



Selección de Resúmenes de Menopausia

Semana del 5 al 11 de mayo 2021

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Case of cholestatic drug-induced liver injury associated with black cohosh. (16)

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Drug-induced liver injury is an uncommon yet fatal cause of liver injury. Black cohosh is a herbal supplement that is derived from *Actaea racemosa*. It has been used for vasomotor symptoms in postmenopausal women, but it can cause liver injury. A 50-year-old Afro-American woman presented with a 2-month history of malaise, itching and severe jaundice. The labs showed elevation of bilirubin and alkaline phosphatase. The patient had a history of black cohosh use for postmenopausal symptoms before she developed her current symptoms. The extensive workup for infective and autoimmune pathology was negative. Black cohosh was discontinued. The patient improved clinically, and her liver enzymes normalised 6 months after the discontinuation of black cohosh. This report emphasises the need to recognise black cohosh as a potential hepatotoxic agent and to monitor the liver enzymes for a patient on black cohosh.

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Association of depression, anxiety and menopausal-related symptoms with demographic, anthropometric and body composition indices in healthy postmenopausal women

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Background: The termination of the menstrual cycle is correlated with a number of physiological alterations and symptoms that can negatively impact emotion and mood. We aimed to investigate the association of anxiety, depression, and menopausal related symptoms with demographic, anthropometric, and body composition indices in healthy postmenopausal women. **Methods:** A total of 320 menopausal women were selected randomly from referrals of health centers between January and June 2018 in Tabriz/Iran. All participants completed a demographic questionnaire. Bioelectrical impedance analysis was applied to evaluate body fat mass (BFM), soft lean mass (SLM), and lean body mass (LBM) of participants. The modified Kupperman index, Beck's depression inventory-II, and Spielberger's state-trait anxiety inventory were applied to measure the severity of menopausal-related symptoms, the frequency, and severity of the symptoms of depression and state (SA) and trait anxiety (TA), respectively. **Results:** Finally, 245 postmenopausal women with age of 55.33 ± 4.48 years and body mass index (BMI) of 27.96 ± 3.22 kg/m² were studied. Women with the age of 55 years and older (OR 3.928, 95% CI 1.504-10.256) and also women with mild physical activity (OR 10.104, 95% CI 3.785-26.976) had a greater possibility of having mild and moderate depression in comparison with women less than 50 years old and women with moderate and severe physical activity. Moderate and severe physical activity was correlated with a lower possibility of having medium upward, relatively severe and severe TA in comparison with participants with mild physical activity in these women (OR 0.372, 95% CI 0.151-0.917). Women with higher BMI and BFM had and more severe menopause-related symptoms ($r: 0.143$, $p: 0.025$ and $r: 0.139$, $p: 0.030$, respectively) and more severe TA symptoms ($r: 0.198$, $p: 0.018$ and $r: 0.151$, $p: 0.021$, respectively). Women with lower LBM ($r: -0.139$, $p: 0.031$) and lower SLM ($r: -0.128$, $p: 0.047$) had more severe depressive symptoms. **Conclusion:** Postmenopausal women with higher age and lower physical activity had a greater possibility of having mild and moderate depression. Lower physical activity was also correlated with a greater possibility of having medium upward to severe TA symptoms. Postmenopausal women with higher BMI and BFM had more severe menopause-related and TA symptoms. Women with lower LBM and SLM had more severe depressive symptoms.

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Strong association between the dietary inflammatory index(DII) and breast cancer: a systematic review and meta-analysis

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association between the Dietary Inflammatory Index (DII) and breast cancer risk has been widely reported in recent years, but there is still controversy about whether a pro-inflammatory diet is a risk factor for breast cancer. We

conducted a meta-analysis to investigate the relationship between the DII and breast cancer risk in pre-menopausal and post-menopausal women. We comprehensively searched PubMed, Embase and the Cochrane Library in January 2021 to identify articles reporting an association between the DII and breast cancer risk. A pooled analysis was conducted with 14 studies covering 312,885 participants. Overall, women in the most pro-inflammatory diet category were at greater risk for breast cancer than those in the most anti-inflammatory category (relative risk [RR]:1.37, 95% confidence interval [CI] 1.17-1.60, $P<0.001$). This association was strong in both pre-menopausal women (RR:1.87, 95% CI 1.17-2.99, $P<0.001$) and post-menopausal women (RR:1.23, 95% CI 1.08-1.40, $P<0.001$). Thus, a strong and independent association was observed between a pro-inflammatory diet (assessed using the DII score) and breast cancer risk, irrespective of menopausal status. Further studies will be required to determine the relationship between a pro-inflammatory diet and different subtypes of breast cancer.

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The risk of carotid plaque instability in patients with metabolic syndrome is higher in women with hypertriglyceridemia

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Background: Metabolic syndrome certainly favors growth of carotid plaque; however, it is uncertain if it determines plaque destabilization. Furthermore, it is likely that only some components of metabolic syndrome are associated with increased risk of plaque destabilization. Therefore, we evaluated the effect of different elements of metabolic syndrome, individually and in association, on carotid plaques destabilization. Methods: A total of 186 carotid endarterectomies from symptomatic and asymptomatic patients were histologically analysed and correlated with major cardiovascular risk factors. Results: Metabolic syndrome, regardless of the cluster of its components, is not associated with a significant increase in risk of plaque destabilization, rather with the presence of stable plaques. The incidence of unstable plaques in patients with metabolic syndrome is quite low (43.9 %), when compared with that seen in the presence of some risk factors, but significantly increases in the subgroup of female patients with hypertriglyceridemia, showing an odds ratio of 3.01 (95% CI, 0.25-36.30). Conclusions: Our data may help to identify patients with real increased risk of acute cerebrovascular diseases thus supporting the hypothesis that the control of hypertriglyceridemia should be a key point on prevention of carotid atherosclerotic plaque destabilization, especially in post-menopausal female patients.

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Vitamin D3 Dose Requirement that Raises 25-Hydroxyvitamin D to Desirable Level in Overweight and Obese Elderly

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Purpose: To investigate the impact of two vitamin D doses, bracketed between the IOM recommended dietary allowance (RDA) and the upper tolerable limit, on vitamin D nutritional status in elderly individuals. Methods: This is a post-hoc analysis on data collected from a 12-month, double-blinded, randomized control trial. 221 ambulatory participants (≥ 65 years), with a mean BMI of 30.2 kg/m², and a mean baseline serum 25-hydroxyvitamin D [25(OH)D] level of 20.4 \pm 7.4 ng/ml, were recruited from 3 out-patient centers in Lebanon. They all received 1,000 mg of elemental calcium from calcium citrate daily, and the daily equivalent of 600 IU or 3,750 IU, of vitamin D₃. Results: Mean 25-hydroxyvitamin D [25(OH)D] level at 12 months was 26.0 ng/ml with low dose and 36.0 ng/ml with high dose, of vitamin D₃. The proportion of participants reaching a value ≥ 20 ng/ml was 86% in the low dose, and 99% in the high-dose arms, with no differences between genders. The increment of 25(OH)D per 100 IU/day was 1ng/ml with the low dose, and 0.41 ng/ml with the high dose. Serum 25 (OH)D levels at 1 year were highly variable in both treatment arms. Baseline 25(OH)D level and vitamin D dose, but not age, BMI, gender, nor season, were significant predictors of serum 25(OH)D level post-intervention. Conclusion: The IOM RDA of 600 IU/day does not bring 97.5% of ambulatory elderly individuals above the desirable threshold of 20 ng/ml. Country-specific RDAs are best derived taking into account the observed variability and predictors of achieved 25(OH)D levels.

Age Ageing. 2021 May 5;50(3):725-732.doi: 10.1093/ageing/afaa237.

Does vascular endothelial dysfunction play a role in physical frailty and sarcopenia? A systematic review

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Background: Frailty is strongly associated with adverse cardiovascular outcomes; however, the underlying pathophysiological processes are largely unknown. Vascular endothelial dysfunction (VED) is the earliest stage of cardiovascular disease (CVD) progression and predicts long-term CVD outcomes. Both these conditions share an elevated inflammatory state as a common pathological factor. Objective: Systematic literature review was conducted to examine the evidence supporting an association between VED and physical frailty and/or sarcopenia, in electronic databases including Scopus, Ovid Medline, CINAHL, ScienceDirect, ProQuest Health & Medicine and Embase from January 1980 to August 2019. Results: A total of 18 studies met the inclusion criteria. VED is independently associated with increased frailty phenotypes and measures of sarcopenia. Several markers of VED, including higher levels of asymmetric dimethylarginine, abnormal ankle brachial index, pulse wave velocity, pulse pressure and lower levels of flow-mediated dilatation, peripheral blood flow and endothelial progenitor cell counts, have been associated with frailty/sarcopenia measurements. Some studies demonstrated the effect of inflammation on the association. Conclusions: Recent studies, although limited, showed that VED could be one of the underlying mechanisms of frailty. It is entirely possible that inflammation-related pathological changes in the vascular endothelium are involved in the early causative mechanisms in physical frailty. The exact mechanism(s) underlying this association are still unclear and will need to be evaluated. The outcomes of these future research studies could potentially inform early preventative strategies for physical frailty and sarcopenia.

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GPÉR: A Novel Target To Treat Cardiovascular Disease In A Sex-Specific Manner?

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As an agonist of the classical nuclear receptors, ER α and ER β , estrogen has been understood to inhibit the development of cardiovascular disease in pre-menopausal women. Indeed, reduced levels of estrogen after menopause are believed to contribute to accelerated morbidity and mortality rates in women. However, estrogen replacement therapy has variable effects on cardiovascular risk in post-menopausal women that include increased serious adverse events. Interestingly, pre-clinical studies have shown that selective activation of the novel membrane-associated G protein-coupled estrogen receptor 1, GPÉR, can promote cardiovascular protection. These benefits are more evident in ovariectomised than intact females or in males. It is therefore possible that selective targeting of the GPÉR in post-menopausal women could provide cardiovascular protection with fewer adverse effects than are caused by conventional 'receptor non-specific' estrogen replacement therapy. This review describes new data regarding the merits of targeting GPÉR to treat cardiovascular disease with a focus on sex differences.

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Severity of climacteric symptoms among Peruvian women from an urban coastal community and a rural Andean community

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Introduction: The aim of this study was to evaluate the severity of climacteric symptoms among two Peruvian communities, adjusted for sociodemographic and clinical variables in climacteric women. Methods: A cross-sectional study was conducted on 90 subjects from two different communities (an urban coastal and a rural Andean district from Peru). The Menopause Rating Scale was used to assess climacteric symptoms. Prevalence ratios with 95% confidence interval (PR 95%CI) were estimated using generalized linear Poisson models with family robust standard errors. Results: A higher probability of severe climacteric symptoms was found in women who were from the Andean community than those who were from the coastal one (PR 2.42, 95%CI 1.47-3.99; p=0.001), which remained in the adjusted model (RP 1.72, 95%CI 1.04-2.86; p=0.035). Conclusion: Understanding the variation of climacteric symptoms among geographically distinct communities could contribute to improving women's quality of life.

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Efficacy and Safety of Denosumab in Osteoporosis or Low Bone Mineral Density Postmenopausal Women

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Denosumab, a human monoclonal antibody, acts against the receptor activator of nuclear factor- κ B ligand and is a promising antiresorptive agent in patients with osteoporosis. This study aimed to update the efficacy and safety of denosumab vs. placebo in osteoporosis or low bone mineral density (BMD) postmenopausal women. PubMed, Embase, Cochrane library, and ClinicalTrials.gov were searched for randomized controlled trials (RCTs) reporting the efficacy and safety data of denosumab vs. placebo in osteoporosis or low BMD postmenopausal women. A random-effects model was used to calculate pooled weight mean differences (WMDs) or relative risks (RRs) with corresponding 95% confidence intervals (CIs) for treatment effectiveness of denosumab vs. placebo. Eleven RCTs including 12,013 postmenopausal women with osteoporosis or low BMD were preferred for the final meta-analysis. The summary results indicated that the percentage change of BMD in the denosumab group was greater than that of BMD in placebo at 1/3 radius (WMD: 3.43; 95%CI: 3.24-3.62; $p < 0.001$), femoral neck (WMD: 3.05; 95%CI: 1.78-4.33; $p < 0.001$), lumbar spine (WMD: 6.25; 95%CI: 4.59-7.92; $p < 0.001$), total hip (WMD: 4.36; 95%CI: 4.07-4.66; $p < 0.001$), trochanter (WMD: 6.00; 95%CI: 5.95-6.05; $p < 0.001$), and total body (WMD: 3.20; 95%CI: 2.03-4.38; $p < 0.001$). Moreover, denosumab therapy significantly reduced the risk of clinical fractures (RR: 0.57; 95%CI: 0.51-0.63; $p < 0.001$), nonvertebral fracture (RR: 0.83; 95%CI: 0.70-0.97; $p = 0.018$), vertebral fracture (RR: 0.32; 95%CI: 0.25-0.40; $p < 0.001$), and hip fracture (RR: 0.61; 95%CI: 0.37-0.98; $p = 0.042$). Finally, denosumab did not cause excess risks of adverse events. These findings suggested that postmenopausal women receiving denosumab had increased BMDs and reduced fractures at various sites without inducing any adverse events.