Selección de Resúmenes de Menopausia

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Does Routine Anti-Osteoporosis Medication Lower the Risk of Fractures in Male Subjects? An Updated Systematic Review With Meta-Analysis of Clinical Trials.

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Background: Several epidemiological articles have reported the correlations between anti-osteoporosis medication and the risks of fractures in male and female subjects, but the specific efficacy of anti-osteoporosis medication for male subjects remains largely unexplored. Objective: The aim of this study was to evaluate the correlation between anti-osteoporosis medication and the risk of fracture in relation to low bone mass [including outcomes of osteoporosis, fracture, and bone mineral density (BMD) loss] in male subjects analyzed in studies within the updated literature. Methods: Randomized controlled trials (RCTs) that analyzed the effectiveness of a treating prescription for male subjects with osteoporosis (or low BMD) and that focused on the outcomes of fracture were included. Relevant studies from Embase, Web of Science, PubMed, and Chinese database of CNKI were retrieved from inception to January 30th, 2019. Two staff members carried out the eligibility assessment and data extraction. The discrepancies were settled by consultation with another researcher. We calculated the pooled relative risks (RRs) based on 95% confidence intervals (CIs). Results: Twenty-seven documents (28 studies) with 5,678 subjects were identified. For the category of bisphosphonates, significant results were observed in pooled analyses for decreased risk of the vertebral fracture domain (RR, 0.44 [95% CI, 0.31-0.62]), nonvertebral fracture domain (RR, 0.63 [95% CI, 0.46-0.87]), and clinical fracture domain (RR, 0.59 [95% CI, 0.48-0.72]) compared with those of controls. Participants with bisphosphonates had a 56% (95% CI = 38-69%) lower risk of vertebral fractures, 37% (95% CI = 13-54%) lower risk of nonvertebral fractures, and 41% (95% CI = 28-52%) lower risk of clinical fractures. Furthermore, meta-analyses also demonstrated a decreased risk of the vertebral fracture domain via treatment with risedronate (RR, 0.45 [95% CI, 0.28-0.72]) and alendronate (RR, 0.41 [95% CI, 0.23-0.74]), but not with calcitriol, calcitonin, denosumab, ibandronate, monofluorophosphate, strontium ranelate, teriparatide, or zoledronic acid, compared with that of controls. Conclusions: This systematic review confirms that bisphosphonates were connected with a decreased risk of vertebral fractures, nonvertebral fractures, and clinical fractures for male subjects with osteoporosis. Future research is needed to further elucidate the role of nonbisphosphonates in treating fractures of osteoporosis subjects.

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Bone health in estrogen-free contraception.

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Estrogens and progestogens influence the bone. The major physiological effect of estrogen is the inhibition of bone resorption whereas progestogens exert activity through binding to specific progesterone receptors. New estrogen-free contraceptive and its possible implication on bone turnover are discussed in this review. Insufficient bone acquisition during development and/or accelerated bone loss after attainment of peak bone mass (PBM) are 2 processes that may predispose to fragility fractures in later life. The relative importance of bone acquisition during growth versus bone loss during adulthood for fracture risk has been explored by examining the variability of areal bone mineral density (BMD) (aBMD) values in relation to age. Bone mass acquired at the end of the growth period appears to be more important than bone loss occurring during adult life. The major physiological effect of estrogen is the inhibition of bone resorption. When estrogen transcription possesses binds to the receptors, various genes are activated, and a variety modified. Interleukin 6 (IL-6) stimulates bone resorption, and estrogen blocks osteoblast synthesis of IL-6. Estrogen may also antagonize the IL-6 receptors. Additionally, estrogen inhibits bone resorption by inducing small but cumulative changes in multiple estrogen-dependent regulatory factors including TNF-α and the OPG/RANKL/RANK system. Review on existing data including information about new estrogen-free contraceptives. All progestins exert activity through binding to specific progesterone receptors; hereby, three different groups of progestins exist: pregnanes, gonanes, and estranes. Progestins also comprise specific glucocorticoid, androgen, or mineralocorticoid receptor interactions. Anabolic action of a progestogen may be

affected via androgenic, anti-androgenic, or synadrogenic activity. The C 19 nortestosterone class of progestogens is known to bind with more affinity to androgen receptors than the C21 progestins. This article reviews the effect of estrogens and progestogens on bone and presents new data of the currently approved drospirenone-only pill. The use of progestin-only contraceptives leading to an estradiol level between 30 and 50 pg/ml does not seem to lead to an accelerate bone loss.

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Estradiol and follicle stimulating hormone as predictors of onset of menopause transition-related bone loss in pre- and perimenopausal women.

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The menopause transition (MT) may be an opportunity for early intervention to prevent rapid bone loss. In order to intervene early, we need to be able to prospectively identify pre- and perimenopausal women who are beginning to lose bone. This study examined whether estradiol (E2), or follicle stimulating hormone (FSH), measured in pre- and perimenopausal women, can predict significant bone loss by the next year. Bone loss was considered significant if BMD decline at the lumbar spine (LS) or femoral neck (FN) from a pre- or early perimenopausal baseline to 1 year after the E2 or FSH measurement was greater than the least detectable change. We used data from 1,559 participants in the Study of Women's Health Across the Nation and tested E2 and FSH as separate predictors using repeated measures modified Poisson regression. Adjusted for MT stage, age, race/ethnicity, and body mass index, women with lower E2 (and higher FSH) were more likely to lose BMD: At the LS, each halving of E2 and each doubling of FSH were associated with 10% and 39% greater risk of significant bone loss, respectively ($p < 0.0001$ for each). At the FN, each halving of E2 and each doubling of FSH were associated with 12% ($p = 0.01$) and 27% ($p < 0.001$) greater risk of significant bone loss. FSH was more informative than E2 (assessed by the area under the receiver-operator curve) at identifying women who were more vs. less likely to begin losing bone, especially at the LS. Prediction was better when hormones were measured in pre- or early perimenopause than in late perimenopause. Tracking within-individual change in either hormone did not predict onset of bone loss better than a single measure. We conclude that measuring FSH in the MT can help prospectively identify woman with imminent or ongoing bone loss at the LS. This article is protected by copyright. All rights reserved.

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Algorithm for the Use of Biochemical Markers of Bone Turnover in the Diagnosis, Assessment and Follow-Up of Treatment for Osteoporosis.

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INTRODUCTION: Increased biochemical bone turnover markers (BTMs) measured in serum are associated with bone loss, increased fracture risk and poor treatment adherence, but their role in clinical practice is presently unclear. The aim of this consensus group report is to provide guidance to clinicians on how to use BTMs in patient evaluation in postmenopausal osteoporosis, in fracture risk prediction and in the monitoring of treatment efficacy and adherence to osteoporosis medication. METHODS: A working group with clinical scientists and osteoporosis specialists was invited by the Scientific Advisory Board of European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). RESULTS: Serum bone formation marker PINP and resorption marker βCTX-I are the preferred markers for evaluating bone turnover in the clinical setting due to their specificity to bone, performance in clinical studies, wide use and relatively low analytical variability. BTMs cannot be used to diagnose osteoporosis because of low sensitivity and specificity, but can be of value in patient evaluation where high values may indicate the need to investigate some causes of secondary osteoporosis. Assessing serum levels of βCTX-I and PINP can improve fracture prediction slightly, with a gradient of risk of about 1.2 per SD increase in the bone marker in addition to clinical risk factors and bone mineral density. For an individual patient, BTMs are not useful in projecting bone loss or treatment efficacy, but it is recommended that serum PINP and βCTX-I be used to monitor adherence to oral bisphosphonate treatment. Suppression of the BTMs greater than the least significant change or to levels in the lower half of the reference interval in young and healthy premenopausal women is closely related to treatment adherence. CONCLUSION: In conclusion, the currently available evidence indicates that the principal clinical utility of BTMs is for monitoring oral bisphosphonate therapy.

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Managing menopausal symptoms after cancer.

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The joint burden of cancer and menopause impacts millions of women globally. This review provides an approach to management of menopausal symptoms after cancer in all settings. This includes an overview of current evidence for both hormonal and non-hormonal treatments for vasomotor symptoms and vaginal dryness after cancer. Systemic menopausal hormone therapy provides symptom control and may be used after most cancers but should be avoided after estrogen receptor-positive breast cancer and after some other estrogen-dependent cancers. Non-hormonal therapies have been minimally studied in women after a cancer diagnosis and, where they have been studied, it is usually in women with breast cancer. Non-hormonal methods to manage vasomotor symptoms include cognitive behavioral therapy, hypnosis, selective serotonin reuptake inhibitors, serotonin noradrenaline reuptake inhibitors, clonidine, and gabapentin. Vaginal estrogen may be useful to address vaginal dryness. However, safety data in breast cancer patients are still lacking and there is currently no consensus. Lubricants may also help with pain with sexual activity. Management of menopausal symptoms after cancer may be challenging and should include information about induced menopause and possible symptoms as well as available treatments. Management then requires a holistic and multidisciplinary approach with individualized care.

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Effects of perimenopausal transdermal estradiol on self-reported sleep, independent of its effect on vasomotor symptom bother and depressive symptoms.

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OBJECTIVE: The aim of this study was to determine the efficacy of transdermal estradiol (E2) plus intermittent progesterone (EPT) for improving self-reported sleep in perimenopausal women, after controlling for vasomotor symptoms (VMS) bother and depressive symptoms. METHODS: Using a double-blind, placebo-controlled design, 172 healthy women meeting STRAW+10 criteria for being in the menopausal transition or early postmenopause were randomized to 12 months of transdermal E2 (0.1 mg/d) + 200 mg progesterone (12 d every 3 mo) or placebo. Using standard questionnaires, self-reported sleep, depression, and VMS bother were obtained at baseline and bimonthly postrandomization. RESULTS: Controlling for baseline levels, EPT (vs placebo) led to reductions in minutes to fall asleep (estimate = -0.12, P=0.002) and number of awakenings (estimate = -0.24, P=0.04) over the 12 months. Controlling for changes in VMS bother and depressive symptoms, EPT still predicted reductions in minutes to fall asleep (estimate = -0.28, P=0.02) and number of awakenings (estimate = -0.11, P=0.02) over the 12 months. CONCLUSIONS: We extend existing research by demonstrating that hormone therapy (HT) in subjective sleep cannot be fully explained by improvements in VMS bother or depressive symptoms. Research to examine the mechanism (s) underlying HT's effects on sleep would have public health significance for perimenopausal women and also advance our general understanding of the pathophysiology of impaired sleep.

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Anti-Osteoporosis Medications Associated with Decreased Mortality after Hip Fracture.

Wang PW1, Li YZ1, Zhuang HF1, Yu HM1, Cai SQ2, Xu H1, Chen ZH1, Lin JK1, Yao XD1.

OBJECTIVE: To study the effect of anti-osteoporosis therapies on mortality after hip fracture. METHODS: This retrospective study was carried out in the Second Affiliated Hospital of Fujian Medical University and enrolled 690 patients 50 years of age and older who were admitted with hip fractures between 2010 and 2015. The patients were followed in 2017: 690 patients aged was from 50 to 103 years. There were 456 women and 234 men. There were 335 patients with fractures of the femoral neck and 355 patients with intertrochanteric fractures of the femur. There were 444 (64.35%) patients who also had internal diseases. The Charlson comorbidity index was 0-6. The anti-osteoporosis medications were classified into no anti-osteoporosis medication, calcium + vitamin D supplementations, non-bisphosphonate medication, and bisphosphonate medication. The physicians followed the patients or family members by personal visit and telephone. Multivariable Cox regression analyses were done with known risk factors for mortality of hip fracture, such as gender, age, number of combined internal diseases, fracture type, place of residence, and Charlson comorbidity index, to show which anti-osteoporosis medications had

significant effects on mortality after adjustment for these variables. RESULTS: Out of 690 patients with hip fractures, 149 patients received no anti-osteoporosis medication, 63 patients received calcium +vitamin D supplementations, 398 patients received non-bisphosphonate medication, and 80 patients received bisphosphonate medication. The patients were followed between 7 months and 52 months, with the average of 28.53 ± 9.75 months. A total of 166 patients died during the follow-up period. Of 166 deaths, 43 occurred within 3 months, 65 within 6 months, and 99 within 1 year after the hip fracture. In this study, fracture type, place of residence, and Charlson comorbidity index were not associated with the mortality, and the male gender, age > 75 years, and ≥ 2 combined internal diseases were the independent factors for deaths post-hip fracture. The cumulative mortality was 36.24% in the patients receiving no anti-osteoporosis medication. The hazard ratio for mortality after hip fracture with bisphosphonate medication, non-bisphosphonate medication, and calcium/vitamin D supplementation was 0.355 (95% CI, 0.194-0.648), 0.492 (95% CI, 0.347-0.699) and 0.616 (95% CI, 0.341-1.114), respectively, as compared with no anti-osteoporosis group. Bisphosphonate and non-bisphosphonate medications for osteoporosis were significantly associated with the reduction of cumulative mortality post-hip fracture ($P < 0.01$). CONCLUSIONS: Bisphosphonate and non-bisphosphonate medications for osteoporosis were significantly associated with decreased mortality after fragility hip fracture.

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Association Between Drug Treatments for Patients With Osteoporosis and Overall Mortality Rates: A Meta-analysis.

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Importance: Previous studies have reported that drug treatments, particularly treatment with bisphosphonates, is associated with reduced overall mortality rates in addition to decreased fracture risk. If so, drug treatments should be recommended for this reason alone, regardless of a patient's risk of fracture. Objective: To assess whether randomized clinical trials demonstrate that treatment with bisphosphonates, particularly zoledronate, is associated with reduced mortality rates. Data Sources: Science Direct, MEDLINE, Embase, and the Cochrane Library were searched for randomized placebo-controlled clinical trials of drug treatments for osteoporosis published after 2009 and published or in press before April 19, 2019. Conference abstracts from annual osteoporosis society meetings were also included in the search. Study Selection: Included studies were clinical trials that (1) were randomized and placebo-controlled; (2) studied drug treatments with proven antifracture efficacy; (3) used agents at the approved dose for treatment of osteoporosis; and (4) had a duration of 1 year or more. Abstracts from the literature searches were reviewed for inclusion and exclusion criteria, and mortality rate data were abstracted from the article by 1 researcher and validated by a second. A total of 2045 records were screened; 38 (1.8%) were included in the meta-analyses. Data Extraction and Synthesis: The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist was followed for abstracting data and assessing data quality and validity. Data were pooled using random-effects models, and between-study variability was assessed using the I2 index. The risk of bias for each study was assessed, and funnel plots and Egger and Begg statistics were used to evaluate publication bias. Main Outcomes and Measures: Associations of all drug treatments, particularly bisphosphonate and zoledronate treatments, with overall mortality. Results: Of 38 clinical trials that included 101 642 unique participants, 38 were included in the meta-analyses of all drug treatments (45 594 participants randomized to placebo; 56 048 to treatment); 21 clinical trials, of bisphosphonate treatments (20 244 participants randomized to placebo; 22 623 to treatment); and 6 clinical trials, of zoledronate treatments (6944 participants randomized to placebo; 6926 to treatment). No significant association was found between all drug treatments for osteoporosis and overall mortality rate (risk ratio [RR], 0.98; 95% CI, 0.91-1.05; $I2 = 0\%$). Clinical trials of bisphosphonate treatment (RR, 0.95; 95% CI, 0.86-1.04) showed no significant association with overall mortality. Also, clinical trials of zoledronate treatment (RR, 0.88; 95% CI, 0.68-1.13) showed no association with overall mortality rate; however, evidence existed for heterogeneity of the results ($I2 = 48.2\%$). Conclusions and Relevance: Results of this meta-analysis suggest that bisphosphonate treatment may not be associated with reduced overall mortality rates in addition to decreased fracture risk and should only be recommended to reduce fracture risk. Additional trials are needed to clarify whether treatment with zoledronate reduces mortality rates.