Selección de Resúmenes de Menopausia

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Bisphosphonates: Future perspective for neurological disorders.

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Neurodegenerative disorders and osteoporosis share some common underlying pathological features including calcium overload, accumulation of toxic chemicals, inflammation and impaired protein prenylation by isoprenoids (farnesyl pyrophosphate and geranylgeranyl pyrophosphate) appear later stage of life. Substantial number of pre-clinical and clinical reports as well as in vitro data univocally acknowledged the negative impact of altered post-translational modification (prenylation) of proteins like small GTPases (Rffhes, Rho, Rac etc.) and cholesterol levels in both serum and brain on CNS integrity. Bisphosphonates (BPs), referred to as gold standard for osteoporosis treatment, have well established role in attenuation of bone resorption and osteoclast apoptosis by inhibition of farnesyl pyrophosphate synthase enzyme (FPPS) in mevalonate pathway. BPs mainly nitrogen containing BPs (NBPs) have potential to offer new therapeutic targets for neurological disorders and received increasing attention in recent years. A year back clinical and pre-clinical studies revealed that NBPs have the potential to alleviate the symptoms of neurological disorders like brain calcification, Alzheimer's disease and Huntington's disease by targeting mevalonate pathway. Though these drugs have well developed role in inhibition of isoprenoids synthesis, these were demonstrated to inhibit acetyl cholinesterase enzyme and cholesterol synthesis in brain that are considered as the critical factors for impairment of cognitive functions which is the hallmark of several neurological disorders. Still the current understanding of BPs' effect in CNS is limited due to lack of studies focusing the molecular and cellular mechanism. The present review aims to reveal the updated discussion on the mechanism contributing BPs' effect in CNS disorders.

Climacteric. 2018 Aug 10:1-7. doi: 10.1080/13697137.2018.1480600. [Epub ahead of print]

The effect of vitamin D2 supplementation on muscle strength in early postmenopausal women: a randomized, double-blind, placebo-controlled trial.

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BACKGROUND: Low serum 25-hydroxyvitamin D [25(OH)D] has been shown to be associated with low muscle mass and loss of muscle strength, resulting in increased disability and frailty in older men and women. Vitamin D deficiency is common in postmenopausal women. The primary objective of the present study was to evaluate the effects of vitamin D supplementation on muscle strength in early postmenopausal women. The effects of vitamin D2 supplementation on muscle mass and muscle cross-sectional area (CSA) were secondarily investigated. METHODS: A 12-week, prospective, randomized, double-blind, placebo-controlled trial was conducted in early postmenopausal women (45-60 years old) with vitamin D deficiency (serum 25(OH)D < 20 ng/ml). A total of 88 subjects were randomized into group I: vitamin D2 supplement 40 000 IU/week (n = 44), or group II: placebo (n = 44). Serum 25(OH)D level, muscle strength, muscle mass and muscle CSA were assessed at baseline and 12 weeks after the supplementation. RESULTS: After 12 weeks of supplementation, 70% of women in group I achieved a sufficient level of serum 25(OH)D (>30 ng/ml). There were significant differences in changes of serum 25(OH)D levels between the two groups ($p < 0.05$). Muscle strength and muscle CSA in group I increased significantly after 12 weeks ($p = 0.015$, 0.045, respectively). However, there were no significant differences in the mean changes of muscle strength, muscle mass and muscle CSA between the two groups ($p = 0.16$, 0.89, 0.84, respectively). CONCLUSION: In this study, we found no obvious effect of vitamin D supplementation on the changes in muscle strength, muscle mass and muscle CSA when compared to placebo. However, there were significant changes in muscle strength and muscle CSA from baseline in the vitamin D supplementation group.

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Osteoporosis and osteopenia in the distal forearm predict all-cause mortality independent of grip strength: 22-year follow-up in the population-based Tromsø Study.

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INTRODUCTION: To investigate if bone mineral density (BMD) levels of the distal forearm, consistent with osteopenia and osteoporosis, can predict mortality and if grip strength is an effect modifier. METHODS: The study population constituted 6565 participants aged 50-79 years at baseline in the Tromsø Study wave 4 conducted in 1994-1995. Forearm BMD measured by SXA was categorized as "normal," "osteopenia," or "osteoporosis" following WHO's definition. Cox regression with all-cause mortality as the outcome over 22 years of follow-up was performed for men and women separately, adjusting for health-related factors, as well as BMD by grip strength interaction. A secondary analysis with a 15-year follow-up also adjusted for hip fractures and osteoporotic fractures. RESULTS: During follow-up, 3176 of participants died (47%). Those categorized as osteoporotic had higher mortality hazard ratio (HR) compared to those with normal BMD; men HR = 1.37 (95% confidence interval (CI) 1.19, 1.58) and women HR = 1.32 (1.14, 1.53) were adjusted for age, body mass index, physical activity, smoking habits, education, health status, chronic diseases, and grip strength. Corresponding HRs for osteopenia were men HR = 1.13 (1.00, 1.27) and women HR = 1.17 (1.01, 1.35). Further adjustments for fractures did only marginally attenuate the results, and HRs were still significant. There was no grip strength by BMD interaction. CONCLUSION: Men and women with low distal forearm BMD values, consistent with osteoporosis or osteopenia, had an increased mortality compared to normal BMD participants. High grip strength did not modify this association, and the association remained after adjustment for a range of health-related factors.

Oncotarget. 2018 Jul 17;9(55):30561-30567. doi: 10.18632/oncotarget.25703. eCollection 2018 Jul 17.

Colorectal tumor prevention by the progestin medroxyprogesterone acetate is critically dependent on postmenopausal status.

Meijer BJ, Wielenga MCB, Hoyer PB, Amos-Landgraf JM, Hakvoort TBM, Muncan V, Heijmans J, et al.

The large randomized placebo controlled trials of the Women's Health Initiative have shown that the combination of estrogen and progestin medroxyprogesterone acetate (MPA) protects from colorectal cancer in postmenopausal women. No effect was observed in women treated with estrogen alone. This suggests that progesterone, or more specifically the progestin MPA may have chemopreventive activity. The effect of MPA on colorectal carcinogenesis has been difficult to study in animal models. Most models are not affected by either depleting female hormones by ovariectomy or treatment with MPA. Importantly, an ovariectomy fails to reproduce one of the hall marks of the postmenopausal state in women with intact ovaries. That is, the continued production of androgens by the atrophic postmenopausal ovaries. Here we show that adenoma incidence is increased in the vinyl cylcohexene diepoxide (VCD) mouse model of the menopause compared to age matched fertile female mice. Treatment with MPA protected VCD treated mice from adenomagenesis, but had no effect on adenoma numbers in age-matched fertile female mice. Our data show that the protective effect of MPA depends on the postmenopausal state and suggest that MPA monotherapy may be studied as a chemopreventive agent in postmenopausal women.

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Relationship between vasomotor symptoms and metabolic syndrome in postmenopausal women.

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Objective. This study was performed to compare the vasomotor symptoms and bone mineral density of postmenopausal women with and without metabolic syndrome. Methods We performed a cross-sectional study of 200 postmenopausal women attending routine health check-ups at Marmara Faculty of Medicine Pendik Training and Research Hospital from June 2015 to December 2015. The vasomotor symptoms scored were hot flashes and night sweats. Metabolic syndrome was defined using the consensus criteria of the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute. Results. Women with vasomotor symptoms had no metabolic syndrome and were younger than those without vasomotor symptoms. There was no significant difference in vasomotor symptoms between patients with osteopenia in the femoral neck, total femur, and spine and patients with normal bone mineral density. The vasomotor symptoms were similar between smokers and

nonsmokers. Conclusion The presence of metabolic symptoms is inversely associated with metabolic syndrome in postmenopausal women. Lipid abnormalities and a high body mass index may be important metabolic components associated with these symptoms. No relationship is present between vasomotor symptoms and the bone mineral density of the spine, femoral neck, and total femur.

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Decreasing trend of bone mineral density in US multiethnic population: analysis of continuous NHANES 2005-2014.

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INTRODUCTION: Osteoporosis prevalence in the USA declined between 1988 and 2006, while the declining trend in hip fracture may have plateaued in 2013-2014. We aimed to examine whether there has been a corresponding change in BMD trajectory for the US population. METHODS: Continuous National Health and Nutrition Examination Survey (NHANES) data from 2005-2006 to 2013-2014 were analyzed to examine BMD trends among US men and women aged 30 years and older and among different race/ethnicity subgroups. ANOVA and Bonferroni adjustments were used to examine the differences in mean BMD, and multiple linear regressions adjusting for potential confounding effects were employed to examine BMD trends. RESULTS: After age standardization, the mean BMD of the femur neck for the first three NHANES cycles was stable (all $p > 0.1$) in both men and women, but significantly decreased in 2013-2014, from 0.864 g/cm2 to 0.846 g/cm2 ($p = 0.0025$) in men and from 0.789 to 0.771 g/cm2 ($p = 0.03$) in women. The overall mean femur neck BMD in 2013-2014 was significantly lower than that in earlier survey cycles in both men and women, even after adjusting for multiple covariates, including age, race, physical activity, previous fracture, BMI, and other variables. Similar results were observed in subgroup analyses of race and sensitivity analyses. CONCLUSIONS: Age-adjusted mean BMD decreased in 2013-2014 in both men and women, and this significant decrease was also observed in sensitivity and subgroup analyses. The decreased BMD in 2013-2014 still remained significant even after being adjusted for multiple potentially confounding effects.

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Insomnia and sexual dysfunction associated with severe worsening of the quality of life in sexually active hysterectomized women.

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Hysterectomy is a common gynecologic surgery carried out to remove the pathologic uterus. Objective: To establish if sleep disorders and sexual function are associated with deterioration of the quality of life (QoL) in hysterectomized and sexually active women. Methods: A cross-sectional study was carried out with inhabitants from two cities of the Colombian Caribbean. The pollsters invited women aged between 40-59 years to participate; in their communities they applied surveys with demographic characteristics: Female Sexual Function Index, Atenas Insomnia Scale and Menopause Rating Scale. Sexually active women were selected; then the association was established with logistic regression. Results: 522 women were studied with an average age of 50 years: 30% oophorectomized, 59.8% Hispanic, 40.2% afro-descendants and 22.2% hormonal therapy users. 80% of them had somato/vegetative, psychological or urogenital deterioration; 29.1% with severe deterioration of QoL and 47.5% with insomnia. Out of 390 (74.7%) with sexual activity, 59.7% suffered from sexual dysfunction. Insomnia: OR:3.05 [95%CI:1.86-4.99], sexual dysfunction OR:3.52 [95%CI:2.01-6.17], dissatisfaction about sexuality OR:4.77 [95%CI:2.08-10.93], low or non-existent sexual desire OR:2.94 [95%CI:1.65-5.25], daytime drowsiness OR:3.15 [95%CI:1.59-6.24] and decrease in daytime well-being OR:3.18 [95%CI:1.79-5.64]. These were factors associated with severe worsening of QoL, while the presence of genital lubrication was protective, OR: 0.44 [95%CI:0.21-0.93], p=0.0332. Conclusion: It was observed that insomnia and sexual dysfunction behaved as factors associated with three times more severe deterioration of the QoL in climacteric and sexually active women previously hysterectomized.

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Serial Studies in Subclinical Atherosclerosis During Menopausal Transition (from the Study of Women's Health Across the Nation).

Khan ZA, Janssen I, Mazzarelli JK, Powell LH, Dumasius A, Everson-Rose SA, Barinas-Mitchell E, et al.

Cardiovascular disease risk increases in women after the menopausal transition; why this inflection point occurs remains uncertain. We aimed to characterize the influence of menopause on vascular aging by prospective assessment of change in indexes of subclinical atherosclerosis across the menopausal transition. We evaluated 411

healthy women from SWAN Heart, an ancillary study of SWAN (Study of Women's Health Across the Nation), for subclinical atherosclerosis at baseline and again after an average of 2.3 years. Carotid intima-media thickness and aortic pulse wave velocity were measured by ultrasound. Coronary artery calcium scores were obtained by computed tomography. Women were grouped by menopausal status as premenopausal, postmenopausal, or having undergone the transition during follow-up. Analyses of changes were adjusted for age at baseline and time between scans. Mean age at baseline was 51 ± 3 years; 93 (23%) subjects transitioned to menopause (Pre-Post), 147 (36%) remained premenopausal (Pre-Pre), while 171 (41%) were postmenopausal at baseline (Post-Post). Blood pressure readings did not differ between groups with similar increase noted in carotid intima-media thickness and log coronary artery calcium + 1 from baseline to follow-up. Change in aortic pulse wave velocity from baseline to follow-up was higher in Pre-Post (121 ± 23 cm/s) compared with Pre-Pre (38 ± 250 cm/s, $p = 0.029$) and Post-Post (41 ± 228 cm/s, $p = 0.045$). In conclusion, changes in aortic stiffness were more sensitive measures of perimenopausal vascular aging than morphologic indexes of subclinical atherosclerosis in women undergoing the menopausal transition. Serial assessment of such changes could potentially elucidate mechanisms of disease and identify women to target for aggressive lifestyle risk factor modification.