

Selección de Resúmenes de Menopausia

Semana del 10 al 16 de julio de 2019

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Differential diagnoses of osteoporosis.

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The differential diagnoses of osteoporosis in geriatric and trauma patients are very important as they may induce different therapies. On average approximately 20% of women and 50% of men, have secondary causes of osteoporosis. The foundation of the diagnostics is a basic osteological laboratory investigation with which the most important secondary causes can be identified. From a geriatric and traumatological point of view vitamin D deficiency with secondary hyperparathyroidism, primary hyperparathyroidism, male hypogonadism, multiple myeloma and monoclonal gammopathy of unclear significance (MGUS) are of particular importance.

BMC Endocr Disord. 2019 Jul 11;19(1):72. doi: 10.1186/s12902-019-0403-2.

The pubertal development mode of Chinese girls with turner syndrome undergoing hormone replacement therapy.

Guo S1, Zhang J1, Li Y1, Ma H1, Chen Q1, Chen H1, Du M2.

BACKGROUND: Further knowledge about the pubertal development mode of girls with Turner syndrome (TS) who have undergone hormone replacement therapy (HRT) is beneficial to the proposal of an optimal HRT regimen. This study examined the pubertal development mode of girls with TS who underwent HRT and evaluated the characteristics of optimal sex induction therapy in girls with TS. **METHOD:** We conducted a retrospective, longitudinal study over the past two decades at The First Affiliated Hospital, Sun Yat-sen University. **PATIENTS:** Seventy-one patients with TS and two groups of normal Chinese girls. **RESULTS:** The total investigation time was 3.00 (2.00, 4.66) years. The interval of each stage was significantly longer ($P < 0.001$) in the girls with TS than that in the normal Chinese girls, except for B2-3 ($P = 0.011$). The uterine volumes of the girls with TS in stages B2 and 3 were greater than those of the control group ($P = 0.046$), whereas the uterine volume of the control group was inversely greater than that of the TS group among those who reached stages B4 and 5 ($P = 0.034$). During HRT, the uterine volume grew significantly from all previous stages except for breast stage 5 (B3 vs. 2: $Z = -2.031$; $P = 0.042$; B4 vs. 3: $Z = -2.273$; $P = 0.023$; B5 vs. 4: $Z = -1.368$; $P = 0.171$). The paired data of 27 girls with TS showed that the uterine volume (17.93 ± 9.31 ml vs. 13.75 ± 6.67 ml) and width (2.54 ± 0.66 cm vs. 2.22 ± 0.36 cm) increased significantly during artificial cycles compared with before artificial cycles ($t = -2.79$ and -2.51 , $P = 0.01$ and 0.018). **CONCLUSION:** HRT led to normal breast development in girls with TS; half of the girls with TS in our study reached Tanner stage B5, although the uterus ultimately developed suboptimally. The girls' breasts and uteruses grew quickly at the beginning of HRT (stages B2-4). An optimal HRT regimen for girls with TS may specifically focus on Tanner stages B2-4 and artificial cycles.

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Effects of ospemifene on bone in postmenopausal women.

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Ospemifene is a selective estrogen-receptor modulator approved for treating menopause-related moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy (VVA), in the United States, and for treating menopause-related, symptomatic VVA in women not appropriate for local estrogen therapy in Europe. This review summarizes the effects of ospemifene on bone, including bone biomarker data from a phase 3 vaginal dryness study. Early-phase studies of postmenopausal women showed that ospemifene dose-dependently decreased bone turnover markers versus placebo, similar to raloxifene. A 12-week, phase 3 study of ospemifene 60 mg/day in postmenopausal women showed improvements in all VVA parameters and significantly greater decreases in seven of nine bone biomarkers versus placebo. Lower bone resorption markers with ospemifene were observed regardless of time since menopause (≤ 5 years or > 5 years) or baseline bone mineral density (BMD) (normal [$n = 18$], osteopenia [$n = 164$], or osteoporosis [$n = 21$]). Biomarker studies ($n = 565$ who took ospemifene) therefore support a potential role for

ospemifene in maintaining bone health (and possibly reducing fracture risk) in postmenopausal women taking it for VVA; however, caution is warranted because data are limited to biochemical markers, rather than fracture and BMD. Although studies show that bone turnover predicts BMD and fractures, any hypothesis about a bone-sparing effect of ospemifene needs testing in rigorous, long-term, phase 3 studies monitoring fractures and BMD.

Cell Rep. 2019 Jul 9;28(2):368-381.e6. doi: 10.1016/j.celrep.2019.06.025.

Estrogen Regulates the Satellite Cell Compartment in Females.

Collins BC1, Arpke RW2, Larson AA3, Baumann CW1, Xie N2, Cabelka CA1, Nash NL1, Juppi HK4, Laakkonen EK4, Sipilä S4, Kovanen V4, Spangenburg EE5, Kyba M2, Lowe DA6.

Skeletal muscle mass, strength, and regenerative capacity decline with age, with many measures showing a greater deterioration in females around the time estrogen levels decrease at menopause. Here, we show that estrogen deficiency severely compromises the maintenance of muscle stem cells (i.e., satellite cells) as well as impairs self-renewal and differentiation into muscle fibers. Mechanistically, by hormone replacement, use of a selective estrogen-receptor modulator (bazedoxifene), and conditional estrogen receptor knockout, we implicate 17 β -estradiol and satellite cell expression of estrogen receptor α and show that estrogen signaling through this receptor is necessary to prevent apoptosis of satellite cells. Early data from a biopsy study of women who transitioned from peri- to post-menopause are consistent with the loss of satellite cells coincident with the decline in estradiol in humans. Together, these results demonstrate an important role for estrogen in satellite cell maintenance and muscle regeneration in females.

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Managing Genitourinary Syndrome of Menopause in Breast Cancer Survivors Receiving Endocrine Therapy.

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Patients with breast cancer receiving antiestrogen therapy, specifically aromatase inhibitors, often suffer from vaginal dryness, itching, irritation, dyspareunia, and dysuria, collectively known as genitourinary syndrome of menopause (GSM). GSM can decrease quality of life and is undertreated by oncologists because of fear of cancer recurrence, specifically when considering treatment with vaginal estrogen therapy because of unknown levels of systemic absorption of estradiol. In this article, we review the available literature for treatment of GSM in patients with breast cancer and survivors, including nonhormonal, vaginal hormonal, and systemic hormonal therapy options. First-line treatment includes nonhormonal therapy with vaginal moisturizers, lubricants, and gels. Although initial studies showed significant improvement in symptoms, the US Food and Drug Administration recently issued a warning against CO₂ laser therapy for treatment of GSM until additional studies are conducted. In severe or refractory GSM, after discussing risks and benefits of vaginal hormonal therapy, the low-dose 10- μ g estradiol-releasing intravaginal tablet or lower-dose 4 μ g estrogen vaginal insert and intravaginal dehydroepiandrosterone (prasterone) are options for treatment, because studies show minimal elevation in serum estradiol levels and significant improvement in symptoms. The decision to offer vaginal estrogen therapy must be individualized and made jointly with the patient and her oncologist.

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Sleep quality and fatigue in women with premature ovarian insufficiency receiving hormone therapy: a comparative study.

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OBJECTIVE: To compare sleep quality and fatigue between women with premature ovarian insufficiency (POI) receiving hormone therapy (HT) and women of the same age with preserved ovarian function. **METHODS:** This was a cross-sectional study of 61 women with POI receiving HT (POI group) and 61 women with preserved ovarian function (control group) who were matched by age (± 2 years). The Pittsburgh Sleep Quality Index (PSQI) and Chalder Fatigue Scale were used to assess sleep quality and fatigue. Apart from correlation analysis, the Mann-Whitney, chi-square, or Fisher test was used to compare the groups. **RESULTS:** Women from the POI and control groups were 35.03 ± 7.68 and 34.49 ± 7.55 years of age, respectively ($P=0.63$). In the PSQI evaluation, the scores were 7.69 ± 4.18 and 8.03 ± 4.53 , respectively ($P=0.79$), showing no difference between the POI and control groups.

However, the POI group had higher and therefore worse scores for the sleep latency component (1.74 ± 0.66 and 1.18 ± 0.87 , respectively; $P < 0.001$) and use of medication to sleep (1.28 ± 0.88 and 0.85 ± 0.8 ; $P = 0.008$). The POI group had a higher fatigue index than that of the control group (5.25 ± 2.78 and 3.49 ± 1.78 , respectively; $P < 0.001$), with sleep quality being classified as poor in 69% and fatigue present in 59% of patients. **CONCLUSIONS:** Women with POI receiving HT have poor sleep quality. They take longer to fall asleep and have a higher fatigue index.

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Prasterone: A Review in Vulvovaginal Atrophy.

Heo YA1.

Vulvovaginal atrophy (VVA) is a progressive condition commonly seen in postmenopausal women. The cessation of ovarian estrogen secretion and a fall in serum levels of dehydroepiandrosterone (DHEA), the remaining source of estrogens and androgens, are thought to promote the development of VVA in this population. Intravaginal prasterone (Intrarosa®) is a synthetic form of DHEA indicated for the treatment of VVA in postmenopausal women presenting with moderate to severe symptoms in the EU; prasterone is also approved in the USA for the treatment of dyspareunia due to menopause. Approval for the treatment of VVA was based on the results of the phase III ERC-231 and -238 trials in which intravaginal prasterone 6.5 mg/day significantly improved the signs and symptoms of VVA (as assessed by the percentage of parabasal and superficial cells, vaginal pH and the severity of dyspareunia) compared with placebo. The beneficial effects of prasterone were also evident during 52 weeks' treatment in the phase III ERC-230 safety trial. Prasterone was generally well tolerated, with the most common treatment-emergent adverse event being application site discharge. During 52 weeks of treatment with prasterone, changes in serum concentrations of estrogenic and androgenic metabolites of DHEA increased from baseline but remained within the normal postmenopausal ranges. Thus, intravaginal prasterone is an effective and generally well-tolerated option for the treatment of VVA in postmenopausal women.

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Urolithiasis increases the risk of subsequent onset of osteoporosis.

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Urolithiasis and osteoporosis are two different pathological entities, but are both important public health issues in older patients. Moreover, the two diseases may share some similar pathogenesis pathway. Currently, few studies focus on the relationship between urolithiasis and osteoporosis. Furthermore, whether the common mobilities influence the long-term osteoporosis rate in urolithiasis patients has never been studied. In the present study, we used the Taiwan National Health Insurance Database (LHID 2000) compiled by the NHI from 1996 to 2013 to determine whether urolithiasis influenced long-term osteoporosis; controls were matched for age, sex, and other comorbidities (including hypertension, diabetes mellitus, dyslipidemia, liver disease, and cardiovascular disease). We included a total of 91,254 patients, including 22,575 patients with urolithiasis and 68,679 control patients. There was a significant difference between the incidence of osteoporosis between the urolithiasis and control groups (adjusted hazard ratio 1.34, 95% CI 1.19-1.79, $p < 0.001$) during the follow up. The incidence rate of osteoporosis during the follow-up period was 8.87 per 1000 person-years in the urolithiasis group and 6.37 per 1000 person-years in the control group. Based on our results, it is evident that urolithiasis significantly increases the subsequent osteoporosis rate. Though the clinical mechanisms are not fully understood, patients who have a history of urolithiasis may need regular follow-up assessment of bone marrow density.

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The Association Between Vitamin D, Frailty and Progression of Frailty in Community-Dwelling Older Women.

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BACKGROUND: Vitamin D (25OHD) plays a role in many physiological functions which decline with age, contributing to frailty and increased risk for negative health outcomes. However, whether 25OHD can be a long-term risk marker for frailty over a longer time-period and whether it is consistent with advancing age is unclear. **OBJECTIVE:** To investigate the association between 25OHD and frailty in women aged 75, followed for 10 years.

DESIGN AND SETTING: Prospective, population-based, cohort study from Malmö, Sweden. **PARTICIPANTS:** Community-dwelling women aged 75(\pm 0.1) (n=1044) with reassessments at ages 80(\pm 0.2) (n=715) and 85(\pm 0.1) (n=382). **METHODS:** Frailty was quantified using a 10-variable frailty-index, ranging from 0 (lowest) to 1 (highest). Women were categorized as vitamin D insufficient (<50nmol/L) or sufficient (\leq 50nmol/L). **RESULTS:** At both ages 75 and 80, 25OHD insufficient women were more frail compared to women with sufficient 25OHD (0.23 vs 0.18; $p<0.001$ and 0.32 vs 0.25; $p=0.001$). At age 80, 25OHD insufficiency was also associated with subsequent frailty 5-years later (0.41 vs 0.32; $p=0.011$). Interestingly, accelerated progression of frailty was not associated with lower 25OHD, neither was 25OHD >75 nmol/L additionally beneficial with regards to frailty. No association between 25OHD and frailty was observed at age 85. Within the frailty-index, variables associated with 25OHD were those related to muscle strength and function. **CONCLUSIONS:** In this prospective observational community cohort study of women aged 75, vitamin D insufficiency was associated with higher frailty in all but the oldest old. This study supports the value of maintaining sufficient vitamin D levels for healthy aging.