bax and the number of caspase-3-positive and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling-positive cells decreased; and short-term and spatial working memory increased. CONCLUSIONS: Combined exercise increases cell proliferation and inhibits apoptosis in the hippocampus and improves cognitive function despite estrogen deficiency.

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Menopausal hot flashes and white matter hyperintensities.

Thurston RC, Aizenstein HJ, Derby CA, Sejdić E, Maki PM.

OBJECTIVE: Hot flashes are classic symptoms of menopause. Emerging data link hot flashes to cardiovascular disease (CVD) risk, yet whether hot flashes are related to brain health is poorly understood. We examined the relationship between hot flashes (measured via physiologic monitor and self-report) and white matter hyperintensities (WMH) among midlife women. METHODS: Twenty midlife women (aged 40-60 y) without clinical CVD, with an intact uterus and ovaries, and not taking hormone therapy were recruited. Women underwent 24 hours of ambulatory physiologic and diary hot flash monitoring to quantify hot flashes; magnetic resonance imaging to assess WMH burden; 72 hours of actigraphy to quantify sleep; and a blood draw, questionnaires, and physical measures to quantify demographics and CVD risk factors. Tests of a priori hypotheses regarding relationships between physiologically monitored and self-reported wake and sleep hot flashes and WMH were conducted in linear regression models. RESULTS: More physiologically monitored hot flashes during sleep were associated with greater WMH, controlling for age, race, and body mass index (β [SE] = 0.0002 [0.0001], P = 0.03]. Findings persisted after controlling for sleep characteristics and additional CVD risk factors. No relationships were observed for self-reported hot flashes. CONCLUSIONS: More physiologically monitored hot flashes during sleep are associated with greater WMH burden among midlife women without clinical CVD. Results suggest that the relationship between hot flashes and CVD risk observed in the periphery may extend to the brain. Future work should consider the unique role of sleep hot flashes in brain health.

Nota de JE: La hiperintensidad de la sustancia blanca se halla en el cerebro de los pacientes con EA y parece aumentar el riesgo de esta enfermedad.