



## Selección de Resúmenes de Menopausia

Semana del 19 al 25 de Noviembre de 2014

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**Obstet Gynecol. 2014 Dec;124(6):1147-1156.**

### Vaginal Estrogen for Genitourinary Syndrome of Menopause: A Systematic Review.

Rahn DD1, Carberry C, Sanses TV, Mamik MM, Ward RM, Meriwether KV, Olivera CK, Abed H, et al.

**OBJECTIVE:** To comprehensively review and critically assess the literature on vaginal estrogen and its alternatives for women with genitourinary syndrome of menopause and to provide clinical practice guidelines. **DATA SOURCES:** MEDLINE and Cochrane databases were searched from inception to April 2013. We included randomized controlled trials and prospective comparative studies. Interventions and comparators included all commercially available vaginal estrogen products. Placebo, no treatment, systemic estrogen (all routes), and nonhormonal moisturizers and lubricants were included as comparators. **METHODS OF STUDY SELECTION:** We double-screened 1,805 abstracts, identifying 44 eligible studies. Discrepancies were adjudicated by a third reviewer. Studies were individually and collectively assessed for methodologic quality and strength of evidence. **TABULATION, NTEGRATION, AND RESULTS:** Studies were extracted for participant, intervention, comparator, and outcomes data, including patient-reported atrophy symptoms (eg, vaginal dryness, dyspareunia, dysuria, urgency, frequency, recurrent urinary tract infection (UTI), and urinary incontinence), objective signs of atrophy, urodynamic measures, endometrial effects, serum estradiol changes, and adverse events. Compared with placebo, vaginal estrogens improved dryness, dyspareunia, urinary urgency, frequency, and stress urinary incontinence (SUI) and urgency urinary incontinence (UUI). Urinary tract infection rates decreased. The various estrogen preparations had similar efficacy and safety; serum estradiol levels remained within postmenopausal norms for all except high-dose conjugated equine estrogen cream. Endometrial hyperplasia and adenocarcinoma were extremely rare among those receiving vaginal estrogen. Comparing vaginal estrogen with nonhormonal moisturizers, patients with two or more symptoms of vulvovaginal atrophy were substantially more improved using vaginal estrogens, but those with one or minor complaints had similar symptom resolution with either estrogen or nonhormonal moisturizer. **CONCLUSION:** All commercially available vaginal estrogens effectively relieve common vulvovaginal atrophy-related complaints and have additional utility in patients with urinary urgency, frequency or nocturia, SUI and UUI, and recurrent UTIs. Nonhormonal moisturizers are a beneficial alternative for those with few or minor atrophy-related symptoms and in patients at risk for estrogen-related neoplasia.

**J Bone Miner Res. 2014 Nov 21. doi: 10.1002/jbmr.2405. [Epub ahead of print]**

### Diagnosis and Management of Osteonecrosis of the Jaw: A Systematic Review and International Consensus.

Khan A1, Morrison A, Hanley D, et al; behalf of the International Task Force on Osteonecrosis of the Jaw.

This paper provides a systematic review of the literature from January 2003 to April 2014 pertaining to the incidence, pathophysiology, diagnosis and treatment of osteonecrosis of the jaw (ONJ), and offers recommendations for its management based on multidisciplinary international consensus. ONJ is associated with oncology-dose parenteral anti-resorptive therapy of bisphosphonates (BP) and denosumab (Dmab). The incidence of ONJ is greatest in the oncology patient population (1-15%) where high doses of these medications are used at frequent intervals. In the osteoporosis patient population, the incidence of ONJ is estimated at 0.001% to 0.01%, marginally higher than the incidence in the general population (<0.001%). New insights into the pathophysiology of ONJ include anti-resorptive effects of BPs and Dmab, effects of BPs on gamma delta T-cells and on monocyte and macrophage function, as well as the role of local bacterial infection, inflammation and necrosis. Advances in imaging include the use of cone beam computerized tomography assessing cortical and cancellous architecture with lower radiation exposure, magnetic resonance imaging, bone scanning and positron emission tomography, although plain films often suffice. Other risk factors for ONJ include glucocorticoid use, maxillary or mandibular bone surgery, poor oral hygiene, chronic inflammation, diabetes mellitus, ill-fitting dentures, as well as other drugs, including anti-angiogenic agents. Prevention strategies for ONJ include elimination or stabilization of oral disease prior to initiation of anti-resorptive agents, as well as maintenance of good oral hygiene. In those patients at high risk for the

development of ONJ, including cancer patients receiving high-dose BP or Dmab therapy, consideration should be given to withholding anti-resorptive therapy following extensive oral surgery until the surgical site heals with mature mucosal coverage. Management of ONJ is based on the stage of the disease, size of the lesions, as well as the presence of contributing drug therapy and comorbidity. Conservative therapy includes topical antibiotic oral rinses and systemic antibiotic therapy. Localized surgical debridement is indicated in advanced non-responsive disease and has been successful. Early data have suggested enhanced osseous wound healing with teriparatide in those without contraindications for its use. Experimental therapy includes bone marrow stem cell intralesional transplantation, low-level laser therapy, local platelet-derived growth factor application, hyperbaric oxygen, and tissue grafting.

**Breast Cancer Res Treat. 2014 Nov 21. [Epub ahead of print]**

### **Reduced progesterone levels explain the reduced risk of breast cancer in obese premenopausal women: a new hypothesis.**

Dowsett M1, Folkard E.

Understanding the complex relationship between obesity and breast cancer is fundamental to our knowledge of the etiology of this malignancy; changes in the composition of the hormonal milieu are implicit in this process. Estrogens are synthesized from androgens by aromatase in the gonads and in peripheral tissues, principally, adipose tissue. Obesity in women, regardless of their age, leads to more aromatase and more extra-glandular estrogen production. In postmenopausal women, in whom ovarian estrogen production is absent, the increased incidence of breast cancer in women with high body mass index has been attributed to the relatively high plasma levels of estradiol from subcutaneous fat. In contrast, obesity in premenopausal women is associated with a previously unexplained reduced incidence of breast cancer. In obese premenopausal women, the cumulative effect of higher levels of estrogens synthesized in the peripheral tissues, together with ovarian estrogen production, results in a negative feedback on the hypothalamic pituitary controlled release of gonadotrophins and a resultant diminution in ovarian steroid production. As a consequence, the normal balance of estrogen and progesterone levels is disrupted: while estrogen levels are normalized, progesterone production is markedly decreased. Progesterone is a promoter of proliferation in the breast. The low levels of progesterone in obese premenopausal women are consistent with, and we propose, are responsible for, the reduction in breast cancer incidence in these women.

**Minerva Endocrinol. 2014 Nov 21. [Epub ahead of print]**

### **The effect of chronic estrogen application on bile and gallstone composition in women with cholelithiasis.**

Sieron D, Czerny B, Sieron-Stoltny K, Karasiewicz M, Bogacz A, Seremak-Mrozikiewicz A, Kotrych D, et al.

Chronic application of third generation progestagens as contraceptives or hormone replacement therapy (HRT) could influence the serum lipid profile, and consequently the bile and gallstone composition. AIMS: To determinate components of serum, bile and gallstones in women of reproductive age or postmenopausal women using hormonal third generation for at least two years. METHODS: We enrolled 101 Caucasian women with cholelithiasis. The study included 45 women of reproductive age and 56 postmenopausal women who were divided into subgroups receiving or not exogenous female hormones. In patients we determined serum levels of  $17\beta$ -estradiol, triglycerides, HDL and LDL cholesterol as well as composition of gallstones and bile. RESULTS: The postmenopausal women showed a significant reduction in the concentration of bile acids in serum while the application of HRT caused an increase in their contents. Serum total and LDL cholesterol in postmenopausal women was higher than in women without hormonal contraception and postmenopausal patients with HRT. Moreover, women taking the exogenous hormones showed a reduced content of calcium ions in both serum, bile and gallstones. CONCLUSIONS: Our observations confirm that the chronic use of oral contraceptives and hormone replacement therapy cause an increase in bile lithogeneity.

**Nutr Res Rev. 2014 Nov 21:1-16. [Epub ahead of print]**

### **Is there a role for vitamin C in preventing osteoporosis and fractures? A review of the potential underlying mechanisms and current epidemiological evidence.**

Finck H, Hart AR, Jennings A, Welch AA.

Osteoporosis and related fractures are a major global health issue, but there are few preventative strategies. Previously reported associations between higher intakes of fruits and vegetables and skeletal health have been suggested to be partly attributable to vitamin C. To date, there is some evidence for a potential role of vitamin C in osteoporosis and fracture prevention but an overall consensus of published studies has not yet been drawn. The present review aims to provide a summary of the proposed underlying mechanisms of vitamin C on bone and reviews the current evidence in the literature, examining a potential link between vitamin C intake and status with osteoporosis and fractures. The Bradford Hill criteria were used to assess reported associations. Recent animal studies have provided insights into the involvement of vitamin C in osteoclastogenesis and osteoblastogenesis, and its role as a mediator of bone matrix deposition, affecting both the quantity and quality of bone collagen. Observational studies have provided some evidence for this in the general population, showing positive associations between dietary vitamin C intake and supplements and higher bone mineral density or reduced fracture risk. However, previous intervention studies were not sufficiently well designed to evaluate these associations. Epidemiological data are particularly limited for vitamin C status and for fracture risk and good-quality randomised controlled trials are needed to confirm previous epidemiological findings. The present review also highlights that associations between vitamin C and bone health may be non-linear and further research is needed to ascertain optimal intakes for osteoporosis and fracture prevention.

**Eur J Clin Nutr. 2014 Nov 5. doi: 10.1038/ejcn.2014.231. [Epub ahead of print]**

### **A fruit, milk and whole grain dietary pattern is positively associated with bone mineral density in Korean healthy adults.**

Shin S, Sung J, Joung H.

**Background/Objectives:** Osteoporosis is a major health problem that will grow in burden with ageing of the global population. Modifiable risk factors for osteoporosis, including diet, have significant implications for disease prevention. We examined associations between dietary patterns and bone mineral density (BMD) in a Korean adult population. **Subjects/Methods:** In total, 1828 individuals from the Healthy Twin Cohort were included as subjects. Information on general characteristics, lifestyles and health status was obtained through a health examination, and BMD was assessed using DEXA. Dietary intake was assessed using a 3-day food record, and dietary patterns were examined by factor analysis. Associations between dietary patterns and BMD were examined using mixed linear regression, adjusting for family and twin structure as well as other potential risk factors for bone health. **Results:** Four dietary patterns were identified (Rice and kimchi; eggs, meat and flour; Fruit, milk and whole grains; and Fast food and soda). The 'Fruit, milk and whole grains' pattern was associated with a reduced risk of having low BMD in men (odds ratio (OR) = 0.38; 95% confidence interval (CI)=0.22-0.67) and women (OR=0.45; 95% CI=0.28-0.72) and was positively associated with BMD at multiple sites. The 'rice and kimchi' pattern had a positive association with only whole-arm BMD in men and women. **Conclusions:** Our results suggest that a dietary pattern with high intake of dairy products, fruits and whole grains may contribute positively to bone health in a Korean adult population, and dietary pattern-based strategies could have potential in promoting bone health.

**Menopause. 2014 Nov 17. [Epub ahead of print]**

### **Effects of estrogen and venlafaxine on menopause-related quality of life in healthy postmenopausal women with hot flashes: a placebo-controlled randomized trial.**

Caan B1, LaCroix AZ, Joffe H, Guthrie KA, Larson JC, Carpenter JS, Cohen LS, Freeman EW, Manson JE, et al.

**OBJECTIVE:** This study aims to evaluate the effects of low-dose estradiol (E2) or venlafaxine on menopause-related quality of life and associated symptoms in healthy perimenopausal and postmenopausal women with hot flashes. **METHODS:** A double-blind, placebo-controlled, randomized trial of low-dose oral 17 $\beta$ -E2 0.5 mg/day and venlafaxine XR 75 mg/day, versus identical placebo, was conducted among 339 women (aged 40-62 y) experiencing two or more vasomotor symptoms (VMS) per day (mean [SD], 8.07 [5.29]) who were recruited at three clinical sites from November 2011 to October 2012. The primary trial outcome, as reported previously, was frequency of VMS at 8 weeks. Here, we report on secondary endpoints of total and domain scores from the Menopause-Specific Quality of Life Questionnaire (MENQOL) and from measures of pain (Pain, Enjoyment in life, and General activity scale), depression (Patient Health Questionnaire-9), anxiety (Generalized Anxiety Disorder Questionnaire-7), and perceived

stress (Perceived Stress Scale). RESULTS: Treatment with both E2 and venlafaxine resulted in significantly greater improvement in quality of life, as measured by total MENQOL scores, compared with placebo (E2: mean difference at 8 wk, -0.4; 95% CI, -0.7 to -0.2;  $P < 0.001$ ; venlafaxine: mean difference at 8 wk, -0.2; 95% CI, -0.5 to 0.0;  $P = 0.04$ ). Quality-of-life domain analyses revealed that E2 had beneficial treatment effects on all domains of the MENQOL except for the psychosocial domain, whereas venlafaxine benefits were observed only in the psychosocial domain. Neither E2 nor venlafaxine improved pain, anxiety, or depressive symptoms, although baseline symptom levels were low. Modest benefits were observed for perceived stress with venlafaxine. CONCLUSIONS: Both low-dose E2 and venlafaxine are effective pharmacologic agents for improving menopause-related quality of life in healthy women with VMS.

**PLoS One. 2014 Nov 17;9(11):e110587. doi: 10.1371/journal.pone.0110587. eCollection 2014.**

### **Visceral fat accumulation is associated with colorectal cancer in postmenopausal women.**

Lee JY, Lee HS, Lee DC, Chu SH, Jeon JY, Kim NK, Lee JW.

**BACKGROUND:** Obesity is a known risk factor for colorectal cancer (CRC), and emerging data suggest that this association is mediated by visceral fat rather than total body fat. However, there is a lack of studies evaluating the association between visceral fat area and the prevalence of CRC. **METHODS:** To investigate the relationship between visceral adiposity and prevalence of CRC, data of 497 women diagnosed with CRC and 318 apparently healthy women were analysed and data of well-balanced 191 pairs of women with CRC and healthy women matched based on propensity scores were additionally analysed. Diagnosis of CRC was confirmed by colonoscopy and histology. Metabolic parameters were assessed, along with body composition, using computed tomography. **RESULTS:** The median visceral fat area was significantly higher in the CRC group compared with the control group before and after matching. The prevalence of CRC increased significantly with increasing visceral fat tertiles after matching ( $p$  for trend  $< 0.01$ ). A multivariate analysis showed that mean visceral fat area of individuals in the 67th percentile or greater group was associated with an increased prevalence of CRC (adjusted odds ratio: 1.80; 95% confidence interval: 1.12-2.91 before matching and adjusted odds ratio: 2.96; 95% confidence interval: 1.38-6.33) compared with that of individuals in the 33th percentile or lower group. **CONCLUSION:** Thus, we conclude that visceral fat area is positively associated with the prevalence of CRC. Although we could not determine the causality, visceral adiposity may be associated with the risk of CRC. Further prospective studies are required to determine the benefits of controlling visceral obesity for reducing CRC risk.