Selección de Resúmenes de Menopausia

Semana del 2 al 8 de mayo de 2018

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Tibolone improves depression in women through the menopause transition: A double-blind randomized controlled trial of adjunctive tibolone.

Kulkarni J, Gavrilidis E, Thomas N, Hudaib AR, Worsley R, Thew C, Bleeker C, Gurvich C.

BACKGROUND: Many women with no past psychiatric history experience severe mood symptoms for the first time in their life during the menopausal transition, with debilitating long-term consequences. Women with a history of depression can experience a relapse or worsening of symptoms during the menopause transition. Traditional antidepressants, SSRIs or SNRIs, are commonly prescribed as the first line response. However, such treatment has shown only small improvements with side effects. Hormone therapies directly targeting the perimenopausal fluctuations in reproductive hormonal systems such as tibolone, have significant potential to treat perimenopausal depression. Our study investigated the use of adjunctive tibolone, selective tissue estrogenic activity regulator, to treat de-novo or relapsing depression occurring during the menopause transition period. METHODS: Women who were going through the menopause transition with depressive symptoms were invited to participate in a double-blind, 12 week randomized control trial with two arms: tibolone (2.5 mg oral/day) or oral placebo (NCT01470092). Forty-four women met inclusion/exclusion criteria; 22 were randomized to tibolone and 22 were randomized to oral placebo. Symptoms were measured with the 'Montgomery- Asberg depression rating scale' (MADRS) as the primary outcome measure. Latent growth curve analysis was used to assess the MADRS scores change over time. RESULTS: Participants in the tibolone group demonstrated a significant improvement in depression scores, as compared to the placebo group, without any significant side effects. LIMITATIONS: This trial only monitored tibolone's effects over 12 weeks. Future research should be conducted over an extended timeframe and explore whether the benefits of tibolone extend to other symptoms of perimenopausal depression. CONCLUSIONS: The use of hormone therapies such as tibolone provide exciting innovations for the treatment of depression during the menopause transition.

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Long-term effect of statins on the risk of new-onset osteoporosis: A nationwide population-based cohort study.

Lin TK, Chou P, Lin CH, Hung YJ, Jong GP.

BACKGROUND: Several observational cohort and meta-analytical studies in humans have shown that statin users have a lower risk of fractures or greater bone mineral densities (BMD) than nonusers. However, some studies including randomized clinical trials have the opposite results, particularly in Asian populations. OBJECTIVE: This study investigates the impacts of statins on new-onset osteoporosis in Taiwan. METHODS: In a nationwide retrospective population-based cohort study, 45,342 subjects aged between 50-90 years having received statin therapy (statin-users) since January 1 2001, and observed through December 31 2013 were selected from the National Health Insurance Research Database of Taiwan. Likewise, 115,594 patients had no statin therapy (statin-non-users) were included as controls in this study. Multivariable Cox proportional hazards analysis for drug exposures was employed to evaluate the association between statin treatment and new-onset of osteoporosis risk. We also used the long-rank test to evaluate the difference of probability of osteoporosis-free survival. RESULTS: During the 13-year follow-up period, 16,146 of all enrolled subjects (10.03%) developed osteoporosis, including 3097 statin-users (6.83%) and 13,049 statin-non-users (11.29%). Overall, statin therapy reduced the risk of new-onset osteoporosis by 48% (adjusted hazard ratio [HR] 0.52; 95% CI 0.50 to 0.54). A dose-response relationship between statin treatment and the risk of new-onset osteoporosis was observed. The adjusted hazard ratios for new-onset osteoporosis were 0.84 (95% CI, 0.78 to 0.90), 0.56 (95% CI, 0.52 to 0.60) and 0.23 (95% CI, 0.21 to 0.25) when cumulative defined daily doses (cDDDs) ranged from 28 to 90, 91 to 365, and more than 365, respectively, relative to nonusers. Otherwise, high-potency statins (rosuvastatin and atorvastatin) and moderate-potency statin (simvastatin) seemed to have a potential protective effect for osteoporosis. CONCLUSIONS: In this population-based cohort study, we found that statin use is associated with a decreased risk of osteoporosis in both genders. The osteoprotective effect of statins seemed to be more prominent with a dependency on the cumulative dosage and statin intensity.

South Asian J Cancer. 2018 Apr-Jun;7(2):91-95. doi: 10.4103/sajc.sajc_109_18.

Practical consensus recommendaton for adjuvant bone-modifying agents in breast cancer.

Bharatuar A, Kar M, Khatri S, Goswami V, Sarin R, Dawood S, Iyenger R, Ganvir M, Parikh PM, Aggarwal S, Talwar.
Bone-modifying therapy is a primary research interest in breast cancer. Several features contribute to the importance of the bone environment in the management of breast cancer. Firstly, bone metastases represent the most common site of breast cancer metastases and secondly, the emergence of cancer treatment-induced bone loss (CTIBL) among breast cancer survivors and patients is of increasing concern. In the adjuvant setting, bisphosphonates can be given to prevent and treat tumor therapy-induced bone loss in premenopausal and postmenopausal women and, owing to their beneficial effect on bone turnover, have also been evaluated for prevention of bone metastases occurrence. Expert oncologists discusses on the update on the approaches of Bone-modifying Agents and its treatment options. This expert group used data from published literature, practical experience and opinion of a large group of academic oncologists to arrive at this practical consensus recommendations for the benefit of community oncologists.

Consult Pharm. 2018 Mar 1;33(3):142-151. doi: 10.4140/TCP.n.2018.142.

Effects of Denosumab After Treatment Discontinuation: A Review of the Literature.

Iranikhah M, Deas C, Murphy P, Freeman MK.
OBJECTIVE: To review and summarize studies on the effects of denosumab on bone mineral density following the discontinuation of therapy. DATA SOURCES: A search of PubMed (1966-July 2017) and International Pharmaceutical Abstracts (1970-July 2017) was conducted using the Medical Subject Headings (MeSH) terms denosumab, osteoporosis, and withholding treatment in combination with free term searches including the words drug holiday, discontinue, discontin*, and drug discontinuation. STUDY SELECTION AND DATA EXTRACTION: An initial review yielded 10 articles. Four articles that addressed the effects of denosumab discontinuation on markers of overall bone health, fracture risk, or bone histology were included in the final review. DATA SYNTHESIS: Denosumab is a monoclonal antibody indicated for the treatment of osteoporosis in men and postmenopausal women. Denosumab has proven beneficial effects on bone remodeling and bone mineral density, and these effects have been noted to be reversed upon treatment discontinuation because of the agent's lack of incorporation into bone matrix. After 12 to 24 months off denosumab therapy, BMD, BTMs levels, as well as histologic and histomorphometric analyses, were reflective of baseline values. The number of studies evaluating the residual skeletal effects of denosumab is limited, and the sample sizes in the articles reviewed were relatively small. CONCLUSION: An evaluation of studies showed that the discontinuation of denosumab results in loss of bone mineral density and a decline to near baseline values within 12 months of discontinuing therapy. Larger extension studies in a more diverse population need to be conducted to extrapolate the data to other patient groups.

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Dietary intake and age at natural menopause: results from the UK Women's Cohort Study.

Dunneram Y, Greenwood DC, Burley VJ, Cade JE.
BACKGROUND: Age at natural menopause is a matter of concern for women of reproductive age as both an early or late menopause may have implications for health outcomes. METHODS: Study participants were women aged 40-65 years who had experienced a natural menopause from the UK Women's Cohort Study between baseline and first follow-up. Natural menopause was defined as the permanent cessation of menstrual periods for at least 12 consecutive months. A food frequency questionnaire was used to estimate diet at baseline. Reproductive history of participants was also recorded. Regression modelling, adjusting for confounders, was used to assess associations between diet and age at natural menopause. RESULTS: During the 4-year follow-up period, 914 women experienced a natural menopause. A high intake of oily fish and fresh legumes were associated with delayed onset of natural menopause by 3.3 years per portion/day (99% CI 0.8 to 5.8) and 0.9 years per portion/day (99% CI 0.0 to 1.8), respectively. Refined pasta and rice was associated with earlier menopause (per portion/day: -1.5 years, 99% CI -2.8 to -0.2). A higher intake of vitamin B6 (per mg/day: 0.6 years, 99% CI 0.1 to 1.2) and zinc (per mg/day: 0.3 years, 99% CI -0.0 to 0.6) was also associated with later age at menopause. Stratification by age at baseline led to attenuated results. CONCLUSION: Our results

suggest that some food groups (oily fish, fresh legumes, refined pasta and rice) and specific nutrients are individually predictive of age at natural menopause.

JAMA Oncol. 2018 Apr 19. doi: 10.1001/jamaoncol.2018.0211. [Epub ahead of print]

Hormone Replacement Therapy After Oophorectomy and Breast Cancer Risk Among BRCA1 Mutation Carriers.

Kotsopoulos J, Gronwald J, Karlan BY, Huzarski T, Tung N, et al; Hereditary Breast Cancer Clinical Study Group.

Importance: Prophylactic bilateral salpingo-oophorectomy is recommended for BRCA1 mutation carriers to prevent ovarian cancer. Whether or not hormone replacement therapy (HRT) initiated after oophorectomy is associated with an increased risk of breast cancer has not been evaluated in a prospective study. Objective: To determine the association between HRT use and BRCA1-associated breast cancer. Design, Setting, and Participants: A prospective, longitudinal cohort study of BRCA1 and BRCA2 mutation carriers from 80 participating centers in 17 countries was conducted between 1995 and 2017 with a mean follow-up of 7.6 years. Participants had sought genetic testing for a BRCA1 or BRCA2 mutation because of a personal or family history of breast and/or ovarian cancer. Carriers of BRCA1 mutation with no personal medical history of cancer who underwent bilateral oophorectomy following enrollment were eligible for the cohort study. Exposures: A follow-up questionnaire was administered every 2 years to obtain detailed information on HRT use. A left-truncated Cox proportional hazard analysis was used to estimate the hazard ratios (HRs) and 95% CIs associated with the initiation of HRT use postoophorectomy. Main Outcomes and Measures: Incident breast cancer. Results: A total of 872 BRCA1 mutation carriers with a mean postoophorectomy follow-up period of 7.6 years (range, 0.4-22.1) were included in this study. Mean (SD) age of participants was 43.4 (8.5) years. Among these, 92 (10.6%) incident breast cancers were diagnosed. Overall, HRT use after oophorectomy was not associated with an increased risk of breast cancer. The HR was 0.97 (95% CI, 0.62-1.52; P = .89) for ever use of any type of HRT vs no use; however, the effects of estrogen alone and combination hormonal therapy were different. After 10 years of follow-up, the cumulative incidence of breast cancer among women who used estrogen-alone HRT was 12% compared with 22% among women who used estrogen plus progesterone HRT (absolute difference, 10%; log rank P = .04). Conclusions and Relevance: These findings suggest that use of estrogen after oophorectomy does not increase the risk of breast cancer among women with a BRCA1 mutation and should reassure BRCA1 mutation carriers considering preventive surgery that HRT is safe. The possible adverse effect of progesterone-containing HRT warrants further study.

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The impact of exercise and vitamin D supplementation on physical function in community-dwelling elderly individuals: A randomized trial.

Aoki K, Sakuma M, Endo N.

BACKGROUND: We investigated the impact of exercise and vitamin D supplementation on physical function and locomotor dysfunction in community-dwelling elderly individuals. METHODS: In total, 148 community-dwelling elderly individuals (aged ≥60 years) who were not taking osteoporosis medications participated in a 24-week intervention. The participants were randomly divided into an exercise group, vitamin D group, and exercise and vitamin D group. The participants and outcome-assessing staff were not blinded to group assignment. Exercise comprised three daily sets each of single-leg standing (1 min/leg/set) and squatting (5-6 repetitions/set); vitamin D supplementation was 1000 IU/day. Participants were contacted every 2 weeks to check on their condition and encourage continued participation. The primary outcome was lower limb muscle strength and mass; secondary outcomes were several physical function measurements, serum 25-hydroxyvitamin D levels, and results of a self-assessment questionnaire completed pre- and post-intervention. RESULTS: We analyzed data from 45, 42, and 43 participants in the exercise, vitamin D, and exercise and vitamin D groups, respectively, who completed the intervention. Locomotive syndrome, which involves reduced mobility due to locomotive organ impairment, was diagnosed in 99 participants (76.2%). Many physical function measurements improved in all groups. Lower limb muscle mass increased significantly in all three groups, with no significant differences between the groups in the degree of change. The average serum 25-hydroxyvitamin D of all vitamin D-supplemented participants increased from 28.1 ng/ml to 47.3 ng/ml after vitamin D supplementation. CONCLUSIONS: Both exercise and vitamin D supplementation independently improved physical function and increased muscle mass in community-dwelling elderly individuals. Moreover, the combination of exercise and vitamin D supplementation might further enhance these positive effects.