Selección de Resúmenes de Menopausia

Semana del 22 al 28 de Julio de 2015

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Cognitive Effects of Hormone Therapy Continuation or Discontinuation in a Sample of Women at Risk for Alzheimer Disease.

Wroolie TE, Kenna HA, Williams KE, Rasgon NL.

OBJECTIVE: Use of estrogen-based hormone therapy (HT) as a protection from cognitive decline and Alzheimer disease (AD) is controversial, although cumulative data support HT use when initiated close to menopause onset with estrogen formulations containing 17β-estradiol preferable to conjugated equine estrogen formulations. Little is known regarding specific populations of women who may derive benefit from HT. METHODS: Women with heightened risk for AD (aged 49-69), all of whom were taking HT for at least 1 year and most of whom initiated HT close to menopause onset, underwent cognitive assessment followed by randomization to continue or discontinue HT. Assessments were repeated at 2 years after randomization. RESULTS: Women who continued HT performed better on cognitive domains composed of measures of verbal memory and combined attention, working memory, and processing speed measures. Women who used 17β-estradiol versus conjugated equine estrogen, whether randomized to continue or discontinue HT, showed better verbal memory performance at the 2-year follow-up assessment. An interaction was also found with HT randomization and family history of AD in a first-degree relative. All female offspring of patients with AD declined in verbal memory; however, women who continued HT declined less than women who discontinued HT. Women without a first-degree relative with AD showed verbal memory improvement (likely because of practice effects) with continuance and declined with discontinuance of HT. CONCLUSION: Continuation of HT use appears to protect cognition in women with heightened risk for AD when initiated close to menopause onset.

Minerva Endocrinol. 2015 Sep;40(3):231-237.

Effectiveness and safety of calcium and vitamin D treatment for postmenopausal osteoporosis.

Cesareo R, Iozzino M, D'onofrio L, Terrinoni I, Maddaloni E, Casini A, Campagna G, Santonati A, Palermo A.

Imbalance of bone resorption and bone formation is responsible for osteoporosis that is characterized by decreased bone mass and mineral density. The aim of this study was to evaluate the available data that could clarify the effectiveness and safety of supplementations with calcium and vitamin D, alone or in combination, to slow down bone loss in postmenopausal and elderly women. Using search key words, we performed a research both in the PubMed and Cochrane Library in order to find all meta-analysis, prospective and randomized clinical studies published from 2000 to 2014 that had investigated the effectiveness of calcium and vitamin D in the treatment of osteoporosis. At the moment it is not possible either to provide reassurance that calcium supplements given with vitamin D do not cause adverse cardiovascular events or to link them with certainty to increased cardiovascular risk. According to the data now available, vitamin D, at dosage of at least 800 IU/day, alone or in combination with antiresorptive drugs, should be administered in osteoporotic and osteopenic patients for a primary and secondary prevention. Further studies are needed and the debate remains ongoing. However, every administration needs the calculation of the absolute fracture risk of the patient. Especially considering the high cost of osteoporosis prevention, more studies are mandatory to clarify indications and contraindications.

Mayo Clin Proc. 2015 Jul 16. doi: 10.1016/j.mayocp.2015.06.002. [Epub ahead of print]

Critical Update of the 2010 Endocrine Society Clinical Practice Guidelines for Male Hypogonadism: A Systematic Analysis.

Seftel AD, Kathrins M, Niederberger C.

"Testosterone Therapy in Men With Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline" (Guidelines), published in 2010, serves as an important guide for the treatment of hypogonadal men. Using the Guidelines as a basis, we searched for the most recent level 1 evidence that continues to support the

recommendations or provide an impetus to modify all or some of them. We performed a systematic analysis with a PubMed query from January 1, 2010, through March 2, 2015, using the following key words: testosterone/deficiency, testosterone/therapeutic use, cardiovascular, morbidity, mortality, screening, sexual function, lower urinary tract symptoms, obstructive sleep apnea, prostate cancer, fertility, bone mineral density, osteoporosis, quality of life, cognitive, erectile dysfunction, and adverse effects. We identified 17 trials representing level 1 evidence that specifically addressed recommendations made in the Guidelines. Trials examining outcomes of testosterone replacement therapy in men with severe lower urinary tract symptoms and untreated obstructive sleep apnea were identified, potentially refuting the current dogma against treatment in the setting of these conditions. Hypogonadal men with type 2 diabetes mellitus and metabolic syndrome were examined in several trials, demonstrating the beneficial effects of therapy on sexual function and insulin sensitivity. Several trials served as reinforcing evidence for the beneficial effects of testosterone therapy on osteoporosis, muscle strength, and symptoms of frailty. As in the Guidelines, inconsistent effects on quality of life, well-being, and erectile function were also noted in publications. Despite controversies surrounding cardiovascular morbidity and treatment in the setting of prostate cancer, no studies examining these issues as primary end points were identified. The low number of eligible studies since 2010 is a limitation of this analysis.

Osteoporos Int. 2015 Jul 23. [Epub ahead of print]

The effect of 8 or 5 years of denosumab treatment in postmenopausal women with osteoporosis: results from the FREEDOM Extension study.

Papapoulos S, Lippuner K, Roux C, Lin CJ, Kendler DL, Lewiecki EM, Brandi ML, Czerwiński E, et al.

The FREEDOM study and its Extension provide long-term information about the effects of denosumab for the treatment of postmenopausal osteoporosis. Treatment for up to 8 years was associated with persistent reduction of bone turnover, continued increases in bone mineral density, low fracture incidence, and a favorable benefit/risk profile. INTRODUCTION: This study aims to report the results through year 5 of the FREEDOM Extension study, representing up to 8 years of continued denosumab treatment in postmenopausal women with osteoporosis. METHODS: Women who completed the 3-year FREEDOM study were eligible to enter the 7-year open-label FREEDOM Extension in which all participants are scheduled to receive denosumab, since placebo assignment was discontinued for ethical reasons. A total of 4550 women enrolled in the Extension (2343 long-term; 2207 cross-over). In this analysis, women in the long-term and cross-over groups received denosumab for up to 8 and 5 years, respectively. RESULTS: Throughout the Extension, sustained reduction of bone turnover markers (BTMs) was observed in both groups. In the long-term group, mean bone mineral density (BMD) continued to increase significantly at each time point measured, for cumulative 8-year gains of 18.4 and 8.3 % at the lumbar spine and total hip, respectively. In the cross-over group, mean BMD increased significantly from the Extension baseline for 5-year cumulative gains of 13.1 and 6.2 % at the lumbar spine and total hip, respectively. The yearly incidence of new vertebral and nonvertebral fractures remained low in both groups. The incidence of adverse and serious adverse events did not increase over time. Through Extension year 5, eight events of osteonecrosis of the jaw and two events of atypical femoral fracture were confirmed. CONCLUSIONS: Denosumab treatment for up to 8 years was associated with persistent reductions of BTMs, continued BMD gains, low fracture incidence, and a consistent safety profile.

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Diagnosis and Management of Subclinical Hypothyroidism in Elderly Adults: A Review of the Literature.

Hennessey JV, Espaillat R.

The estimated prevalence of subclinical hypothyroidism (SCH) in the general population is 3% to 8%. As the average age of the population in the United States and other countries continues to increase, the overall prevalence of SCH may also be expected to increase. Although age-related changes in thyroid function are well described, normal thyroid-stimulating hormone (TSH) reference limits, derived for age-specific populations, are not routinely used to identify thyroid dysfunction in elderly adults. Therefore, currently accepted values for the upper limit of normal of TSH may be inappropriate for diagnosing SCH in individuals aged 65 and older, resulting in potential overestimation of the prevalence of SCH in this population. This review discusses the current evidence of the effects of SCH on cardiovascular health and neuropsychiatric function in older adults. Although the results of

some studies are conflicting, the overall evidence suggests that the consequences of SCH may be different for elderly adults than for younger populations. Treatment of SCH in older individuals requires special consideration with regard to thyroid hormone replacement therapy and expected clinical outcomes. Although careful identification of individuals with persistent SCH who could benefit from levothyroxine treatment is necessary, current evidence suggests that individuals with TSH levels greater than 10 mIU/L who test positive for antithyroid antibodies or are symptomatic may benefit from levothyroxine treatment to reduce the risk of progression to overt hypothyroidism, decrease the risk of adverse cardiovascular events, and improve their quality of life. After treatment is initiated, careful monitoring is essential.

Clin Breast Cancer. 2015 Jun 18. doi: 10.1016/j.clbc.2015.06.005. [Epub ahead of print]

Genitourinary Syndrome of Menopause in Breast Cancer Survivors: Are We Facing New and Safe Hopes?

Biglia N, Bounous VE, Sgro LG, D'Alonzo M, Pecchio S, Nappi RE.

Breast cancer survivors (BCSs) often suffer from menopausal symptoms induced by systemic treatments, with a consequent negative effect on quality of life. Since the introduction of aromatase inhibitors as the standard therapy for hormone-dependent tumors, genitourinary syndrome of menopause (GSM) has become a main problem for BCSs. This new terminology refers to the wide range of vaginal and urinary symptoms related to menopause, which can be relieved by estrogen therapy. Unfortunately, systemic hormone therapy is contraindicated for BCSs and also vaginal estrogens at standard dosage might influence the risk of recurrence because they cause a significant increase of circulating estrogens. Nonhormonal vaginal moisturizers or lubricants are the first choice for BCSs but only have limited and short-term efficacy. New strategies of management of GSM are now available, including: (1) low-dose or ultra low-dose vaginal estrogens; (2) oral selective estrogen receptor modulators (ospemifene); (3) androgen therapy; (4) physical treatment with vaginal laser; and (5) psychosocial interventions. In this review we discuss and analyze these different options.

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Allogeneic Mesenchymal Precursor Cells in Type 2 Diabetes: A Randomized, Placebo-Controlled, Dose Escalation Safety and Tolerability Pilot Study.

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OBJECTIVE: To assess the safety, tolerability, and feasibility of adult allogeneic bone marrow-derived mesenchymal precursor cells (MPCs) in type 2 diabetes inadequately controlled with metformin either alone or with one additional oral antidiabetic agent. RESEARCH DESIGN AND METHODS: The study was a dose-escalating randomized placebo-controlled trial assessing one intravenous (IV) infusion of MPCs (rexlemestrocel-L; Mesoblast Inc.) 0.3 × 106/kg (n = 15), 1.0 × 106/kg (n = 15), or 2.0 × 106/kg (n = 15) or placebo (n = 16). Study duration was 12 weeks. RESULTS: Subjects (21 women, 40 men) with a mean ± SD baseline HbA1c 8.3 ± 1.0% (67 ± 10.9 mmol/mol), BMI 33.5 ± 5.5 kg/m2, and diabetes duration 10.1 ± 6.0 years were enrolled at 18 U.S. sites. No acute adverse events (AEs) were associated with infusion. No serious AEs, serious hypoglycemia AEs, or discontinuations due to AEs over 12 weeks were found. No subjects developed donor-specific anti-HLA antibodies or became sensitized. The safety profile was comparable among treatment groups. Compared with placebo, a single IV infusion of rexlemestrocel-L reduced HbA1c at all time points after week 1. The adjusted least squares mean ± SE dose-related differences in HbA1c from placebo in the rexlemestrocel-L groups ranged from -0.1 ± 0.2% (-1.1 ± 2.2 mmol/mol) to -0.4 ± 0.2% (4.4 ± 2.2 mmol/mol) at 8 weeks and from 0.0 ± 0.25% to -0.3 ± 0.25% (-3.3 ± -2.7 mmol/mol) at 12 weeks ($P < 0.05$ for 2.0 × 106/kg dose at 8 weeks). The clinical target HbA1c <7% (53 mmol/mol) was achieved by 33% (5 of 15) of the subjects who received the 2.0 × 106/kg dose vs. 0% of those who received placebo ($P < 0.05$). CONCLUSIONS: This short-term study demonstrates the safety and feasibility of up to 246 million MPCs in subjects with type 2 diabetes.