



Selección de Resúmenes de Menopausia

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Effects of selective serotonin reuptake inhibitors and other antidepressant drugs on the risk of hip fracture: a case-control study in an elderly Mediterranean population

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 Objectives: To describe the association between exposure to different antidepressant drugs and hip fracture in an elderly Mediterranean population. Methods: Cases were all patients aged 50-95 years admitted to the emergency room of our hospital with hip fracture not related to a high intensity trauma during 2010. For each case, four controls were identified from primary care electronic medical records matched by age (± 3 years), gender, date of consultation at the primary care centre (± 1 month) and primary care centre. Pharmacological treatments received within the previous 5 years were retrieved from the prescription records. Crude and adjusted risks associated with exposures were calculated by conditional logistic regression. ORs were adjusted by matching variables and by significant risk factors identified in the bivariate analysis (prescription of ≥ 4 drugs, osteoporosis, diabetes mellitus and previous fracture). Results: 136 cases and 544 controls were analysed. Adjusted OR (95% CI) for hip fracture associated with exposure to any antidepressants was 2.42 (1.24 to 4.73); for selective serotonin reuptake inhibitors (SSRIs) it was 3.52 (1.67 to 7.41), for non-selective monoamine reuptake inhibitors 1.07 (0.18 to 6.46) and for other antidepressants 0.82 (0.27 to 2.48). Sertraline (OR 3.88 (1.15 to 13.09)) was the only active principle with significant adjusted risk. When only exposures > 6 months were considered, significant risks persisted for SSRIs (OR 2.64 (1.10 to 6.37)). Conclusions: The results of this study are coincident with other studies in which SSRIs, but not other types of antidepressants, are associated with an increased risk of hip fracture in our setting.

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Controversies in Vitamin D: A Statement From the Third International Conference

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 The Third International Conference on Controversies in Vitamin D was held in Gubbio, Italy, September 10-13, 2019. The conference was held as a follow-up to previous meetings held in 2017 and 2018 to address topics of controversy in vitamin D research. The specific topics were selected by the steering committee of the conference and based upon areas that remain controversial from the preceding conferences. Other topics were selected anew that reflect specific topics that have surfaced since the last international conference. Consensus was achieved after formal presentations and open discussions among experts. As will be detailed in this article, consensus was achieved with regard to the following: the importance and prevalence of nutritional rickets, amounts of vitamin D that are typically generated by sun exposure, worldwide prevalence of vitamin D deficiency, the importance of circulating concentrations of 25OHD as the best index of vitamin D stores, definitions and thresholds of vitamin D deficiency, and efficacy of vitamin D analogues in the treatment of psoriasis. Areas of uncertainty and controversy include the following: daily doses of vitamin D needed to maintain a normal level of 25OHD in the general population, recommendations for supplementation in patients with metabolic bone diseases, cutaneous production of vitamin D by UVB exposure, hepatic regulation of 25OHD metabolites, definition of vitamin D excess, vitamin D deficiency in acute illness, vitamin D requirements during reproduction, potential for a broad spectrum of cellular and organ activities under the influence of the vitamin D receptor, and potential links between vitamin D and major human diseases. With specific regard to the latter area, the proceedings of the conference led to recommendations for areas in need of further investigation through appropriately designed intervention trials.

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Longitudinal changes over three years in sex steroid hormone levels in women aged 70 years and over

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Objective: Sex steroid levels in women vary with increasing age from the age of 70 years (70+). Whether this reflects change within individuals with age or a survival advantage is not known. This study aimed to determine the stability of circulating sex steroids and SHBG over time in individual women aged 70+. **Design:** A prospective cohort study. **Participants:** 400 women, aged 70+ not using any sex steroid, anti-androgen/estrogen or glucocorticoid therapy. **Main outcome measurements:** Sex steroid concentrations, measured by liquid chromatography-tandem mass spectrometry and sex hormone binding globulin (SHBG) by immunoassay, in paired blood samples drawn 3 years apart and analysed together. **Results:** 400 women, median (IQR) age 78.0 (8.6) years, were included in the analysis. Mean testosterone concentrations were statistically significantly higher in follow-up samples compared with baseline. The change was modest (mean change 31 pmol/L, 95% confidence interval (CI) 2.4 to 59.8; $p=0.034$) and an increase was not observed in all women. There was a statistically significant decline in mean body mass index (mean change -0.4 kg/m², 95% CI 0.6 to -0.3 ; $p<0.001$) and a significant increase in the mean serum SHBG concentration (mean change 4, 95% CI 3 to 5; $p<0.001$). The change observed in testosterone was not explained by the observed change in SHBG. There was no significant change in the mean estrone or dehydroepiandrosterone concentration. **Conclusions:** Testosterone concentrations in women aged 70+ were more likely to increase than decrease. Whether increasing testosterone concentrations in older women confer a survival advantage needs investigation.

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High-density lipoprotein cholesterol and arterial calcification in midlife women: the contribution of estradiol and C-reactive protein

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Objective: Studies suggest a reversal in the protective association of high-density lipoprotein cholesterol (HDL-C) and cardiovascular disease in women traversing menopause. Decreasing estrogen levels during the transition, as well as inflammation, may explain this reversal. We tested whether either estradiol or C-reactive protein (CRP) concentrations modified the association of HDL-C with aortic (AC) or coronary artery calcification (CAC). **Methods:** A total of 478 participants between ages 46 to 59 from the Study of Women's Health Across the Nation Heart baseline visit were included. AC and CAC presence were defined as Agatston score of 100 or higher and 10 or higher, respectively. Logistic regression was used for analysis. **Results:** A total of 112 (23.53%) participants had AC 100 or higher and 104 (21.76%) had CAC 10 or higher. In unadjusted models, a 1-mg/dL higher in HDL-C was associated with 3% lower odds of AC (95% CI: 0.95-0.99) and 4% lower odds of CAC (95% CI: 0.95-0.98). In adjusted models, a significant interaction between HDL-C and estradiol with respect to AC but not CAC was detected, such that higher HDL-C level was protective at the highest estradiol quartile (odds ratio: 0.91, 95% CI: 0.84-0.99 per 1 mg/dL higher HDL-C, $P=0.03$) but tended to associate with greater risk at the lowest quartile (odds ratio: 1.04, 95% CI: 0.98-1.10 per 1 mg/dL higher HDL-C, $P=0.16$). CRP did not modify any association. **Conclusions:** The protective cardiovascular association of higher HDL-C levels on AC was modified by estradiol but not CRP concentrations. The pathways through which estradiol might influence this association should be further investigated.

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Short-term impact of surgically induced menopause on cognitive function and wellbeing in women at high risk for ovarian cancer following risk-reducing bilateral salpingo-oophorectomy

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Objective: Risk-reducing bilateral salpingo-oophorectomy (RRSO) is an effective strategy to prevent pelvic serous carcinoma for women at high risk of developing ovarian cancer; however, it results in premature menopause. Data is lacking to adequately counsel these women about potential effects of premature menopause on cognition and quality of life. **Methods:** A prospective study in premenopausal women at high risk of ovarian cancer to determine changes in cognition over time after RRSO and the impact of hormone therapy (HT) on cognition. Participants were surveyed before and after surgery using the Functional Assessment of Cancer Therapy-Cognitive questionnaire and questions regarding domains of wellbeing at 6, 12 and 18 months. Data was tested for changes across time using mixed model

regression and logistic regression. Results: Fifty-seven women were included. Sixty-three percent of participants used HT. At 6 months postoperatively, perceived cognitive impairment declined by 5.5 points overall (4.4 in non-HT users and 6 in HT users), $P = 0.003$. The other domains of cognition assessed did not change significantly over time and the use of HT did not impact scores. Sleep disruption was common in this cohort and was not mitigated by HT. Self-reported depression improved after RRSO ($P = 0.004$). Conclusion: Women at high risk of ovarian cancer who choose RRSO may experience declines in cognition within the first 6 months of surgical menopause. HT may cause small declines in perceived cognitive impairment at 6 months after RRSO. Women can expect more sleep disruption after menopause, which is not mitigated by HT.

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Levonorgestrel intrauterine system for endometrial protection in women with breast cancer on adjuvant tamoxifen

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Background: Adjuvant tamoxifen reduces the risk of breast cancer recurrence in women with oestrogen receptor-positive breast cancer. Tamoxifen also increases the risk of postmenopausal bleeding, endometrial polyps, hyperplasia, and endometrial cancer. The levonorgestrel-releasing intrauterine system (LNG-IUS) causes profound endometrial suppression. This systematic review considered the evidence that the LNG-IUS prevents the development of endometrial pathology in women taking tamoxifen as adjuvant endocrine therapy for breast cancer. Objectives: To determine the effectiveness and safety of the levonorgestrel intrauterine system (LNG-IUS) in pre- and postmenopausal women taking adjuvant tamoxifen following breast cancer for the outcomes of endometrial and uterine pathology including abnormal vaginal bleeding or spotting, and secondary breast cancer events. We included four RCTs (543 women analysed) in this review. **AUTHORS' CONCLUSIONS:** The LNG-IUS probably slightly reduces the incidence of benign endometrial polyps and endometrial hyperplasia in women with breast cancer taking tamoxifen. At 12 and 24 months of follow-up, the LNG-IUS probably increases abnormal vaginal bleeding or spotting among women in the treatment group compared to those in the control. Data were lacking on whether the LNG-IUS prevents endometrial cancer in these women. There is no clear evidence from the available RCTs that the LNG-IUS affects the risk of breast cancer recurrence or breast cancer-related deaths. Larger studies are necessary to assess the effects of the LNG-IUS on the incidence of endometrial cancer, and to determine whether the LNG-IUS might have an impact on the risk of secondary breast cancer events.