Selección de Resúmenes de Menopausia

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Risk-Reducing Salpingo-Oophorectomy and the Use of Hormone Replacement Therapy Below the Age of Natural Menopause: Scientific Impact Paper No. 66

R Manchanda, F Gaba, V Talaulikar, J Pundir, S Gessler, M Davies, U Menon.

This paper deals with the use of hormone replacement therapy (HRT) after the removal of fallopian tubes and ovaries to prevent ovarian cancer in premenopausal high risk women. Some women have an alteration in their genetic code, which makes them more likely to develop ovarian cancer. Two well-known genes which can carry an alteration are the BRCA1 and BRCA2 genes. Examples of other genes associated with an increased risk of ovarian cancer include RAD51C, RAD51D, BRIP1, PALB2 and Lynch syndrome genes. Women with a strong family history of ovarian cancer and/or breast cancer, may also be at increased risk of developing ovarian cancer. Women at increased risk can choose to have an operation to remove the fallopian tubes and ovaries, which is the most effective way to prevent ovarian cancer. This is done after a woman has completed her family. However, removal of ovaries causes early menopause and leads to hot flushes, sweats, mood changes and bone thinning. It can also cause memory problems and increases the risk of heart disease. It may reduce libido or impair sexual function. Guidance on how to care for women following preventative surgery who are experiencing early menopause is needed. HRT is usually advisable for women up to 51 years of age (average age of menopause for women in the UK) who are undergoing early menopause and have not had breast cancer, to minimise the health risks linked to early menopause. For women with a womb, HRT should include estrogen coupled with progestogen to protect against thickening of the lining of the womb (called endometrial hyperplasia). For women without a womb, only estrogen is given. Research suggests that, unlike in older women, HRT for women in early menopause does not increase breast cancer risk, including in those who are BRCA1 and BRCA2 carriers and have preventative surgery. For women with a history of receptor-negative breast cancer, the gynaecologist will liaise with an oncology doctor on a case-by-case basis to help to decide if HRT is safe to use. Women with a history of estrogen receptor-positive breast cancer are not normally offered HRT. A range of other therapies can be used if a woman is unable to take HRT. These include behavioural therapy and non-hormonal medicines. However, these are less effective than HRT. Regular exercise, healthy lifestyle and avoiding symptom triggers are also advised. Whether to undergo surgery to reduce risk or not and its timing can be a complex decision-making process. Women need to be carefully counselled on the pros and cons of both preventative surgery and HRT use so they can make informed decisions and choices.

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Factors influencing the levothyroxine dose in the hormone replacement therapy of primary hypothyroidism in adults

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Levothyroxine (LT4) is a safe, effective means of hormone replacement therapy for hypothyroidism. Here, we review the pharmaceutical, pathophysiological and behavioural factors influencing the absorption, distribution, metabolism and excretion of LT4. Any factor that alters the state of the epithelium in the stomach or small intestine will reduce and/or slow absorption of LT4; these include ulcerative colitis, coeliac disease, bariatric surgery, Helicobacter pylori infection, food intolerance, gastritis, mineral supplements, dietary fibre, resins, and various drugs. Once in the circulation, LT4 is almost fully bound to plasma proteins. Although free T4 (FT4) and liothyronine concentrations are extensively buffered, it is possible that drug- or disorder-induced changes in plasma proteins levels can modify free hormone levels. The data on the clinical significance of genetic variants in deiodinase genes are contradictory, and wide-scale genotyping of hypothyroid patients is not currently justified. We developed a decision tree for the physician faced with an abnormally high thyroid-stimulating hormone (TSH) level in a patient reporting adequate compliance with the recommended LT4 dose. The physician should review medications, the medical history and the serum FT4 level and check for acute adrenal insufficiency, heterophilic anti-TSH antibodies, antibodies against gastric and intestinal components (gastric parietal cells, endomysium, and tissue transglutaminase 2), and Helicobacter pylori infection. The next step is an LT4 pharmacodynamic absorption test; poor LT4 absorption should prompt a consultation

with a gastroenterologist and (depending on the findings) an increase in the LT4 dose level. An in-depth etiological investigation can reveal visceral disorders and, especially, digestive tract disorders.

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Menopausal hormone therapy and risk of oesophageal adenocarcinoma in a population-based cohort study

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Background: Oesophageal adenocarcinoma is characterised by a strong male predominance. We aimed to test the hypothesis that menopausal hormonal therapy decreases the risk of oesophageal adenocarcinoma. Methods: This population-based cohort study included all women who used systemic menopausal hormonal therapy (exposed) in Sweden between 2005 and 2018. For each exposed participant, five randomly selected female age-matched non-users of menopausal hormonal therapy (unexposed) were included. Cox regression provided hazard ratios (HR) with 95% confidence intervals (CI) adjusted for age, smoking-related diagnoses, Helicobacter pylori eradication, use of non-steroidal anti-inflammatory drugs/aspirin, use of statins and hysterectomy. Results: The study included 296,964 users of menopausal hormonal therapy and 1,484,820 non-users. Ever-users of menopausal hormonal therapy had an overall decreased risk of oesophageal adenocarcinoma (HR 0.78, 95% CI 0.63-0.97), which remained unchanged after further adjustment for gastro-oesophageal reflux disease (HR 0.78, 95% CI 0.63-0.97) and obesity/diabetes (HR 0.79, 95% CI 0.63-0.98). Decreased HRs were indicated both in users of oestrogen only (HR 0.82, 95% CI 0.60-1.12) and oestrogen combined with progestogen (HR 0.75, 95% CI 0.56-1.00). The risk reduction was more pronounced in users younger than 60 years (HR 0.57, 95% CI 0.38-0.86). Conclusions: Menopausal hormone therapy in women may decrease the risk of oesophageal adenocarcinoma.

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Linking physical activity to breast cancer via sex hormones part 1: The effect of physical activity on sex steroid hormones

Christopher T V Swain 1, Ann E Drummond 1, Leonessa Boing 2, Roger L Milne 1, Dallas R English 3, et al.

The effect of physical activity on breast cancer risk may be partly mediated by sex steroid hormones. This review synthesised and appraised the evidence for an effect of physical activity on sex steroid hormones. Systematic searches were performed using MEDLINE (Ovid), EMBASE (Ovid), and SPORTDiscus to identify experimental studies and prospective cohort studies that examined physical activity and estrogens, progestins, and/or androgens, as well as sex hormone binding globulin (SHBG) and glucocorticoids in pre- and post-menopausal women. Meta-analyses were performed to generate effect estimates. Risk of bias was assessed, and the GRADE system was used to appraise quality of the evidence. Twenty-eight randomized controlled trials (RCTs), 81 non-randomized interventions, and six observational studies were included. Estrogens, progesterone, and androgens mostly decreased, and SHBG increased, in response to physical activity. Effect sizes were small, and evidence quality was graded moderate or high for each outcome. Reductions in select sex steroid hormones following exercise supports the biological plausibility of the first part of the physical activity - sex hormone - breast cancer pathway. The confirmed effect of physical activity on decreasing circulating sex steroid hormones supports its causal role in preventing breast cancer.

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Linking physical activity to breast cancer via sex steroid hormones Part 2: The effect of sex steroid hormones on breast cancer risk

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We undertook a systematic review and appraised the evidence for an effect of circulating sex steroid hormones and sex hormone binding globulin (SHBG) on breast cancer risk in pre- and post-menopausal women. Systematic searches identified prospective studies relevant to this review. Meta-analyses estimated breast cancer risk for women with the highest compared to the lowest level of sex hormones and the DRMETA Stata package was used to graphically represent the shape of these associations. The ROBINS-E tool assessed risk of bias, and the GRADE system appraised the strength of evidence.In pre-menopausal women, there was little evidence that estrogens, progesterone or SHBG

were associated with breast cancer risk, whereas androgens showed a positive association. In post-menopausal women, higher estrogens and androgens were associated with an increase in breast cancer risk, whereas higher SHBG was inversely associated with risk. The strength of the evidence quality ranged from low to high for each hormone. Dose-response relationships between sex steroid hormone concentrations and breast cancer risk were most notable for post-menopausal women. These data support the plausibility of a role for sex steroid hormones in mediating the causal relationship between physical activity and the risk of breast cancer.

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Management of pre-, peri-, and post-menopausal abnormal uterine bleeding: When to perform endometrial sampling?

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Abnormal uterine bleeding (AUB) is defined as abnormal volume, duration, or frequency of menstrual period and is a common symptom in women of all ages (premenopausal, perimenopausal, and postmenopausal). The acronym PALM-COEIN, introduced by the International Federation of Gynecology and Obstetrics (FIGO), facilitates the evaluation and differential diagnosis of AUB, mostly in premenopausal women with AUB. Endometrial evaluation (including ultrasound or hysteroscopic imaging and tissue sampling) for subtle pathology is proposed in patients who are at high risk for endometrial cancer and in patients at low risk who present with AUB and who present poor correspondence in medical treatment. Many new diagnostic modalities are available in clinicians in order to help the assessment of women presenting with abnormalities in their menstrual pattern. The present study reviews the optimal management of women presenting with AUB, taking into consideration the actual need for invasive management in these women, who of them require it, and who can be diagnosed without histological verification. The importance of endometrial tissue sampling in women who present with AUB as well as the best timing for a clinician to conduct a biopsy are two axons analyzed below, according to the latest worldwide guidelines and major publications about this subject.

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Handgrip strength, dynapenia, and related factors in postmenopausal women

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Objective: This study aimed to evaluate the prevalence of dynapenia and factors related to low dominant handgrip strength (HGS) in postmenopausal women. Methods: A cross-sectional study was performed on 249 postmenopausal women aged 50 to 84 years. The following variables were recorded: age, age at menopause, smoking status, and the HGS measured with a digital dynamometer, body mass index, and adiposity assessed by bioelectric impedance. The physical activity level was evaluated by using the International Physical Activity Questionnaire. Bone mineral density was reported as T-scores, and blood biochemical parameters (calcium, phosphorus, vitamin D, and parathormone levels) were measured. Results: 31.3% of women had dynapenia, and those aged ≥65 years had lower HGS ($P < 0.001$). Age at menopause was also associated with HGS, with those with menopause < 51 showing lower HGS ($P = 0.005$). Likewise, fat content ≥ 40%, and osteopenia/osteoporosis were also related to lower strength ($P < 0.001$). There was no statistically significant difference among HGS with respect to body mass index, smoking status, and plasma levels of vitamin D. A logistic regression model with lower Akaine Information Criterion showed that for every year in age and for each 1% of adiposity, women were more likely to have dynapenia with odd ratio (OR): 1.09; 95% and confidence interval (CI): 1.04 to 1.14 and OR: 1.06; 95% CI: 1.00 to 1.13, respectively. Conversely, women with higher femoral neck T-score were less likely to have dynapenia (OR: 0.53; 95% CI: 0.35-0.78). Conclusions: HGS was associated with age at menopause, bone mineral density, and adiposity adjusted by age. The age and adiposity were significantly associated with a higher risk of dynapenia, whereas women with higher femoral neck T-score were less likely to have dynapenia.

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The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis

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Background: Osteoporosis affects all sections of society, including families with people affected by osteoporosis, government agencies and medical institutes in various fields. For example, it involves the patient and his/her family

members, and government agencies in terms of the cost of treatment and medical care. Providing a comprehensive picture of the prevalence of osteoporosis globally is important for health policymakers to make appropriate decisions. Therefore, this study was conducted to investigate the prevalence of osteoporosis worldwide. Methods: A systematic review and meta-analysis were conducted in accordance with the PRISMA criteria. The PubMed, Science Direct, Web of Science, Scopus, Magiran, and Google Scholar databases were searched with no lower time limit up till 26 August 2020. The heterogeneity of the studies was measured using the I2 test, and the publication bias was assessed by the Begg and Mazumdar's test at the significance level of 0.1. Results: After following the systematic review processes, 86 studies were selected for meta-analysis. The sample size of the study was 103,334,579 people in the age range of 15-105 years. Using meta-analysis, the prevalence of osteoporosis in the world was reported to be 18.3 (95% CI 16.2-20.7). Based on 70 studies and sample size of 800,457 women, and heterogenicity I2: 99.8, the prevalence of osteoporosis in women of the world was reported to be 23.1 (95% CI 19.8-26.9), while the prevalence of osteoporosis among men of the world was found to be 11.7 (95% CI 9.6-14.1 which was based on 40 studies and sample size of 453,964 men.). The highest prevalence of osteoporosis was reported in Africa with 39.5% (95% CI 22.3-59.7) and a sample size of 2989 people with the age range 18-95 years. Conclusion: According to the medical, economic, and social burden of osteoporosis, providing a robust and comprehensive estimate of the prevalence of osteoporosis in the world can facilitate decisions in health system planning and policymaking, including an overview of the current and outlook for the future; provide the necessary facilities for the treatment of people with osteoporosis; reduce the severe risks that lead to death by preventing fractures; and, finally, monitor the overall state of osteoporosis in the world. This study is the first to report a structured review and meta-analysis of the prevalence of osteoporosis worldwide.