Selección de Resúmenes de Menopausia

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Effects of 2-methoxyestradiol on hydrogen peroxide induced neuronal cell death and tau hyperphosphorylation

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Aims: Alzheimer's Disease (AD) is characterized by progressive cognitive impairment, and memory loss. It has been shown that depletion of estrogens renders women vulnerable to AD with menopause women presenting higher risk for AD development than men. However, women under hormone replacement therapy (HRT) with 17β-estradiol (E2) show lower risk for AD, implying that E2 may be protective. It has been shown that E2 exerts its effects through the estrogen receptor (ER) but also via its biologically active metabolites, 2-hydroxyestradiol (2OH), and 2-methoxyestradiol (2ME). We hypothesized that the neuroprotective effects of E2 are partly attributed to its metabolites. Materials and methods: SH-SY5Y neuronal cells were subjected oxidative stress (OS) cell death by hydrogen peroxide (H2O2), in the presence or absence of E2, 2ME and 2OH. Viability was assessed by trypan blue and thiazolyl blue tetrazolium bromide assays, intracellular OS with the Dichlorodihydrofluorescein Diacetate (DCFDA) assay, and Bax, p53 and PUMA quantified by RT-PCR. Tau hyperphosphorylation was studied by western blot. Key findings: E2 and its metabolites 2OH and 2ME protect from cell death as assessed by the viability assays. Their effect was partly attributed to their antioxidant properties evidenced by the reduction of intracellular OS. Treatment with 2ME resulted in a reduction of Bax, but not p53 or PUMA in cells challenged with OS. Finally, 2ME was able to inhibit tau hyperphosphorylation as well. Significance: E2 protects neuron cells partly through its metabolites. Further studies are needed to fully delineate the mechanism for this protection.

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The clinical management of testosterone replacement therapy in postmenopausal women with hypoactive sexual desire disorder: a review

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As women age, there is an overall decrease in androgen production due to decline of ovarian and adrenal function during menopause. Androgens have been demonstrated to play an important role in sexual motivation in women. As a result, many postmenopausal women experience Female Sexual Dysfunction (FSD) which are a group of disorders that pertain to sexual arousal, desire, orgasm, and pain. A prevalent manifestation of FSD is Hypoactive Sexual Desire Disorder (HSDD) or the absence of sexual fantasies, thoughts, and/or desire for or receptivity to sexual activity. There is gaining interest in the use of Testosterone Replacement Therapy (TRT) for the treatment of HSDD in postmenopausal women. This article reviews the literature on the relationship of androgen decline and HSDD, describes our methodology for evaluation, diagnosis of HSDD, and the use of TRT in treating postmenopausal women with HSDD. Our results conclude that testosterone is a vital hormone in women in maintaining sexual health and function. TRT is an effective treatment option for postmenopausal people with HSDD. There is still limited data on the effectiveness in premenopausal people with HSDD. Further research in the strengths and weaknesses for the long-term effect of TRT in women of all ages is needed.

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Female Reproductive Events and Subclinical Atherosclerosis of the Brain and Carotid Arteriopathy: the Ohasama Study

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Aims: Few studies have investigated the subclinical atherosclerotic changes in the brain and carotid artery, and in East Asian populations. We sought to investigate whether gravidity, delivery, the age at menarche and menopause and estrogen exposure period are associated with subclinical atherosclerosis of the brain and carotid arteriopathy. Methods: This cross-sectional study formed part of a cohort study of Ohasama residents initiated in 1986. Brain atherosclerosis

and carotid arteriopathy were diagnosed as white matter hyperintensity (WMH) and lacunae evident on brain magnetic resonance imaging (MRI) and carotid intimal media thickness (IMT) or plaque revealed by ultrasound, respectively. The effect of the reproductive events on brain atherosclerosis and carotid arteriopathy was investigated using logistic regression and general linear regression models after adjusting for covariates. Results: Among 966 women aged ≥ 55 years in 1998, we identified 622 and 711 women (mean age: 69.2 and 69.7 years, respectively) who underwent either MRI or carotid ultrasound between 1992-2008 or 1993-2018, respectively. The highest quartile of gravidity (≥ 5 vs. 3) and delivery (≥ 4 vs. 2), and the highest and second highest (3 vs. 2) quartiles of delivery were associated with an increased risk of WMH and carotid artery plaque, respectively. Neither of age at menarche, menopause, and estrogen exposure period estimated by subtracting age at menarche from age at menopause was associated with atherosclerotic changes of brain and carotid arteries. Conclusions: Higher gravidity and delivery are associated with subclinical atherosclerosis of the brain and carotid plaque.

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Body fatness associations with cancer from recent epidemiologic studies

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This narrative review highlights current evidence linking greater body fatness to risk of various cancers, with focus on evidence from recent large cohort studies and pooled analyses of cohort studies as well as Mendelian randomization studies (which utilized genetic variants associated with body mass index to debrief the causal effect of higher body fatness on cancer risk). This review also provides insights into the biological mechanisms underpinning the associations. Data from both observational and Mendelian randomization studies support the associations of higher body mass index with increased risk of many cancers with the strongest evidence for digestive system cancers, including esophageal, stomach, colorectal, liver, gallbladder, and pancreatic cancer, as well as kidney, endometrial, and ovarian (weak association) cancer. Evidence from observational studies suggests that greater body fatness has contrasting effects on breast cancer risk depending on menopausal status and on prostate cancer risk depending on disease stage. Experimental and Mendelian randomization studies indicate that adiponectin, insulin, and sex hormone pathways play an important role in mediating the link between body fatness and cancer risk. The possible role of specific factors and pathways, such as other adipocytokines and hormones and the gut microbiome in mediating the associations between greater body fatness and cancer risk is yet uncertain and needs investigation in future studies. With rising prevalence of overweight and obesity worldwide, the proportion of cancer caused by excess body fatness is expected to increase. There is thus an urgent need to identify efficient ways at the individual and societal level to improve diet and physical activity patterns to reduce the burden of obesity and accompanying comorbidities, including cancer.

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Roles of Hormone Replacement Therapy and Menopause on Osteoarthritis and Cardiovascular Disease Outcomes: A Narrative Review

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Osteoarthritis (OA) is a highly prevalent condition characterized by degradation of the joints. OA and cardiovascular disease (CVD) are leading contributors to disease burden worldwide, with a high level of overlap between the risk factors and occurrence of both conditions. Chief among the risk factors that contribute to OA and CVD are sex and age, which are both independent and interacting traits. Specifically, the prevalence of both conditions is higher in older women, which may be mediated by the occurrence of menopause. Menopause represents a significant transition in a women's life, and the rapid decline in circulating sex hormones, estrogen and progesterone, leads to complex physiological changes. Declines in hormone levels may partially explain the increase in prevalence of OA and CVD in post-menopausal women. In theory, the use of hormone therapy (HT) may buffer adverse effects of menopause; however, it is unclear whether HT offers protective effects for the onset or progression of these diseases. Studies have shown mixed results when describing the influence of HT on disease risk among post-menopausal women, which warrants further exploration. The roles that increasing age, female sex, HT, and CVD play in OA risk demonstrate that OA is a multifaceted condition. This review provides a timely consolidation of current literature and suggests aims for future research directions to bridge gaps in the understanding of how OA, CVD, and HT interact in post-menopausal women.

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The relationship between tobacco and breast cancer incidence: A systematic review and meta-analysis of observational studies

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Background: The effect of tobacco on breast cancer (BC) is controversial. The purpose of this study was to investigate the relationship between tobacco and BC. Methods: A search was conducted in PubMed, EBSCO, Web of Science and Cochrane Library databases before February 2022. The adjusted odd ratio (OR) and corresponding 95% confidence interval (CI) were used to examine the relationship between active or passive smoking and BC risk. Results: A total of 77 articles composed of 2,326,987 participants were included for this meta-analysis. Active (OR=1.15, 95% CI=1.11-1.20, p<0.001) and passive (OR=1.17, 95% CI=1.09-1.24, p<0.001) smoking increased the risk of BC in the female population, especially premenopausal BC (active smoking: OR=1.24, p<0.001; passive smoking: OR=1.29, p<0.001), but had no effect on postmenopausal BC (active smoking: OR=1.03, p=0.314; passive smoking: OR=1.13, p=0.218). Active smoking increased the risk of estrogen receptor-positive (ER+) BC risk (OR=1.13, p<0.001), but had no effect on estrogen receptor-negative (ER-) BC (OR=1.08, p=0.155). The risk of BC was positively associated with the duration and intensity of smoking, negatively associated with the duration of smoking cessation. Active smoking increased the risk of BC in the multiparous population (OR=1.13, p<0.001), but had no effect on the nulliparous population (OR=1.05, p=0.432), and smoking before the first birth (OR=1.22, 95% CI=1.17-1.27) had a greater impact on the risk of BC than smoking after the first birth (OR=1.08, 95% CI=1.04-1.12). Conclusion: Smoking (active and passive) increased the risk of BC in women. The effect of smoking on BC was influenced by smoking-related factors (duration, intensity, years of quitting), population-related factors (fertility status), and BC subtypes.