

Selección de Resúmenes de Menopausia

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Impact of Dietary Protein on Osteoporosis Development

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Osteoporosis is a frequent yet unsolved health problem among older people. The influence of dietary protein still raises many questions regarding its quality and quantity in the context of bone health. The aim of this manuscript is to review the latest evidence on plant and animal protein influences on bone health in various groups of patients. The review is based on original studies, meta-analyses, randomized controlled trials, and prospective cohort studies published in PubMed and Cochrane databases during the last five years. Combining plant and animal protein with physical activity has the best effect on bones (muscle strengthening and reducing the risk of falls), while high protein intake can have adverse effects during bed rest. Despite the content of isoflavones, plant protein is not more beneficial than animal protein (dairy products) and can increase bone resorption markers. Hypoestrogenism due to menopause or eating disorders leads to low bone density and an increased risk of osteoporosis. A well-balanced diet with sufficient energy supply and protein intake (both of plant and animal origins) and adequate physical activity are crucial to ensure bone health. Dietary interventions should consider the quantity and quality of protein in patients with other comorbidities, particularly in an aging society.

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Long-Term Consumption of Green Tea Can Reduce the Degree of Depression in Postmenopausal Women by Increasing Estradiol

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Postmenopausal women face a higher risk of depression due to a combination of social and physiological factors. As a beverage rich in a variety of bioactive substances, green tea has significant effects on metabolism, inflammation and endocrine, and may reduce the risk of depression, but few studies have looked at the effects of green tea on postmenopausal women. Therefore, we designed this study to investigate the effects of long-term green tea consumption on inflammation, endocrine and depression levels in postmenopausal women. We investigated a tea-producing village and eventually included 386 postmenopausal women, both in the tea drinking and control groups. The results showed that there were significant differences in the degree of insomnia, degree of depression, BMI, SII and estradiol between the two groups. And, green tea consumption may reduce the risk of depression through the mediating pathway of sleep, SII and estradiol. In summary, long-term green tea consumption can reduce the risk of depression in postmenopausal women by reducing inflammation and increasing estradiol. This kind of living habit deserves further promotion.

Complement Ther Med. 2023 Nov 8;79:103002. doi: 10.1016/j.ctim.2023.103002. Online ahead of print.

A dietary intervention for postmenopausal hot flashes: A potential role of gut microbiome. An exploratory analysis

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Objective: This study examined the role of gut microbiome changes in mediating the effects of a dietary intervention on the frequency and severity of postmenopausal vasomotor symptoms METHODS: Postmenopausal women (n = 84) reporting ≥ 2 moderate-to-severe hot flashes daily were randomly assigned, in 2 successive cohorts, to an intervention including a low-fat, vegan diet and cooked soybeans (½ cup [86 g] daily) or to stay on their usual diet. Over a 12-week period, frequency and severity of hot flashes were recorded with a mobile application. In a subset of 11 women, gut microbiome was analyzed at baseline and after 12 weeks of the dietary intervention (low-fat vegan diet with soybeans), using deep shotgun metagenomic sequencing. Differences in the microbiome between baseline and 12 weeks were assessed by comparing alpha diversity with Wilcoxon signed rank tests, beta diversity with permanovaFL, and taxon abundance with Wilcoxon signed rank tests. Pearson correlations were used to assess the association between changes in hot flashes and gut bacteria. Results: In the subset for which microbiome testing was done, total hot flashes decreased by 95 % during the dietary intervention (p = 0.007); severe hot flashes disappeared (from 0.6 to 0.0/day; p = 0.06); and moderate-to-severe hot flashes decreased by 96 % (p = 0.01). Daytime and nighttime hot flashes were reduced by 96 %

($p = 0.01$) and 94 % ($p = 0.004$), respectively. Alpha and beta diversity did not significantly differ in the intervention group between baseline and 12 weeks. Two families (Enterobacteriaceae and Veillonellaceae), 5 genera (Erysipelatoclostridium, Fusicatenibacter, Holdemanella, Intestinimonas, and Porphyromonas), and 6 species (Clostridium asparagiforme, Clostridium innocuum, Bacteroides thetaiotaomicron, Fusicatenibacter saccharivorans, Intestinimonas butyrificiproducens, Prevotella corporis, and Streptococcus sp.) were differentially abundant, but after correction for multiple comparisons, these differences were no longer significant. Changes in the relative abundance of Porphyromonas and Prevotella corporis were associated with the reduction in severe day hot flashes both unadjusted ($r = 0.61$; $p = 0.047$; and $r = 0.69$; $p = 0.02$), respectively), and after adjustment for changes in body mass index ($r = 0.63$; $p = 0.049$; and $r = 0.73$; $p = 0.02$), respectively). Changes in relative abundance of Clostridium asparagiforme were associated with the reduction in total severe hot flashes ($r = 0.69$; $p = 0.019$) and severe night hot flashes ($r = 0.82$; $p = 0.002$) and the latter association remained significant after adjustment for changes in body mass index ($r = 0.75$; $p = 0.01$). Conclusions: This exploratory analysis revealed potential associations between changes in vasomotor symptoms in response to a diet change and changes in the gut microbiome. Larger randomized clinical trials are needed to investigate these findings.

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Long-term consequences of osteoporosis therapy with bisphosphonates

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Bisphosphonates (BPs) are medications widely used in clinical practice to treat osteoporosis and reduce fragility fractures. Its beneficial effects on bone tissue have been consolidated in the literature for the last decades. They have a high affinity for bone hydroxyapatite crystals, and most bisphosphonates remain on the bone surface for a long period of time. Benefits of long-term use of BPs: Large and important trials (Fracture Intervention Trial Long-term Extension and Health Outcomes and Reduced Incidence with Zoledronic acid Once Yearly-Pivotal Fracture Trial) with extended use of alendronate (up to 10 years) and zoledronate (up to 6 years) evidenced significant gain of bone mineral density (BMD) and vertebral fracture risk reduction. Risks of long-term use of BPs: The extended use of antiresorptive therapy has drawn attention to two extremely rare, although severe, adverse events. That is, atypical femoral fracture and medication-related osteonecrosis of the jaw are more common in patients with high cumulative doses and longer duration of therapy. BPs have demonstrated safety and effectiveness throughout the years and evidenced increased BMD and reduced fracture risks, resulting in reduced morbimortality, and improved quality of life. These benefits overweight the risks of rare adverse events.

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Relationship between menopausal hormone therapy and incidence of fractures in postmenopausal women

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Objective: Long-term protective effects of menopausal hormone therapy (MHT) at fractures with different doses and components are controversial. We analyzed the effect of MHT on the incidence of spine and femur fractures according to MHT type, age at commencement, duration and dose of hormones in Korean women. Method: This retrospective study evaluated propensity score-matched patients with MHT from the Korean National Health Insurance Service database. Among women aged ≥ 50 years with menopause between 2004 and 2007, spine and femur fracture incidence until 2017 was analyzed in 36,446 women who had received MHT for >1 year. Estrogen-progesterone therapy (EPT), estrogen-only therapy (ET) or tibolone therapy was conducted. Results: EPT significantly lowered the incidence of spine and femur fractures with a conventional dose, but not with a low dose. Tibolone significantly decreased the incidence of spine fractures in women aged 50-59 years when used for >5 years, and the incidence of femur fractures in women older than 60 years when used for >3 years. ET significantly lowered the risk of femur fractures when estradiol was used for >5 years. Conclusion: In menopausal women, all MHT including conventional-dose EPT, ET and tibolone tended to lower the incidence of fractures. The effects, however, varied with the type of fracture and type of MHT.

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Trajectories of Blood Lipids Profile in Midlife Women: Does Menopause Matter?

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Background It remains controversial whether changes of lipids over menopause transition (MT) are more age-related or more menopause-related. We aimed to classify women into different trajectory groups based on pattern and level of total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B (ApoB), high-density lipoprotein cholesterol (HDL-C), triglyceride, and apolipoprotein A-I over the MT, as well as examine the effect of MT-related factors on lipid trajectory groups and levels. Methods and Results The cohort included 2582 subjects from the Study of Women's Health Across the Nation. Different trajectory patterns of lipids during the MT were determined using the latent class growth mixture model. The predictors of distinct blood lipids trajectory groups were determined by multiple linear regression models and multinomial logistic regression models. Women were categorized into either inverse U-shape or progressing trajectory group in each blood lipids measurement. The inverse U-shape total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, high-density lipoprotein cholesterol, log(TG), and apolipoprotein A-I trajectories showed an increasing trend before menopause but a decreasing trend after menopause. The U-shape total cholesterol, low-density lipoprotein cholesterol, and apolipoprotein B trajectories started to rise 5 years before menopause. Age at menopause, follicle-stimulating hormone, vasomotor symptoms, and estradiol predicted the shape and level of the women's lipids over the MT. Conclusions Distinct lipid trajectories were identified during the MT, and the existence of at least 1 trajectory in each lipid parameters suggested a contribution of menopause. Our study highlights the need for earlier and continuous surveillance of lipids during the MT.

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Association Between Premature Menopause and Cardiovascular Diseases and All-Cause Mortality in Korean Women

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Background Mortality from cardiovascular diseases in Asian populations is considerable. Menopause is a risk-enhancing factor for cardiovascular disease, but it is unclear whether menopause is an independent risk factor for cardiovascular disease and mortality in Asian women. Methods and Results A total of 1 159 405 postmenopausal women, who had participated in the health examinations of the Korean National Health Insurance Service in 2009, were analyzed, and their reproductive histories were taken. A multivariable Cox proportional hazard model assessed the hazard ratios (HRs) of myocardial infarction (MI), ischemic stroke, and all-cause mortality, according to the history of premature menopause and age at menopause. After an average 10-year follow-up, there were 31 606, 45 052, and 77 680 new cases of MI, ischemic stroke, and all-cause mortality, respectively. The women with premature menopause exhibited increased risks of MI (HR, 1.40 [95% CI, 1.31-1.50]), ischemic stroke (HR, 1.24 [95% CI, 1.17-1.31]), and all-cause mortality (HR, 1.19 [95% CI, 1.14-1.24]) when compared with women with menopause aged ≥ 50 years. The highest risk was evident with menopause between the ages of 30 and 34 years (HR for MI, 1.52 [95% CI, 1.30-1.78]; HR for ischemic stroke, 1.29 [95% CI, 1.12-1.48]; HR for all-cause mortality, 1.33 [95% CI, 1.20-1.47]) when compared with women with menopause aged ≥ 50 years. Conclusions Earlier age at menopause was associated with increased risks for MI, ischemic stroke, and all-cause mortality. Future guidelines and risk assessment tools should consider menopause as an independent risk factor of cardiovascular disease in Korean women.

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Changes in menopausal symptoms comparing oral estradiol versus transdermal estradiol

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Objective: This study aimed to compare the efficacy and safety of oral and transdermal estradiol in alleviating menopausal symptoms. Method: A total of 257 recently menopausal women were randomized into two groups. The t-E2 group received transdermal estradiol (2.5 g per day) (n = 128) and the o-E2V group received oral estradiol valerate (2 mg per day) (n = 129) for 24 weeks; both groups received micronized progesterone (200 mg per day). The primary outcome measure is the change in the modified Kupperman Menopausal Index (KMI) after 24 weeks of treatment. Menopausal symptoms were recorded at screening and at 4, 12 and 24 weeks using both the KMI and the Menopause Rating Scale (MRS). Results: Significant amelioration was observed by KMI and MRS scores for both groups after treatment (p < 0.001). The mean KMI scores showed no difference between the two groups. The mean MRS scores were similar between the two groups at baseline and after 4 weeks of treatment. The results showed statistical differences after 12 weeks and 24 weeks of treatment (p = 0.005 and p = 0.011). Both the after-treatment scores minus the baseline scores of KMI and MRS and the incidence of adverse effects showed no difference between the two groups. Conclusions: This study shows

that both transdermal and oral estradiol are effective in relieving menopausal symptoms, with little difference in treatment efficacy and safety.

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Menopausal Vasomotor Symptoms and Plasma Alzheimer's Disease Biomarkers

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Background: Identifying risk factors for Alzheimer's disease (AD) in women is important as women comprise two thirds of individuals with AD. Prior work links vasomotor symptoms (VMS), the cardinal menopausal symptom, with poor memory performance and with alterations in brain structure, function, and connectivity. These associations are evident when VMS are monitored objectively with ambulatory skin conductance monitors. Objective: To determine whether VMS are associated with AD biomarkers. Study design: Between 2017 and 2020 the MsBrain study enrolled 274 community-dwelling women aged 45-67 who had a uterus and at least one ovary and were late perimenopausal or postmenopausal. Key exclusion criteria included neurological disorder, surgical menopause, and recent use of hormonal or non-hormonal VMS treatment. Women underwent 24 hours of ambulatory skin conductance monitoring to assess VMS. Plasma concentrations of AD biomarkers including amyloid β ($A\beta$) 42/40 ratio, phosphorylated tau (p-tau 181 and 231), glial fibrillary acidic protein (GFAP), and neurofilament light (NfL) were measured using single molecule array (Simoa) technology. Associations between VMS and AD biomarkers were assessed via linear regression models adjusted for age, race/ethnicity, education, body mass index, apolipoprotein E4 status, and in additional models, estradiol and sleep. Results: A total of 248 (mean age=59.06 years, 81% white, 99% postmenopausal) of enrolled MsBrain participants contributed data. Objectively-assessed VMS occurring during sleep were associated with significantly lower $A\beta$ 42/ $A\beta$ 40, [B(SE)=-.0010 (.0004), p =.018, multivariable], suggestive of greater brain $A\beta$ pathology. Findings remained significant after additional adjustments for estradiol and sleep. Conclusions: Nighttime VMS may be a marker of women at risk of AD. It is yet unknown if these associations are causal.

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Systematic review and meta-analysis of the effects of menopause hormone therapy on risk of Alzheimer's disease and dementia

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Introduction: Despite a large preclinical literature demonstrating neuroprotective effects of estrogen, use of menopausal hormone therapy (HT) for Alzheimer's disease (AD) risk reduction has been controversial. Herein, we conducted a systematic review and meta-analysis of HT effects on AD and dementia risk. Methods: Our systematic search yielded 6 RCT reports (21,065 treated and 20,997 placebo participants) and 45 observational reports (768,866 patient cases and 5.5 million controls). We used fixed and random effect meta-analysis to derive pooled relative risk (RR) and 95% confidence intervals (C.I.) from these studies. Results: Randomized controlled trials conducted in postmenopausal women ages 65 and older show an increased risk of dementia with HT use compared with placebo [RR = 1.38, 95% C.I. 1.16-1.64, p < 0.001], driven by estrogen-plus-progestogen therapy (EPT) [RR = 1.64, 95% C.I. 1.20-2.25, p = 0.002] and no significant effects of estrogen-only therapy (ET) [RR = 1.19, 95% C.I. 0.92-1.54, p = 0.18]. Conversely, observational studies indicate a reduced risk of AD [RR = 0.78, 95% C.I. 0.64-0.95, p = 0.013] and all-cause dementia [RR = .81, 95% C.I. 0.70-0.94, p = 0.007] with HT use, with protective effects noted with ET [RR = 0.86, 95% C.I. 0.77-0.95, p = 0.002] but not with EPT [RR = 0.910, 95% C.I. 0.775-1.069, p = 0.251]. Stratified analysis of pooled estimates indicates a 32% reduced risk of dementia with midlife ET [RR = 0.685, 95% C.I. 0.513-0.915, p = 0.010] and non-significant reductions with midlife EPT [RR = 0.775, 95% C.I. 0.474-1.266, p = 0.309]. Late-life HT use was associated with increased risk, albeit not significant [EPT: RR = 1.323, 95% C.I. 0.979-1.789, p = 0.069; ET: RR = 1.066, 95% C.I. 0.996-1.140, p = 0.066]. Discussion: These findings support renewed research interest in evaluating midlife estrogen therapy for AD risk reduction.

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Use of MHT in women with cardiovascular disease: a systematic review and meta-analysis

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This systematic review assesses the effect of menopausal hormone therapy (MHT) on cardiovascular outcomes and risk factors in postmenopausal women with cardiovascular disease (CVD). The Medline, Embase and Cochrane databases

were searched from inception to December 2022 for randomized controlled trials (RCTs) and observational studies using methodology from a previous Cochrane review. Quality assessment used the Cochrane risk of bias tool and Newcastle-Ottawa scale, respectively. From 5647 studies identified, 29 (23 RCTs and six observational studies) were included. Most studies were conducted in North America or Europe and investigated oral estrogens. Participants were older with varying frequency of cardiac risk factors and underlying CVD. No significant difference was observed between MHT users and controls regarding primary outcomes of non-fatal myocardial infarction, cardiovascular death or stroke. No difference in frequency of angina, heart failure and transient ischemic attacks was observed. Inconsistent effects of MHT on angiographic progression were seen and varied with glycemic status. Estradiol had a positive effect on flow-mediated dilatation. Limited studies identified differing effects of MHT on cardiac risk factors, varying with estrogen preparation. This study confirms no benefit of MHT for secondary CVD prevention, highlighting evidence limitations and the importance of shared decision-making when managing menopausal symptoms in women with CVD.