Selección de Resúmenes de Menopausia

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Early changes in bone turnover and bone mineral density after discontinuation of long-term oral bisphosphonates: a post hoc analysis

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Introduction: The short-term effects of discontinuing long-term bisphosphonates are poorly characterized. This post hoc analysis investigated 1-12-month changes in bone mineral density (BMD) and bone turnover markers (BTM) after alendronate (ALN) discontinuation. Methods: Data were from a randomized, double-blind trial of MK-5442 (calcium-sensing receptor antagonist) following oral bisphosphonates, with placebo and continued ALN controls (ClinicalTrials.gov NCT00996801). Postmenopausal women with osteoporosis had received oral bisphosphonate (≥ 3-4 preceding years; ALN for the 12 months pre-screening), continuing on ALN 70 mg/week (n = 87) or placebo (n = 88). Results: At 12 months, least-squares mean percent changes from baseline BMD (placebo vs. ALN) were lumbar spine (LS): - 0.36 vs. 1.29, total hip: - 1.44 vs. 0.46, and femoral neck (FN): - 1.26 vs. - 0.08 (all P < 0.05). BTM levels increased by 1-3 months, to 12 months, with placebo vs. ALN (P < 0.001). FN BMD decline was greater in the placebo subgroup with higher urinary N-terminal cross-linked telopeptides of type I collagen/creatinine [uNTx/Cr] (P < 0.01), and higher serum N-terminal pro-peptide of type 1 collagen [P1NP] levels (P < 0.05), at baseline. There was a trend toward greater FN BMD loss with higher BTM levels at 3 and/or 6 months. Younger age and higher LS BMD at baseline were associated with greater LS BMD loss at 12 months (P = 0.04 and < 0.01, respectively); higher baseline FN BMD predicted greater FN BMD loss (P = 0.04). Conclusion: Early changes in BTM levels and BMD were observed after discontinuation of long-term ALN. Further characterization of factors associated with patients' risk of bone loss upon bisphosphonate discontinuation is warranted.

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The Roles of Epigenetics Regulation in Bone Metabolism and Osteoporosis

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Osteoporosis is a metabolic disease characterized by decreased bone mineral density and the destruction of bone microstructure, which can lead to increased bone fragility and risk of fracture. In recent years, with the deepening of the research on the pathological mechanism of osteoporosis, the research on epigenetics has made significant progress. Epigenetics refers to changes in gene expression levels that are not caused by changes in gene sequences, mainly including DNA methylation, histone modification, and non-coding RNAs (lncRNA, microRNA, and circRNA). Epigenetics play mainly a post-transcriptional regulatory role and have important functions in the biological signal regulatory network. Studies have shown that epigenetic mechanisms are closely related to osteogenic differentiation, osteogenesis, bone remodeling and other bone metabolism-related processes. Abnormal epigenetic regulation can lead to a series of bone metabolism-related diseases, such as osteoporosis. Considering the important role of epigenetic mechanisms in the regulation of bone metabolism, we mainly review the research progress on epigenetic mechanisms (DNA methylation, histone modification, and non-coding RNAs) in the osteogenic differentiation and the pathogenesis of osteoporosis to provide a new direction for the treatment of bone metabolism-related diseases.

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Effect of metformin and insulin vs. placebo and insulin on whole body composition in overweight patients with type 2 diabetes: a randomized placebo-controlled trial

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Introduction: Glucose-lowering medications affect body composition. We assessed the long-term effects of metformin compared with placebo on whole body bone and body composition measures in patients with type 2 diabetes mellitus.

Methods: This was a sub-study of the Copenhagen Insulin and Metformin Therapy trial, which was a double-blinded randomized placebo-controlled trial assessing 18-month treatment with metformin compared with placebo, in combination with different insulin regimens in patients with type 2 diabetes mellitus (T2DM). The sub-study evaluates the effects on bone mineral content (BMC), density (BMD), and body composition f rom whole body dual-energy X-ray absorptiometry (DXA) scans which were assessed at baseline and after 18 months.Results: Metformin had a small, but positive, ($p < 0.05$) effect on subtotal, appendicular, and legs BMC and BMD compared with placebo. After adjustment for sex, age, vitamin D, smoking, BMI, T2DM duration, HbA1c, and insulin dose, the effects on appendicular BMC and BMD persisted ($p < 0.05$ for both). The changes in appendicular BMC and BMD corresponded approximately to a 0.7% and 0.5% increase in the metformin group and 0.4% and 0.4% decrease in the placebo group, respectively. These effects were mostly driven by an increase in BMC and BMD in the legs and a loss of BMC and BMD in the arms. During 18 months, all participants increased in weight, fat mass (FM), FM%, and lean mass (LM), but decreased in LM%. The metformin group increased less in weight (subtotal weight (weight-head) - 2.4 [- 3.5, - 1.4] kg, p value < 0.001) and FM (- 1.5 [- 2.3, - 0.8] kg, p value < 0.001) and decreased less in LM% (0.6 [0.2, 1.1] %, p value < 0.001) compared with the placebo group. Conclusion: Metformin treatment had a small positive effect on BMC and BMD in the peripheral skeleton and reduced weight gain compared with placebo in insulin-treated patients with T2DM.

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Interactions between estradiol, diabetes, and brain aging and the risk for cognitive impairment

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The Women's Health Initiative Memory Study reported that older women using conjugated equine estrogens hormone therapy (HT) with or without medroxyprogesterone acetate were at increased risk for probable dementia and smaller brain volumes. These adverse effects were greatest among women who had type 2 diabetes mellitus (T2DM) at baseline or who developed the disease during follow-up. This review summarizes existing literature from randomized trials, observational studies, and preclinical studies to provide a fundamental understanding of the effects of the interaction between T2DM and HT on cognitive and metabolic health changes in brain aging.

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What happens after menopause? (WHAM): A prospective controlled study of depression and anxiety up to 12 months after premenopausal risk-reducing bilateral salpingo-oophorectomy

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Objective: Risk-reducing bilateral salpingo-oophorectomy (RRBSO) substantially reduces ovarian cancer risk in women with pathogenic gene variants and is generally recommended by age 34-45 years. Natural menopause is a vulnerable period for mood disturbance, but the risk of depression and anxiety in the first 12 months after RRBSO and potential modifying effect of hormone therapy are uncertain. Methods: Prospective controlled observational study of 95 premenopausal women planning RRBSO and a Comparison group of 99 premenopausal women who retained their ovaries,- 95% of whom were at population level risk of ovarian cancer. Clinically significant symptoms of depression and anxiety were measured using standardised instruments at baseline, 3, 6 and 12 months. Chi-square tests and adjusted logistic regression models compared differences between groups. Results: Baseline symptoms and previous depression or anxiety did not differ between groups. At 3 months after RRBSO clinically significant depressive symptoms were doubled (14.5% vs 27.1%, $p = 0.010$), which persisted at 12 months. Depressive symptoms were stable in comparisons. At 3 months after RRBSO, clinically significant anxiety symptoms almost trebled (6.1% vs 17.7%, $p = 0.014$) before plateauing at 6 months and returning to baseline at 12 months. Compared to comparisons, RRBSO participants were at 3.0-fold increased risk of chronic depressive symptoms (Wald 95% CI 1.27-7.26), 2.3-fold increased risk of incident depression (95% Wald CI 1.08-5.13) and 2.0-fold increase of incident anxiety (Wald 95% CI 0.78-5.00). Depression and anxiety were slightly more common in Hormone Therapy users after RRBSO vs non-users. Conclusions: RRBSO leads to a rapid increase in clinically significant depressive and anxiety symptoms despite Hormone Therapy use.

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A meta-analysis on the prevalence of depression in perimenopausal and postmenopausal women in India

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Introduction: The mental health of perimenopausal and postmenopausal women is a relatively understudied area. This review formally explores the prevalence of depression in perimenopausal and postmenopausal women in India. Methods: Databases like PubMed, Embase, Cochrane library, Web of Science and Scopus were systematically searched for cross-sectional or cohort studies, providing prevalence of depression in Indian perimenopausal and postmenopausal women. Systematic study selection and data extraction procedures were followed. Quality assessment of individual study was done using AXIS tool. For pooling of effect sizes, the random effects model was used. Funnel plot and Egger's test were used to ascertain publication bias. Subgroup analyses and meta-regression analysis were used to explore heterogeneity in the summary estimates. Results: After a thorough search, ten studies were found to be eligible and included in this review. Pooled estimate for prevalence of depression (random effects model) in perimenopausal and postmenopausal women in India is 42.47 % (95 % CI: 28.73-57.49, I2 = 97.7 %). On visual inspection of the funnel plot and interpreting egger's test (bias: 3.49, SE bias: 3.68, p = 0.37), there was absence of publication bias. Conclusion: We documented 42.47 % pooled prevalence of depression in perimenopausal and postmenopausal women in India.

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Efficacy of Denosumab Therapy Following Treatment with Bisphosphonates in Women with Osteoporosis: A Cohort Study

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Denosumab is a human monoclonal antibody that neutralizes RANKL, a cytokine able to interact with the RANK receptor on preosteoclasts and osteoclasts, decreasing their recruitment and differentiation, leading to a decreased bone resorption. The aim of this observational real-life study was to analyze adherence to denosumab therapy and assess its efficacy in increasing bone mineral density (BMD) and modulating biochemical skeletal markers following previous treatments with bisphosphonates in a group of post-menopausal women with osteoporosis. Women were recruited in the specialized center from March 2012 to September 2019. Biochemical markers were recorded at baseline and every six months prior to subsequent drug injection. Dual X-ray absorptiometry was requested at baseline and after 18/24 months. Comparing BMD at baseline and after denosumab therapy in naive patients and in those previously treated with bisphosphonates, a positive therapeutic effect was observed in both groups. The results of our real-life study demonstrate, as expected, that BMD values significantly increased upon denosumab treatment. Interestingly, denosumab showed an increased efficacy in patients previously treated with bisphosphonates. Moreover, biochemical markers data indicate that osteoporotic patients, without other concomitant unstable health conditions, could be evaluated once a year, decreasing the number of specialistic center access.