Selección de Resúmenes de Menopausia

Semana del 10 a 16 de julio, 2024

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Drug Des Devel Ther. 2024 Jul 10:18:2891-2904. doi: 10.2147/DDDT.S460681. eCollection 2024. -22

Pharmacokinetics and Safety of Estradiol Valerate Tablet and Its Generic: A Phase 1 Bioequivalence Study in Healthy Chinese Postmenopausal Female Subjects

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Purpose: Estradiol valerate (Progynova®) is used as hormone therapy to supplement estrogen deficiency. This study aimed to assess the bioequivalence of an estradiol valerate tablet and its generic form, under fasting and fed conditions. Methods: A randomized, open-label, single-dose, 2-period crossover study was conducted on healthy postmenopausal Chinese female volunteers under fasting and fed conditions. For each period, the subjects received either a 1 mg tablet of estradiol valerate or its generic. Blood samples were collected before dosing and up to 72 hours after administration. Plasma levels of total estrone, estradiol, and unconjugated estrone were quantified using a validated liquid chromatography-tandem mass spectrometry method. Results: A total of 54 volunteers were enrolled in this study. The primary pharmacokinetic parameters, including Cmax, AUC0-t, and AUC0-∞, were similar for the two drugs under both fasting and fed conditions, with 90% confidence intervals for the geometric mean ratios of these parameters, all meeting the bioequivalence criterion of 80-125%. A total of 48 adverse events (AEs) were reported in the fed study compared with 24 AEs in the fasting study. Conclusion: Estradiol valerate and its generic form were bioequivalent and well tolerated under both fasting and fed conditions.

BMC Womens Health. 2024 Jul 13;24(1):399. doi: 10.1186/s12905-024-03243-4.

The impact of physical activity and exercise interventions on symptoms for women experiencing menopause: overview of reviews

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Background: Women experiencing problematic menopausal symptoms report lower health-related quality of life and greater healthcare use than women without symptoms. Not all women want to or are able to take hormone replacement therapy. Strengthening the evidence for menopause symptom-management options, including physical activity, improves agency for women. Aim: This overview assesses effectiveness of physical activity and exercise interventions targeting women experiencing menopause symptoms. Methods: Medline, Embase, CINAHL, Scopus, The Cochrane Database of Systematic Reviews and Social Science Citation Index were searched (June 2023) for systematic reviews of physical activity and exercise interventions targeting women experiencing menopause. Reviews were assessed using AMSTAR-2 and a best-evidence approach to synthesis without meta-analysis (SWIM) was adopted. The protocol was registered on PROSPERO (CRD42022298908).Results: Seventeen reviews included 80 unique relevant primary studies with 8983 participants. There is evidence showing improvement of physical, urogenital, and total symptoms following yoga interventions. Evidence for vasomotor and psychological symptoms was inconclusive. Findings for aerobic exercise were inconclusive although there were some examples of beneficial effects on total and vasomotor symptoms. Evidence was very limited for other types of physical activity and impact on physical, sexual and urogenital symptoms. Conclusion: There is some evidence that yoga, and to lesser extent, aerobic exercise may be beneficial for some menopause symptoms, but there is insufficient evidence to recommend a particular form of exercise. Current reviews categorise women on menopause status; broadening this to include ethnicity, income status, employment and other factors will allow better understanding of context for successful interventions.

J Clin Endocrinol Metab. 2024 Jul 12:dgae480. doi: 10.1210/clinem/dgae480. Online ahead of print.

Breast Cancer is Increased in Women with Primary Ovarian Insufficiency

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Context: DNA damage/repair gene variants are associated with both primary ovarian insufficiency (POI) and cancer risk. Objective: We hypothesized that a subset of women with POI and family members would have increased risk for cancer.Design: Case-control population-based study using records from 1995-2022. Setting: Two major Utah academic

healthcare systems serving 85% of the state. Subjects: Women with POI (n=613) were identified using ICD codes and reviewed for accuracy. Relatives were linked using the Utah Population Database. Intervention: Cancer diagnoses were identified using the Utah Cancer Registry. Main outcome measures: The relative risk of cancer in women with POI and relatives was estimated by comparison to population rates. Whole genome sequencing was performed on a subset of women. Results: Breast cancer was increased in women with POI (OR [95%CI] 2.20 [1.30, 3.47]; p=0.0023) and there was a nominally significant increase in ovarian cancer. Probands with POI were 36.5±4.3 years and 59.5±12.7 years when diagnosed with POI and cancer, respectively. Causal and candidate gene variants for cancer and POI were identified. Among second-degree relatives of these women, there was an increased risk of breast (1.28 [1.08, 1.52]; p=0.0078) and colon cancer (1.50 [1.14, 1.94]; p=0.0036). Prostate cancer was increased in first- (1.64 [1.18, 2.23]; p=0.0026), second- (1.54 [1.32, 1.79]; p<0.001), and third-degree relatives (1.33 [1.20, 1.48]; p<0.001). Conclusions: Data suggest common genetic risk for POI and reproductive cancers. Tools are needed to predict cancer risk in women with POI and potentially to counsel about risks of hormone replacement therapy.

Climacteric. 2024 Jun 19:1-7. doi: 10.1080/13697137.2024.2354728. Online ahead of print.

Hormone replacement therapy and myocardial infarction and stroke in postmenopausal Korean women

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Objective: This study aimed to investigate the association of hormone replacement therapy (HRT) use, type, duration and age of commencement with myocardial infarction (MI) and stroke in postmenopausal Korean women. Methods: This nested case-control study used data from the National Health Insurance Service database to analyze 2017 data from women aged ≥50 years and diagnosed with natural menopause between 2004 and 2007. Among 356,160 eligible women, 36,446 used HRT for ≥1 year and 319,714 did not (controls). These two groups were matched 1:1 for statistical analysis. Type and duration were categorized into three categories. Results: Women who started estrogen-progestogen therapy (EPT) or estrogen therapy (ET) in their 50s, or EPT or tibolone in their ≥60s exhibited a lower stroke risk than controls. MI risk was lower among women who used tibolone - regardless of duration - or EPT or ET for 1-3 years than among controls. Stroke risk was lower with tibolone use for ≥5 years or with EPT or ET use for 1-3 years or ≥5 years than non-users. Conclusion: Our study may support the beneficial effect of HRT by showing that Korean postmenopausal women who used HRT at a relatively younger and healthier age had a relative benefit for MI and stroke.

BMC Public Health. 2024 Jul 8;24(1):1816. doi: 10.1186/s12889-024-19348-2.

Effects of exercise on depression and anxiety in postmenopausal women: a pairwise and network meta-analysis of randomized controlled trials

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Background: Exercise has been identified as a promising non-pharmacological therapy for the management of depression, but there is still controversy over which type is most effective. We aimed to compare and rank the types of exercise that improve depression in postmenopausal women by quantifying information from randomized controlled trials (RCTs). Methods: The PubMed, Web of Science, SPORTDiscus, CNKI, The Cochrane Library, PsycINFO, EMBASE, and CINAHL Plus databases were searched to identify articles published from inception to 1 March 2024 reporting RCTs that examined the effectiveness of exercise on depression in postmenopausal women. The risk of bias was assessed using the revised Cochrane risk-of-bias tool for RCTs. The quality of the evidence for each comparison was graded using the online confidence in network meta-analysis tool (CINeMA). Standardized mean differences (SMDs) were calculated using the mean and standard deviation of pre-to-post intervention changes and then pooled using a random effects model in a pairwise meta-analysis using Review Manager 5.4. Then, a frequentist network meta-analysis was conducted using a random effects model was conducted to evaluate the efficacy of different exercise types using the network package of Stata 15. Results: This study included 26 studies involving 2,170 participants. The pairwise meta-analysis revealed that exercise had a significant positive effect on depression in postmenopausal women (SMD = -0.71, 95% confidence interval [CI] = -0.94 to -0.48; I2 = 78%). The network meta-analysis revealed that mind-body exercise (SMD = -0.97, 95% CI = -1.28 to -0.67), aerobic exercise (SMD = -0.58, 95% CI = -0.88 to -0.27) and multicomponent exercise (SMD = -0.57, 95% CI = -1.15 to -0.002) significantly reduced depression compared to the control intervention. Mind-body exercise had the highest probability of being the most effective intervention. Exercise interventions also showed positive effects on anxiety. Most studies were judged to have some concerns regarding their risk of bias, and the confidence in evidence was often very low according to CINeMA. Conclusion: For

postmenopausal women, there is very low to moderate quality evidence that exercise interventions are an effective antidepressant therapy, with mind-body exercise most likely being the optimal type.

Ceska Gynekol. 2024;89(2):156-159. doi: 10.48095/cccg2024156.

Usage of the levonorgestrel releasing intrauterine system in perimenopause

Tomáš Fait

Levonorgestrel releasing intrauterine system have excellent contraceptive efficacy with simultaneous lowering of menstruation's blood loss. It could be used for therapy of endometrial hyperplasia in perimenopause. In position of gestagen part of the hormone replacement therapy it has high control of endometrial proliferation. It is conjoined with the zero increasing of risk of thromboembolic disease in combination with transdermal oestrogen's application.

Gynecol Endocrinol. 2024 Dec;40(1):2375577. doi: 10.1080/09513590.2024.2375577. Epub 2024 Jul 8.

Ultra-low-dose continuous combined estradiol and dydrogesterone in postmenopausal women: A pooled safety and tolerability analysis

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Objective: To assess the safety and tolerability of ultra-low dose estradiol and dydrogesterone (E0.5 mg/D2.5 mg) among postmenopausal women. Methods: This pooled analysis of data from three clinical studies assessed the effects of continuous combined ultra-low-dose estradiol and dydrogesterone among postmenopausal women. Participants received E0.5 mg/D2.5 mg or placebo for 13 weeks (double-blind, randomized, European study), E0.5 mg/D2.5 mg or placebo for 12 weeks (double-blind, randomized, Chinese study), or E0.5 mg/D2.5 mg for 52 weeks (open-label, European study). Safety outcomes included treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), treatment discontinuation due to a TEAE, and adverse events of special interest (AESIs). Results: Overall, 1027 women were included in the pooled analysis (E0.5 mg/D2.5 mg, n = 736; placebo, n = 291). Mean treatment exposure was 288.9 days in the E0.5 mg/D2.5 mg group and 86.6 days in the placebo group. The proportion of women experiencing ≥1 TEAE was similar in the E0.5 mg/D2.5 mg and placebo groups (50.1% vs 49.5%, respectively). TESAEs occurred in 12 (1.6%) women receiving E0.5 mg/D2.5 mg and 9 (3.1%) women receiving placebo. Discontinuation of study treatment was infrequent in both groups (E0.5 mg/D2.5 mg: 1.5%; placebo: 2.4%). The occurrence of breast pain was more common in the E0.5 mg/D2.5 mg group than in the placebo group (2.0% vs 0.3%) as was uterine hemorrhage (6.5% vs 2.4%). The incidence of acne, hypertrichoses and weight increased was similar between groups. Conclusions: Across three studies, ultra-low-dose estradiol plus dydrogesterone was well tolerated among postmenopausal women, with no increase in TEAEs or TESAEs compared with placebo.