Selección de Resúmenes de Menopausia

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Estradiol Replacement Modulates Synaptic Transmission-Related Proteins in the Hippocampus of Ovariectomized Rats: An Exploratory Proteomic Approach

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The loss of ovarian hormones in postmenopause influences cognition, emotion and energy homeostasis, processes integrated by the hippocampus. The mechanisms by which estradiol influences this area have not been fully understood. The present study aimed at investigating the effects of estradiol on the rat hippocampus proteome of ovariectomy-induced menopause either followed by estradiol replacement or not. Eighteen 3-month-old female Wistar rats were either ovariectomized or sham operated and fed with standard chow for 3 months. A subgroup of ovariectomized rats received estradiol replacement. The hippocampi were processed using data independent acquisition MS-based proteomics and differentially expressed proteins were submitted to bioinformatics analysis for a pathway-based functional understanding of the estradiol effects. Proteomic analysis revealed that 49 hippocampal proteins were modulated by ovariectomy and estradiol replacement. Functional analysis of the differentially expressed proteins revealed the enrichment of terms related to energy metabolism (comprising glycolysis/gluconeogenesis, pyruvate metabolism, oxidative phosphorylation, and response to oxidative stress) and neuron projection (comprising cytoskeleton organization, regulation of vesicle-mediated transport, and modulation of chemical synaptic transmission). The present dataset indicates that, at the hippocampus, estradiol affects mitochondrial dynamics, lipid metabolism and intracellular trafficking machinery and influences dendritic and synaptic transmission and brain plasticity. Some alterations observed in proteins have not yet been described in the hippocampus in the context of menopause and estradiol replacement. These data provide new insights into the mechanisms involved with menopause effects and may help future studies related to drug development for the prevention and treatment of postmenopause associated symptoms.

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Cost-Effectiveness Analysis of Menopausal Hormone Therapy

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Objective: To evaluate the cost effectiveness of menopausal hormone therapy (MHT) based on the risk-benefit profiles of current MHT formulations. Methods: We used a Markov model to examine the cost effectiveness of MHT for hypothetical 50-year-old women with vasomotor symptoms compared with transdermal estradiol (E2) alone for patients without a uterus and transdermal E2 in combination with micronized progesterone for patients with a uterus, assuming 5 years of use. Using a health system perspective, we expressed the effectiveness in quality-adjusted life years (QALYs), and the willingness-to-pay threshold was set to $100,000 per QALY gained. We derived probabilities, cost data, and utilities from the literature and estimated the incremental cost-effectiveness ratios between the MHT and no MHT strategies as our primary outcome. Secondary outcomes included the number of cases of cardiovascular disease, breast cancer, colon cancer, and hip fracture and the number of deaths. Results: Use of MHT demonstrated absolute dominance over not using MHT for both the E2 and E2+micronized progesterone arms. Per 10,000 patients over a lifetime, E2 compared with no MHT was $135,396,560 less expensive, resulted in a gain of 33,196 QALYs, and was associated with 259 fewer cases of atherosclerotic cardiovascular disease (ASCVD), 105 fewer colon cancer cases, 87 more breast cancer cases, 181 fewer hip fractures, and 647 fewer deaths. Micronized progesterone compared with no MHT was $127,738,990 less expensive, resulted in a gain of 33,083 QALYs, and was associated with 285 fewer cases of ASCVD, 18 more colon cancer cases, 46 more breast cancer cases, 183 fewer hip fractures, and 615 fewer deaths. Sensitivity analysis showed that variables related to ASCVD had the most effect on the model. Probabilistic sensitivity analysis revealed absolute dominance for both MHT strategies at all willingness-to-pay thresholds up to $200,000. Conclusion: Our model suggests that MHT is cost effective for typical patients experiencing menopausal symptoms with initiation of MHT at age 50 years and use for 5 years. The reduction in ASCVD risk by MHT is the largest driver of cost effectiveness in the model.

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Menopausal Estrogen Therapy and Risk of Breast Cancer

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Recent evidence suggests that use of menopausal estrogen-only therapy in patients who have undergone hysterectomy reduces breast cancer risk among patients at population risk for breast cancer as well as in those with pathogenic high-risk BRCA variants. A meta-analysis of 10 randomized trials of estrogen therapy compared with placebo among 14,282 participants at population risk noted that 3.6% those randomized to estrogen alone were diagnosed with breast cancer, compared with 4.7% of those randomized to placebo (relative risk 0.77; 95% CI, 0.65-0.91, P=.002). A matched prospective cohort study of 676 patients with BRCA mutations and intact breasts who used menopausal hormone therapy (MHT) found that the estimated 15-year cumulative incidence of breast cancer with estrogen alone compared with no MHT was 24.3%, compared with 47.3% in the matched nonusers of MHT (P<.0001). This evidence underscores the need for more data that specifically assess the effect of estradiol therapy among patients who have undergone hysterectomy. Until such data are available, counseling patients at risk for breast cancer who have completed childbearing and are planning surgery for benign gynecologic conditions should involve shared decision-making that addresses the future risk of breast and endometrial cancers, cardiovascular disease, as well as the morbidity associated with hysterectomy. When appropriate, such counseling should also describe the availability of uterine-sparing alternatives.

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Sex hormones and their receptors in osteoarthritis: current research progress

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Osteoarthritis (OA) is the most prevalent degenerative joint disease worldwide and a leading cause of pain, disability, and reduced quality of life, with pronounced sex-specific differences in incidence and clinical presentation. Epidemiological evidence shows a sharp increase in OA prevalence in women after menopause, whereas in men, the elevated risk at older age is more closely associated with declines in bone mass, muscle strength, and biomechanical stability. Increasing experimental and clinical studies indicate that sex hormones-including estrogen, androgens, and progesterone-and their respective receptors [estrogen receptor (ER), androgen receptor (AR), and progesterone receptor (PR)] play essential roles in maintaining joint homeostasis and modulating OA pathogenesis. At the molecular level, these hormones regulate chondrocyte proliferation, differentiation, apoptosis, extracellular matrix (ECM) metabolism, synovial inflammation, and subchondral bone remodeling through diverse genomic and non-genomic signaling pathways. Dysregulation of hormone signaling, particularly estrogen deficiency or receptor imbalance, contributes to cartilage degeneration, aberrant bone remodeling, and inflammatory activation, thereby promoting OA progression. Notably, hormone-related effects appear to be tissue-specific, receptor subtype-dependent, and stage-dependent, underscoring the complexity of endocrine regulation in joint diseases. This review summarizes recent advances in the roles of sex hormones and their receptors in OA, integrating evidence from molecular mechanisms, experimental studies, and clinical research. It aims to provide a comprehensive framework for understanding sex differences in OA and to support the development of sex-specific and mechanism-based therapeutic strategies.

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Estrogen Withdrawal-Induced Cognitive Impairment in Menopausal Women: Mechanisms and Prospects for Integrated Interventions

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A marked reduction in estrogen levels during perimenopause substantially elevates the risk of Alzheimer's disease (AD) and cognitive dysfunction in women. While the endocrine etiology is well established, applying this understanding to effective clinical prevention remains difficult. Recent findings of diminished cerebral glucose metabolism and lower mitochondrial cytochrome oxidase activity in menopausal women have shifted research attention toward mitochondrial homeostasis disruption and neuroimmune-inflammatory network imbalance as central mechanisms underlying menopausal cognitive decline. This article examines the characteristics and underlying mechanisms of mitochondrial and immune imbalances induced by estrogen withdrawal during menopause. Estrogen deficiency is shown to disrupt mitochondrial-immune homeostasis, particularly via ERβ-mediated mitochondrial oxidative phosphorylation system (OXPHOS) dysfunction and subsequent excessive activation of the NLRP3 inflammasome. The analysis further addresses enhanced inflammatory signaling resulting from excessive reactive

oxygen species generation and mitochondrial DNA (mtDNA) release, as well as reduced synaptic plasticity due to impaired neurotransmitter synthesis and an inflammatory microenvironment. Additionally, the dysregulation of the estrogen-neuromodulatory system in menopausal cognitive decline is investigated. Recent studies demonstrate that intervention strategies targeting estrogen receptors, especially selective ERβ agonists, possess significant neuroprotective potential. Future approaches should incorporate biomarkers, including neuroimaging and genetic polymorphisms, to facilitate risk-stratified and individualized precision medicine. This integration may enhance the prevention or delay of menopause-associated cognitive decline in women.

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Estrogen deficiency-induced lipid dysregulation in menopause: Mechanisms, metabolic consequences, and therapeutic strategies

Menopause is a universal physiological transition marked by the permanent cessation of ovarian estrogen secretion, with far-reaching consequences for cardiometabolic health. Among these consequences, lipid dysregulation stands as one of the most clinically significant, substantially elevating the risk of cardiovascular disease and metabolic syndrome in postmenopausal women. Estrogen deficiency disrupts hepatic lipid metabolism, alters lipoprotein particle composition, promotes visceral adiposity, and triggers a chronic low-grade inflammatory state, collectively establishing an atherogenic lipid profile. Although the broad association between menopause and dyslipidemia has long been recognized, the precise cellular and molecular mechanisms underlying this relationship remain incompletely characterized. This review synthesizes current evidence on the pathophysiological mechanisms linking estrogen deficiency to lipid dysregulation in menopause, encompassing alterations in LDL and HDL metabolism, triglyceride accumulation, changes in lipoprotein lipase (LPL) activity, hepatic lipid accumulation, and the roles of estrogen receptor signaling in adipose tissue and liver. Current and emerging therapeutic strategies are also discussed, including hormone replacement therapy (HRT), lifestyle modifications, lipid-lowering pharmacotherapy, and novel molecular targets. Advancing the mechanistic understanding of these processes is essential to developing precision therapeutic approaches that effectively address the heightened cardiometabolic risk in postmenopausal women.

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Systemic menopausal hormone therapy treatment patterns in Danish women-A nationwide drug utilization study

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Objectives: This paper aims to describe the treatment patterns of contemporary systemic menopausal hormone therapy (MHT) in Denmark. Study design: This study is a nationwide drug utilization study including an open cohort of all Danish women aged >40 years between 2000-2024. Main outcome measures: This study analysed the use of systemic MHT, identified by prescription redemption and categorized by route of administration. Results: During the study period, n = 2 350 335 women reached the age of >40 years and n = 454 592 (19.3%) women used MHT at least once. The prevalence declined from 107.7 per 1000 women in the total cohort on 1 January 2000, to 17.8 per 1000 women on 1 January 2024. The corresponding prevalences for the age group 51-60 years decreased from 191.0 per 1000 women to 33.8 per 1000 women during the same period. The incidence declined from 15.7 per 1000 person-years in 2000 to 4.3 per 1000 person-years in 2023 and then increased to 8.5 per 1000 person-years in 2024. The corresponding numbers for the age group 51-60 years were 33.9 per 1000 person-years in 2000, 9.3 per 1000 person-years in 2023, and 20.2 per 1000 person-years in 2024. In 2022-2024 more women initiated transdermal (2022: 56%; 2023: 63%; 2024: 75%) than oral therapy. For women who initiated treatment before 2015, the cumulative duration of use was often <1 year (37%). Conclusions: Prevalence and incidence of systemic MHT declined over time in Denmark, except in 2024 where the incidence increased. In recent years, more women started transdermal than oral therapy. Cumulative duration of use was often less than 1 year.

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Hormone replacement therapy in healthy BRCA1 and 2 mutation carriers after risk-reducing salpingo-oophorectomy: A 5 Ws and 2 Hs practitioner toolkit

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The management of menopausal symptoms in healthy women carrying BRCA1 or BRCA2 mutations is clinically challenging, particularly in those undergoing risk-reducing salpingo-oophorectomy. This preventive surgery is recommended because it lowers the risk of ovarian cancer, halves the risk of breast cancer and decreases the risk of all-cause mortality; nevertheless, it induces premature menopause, which does have health consequences. Given the negative impact of premature surgical menopause on BRCA1 and 2 mutation carriers' health and quality of life, this population could greatly benefit from hormone replacement therapy. However, its use in this context remains limited, mainly due to patients' and physicians' concerns about its oncological safety. Current evidence suggests that a short course of hormone replacement therapy does not increase breast cancer risk in BRCA mutation carriers after risk-reducing salpingo-oophorectomy. Therefore it can be proposed to BRCA mutation carriers until the age of natural menopause. This review represents a guide to daily practice by answering questions - the 5 Ws (why, when, who, what and where) and 2 Hs (how and how much) - to help physicians in their counselling on hormone replacement therapy and its prescription for this special population.