



## Selección de Resúmenes de Menopausia

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### Identification of risk factors for falls in postmenopausal women: a systematic review and meta-analysis.

Zhao J1,2, Liang G2,3, Huang H1,2, Zeng L2,3, Yang W2,3, Pan J2,3, Liu J4,5.

The purpose of this study was to identify risk factors for falls in postmenopausal women and provide evidence for the primary prevention of falls in postmenopausal women. The protocol for this meta-analysis is registered with PROSPERO (CRD42020170927). We searched PubMed, the Cochrane Library and EMBASE for observational studies on the risk factors for falls in postmenopausal women. Review Manager 5.3 was used to calculate the relative risk (RR) or weighted mean difference (WMD) of potential risk factors related to falls. STATA 14.0 was used for the quantitative evaluation of publication bias. Eleven studies with 42,429 patients from 7 countries were included. The main risk factors for falls in postmenopausal women were patient sociodemographic risk factors (age: WMD = 0.37, 95% CI 0.07 to 0.68; body weight: WMD = 0.88, 95% CI 0.56 to 1.12; BMI: WMD = 0.34, 95% CI 0.21 to 0.46; exercise: RR = 0.97, 95% CI 0.94 to 0.99; and FES-I: WMD = 6.60, 95% CI 0.72 to 12.47) and medical risk factors (dietary calcium intake: WMD = - 16.91, 95% CI - 25.80 to - 8.01; previous fracture history: RR = 1.21, 95% CI 1.13 to 1.29; previous falls: RR = 2.02, 95% CI 1.91 to 2.14; number of diseases, > 2: RR = 1.17, 95% CI 1.11 to 1.23; and number of reported chronic health disorders: WMD = 0.30, 95% CI 0.10 to 0.49). Knowledge of the many risk factors associated with falls in postmenopausal women can aid in fall prevention. However, we cannot rule out some additional potential risk factors (age at the onset of menopause, years since last menstruation, hormone therapy and BMD) that need further clinical research.

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### Serum levels of allopregnanolone, progesterone and testosterone in menstrually-related and postmenopausal migraine: A cross-sectional study.

Rustichelli C1, Bellei E2, Bergamini S2, Monari E2, Baraldi C3, Castro FL4, Tomasi A2, Ferrari A5.

**BACKGROUND:** Reduced blood or cerebrospinal fluid levels of allopregnanolone are involved in menstrual cycle-linked CNS disorders, such as catamenial epilepsy. This condition, like menstrually-related migraine, is characterized by severe, treatment-resistant attacks. We explored whether there were differences in allopregnanolone, progesterone and testosterone serum levels between women with menstrually-related migraine (MM, n = 30) or postmenopausal migraine without aura who had suffered from menstrually-related migraine during their fertile age (PM, n = 30) and non-headache control women in fertile age (FAC, n = 30) or post-menopause (PC, n = 30). **METHODS:** Participants were women with migraine afferent to a headache centre; controls were female patients' acquaintances. Serum samples obtained were analyzed by HPLC-ESI-MS/MS. **RESULTS:** In menstrually-related migraine and postmenopausal migraine groups, allopregnanolone levels were lower than in the respective control groups (fertile age and post-menopause) ( $p < 0.001$ , one-way analysis of variance followed by Tukey-Kramer post-hoc comparison test) while progesterone and testosterone levels were similar. By grouping together patients with migraine, allopregnanolone levels were inversely correlated with the number of years and days of migraine/3 months ( $p \leq 0.005$ , linear regression analysis). **CONCLUSION:** Decreased GABAergic inhibition, due to low allopregnanolone serum levels, could contribute to menstrually-related migraine and persistence of migraine after menopause. For the management of these disorders, a rise in the GABAergic transmission by increasing inhibitory neurosteroids might represent a novel strategy.

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### Vasomotor Menopausal Symptoms and Risk of Cardiovascular Disease: A pooled analysis of six prospective studies.

Zhu D1, Chung HF2, Dobson AJ2, Pandeya N3, Anderson DJ4, Kuh D5, Hardy R6, Brunner EJ7, Avis NE8, et al.

**BACKGROUND:** Menopausal vasomotor symptoms (VMS, i.e., hot flashes and night sweats) have been associated with unfavorable risk factors and surrogate markers of cardiovascular disease (CVD), but their association with clinical CVD events is unclear. We aimed to examine the associations between different component of VMS and timing of

VMS and risk of CVD. **STUDY DESIGN:** We harmonized and pooled individual-level data from 23 365 women in six prospective studies which contributed to the InterLACE consortium. Women who experienced CVD events before baseline were excluded. The associations between frequency (never, rarely, sometimes and often), severity (never, mild, moderate and severe), and timing (before or after age of menopause, i.e., early or late onset) of VMS and incident CVD were analysed. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). **RESULTS:** In the adjusted model, no evidence of association was found between frequency of hot flushes and incident CVD, while women who reported night sweats "sometimes" (HR 1.22, 95% CI 1.02-1.45) or "often" (1.29, 1.05-1.58) had higher risk of CVD. Increased severity of either hot flushes or night sweats was associated with higher risk of CVD. The hazards ratios of CVD in women with severe hot flushes, night sweats and any VMS were 1.83 (1.22, 2.73), 1.59 (1.07, 2.37) and 2.11 (1.62, 2.76) respectively. Women who reported severity for both hot flushes and night sweats had a higher risk of CVD (1.55, 1.24-1.94) than those with hot flushes alone (1.33, 0.94-1.88) and night sweats alone (1.32, 0.84-2.07). Women with either early onset (1.38, 1.10-1.75) or late onset (1.69, 1.32-2.16) VMS had an increased risk of incident CVD, compared with women who did not experience VMS. **CONCLUSION:** Severity rather than frequency of VMS (hot flushes and night sweats) was associated with increased risk of CVD. VMS with onset before or after menopause were also associated with increased risk of CVD.

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### **Prevalence of ocular surface disease symptoms in peri- and postmenopausal women.**

Garcia-Alfaro PI, Bergamaschi L, Marcos C, Garcia S, Rodríguez I.

**OBJECTIVE:** The objective of the study was to determine the prevalence of ocular surface disease (OSD) symptoms and the possible existence of differences between peri- and postmenopausal women, based on the result of the Ocular Surface Disease Index (OSDI). **METHODS:** A transversal observational study based on the results of an e-mail survey between October 2018 and January 2019 involving 1,947 women. The study was performed on a group of peri- and postmenopausal women aged between 45 and 79 years. The personal data in the survey included age, menopause status, age at menopause, prediagnosis of dry eye, undergoing dry eye treatment, and the OSDI questionnaire. Student's t test and Chi squared test were used to compare means or percentages between results on the survey and peri- and postmenopausal women. Finally, a univariate logistic regression was carried out to estimate the prevalence of OSD. The OSDI score is assessed on a scale of 0 to 100. **RESULTS:** The mean age of the entire sample was 54.2±6.8 years, with a mean age at menopause of 49.45±4.02 years. The mean OSDI score was 29.2±19.4, considered as moderate dry eye. The global prevalence of OSD symptoms was 64% (1,247/1,947), which increased significantly in postmenopausal women, being 66.8% (820/1,228) (P = 0.001). The probability of OSD symptoms prevalence increases with age (odds ratio: 1.02; 95% CI [1.01-1.03]). The greater the age at menopause, the lower the probability of OSD symptoms prevalence (odds ratio: 0.96 95% CI [0.93-0.99]). **CONCLUSIONS:** Sixty-four percent of the pre- and postmenopausal women studied had OSD symptoms. There was a correlation between OSD symptoms and age, postmenopause, and earlier age at menopause, which was associated with an increased prevalence.

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### **Bone mass in women with premature ovarian insufficiency: a comparative study between hormone therapy and combined oral contraceptives.**

Gazarra LBC1, Bonacordi CL, Yela DA, Benetti-Pinto CL.

**OBJECTIVE:** The aim of the study was to evaluate whether combined oral contraceptives (COCs) can be used as hormone therapy (HT) to preserve bone mineral density (BMD) in women with premature ovarian insufficiency (POI). **METHODS:** An observational study of women with POI comparing the use of COC (ethinylestradiol 30 µg + levonorgestrel, continuously) with: low-dose HT (continuous conjugated estrogen 0.625mg plus medroxyprogesterone or continuous estradiol [E2] 1mg+norethisterone), high-dose HT (continuous conjugated estrogen 1.25mg+medroxyprogesterone or continuous E2 2mg+norethisterone), tibolone 2.5mg, or no treatment. Bone density scans were performed every 2±1 years. The difference between final and initial (delta) BMD values was calculated for the lumbar spine, total femur, and femoral neck. Generalized estimating equations were used to analyze the effect of treatment over time. Variables without normal distribution were transformed into ranks. **RESULTS:** Overall, 420 scans (210 deltas) of 119 women were analyzed. The women were 30.3±9.2 years old (mean±SD). BMD deltas at the lumbar spine and total femur were greater in the COC and high-dose HT groups. At the lumbar spine, the differences between two scans were greater in the COC group when compared to low-dose HT group: -0.043 (95% CI -0.062 to -0.024), untreated: -0.056 (-0.080 to -0.032), and tibolone: -0.050 (-0.094 to -0.006) groups. Total femur BMD

decreases and the delta were lower in the low-dose HT group -0.038 (-0.052 to -0.024) when compared to COC. CONCLUSION: Continuous COC was associated with increased BMD in women with POI compared to low-dose HT, with similar improvement in the COC and high-dose HT groups.

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### **Pharmacological prevention of fractures in patients undergoing glucocorticoid therapies: a systematic review and network meta-analysis.**

Deng J1, Silver Z2, Huang E1, Zheng E3, Kavanagh K2, Wen A1, Cheng W4, Dobransky J4, Sanger S5, OBJECTIVE: To perform a network meta-analysis (NMA) on the efficacy of antiosteoporotic interventions in the prevention of vertebral and non-vertebral fractures in adult patients taking glucocorticoids (GCs). METHODS: We performed NMAs based on a prospectively developed protocol. A librarian-assisted database search of MEDLINE, EMBASE, Web of Science, Cumulative Index of Nursing and Allied Health Literature (CINAHL), the Cochrane Central Register of Controlled Trials (CENTRAL) and Chinese databases was conducted for randomized controlled trials (RCTs) comparing antiosteoporotic interventions in adult patients taking GCs. Outcomes were vertebral and non-vertebral fracture incidences. RESULTS: We included 56 RCTs containing 6479 eligible patients in our analysis. We found that alendronate and teriparatide were associated with decreased odds of both vertebral and non-vertebral fractures. Denosumab and risedronate were associated with decreased odds of vertebral fractures, while etidronate, ibandronate and alfacalcidol were associated with decreased odds of non-vertebral fractures. We observed low network heterogeneity as indicated by the I<sup>2</sup> statistic, and we did not detect evidence of publication bias. All outcomes were based on a moderate quality of evidence according to GRADE. CONCLUSION: Bisphosphonates, teriparatide and denosumab are associated with decreased odds of fracture in patients undergoing GC therapy. Vitamin D metabolites and analogues (e.g. alfacalcidol) may have greater anti-fracture efficacy compared with plain vitamin D.

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### **Cellular senescence in age-related disorders: Targeting senescent cells to alleviate aging.**

Kaur J1, Farr JN2.

Much of the population is now faced with an enormous burden of age-associated chronic diseases. Recent discoveries in geroscience indicate that healthspan in model organisms such as mice can be manipulated by targeting cellular senescence, a hallmark mechanism of aging, defined as an irreversible proliferative arrest that occurs when cells experience oncogenic or other diverse forms of damage. Senescent cells and their pro-inflammatory secretome have emerged as contributors to age-related tissue dysfunction and morbidity. Cellular senescence has causal roles in mediating osteoporosis, frailty, cardiovascular diseases, osteoarthritis, pulmonary fibrosis, renal diseases, neurodegenerative diseases, hepatic steatosis, and metabolic dysfunction. Therapeutically targeting senescent cells in mice can prevent, delay, or alleviate each of these conditions. Therefore, senotherapeutic approaches, including senolytics and senomorphics, that either selectively eliminate senescent cells or interfere with their ability to promote tissue dysfunction, are gaining momentum as potential realistic strategies to abrogate human senescence to thereby compress morbidity and extend healthspan.

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### **Estrogen for the prevention of recurrent urinary tract infections in postmenopausal women: a meta-analysis of randomized controlled trials.**

Chen YY1,2,3,4, Su TH1,2,3,4, Lau HH5,6,7,8.

Introduction and hypothesis: Recurrent urinary tract infections (rUTIs) are commonly encountered in postmenopausal women. Optimal non-antimicrobial prophylaxis for rUTIs is an important health issue. The aim of this study was to evaluate the use of estrogen in the prevention of rUTIs versus placebo. METHODS: Eligible studies published up to December 2019 were retrieved through searches of MEDLINE, Embase, and Cochrane Central Register of Controlled Trials and Database of Systematic Reviews. We included randomized controlled trials of estrogen therapies versus placebo regarding the outcomes of preventing rUTIs. Changes in vaginal pH and estrogen-associated adverse events were also analyzed. RESULTS: Eight studies including 4702 patients (2367 who received estrogen and 2335 who received placebo) were identified. Five studies including 1936 patients evaluated the use of vaginal estrogen, which resulted in a significant reduction in rUTIs (relative risk, 0.42; 95% CI, 0.30-0.59). Three studies including 2766

patients evaluated the outcomes of oral estrogen in the prevention of UTIs and showed no significant difference in the number of rUTIs compared to treatment with placebo (relative risk, 1.11; 95% CI, 0.92-1.35). Two studies reviewed changes in vaginal pH and showed a lower pH (mean difference, -1.81; 95% CI, -3.10--0.52) after vaginal estrogen therapy. Adverse events associated with vaginal estrogen were reported, including vaginal discomfort, irritation, burning, and itching. There was no significance increase in the vaginal estrogen group (relative risk, 3.06; 95% CI, 0.79-11.90). CONCLUSIONS: Compared with placebo, vaginal estrogen treatment could reduce the number of rUTIs and lower the vaginal pH in postmenopausal women.